Interventional procedure overview of image-guided percutaneous laser ablation of primary and secondary liver tumours

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Table 1 Abbreviations

Abbreviation	Definition
CI	Confidence interval
CRC	Colorectal cancer
HCC	Hepatocellular carcinoma
INR	International normalised ratio
Nd:YAG	neodyminum-doped: yttrium-aluminum-garnet
PEI	Percutaneous ethanol injection
RECIST	Response evaluation criteria in solid tumors
RFA	Radiofrequency ablation
SD	Standard deviation
SIR	Society of Interventional Radiology
TACE	Transcatheter arterial chemoembolisation

Indications and current treatment

The most common type of primary liver cancer is hepatocellular carcinoma (HCC). Secondary cancer in the liver can arise from any primary site, but it most commonly spreads from cancers of the bowel, breast, lung, pancreas, stomach, ovary, and neuroendocrine tumours (Source: Cancer Research UK website).

Treatment for primary liver cancer depends on several factors, including the exact location and stage of the cancer, the patient's liver function and any patient-related comorbidities. The treatment options include:

- surgical excision
- chemotherapy (conventional or hepatic artery infusion)
- transarterial chemoembolisation (TACE)
- selective internal radiation therapy
- percutaneous ethanol injection
- local ablation techniques such as cryotherapy, radiofrequency, and microwave ablation.

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A liver transplant (with curative intent) may be appropriate for some people.

Treatment for secondary liver cancer depends on the site of the primary cancer, which parts of the liver are affected and whether the cancer has metastasised further. The most common treatment is chemotherapy, but other treatments include surgery, hormonal therapies, targeted therapies, ablation and embolisation treatments.

What the procedure involves

Image-guided percutaneous laser ablation is done under general anaesthesia or local anaesthesia with sedation. Depending on the size of the tumour, 1 or more (usually up to 4) optical fibres are percutaneously inserted into the liver using a small introducer needle. The fibre distance and energy delivery per fibre are adjusted to shape the area to be ablated. The fibres deliver laser energy for several minutes to heat the tissue until it is destroyed with a sufficient safety margin. The fibres work simultaneously to amplify the ablation volume. Image guidance is used to check the positioning of the fibres, monitor the treatment, and verify the effective ablation area. The aim is to destroy the tumour.

Unmet need

People with early-stage liver cancer usually have surgery to remove the tumour. People with more advanced liver cancer are more likely to be offered chemotherapy. Other treatments include chemoembolisation, radioembolisation and targeted therapy drugs. There are several types of local ablation techniques, which can be used to treat small tumours. Image-guided percutaneous laser ablation may be an option when surgery is unsuitable. It can be done without a general anaesthetic and uses thinner needles than microwave ablation and RFA. Its localised action means it can be used for tumours that are close to structures at risk. It may also be a bridging option for people waiting for a liver transplant.

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Outcome measures

The main efficacy outcomes included complete tumour ablation, local tumour progression, local or distant recurrence, overall survival, and disease-free survival. Safety outcomes included mortality, bleeding, infection, and damage to surrounding tissues. The efficacy outcome measures used are detailed in the following paragraphs.

The response evaluation criteria in solid tumours (RECIST) are used for measuring tumour response using X-ray, CT, and MRI. There are 4 categories:

- complete response: disappearance of all target lesions
- partial response: 30% decrease in the sum of the longest diameter of target lesions
- progressive disease: 20% increase in the sum of the longest diameter of target lesions
- stable disease: small changes that do not meet the above criteria.

In modified RECIST (mRECIST) criteria, the response of target lesions is evaluated from the percentage change in the sum of the diameters of the viable portions (portions enhanced during the arterial phase).

The World Health Organization criteria for tumour response assessment are:

- complete response: disappearance of target tumour
- partial response: more than 50% reduction in tumour size
- no response or stable disease: less than 50% reduction in tumour size and less than 25% increase in tumour size
- progressive disease: more than 25% increase in tumour size.

Objective response is the aggregation of complete response and partial response results.

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The Child-Pugh scoring system (also known as the Child-Pugh-Turcotte score) was designed to predict mortality in people with cirrhosis. The score is determined by scoring 5 clinical measures of liver disease and the possibility of eventual liver failure. A score of 1, 2, or 3 is given to each measure, with 3 being the most severe. There are 3 categories according to the final score: A is the least severe, B indicates moderately severe liver disease and C is the most severe.

Evidence summary

Population and studies description

This interventional procedures overview is based on about 3,000 people from 4 randomised controlled trials (Di Costanzo 2015, Orlacchio 2014, Ferrari 2007, Zou 2017), 1 quasi-randomised controlled trial (Ferrari 2006), 1 retrospective non-randomised comparative study (Adwan 2022), 1 case-control study (Morisco 2018), 5 cohort studies (Pacella 2009, Francica 2012, Vogl 2004, Vogl 2014, Vogl 2013) and 1 case report (Helmberger 2002). Of these 3,000 people, about 2,500 had the procedure. There is likely to be some population overlap between the studies. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 13 studies as the key evidence in table 2 and table 3, and lists 40 other relevant studies in table 5.

Most of the studies were from Italy or Germany, with 1 randomised controlled trial from China. All 4 randomised controlled trials included people with HCC and compared laser ablation with RFA. The non-randomised studies included people with HCC and metastatic liver tumours, and comparators included microwave ablation, TACE, and percutaneous ethanol injection. Most of the studies included people with up to 5 small tumours (maximum diameters ranged from 3 cm to 5 cm) and with Child-Pugh class A or B cirrhosis. An exception was the case-control study by Morisco (2018), which compared laser ablation with TACE in a

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population with a solitary HCC 40 mm or larger. The retrospective cohort study by Francica (2012) aimed to compare outcomes of laser ablation in HCC tumours at high-risk locations compared with those at standard risk locations. Several studies reported follow up beyond 5 years.

In the study by Ferrari (2006), which has been described as quasi-randomised, computer randomisation was used for most treatments but there were some exceptions. Tumours with a difficult percutaneous approach were treated with TACE, and an alternative treatment to laser ablation was used for superficial lesions next to large vessels and cholecysts.

The cohort study by Vogl (2014) specifically stated that 57% (n=337) of people had treatment with a curative intention aiming to eliminate disease from the liver and 43% (n=257) had treatment with a palliative intention.

Table 2 presents study details.

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Figure 1 Flow chart of study selection

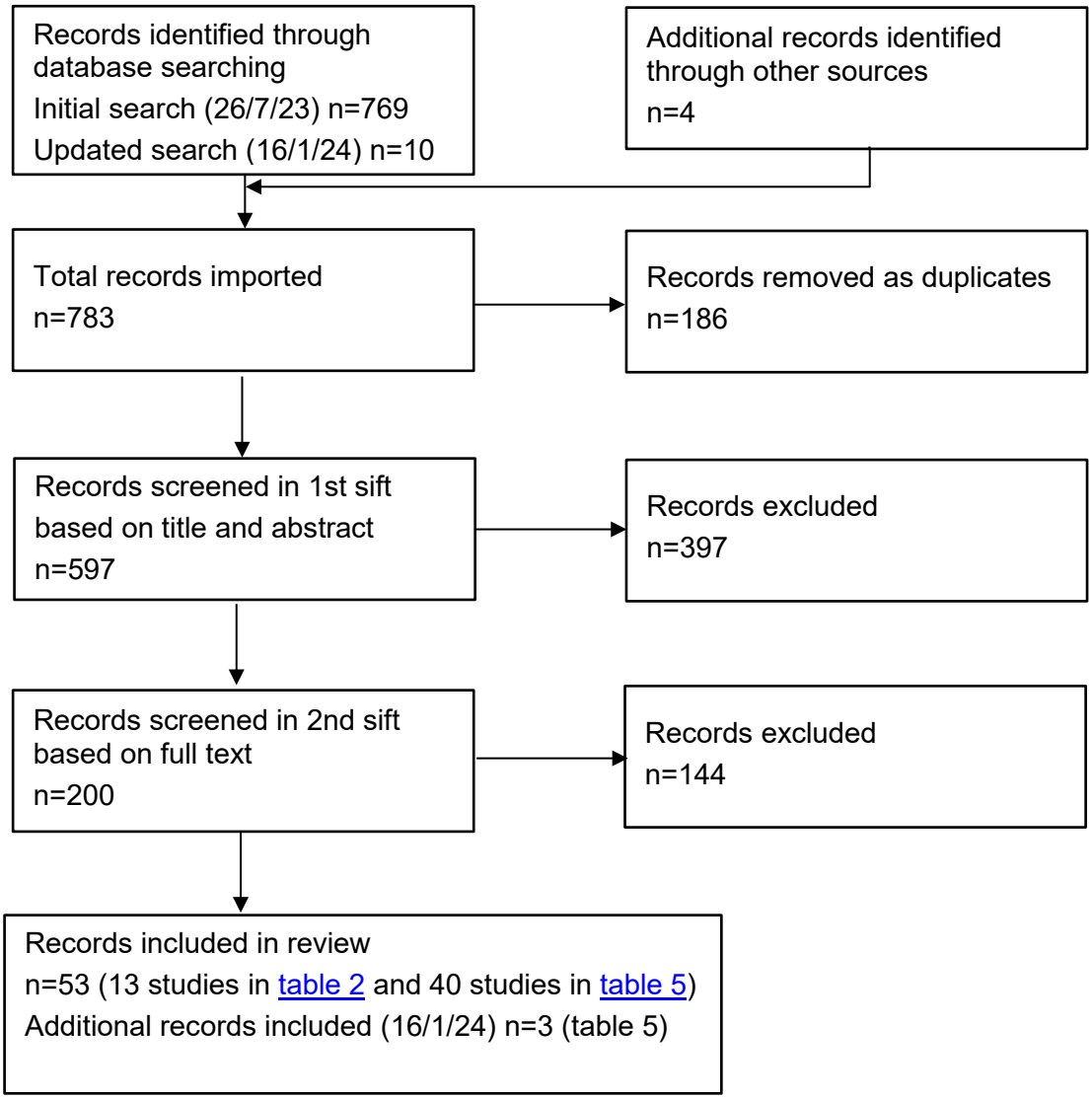

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Table 2 Study details

Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
1	Di Costanzo G, 2015 Italy	n=140 (157 tumours) 100:40 HCC	Median 70 (range 36 to 84)	Non-inferiority randomised controlled trial (single centre) January 2009 to September 2012	Patients with cirrhosis and unresectable HCC or who refused surgery; solitary HCC 5 cm or smaller, or 1 to 3 tumours each 3 cm or smaller in diameter; Child-Pugh class A or B; platelet count above 40,000 per microlitre and INR below 2.0; no previous HCC treatment.	• Laser ablation, with Echolaser (Elesta, Italy) using 1 to 4 fibres (n=70 patients, 80 tumours) • RFA, using a single electrode (n=70 patients, 77 tumours) All procedures were done under ultrasound guidance.	Up to 59 months
2	Orlacchio A, 2014 Italy	n=30 (30 tumours) 21:9 HCC	Mean 72.4 (range 52 to 78)	Randomised controlled trial (single centre) 2009 to 2011	Patients with cirrhosis and single HCC tumour with maximum diameter 40 mm; Child-Pugh class A or B.	• Laser ablation, with Echolaser XVG system, using 2 to 4 fibres (n=15) • RFA, using a single expandable electrode (n=15)	Up to 12 months

