ACE BRIEF FOR NEW AND EMERGING HEALTH TECHNOLOGIES

Edison Histotripsy System (HistoSonics) for non-invasive destruction of liver tumours

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Contents

Summary of Key Points

- Malignant liver tumours pose a significant health burden in Singapore, ranking among the top five cancer deaths.
- In patients with early-stage primary liver cancer, and those with secondary liver cancer with ≤3 liver lesions of ≤3 cm each, ablation therapy may be a viable treatment option.
- The Edison Histotripsy System (herein referred to as Edison) is an FDA-registered platform that uses focused ultrasound pulses to ablate liver tumours at the sub-cellular level. It is indicated for the non-invasive destruction of liver tumours, including unresectable liver tumours.
- Based on two single-arm trials in patients with ≤3 liver tumours of ≤3 cm each, who were contraindicated or unresponsive to standard of care (SOC) treatment (total n=55; tumours=63), Edison appeared to be effective in ablating target liver tumours, despite some safety issues.
    - Edison-related major adverse events were reported in 13% of patients (6/47). All occurred in the first 30 days post-procedure with one patient each reporting sepsis, pleuritic pain, abdominal pain, portal vein thrombosis, post-operative thrombosis, or fatal hepatic failure.
    - Edison-related non-major complications included procedural and abdominal pain, and occurred in 26% and 22% of patients, respectively.
    - One-year overall survival was 58.6% (95% CI: 43.0% to 71.3%) and freedom from local tumour progression post-Edison was 63.4% (95% CI: 43.5% to 78.0%).
    - High procedural success rates were reported across both trials, with technical success achieved in 96% of tumours overall.
    - No significant difference was reported in quality of life and median pain before and after the procedure.
- The cost-effectiveness of Edison for liver tumours was uncertain. Based on the USA Medicare database, it is likely that the cost of a histotripsy procedure using Edison could be 3 to 9 times higher than forlocal SOC ablation procedures.
    - Histotripsy procedure using Edison cost per patient is estimated to be between USD$9,527 (SGD$12,960) to USD$17,500 (SGD$23,805), at ambulatory surgical centres and hospital outpatient departments, respectively. Local costs of ablation therapy range between SGD$2,556 to SGD$3,946 in patients from subsidised wards.
    - USA Medicare covers the remaining cost of Edison above patient co-payment of USD$1,676 (SGD$2,280) to USD$1,878 (SGD$2,555).
- Key uncertainties regarding use of Edison include its relative benefits against other ablative therapies, and the applicability of the findings to the local target population.
    - One local trial of Edison in patients (n=40) with liver tumours contraindicated or unresponsive to other treatments is commencing soon.
- Implementation considerations include potentially high capital cost of technology (up to SGD$2.7M to SGD$4.0M/system). Consumables cost about USD$6K (SGD$7,948) per use.
- Based on feedback from established centres in US and Hong Kong, a local clinician indicated that the learning curve to use Edison is expected to be shorter compared to existing modalities, such as ablation, radioembolisation and surgery.

I. Background

Between 2018 and 2022, primary liver cancer was the third highest leading cause of cancer death in males (12.3% of cancer-related deaths) and fifth among females (5.8% of cancer-related deaths) in Singapore.[1]

Malignant liver tumours can originate in the liver (primary liver cancer) or spread to the liver (secondary liver cancer) from other sites.[2] Among primary liver cancers, there are two main types: hepatocellular carcinoma (HCC), which is more common, and cholangiocarcinoma. For secondary liver cancer, the most common types of primary cancers causing liver metastasis include colorectal, lung, and pancreatic cancers.[3] Globally, it is estimated that between 20% to 50% of patients with primary lung, colorectal, or pancreatic cancers will eventually develop liver metastases.[4-6]

Liver tumours are typically diagnosed through imaging, blood tests, and liver biopsies.[7] For most patients with early-stage or locally advanced primary liver cancer with varying degrees of liver function, resections and transplants are the typical treatments of choice. Ablation therapy might be preferred in some patients with early-stage primary liver cancer.[7] It might also be used as an adjunct treatment in certain patients with secondary liver cancer, as well as for patients who are not good candidates for surgery, those awaiting surgery, or those with recurrent tumours after a previous surgery.[8, 9]

Currently, thermal ablation using either radiofrequency or microwaves is the main ablation technique used to treat liver cancer in Singapore.[10] However, the main disadvantage of thermal ablation is the heat-sink effect, which refers to incomplete ablation of tumours located near large blood vessels due to the cooling effect of blood flow,[11] which negatively impacts on ablation efficacy and clinical outcomes.[12]

II. Technology

The Edison Histotripsy System by HistoSonics (herein referred to as Edison) is a platform that uses focused ultrasound pulses to ablate liver tumours at the sub-cellular level.[13] Specifically, when ultrasound waves generated by Edison reach the targeted tissue, they cause vibrations that create high pressure. This pressure creates micro-bubbles that expand and collapse rapidly, forming a bubble cloud that moves through the targeted tissue. The vibrations, expansion, and collapse induce mechanical disruption in target tissue, which only occurs within the bubble cloud, avoiding damage to non-target tissue. Destruction of the cancer cells results in an acellular lysate with limited to no recognisable cellular structures. This is subsequently removed by the lymphatic system.

