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HISTOTRIPSY: CURRENT STATUS, CLINICAL APPLICATIONS, AND FUTURE PERSPECTIVES: A NARRATIVE REVIEW

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ABSTRACT

Background: A significant proportion of solid tumors remain inoperable or resistant to systemic treatment, highlighting the need for effective local therapies. Histotripsy is an innovative, non-invasive, non-thermal ultrasound-based technique that uses acoustic cavitation to mechanically fragment tissue with high spatial precision and minimal collateral damage.

Aim: The aim of this review is to present the physical principles underlying histotripsy, describe its biological effects on tissues, summarize current clinical applications, and discuss potential future indications for this innovative, non-invasive therapeutic technology.

Materials and methods: The study was conducted as a narrative review of the literature on histotripsy. In February 2026, a non-systematic search of the PubMed and Google Scholar databases was conducted. Particular emphasis was placed on studies published within the last five years, including original articles, clinical trials, and review articles.

Results: In the first prospective clinical trial, Hope4Liver, which used histotripsy to treat hepatocellular carcinoma and liver metastases, a primary efficacy rate of 95.5% and a complication rate of 6.8% were reported.

Conclusions: Histotripsy is a highly promising, non-invasive ablation technique that enables precise, non-thermal tissue destruction while preserving surrounding structures. Current data remain limited, and long-term results are lacking. Further large-scale prospective studies are needed to define the role of this technique and compare its efficacy with established treatment methods.

KEYWORDS

Histotripsy, Non-Invasive Ablation, Ultrasound Therapy, Acoustic Cavitation, Liver Tumors, Minimally Invasive Treatment

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1. Introduction

Radical surgical resection, systemic chemotherapy, and ionizing radiation are the three main methods of oncologic treatment. Despite this, a significant proportion of solid tumors remain ineligible for surgery or show a limited response to systemic therapy, highlighting the need to develop new, effective local treatment methods. For this reason, increasing attention is being paid to the development of innovative local and regional therapies capable of selectively destroying tumor tissue while minimizing damage to surrounding healthy structures (1–3).

Minimally invasive ablation techniques are important components of modern cancer treatment. Thermal ablation methods, including radiofrequency ablation, microwave ablation, and cryoablation, are currently recommended as potentially curative options for selected patients with certain types of tumors. In addition, other energy-based methods, such as laser ablation, gamma radiation, and high-intensity focused ultrasound (HIFU), are widely used in clinical practice (4). Importantly, these techniques have a local effect on tumor tissue, which reduces systemic toxicity associated with chemotherapy and lowers the incidence of complications associated with extensive surgical procedures (5,6). These techniques can also be used for cytoreduction in patients with inoperable tumors, reducing the tumor burden and possibly increasing the effectiveness of systemic therapies. However, despite these advantages, current techniques are associated with significant limitations (3,7). Factors such as tumor stage, organ function, the operator's experience, and difficult anatomical locations, limit the use of ablation and contribute to unpredictable treatment (2,8). Thermal techniques pose challenges in accurately predicting ablation margins and defining a well-defined target zone, as different tissue types exhibit variable thermal conductivity and impedance, leading to heterogeneity in temperature distribution(3). Furthermore, these methods are sensitive to the “heat sink” effect, in which blood flow in adjacent vessels diffuses heat energy, lowering the temperature of the target lesion. This phenomenon reduces treatment efficacy near vascular structures and may increase the risk of residual disease or tumor progression. Additionally, current ablation therapies have limited use in treating lesions affecting critical anatomical structures, such as major blood vessels.(1,6,8–11).

Minimally invasive methods are generally associated with a relatively low complication rate; however, there remains significant potential to improve safety through the refinement of existing techniques as well as the development of new, less invasive local therapies (11,12). These limitations have driven the development of new non-thermal ablation technologies that enable the precise destruction of tissue while protecting key anatomical structures.

Histotripsy is a new, non-invasive therapeutic method that uses high-energy focused ultrasound waves to mechanically break down tissue (1,11). This technique offers high spatial accuracy with minimal collateral damage, enabling safer and more effective localized treatment of tumors compared to conventional ablative or locoregional methods (3).

The purpose of this review is to present the physical principles underlying histotripsy, describe its biological effects on tissues, summarize current clinical applications, and discuss potential future indications for this innovative, non-invasive therapeutic technology.

