
Medical Policy



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***Current Policy Effective Date: 7/1/26**
(See policy history boxes for previous effective dates)

Title: Nonthermal Histotripsy for Primary and Metastatic Liver Tumors (i.e., Edison System)

Description

Histotripsy is an incisionless non-thermal procedure that uses ultrasound to induce mechanical cavitation resulting in the transformation of targeted tissue into acellular debris. The HistoSonics Edison® (Ann Arbor, MI, USA) platform is an FDA-approved (2023) histotripsy device that utilizes cavitation cloud histotripsy, a form of histotripsy that combines shock-scattering and intrinsic threshold histotripsy. It is a treatment used to selectively destroy cancer cells, including malignant liver lesions.

Medical Policy Statement

Nonthermal histotripsy, with an FDA approved device (i.e. Edison System), is established as a therapeutic option for primary and metastatic liver tumors when criteria are met.

Inclusionary and Exclusionary Guidelines

Inclusions:

Nonthermal histotripsy (i.e., Edison System) of primary or metastatic tumors of the liver may be considered established when **ALL** the following are met:

- Individuals for whom traditional surgical methods, chemotherapy, and other treatments, such as ablation would be too risky or pose unacceptably increased risks or have been ineffective.
- 18 years of age or older

- Tumor is less than or equal to 3 cm in longest diameter
- No more than 3 tumors are targeted for index procedure, regardless of how many tumors are present
- No evidence of end stage liver or kidney disease
- ECOG Performance Status 0-2^a and life expectancy of > 6 months

^a A score on the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale, which is used to assess how a patient's disease affects their ability to perform daily activities. The scale ranges from 0 to 5, with 0 indicating fully active and 5 indicating death. An ECOG score of 0-2 generally indicates that the patient is still able to perform most daily activities and may still be able to work, although some may experience fatigue or limitations.

Exclusions:

- The above criteria are not met.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

0686T*

Other codes (investigational, not medically necessary, etc.):

N/A

* Note: 0686T is payable as of 2/1/25

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Background

The HistoSonics Edison® (Ann Arbor, MI, USA) platform uses an ultrasound to generate acoustic based waves which causes micro-bubbling and emulsifies liver tumors into liquid material. The acellular debris is then absorbed by the body. This targeted non-invasive therapy mechanically breaks down cancerous tissue; without heat or radiation, making it safer for surrounding tissues. It presents a unique advantage over existing therapies which involve heat and/or radiation which carry the risk of damage to the surrounding normal tissue and blood vessels.

Hepatocellular cancer (HCC) is the most common liver cancer. Other primary liver cancers include intrahepatic cholangiocarcinoma (bile duct cancer), angiosarcoma and hepatoblastoma. Treatment is varied depending on the diagnosis. Generally, hepatocellular cancer is initially evaluated for surgical resection or liver transplantation. When that is not feasible, locoregional treatment such as ablation, arterial directed therapy or radiotherapy are then considered. When those treatments are not feasible and beneficial to achieve an improved outcome, immunotherapy and chemotherapy provide options.

Advanced cancer is when evidence of its presence is found beyond the primary site or origin, so it is no longer localized. Regional spread of the cancer is to nearby structures or lymph nodes. Distant spread of the cancer, also referred to as metastasis, is to distant parts of the body. The liver is a common site for metastasis. Cancers that spread to the liver most often are colorectal, breast, esophageal, stomach, pancreas, lung, kidney, and melanoma skin cancers according to the American Cancer Society (2025). Those cancers that have metastasized to the liver are also referred to as secondary liver cancers. Secondary liver cancers are more common than primary liver cancers in the United States and Europe.

Treatment of metastases caused by secondary liver cancers varies according to the number, size, and location within the liver. Surgery, ablation, embolization, chemotherapy and radiation to the whole liver or stereotactic radiation to the metastasis are all possible interventions. Clinical decision making that weighs the risk of the procedure and the benefits of its outcome are critical to the correct selection. Frequently, there is a balance as to reduction/removal of the metastasis and the impact on the resultant function of the liver. As a result, procedures that minimize toxicity to normal liver tissue and maintain adequate liver function are more likely chosen.

