Regence

Medical Policy Manual Medicine, Policy No. 178

Histotripsy for Tumor Treatment

Effective: July 1, 2026

Next Review: April 2027
Last Review: June 2026

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Histotripsy is a non-invasive treatment that uses focused ultrasound pulses to mechanically break down targeted tissue through the creation and collapse of microscopic bubbles. Histotripsy is proposed for the treatment of malignant lesions.

MEDICAL POLICY CRITERIA

The use of histotripsy is considered **investigational** for any indication.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Radiofrequency Ablation (RFA) of Tumors Other than Liver, Surgery, Policy No. 92
2. Cryosurgical Ablation of Miscellaneous Solid Tumors, Surgery, Policy No. 132
3. Magnetic Resonance (MR) Guided Focused Ultrasound (MRgFUS) and High Intensity Focused Ultrasound (HIFU) Ablation, Surgery, Policy No. 139
4. Microwave Tumor Ablation, Surgery, Policy No. 189
5. Ablation of Primary and Metastatic Liver Tumors, Surgery, Policy No. 204

BACKGROUND

Histotripsy is a non-invasive medical treatment that uses focused ultrasound technology to precisely destroy targeted tissue. The technique works by delivering rapid, high-intensity ultrasound pulses that create tiny bubbles in the tissue. These bubbles quickly expand and collapse in a process called cavitation, which mechanically breaks down the targeted tissue into a liquid-like state without using heat or causing significant damage to surrounding healthy tissue.

The Edison® System (HistoSonics, Inc) operates by delivering high-amplitude, microsecond ultrasound pulses that create controlled acoustic cavitation, forming "bubble clouds" at targeted locations. These bubble clouds, consisting of microbubbles that rapidly expand and collapse, exert mechanical stress on the liver tissue, ultimately destroying it and creating an acellular lysate. The system is integrated with a GE LOGIQ E10s ultrasound system allowing for precise targeting and treatment delivery through system software that controls the treatment arm's movement through the planned treatment volume.[1]

REGULATORY STATUS

The Edison® System (HistoSonics®, Ann Arbor, MI)

- In October 2023 the Food and Drug Administration issued de novo marketing authorization for the Edison System for focused ultrasound system for non-thermal, mechanical tissue ablation. This device uses focused ultrasound to mechanically ablate soft tissue. The device is not intended to thermally ablate tissue. (DEN220087)
- In October 2024 the Edison® System was granted 510 (k) premarket approval for non-invasive destruction of liver tumors, using a non-thermal, mechanical process of focused ultrasound. This approval was based on the predicate Edison System. (K241902)[1]

EVIDENCE SUMMARY

SYSTEMATIC REVIEWS

There are no systematic reviews for this indication.

Nonrandomized Studies

Ziemlewicz (2025) published a single-arm trial (#HOPE4LIVER) evaluating histotripsy for treating primary and metastatic liver tumors in 47 patients (19 with hepatocellular carcinoma, 28 with metastatic disease) across 14 sites in the United States and Europe.[2] The primary study endpoints of technical success in treating the targeted tumor and 30-day complications were evaluated on the first 44 pooled patients enrolled, and the results were previously published (see below). For the current study 52 tumors were treated in patients who were ineligible for or had declined standard therapies, with 89.5% (17/19) of hepatocellular carcinoma patients and 96.4% (27/28) of metastatic patients having multifocal hepatic tumors at treatment. At the 30-day, 6-month, and 12-month visits, there were 47 (no withdrawals), 37 (9 deaths and 1 withdrawal), and 27 (9 deaths and 1 withdrawal) active patients, respectively. The 1-year local control rate was 63.4% using the primary assessment method and 90% using the post hoc method. There were six serious adverse device-related effects within 30 days of treatment which included hepatic failure, portal vein thrombosis, postoperative thrombosis,

procedural pain, sepsis, and pleuritic pain. Only one nonserious adverse device-related effect was observed after 30 days of treatment. Overall survival at 1-year was 73.3% for patients with hepatocellular carcinoma and 48.6% for patients with metastatic disease. Progression of disease outside the liver was not tracked within the trial, thus metrics such as progression-free survival cannot be calculated. The patient population was 95% White, which may limit generalizability of the outcomes

Wehrle (2025) published a retrospective safety analysis of histotripsy for liver tumors in 230 patients from nine centers who underwent treatment for 510 tumors across 18 centers.[3] The tumors included colorectal metastases (n = 140), neuroendocrine tumors (n = 46), hepatocellular carcinomas (n = 31), pancreatic tumors (n = 30), and breast metastases (n = 26). Within 30 days of treatment, 12 of 230 patients (5.2%) experienced complications of any grade, with nine patients (75%) having minor complications (Clavien-Dindo grade ≤ II), median and mean Comprehensive Complication Index of 0.00 (IQR 0.00-0.00) and 0.00 (95% CI 0.00-0.75), and three major complications (Clavien-Dindo grade > II, 1.3%) consisting of deaths due to disease progression in patients treated with palliative intent for advanced disease. Study limitations include the short 30-day follow-up period for safety outcomes, self report of complications, lack of long-term oncologic outcome data in this initial report, potential selection bias as all patients were treated in the early post-FDA approval period, and the absence of a control group for comparison with other liver-directed therapies. The authors indicate that future studies should evaluate the treatment response to histotripsy, recurrence, and progression-free survival.