2. Research materials and methods

2.1 Data collection

This study was conducted as a narrative review of the literature on histotripsy as a new ablative method used in oncology and related fields. In February 2026, a non-systematic search of the PubMed and Google Scholar databases was conducted to identify relevant publications. Particular emphasis was placed on studies published within the last five years, and those representing key technological or clinical milestones in the development of this technique. To ensure a broad clinical and scientific context, relevant original articles, clinical trials, and review articles were included, with priority given to these studies. Additional sources were identified through manual analysis of the reference lists of selected publications.

3. Background and general characteristics of histotripsy

Histotripsy is an innovative, non-invasive, non-thermal, and non-ionizing therapeutic technique that uses ultrasound, employing short, high-pressure acoustic pulses to induce cavitation and mechanically fragment tissue. Although it belongs to the wider group of high-intensity focused ultrasound (HIFU) technologies, it differs fundamentally from them in its mechanism of action.

Histotripsy does not induce coagulative necrosis through thermal action. Histotripsy relies on the precise delivery of high-amplitude ultrasonic pulses to the focal area, leading to the formation, oscillation, and collapse of microbubbles. This process causes the mechanical disruption of cell membranes and extracellular structures (1,3,8,13).

The first study on histotripsy was published in 2004. The term “histotripsy” derives from Greek, where the prefix “histo” means tissue, and “trypsis” refers to crushing or fragmentation, which accurately describes the basic mechanism of physically breaking down tissue(14). A significant milestone in the development of histotripsy occurred on October 9, 2023, when the U.S. Food and Drug Administration (FDA) approved histotripsy for the treatment of liver tumors. This decision was based on the results of the HOPE4LIVER study, which demonstrated a high technical success rate (95.5%), a good safety profile (6.8% serious adverse events), and effective ablation of primary and metastatic liver lesions (15).

3.1 Physical Principles and Mechanism of Action

The fundamental mechanism of histotripsy is acoustic cavitation. Precisely directed, high-amplitude ultrasonic pulses that surpass the cavitation threshold in the focal zone lead to the formation of microbubbles. These bubbles rapidly expand and collapse within microseconds, generating intense mechanical forces. These forces rupture cell membranes, destroy intracellular components, and fragment the extracellular matrix. Finally, the treated tissue transforms into a homogeneous, cell-free homogenate (Fig. 1)

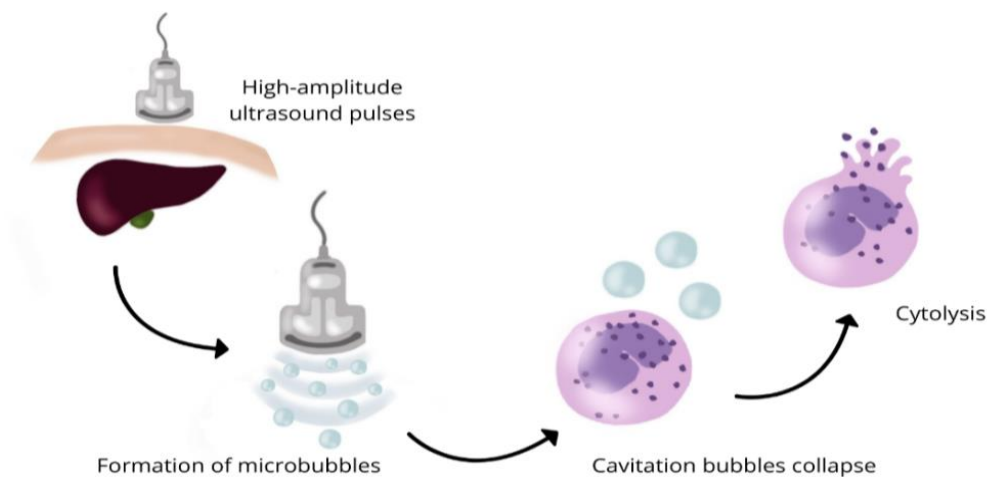


Fig. 1. Histotripsy utilizes focused, short, high-amplitude, low-duty-cycle ultrasound pulses to induce the rapid formation and collapse of cavitation bubbles. These bubbles generate intense, localized mechanical forces that disrupt cellular structures and cause precise tissue destruction.

Importantly, this process is concentrated on a precisely defined target area, allowing for high-precision tissue destruction with minimal damage to surrounding structures (2, 3, 6, 10).