The platform has four main components (Figure 1): (1) a diagnostic imaging source (GE LOGIQ E10s) that is provided with each Edison Histotripsy System; (2) the Edison System transducer; (3) a treatment head which simultaneously delivers ultrasound to targeted liver tissue and provides real-time imaging to the treating physician via an ultrasound probe; and (4) a cart to create the medium (a single-use membrane) which couples the therapeutic head to the patient and allows ultrasound delivery.[14] Histotripsy using the Edison is performed under general anaesthesia and requires no incisions or needles.[15] During the procedure, the

treatment head encased in the coupling membrane is applied to the patient to deliver ultrasound pulses for tumour ablation (Figure 2). Most patients may only require a single session for multiple tumours. However, procedural time and number of sessions vary based on patient-specific factors such as numbersize and positioning of the tumours.[16] but Patients may return home on the same day or the day after the procedure and resume their normal activities shortly after.

The advantage of histotripsy, as compared to traditional thermal ablation techniques, is the lack of heat-sink susceptibility and the precise nature of ablation margins, allowing histotripsy to be carried out next to critical structures.[13]

Figure 1: The four-component Edison system. From left to right: a) diagnostic imaging source, b) the Edison System transducer, c) treatment head and d) fluidics cart to create the coupling medium.

Figure 2: Illustration of a patient undergoing treatment via Edison. (a) Placement of the therapeutic probe over localisation of tumour, (b) Ultrasound imaging probe and screen, (c) Schematic of focused-ultrasound waves ablating target site

III. Regulatory and Subsidy Status

The first version of Edison was granted marketing authorisation by the FDA under the De Novo Classification Request process (DEN220087).[15] Since then, two newer versions have been approved by the FDA (K233466 and K241902).[17, 18] They have been assessed as substantially equivalent to the first version by the FDA, albeit with reduced therapy time and increased size of the bubble cloud. Based on the FDA, Edison is indicated for the non-invasive destruction of liver tumours, including unresectable liver tumours, using a non-thermal, mechanical process of focused ultrasound.

In the USA, Medicare (public insurance) states that on average, a patient undergoing histotripsy pays between USD$1,676 (SGD$2,280) to USD$1,878 (SGD$2,555)[a] at ambulatory surgical centres and hospital outpatient departments, respectively, with Medicare covering

[a] Based on Monetary Authority of Singapore's 2024 to 2025 exchange rate: USD$1=SGD$1.3603

the rest of the treatment.[19] Although not explicitly stated, the cost is likely to reflect a per session cost, given that the number of sessions may vary from patient to patient. For patients in the USA covered by private insurance, coverage is unclear as it is still being established by insurers.[16]

IV. [2]Stage of Development in Singapore

☐	Yet to emerge	☐	Established
☒	Investigational / Experimental (subject of clinical trials or deviate from standard practice and not routinely used)	☐	Established *but* modification in indication or technique
☐	Nearly established	☐	Established *but* should consider for reassessment (due to perceived no/low value)

V. Treatment Pathway

The current local management pathway for liver tumours is summarised in Appendix A. It is primarily based on National Cancer Centre Singapore's clinical practice guidelines (CPG)[7], supplemented by CPGs from the European Association for the Study of the Liver for primary liver cancer[20], and the Japanese Society of Hepato-Biliary Pancreatic Surgery for secondary liver cancer[8]. The pathway was validated by local clinicians' input (Personal Communication: Senior Consultants from National Cancer Centre Singapore and National University Cancer Institute Singapore, March 2025).

In general, for patients diagnosed with a liver tumour, standard of care (SOC) includes surgery, ablative therapy, localised or systemic chemotherapy, radiation therapy, or palliative care. The choice is dependent on patient and tumour characteristics, including staging. Broadly, patients with early-stage primary disease are those with a single tumour of ≤5 cm or 3 or fewer tumours of ≤3 cm, and with no vascular invasion and no distant metastases.[7] Among patients with early-stage primary disease, those with good liver function and good general health may undergo surgical resection (adequate liver remnant) or, for selected cases, surgical transplantation (marginally adequate liver remnant or close vascular margins). These patients may also undergo radiation therapy (Personal Communication: Senior Consultant from National University Cancer Institute Singapore, May 2025). For those with unresectable disease due to poor liver function or general health, and/or inadequate liver remnant, ablative therapy is an option if they meet the size criteria (3 or fewer tumours of ≤3 cm). These patients may also undergo surgical transplantation.[20]

Patients with early-stage unresectable disease that is not suitable for ablation or transplantation may undergo radiation therapy, or chemoembolisation (in select cases).