Hepatocellular carcinoma (HCC) is an aggressive disease that can be resistant to conventional chemotherapy and radiotherapy. Queen et al (2025) discusses how a recently FDA-approved non-thermal, non-invasive, focused ultrasound treatment (i.e. Edison System) may be a solution to overcoming refractory HCC. While surgical resection and trans-arterial therapy can improve overall survival, the biological aspects of HCC contribute to the complexity of its management and limit the effectiveness of current treatment options. The current evidence supports that the novel histotripsy approach offers several key advantages that address the limitations of the current treatment strategies for HCC. Clinical trials have highlighted the ability of this technology to destroy solid tumors and induce remission with minimal side effects. In addition, current preclinical studies point to the potent immunostimulatory effects of histotripsy, including the induction of abscopal effects. Authors indicate that this poses significant promise in treating tumor metastasis.

Another significant role for histotripsy is with liver transplantations. A liver transplantation for cancer related diagnoses can be a curative option. Hepatocellular cancer as the most common primary liver cancer is the most frequently identified cancer for this intervention. To maintain eligibility for a liver transplant according to the United Network for Organ Sharing guidelines and to receive priority listing on the wait list, the liver lesions must be limited by number and size. Various locoregional techniques have been identified to control the growth of these metastases such as chemical ablation, thermal ablation, chemoembolization, radiation microspheres and external beam radiation. These ablative procedures are essential to successfully bridge an individual to liver transplantation.

The Edison System is a non-invasive, non-thermal soft tissue-destruction device that uses pulsed sound waves to induce a “bubble cloud” from gases produced from targeted tissues (i.e., tumors). Those pulsed sound waves create small cavities that rapidly fill with vapor, and cavitation is induced when these vapor-filled cavities collapse. Targeted tissues are destroyed without the use of heat through high pressure point mechanical forces during this process. Soft tissue targets can be precisely selected, avoiding damage to the surrounding normal

structures. Unlike other ablative technologies, physicians can monitor the tissue destruction under continuous real-time visualization and control using radiological imaging.

United Network for Organ Sharing (UNOS) is the non-profit scientific and educational organization that administers the Organ Procurement and Transplantation Network (OPTN) under contract with the federal government. UNOS manages the national transplant waitlist, securely maintains databases, and monitors organ matches to ensure policies are followed including equitable allocation.

As of 2024, liver histotripsy has been recognized by UNOS/OPTN as an allowable locoregional treatment for liver lesions. The use of liver directed histotripsy is now recognized as an acceptable step to control liver lesions and fulfill criteria to maintain an individual's prioritized status on the wait list for a liver transplant.

Currently, there exist 3 major classifications of histotripsy, which vary based on the aforementioned parameters; these include shock-scattering histotripsy, boiling histotripsy, and intrinsic threshold histotripsy.

Summary of Evidence

For individuals who have primary or metastatic tumors of the liver who have failed to respond to or are intolerant to other available standard of care options, clinical trials, a systematic review, case studies and prospective studies were reviewed. The primary endpoint of a phase 1 clinical study was the determination of the acute technical success of a single treatment using the VORTX RxVR histotripsy device, as assessed on magnetic resonance (MR) imaging. In the #HOPE4LIVER trial, histotripsy results in local control of liver tumors at 1 year, which is consistent with current locoregional therapies. Authors concluded that the histotripsy device performed consistently and reliably in destroying all targeted liver tumors precisely and without liver toxicities or other significant adverse events. Histotripsy has shown to be a non-invasive treatment option, demonstrating the ability to treat a targeted volume of the liver tissue successfully and safely. Also, the use of non-invasive nature of histotripsy with its high precision and capability to spare critical vessels and bile ducts will improve the treatment for individuals with primary and metastatic liver tumors. There is sufficient evidence to determine that the technology results in an improvement in net health outcomes

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

Acoustic cavitation is the generation, oscillation, and collapse of microbubbles activated by ultrasound. Ultrasound imaging is typically used to guide and monitor

the histotripsy procedure in real-time. The material in the histotripsy ablation zone is absorbed by the body within 1–2 months, leaving a minimal remnant scar. In contrast to many existing minimally-invasive techniques, histotripsy can noninvasively eradicate tissue.

The HistoSonics Edison® (Ann Arbor, MI, USA) platform has shown significant promise in treating HCC in clinical trials. However, one limitation of this system is that it relies on ultrasound (US) guidance to detect the area for treatment. Not all liver tumors are well-visualized with US, meaning some individuals are not candidates for this treatment. Additional limitations include the risk of injury to adjacent structures and sound interference.