3.2 Acoustic Histotripsy Strategies

Depending on the acoustic parameters and the dominant physical mechanisms, three main methods of histotripsy can be distinguished: cavitation histotripsy (CH), boiling histotripsy (BH), and hybrid histotripsy (HH). These techniques differ mainly in pulse duration, pressure amplitude, and bubble formation mechanisms, although ultimately they all lead to mechanical tissue fragmentation(16).

3.2.1 Cavitation Histotripsy (CH)

Cavitation histotripsy utilizes very short ultrasound pulses (typically a few to several acoustic cycles) with high-peak negative pressures. These conditions promote the formation of dense microbubble clouds in the target tissue. The bubbles originate from pre-existing gas nuclei collapse rapidly, generating forces that mechanically destroy biological structures.

Two main variants of CH are distinguished. In threshold histotripsy, a single pulse exceeds the cavitation threshold, producing bubble clouds directly from intrinsic cavitation nuclei at high negative pressures. This enables extremely precise submillimeter-scale lesions and represents the most accurate and clinically advanced form of the technique.

In contrast, the shock-scattering approach employs slightly longer pulses at lower pressure values. In this case, initially formed bubbles scatter and amplify incoming shock waves, promoting progressive cavitation cloud formation over multiple pulses. While this approach increases treatment efficiency, it is associated with slightly reduced spatial precision(10,13,17).

A characteristic feature of CH is complete liquefaction of tissue within the focal zone with a very narrow transition margin. It is worth noting that collagen rich structures, such as blood vessels and ducts, exhibit relative resistance, suggesting a certain level of tissue selectivity (2,3,6,7,18,19).

3.2.2 Boiling Histotripsy (BH)

Boiling histotripsy offers an alternative approach. It uses significantly longer ultrasound pulses at lower pressure amplitudes. This leads to the formation of millimeter-sized vapor bubbles at the focal point as a result of rapid, localized heating caused by the nonlinear propagation of the shock wave. Although there is a transient thermal component, the dominant mechanism of tissue destruction remains a mechanical one. Compared to cavitation histotripsy, boiling histotripsy allows for the treatment of larger tissue volumes more quickly, although this results in a slight decrease in spatial precision (5,10,19).

3.2.3 Hybrid Histotripsy (HH)

Hybrid histotripsy is a new, still experimental method that combines aspects of both CH and BH. It uses pulses of moderate duration and pressure amplitude, often in combination with complex pulse sequences or multiple frequencies, which enhances cavitation efficiency (10).

4. Discussion

Histotripsy is an innovative, non-invasive, non-ionizing, and non-thermal ablation method that uses focused ultrasound waves to induce acoustic cavitation. This leads to the precise mechanical destruction of target tissues. Currently, its most advanced and clinically well-established application is the treatment of primary and metastatic liver cancers.(2,3)

4.1 Liver

The THERESA study is the first study to evaluate the use of histotripsy in humans with liver tumors. In this study, a system developed by HistoSonics was used to perform ultrasound-guided percutaneous histotripsy in eight patients with a total of 11 primary or metastatic liver tumors. The median tumor size was approximately 1.4 cm. All procedures were performed under general anesthesia, and tumor localization was achieved using a diagnostic ultrasound device. Technical success was defined as the creation of a precisely targeted zone of tissue destruction within the planned treatment volume, confirmed by magnetic resonance imaging within 24–36 hours after the procedure. Imaging revealed clearly defined, non-enhanced cavities that corresponded exactly to the target ablation areas. It is important to note that no device-related adverse events or Grade 3 adverse events were reported. This confirms the favorable safety profile of histotripsy. However, two cases of local tumor progression were noted. In one case, incomplete ablation resulted from non-optimal ultrasound visualization, which led to a part of the tumor being left untreated. In the second case, the progression was difficult to distinguish from the growth of an adjacent, untreated lesion(16).