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
						All procedures were done under combined ultrasound and CT guidance. Lesions that showed a partial response at 30 days were retreated with the same technique.	
3	Ferrari F, 2007 Italy	n=81 (95 tumours) 56: 25 HCC	Mean 69.3 (range 51 to 82)	Randomised controlled trial January 2003 to December 2005	Patients with cirrhosis and a single HCC tumour with a maximum diameter of 40 mm or with a maximum of 3 HCC tumours each measuring no more than 30 mm in diameter and who had not had previous treatment for HCC; performance status between 0 and 2, cardiac and pulmonary function between 0 and 2	• Laser ablation using a Nd-YAG laser (DEKA-M.E.L.A, Italy); n=41, 66 treatment sessions. Up to 4 fibres were positioned inside the tumour. • RFA, using single or cluster closed tip, internally cooled electrodes, n=40. Additional treatment sessions were	Up to 60 months

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
					(World Health Organization) and age ranging from 19 to 82 years. Prothrombin time less than 40% (INR greater than 1.99) or platelet count less than 40,000/ml caused treatment to be delayed until adequate values had been restored in 22 patients. Patients with evidence of vascular tumour extension, invasion of the main bile duct or extrahepatic metastases on CT were excluded.	offered if ablation was incomplete after the initial session. Both procedures were done under ultrasound guidance.	
4	Zou D, 2017 China	n=74 (69 had a single tumour) 58: 16 HCC	Range 37 to 76	Randomised controlled trial October 2013 to March 2016	HCC and increased alphafetoprotein; diameter of single tumour foci, or the sum of diameters of 2 adjacent tumour foci was less than 3 cm, without	• Laser ablation using EchoLaser X4 system (ESAOTE S.P.A, Italy); n=35	3 months

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
					infiltration of blood vessels and bile ducts, abdominal lymph nodes or distant transfer; patients chose laser ablation or RFA as the first treatment and had no previous treatment history; Child-Pugh of liver function was A or B level.	1 to 3 needles were placed under ultrasound guidance and the procedure was monitored continuously with real-time ultrasound guidance. • RFA using 1 or 2 electrode needles; n=39	
5	Ferrari F, 2006 Italy	n=131 (148 tumours) 94:37 HCC 1 patient was waiting for a liver transplant.	Mean 67.8 (range 44 to 82)	Quasi-randomised controlled trial (mostly randomised with some exceptions) November 1998 to March 2004	Single HCC tumour with maximum diameter of 40 mm or multiple tumours (maximum 3) each with a diameter of 30 mm or smaller; Child-Pugh class A or B, Patient Performance Status of 0 to 2, cardiac and lung function of 0 to 2 (World Health Organisation) and	• Laser ablation under ultrasound guidance, with a multifrequency convex probe with a lateral needle guide system (n=46, 50 tumours) • TACE (n=18, 20 tumours) • PEI under ultrasound	Up to 84 months

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
					age between 18 and 80.	guidance (n=34, 38 tumours) • Combined TACE and PEI (n=33, 40 tumours)	
6	Adwan H, 2022 Germany	n=303 (510 tumours) 239:64 HCC	Mean 67.5 (laser ablation), 66 (microwave ablation)	Retrospective non-randomised comparative study	Early or intermediate tumour stage with HCC maximum axial diameter 5 cm, maximum 5 tumours, and adequate coagulation (INR 1.5 or less, or thrombocytes 50,000 per microlitre or more).	• Laser ablation under MRI guidance (n=53, 75 tumours, 76 sessions) Nd-YAG laser, Avanto, Siemens, using SOMATEX laser application kit. Puncture of the tumour and insertion of the laser applicator was done under CT guidance. • Microwave ablation under CT guidance (n=250, 435 tumours 445 sessions).	Mean 35.7 months (laser), 31.5 months (microwave)

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
						CT fluoroscopic scans were repeatedly done to monitor ablation.	
7	Pacella C, 2009 Italy	n=432 (548 tumours) 278:154 HCC 52 people were potentially eligible for liver transplant.	Mean 67.7	Retrospective (from 1994 to January 2004) and prospective (from February 2004 onwards) multicentre cohort study 1994 to 2005	Cirrhosis and early HCC (single tumour 4 cm or less or 1 to 3 tumours, each 3 cm or less in diameter) and surgery was not an option. Exclusion criteria included extrahepatic metastases; local, segmental, or lobar portal venous thrombosis; uncontrolled liver disease decompensation; severe clotting impairment; renal failure; or Child-Turcotte-Pugh class C cirrhosis.	Laser ablation using a Nd:YAG, laser (DEKA-M.E.L.A., Italy) and an optical beam-splitting device (SMART 1064 HCC; DEKA-M.E.L.A.) with 4 separate fibres. One to 4 needles were placed under ultrasound guidance and the procedure was monitored continuously with real-time ultrasound guidance.	Median 36 months (reverse Kaplan-Meier estimate), range 1 to 109 months.

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
8	Morisco F, 2018 Italy	n=82 (82 tumours) 58: 24 HCC	Median 72 (range 49 to 88)	Retrospective case-control study (historical control group) January 2009 to December 2012	Unresectable HCC or refusal of surgery; solitary HCC 40 mm or larger; Barcelona Clinic Liver Cancer stage A or B; Child–Pugh class A or B cirrhosis; platelet count more than 40,000 per microlitre and INR less than 2.0; no history of previous HCC treatment. Exclusion criteria included: history of encephalopathy or refractory ascites; vascular invasion or extrahepatic metastasis; severe comorbidities reducing life expectancy.	• Laser ablation using 4 or 8 fibres (n=41); 25 patients had 2 treatment sessions and 7 had 3 sessions. • TACE (n=41); all patients had at least 2 treatment sessions	Mean 37.4 months
9	Francica G, 2012 Italy	n=164 (182 tumours) 90:74 HCC	Mean 68.6 (range 42 to 84)	Retrospective cohort study January 1996 to June 2008	Single HCC tumour 4 cm or less in diameter or multiple tumours (no more	Laser ablation with Nd:YAG laser (279 sessions)	Median 81 months (range 6 to 144)

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
		n=106 with tumour at high-risk location, 58 at standard risk location			than 3) each 3 cm or less in diameter irrespective of location; Child-Pugh class A or B cirrhosis; lack of extrahepatic metastases and lack of local, segmental, or lobar portal venous thrombosis; and follow up of at least 6 months. A high-risk location was defined as less than 5 mm from large vessels or vital structures.	2, 3 or 4 optic fibres advanced in needles were positioned under ultrasound guidance and the procedure was monitored continuously with real-time ultrasound guidance.	
10	Vogl T, 2004 Germany	n=603 (1,801 tumours) 432: 171 CRC liver metastases	Mean 61.2 (range 31 to 89)	Cohort study June 1993 to February 2002 173 patients had already had treatment as part of earlier clinical trials.	Recurrent liver metastases after partial liver resection, metastases in both liver lobes, locally nonresectable tumours, general contraindications for surgery or refusal to	Laser ablation using non-irrigated laser application system with limited power settings (n=56 [group 1]), or internally cooled laser application system (n=117 already treated [group 2] and n=430	Up to 7.6 years

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
					have surgical resection. Exclusion criteria included more than 5 tumours larger than 5 cm in greatest diameter or known extrahepatic tumour spread.	prospectively treated [group 3]); 1,555 treatment sessions. Group 3 had more aggressive treatment than group 2, with more applicators per tumour. The needles were placed under CT guidance and MRI was used to monitor the procedure.	
11	Vogl T, 2014 Germany	n=594 (1,545 tumours) 406: 188 CRC liver metastases	Mean 61.2 (range 25 to 87)	Single centre cohort study January 1999 to December 2010	Recurrent liver metastases after partial liver resection, metastases in both liver lobes, locally nonresectable tumours, general contraindications for surgery or refusal to have surgical resection, maximum of 5 tumours, tumour	MRI-guided laser ablation using a Nd:YAG laser (Dornier MedTech, Germany); mean number of sessions per patient=2.26 (range 1 to 7). Needle puncture was done with CT guidance. For large tumours, multiple	Mean 22.5 months (range 0 to 121)

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
					size 5 cm or less in diameter.	applicators were used.	
12	Vogl T, 2013 Germany	n=401 (809 tumours) 58: 343 Liver metastases from primary sites other than CRC (mainly breast)	Mean 57.3 (range 26 to 86)	Cohort study January 2000 to January 2011	Maximum of 5 tumours, metastases of 5 cm or less in diameter, recurrent liver metastases after partial liver resection, metastases in both liver lobes, and general contraindications for surgery. Exclusion criteria: CRC liver metastases, poor general condition (Karnofsky status less than 70%).	MRI-guided laser ablation using a Nd:YAG laser (Dornier MedTech, Germany); 736 treatment sessions. Needle puncture was done with CT guidance. For large tumours, multiple applicators were used. The mean and median number of applicators per tumour was 2 (range 1 to 5).	Survival up to 5 years was reported
13	Helmberger T, 2002	n=1 male Liver metastases (history of renal cell carcinoma)	57	Case report	The patient had 5 liver metastases (maximum diameter 5 cm), in both liver lobes and located in central hepatic areas, surgical	Laser ablation using a Nd:YAG laser (Dornier MedTech, Germany). An introducer sheath was placed into each tumour under CT guidance, to	Perioperative

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Study no.	First author, date country	Patients (men: women)	Age (years)	Study design	Inclusion criteria	Intervention	Follow up
					resection was not considered.	direct the laser fibre into the tumour. The position of the laser fibre was controlled by CT fluoroscopy for each placement during and at the end of the ablation process.	

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Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Di Costanzo, 2015	**Complete tumour ablation** (absence of any contrast enhancement within or at the periphery of the HCC nodule, assessed by CT or MRI): • Laser ablation=95.7% (67 out of 70; 95% CI 88.1 to 98.5) of patients and 96.3% (77 out of 80; 95% CI 89.6 to 98.7) of nodules • RFA=97.1% (68 out of 70; 95% CI 90.2 to 99.2) of patients and 97.4% (75 out of 77; 95% CI 91.0 to 99.3) of nodules Overall treatment sessions to obtain complete tumour ablation: • Laser ablation=82 • RFA=72, p=0.058 4 people had liver transplant (3 laser ablation and 1 RFA). Evaluation of explanted livers showed complete necrosis of treated nodules. **Local tumour progression:** • Laser ablation=22.9% (16 out of 70) • RFA=25.7% (18 out of 70), p=0.956 **Mean time to local progression (months):** • Laser ablation=45.9 (95% CI 40.6 to 51.2)	There were no treatment-related deaths. **Moderate pain (SIR Class A):** • Laser ablation=33% • RFA=36% **Self-limiting fever lasting less than 15 days (SIR Class A):** • Laser ablation=35% • RFA=32% **Subcutaneous tumour seeding (SIR Class C):** • Laser ablation=1.4% (1 out of 70) • RFA=1.4% (1 out of 70) In both cases, it was surgically removed.