Those with primary liver cancer beyond early-stage (locally advanced or distant metastases) are typically not candidates for current ablative therapy methods. Instead, they may undergo alternative treatment such as chemotherapy, radiotherapy, palliative therapy, or supportive care, depending on their liver function and extent of disease.

For patients with secondary liver cancer, however, a Japanese CPG provided a weak recommendation that ablation may be used as an adjunct treatment for certain patients; however, surgical resection is a preferred option.[8]

Local clinicians opined that Edison could be used as an alternative to current ablative methods as a same-line treatment option for some patients with unresectable disease due to poor liver function or general health, and/or inadequate future liver remnant if they meet the size criteria (3 or fewer tumours of ≤3 cm). (Personal Communication: Senior Consultants from National Cancer Centre Singapore and National University Cancer Institute Singapore, March and June 2025).[22] Based on the FDA-approved indication, Edison may also be suitable for patients with unresectable disease beyond early-stage.

VI. Summary of Evidence

This assessment was conducted using the Population, Intervention, Comparator and Outcome (PICO) criteria (Table 1). Literature searches were conducted in health technology assessment (HTA) databases, Cochrane Library and Embase.

Table 1: Summary of PICO criteria

Population	Patients with liver tumours, including unresectable liver tumours
Intervention	Histotripsy using focused ultrasound pulses with Edison Histotripsy System (any version)
Comparator	Primary: Other ablative methods Secondary: Other SOC therapies including surgery, radiation therapy, chemotherapy and no treatment
Outcome	Safety Clinical effectiveness ● Overall survival ● Disease-free survival ● Recurrence rate ● Technical success of liver ablation ● Local tumour progression ● Liver function ● QoL ● Other patient-related outcomes Economic outcomes: Costs, cost-effectiveness
Abbreviations:; SOC, standard of care; QoL, quality of life	

The key evidence base comprised three publications from two single-arm trials: a 2023 feasibility trial (THERESA); n=8, 11 tumours)[21] and a pivotal trial (HOPE4LIVER), with two publications by Mendiratta-Lala et al. (2024)[22] and Ziemlewicz et al. (2025)[23]. The publication by Mendiratta-Lala et al. [22] reported on outcomes up to 30 days (n=44; 49 tumours) while Ziemlewicz et al. [23] reported on outcomes at up to a year of follow-up (n=47, 52 tumours). For this brief, safety and effectiveness data for the HOPE4LIVER trial will be sourced primarily from Ziemlewicz et al.[23], unless otherwise stated. Information from Mendiratta-Lala et al.[22] will supplement any missing information, particularly for detailed

early safety and effectiveness outcomes (≤30 days). THERESA and HOPE4LIVER were both sponsored by the manufacturer, HistoSonics.[21-23] The specific model of Edison was not reported in either trial. Other study details are summarised in Appendix B.

Both trials included patients aged between 60 and 64 years with ≤3 liver tumours of ≤3 cm in diameter each, and unresponsive or contraindicated for other treatments. All patients were administered a single Edison session No concurrent therapy was used for the first 30 days after Edison, but patients were eligible for additional treatments beyond this time point.

No comparative study, health technology assessment (HTA) or full-text systematic reviews and/or meta-analyses were identified.

Safety

Safety outcomes were reported as any adverse event (AE) experienced during study follow-up, which was one year for HOPE4LIVER (n=47) and up to two months for THERESA (n=8).[21, 23] The studies defined favourable safety profiles using different criteria: THERESA[21] required 0% occurrence of specific SAEs (e.g. major bleeding and death), while HOPE4LIVER[22] defined it as ≤25% of Edison-attributable SAEs graded as Common Terminology Criteria for Adverse Events (CTCAE) ≥3. The definitions of key outcomes are summarised in Table 2. Neither study reported their methodology for determining Edison-related AEs. All safety events reported are summarised in Table 3.