Sandilos et al (2024) deliberated on the potential positive effects of mechanical, nonthermal histotripsy. Aside from the immediately appreciable effect on tissue volume loss, the authors concluded that the effect of technology has contributed to additional exploitable immunologic benefits. Histotripsy has been shown to stimulate an immune response and induce abscopal effects (affecting not only the targeted tumor, but also tumors that were not targeted). Thus, the potential effects of the histotripsy stimulation may help the body's immune regulatory system attack remaining cancer cells which may have positive implications for future cancer treatment. Additional advantages of this procedure include its minimal side effects which include being well-tolerated, non-invasive, shorter recovery period for patients, minimal complications such as bleeding and pain at the treatment site. Histotripsy has been investigated for many pre-clinical applications, including treatment for tumors in the liver and potential immune responses to tumor antigens.

Clinical Context and Therapy Purpose

The purpose of histotripsy is to provide alternative treatment options for individuals with primary or metastatic liver cancers who have failed existing standard of care treatment.

The following PICO was used to select literature to inform this review:

The #HOPE4LIVER Single-Arm Pivotal Trial for Histotripsy of Primary and Metastatic Liver Tumors.

Review of Evidence

Vidal-Jove et al (2022) evaluated a multicenter phase I trial (Theresa Study). Eleven tumors were targeted in the 8 individuals who all had unresectable end-stage multifocal liver tumors: colorectal liver metastases (CRLM) in 5 patients (7 tumors), breast cancer metastases in 1 (1 tumor), cholangiocarcinoma metastases in 1 (2 tumors), and hepatocellular carcinoma (HCC) in 1 (1 tumor). Median age of the participants was 60.4 years with an average targeted tumor diameter of 1.4 cm. The primary endpoint was acute technical success, defined as creating a zone of tissue destruction per planned volume assessed by MRI 1-day post-procedure over an 8 weeks' time-frame. Safety (device-related adverse events) through 2 months was a secondary endpoint. Hepatic histotripsy, was performed with a prototype system (HistoSonics, Inc., Ann Arbor, MI). The primary endpoint of the study was the determination of the acute technical success of a single treatment using the VORTX RxVR histotripsy device, as assessed on magnetic resonance (MR) imaging using a 1.5 T MR scanner with maximum slice thickness of 5 mm one day post procedure. Secondary endpoints included adverse events, assessment of the local tumor progression, assessment of liver function, assessment of possible immune response to treatment, evaluation of quality of life, and assessment of pain and analgesic requirements post procedure. There were no adverse events determined to be probably or definitely device-related, giving the histotripsy procedure an excellent safety

profile. Liver function elevations were observed in all participants as expected given histotripsy's mechanism of action that completely destroys hepatocytes. Authors concluded that the histotripsy device performed consistently and reliably in destroying all targeted liver tumors precisely and without liver toxicities or other significant adverse events. Advantages of histotripsy are that the treatment effect can be monitored real-time under ultrasound which ensures that the target is treated appropriately while minimizing if not eliminating the risk of injury to adjacent tissue. Authors indicated that regardless of the multiple limitations of the study, this trial demonstrated that hepatic histotripsy can effectively destroy a targeted tissue volume with no device-related adverse events in a small number of patients. Given histotripsy's novel, noninvasive approach, more extensive multicenter clinical trials validating these results are warranted.