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First author, date	Efficacy outcomes	Safety outcomes
	• RFA=39.6 (95% CI 34.1 to 45.0), p=0.376 *Note: There are some discrepancies in the reported results and the numbers above were taken from Table 2 of the publication.* **Mean overall survival (months):** • Laser ablation=42.2 (95% CI 37.2 to 47.2) • RFA=42.8 (95% CI 38.3 to 47.3), p=0.346 **1-year survival probability:** • Laser ablation=94% • RFA=94% **3-year survival probability:** • Laser ablation=80% • RFA=89% **Mortality during study period:** • Laser ablation=34.3% (7 cancer progression, 10 liver failure, 2 cancer progression and liver failure, 2 variceal bleeding, 3 other causes) • RFA=26% (6 cancer progression, 3 liver failure, 5 cancer progression and liver failure, 1 variceal bleeding, 3 other causes)	

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First author, date	Efficacy outcomes	Safety outcomes
Orlacchio, 2014	**Technical success**=100% **Complete response at 30 days** (assessed by CT, evaluated according to the mRECIST criteria): • Laser ablation=66.7% (10 out of 15) • RFA=86.7% (13 out of 15) **Complete response after second treatment session:** • Laser ablation=86.7% (13 out of 15) • RFA=93.3% (14 out of 15), p=not significant Number of treatment sessions per tumour needed to obtain complete ablation: • Laser ablation=1.38 • RFA=1.21 The 3 tumours that did not show a complete response were treated with chemoembolisation. No patients died during the first 12 months of follow up. **Cumulative rates of freedom from local disease progression:** • 3 months: laser ablation=85%, RFA=92% • 6 months: laser ablation=62%, RFA=86%	There were no major complications and no procedure-related deaths. **Minor complications** Asymptomatic perihepatic fluid collection: • Laser ablation, n=1 • RFA, n=3 Subcapsular haematoma: • Laser ablation, n=0 • RFA, n=1 Asymptomatic pleural effusion: • Laser ablation, n=1 • RFA, n=4 **Side effects** Vasovagal reaction: • Laser ablation, n=1 • RFA, n=2 Postablation syndrome: • Laser ablation, n=1

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First author, date	Efficacy outcomes	Safety outcomes
	• 12 months: laser ablation=54%, RFA=86%, p=0.083 The cumulative rates of freedom from local disease progression at 12 months were higher for patients with tumours 20 mm or less in diameter. For tumours 21 mm or more in diameter, there was a higher rate of recurrence in the laser ablation group compared with RFA (p=0.0081).	• RFA, n=12
Ferrari, 2007	**Complete tumour ablation** (assessed by CT, defined as no contrast uptake seen in the ablation zone during the early arterial phase): • Laser ablation=78% (35 out of 45); 10 additional sessions • RFA=94% (47 out of 50); 3 additional sessions **Disease recurrence (local tumour progression or new HCC tumour):** • Laser ablation=26.8% (11 out of 41) • RFA=22.5% (9 out of 40) Of the 15 cases of local tumour progression, 60% were diagnosed at 12 to 24 months after treatment and the remaining 40% within the first 12 months; no local tumour progression was observed later than 24 months after treatment. **Disease-free interval:** • Laser ablation=15.45 months (SD 7.99)	No deaths or major or minor complications occurred during the procedures, and no cases of neoplastic seeding have been observed to date.

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First author, date	Efficacy outcomes	Safety outcomes
	• RFA=17.78 months (SD 8.52) **Cumulative survival rates** • 12 months: Laser=88.6%, RFA=92.2% • 24 months: Laser=70.4%, RFA=75.0% • 36 months: Laser=56.6%, RFA=61.3% • 48 months: Laser=40.2%, RFA=54.6% • 60 months: Laser=22.9%, RFA=40.9% (at 55 months) p=0.3299 Univariate analysis of survival revealed statistically significant differences between the Child-Pugh A and B groups (p<0.0001), between HCC nodules measuring 25 mm or less and more than 25 mm (p=0.0001) and between patients with a single tumour and with 2 tumours (p=0.0484). The Cox model showed that Child-Pugh class was the most important prognostic survival factor.	
Zou, 2017	**Complete response at 3 months** (according to mRECIST criteria): • Laser ablation=88.6% (31 out of 35) • RFA=92.3% (36 out of 39), p=0.583 **Alphafetoprotein levels 3 months after treatment (µg/l):** • Laser ablation=770.36 (baseline 973.67, p<0.001) • RFA=781.52 (baseline 983.78, p<0.001) The difference between the groups was not statistically significant.	**Adverse reactions** **Fever** • Laser=11.4% (4 out of 35) • RFA=12.8% (5 out of 39), p=0.855 **Nausea** • Laser=48.6% (17 out of 35) • RFA=48.7% (19 out of 39), p=0.990

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First author, date	Efficacy outcomes	Safety outcomes
	Carcinoembryonic antigen levels 3 months after treatment (U/l): • Laser ablation=182.68 (baseline 289.81, p<0.001) • RFA=180.65 (baseline 282.10, p<0.001) The difference between the groups was not statistically significant. **Proportion of patients who reported great or general satisfaction 3 days after treatment:** • Laser ablation=94.3% (33 out of 35) • RFA=69.2% (27 out of 39), p=0.022	**Vomiting** • Laser=28.6% (10 out of 35) • RFA=30.8% (12 out of 39), p=0.836 **Diarrhoea** • Laser=2.9% (1 out of 35) • RFA=2.6% (1 out of 39), p=0.522 **Abdominal pain** • Laser=74.3% (26 out of 35) • RFA=74.4% (29 out of 39), p=0.994 **Skin rash** • Laser=2.9% (1 out of 35) • RFA=7.7% (3 out of 39), p=0.687
Ferrari, 2006	**Complete necrosis after first treatment session** (assessed by CT, defined as no contrast impregnation in the tumour site in the early arterial phase (25 to 30 seconds after contrast injection): • Laser ablation=92% (46 out of 50) of tumours • TACE=70% (14 out of 20) of tumours • PEI=74% (28 out of 38) of tumours • Combined TACE and PEI=80% (32 out of 40) of tumours Further treatment sessions were offered after partial responses.	There were no deaths or major complications during the procedures. There were 2 minor complications after TACE (cholecystitis). Side effects of TACE included nausea, mild pain in the right hypochondrium and fever in the hours immediately following

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First author, date	Efficacy outcomes	Safety outcomes
	Mean number of treatments per tumour: • Laser ablation=1.2, TACE=1.3, PEI=2.8, Combined TACE and PEI=5.3 **Recurrence-free interval (months):** • Laser ablation=13.7 (8.7) • TACE=18.0 (SD 5.5) • PEI=27.0 (SD 13.5) • Combined TACE and PEI=13.9 (SD 8.9) • Total=15.7 (SD 9.4) **Disease-free interval (months):** • Laser ablation=14.3 (SD 8.0) • TACE=18.0 (SD 5.5) • PEI=29.8 (SD 13.4) • Combined TACE and PEI=15.4 (SD 16.1) • Total=17.0 (SD 13.7) **Cumulative survival at 12, 36 and 60 months (%):** • Laser ablation=90.0, 53.3, 31.0 • TACE=66.7, 11.1, 0 • PEI=71.0, 29.4, 18.4	treatment. Severity of symptoms was directly proportional to the volume of the treated tumour. There were no cases of neoplastic cellular seeding in patients who had treatment with either PEI or laser ablation.

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First author, date	Efficacy outcomes	Safety outcomes
	• Combined TACE and PEI=90.8, 41.4, 19.3 • Total=81.9, 35.7, 20.8 The survival rate for Child–Pugh class A was statistically significantly higher (p<0.0001) than for Child–Pugh class B. Those who had laser ablation or combined therapy survived longer than those who had TACE (p=0.0001 and 0.0096, respectively). Laser ablation was associated with longer survival than PEI (p=0.0274).	

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First author, date	Efficacy outcomes	Safety outcomes
Adwan, 2022	**Mean diameter of ablation area (cm):** • Laser ablation=5.3 • Microwave ablation=4.4, p=0.0001 **Technical success:** • Laser ablation=100% (76 out of 76) • Microwave ablation=100% (445 out of 445) **Initial complete ablation** (assessed using contrast enhanced MRI): • Laser ablation=98.7% (74 out of 75) • Microwave ablation=97.7% (425 out of 435) **Local tumour progression** (defined as a new HCC tumour directly adjacent to the ablation area or an increase in the size of the ablation area at the follow up): • Laser ablation=3.8% (2 out of 53) • Microwave ablation=6.0% (15 out of 250) **Intrahepatic distant recurrence:** • Laser ablation=64.2% (34 out of 53) • Microwave ablation=46.0% (115 out of 250) **Overall survival at 1, 3 and 5 years from date of diagnosis:**	There were no procedure-related deaths in either group. **Overall complication rate:** • Laser ablation=7.9% (6 out of 76) • Microwave ablation=2.9% (13 out of 445), p=0.045 There was 1 major complication, which was in the microwave ablation group (haemorrhagic pleural effusion, treated with thoracic drainage). **Mild haemorrhage:** • Laser ablation=2.6% (2 out of 76) • Microwave ablation=1.4% (6 out of 445) **Pleural effusion:** • Laser ablation=5.3% (4 out of 76) • Microwave ablation=1.4% (6 out of 445)

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First author, date	Efficacy outcomes	Safety outcomes
	• Laser ablation=96.2%, 54.7%, 30.2% • Microwave ablation=94.3%, 65.4%, 49.1%, p=0.002 **Overall survival at 1, 3 and 5 years from ablation date:** • Laser ablation=85.0%, 37.7%, 17.0% • Microwave ablation=86.6%, 53.4%, 40.4%, p=0.001 **Disease-free survival at 1, 3 and 5 years from ablation date:** • Laser ablation=54.7%, 30.2%, 17.0% • Microwave ablation=45.9%, 30.6%, 24.8%, p=0.719 **Local tumour progression-free survival at 1, 3 and 5 years from ablation date:** • Laser ablation=96.2%, 96.2%, 96.2% • Microwave ablation=95.2%, 93.8%, 93.8%, p=not significant **Intrahepatic distant recurrence-free survival at 1, 3 and 5 years from ablation date:** • Laser ablation=64.2%, 49.0%, 39.6% • Microwave ablation=55.6%, 46.4%, 42.4%, p=not significant	
Pacella, 2009	**Initial complete response** (assessed by CT, according to modified World Health Organization criteria, classified as no areas of enhancement within or at the periphery of the ablation zone) =	**Complications** • Treatment-related death, n=1 (4 days after the procedure, the patient had acute liver

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First author, date	Efficacy outcomes	Safety outcomes
	78.2% (338 out of 432) of patients, 79.6% (436 out of 548) of tumours **Complete ablation by tumour size** • 2 cm or smaller=85.1% (183 out of 215) • Between 2.1 and 3.0 cm=81.8% (198 out of 242) • Between 3.1 and 4.0 cm=60.4% (55 out of 91) The probability of achieving a complete tumour ablation was statistically significantly greater in patients with a single tumour compared with patients with multiple tumours (p=0.015). **Survival** At the time of the analysis, 9 patients (2.1%) had had liver transplantations and 7 patients (1.6%) had been lost to follow up. 43.5% (188/432) of patients had died. Causes of death included HCC (n=88), extrahepatic metastases (n=11), and underlying cirrhosis and liver failure (n=56). **Median overall survival**=47 months (95% CI 41 to 53) • Child-Turcotte-Pugh class A=53 months (95% CI 44 to 62) • Child-Turcotte-Pugh class B=40 months (95% CI 33 to 47), p=0.088 **3-year cumulative survival**=61% **5-year cumulative survival**=34% Multivariate Cox analysis showed that the independent predictors of survival were serum albumin level greater than 3.5 g/dl	decompensation associated with severe respiratory failure; also reported in Francica et al., 2012) • Major complications needing specific treatment=1.6% (7 out of 432) • Minor complications=98.1% (424 out of 432; most commonly asymptomatic pleural effusion [n=265]) **Major complications within 24 hours of procedure** • Pancreatitis=0.2% (1 out of 432) • Intrahepatic haematoma=0.2% (1 out of 432) • Peritoneal bleeding=0.2% (1 out of 432) **Major complications within 30 days of procedure** • Transient decompensation of liver function (SIR class C)=0.5% (2 out of 432)

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First author, date	Efficacy outcomes	Safety outcomes
	(p=0.002), complete tumour ablation (p=0.001), and age less than 73 years (p=0.001). **Recurrence and disease-free survival** Tumour recurrence (local and distant)=20% (67 out of 338) Median time to recurrence=24 months (95% CI 20 to 28) Median disease-free survival time=26 months (95% CI 22 to 30)	• Transient decompensation of liver function (SIR class D)=0.5% (2 out of 432) • Acute liver decompensation (SIR class F)=0.2% (1 out of 432)
Morisco, 2018	**Complete response** (**according to the modified Response Evaluation Criteria in Solid Tumours):** • Laser ablation=63.4% (21 out of 41) • TACE=19.5% (8 out of 41), p<0.001 **Response rate in tumours with diameter between 51 and 60 mm:** • Laser ablation=75% • TACE=14.3%, p=0.013 **Disease recurrence in successfully patients:** • Laser ablation=19.2% (5 out of 26) • TACE=75% (6 out of 8), p<0.0001 **Mean time to recurrence:** • Laser ablation=42.2 months (95% CI 34.3 to 50.1) • TACE=26.8 months (95% CI 18.6 to 34.9), p=0004	No safety outcomes were reported.