Table 2: Safety and effectiveness outcomes and corresponding measurement tools

Study ID	Outcome	Measurement tool	Definition
Primary safety outcomes			
THERESA[21]	Favourable safety profile at 8 weeks	NR	0% SAE defined as major bleeding requiring transfusion within 48 hours of Edison treatment, visceral perforation due to Edison, major bile duct injury or death directly resulting from Edison
HOPE4LIVER [22, 23]	Favourable safety profile at 30 days		≤25% of SAE assessed as CTCAE grade ≥3 (severe to medically significant to life-threatening) attributable to Edison
Primary effectiveness outcome			
HOPE4LIVER [22, 23]	OS at 30, 90, 180 and 365 days	Kaplan Meier method[a]	Survival rate at various timepoints
	Freedom from LTP at 30, 180 and 365 days	Kaplan Meier method based on MRI or CT scans[b]	Absence of viable tumour for both primary and post-hoc assessment
	Treatment success at ≤36 hours	MRI or CT scans	The proportion of tumours where the post-Edison treatment volume was greater than or equal to the pre-treatment planning volume, relative to the total number of treated tumours[25, 26]
THERESA[21]	Treatment success at 24 hours		
Secondary effectiveness outcomes			
THERESA[21]	LTP at 30 days	MRI or CT scans	Visualisation of tumour within an area where complete tumour ablation was thought to have been achieved (i.e. treatment volume)[12]
HOPE4LIVER [22, 23]	Technique efficacy at 30, 180 and 365 days		A lack of nodular or mass-like area of enhancement within or along the edge of the treatment volume assessed.[25]
THERESA[21]	Liver function	Liver function tests	

	QoL	EORTC QLQ-C30	
	Pain	100mm VAS	

Abbreviations: 100mm VAS; 100-millimetre visual analogue scale; AE, adverse event; CT, computerised tomography; CTCAE, Common Terminology Criteria for Adverse Events; EORTC, European Organisation for Research and Treatment of Cancer; LTP, local tumour progression; MRI, magnetic resonance imaging; NR, not reported; OS, overall survival; QoL, quality of life; SAE, serious adverse event

Notes:

a. Day zero as the date of procedure, with patients censored at the latest date of study exit (if not death), last visit, or last reported adverse event onset.
b. For freedom from LTP, both a primary assessment (a single-read model with two experienced board-certified radiologists with a medical director to provide feedback) and post-hoc analysis (after 1 year of follow-up by an experienced reader) to allow for an experienced reader and to allow for evaluation of each patient over the entire post-treatment course.

SAEs

There were 10 serious AEs (SAEs) reported across both trials during follow-up.[21-23] Six of the SAEs, all reported in HOPE4LIVER,[23] were assessed as Edison-related; resulting in 12.8% Edison-related SAE in [23] that study population at 30 days. [23]

Of the six Edison-related SAEs, three were assessed using CTCAE (as reported by Mendiratta-Lala et al.)[22] and ranged between CTCAE grades 3 and 5. One CTCAE grade 3 SAE of sepsis was reported in a patient with an implanted biliary stent requiring pharmacological treatment, and a second patient reported pleuritic pain requiring hospitalisation. In addition, a CTCAE grade 5 SAE of hepatic failure at day 12 post-treatment developed in a third patient, resulting in death at day 37. The authors reported that this patient had poor underlying liver function, despite meeting the inclusion criteria for enrolling in the trial. The three non-CTCAE graded Edison-related SAEs included portal vein thrombosis, post-operative thrombosis and procedural pain.[23]

Of the four other non-Edison-related SAEs, two were reported in HOPE4LIVER,[23] including bleeding related to a primary pancreatic tumour and progression of metastatic colorectal cancer, leading to death in both patients (specific CTCAE grades were not reported). The other two (CTCAE grade 3) were reported in THERESA[21], and included a dental abscess and hypercalcaemia in a patient with Crohn's disease, occuring at 32- and 22-days post-Edison.

Based on the definitions reported in Table 2, both trials concluded a favourable safety profile for Edison, given that there were 0% Edison-related SAEs in THERESA[21] and 12.8% in HOPE4LIVER.[26] It is worth noting that, despite including similar populations, the trials adopted very different thresholds (0% in THERESA[21] and ≤25% in HOPE4LIVER[22]) for the same outcome.

AEs

HOPE4LIVER[23] reported 43 Edison-related non-serious AEs (CTCAE grades ≤2), with the most common being procedural pain (25%, n=12) and abdominal pain (22%, n=11). Most (42 of 43) of these AEs occurred at 30 days/one month, while one (biloma) occurred at day 188 (beyond six months).[23] THERESA[21] did not report the total number of non-serious AEs, which were all non-hepatic and resolved within one week.[21]

Other AE revealed by exploratory analysis

In addition, Mendiratta-Lala et al.[22] also reported that six patients (n=44; 14%) had damage to the liver tissue outside the expected margin.[6] This damage was defined as imaging changes post-Edison compared to baseline. Of these six patients, one had mistargeted histotripsy treatment, while the remaining five had perfusion changes contiguous to the treatment area.