Mendiratta-Lala et al (2024) discussed a prospective, multicenter, single-arm study in which 14 sites in Europe and the United States recruited 44 participants from January 2021 to July 2022. Twenty-one participants were from the United States, 23 were from the European Union or England with a total of 22 females, 22 males and mean age of 64 years $\pm$ 12 [SD]. The majority had Child-Pugh class A disease (86%). Eighteen participants (41%) had hepatocellular carcinoma and 26 (59%) had non-hepatocellular carcinoma liver metastases. In total, 49 tumors were treated. The maximum pretreatment tumor diameter was 1.5 cm $\pm$ 0.6 and the maximum post-histotripsy treatment zone diameter was 3.6 cm $\pm$ 1.4. Up to 3 tumors smaller than 3 cm in size could be treated. CT or MRI and clinic visits were performed at 1 week or less pre-procedure, at index-procedure, 36 hours or less post-procedure, and 30 days post-procedure. There were co-primary end points of technical success of tumor treatment and absence of procedure-related major complications within 30 days, with performance goals of greater than 70% and less than 25%, respectively. The technical success end point was achieved in 42 of 44 tumors (95%; 95% CI: 84, 100). Procedure-related major complications such as abdominal pain and pain at the site of the procedure were reported in 3 of 44 participants (7%; 95% CI: 2,18), both meeting the performance goal. Notable limitations of the study include the small sample size and short-term post-procedure follow-up. Authors concluded that the study confirms the technical success and safety of histotripsy for the noninvasive mechanical destruction of liver tumors. It is believed that pending early clinical adoption, larger trials with longer follow-up in typical candidates for local-regional treatment will provide further outcome data to help define the role of this emerging technology.

Uysal et al (2025) reported on a case study which describes the first use of histotripsy as a bridging therapy prior to liver transplantation for hepatocellular carcinoma (HCC). A 59-year-old Caucasian female with morbid obesity (BMI 55 kg/m²) and cirrhosis from metabolic dysfunction-associated steatotic liver disease, complicated by hepatic encephalopathy, thrombocytopenia, and portal hypertension underwent an MRI which showed a 2 cm LIRAD-5/OPTN-5b lesion consistent with HCC. She had an initial AFP of 12.1 ng/ml. The patient underwent liver histotripsy with an ablative margin of 0.5 cm. One month later, she received an orthotopic liver transplant from a donation after cardiac death donor. The explanted liver demonstrated total necrosis of the area treated with histotripsy. There was no evidence of viable tumor cells at the site of the original tumor on H&E staining and low magnification view of the region of interest showed a necrotic nodule from the treated HCC. Although locoregional treatments such as radiofrequency ablation, microwave ablation, transarterial chemoembolization, and TARE are well-established options for bridging individuals to liver transplantation, they have notable limitations including their invasive nature, significant radiation exposure, limited real-time visualization of therapeutic effects and inconsistent tumor

control. Furthermore, these treatments often necessitate the suspension of systemic therapies, such as chemotherapy or immunotherapy, which can disrupt potential synergistic effects during a critical period. Authors concluded that this case highlights the successful use of histotripsy, suggesting it could be a valuable addition to existing HCC treatments, especially given its non-invasive nature and the risks associated with other bridging therapies.

Ziemlewicz (2025) reported on the 1-year clinical outcomes from the #HOPE4LIVER trial. Among 47 participants, the 1-year local tumor control rate was 63% by initial review and 90% after expert reassessment. This difference was explained as being due to a learning curve in interpreting the appearance of tissue disruption caused by the histotripsy treatment. One-year survival was 73% for hepatocellular carcinoma and 49% for metastatic disease. Most treatment zones showed progressive shrinkage (over 95% volume reduction), and nearly all adverse effects occurred within 30 days of treatment, primarily mild abdominal pain or fever. Only six serious device-related events were reported, and no delayed toxicities were found. Overall, histotripsy provided tumor control and safety outcomes comparable to current local liver therapies. Histotripsy results in local control of liver tumors at 1 year, which is consistent with current locoregional therapies. The safety profile is favorable, and survival at 1 year is comparable with other therapies for similar disease stages.

Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT04572633	The HistoSonics System for Treatment of Primary and Metastatic Liver Tumors Using Histotripsy (#HOPE4LIVER US)	47	Sept 2027
NCT04573881	The HistoSonics System for Treatment of Primary and Metastatic Liver Tumors Using Histotripsy (#HOPE4LIVER EU/UK) (#HOPE4LIVER)	24	Aug 2027

Regulatory Status

The HistoSonics Edison System was approved by the U.S. Food and Drug Administration (FDA) through the De Novo pathway 513(f)(2) on October 6, 2023. Because there are no other equivalent devices, the De Novo 513(f)(2), rather than the 510(k)-approval pathway, was required. The FDA classifies the Edison, as a focused ultrasound system for non-invasive, non-thermal, mechanical tissue ablation of liver tumors, including unresectable liver tumors.

In 2024, the Edison System (HistoSonics, Inc) was granted FDA 510(k) approval (K233466) for the non-invasive destruction of liver tumors, including unresectable liver tumors, using a non-thermal, mechanical process of focused ultrasound.