These results were later extended in the multicenter HOPE4LIVER clinical trial, which included 45 patients with 84 liver lesions, including hepatocellular carcinoma (37) and metastatic lesions (47). In this study, histotripsy was technically successful in 98.8% of patients. By day 30 post-procedure, 90.5% of lesions had shrunk by at least 50%, and more than one-third had shrunk by over 75%. Importantly, no serious device-related adverse events were reported, further confirming the efficacy and safety of this method in a wider clinical population (8). Long-term results of this study, including data from a one-year follow-up of 19 patients with hepatocellular carcinoma and 28 with metastatic disease, showed a local control rate of 63.4% based on primary evaluation criteria and 90% based on a post hoc analysis. After 30 days, only one non-serious device-related adverse event was reported, compared with six serious adverse events during the first 30 days. The overall one-year survival rate was 73.3% for patients with HCC and 48.6% for patients with metastatic disease, confirming long-term safety and clinical efficacy over time (12).

These results are further supported by real-world safety data from a recent international retrospective cohort study involving 230 patients treated at nine centers. Among these patients, 31 had hepatocellular carcinoma, and the remainder had colorectal metastases, neuroendocrine tumors, pancreatic tumors, and breast metastases. Within 30 days of treatment, complications were observed in 12 patients (5.2%), of whom 9 were non-life-threatening. The three main complications were deaths attributed to disease progression in patients with advanced-stage cancer who were receiving palliative care. Given the extensive preexisting intrahepatic and extrahepatic disease in these cases, these events were considered consistent with the natural course of the disease rather than treatment-related toxicity. Overall, these results confirm the repeatability and safety of histotripsy across multiple centers and among different operators, supporting its potential for wider clinical application (20).

4.2 Kidney

Based on robust clinical evidence regarding its use in the treatment of liver diseases, research has begun into the potential application of histotripsy in other organ systems, including the kidneys. Preclinical studies and early clinical trials indicate promising potential for the use of this method in the treatment of kidney tumors.

Ongoing clinical trials are evaluating the use of histotripsy in patients with renal cell carcinoma. The first study, titled “Clinical Ablation Using Histotripsy for Noninvasive Treatment of Renal Tumors” (CAIN, NCT05432232), is a prospective study involving patients with non-metastatic renal tumors measuring ≤ 3 cm.

The study focuses on safety, technical success, and early efficacy, with endpoints including complete tumor coverage on imaging and the absence of Grade 3 or higher complications (21).

The second study, titled “The HistoSonics Edison System for the Treatment of Primary Solid Kidney Tumors Using Histotripsy (#HOPE4KIDNEY, NCT05820087), is a prospective, multicenter, single-arm clinical trial designed to further evaluate the efficacy and safety of the Edison system in the treatment of primary solid renal tumors. The protocol includes a series of check-ups at 14, 30, 90, and 180 days, followed by annual evaluations over a five-year period to evaluate long-term outcomes (22). These studies represent the first systematic attempts to implement histotripsy into urologic oncology practice.

4.3 Pancreas

In addition to its applications in the kidneys, histotripsy is also being studied for use in the pancreas to treat pancreatic ductal adenocarcinoma. Preliminary preclinical results indicate that histotripsy enables precise, non-thermal tumor ablation while preserving adjacent critical structures, which is particularly important in this anatomically complex area.

The first prospective, multicenter, single-arm study of the HistoSonics Edison™ for the treatment of pancreatic ductal adenocarcinoma using histotripsy is the GANNON study (NCT06282809), which evaluates the safety of histotripsy in patients with inoperable locally advanced (stage III) or oligometastatic (stage IV) disease. The study began in December 2024, with preliminary completion expected in August 2026 and final completion in January 2027. Post-procedure imaging is performed within 36 hours, followed by structured follow-up at 7, 14, 30th, 60th, 120th, and 180th days to evaluate both safety and early efficacy outcomes (23).

4.4 Benign prostate hypertrophy (BPH)

In addition to oncological indications, histotripsy is also being investigated for benign conditions, such as benign prostatic hyperplasia. The study “Treatment of Benign Prostatic Hyperplasia with Histotripsy Using the Vortx Rx System” (NCT01896973) is a prospective study evaluating safety and preliminary efficacy in patients with symptomatic benign prostatic hyperplasia. In 25 patients, non-invasive ablation of prostate tissue was performed under ultrasound guidance. Most patients (68%) underwent the procedure under general anesthesia, while 32% received sedation. No serious intraoperative complications were reported. The study demonstrated a reduction in the International Prostate Symptom Score of 52.4% after 1 month, 50.8% after 3 months, and 44.0% after 6 months compared to baseline. These results confirm the safety and early clinical efficacy of histotripsy in this indication (24).