Table 3: Summary of safety outcomes

Trial	Follow-up time	Outcome	Effect estimates
HOPE4LIVER[22, 23]	1 year[a]	AE	201 AEs in 47 patients Edison-related: 49 (24% of all AE) ● SAE: 6 SAEs in 47 patients ○ 2 CTCAE grade 3 events: sepsis and pleuritic pain ○ 1 CTCAE grade 5 event: hepatic failure ○ 3 non-CTCAE graded events: portal vein thrombosis, post-operative thrombosis and procedural pain ● Non-serious AE: 43 AEs in 47 patients ○ 26% procedural pain (n=12) ○ 22% abdominal pain (n=11) ○ 12% pyrexia (n=6)
	30 days[a]	Possible safety issues not reported as AE	Damage to liver tissue (outside of the expected margin reported in 14% of patients (6/44)
THERESA[21]	8 weeks	AE	2 SAE ● Edison-related: 0 ● 2 SAEs; no Edison-related ○ 2 CTCAE grade 3 events Other AE events (number NR): ● CTCAE grades 1 to 2
Abbreviations: AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; NR, not reported Notes: a. For 30 days of follow-up: n=44 with 49 tumours, for 1-year follow-up: n=47 with 52 tumours			

Effectiveness

HOPE4LIVER[23] reported overall survival (OS) and freedom from local tumour progression (LTP) among 47 patients, with day zero defined as the date of the Edison procedure.[23] Other primary outcomes across both trials included tumour-level. technical success rate at 24 hours (THERESA)[21] or ≤36 hours (HOPE4TRIAL)[22].THERESA[21] additionally assessed tumour-level LTP, liver function, quality of life (QoL) and pain.[21] The definitions and measurement tools used for key effectiveness are summarised in Table 2, while results are summarised in Table 4.

Overall survival

The median survival time for all patients in HOPE4LIVER was 20.7 months (n=47).[23]

Overall patient survival was 93.6% (95% CI: 81.5% to 97.9%), 83.0% (95% CI: 68.8% to 91.1%) and 58.6% (95% CI: 43.0% to 71.3%), at three months, six months and one year, respectively.

In patients with HCC (n=19), overall survival at 12 months was 73.3%. In patients with secondary liver cancer (n=28), overall survival was 48.6% (95% CI: 29.0% to 65.6%) at one year follow-up. The author cited that Edison appears to result in similar one-year OS rates compared to systemic immunotherapy in HCC patients (50% to 75%), and similar technical success rates compared to other SOC ablation modalities (48% to 95% across tumour types).

Local tumour progression

In HOPE4LIVER, at the patient-level, freedom from LTP was 63.4% (95% CI: 43.5% to 78.0%) at one year, based on the primary assessment.[23] This contrasted with the one-year freedom from LTP of 90.0% (95% CI: 75.3% to 96.2%) reported from the post-hoc assessment. The authors attributed the difference to visible blood vessels in the treatment zone initially interpreted as LTP at primary assessment.

In THERESA, at tumour-level, 20% LTP by one month was reported in two separate patients.[21] The authors considered the reasons for the failure as ablation mistargeting due to poor imaging for one patient, and growth of an adjacent untreated tumour for the other.

Procedure-related outcomes

Histotripsy demonstrated high procedural success rates across both trials. Technical success was achieved in 96% (53/55) of tumours overall,[21, 22] with complete treatment coverage achieved in all cases, except for two tumours in HOPE4LIVER[22] that were mistargeted.[21, 22] Regarding technique efficacy, HOPE4LIVER[23] reported increasing rates at the periphery of the treatment zone over time, from 79.2% at one month to 91.7% at one year among evaluable tumours.[23] Technique efficacy was considered able to improve with greater procedural experience. Further details on technical success and technique efficacy are available in Appendix C.

Liver function

THERESA reported elevations of transaminase 24 hours post-Edison among all eight patients. However, this level returned to baseline within a week and remained normal throughout the follow-up period out to two months.[21] The authors assessed this as an expected side effect from Edison, given that it destroys hepatocytes. No liver biomarkers changed significantly from baseline throughout follow-up.

Quality of life

In THERESA, QoL scores (European Organisation for Research and Treatment of Cancer QLQ-C30) showed no significant changes in overall score, or any sub-dimension score, from baseline to two months (overall baseline: n=8, 68 ± 13; overall two months: n=5, 61 ± 22,).[21]

Pain

In THERESA, pain scores (measured using Visual Analogue Scale) showed a median increase of 30 mm (n=7; IQR: 0 mm to 40 mm) from 24 hours to one week post-Edison.[21] Most patients (62.5%) required non-narcotic pain medication during the first week. Based on the

literature, a score of 30 mm (3 cm) is typically representative of mild pain with minimal impact on activities of daily living.[24]