Product code: QGM

Supplemental Information

Organ Procurement and Transplantation Network

Effective August 1, 2024, the organ procurement and transplantation network (OPTN)'s Waiting List, known as the Waitlist, lists "Histotripsy and Other as loco-regional treatment options for initial and extension exception requests for liver candidates. OPTN proposes adding the options of "Histotripsy" and "Other" to the locoregional treatments section within the HCC initial and extension exception forms in the OPTN computer system. Requirements for Hepatocellular Carcinoma (HCC) MELD or PELD Score Exceptions outlines the required criteria for a candidate to automatically be approved for an initial HCC exception as well as extension requests. One of these criteria is that the candidate must undergo a thorough assessment that includes an indication whether the candidate has undergone locoregional therapy. While policy does not mandate specific types of therapy, the HCC exception forms collect more granular information. These exceptions should be automatically approved if the candidate meets all other criteria outlined.

Government Regulations

National:

Centers for Medicare & Medicaid Services: Approved IDE Studies

Refer to the Medicare IDE approved Studies site for full details.

CMS may consider for Medicare coverage certain devices with an FDA-approved investigational device exemption (IDE) that have been categorized as Category B (Nonexperimental/investigational) device.

Category B (Nonexperimental/investigational) device refers to a device for which the incremental risk is the primary risk in question (that is, initial questions of safety of that device type have been resolved), or it is known that the device type can be safe and/or effective (e.g. FDA premarket approval or clearance for that device type has been granted).

"The HistoSonics System for Treatment of Primary and Metastatic Liver Tumors Using Histotripsy (#HOPE4LIVER)" clinical trial NCT04573881 with an estimated completion date of July 2026 is listed as a category B on Medicare's website for approved studies. The covered trial is investigating the efficacy and safety of the HistoSonics System for the treatment of primary or metastatic tumors located in the liver. The population of interest is ≥ 18 years of age and have been diagnosed with hepatocellular carcinoma or liver metastases from other primary cancers.

Local:

No Local Determination noted for the use of histotripsy with primary and metastatic liver cancer was found.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Cryosurgical Ablation of Primary or Metastatic Liver Cancer
 - Radioembolization for Primary and Metastatic Tumors of the Liver
 - Radiofrequency Ablation of Primary and Metastatic Liver Tumors
 - Transcatheter Arterial Chemoembolization of Hepatic Tumors (TACE)
 - Transplant-Heart-Liver (Combined)
 - Transplant-Liver
 - Transplant-Liver-Kidney (Combined)
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References

1. Akdas, S. "Bubble Trouble for Cancer: Is Histotripsy Hype or Hope?" *Breaking Cancer News*. 2024. <https://breakingcancernews.com/2024/11/10/bubble-trouble-against-cancer-is-histotripsy-hype-or-hope/>. Accessed March 28, 2026.
2. American Cancer Society. "Liver Metastases." 2025. <https://www.cancer.org/cancer/managing-cancer/advanced-cancer/liver-metastases.html>. Accessed March 28, 2026.
3. Centers for Medicare & Medicaid Services." IDE Study: The HistoSonics System for Treatment of Primary and Metastatic Liver Tumors Using Histotripsy (#HOPE4LIVER). G200253-NCT04573881." 2021. <https://www.cms.gov/https/wwwcmsgov/medicare/coverage/ide/approved-ide-studies/g200253-nct04573881>. Accessed March 28, 2026.
4. Cornell Law School. Legal Information Institute. 42 CFR § 405.201 - Scope of subpart and definitions. <https://www.law.cornell.edu/cfr/text/42/405.201>. Accessed March 28, 2026.
5. HistoSonics. "Histotripsy at Work." <https://histosonics.com/the-science/>. Accessed March 28, 2026.
6. Khokhlova, V, Fowlkes, B., et al, "Histotripsy Methods in Mechanical Disintegration of Tissue: Towards Clinical Applications." *International Journal of Hyperthermia*, 2015 Mar; 31 (2): 145-162. PMID: 25707817.
7. Mendiratta-Lala, M., Wiggermann, P., et al. "The #HOPE4LIVER Single Arm Pivotal Trial for Histotripsy of Primary and Metastatic Liver Tumors". *Radiology*, 2024 Sep;312(3)
8. National Library of Medicine. The HistoSonics System for Treatment of Primary and Metastatic Liver Tumors Using Histotripsy (#HOPE4LIVER EU/UK) (#HOPE4LIVER). NCT04573881. 2021. <https://clinicaltrials.gov/study/NCT04573881>. Accessed March 28, 2026.
9. Qu, S., Worlikar, T., et al. "Non-Thermal Histotripsy Tumor Ablation Promotes Abscopal Immune Responses that Enhance Cancer Immunotherapy." *Immunotherapy Cancer*. 2020 Jan;8 (1) PMID: 31940590
10. Queen H, Ferris SF, Cho CS, Ganguly A. "The Emerging Role of Histotripsy in Liver Cancer Treatment: A Scoping Review." *Cancers (Basel)*. 2025 Mar 7;17(6):915. PMID: 40149252
11. Roberts, W. "Development and Translation of Histotripsy: Current Status and Future Directions." *Curr Opin Urol*. 2014 Jan 24(1):104-110. PMID: 24231530.
12. Sandilos, G., Butchy, MV., et al. "Histotripsy -Hype or hope? Review of Innovation and Future Implications." *Journal of Gastrointestinal Surgery*, 2024 Aug 28(8):1370-1375. PMID: 38862075.