Mendiratta-Lala (2024) published the results of a prospective multicenter, single arm trial (#HOPE4LIVER).[4] A total of 44 participants with up to three tumors smaller than 3 cm in size were treated with histotripsy. Participants included individuals with hepatocellular carcinoma (n = 18) or with liver metastases from non–hepatocellular carcinomas (n = 26). All participants underwent a single session of histotripsy. Technical efficacy at 30 days was 83%. A total of 101 adverse events were reported within 30 days postoperative, with 94 (93.1%) categorized as nonserious. Three of the serious adverse events were classified as primary safety end-point failures (Sepsis, pleuritic pain and hepatic failure leading to death 37 days post procedure). The remaining four serious adverse events were splenic hematoma, melena, procedural pain, and progression of metastatic colorectal cancer. Limitations include outcomes focused only on early performance metrics rather than long-term clinical outcomes, the patient cohort primarily consisted of stage IV metastatic disease cases, which may not represent typical ablation treatment candidates and the absence of a control group limits the ability to compare histotripsy's effectiveness against established ablative technologies.

Vidal-Jove (2022) published a first-in-human phase I trial evaluating histotripsy, a noninvasive focused ultrasound therapy, for treating liver tumors.[5] The study, known as the Theresa Study, included 8 of 14 recruited patients (median age 60.4 years) with unresectable end-stage multifocal liver tumors, targeting eleven tumors total with an average diameter of 1.4 cm. The distribution of cases included 5 patients with colorectal liver metastases (7 tumors), 1 patient with breast cancer metastases (1 tumor), 1 with cholangiocarcinoma metastases (2 tumors), and 1 with hepatocellular carcinoma (1 tumor). Using a prototype system from HistoSonics, Inc., the study achieved its primary endpoint of creating planned tissue destruction zones in 100% of procedures, as verified by MRI one day post-procedure. The treatment demonstrated a favorable safety profile with zero device-related adverse events during the eight-week follow-up period, and 2 of 8 patients showed continuous decline in tumor

markers. Limitations include small sample size and the non-randomized design. Trial Registration: Study to Evaluate VORTX Rx (Theresa). NCT03741088.

PRACTICE GUIDELINE SUMMARY

National Comprehensive Cancer Network (NCCN)

- The NCCN Practice guidelines for Hepatocellular Carcinoma (V1. 2026) do not address histotripsy.[6]
- The NCCN practice guidelines for Kidney Cancer (V2. 2026) do not address histotripsy.[7]
- The NCCN practice guidelines for Pancreatic Adenocarcinoma (V1.2026) do not address histotripsy.[8]

SUMMARY

There is not enough research to show that histotripsy is a safe and effective treatment for renal, hepatic or pancreatic malignant tumors. No U.S. evidence based clinical practice guidelines recommend the use of histotripsy for any indication. Therefore, the use of histotripsy for any indication is considered investigational.

REFERENCES

1. FDA 510(k) premarket notification for Edison System [cited 04/06/2026]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf24/K241902.pdf.
2. Ziemlewicz TJ, Critchfield JJ, Mendiratta-Lala M, et al. The #HOPE4LIVER Single-arm Pivotal Trial for Histotripsy of Primary and Metastatic Liver Tumors: One-year Update of Clinical Outcomes. *Ann Surg.* 2025;282(6):908-16. PMID: 40201962
3. Wehrle CJ, Burns K, Ong E, et al. The first international experience with histotripsy: a safety analysis of 230 cases. *J Gastrointest Surg.* 2025;29(4):102000. PMID: 39978577
4. Mendiratta-Lala M, Wiggermann P, Pech M, et al. The #HOPE4LIVER Single-Arm Pivotal Trial for Histotripsy of Primary and Metastatic Liver Tumors. *Radiology.* 2024;312(3):e233051. PMID: 39225612
5. Vidal-Jove J, Serres X, Vlaisavljevich E, et al. First-in-man histotripsy of hepatic tumors: the THERESA trial, a feasibility study. *Int J Hyperthermia.* 2022;39(1):1115-23. PMID: 36002243
6. National Comprehensive Cancer Network (NCCN) Guidelines for Hepatocellular Carcinoma (V1. 2026). [cited 05/07/2026]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf.
7. National Comprehensive Cancer Network (NCCN) Guidelines for Kidney Cancer (V2. 2026). [cited 05/07/2026]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
8. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma (V1.2026). [cited 05/07/2026]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf.

CODES

Codes	Number	Description
CPT	0686T	Histotripsy (ie, non-thermal ablation via acoustic energy delivery) of malignant hepatocellular tissue, including image guidance
	0888T	Histotripsy (ie, non-thermal ablation via acoustic energy delivery) of malignant renal tissue, including imaging guidance
	1037T	Histotripsy (ie, non-thermal ablation via acoustic energy delivery) of malignant pancreatic tissue, including imaging guidance
HCPCS	None	

Date of Origin: *April 2025*