Table 4: Summary of effectiveness evidence on Edison

Study ID, study design	Follow-up time	Outcome	Effect estimates
HOPE4LIVER[22, 23]	1 year	Survival	Survival rate: ● 1 month (n=47): 100.0% ● 3 months (n=44): 93.6% (95% CI: 81.5% to 97.9%) ● 6 months (n=38): 83.0% (95% CI: 68.8% to 91.1%) ● 1 year (n=21): 58.6% (95% CI: 43.0% to 71.3%)
		Freedom from LTP	Primary assessment: ● 1 month (n=39): 86.7% (95% CI: 72.7% to 93.8%) ● 6 months (n=28): 81.5% (95% CI: 66.3% to 90.4%) ● 1 year (n=11): 63.4% (95% CI: 43.50% to 78.0%) Post-hoc assessment: ● 1 month (n=43): 95.6% (95% CI: 83.4% to 98.9%) ● 6 months (n=34): 92.9% (95% CI: 79.5% to 97.7%) ● 1 year (n=18): 90.0% (95% CI: 75.3% to 96.2%)
		Technique efficacy	Primary assessment: ● 1 month (n=48 tumours): 79.2% ● 6 months (n=35 tumours): 80.0% ● 1 year (n=24 tumours): 91.7% Post-hoc assessment: ● 1 month (n=48 tumours): 89.6% ● 6 months (n=35 tumours): 91.7% ● 1 year (n=24 tumours): 96.0%
	30 days	Technical success rate at 36 hours	95% among 44 tumours (95% CI: 84% to 100%)
THERESA[21]	8 weeks	Technical success rate at 24 hours	100% among 11 tumours
		LTP	● 1-week & 1-month: 20% (n=10 tumours) ● 2-month: No LTP in any treated tumour
		Liver function	Transaminase: Elevation in 100% of patients at 24 hours from, but returned to normal limits till end of follow-up
		QoL	No significant differences between: ● Baseline: 68±13 (n=8) ● 2-month: 61±22 (n=5)
		Median pain	● Baseline: 0 (IQR: 1 to 10) (n=8) ● 24-hour & 1-week: 30 (IQR: 0 to 40) (n=7)
AbbreviationsCI, confidence interval; GGT, gamma-glutamyl transferase; INR, international normalised ratio; IQR, interquartile range; LTP, local tumour progression; QoL, quality of life; NR, not reported			

Limitations of evidence

Current evidence is limited by the small number of studies with small sample sizes, relatively short follow-up periods, and a lack of comparison to other ablation or SOC therapies. Furthermore, applicability of the results to the local population is questionable given that there was no Asian representation in either trial, with 100% (n=8) of patients in THERESA and 96% (n=47) in HOPE4LIVER being Caucasian.[21-23] This absence of data is particularly significant, as Asian populations have been reported to exhibit differences in clinical characteristics such as tumour differentiation and vascular invasion, compared to other ethnicities.[25]

Cost-effectiveness

No economic analysis was identified for Edison.

Ongoing trial(s)

A scan of ClinicalTrials.gov (as of March 2025) identified three ongoing manufacturer-sponsored trials (Table 5). The largest study (NCT06486454) in patients with liver tumours (n=5,000) will be completed in 2031. However, as it is a single-arm study with outcomes assessed at only 36 hours after Edison administration, it is unlikely to address the key evidence gap of comparative evidence between Edison with other SOC therapies, including ablation technique. Two other trials explore the use of Edison in renal and pancreatic tumours.

HOPE4LIVER is also expected to provide 5 years of follow-up data.[27]

Table 5: Ongoing trials for the use of Edison

Study (Trial ID)	Population & estimated enrolment	Brief description	Estimated study completion date	Remarks
Real-world Evaluation of the HistoSonics Edison System for Treatment of Liver Tumours Across Multidisciplinary Users (BOOMBOX: Master Study) NCT06486454	Adults aged ≥22 years with diagnosis of primary or metastatic or benign liver tumours (n=5,000)	Prospective, observational, single arm study aiming to understand how different patient characteristics and procedural characteristics may affect histotripsy success at 36 hours post-histotripsy.	November 2031	Sponsored by the manufacturer. Recruiting currently
The HistoSonics Edison™ System for Treatment of Primary Solid Renal Tumours Using Histotripsy (#HOPE4KIDNEY) NCT05820087	Adults aged ≥22 years with diagnosis of only one non-metastatic solid renal mass ≤3cm (n=68)	Prospective, single-arm, interventional, open-label study aiming to assess efficacy of histotripsy on renal tumours	May 2025	Sponsored by the manufacturer. Recruiting currently
The HistoSonics Edison™ System for Treatment of Pancreatic Adenocarcinoma Using Histotripsy (GANNON) NCT06282809	Adults aged ≥18 years diagnosed with unresectable pancreatic adenocarcinoma, locally advanced (Stage 3) or oligometastatic disease (Stage 4) (n=50)	Prospective, single-arm, interventional, open-label study aiming to assess feasibility of histotripsy on pancreatic adenocarcinomas	January 2026	Sponsored by the manufacturer. Recruiting currently

Furthermore, an efficacy trial of Edison in the local population, conducted by two of Singapore's public cancer centres, National Cancer Centre Singapore (NCCS) and National University Cancer Institute (NCIS), will commence in the second half of 2025. The trial population will be 40 patients with liver tumours not responsive or suitable for current treatments, who would either have (1) late-stage liver cancer or (2) secondary liver cancer and are using Edison as an adjunct. The tumours will follow the current ablation criteria (3 or fewer tumours of ≤3cm). This local trial will evaluate Edison's local safety and efficacy profile, possibly bridging key gaps in knowledge on the use of Edison in Asians. The trial also aims to assess if Edison can stimulate the immune system to attack non-targeted tumours. This trial will be extended to include kidney and pancreatic cancers.