4.5 Aortic stenosis

The potential of histotripsy has also been investigated in cardiological applications. In the clinical trial „Valvosoft First-In-Man Study in Severe Symptomatic Aortic Stenosis” (NCT03779620), the efficacy and safety of non-invasive ultrasound therapy for the treatment of severe symptomatic aortic stenosis caused by calcification were evaluated using the Valvosoft device in elderly patients who were ineligible for standard procedures. The procedure was performed successfully, with no serious device-related complications, indicating a good safety profile. At the one-month follow-up, 6 out of 10 patients showed significant improvement in aortic valve area and a reduction in transvalvular pressure gradients (25).

Histotripsy has also been studied in the preclinical phase and applied to a wide range of conditions, including pancreatic cancer (26), intracranial malignant tumors (27), neurological disorders (27), thrombosis (17), hematomas (28), congenital heart defects in newborns and fetuses (29), valvular diseases (25), and kidney stones (30). These growing applications highlight the versatility of this technology and support its further clinical development across many fields of medicine.

4.6 Advantages of Histotripsy

The use of histotripsy has many advantages for patients undergoing treatment due to its non-invasive nature and fewer complications compared to surgical or percutaneous methods (3). The elimination of the necessity for surgical or percutaneous access associated with the histotripsy procedure reduces the risk of pain and bleeding. The primary advantage of histotripsy is its ability to generate well separated ablation zones while maintaining the safety of critical structures such as blood vessels, biliary ducts and lymphatic ducts. It is most significant in the management of centrally located tumours, where the proximity of critical anatomical structures increases the risk of serious complications (2, 7, 15). Furthermore, histotripsy allows for real-time imaging, enabling precise control of ablation margins and minimising damage to surrounding tissues (3, 6, 16).

Evidence from real-world multicenter analyses involving larger patient cohorts has confirmed low complication rates, further supporting the favorable safety profile of this modality. Nevertheless, it should be emphasized that the majority of currently available data originate from single-arm, non-randomized studies, which limits direct comparisons with established standard therapies.

4.7 Limitations

Despite its significant potential, histotripsy is associated with several major limitations. A key challenge is the need to achieve an adequate acoustic window, as high peak focal pressures are required to induce effective cavitation. (2). For this reason, factors such as lesion depth, echogenicity, and the presence of anatomical barriers, including ribs or intestines have a major impact on the feasibility and efficacy of the procedure. Lesions located in anatomically challenging areas, such as the dome of the liver or deep liver segments, may therefore pose a challenge or make the procedure impossible(1,7). Furthermore, this procedure is typically performed under general anesthesia with controlled ventilation to minimize respiratory motion and achieve the highest possible targeting accuracy, although motion management remains a significant technical challenge (3,7). Tumor size represents another significant limitation. While lesions up to approximately 3–4 cm in size can typically be treated in a single session, larger tumors require multiple overlapping ablations, which increases the procedural complexity and duration. These limitations underscore the need for further advances in real time imaging, movement compensation, and aberration correction to improve accuracy and expand the clinical application of histotripsy (1).

Although histotripsy offers advantages in terms of safety and minimal invasiveness compared to established methods such as thermal ablation, arterial chemoembolization, and surgical resection, these traditional methods are supported by more robust long term data. Furthermore, compared to existing treatment methods, histotripsy lacks data on long-term outcomes and standard procedures. And since most preclinical and clinical studies to date have evaluated it as a standalone cancer therapy, further research is needed to assess its potential in combination with surgery, radiation therapy, chemotherapy, and transvascular procedures to improve patient outcomes while providing solid clinical evidence and patient safety (2,7).

4.8 Future directions

Histotripsy is becoming a valuable option for certain patients, particularly those who are not eligible for surgery or other ablative therapies. In the future, it may serve as a bridging or supportive method within multidisciplinary treatment strategies. Technological advances and expanding clinical trials are expected to extend its use in oncological and non-oncological conditions. Histotripsy is more likely to complement existing therapies rather than replace standard methods. Future studies should prioritize long-term oncological outcomes, reproducibility of results across different centers and cost-effectiveness. Efforts to simplify and increase the accessibility of treatment delivery systems are also important (1,3).