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First author, date	Efficacy outcomes	Safety outcomes
	Mean disease-free survival: • Laser ablation=31.5 months (95% CI 24.1 to 38.8) • TACE=14.2 months (95% CI 9.7 to 18.7), p<0.0001 **Mean overall survival:** • Laser ablation=39.7 months (95% CI 33.1 to 46.4) • TACE=37.0 months (95% CI 30.7 to 43.3), p=0.725 **Overall survival probability rates:** • 1 year: laser ablation=90.2%, TACE=85.4% • 2 years: laser ablation=65.5%, TACE=65.9% • 3 years: laser ablation=55.4%, TACE=48.8% During the study period 50 patients died; 24 patients in the laser ablation group (12 HCC progression, 6 liver failure and 6 unknown causes) and 26 in the TACE group (16 HCC progression, 9 liver failure and 1 unknown cause).	
Francica, 2012	**Complete ablation** (assessed by CT, defined as no areas of enhancement at the periphery of the target area) = 93.4% (170 out of 182) of tumours **Mean number of ablation sessions per tumour**=1.58 (range 1 to 3) **Complete response**=92.7% (152 out of 164) of patients • High-risk location group=91.5% (97 out of 106) of patients, 92.2% (107 out of 116) of tumours	**Periprocedural major complications (within 30 days; per patient):** • Death=0.6% (1 out of 164); the patient died 4 days after the laser ablation procedure of acute liver decompensation associated with severe

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First author, date	Efficacy outcomes	Safety outcomes
	• Standard risk location group=94.8% (55 out of 58) of patients, 95.5% (63 out of 66) of tumours, p=0.271 between groups Tumour size did not affect the probability of complete response. **Local tumour progression**=10.6% (18/170) of tumours There was no statistically significant difference in the cumulative incidence of local tumour progression among tumours at high-risk sites compared with elsewhere (p=0.499). Among the variables possibly associated with local tumour progression, only tumour size showed a trend at multivariate analysis (p=0.056) for an association to local recurrence. There was no statistically significant difference between the risk groups in terms of local tumour progression-free survival. **Further treatment** Twelve of the 18 tumours with local progression had further treatment: 5 had TACE and 7 had laser ablation; complete ablation was achieved in all those treated with laser ablation.	respiratory failure (also reported in Pacella et al., 2009). • Main bile duct injury=0.6% (1 out of 164) These were both in the high-risk group. **Minor complications (per session):** • Effusion beneath Glisson capsule=1.8% (5 out of 279) • Subcapsular hematoma=0.4% (1 out of 279) • Partial necrosis of contiguous kidney=0.4% (1 out of 279) • Ascites=1.1% (3 out of 279; 1 was in the high-risk group) • Gastric wall burn=0.4% (1 out of 279) **Side effects (per session):** • Abdominal pain=0.4% (1 out of 279) • Mild to moderate increase in body temperature=8.6% (24 out of 279; 9 in high-risk group)

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First author, date	Efficacy outcomes	Safety outcomes
		• Pleural effusion=18.3% (51 out of 279; 11 in high-risk group)
Vogl, 2004	**Local recurrence rate at 3 and 6 months by tumour size (groups 2 and 3):** • 0 to 2 cm (n=474) = 1.3% and 1.9% • 2 to 3 cm (n=539) = 2.0% and 2.4% • 3 to 4 cm (n=327) = 1.2% at 3 and 6 months • More than 4 cm (n=294) = 3.7% and 4.4% There were no further local recurrences after 6 months. **Mean survival from date of diagnosis of metastasis** for all patients=4.4 years (95% CI 4.0 to 4.8) • 1-year survival=94% • 2-year survival=77% • 3-year survival=56% • 5-year survival=37% **Median survival**=3.5 years (95% CI 3.0 to 3.9) **Mean survival from first laser ablation**=3.8 years (95% CI 3.4 to 4.2) • 1-year survival=86% • 2-year survival=64% • 3-year survival=49% • 5-year survival=33% **Median survival**=2.9 years (95% CI 2.4 to 3.3)	**Clinically relevant complications (per session):** • Pleural effusion=1.1% (17 out of 1,555) • Intra-abdominal bleeding=0.1% (2 out of 1,555) • Liver abscess=0.4% (6 out of 1,555) • Death within 30 days=0.1% (2 out of 1,555); 1 patient died 4 weeks after the procedure from peritonitis and respiratory failure, after developing leakage in the jejunum. The other patient died from suspected sepsis, but this was unconfirmed. • Pneumothorax=0.1% (1 out of 1,555) • Injury to bile duct=0.1% (1 out of 1,555) • Bronchial-biliary fistula=0.1% (1 out of 1,555) No seeding of metastases along the cannulation tract was identified.

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First author, date	Efficacy outcomes	Safety outcomes
Vogl, 2014	**Median overall survival from first laser ablation**=25 months (95% CI 22.5 to 27.5) **Mean survival**=29.3 months (range 0.03 to 121) • 1-year overall survival=78% • 2-year overall survival=50.1% • 3-year overall survival=28% • 4-year overall survival=16.4% • 5-year overall survival=7.8% Median survival in those who had treatment with curative intent (n=337) = 29 months (95% CI 25.4 to 32.6); mean=32.6 (range 2 to 121) Median survival in those who had treatment with palliative intent (n=257) = 21 months (95% CI 18.5 to 23.5); mean 24.1 (range 0.03 to 64), p<0.001 A multivariate Cox model identified the most significant prognostic factors for overall survival as the number (p<0.001) and diameter (p<0.001) of metastases as well as the primary surgical lymph node stage (p<0.003). **Median progression-free survival**=13 months (95% CI 11.1 to 14.9) **Mean progression-free survival**=33.7 months (range 0.03 to 54) • 1-year progression-free survival=51.3%	No safety outcomes were reported.

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First author, date	Efficacy outcomes	Safety outcomes
	• 2-year progression-free survival=35.4% • 3-year progression-free survival=30.7% • 4-year progression-free survival=25.4% • 5-year progression-free survival=22.3% New intrahepatic tumours were detected in 343 patients (58%) during follow up; 2% (n=12) of all patients developed a local recurrence. The diameter and the initial number of metastases were the most important prognostic factors for progression-free survival. **Further treatment** 271 patients (46%) had further treatment after the final laser ablation because they showed signs of progressive disease (12% had systemic chemotherapy, 29% had TACE and 5% had both).	
Vogl, 2013	**Median overall survival** from first laser ablation= 37.6 months (range 0.03 to 1631.9) **Mean overall survival**=62.0 months (SD 25.9) • 1-year overall survival=86.5% • 2-year overall survival=67.2% • 3-year overall survival=51.9% • 4-year overall survival=39.9% • 5-year overall survival=33.4% Statistically significant prognostic factors for the long-term survival up to a very high probability: initial number of metastases (p=0.008), mean volume of metastasis (p<0.001), the quotient of	No safety outcomes were reported.

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First author, date	Efficacy outcomes	Safety outcomes
	the total volumes of necroses and metastases (p<0.001), and the T stage of the primary tumour according to the TNM classification (p<0.001). **Median progression-free survival**=12.2 months (range 0.03 to 133.8) **Mean progression-free survival**=35.2 months (SD 18.2) • 1-year progression-free survival=50.6% • 2-year progression-free survival=33.8% • 3-year progression-free survival=26% • 4-year progression-free survival=20.4% • 5-year progression-free survival=17% The Cox regression model identified the mean volume of metastasis (p<0.001), the quotient of total volumes (p=0.02), and the initial number of metastases (p=0.001) as statistically significant prognostic factors. The location of the primary tumour had no prognostic value.	
Helmberger, 2002	The aim of the procedure was to reduce the total tumour load rather than complete tumour destruction, to possibly qualify the patient for further selective chemotherapy. After the laser ablation, the patient was offered superselective chemoembolisation of the metastases. Two years later, and after 19 sessions of superselective chemoembolisation, the metastases	**Massive cardiac air embolism** A spiral CT scan was done immediately after the last laser fibre was removed but removed but with the introducer sheath still in place. The scan revealed air within the right atrium, the right ventricle, and the hepatic veins. The scan was

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First author, date	Efficacy outcomes	Safety outcomes
	were still under local control without signs of significant progression.	interrupted and at the same time, the patient became pulseless and unconscious. The right ventricle was percutaneously punctured with a needle. Mechanical cardiopulmonary resuscitation was not done, to prevent air embolisation into the pulmonary veins. Within 1 minute 250 ml air had been evacuated and, after external electrical defibrillation, regular heart action was re-established. The patient recovered completely within minutes and remained hemodynamically stable. After 1 hour, he was fully oriented except for an amnesia of the procedure and the subsequent 10 minutes.

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Procedure technique

Of the 13 studies, 7 stated that the laser ablation was done under ultrasound guidance and 4 stated that the ablation was done under MRI guidance, with the needles being placed under CT guidance. Of the 7 using ultrasound, 3 stated that an Echolaser system was used, which consists of an ultrasound device and a diode laser unit (Di Costanzo 2015, Orlacchio 2014, Zou 2017). Other studies stated that a Nd:YAG laser was used. Most studies described using up to 4 fibres for ablation.

Efficacy

Complete tumour ablation

The rates of complete tumour ablation were reported in 9 studies and ranged from 67% to 99%.

In the randomised controlled trial of 140 people with HCC (157 tumours), complete tumour ablation was reported in 96% (67 out of 70; 95% CI 88 to 99) of people who had laser ablation and 97% (68 out of 70; 95% CI 90 to 99) of people who had RFA. More treatment sessions were needed in the laser group to obtain complete tumour ablation (82 compared with 72 in the RFA group, p=0.058; Di Costanzo 2015). In the randomised controlled trial of 30 people with HCC (30 tumours), a complete response at 30 days was reported in 67% (10 out of 15) of those who had laser ablation and 87% (13 out of 15) of those who had RFA. After a second treatment session, the rates were 87% (13 out of 15) in the laser ablation group and 93% (14 out of 15) in the RFA group (p=not significant; Orlacchio 2014). In the randomised controlled trial of 81 people with HCC (95 tumours), complete ablation was reported in 78% (35 out of 45) of tumours in the laser ablation group and 94% (47 out of 50) of tumours in the RFA group (Ferrari 2007). In the randomised controlled trial of 74 people with HCC, a complete response at 3 months was reported for 89% (31 out of 35) of those who had laser ablation and 92% (36 out of 39) of those who had RFA (p=0.583; Zou

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2017). In the quasi-randomised controlled trial of 131 people with HCC, complete necrosis after the first treatment session was reported in 92% (46 out of 50) of tumours treated by laser ablation, 70% (14 out of 20) of tumours treated by TACE, 74% (28 out of 38) of tumours treated by PEI and 80% (32 out of 40) of tumours treated by combined TACE and PEI (Ferrari 2006). In the non-randomised comparative study of 303 people with HCC (510 tumours), initial complete ablation was reported for 99% (74 out of 75) of tumours treated by laser ablation and 98% (425 out of 435) of tumours treated by microwave ablation (Adwan 2022). In the case-control study of 82 people with a solitary HCC 40 mm or larger, a complete response was reported in 63% (21 out of 41) of those who had laser ablation and 20% (8 out of 41) of those who had TACE ($p<0.001$). The response rates for tumours between 51 mm and 60 mm in diameter were 75% after laser ablation and 14% after TACE ($p=0.013$; Morisco 2018).

