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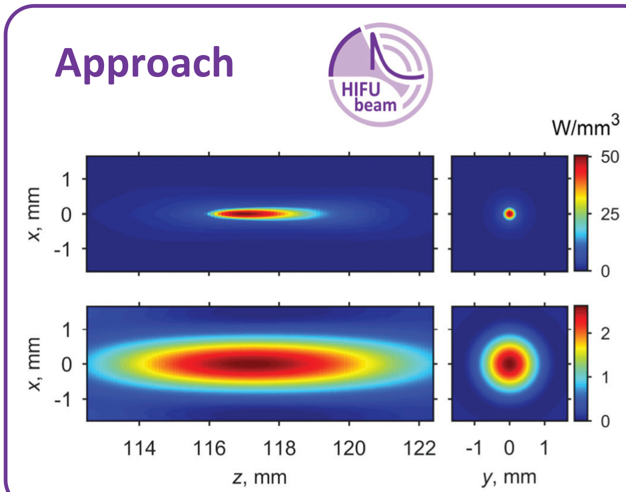
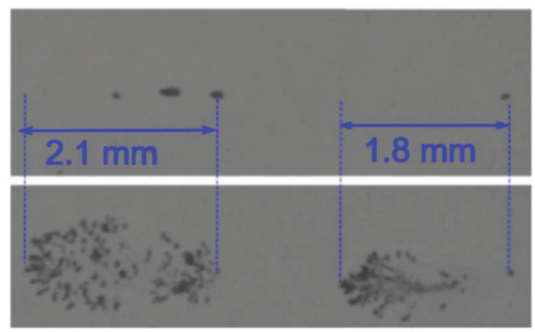
Special Issue on Histotripsy

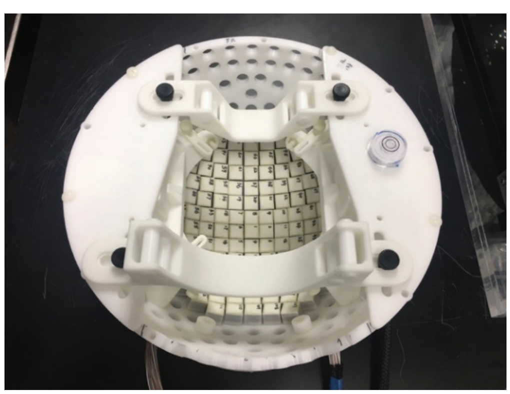
Approach



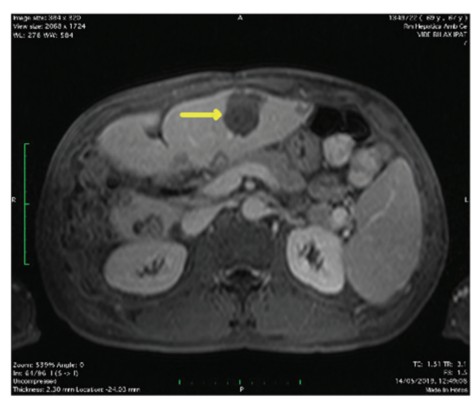
Mechanisms



Hardware



Application



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Histotripsy: Approaches, Mechanisms, Hardware, and Applications

Histotripsy is a therapeutic ultrasound technology to liquefy tissue into acellular debris using sequences of high-power focused ultrasound pulses. The research on histotripsy has been rapidly growing in the past decade. In contrast to conventional high intensity focused ultrasound (HIFU) thermal therapy, the major mechanism of histotripsy is mechanical, which enables localized tissue disintegration at the target sites without thermal damage to the overlaying and surrounding tissues. Two major approaches, cavitational histotripsy and boiling histotripsy, with two different mechanisms, have been extensively explored lately. Histotripsy therapy is being evaluated for treating cancer, thrombosis, hematomas, abscess, enhanced immune response, and neurological applications in preclinical studies with small and large animal models. First clinical trials using histotripsy for benign prostatic hyperplasia and liver cancer have been undertaken. In addition to complete tissue liquefaction, a mechanism of a partial mechanical tissue damage is being explored for a broader range of applications such as non-invasive biopsy, drug delivery, and biofabrication. Specialized hardware and software are being developed. This Special Issue covers the latest research on approaches, mechanisms, hardware, and applications of histotripsy. Four figures on the cover page illustrate examples of research in these directions from representative articles of the issue.

The Approach figure (top left) illustrates strong enhancement and spatial localization of tissue heating at the focus by nonlinear waves with high-amplitude shocks (top) *versus* harmonic waves (bottom). Such rapid heating has been used in boiling histotripsy and in developing methods for fast volumetric thermal tissue ablation in existing clinical HIFU systems. The image is modified from the paper titled “HIFU Beam: A simulator for Predicting Axially Symmetric Nonlinear Acoustic Fields Generated by Focused Transducers in a Layered Medium,” by P. V. Yuldashev, M. M. Karzova, W. Kreider, P. B. Rosnitskiy, O. A. Sapozhnikov, and V. A. Khokhlova.

The Mechanism figure (top right) shows a proliferation process of two cavitation bubbles (left and right) in gel imaged by a high-speed camera. The frames correspond to the initial (top) and proliferated (bottom) bubbles that have shifted axially over the 1 ms pulse. Such proliferating behavior is determined by the degree of nonlinear distortion of HIFU focal waveform and provides a mechanism for pHIFU-based drug delivery and less disruptive tissue stimulation. The image is modified from the paper titled “Inertial Cavitation Behaviors Induced by Nonlinear Focused Ultrasound Pulses,” by C. R. Bawiec, P. B. Rosnitskiy, A. T. Peek, A. D. Maxwell, W. Kreider, G. R. ter Haar, O. A. Sapozhnikov, V. A. Khokhlova, and T. D. Khokhlova.

The Hardware figure (bottom left) shows the first transcranial MR-compatible histotripsy array, which was used, for the first time, to show the *in vivo* feasibility of successful ablation in an intact porcine brain through excised human skull using MR-guided transcranial histotripsy. This image is modified from the paper titled “Transcranial MR-Guided Histotripsy System,” by N. Lu, T. L. Hall, D. Choi, D. Gupta, B. J. Daou, J. R. Sukovich, A. Fox, T. I. Gerhardson, A. S. Pandey, D. C. Noll, and Z. Xu.

The Application figure (bottom right) shows an MR image of a post-histotripsy liver tumor treatment (arrow) in a human patient. This result is from the first human trial (NCT03741088, Spain) of both histotripsy cancer treatment and hepatic histotripsy. The trial results provide the first evidence of the safety and feasibility of histotripsy tumor treatment in humans, leading to local tumor regression and control/shrinkage of distant tumors (abscopal effect). This image is modified from the paper titled “Liver Histotripsy Mediated Abscopal Effect–Case Report,” by J. Vidal-Jové, X. Serres-Créixams, T. J. Ziemlewicz, and M. Cannata.