5. Conclusions

To summarize, histotripsy is a recently developed, non-invasive ablation method that enables precise targeting and has a very good safety profile. Initial clinical studies have shown that tissue destruction occurs efficiently and non-thermally, with less damage to adjacent structures than other established minimally invasive methods. Although the initial results appear promising, more evidence is needed before histotripsy can be used in everyday practice. Nevertheless, determining the role of histotripsy as a primary or supportive treatment remains a challenge. To ensure the safety of histotripsy, it is necessary to develop optimal treatment protocols and conduct a comprehensive comparison of its efficacy with other minimally invasive treatment methods. Large-scale randomized trials involving long-term follow-up are required.

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- Pallumeera, M., Hong, M., & Giang, J. C. (2025). Histotripsy : Recent advances , clinical applications , and future prospects. 1–18.
- Worlikar, T., Loudon, N., Khaykin, V. M., Zhang, B. S. M., & Cho, C. S. (2025). Development of Histotripsy as a local-regional liver cancer therapy : Preclinical to clinical translation. 1–15.
- Sandilos, G., Butchy, M. V., Koneru, M., Gongalla, S., Sensenig, R., & Ki, Y. (2024). Histotripsy – hype or hope? review of innovation and future implications. *J Gastrointest Surg.* 28(8), 1370–5. <https://doi.org/10.1016/j.gassur.2024.05.038>
- Chlorogiannis D dimitris, & Sotirchos, V. S. (2024). Oncologic outcomes after percutaneous ablation for colorectal liver metastases : An updated comprehensive review. 1–12.
- Iqbal, M. F., Shafique, M. A., Abdur Raqib, M., Fadlalla Ahmad, T. K., Haseeb, A., M A Mhjoob, A., et al. (2024). Histotripsy: An innovative approach for minimally invasive tumour and disease treatment. *Ann Med Surg.* 86(4), 2081–7.
- Eigner, E., Malshy, K., Bandari, J., Fazaa, N., Nsair, A., Hines, L., et al. (2025). Review and mini-review Histotripsy in the management of rcc : A new frontier in focused therapies. (August), 1–6.
- Uysal, M., Wehrle, C. J., Satish, S., Knott, E., Hong, H., Allkushi, E., et al. (2025). Histotripsy of liver tumors : Patient selection , ethical discussions , and how we do it.
- Wah, T. M., Pech, M., Thormann, M., & Serres, X. (2023). Interventional oncology a multi-centre , single arm , non-randomized , prospective european trial to evaluate the safety and efficacy of the HistoSonics system in the treatment of primary and metastatic liver cancers (# HOPE4LIVER). *Cardiovasc Intervent Radiol.* 46(2), 259–67. <https://doi.org/10.1007/s00270-022-03309-6>
- Vidal-jové, J., Serres-créixams, X., Ziemlewicz, T. J., & Cannata, J. M. (2021). Liver Histotripsy mediated abscopal effect — case report. 68(9), 3001–5.
- Xu, Z., Khokhlova, T. D., Cho, C. S., & Khokhlova, V. A. (2025). Histotripsy : A method for mechanical tissue ablation with ultrasound. 26(1), 141–67.
- Wehrle, C. J., Ahmed, A. F. S., Knott, E., Hong, H., Uysal, M., Schlegel, A., et al. (2026). The first full year of Histotripsy for liver tumors : Local tumor control and preliminary oncologic efficacy. *Surgery.* 191, 109898. <https://doi.org/10.1016/j.surg.2025.109898>
- Ziemlewicz, T. J., Critch, J. J., Mendiratta-lala, M., Wiggermann, P., Pech, M., Serres-créixams, X., et al. (2025). The # HOPE4LIVER single-arm pivotal trial for Histotripsy of primary and metastatic liver tumors one-year update of clinical outcomes. 282(6), 908–16.
- Imran, K. M., Ganguly, A., Paul, T., Powar, M., Vlaisavljevich, E., Arbor, A., et al. (2024). Magic bubbles: Utilizing Histotripsy to modulate the tumor microenvironment and improve systemic anti-tumor immune responses. 40(1), 1–17.
- Xu, Z., Ludomirsky, A., Eun, L. Y., Hall, T. L., Tran, B. C., Fowlkes, J. B., et al. (2004). Controlled ultrasound tissue erosion. *IEEE Trans Ultrason Ferroelectr Freq Control.* 51(6), 726–36.
- Mendiratta-lala, M., White, S. B., Thormann, M., Torzilli, G., & Ziemlewicz, T. J. (2024). The # HOPE4LIVER single-arm pivotal trial for Histotripsy of primary and metastatic liver tumors. (3).