In 2 single-arm studies of people with HCC, the complete response after laser ablation was 80% (436 out of 548; Pacella 2009) and 93% (170 out of 182) of tumours (Francica 2012).

Local tumour progression or recurrence

Local tumour progression, progression-free survival or recurrence was reported as an outcome in 10 studies.

In the randomised controlled trial of 140 people with HCC, local tumour progression was reported in 23% (16 out of 70) of people who had laser ablation and 26% (18 out of 70) of people who had RFA ($p=0.956$). The mean time to local progression was similar between the groups (46 months for laser ablation and 40 months for RFA, $p=0.376$; Di Costanzo 2015). In the randomised controlled trial of 30 people with HCC, cumulative rates of freedom from local disease progression at 3, 6 and 12 months after treatment were 85%, 62% and 54% in the laser ablation group, and 92%, 86% and 86% respectively in the RFA group ($p=0.083$). For tumours 21 mm or more in diameter, there was a higher

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rate of recurrence in the laser ablation group compared with RFA (p=0.0081; Orlacchio 2014). In the randomised controlled trial of 81 people with HCC, disease recurrence (local tumour progression or new HCC) was reported in 27% (11 out of 41) of those who had laser ablation and 23% (9 out of 40) of those who had RFA. All local tumour progression was observed within 24 months after treatment (Ferrari 2007). In the non-randomised comparative study of 303 people with HCC, local tumour progression was reported in 4% (2 out of 53) of those who had laser ablation and 6% (15 out of 250) of those who had microwave ablation. Local tumour progression-free survival at 1, 3 and 5 years from ablation date was similar between the groups (Adwan 2022). In the case-control study of 82 people with a solitary HCC 40 mm or larger, the rate of disease recurrence after initially successfully treatment was 19% (5 out of 26) in the laser ablation group and 75% (6 out of 8) in the TACE group (p<0.0001; Morisco 2018).

In the cohort study of 164 people with HCC (182 tumours), the rate of local tumour progression was 11% (18 out of 170). There was no statistically significant difference in the cumulative incidence of local tumour progression among tumours at high-risk sites compared with elsewhere (p=0.499; Francica 2012). In the cohort study of 432 people with HCC, the rate of recurrence (local and distant) was 20% (67 out of 338). The mean time to recurrence was 24 months (95% CI 20 to 28; Pacella 2009).

In the cohort study of 603 people with CRC liver metastases, local recurrence rate at 6 months was 2% for tumours 0 cm to 2 cm in diameter, 2% for tumours between 2 cm to 3 cm, 1% for tumours between 3 cm and 4 cm and 4% for tumours larger than 4 cm in diameter (Vogl 2004). In the cohort study of 594 people with CRC liver metastases (1,545 tumours), the median progression-free survival was 13 months (95% CI 11 to 15). Progression-free survival was 51% at 1 year, 35% at 2 years, 31% at 3 years, 25% at 4 years and 22% at 5 years (Vogl 2014). In the cohort study of 401 people with liver metastases from primary sites other than CRC (809 tumours), median progression-free survival

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was 12 months (range 0 to 134). Progression-free survival was 51% at 1 year, 34% at 2 years, 26% at 3 years, 20% at 4 years and 17% at 5 years (Vogl 2013).

Disease-free survival

Disease-free survival was reported in 3 studies. In the non-randomised comparative study of 303 people with HCC, disease-free survival at 1, 3 and 5 years from ablation date was 55%, 30% and 17% in the laser ablation group, compared with 46%, 31% and 25% in the microwave ablation group (p=0.719; Adwan 2022). In the case-control study of 82 people with a solitary HCC 40 mm or larger, mean disease-free survival was 31.5 months (95% CI 24.1 to 38.8) in the laser ablation group and 14.2 months (95% CI 9.7 to 18.7) in the TACE group (p<0.0001; Morisco 2018).

In the cohort study of 432 people with HCC, median disease-free survival time was 26 months (95% CI 22 to 30; Pacella 2009).

Overall survival

Overall survival was reported in 9 studies. In the randomised controlled trial of 140 people with HCC, mean overall survival was 42 months (95% CI 37 to 47) in the laser ablation group and 43 months (95% CI 38 to 47) in the RFA group (p=0.346). The 1-year survival probability was 94% in both groups and the 3-year survival probability was 80% in the laser group and 89% in the RFA group (Di Costanzo 2015). In the randomised controlled trial of 81 people with HCC, the cumulative survival rates at 1 to 5 years were higher in the RFA group than the laser ablation group, but the difference was not statistically significant (Ferrari 2007). In the quasi-randomised controlled trial of 131 people with HCC, cumulative survival at 1, 3 and 5 years was 90%, 53% and 31% for those who had treatment with laser ablation, 67%, 11% and 0% for those who had treatment with TACE, 71%, 29% and 18% for those who had treatment with PEI, and 91%, 41% and 19% for those who had treatment with combined TACE and PEI. Those who had laser ablation or combined therapy survived longer than those who had

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TACE (p=0.0001 and 0.0096, respectively), and laser ablation was associated with longer survival than PEI (p=0.0274; Ferrari 2006). In the non-randomised comparative study of 303 people with HCC, overall survival at 1, 3 and 5 years from diagnosis was 96%, 55% and 30% in the laser ablation group, compared with 94%, 65% and 49% in the microwave ablation group (p=0.002). Overall survival at 1, 3 and 5 years from ablation date was 85%, 38% and 17% in the laser ablation group, compared with 87%, 53% and 40% in the microwave ablation group (p=0.001; Adwan 2022). In the case-control study of 82 people with a solitary HCC 40 mm or larger, mean overall survival was 40 months (95% CI 33 to 46) in the laser ablation group and 37 months (95% CI 31 to 43) in the TACE group (p=0.725). Overall survival probability at 1, 2 and 3 years was 90%, 66% and 55% in the laser group, compared with 85%, 66% and 49% in the TACE group (Morisco 2018).

In the cohort study of 432 people with HCC (548 tumours), median overall survival was 47 months (95% CI 41 to 53), 3-year cumulative survival was 61% and 5-year cumulative survival was 34%. Survival duration was statistically significantly longer in patients with main tumour size of 2.0 cm or less compared with 3.1 cm to 4.0 cm (p=0.003), and in those with main tumour size of 2.1 cm to 3.0 cm compared with 3.1 cm to 4.0 cm (p=0.027; Pacella 2009).

In the cohort study of 603 people with CRC liver metastases, mean survival from date of diagnosis of metastasis was 4.4 years (95% CI 4.0 to 4.8) and median survival was 3.5 years (95% CI 3.0 to 3.9). Survival at 1, 2, 3, and 5 years was 94%, 77%, 56% and 37%, respectively. Mean survival from date of first laser ablation was 3.8 years (95% CI 3.4 to 4.2) and median survival was 2.9 years (95% CI 2.4 to 3.3). Survival at 1, 2, 3, and 5 years was 86%, 64%, 49% and 33%, respectively (Vogl 2004). In the cohort study of 594 people with CRC liver metastases, the median overall survival from first laser ablation was 25 months (95% CI 22.5 to 27.5). Mean survival was 29.3 months (range 0 to 121). Overall survival was 78% at 1 year, 50% at 2 years, 28% at 3 years, 16% at 4 years and

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8% at 5 years (Vogl 2014). In the cohort study of 401 people with liver metastases from primary sites other than CRC, median overall survival from first laser ablation was 37.6 months (range 0 to 1,632). Mean overall survival was 62 months (SD 25.9). Overall survival was 87% at 1 year, 67% at 2 years, 52% at 3 years, 40% at 4 years and 33% at 5 years. Statistically significant prognostic factors for long-term survival were the initial number of metastases ($p=0.008$), mean volume of metastasis ($p<0.001$), the quotient of the total volumes of necroses and metastases ($p<0.001$), and the T stage of the primary tumour according to the TNM classification ($p<0.001$; Vogl 2013).

Patient satisfaction

In the randomised controlled trial of 74 people with HCC, the proportion of people who reported great or general satisfaction 3 days after treatment was 94% in the laser group and 69% in the RFA group ($p=0.022$; Zou 2017).

Safety

Complications that were described as major or clinically relevant have been summarised below.

Mortality

One treatment-related death was reported in the cohort study of 432 people. Acute liver decompensation associated with severe respiratory failure happened 4 days after the procedure (Pacella 2009). Death within 30 days was reported after less than 1% (2 out of 1,555) of treatment sessions in the cohort study of 603 people. One person died 4 weeks after the procedure from peritonitis and respiratory failure, after developing leakage in the jejunum. The other person died from suspected sepsis, but this was unconfirmed (Vogl 2004).

Cardiac air embolism

A case report of massive cardiac air embolism after laser ablation was published in 2002. The air embolism was identified during the CT scan that was done

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immediately after the procedure. The right ventricle was percutaneously punctured with a needle and the air was evacuated. After external electrical defibrillation, the patient recovered and remained haemodynamically stable (Helmberger 2002).

Pancreatitis

Pancreatitis within 24 hours of laser ablation, categorised as a major complication, was reported in 1 person in the cohort study of 432 people (Pacella 2009).

Intrahepatic haematoma

Intrahepatic haematoma within 24 hours of laser ablation, categorised as a major complication, was reported in 1 person in the cohort study of 432 people (Pacella 2009).

Bleeding

Major peritoneal bleeding within 24 hours of laser ablation was reported in 1 person in the cohort study of 432 people (Pacella 2009). Clinically relevant intra-abdominal bleeding was reported after less than 1% (2 out of 1,555) of treatment sessions in the cohort study of 603 people (Vogl 2004).

Transient decompensation of liver function

Major transient decompensation of liver function was reported in 1% (4 out of 432) of people within 30 days of laser ablation.

Bile duct injury

Main bile duct injury was reported in 1 person, who had a tumour in a high-risk location, after laser ablation in the cohort study of 164 people (Francica 2012). Injury to the bile duct was reported in 1 person in the cohort study of 603 people (Vogl 2004).

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Pleural effusion

Clinically relevant pleural effusion was reported after 1% (17 out of 1,555) of treatment sessions in the cohort study of 603 people (Vogl 2004).

Liver abscess

Liver abscess, described as clinically relevant, was reported after less than 1% (6 out of 1,555) treatment sessions in the cohort study of 603 people (Vogl 2004).

Pneumothorax

Pneumothorax, described as clinically relevant, was reported in 1 person in the cohort study of 603 people (Vogl 2004).

Bronchial-biliary fistula

Bronchial-biliary fistula, described as clinically relevant, was reported in 1 person in the cohort study of 603 people (Vogl 2004).