13. United Network for Organ Sharing (UNOS). "Liver treatment options added for HCC exception candidates." 2024. [https://unos.org/unet-system-changes/liver-treatment-options-to-be-added-for-hcc-exception-candidates/#:~:text=Effective%20August%201%2C%202024%2C%20the,with%20hepatocellular%20carcinoma%20\(HCC\),](https://unos.org/unet-system-changes/liver-treatment-options-to-be-added-for-hcc-exception-candidates/#:~:text=Effective%20August%201%2C%202024%2C%20the,with%20hepatocellular%20carcinoma%20(HCC),) Accessed April 10, 2025. No longer populates as of March 27, 2026.
14. U.S. Food & Drug Administration. "Edison System". DEN220087. 2023. https://www.accessdata.fda.gov/cdrh_docs/pdf22/DEN220087.pdf. Accessed March 28, 2026.
15. U.S. Food & Drug Administration. "Edison System". K233466. 2024. https://www.accessdata.fda.gov/cdrh_docs/pdf23/K233466.pdf. Accessed March 28, 2026.
16. U.S. Food & Drug Administration. Investigational Device Exemption (IDE). <https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/investigational-device-exemption-ide>. Accessed March 28, 2026.
17. Uysal, M., Wehrle, C.J. Coppa, C. et al. "Bridging therapy with histotripsy prior to liver transplantation for hepatocellular carcinoma: a first case report." *Exp Hematol Oncol* 14, 20 (2025) PMID 40001149.
18. Vidal-Jove, J., Serres, X., et al. "First -in-Man Histotripsy of Hepatic Tumors: The THERESA trial, a feasibility study." *Int J Hyperthermia*. 2022; 39(1),1115-1123. PMID: 36002243.
19. Wah TM, Pech M, Thormann M, et al. "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*. 2023 Feb;46(2):259-267. Nov 15. PMID: 36380155.
20. Xu, Z., Hall, T. L., Vlaisavljevich, E., & Lee, F. T. "Histotripsy: The First Noninvasive, Non-ionizing, Non-thermal Ablation Technique based on Ultrasound." *Inte J of Hyperthermia* 2021 April ; 38(1), 561–575. PMID: 33827375.
21. Ziemlewicz TJ, Critchfield JJ, Mendiratta-Lala M, et al. The #HOPE4LIVER single-arm pivotal trial for histotripsy of primary and metastatic liver tumors: 1-year update of clinical outcomes. *Ann Surg*. April 9. 2025 PMID 40201962

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 3/27/26, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
7/1/25	4/15/25		Joint policy established Vendor: N/A
7/1/26	4/21/26		Routine maintenance (slp/lk)

Next Review Date: 2nd Qtr, 2027

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: NONTHERMAL HISTOTRIPSY FOR PRIMARY AND METASTATIC LIVER TUMORS
(I.E., EDISON SYSTEM)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply
BCNA (Medicare Advantage)	Refer to Government Regulation section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.
- Duplicate (back-up) equipment is not a covered benefit.