Summary

The overall evidence base comprised two small (n=55, total) single-arm studies with a follow-up of up to one year. Overall, six SAEs among 47 patients (12.8%) were assessed as Edison-related, with both trials concluding a favourable safety profile for the procedure. OS at one year for all patients was 58.6%, 73.3% for patients with HCC and 48.6% for patients with secondary liver cancer. At one-year follow-up, freedom from LTP was 63.4% based on primary assessment. At tumour-level, Edison achieved an overall 96% technical success rate for both primary and secondary liver tumours.

A key limitation is the lack of comparative evidence of the Edison to SOC ablative techniques. Beyond study design, the applicability of these findings remains uncertain. For example, the trials did not include any Asian populations, who may exhibit different characteristics such as tumour differentiation and vascular invasion compared to other populations.

VII. Estimated Costs

The capital cost of Edison was not identified, but local media have reported that two philanthropic organisations have committed SGD$12M to bring Edison trials to two sites locally.[26] This funding may cover both capital costs for Edison and other trial-related costs; if capital costs were a substantial portion, a single Edison system may cost SGD$2.7M to SGD$4.0M.

In the USA, the typical histotripsy procedural cost* using Edison ranges from USD$9,394 (SGD$12,779) at ambulatory surgical centres to USD$17,500 (SGD$23,805) at hospital outpatient departments.[19] Although not explicitly stated, the costs for Edison are likely to reflect per per-session costs. Depending on the severity of the patient's condition, multiple tumours can be treated in a single session.[26, 27] According to a local clinician, consumables alone cost approximately USD$6,000 (SGD$7,948) per use (Personal Communication: Senior Consultant from NCCS, June 2025). Edison charges appear to be approximately 2.7 times the cost of thermal ablation (percutaneous radiofrequency) for one or more liver tumour in the US, with Medicare reporting total costs ranging from USD$3,562 (SGD$4,845) to USD$6,536 (SGD$8,891) in the ambulatory surgical centres and hospital outpatient departments respectively.[28] In Singapore, based on the Table of Surgical Procedures, current ablation

procedure charges for patients in subsidised B2 and C wards vary between SGD$2,556 to SGD$3,946 (Table 6).[29] Based on the prices in US, the procedures could be up to three to nine times more expensive than other local ablative procedures in Singapore.

Table 6: Estimated cost of ablation therapy for liver tumours in public hospitals in Singapore

Estimated cost for TOSP Code SF706L- Liver, Tumour, Imaging Guided Percutaneous Local Ablation, Simple (Radiofrequency, Cryotherapy, Microwave, Laser, Alcohol, Etc)	
Ward type	Typical bill range
B2	SGD$2,665 to SGD$3,946
C	SGD$2,556 to SGD$3,433
Abbreviations: TOSP, Table of Surgical Procedures	

VIII. Implementation Considerations

Certain implementation issues might be pertinent to this technology, including the need for capital investment to purchase potentially expensive equipment. One clinician, drawing on experience from US and Hong Kong centres, reported that the practitioner learning curve for using Edison may be shorter than for conventional treatments such as ablation, radioembolisation, and surgery (Personal Communication: Senior Consultant from NCCS, June 2025). Authors of the HOPE4LIVER studynoted that technique efficacy could be improved with procedural experience, particularly in targeting ablation sites.

IX. Concurrent Developments

No other mechanical tumour ablation methods were identified for patients with liver tumours.

X. Additional Information

Based on both trials, the median or mean treatment time with Edison can range between 25 minutes to 34 minutes, per tumour.

Local clinicians opined that annually there would be 30 to 50 patients not suitable for thermal ablation who would be eligible for Edison. (Personal Communication: Senior Consultant from NCCS, March, May and June 2025). Long-term oncological data for Edison are anticipated to become available within 2 to 3 years, and it is already replacing conventional ablative procedures at some US centres. (Personal Communication: Senior Consultant from NCCS, June 2025). However, local clinicians also indicated that they would classify Edison as an alternative treatment option rather than SOC given concerns of SAE rates, cost and availability of other non-invasive techniques.