Tumour seeding

Subcutaneous tumour seeding was reported in 1 person who had laser ablation and 1 who had RFA in the randomised controlled trial of 140 people with HCC. In both people, it was surgically removed (Di Costanzo 2015). Three studies including 690 people who had laser ablation specified that no tumour seeding had been observed (Vogl 2004, Ferrari 2006 and 2007).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They did not describe any additional anecdotal or theoretical adverse events.

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Three professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- Most of the data included in the key evidence is from Europe.
- There are several randomised controlled trials comparing laser ablation with RFA for treating HCC. No randomised controlled trials were identified for metastatic liver cancer.
- In the non-inferiority randomised controlled trial by Di Costanzo (2015), the 2 treatment groups were not entirely balanced because of the random inclusion of more large and high-risk located tumours in the laser ablation group.
- The retrospective case-control study by Morisco (2018) used multicentre historical controls treated with TACE to compare with laser ablation at a single centre, which may have introduced some bias.
- Different techniques were used to do laser ablation, including different laser systems and different types of imaging.
- Some studies included people who had already had treatment for liver cancer, but some excluded those who had previous treatment.
- Some studies included people who had refused surgery as well as those for whom surgery was unsuitable. The outcomes may be different in these separate groups.
- Most studies included people with up to 5 small tumours (generally up to 50 mm in diameter). One study compared laser ablation with TACE for a solitary large HCC (up to 76 mm; Morisco 2018). The randomised controlled trial by Orlacchio (2014) only included people with a single HCC tumour with maximum diameter 40 mm. It is likely that multifocal HCC has a different biological behaviour compared with unifocal HCC, with worse trends in terms of both survival and recurrence.
- Most studies excluded people with Child-Pugh class C liver disease.

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- Some studies reported response rates after the first treatment session, but others reported the rates after additional sessions.
- One author noted that particularly for HCC, disease-free survival time and overall survival may be related to the aetiology and severity of the liver failure associated with cirrhosis and histological type of tumour. Survival rates can be influenced by the onset of other tumours, both primary and secondary, or complications resulting from liver failure. Local disease progression-free survival or recurrence-free survival may be a better outcome measure for local ablation procedures.
- Several studies reported follow up of 5 years or longer.
- No potential conflicts of interest were declared in the key evidence papers.
- No ongoing key trials were identified.

Related NICE guidance

Interventional procedures

- NICE interventional procedures guidance on melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic cancer in the liver (Recommendation: special arrangements for metastases from ocular melanoma, research for other liver tumours).
- NICE interventional procedures guidance on selective internal radiation therapy for unresectable colorectal metastases in the liver (Recommendation: special arrangements for people who cannot have chemotherapy, research for people who can have chemotherapy).
- NICE interventional procedures guidance on irreversible electroporation for primary liver cancer (Recommendation*:* research only).
- NICE interventional procedures guidance on selective internal radiation therapy for unresectable primary intrahepatic cholangiocarcinoma (Recommendation: research only).

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- NICE interventional procedures guidance on microwave ablation for treating liver metastases (Recommendation: standard arrangements).
- NICE interventional procedures guidance on selective internal radiation therapy for primary hepatocellular carcinoma (Recommendation: standard arrangements).
- NICE interventional procedures guidance on irreversible electroporation for treating liver metastases (Recommendation: research only).
- NICE interventional procedures guidance on cryotherapy for the treatment of liver metastases (Recommendation: special arrangements).
- NICE interventional procedures guidance on radiofrequency ablation for colorectal liver metastases (Recommendation: standard arrangements).
- NICE interventional procedures guidance on ex-vivo hepatic resection and reimplantation for liver cancer (Recommendation: special arrangements).
- NICE interventional procedures guidance on microwave ablation of hepatocellular carcinoma (Recommendation: standard arrangements).
- NICE interventional procedures guidance on radiofrequency-assisted liver resection (Recommendation: standard arrangements).
- NICE interventional procedures guidance on laparoscopic liver resection (Recommendation: standard arrangements).
- NICE interventional procedures guidance on radiofrequency ablation of hepatocellular carcinoma (Recommendation: standard arrangements).

Technology appraisals

- NICE technology appraisal guidance on cabozantinib for previously treated advanced hepatocellular carcinoma.
- NICE technology appraisal guidance on selective internal radiation therapies for treating hepatocellular carcinoma.
- NICE technology appraisal guidance on atezolizumab with bevacizumab for treating advanced or unresectable hepatocellular carcinoma.

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- NICE technology appraisal guidance on regorafenib for previously treated advanced hepatocellular carcinoma.
- NICE technology appraisal guidance on lenvatinib for untreated advanced hepatocellular carcinoma.
- NICE technology appraisal guidance on Sorafenib for treating advanced hepatocellular carcinoma.

NICE guidelines

- NICE guideline on colorectal cancer (Recommendation: consider chemotherapy with local ablative techniques for people with colorectal liver metastases that are unsuitable for liver resection after discussion by a specialist multidisciplinary team).

Professional societies

- British Society of Interventional Radiology
- British Society of Gastrointestinal and Abdominal Radiology
- British Society of Gastroenterology
- Association of Upper Gastrointestinal Surgeons of Great Britain & Ireland
- Royal College of Radiology.

Company engagement

NICE asked 2 companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

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analysis of prognostic factors for long-term survival and progression-free survival. Investigative Radiology 48: 406–12

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Methods

NICE identified studies and reviews relevant to image-guided percutaneous laser ablation of primary and secondary liver tumours from the medical literature. The following databases were searched between the date they started to 16 January 2024: MEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with primary or secondary liver cancer.
- Intervention or test: image-guided percutaneous laser ablation.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

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Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE ALL (Ovid)	16/01/2024	1946 to Jan 12. 2024
EMBASE (Ovid)	16/01/2024	1974 to Jan 12, 2024
EMBASE Conference (Ovid)	16/01/2024	1974 to Jan 12, 2024
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	16/01/2024	Issue 1 of 12, 2024
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	16/01/2024	Issue 1 of 12, 2024
International HTA database (INAHTA)	16/01/2024	-

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

1 exp Liver Neoplasms/
2 ((liver or hepatic* or bile or hepatocellular) adj4 (secondar* or primar* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metastas* or lesion*)).tw.
3 Bile Duct Neoplasms/
4 (hepatoma* or cholangiocarcinoma* or hepatocarcinoma* or HCC).tw.
5 Carcinoma, Hepatocellular/
6 or/1-5
7 Catheter Ablation/
8 ((catheter* or needle* or electrode* or heat* or thermo* or thermal* or (transvenous adj1 electric*)) adj4 ablat*).tw.
9 (thermoablat* or thermotherap*).tw.
10 LITT.tw.
11 Ablation Techniques/
12 (percutan* adj4 (ablat* or therap* or treat*)).tw.
13 (PLA or EUSLA).tw.
14 (ultrasound* or ultra-sound* or ultrason* or sonograph* or echograph* or echotomograph*).tw.
15 Ultrasonography/

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16 ultrasonography, interventional/ or endoscopic ultrasound-guided fine needle aspiration/
17 Ultrasonic Therapy/
18 (ultrasonic* adj4 (therap* or ablat* or treat*)).tw.
19 or/7-18
20 exp Laser Therapy/
21 (laser* adj4 (therap* or ablat* or treat*)).tw.
22 20 or 21
23 19 and 22
24 6 and 23
25 Echolaser*.tw.
26 24 or 25
27 Animals/ not Humans/
28 26 not 27
29 limit 28 to english language

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Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (table 2 and table 3) are listed in table 5.

Observational studies with population size 30 or fewer and papers published before 2000 were excluded.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Arienti V, Pretolani S, Pacella CM et al. (2008) Complications of laser ablation for hepatocellular carcinoma: a multicenter study. Radiology 246: 947–55	**HCC** Retrospective and prospective cohort study n=520 Follow up: 12 months	Major complication rate=1.5% (15/1,004), associated with excess energy and high-risk location. Minor complication rate=6.2% (62/1,004), associated with excess energy, high bilirubin level, and low prothrombin time. Primary effectiveness rates were 60% in all HCCs and 81% in HCCs smaller than 3 cm.	A study from the same population is included (Pacella 2009)
Caspani B, Lerardi AM, Motta F et al. (2010) Small nodular hepatocellular carcinoma treated by laser thermal ablation in high-risk locations: preliminary results. European Radiology 20: 2286–92	**HCC** Case series n=49 Follow up: 12 months	Laser ablation can be considered a safe treatment in "critical nodules".	Small case series.
Chai W, Zhao Q, Song H et al. (2019) Treatment response and preliminary	Prospective case series n=92	Patients in the endoscopic ultrasound guided laser ablation and percutaneous ultrasound	Small study, comparing laser ablation under

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efficacy of hepatic tumour laser ablation under the guidance of percutaneous and endoscopic ultrasonography. World Journal of Surgical Oncology 17: 133	Follow up: 12 months	guided laser ablation groups shared a similar treatment response and preliminary efficacy in the treatment of hepatic tumours.	endoscopic ultrasound guidance with conventional ultrasound guidance.
Christophi C, Nikfarjam M, Malcontenti-Wilson C et al. (2004) Long-term survival of patients with unresectable colorectal liver metastases treated by percutaneous interstitial laser thermotherapy. World Journal of Surgery 28: 987–94	**CRC liver metastases** Prospective case series n=80 Follow up: median 35 months	Median disease-free survival=24.6 months, with a 5-year survival of 3.8%. Poor tumour differentiation and the presence of more than 2 hepatic metastases were associated with lower overall survival ($p<0.01$). Fourteen patients who had treatment for postoperative hepatic recurrences had the best outcome, with a median overall survival of 36.3 months and a 5-year survival of 17.2%.	Larger or more recent studies are included.
Di Costanzo GG, Francica G, Pacella CM (2014) Laser ablation for small hepatocellular carcinoma: State of the art and future perspectives. World Journal of Hepatology 6: 704–15	**HCC** Review	According to internationally endorsed guidelines, percutaneous thermal ablation is the mainstay of treatment in patients with small HCC who are not candidates for surgical resection or transplantation. Laser ablation represents one of currently available loco-ablative techniques. A review of published data suggests that laser ablation is equivalent to the more popular and widespread RFA in both local tumour control and long-term outcome in the percutaneous treatment of early HCC. In addition,	No meta-analysis; all relevant studies are included.

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		the LA technique using multiple thin laser fibres allows improved ablative effectiveness in HCCs greater than 3 cm.	
Di Costanzo GG, D'Adamo G, Tortora R et al. (2013) A novel needle guide system to perform percutaneous laser ablation of liver tumors using the multifiber technique. Acta radiologica 54: 876–81	**HCC and liver metastases** n=116	Complete tumour ablation was achieved in a single session in 112 (88%) lesions (94% for nodules 3 cm or smaller and 80% for those larger than 3 cm. Of note, complete ablation was achieved in 92% of nodules up to 5 cm.	Larger or more recent studies are included.
Dick EA, Joarder R, de Jode M et al. (2003) MR-guided laser thermal ablation of primary and secondary liver tumours. Clinical Radiology 58: 112–20	**Primary and secondary liver tumours** n=35 Follow up: 5.8 months	MR-guided laser ablation produces a better survival in patients with HCC than would be expected in patients who did not have treatment and has a mean survival in patients with metastases at least equal to the longest median survival in patients who did not have treatment.	More recent or larger studies are included.
Eichler K, Zangos S, Gruber-Rouh T et al. (2012) Magnetic resonance-guided laser-induced thermotherapy in patients with oligonodular hepatocellular carcinoma: long-term results over a 15-year period. Journal of clinical gastroenterology 46: 796-801	**HCC** Prospective case series n=113	The mean survival rate from date of diagnosis of the HCC treated with laser ablation, was 4.9 years (95% CI 3.6 to 5.1). The median survival rate was 3.5 years (95% CI 2.7 to 4.2). One-year survival was 95%; 2-year survival 72%, 3-year survival 54%; and 5-year survival 30%.	Larger studies are included.
Eichler K, Mack MG, Straub R et al. (2001) Oligonodular hepatocellular carcinoma (HCC):	**HCC** Prospective case series n=39	Complete necrosis was achieved in 97.5% of tumours with a 5 mm safety margin, resulting in a complete destruction	More recent or larger studies are included.