16. Vidal-jove, J., Serres, X., Vlaisavljevich, E., Cannata, J., Duryea, A., Miller, R., et al. (2022). First-in-man Histotripsy of hepatic tumors : The THERESA trial , a feasibility study. *Int J Hyperth.* 39(1), 1115–23. <https://doi.org/10.1080/02656736.2022.2112309>
17. Bollen, V., Hendley, S. A., Paul, J. D., Maxwell, A. D., Haworth, K. J., Holland, C. K., et al. (2020). In vitro thrombolytic efficacy of single- and five-cycle Histotripsy pulses and rt-PA. *Ultrasound Med Biol.* 46(2), 336–49.
18. Serres-créixams, X., Vidal-jové, J., Ziemlewicz, T. J., Cannata, J. M., Miguel, J., Uriarte, I., et al. (2021). Contrast - enhanced ultrasound : A useful tool to study and monitor hepatic tumors treated with Histotripsy. 3010(c).
19. Kumar, Y. N., Singh, Z., Wang, Y. N., Kanabolo, D., Chen, L., Bruce, M., et al. (2024). Open a comparative study of Histotripsy parameters for the treatment of fibrotic ex - vivo human benign prostatic hyperplasia tissue. *Sci Rep.* 1–13. <https://doi.org/10.1038/s41598-024-71163-2>
20. Wehrle, C. J., Burns, K., Ong, E., Couillard, A., Parikh, N. D., Caoili, E., et al. (2025). The first international experience with histotripsy_ a safety analysis of 230 cases. *J Gastrointest Surg.* 29(4), 102000. <https://doi.org/10.1016/j.gassur.2025.102000>
21. The HistoSonics Investigational System for Treatment of Primary Solid Renal Tumors Using Histotripsy (CAIN) (n.d.). <https://clinicaltrials.gov/study/NCT05432232?intr=Histotripsy&page=1&rank=3>
22. The HistoSonics EdisonTM System for Treatment of Primary Solid Renal Tumors Using Histotripsy (#HOPE4KIDNEY) (#HOPE4KIDNEY) (n.d.). <https://clinicaltrials.gov/study/NCT05820087?intr=Histotripsy&page=1&rank=2>
23. The HistoSonics EdisonTM System for Treatment of Pancreatic Adenocarcinoma Using Histotripsy (GANNON) (n.d.). <https://clinicaltrials.gov/study/NCT06282809>
24. Schuster, T. G., Wei, J. T., Hendlin, K., Jahnke, R., & Roberts, W. W. (2018). Prostatic enlargement using the. *Urology.* 114, 184–7. <https://doi.org/10.1016/j.urology.2017.12.033>
25. Messas, E., IJsselmuiden, A., Goudot, G., Vlieger, S., Zarka, S., Puymirat, E., et al. (2021). Feasibility and performance of noninvasive ultrasound therapy in patients with severe symptomatic aortic valve stenosis: A first-in-human study. *Vol. 143, Circulation. United States.* . p. 968–70.
26. Gannon, J., Paul, T., Mohammad, K., Edwards, M., Ziemlewicz, T., Trusiano, B., et al. (2026). Ultrasound in medicine & biology non-invasive pancreas ablation using Histotripsy : Pre-clinical safety study in an in vivo porcine model. *Ultrasound Med Biol.* 52(1), 62–71. <https://doi.org/10.1016/j.ultrasmedbio.2025.07.026>
27. Sukovich, J. R., Cain, C. A., Pandey, A. S., Camelo-piragua, S., Allen, S. P., Hall, T. L., et al. (2020). In vivo Histotripsy brain treatment. 131(4), 1331–8.
28. Hunter, C., Bruce, M., Khokhlova, V. A., & Thomas, J. (2021). Effect of stiffness of large extravascular hematomas on their susceptibility to boiling. 50(8), 2007–16.
29. Xu, Z., Owens, G., Gordon, D., Cain, C., & Ludomirsky, A. (2010). Noninvasive creation of an atrial septal defect by Histotripsy in a canine model. *Circulation.* 121(6), 742–9.
30. Matula, T. J., Wang Y nam, Khokhlova, T., Leotta, D. F., Brayman, A. A., Bruce, M., et al. (2022). Hhs public access. 47(3), 603–19.