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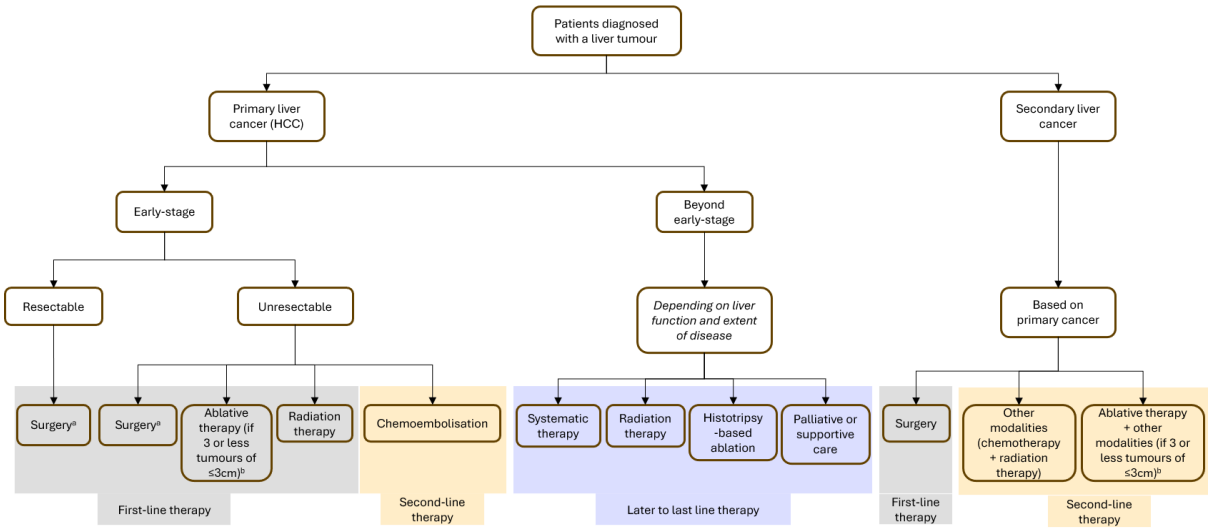
APPENDIX

Appendix A: Treatment pathway



Notes:

a. Surgery refers to either resective surgery or liver transplantation.

b. Includes ablative therapy only, histotripsy only or both.

Abbreviation: HCC, hepatocellular carcinoma

Appendix B: Summary of study designs for three included publications

Study ID, study design	Follow-up	Population (n)
Ziemlewicz (2025)[a] Mendiratta-Lala (2024)[a] HOPE4LIVER[26,27] Prospective, non-randomised, single-arm, multi-centre pivotal trial	1 year	Patients (≥18 years) with ≤3 unresectable end-stage multifocal liver tumours (≤3 cm in diameter) that has not responded to/intolerant of/relapsed from available therapies including surgery, locoregional therapies[b], chemotherapy or immunotherapy (n=47; 52 tumours)
Vidal-Jove (2022) THERESA[25] Prospective, non-randomised, single-arm, multi-centre feasibility trial	2 months	Patients (≥18 years) with ≤3 unresectable end-stage multifocal liver tumours (≤3 cm in diameter) not suitable for other therapies including surgery or locoregional therapies[b] (n=8; 11 tumours)
Notes: a. Mendiratta-Lala (2024) reported on outcomes up to 30 days (n=44; 49 tumours) while Ziemlewicz (2025) reported on outcomes up to a year of follow-up (n=49, 52 tumours). The difference in patient numbers between the two publications appeared to be due to additional enrolment after the initial 44 patients. b. Locoregional therapies entail other ablation techniques, chemoembolisation or radioembolisation.		

Appendix C: Detailed procedure-related outcomes

Technical success rate

Across both studies, an overall technical success rate of 96% (53/55 tumours) was achieved by histotripsy, with 100% reported at 24 hours in THERESA and 95% at ≤36 hours in HOPE4LIVER (as reported by Mendiratta-Lala,2024). In HOPE4LIVER, the performance goal of 70% treatment success rate was also met. The two tumours that did not achieve technical success in HOPE4LIVER were not fully covered by the histotripsy treatment zone due to mistargeting. No further details on these patients were provided in the publications.

At the patient-level, 95% (n=40; 95% CI: 84% to 99%) of individuals in HOPE4LIVER had treatment success.

Technique efficacy

HOPE4LIVER reported technique efficacy at the periphery of the treatment zone of 79.2%, 80.0% and 91.7% among 48 tumours at one month, 35 tumours at six months and 24 tumours at one year, respectively. This contrasted with post-hoc assessment at the same time points (as reported in Table 4), with the authors indicating modest agreement between the two assessment readings (70.8% to 84.0%). The authors also reported that the disagreement in assessing this parameter occurred in cases where the primary assessment reported the presence of enhancement, but post-hoc identified no tumour.

Among the original 52 tumours at 30 days, the exclusion criteria of four lesions were not clearly stated in the study analysis, but reporting by Mendiratta-Lala (2024) of early 30-day results indicates that some lesions were excluded due to lack of or inadequate imaging results. The authors noted that technique efficacy could be improved with procedural experience.