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MR-guided laser-induced thermotherapy (LITT). Radiologe 41: 915–22		of the tumour without local recurrences. Mean survival was 4.4 years (95% CI 3.6 to 5.2 years) after the time of diagnoses of the HCC (Kaplan-Meier-method).	
Ferrari FS, Stella A, Gambacorta D et al. (2004) Treatment of large hepatocellular carcinoma: comparison between techniques and long term results. La Radiologia medica 108: 356–71	**HCC** Randomised controlled trial n=89	For laser ablation, complete necrosis was 86%. Cumulative survival rates were 86%, 33%, and 12% at 1, 3 and 5 years, respectively. Combined therapy and laser ablation were most effective.	A more recent study from the same author is included.
Francica G, Petrolati A, Di Stasio E et al. (2012) Influence of ablative margin on local tumor progression and survival in patients with HCC <=4 cm after laser ablation. Acta Radiologica 53: 394–400	**HCC** Cohort study n=116 Follow up: mean 42 months	An ablative margin 7.5 mm or more was useful in preventing local tumour progression but did not affect long-term survival in patients with HCC 4 cm or smaller treated with laser ablation.	Small study, assessing influence of ablative margin.
Francica G, Iodice G, Delle Cave M et al. (2007) Factors predicting complete necrosis rate after ultrasound-guided percutaneous laser thermoablation of small hepatocellular carcinoma tumors in cirrhotic patients: a multivariate analysis. Acta Radiologica 48: 514–19	**HCC** Retrospective case series n=60	The effectiveness of ultrasound-guided laser ablation for HCC tumours 4 cm or less was negatively affected by both operator-related (the beginning of the operator's experience with the technique) and tumour-related factors (non-naive, infiltrating HCC tumours).	Larger or more recent studies are included.
Giorgio A, Tarantino L, de Stefano G et al. (2003) Complications after interventional sonography of focal	**Primary and secondary liver tumours** Review	Major complications after liver tumour ablative procedures included 10 cases of acute liver failure, 2 cases of acute tubular necrosis, 2 cases	Review includes a mix of procedures.

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liver lesions: a 22-year single-center experience. DOI: 10.7863/jum.2003.22.2.193	n=13,222 (122 laser ablation)	of self-limiting hemoperitoneum, 2 cases of paralytic ileum, 2 abscesses, and 1 case of cholangitis. 3% of 122 had major complications after laser ablation (self-limiting paralytic ilea [n=2] and acute liver failure treated with medication [n=2 patients with Child-Pugh class C cirrhosis).	
Giorgio A, Tarantino L, de Stefano G et al. (2000) Interstitial laser photocoagulation under ultrasound guidance of liver tumors: results in 104 treated patients. European Journal of Ultrasound 11: 181–8	**Primary and secondary liver tumours** Case series n=104	CT showed complete necrosis in 70 out of 85 HCC nodules in 65 treated patients and in 24 out of 31 patients with metastases. Three patients with Child class C had severe liver failure, 1 was associated with transient paralytic ileum. One of these patients died 2 months after treatment. Two patients with metastasis did not complete treatment because of a complication (1 paralytic ileum, 1 gastric haemorrhage).	More recent or larger studies are included.
Kim Ha Il, An Jihyun, Han Seungbong et al. (2023) Loco-regional therapies competing with radiofrequency ablation in potential indications for hepatocellular carcinoma: a network meta-analysis. Clinical and Molecular Hepatology 29: 1013–28	**HCC** Systematic review and network meta-analysis 19 randomised controlled trials (n=2,793)	The results suggest that chemoembolisation combined with RFA is the best option for local treatment of early HCC. Cases with potential contraindications for RFA may benefit from a tailored approach using thermal or radiation modalities. For imaging-guided percutaneous ablation techniques, direct and indirect comparison data	Only 1 randomised controlled trial was included on laser ablation, which is already described in the key evidence.

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		revealed no statistically significant differences in both survival and progression endpoints. Each technique has its own advantages and limitations compared with RFA.	
Lichun D, Dazhong Z, Wei SS et al. (2017) Clinical observation of laser ablation combined with chemotherapy in postoperative colorectal cancers with liver metastasis. Minerva Chirurgica 72: 18–23	**CRC liver metastases** Observational study n=85	Laser ablation in combination with chemotherapy of colorectal carcinoma liver metastases is effective and well-tolerated.	Study assesses laser ablation in combination with chemotherapy.
Loveman E, Jones J, Clegg AJ et al. (2014) The clinical effectiveness and cost-effectiveness of ablative therapies in the management of liver metastases: systematic review and economic evaluation. Health technology assessment (Winchester, England) 18: vii-283	**Liver metastases** 2 case series (n=705 and 232, with some patient overlap)	No comparative studies of laser ablation were identified. Two prospective case series, which provide very low-quality evidence, were included from the same institution. The most common adverse event was non-symptomatic pleural effusion, which occurred 41 (9%) times in 452 treatment sessions. There were 20 (4%) events of small non-symptomatic subscapular haematoma.	Review only includes 2 case series on laser ablation.
Luerken L, Haimerl M, Doppler M et al. (2022) Update on Percutaneous Local Ablative Procedures for the Treatment of Hepatocellular Carcinoma. RoFo: Fortschritte auf dem Gebiete der Rontgenstrahlen und	**HCC** Review	Laser ablation is a potential alternative in patients with liver cirrhosis and smaller HCCs. Despite the promising results, laser ablation is not mentioned in the current S3 guideline, partly because of the high level of required equipment; but it	The review includes 2 randomised controlled trials on laser ablation, both of which are included in the key evidence.

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der Nuklearmedizin 194: 1075–86		is rarely used and has been superseded in many centres by microwave ablation or RFA.	
Luo W, Zhang Y, He G et al. (2017) Effects of radiofrequency ablation versus other ablating techniques on hepatocellular carcinomas: a systematic review and meta-analysis. World Journal of Surgical Oncology 15: 126	**HCC** Systematic review n=30 articles (3 on laser ablation)	Lower complete tumour ablation rates and higher local tumour recurrence rates were observed in the laser ablation group. Higher overall survival was seen in the in RFA group, particularly among larger HCCs ($p<0.05$). A tendency of fewer complications was detected in the laser ablation group. Thin needles for laser ablation may improve the ablative effects on tumours with irregular shape or in high-risk locations.	Review only includes 3 randomised controlled trials on laser ablation, all of which are included in the key evidence.
Mack MG, Straub R, Eichler K et al. (2004) Breast cancer metastases in liver: laser-induced interstitial thermotherapy--local tumor control rate and survival data. Radiology 233: 400-9	**Breast cancer liver metastases** Case series n=232	Local recurrence rate at 6-month follow up =2.3% for metastases up to 2 cm in diameter, 4.3% for metastases 2 cm to 3 cm in diameter, 3.2% for metastases 3 cm to 4 cm in diameter, and 1.9% for metastases larger than 4 cm in diameter. No additional local tumour progression was observed beyond 6 months. Mean survival rate from diagnosis of the metastases treated with laser ablation=4.9 years (95% CI 4.3 to 5.4). Median survival=4.3 years. 1-year survival= 96%, 2-year survival=80%, 3-year survival=63%, 5-year survival=41%. Mean survival after the first	More recent or larger studies are included.

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		laser ablation=4.2 years (95% CI 3.6 to 4.8).	
Mack MG, Straub R, Eichler K; et al. (2001) Percutaneous MR imaging-guided laser-induced thermotherapy of hepatic metastases. Abdominal Imaging 26: 369–74	**Liver metastases** Case series n=705	The overall rate of complications and side effects was 7.5%. The rate of clinically relevant complications was 1.3%. Local tumour control rate was 99% after 3 months and 98% after 6 months. In patients with CRC liver metastases, the mean survival was 41.8 months (95% CI 37.3 to 46.4 months). The 1-year survival rate was 93%, the 2-year survival rate was 74%, the 3-year survival rate was 50%, and the 5-year survival was 30%. In patients with liver metastases from breast cancer, the mean survival was 4.3 years (95% CI 3.6 to 5.0).	More recent studies are included.
Majumdar A, Roccarina D, Thorburn D et al. (2017) Management of people with early- or very early-stage hepatocellular carcinoma. Cochrane Database of Systematic Reviews Issue 3. Art. No. CD011650. DOI: 10.1002/14651858.CD011650.pub2 Accessed 29 September 2023.	**HCC** Systematic review 20 references (18 trials; 2 on laser ablation)	High-quality randomised clinical trials designed to measure clinically important differences in all-cause mortality and following the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials), and CONSORT guidelines, are needed. Future trials on early HCC should follow up people for at least 4 to 5 years because most deaths occur beyond 3 years. They should also include other patient-oriented outcomes such as health related quality of life.	Review only included 2 trials on laser ablation, both of which are included in the key evidence.
Pacella CM, Bizzarri G, Francica G et al. (2006) Analysis of	**HCC** Prospective case series	Median overall survival=39 months (95% CI 30 to 47) The 1-, 2-, 3-	Larger or more recent studies are included.

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factors predicting survival in patients with hepatocellular carcinoma treated with percutaneous laser ablation. Journal of Hepatology 44: 902–9	n=148	, 4-, and 5-year cumulative survival rates were 89, 75, 52, 43, and 27%, respectively. From multiple regression analysis, the independent predictors of survival were found to be tumour grading (p=0.002; risk ratio [RR] 0.37, 95% CI 0.20 to 0.70), bilirubin levels 2.5mg/dl or lower (p=0.014; RR 1.58, 95% CI 1.09 to 2.28), and the achievement of complete tumour ablation (p=0.020; RR 0.53, 95% CI 0.31 to 0.90). An initial complete tumour ablation was the only factor associated with longer survival in patients with Child-Turcotte-Pugh class A cirrhosis (p=0.012; hazard ratio 0.48, 95% CI 0.23 to 1.03).	
Pacella CM, Valle D, Bizzarri G et al. (2006) Percutaneous laser ablation in patients with isolated unresectable liver metastases from colorectal cancer: Results of a phase II study. Acta Oncologica 45: 77–83	**CRC liver metastases** Prospective case series n=44	After treatment, 61% (46/75) of the tumours were ablated completely. The likelihood of achieving a complete ablation was significantly higher when metastases had a diameter less than 3 cm (p=0.004). Overall survival was 30.0 months in patients with a complete ablation and 20.2 months in those with a partial ablation (p=0.002).	Larger or more recent studies are included.
Pacella CM, Bizzarri G, Francica G et al. (2005) Percutaneous laser ablation in the treatment of	**HCC** Retrospective case series n=82	Percutaneous laser ablation is a highly effective treatment in HCC with a tumour size of 4.0 cm or smaller. In this setting, 2 variables,	Larger or more recent studies are included.

