

FOCUS ON HISTOTRIPSY

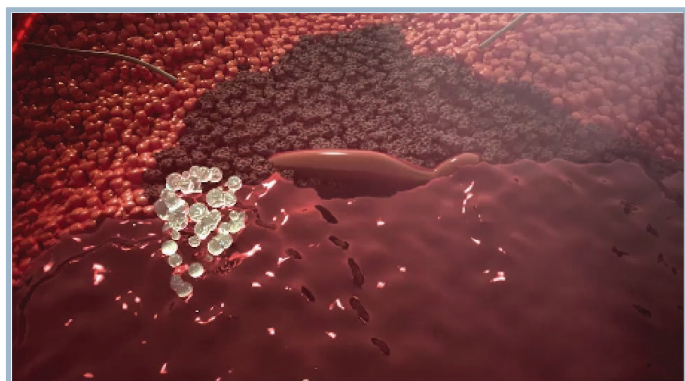
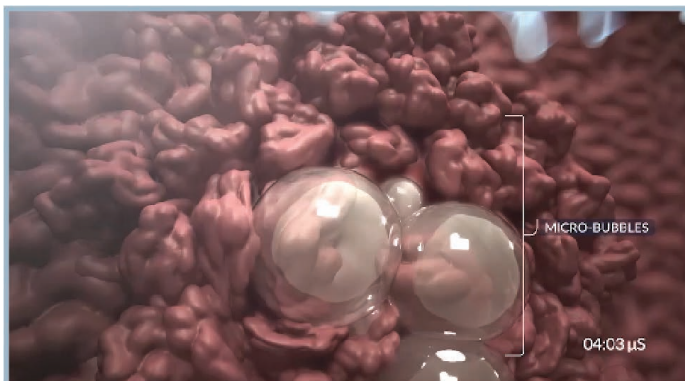
Bubbles have never been so powerful

THE SCIENCE

Histotripsy is a novel form of focused ultrasound that uses high amplitude, very short pulses designed to mechanically liquefy and destroy targeted tissue.

Specifically, as the focused ultrasound energy converges at a known focal point, high pressure causes extremely small, naturally occurring gas bubbles to expand many times larger through a phenomenon called acoustic cavitation.

As the ultrasound waves converge on the targeted tissue, the rapid expansion and collapse of the micro-bubbles forms a “bubble cloud” which imparts mechanical forces on the cells, resulting in instantaneous cell destruction and leaving behind an acellular lysate.



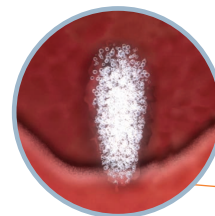
Histotripsy’s unique mechanism of action destroys targeted tissue only within the bubble cloud, which enables highly precise treatments while avoiding damage to non-targeted tissue. Histotripsy is performed non-invasively, and it does not use ionizing radiation or heat to destroy targeted tissue.



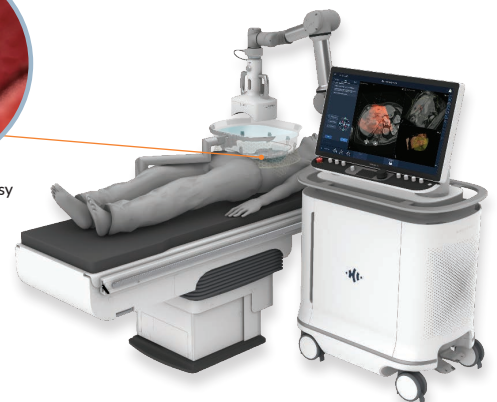
HARNESSING THE POWER

Using the Edison® System, the physician views real-time diagnostic ultrasound to localize the targeted tissue and to plan the treatment volume (including any margin the physician determines appropriate). During planning, the physician also establishes the minimum threshold voltage required to sustain the bubble cloud in the targeted tissue – this leverages histotripsy’s “threshold effect” that removes targeted liver tumors while tending to preserve collagenous vessels and ducts.¹

During treatment, the physician monitors treatment via real-time diagnostic ultrasound as the precision treatment arm continuously moves the bubble cloud automatically to encompass the entire planned treatment volume. The destructive effects of histotripsy is confined to the tissue within the planned treatment volume.



Rendering of histotripsy bubble cloud



POST-TREATMENT

After treatment has concluded, the physician uses live ultrasound to confirm treatment. The volume where soft tissue was mechanically destroyed will typically appear hypoechoic (dark). The images below demonstrate histotripsy results in (A1) a patient MRI and contrast-enhanced ultrasound demonstrating precision treatment and (A2) an immediate tissue response with preserved patent vessel traversing the treatment zone. The final images (A3) are of an ex-vivo animal model and are representative of collagen structures and larger vessels which tend to remain preserved after histotripsy.

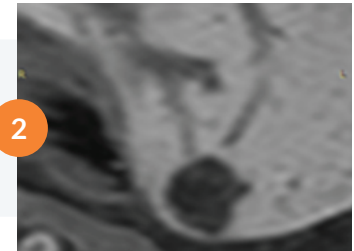
A1

ThERESA Trial²

MRI images of pre and post liver tissue treatment.



Red circle designates the planned treatment area.



The treatment zone encompasses the planned treatment area but does not impact other tissue, including the adjacent liver capsule.

A2

ThERESA Trial

Contrast-enhanced ultrasound (CEUS) pre and post liver tumor and tissue treatment.



Red circle designates the planned treatment area.

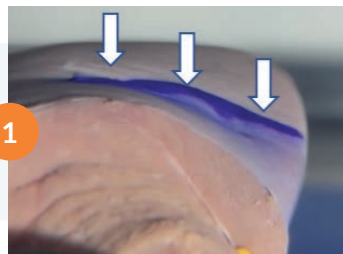


Hypoechoic appearance post-treatment.

A3

Benchtop Bovine Liver

Post liver tissue treatment.



Histotripsy treatment completed just below liver capsule, which remains intact.



Patent vessels traversing through treatment zone visualized after washout of acellular lysate.

REFERENCES

1. Vlaisavljevich E, et al. Effects of tissue mechanical properties on susceptibility to histotripsy-induced tissue damage. *Phys Med Biol.* 2014;59(2):253-270. doi:10.1088/0031-9155/59/2/253
2. Vidal-Jove J, et al. First-in-man histotripsy of hepatic tumors: the ThERESA trial, a feasibility study. *Int J Hyperthermia.* 2022;39(1):1115-1123. doi:10.1080/02656736.2022.2112309

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

The Edison System is intended for the non-invasive mechanical destruction of liver tumors, including the partial or complete destruction of unresectable liver tumors via histotripsy. The FDA has not evaluated the Edison System for the treatment of any disease including, but not limited to, cancer or evaluated any specific cancer outcomes (such as local tumor progression, 5-year survival or overall survival). The System should only be used by persons who have completed training performed by HistoSonics, and its use guided by the clinical judgment of an appropriately trained physician. Refer to the device Instructions for Use for a complete list of warnings, precautions and a summary of clinical trial results, including reported adverse events.