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hepatocellular carcinoma with small tumors: analysis of factors affecting the achievement of tumor necrosis. Journal of Vascular and Interventional Radiology 16: 1447–57		tumour size and tumour location, affect the achievement of complete tumour ablation and the number of treatments required to obtain tumour necrosis.	
Pacella CM, Bizzarri G, Magnolfi F et al. (2001) Laser thermal ablation in the treatment of small hepatocellular carcinoma: results in 74 patients. Radiology 221: 712–20	**HCC** Case series n=74 Follow up: mean 25 months	During follow up 84 tumours (91%) decreased in size. The local recurrence rates ranged from 1.6% to 6.0%. Recurrence rates in other liver segments ranged from 24% to 73%. Cancer-free survival rates ranged from 73% to 24%. Overall survival rates were 99%, 68%, and 15% at 1, 3, and 5 years, respectively. Twenty-one patients (28%) died.	Larger or more recent studies are included.
Pech M, Wieners G, Kryza R et al. (2008) CT-guided brachytherapy (CTGB) versus interstitial laser ablation (ILT) of colorectal liver metastases: an intraindividual matched-pair analysis. Strahlentherapie und Onkologie: Organ der Deutschen Rontgengesellschaft 184: 302–6	**CRC liver metastases** Non-randomised comparative study n=36 Follow up: median 14 months	Only 5 of 18 patients (28%) showed local tumour progression after CT-guided brachytherapy, compared with 10 of 18 patients (56%) after laser ablation.	Small, non-randomised study comparing laser ablation with brachytherapy.
Pech M, Wieners G, Freund T et al. (2007) MR-guided interstitial laser thermotherapy of	**CRC liver metastases** Case series n=66	The overall median progression-free survival was 6.1 months. Median survival was 23 months (95% CI 17 to	More recent or larger studies were included.

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colorectal liver metastases: efficiency, safety and patient survival. European Journal of Medical Research 12: 161–8	Follow up: median 8.7 months	29 months). The rate of major complications was 2% (n=2) and peri-procedural mortality (30 days) was 3% (n=2). After 3, 6, 9, and 12 months, local tumour control was 98%, 91%, 76%, and 69%, respectively.	
Puls R, Langner S, Rosenberg CH et al (2005) Laser ablation of liver metastases from colorectal cancer with MR thermometry: 5-year survival. Journal of Vascular and Interventional Radiology 16:981–990	**CRC liver metastases** Case series n=87	Technical success=99% Local tumour progression rate was 10% after 6 months. Major complications included large pleural effusion, large subcapsular hematoma, abscess, large pneumothorax, pleuritis with fever, intrahepatic haemorrhage, and biloma. Mean survival from the time of diagnosis of the primary tumour was 50.6 months for all patients who had treatment (95% CI 44.9 to 56.3 months). Median survival time was 54 months and survival rates were 96% at 1 year, 86% at 2 years, 72% at 3 years, 50% at 4 years, and 33% at 5 years. The mean survival time after the first treatment was 31.1 months (95% CI 26.9 to 35.3 months).	More recent or larger studies were included.
Ricke J, Wust P, Stohlmann A et al. (2004) CT-guided interstitial brachytherapy of liver malignancies alone or in combination with	**Primary and secondary liver tumours** Non-randomised comparative study n=37	CT-guided brachytherapy using 3D CT data for dosimetry is safe and effective alone or in combination with laser ablation.	Small study, assessing interstitial brachytherapy alone or in combination with laser therapy.

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thermal ablation: phase I-II results of a novel technique. International Journal of Radiation Oncology, Biology, Physics 58: 1496–505	Follow up: 6 months		
Vogl TJ, Gruber-Rouh T, Naguib NNN et al. (2023) Liver metastases of neuroendocrine tumors: Conventional transarterial chemoembolization and thermal ablation RoFo Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgebenden Verfahren DOI: 10.1055/a-2193-0722	**Neuroendocrine liver metastases** Retrospective cohort study n=130	The number of liver lesions and therapeutic intention were prognostic factors for survival. A high rate of complete ablation in thermoablative procedures was achieved. Laser ablation compared to microwave ablation was associated with more complications.	All patients had conventional transarterial chemo-embolisation; 40 had additional thermal ablation (including 20 who had laser ablation).
Vogl TJ, Kreutztrager M, Gruber-Rouh T et al. (2014) Neoadjuvant TACE before laser induced thermotherapy (LITT) in the treatment of non-colorectal non-breast cancer liver metastases: feasibility and survival rates. European Journal of Radiology 83: 1804–10	**Non-CRC, non-breast liver metastases** Non-randomised comparative study n=110	Transarterial chemoembolisation with different protocols alone and in combination with laser ablation is a feasible palliative treatment option resulting in a median survival of 21.1 months for unresectable liver metastases of non-colorectal and non-breast cancer origin.	Study focuses on TACE with or without laser ablation.
Vogl TJ, Farshid P, Naguib NNN et al. (2014) Thermal ablation of liver metastases from colorectal cancer:	**CRC liver metastases** Review	Reviewed literature showed a local progression rate between 2.8% and 29.7% of RF-ablated liver lesions at 12 to 49 months follow up,	No meta-analysis.

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radiofrequency, microwave and laser ablation therapies. La Radiologia Medica 119: 451–61		2.7% to 12.5% of microwave ablated lesions at 5 to 19 months follow up and 5.2% of lesions treated with laser ablation at 6-month follow up. Major complications were observed in 4% to 33% of patients who had treatment with RF ablation, 0% to 19% of patients who had treatment with microwave ablation and 0.1 to 3.5% of lesions treated with laser ablation. The mean of 1-, 3- and 5-year survival rates for RFA, microwave and laser ablated lesions was (93, 45, 31%), (79, 39, 21%) and (94, 62, 29%), respectively. The median survival in these methods was 33.2, 29.5 and 33.7 months, respectively.	All relevant articles have been included.
Vogl TJ, Farshid P, Naguib Nagy NN et al. (2013) Thermal ablation therapies in patients with breast cancer liver metastases: a review. European Radiology 23: 797–804	**Breast cancer liver metastases** Review	The reviewed literature showed positive response rates of 63% to 97% in RF-ablated lesions, 98% in laser ablated lesions and 34.5% to 62.5% in microwave ablated lesions. Median survival was 10.9 to 60 months using RFA, 51 to 54 months after laser ablation and 41.8 months using microwave. Five-year survival rates were 27 to 30%, 35% and 29%, respectively. Local tumour progression ranged from 13.5% to 58% using RFA, 2.9%	More recent studies are included.

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		with laser and 9.6% with microwave.	
Vogl TJ, Naguib NNN, Nour-Eldin NEA et al. (2011) Repeated chemoembolization followed by laser-induced thermotherapy for liver metastasis of breast cancer. AJR. American Journal of Roentgenology 196: w66–72	**Breast cancer liver metastases** Prospective case series n=161	Transarterial chemoembolisation can be used for sufficient downstaging of liver metastatic lesions of breast cancer to allow laser-induced thermotherapy.	Study assesses use of TACE before laser ablation.
Vogl TJ, Eichler K, Zangos S et al. (2005) Interstitial laser therapy of liver tumors. Medical Laser Application 20: 115–18	**Liver metastases** n=1,632	MR-guided laser-induced thermotherapy is a safe method for the treatment of liver tumours and yields a low rate of major and minor complications because of its minimal invasive character.	Other studies published by the same author with more outcomes are included.
Vogl TJ, Straub R, Zangos S et al. (2004) MR-guided laser-induced thermotherapy (LITT) of liver tumours: experimental and clinical data. International Journal of Hyperthermia 20: 713–24	**Liver metastases** n=1,259	Local tumour control rate=98.7% at 3 months and 97.3% at 6 months. The mean survival rate=4.4 years (95% CI 4.1 to 4.8 years) and median survival=3.0 years. No statistically significant difference in survival rates was observed in patients with CRC liver metastases compared with other primary tumours. The rate of clinically relevant side effects and complications needing secondary treatment was 2.2%.	Other studies published by the same author are included.
Vogl T, Straub R, Eichler K et al. (2002) Malignant liver tumors treated with MR imaging–guided laser-induced	**Malignant liver tumours** Cohort study n=899	Major complications included 3 deaths (0.1%) within 30 days, pleural effusion needing thoracentesis in 16 (0.8%) cases, hepatic	More recent studies are included.

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thermotherapy: experience with complications in 899 patients (2,520 lesions). Radiology 225 (no. 2)		abscess needing drainage in 15 (0.7%) cases, bile duct injury in 4 (0.2%) cases, segmental infarction in 3 (0.1%) cases, and haemorrhage needing transfusion in 1 (0.05%) case. Minor complications included postprocedural fever in 710 (33%), pleural effusion not needing thoracentesis in 155 (7%), subcapsular hematoma in 69 (3%), subcutaneous haematoma in 24 (1%), pneumothorax in 7 (0.3%), and haemorrhage in 2 (0.1%) cases.	
Vogl TJ, Eichler K Straub R et al. (2001) Laser-induced thermotherapy of malignant liver tumors: general principals, equipment(s), procedure(s)--side effects, complications and results. European Journal of Ultrasound 13: 117–27	**Primary and secondary liver tumours** Case series n=676	There were no relevant clinical complications. Mean survival=35 months MRI-guided, or ultrasound-guided laser ablation appears to be a safe and effective treatment protocol for liver metastases and oligonodular HCC.	More recent studies are included.
Wade R, South E, Anwer S et al. (2023) Ablative and non-surgical therapies for early and very early hepatocellular carcinoma: a systematic review and network meta-	**HCC** Systematic review and network meta-analysis 37 randomised controlled trials and 14 non-	Data comparing radiofrequency ablation with microwave ablation, laser ablation or proton beam therapy were limited. Adverse events were reported inconsistently. There is evidence that percutaneous ethanol	Only 3 randomised controlled trials were included on laser ablation, all of which are already described in

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analysis. Health Technology Assessment 27(29)	randomised studies	injection and percutaneous acid injection are inferior to radiofrequency ablation, microwave ablation and resection. The uncertainty associated with the available data was demonstrated in the network meta-analysis results, where credible intervals were generally wide and most crossed the line of no effect. The estimated treatment effectiveness ranking was also very uncertain, with very wide credible intervals for most interventions.	the key evidence.
Wietzke-Braun P, Schindler C, Raddatz D et al. (2004) Quality of life and outcome of ultrasound-guided laser interstitial thermo-therapy for non-resectable liver metastases of colorectal cancer. European Journal of Gastroenterology & Hepatology 16: 389-95	**CRC liver metastases** Prospective case series n=45 Follow up: 6 months	Median survival after laser ablation=8.5 months (range 1.5 to 18). In the multivariate analyses, quality-of-life symptoms and functioning scales did not deteriorate in patients alive at 6 months after laser ablation. Univariate analyses outlined a significant increase of the pain subscale before and at 1 week after laser ablation.	Small case series with short term follow up.
Wietzke-Braun P, Ritzel U, Nolte W et al. (2003) Ultrasound-guided laser interstitial thermo therapy for treatment of non-resectable primary and secondary liver tumours--a feasibility study. Ultraschall in	**Primary and secondary liver tumours** Case series n=60	There were no serious adverse events and no deaths within 30 days.	Small feasibility study.

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der Medizin 24: 107–12			
Zangos S, Mack MG, Balzer JO et al. (2004) Neoadjuvant transarterial chemoembolization (TACE) before percutaneous MR-guided laser-induced thermotherapy (LITT): Results in large-sized primary and secondary liver tumors. Medical Laser Application 19: 98–108	**Primary and secondary liver tumours** Case series n=289	The combined treatment protocol (TACE followed by MRI-guided laser ablation) appears to be a safe and effective treatment of large unresectable liver tumours. The combination of TACE and laser ablation results in significant superior survival rates in comparison to the results of TACE alone. HCC showed a better response to the treatment than liver metastases.	The focus of the study is the effect of neoadjuvant TACE before laser ablation.

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