

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of microwave ablation for treating liver metastases

Liver metastases are cancers that have spread (metastasised) to the liver from a cancer in another part of the body, often from the colon or rectum. Microwave ablation uses heat energy to destroy cancer cells. It can be done using a probe inserted through the skin (keyhole surgery), or during open abdominal surgery.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in April 2015 and updated in January 2016.

Procedure name

- Microwave ablation for treating liver metastases

Specialist societies

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

Description

Indications and current treatment

Liver metastases are a common manifestation of many primary cancers. The liver is the main site for metastases originating from colorectal or other gastrointestinal tract cancers.

The number, location and size of the metastases as well as the patient's general health and the site of the primary cancer all influence the choice of treatment for liver metastases. For a minority of patients, surgical resection with curative intent may be possible. Whilst non-surgical ablative techniques may be used with curative intent, for most patients treatment is palliative. Options for palliative treatment include systemic chemotherapy, external beam radiotherapy, thermal ablation techniques (such as radiofrequency or cryotherapy), arterial embolisation techniques, and selective internal radiation therapy. Multiple treatment modalities may be used for individual patients.

Thermal ablation techniques are normally used in patients for whom surgery would not be suitable, or for treating recurrence following surgical resection. They may also be used as an adjunct to hepatic resection, either to downstage the disease to facilitate liver resection or to ablate small-volume disease in the liver remnant after resection.

What the procedure involves

Microwave ablation aims to destroy tumour cells using heat, which creates localised areas of tissue necrosis with minimal damage to surrounding normal tissues.

The procedure can be done using local anaesthesia or with the patient under general anaesthesia, either percutaneously or during open or laparoscopic surgery. A probe is advanced into each targeted lesion under imaging guidance and the tumour is ablated by delivering high-frequency microwave energy. Multiple pulses of energy may be delivered during a session, and multiple probes can be used to treat larger tumours.

A variety of different microwave devices can be used for this procedure.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to microwave ablation for treating liver metastases. The following databases were searched, covering the period from their start to 5 January 2016: MEDLINE,

IP overview: microwave ablation for treating liver metastases

PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with liver metastases.
Intervention/test	Microwave ablation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 4003 patients from 1 randomised controlled trial (RCT)¹, 5 non-randomised comparative studies²⁻⁶, and 6 case series⁷⁻¹¹.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on microwave ablation for treating liver metastases

Study 1 Shibata T (2000) - included in 2011 overview

Details

Study type	Randomised controlled trial
Country	Japan
Recruitment period	1990–1997
Study population and number	n=30 (14 MW coagulation, 16 liver resection) patients with primary colorectal carcinoma and liver metastases
Age and sex	Mean 61 years; 53% (16/30) male
Patient selection criteria	Patients with multiple (fewer than 10) metastatic liver tumours from colorectal primaries (at least 1 confirmed histologically), largest tumour < 80 mm, and no signs of cirrhosis or chronic hepatitis.
Technique	Open microwave coagulation using a tissue coagulator for a net period between 2 and 20 minutes at between 60 W and 100 W vs hepatic resection including lobectomy, segmentectomy, subsegmentectomy, and/or wedge resection as clinically indicated.
Follow-up	Not reported (imaging follow-up every 3 months)
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: 25% (10/40) of patients dropped out during the surgery phase, outcomes for these patients were not compared.

Study design issues:

- Randomisation was by computer generated sequence.
- Patients with all liver cancer types were randomised and only those with colorectal metastases were reported here.
- Cumulative survival calculated by Kaplan–Meier method.
- No details given of concomitant treatment.

Study population issues: There were no significant differences in clinical or demographic characteristics between the groups at baseline.

Other issues:

- MW intervention characteristics differed for treatment of superficial and deeply seated tumours.
- Authors recommended caution in applying microwave coagulation to tumours near a large branch of a bile duct.

Key efficacy and safety findings

Efficacy	Safety																																																								
<p>Number of patients analysed: 30 (14 versus 16)</p> <p>Survival</p> <p>Mean survival time</p> <ul style="list-style-type: none"> MW group: 27 months Hepatectomy group: 25 months p = 0.83 <p>Estimated survival rates</p> <table border="1" data-bbox="94 562 527 709"> <thead> <tr> <th></th> <th>Microwave</th> <th>Hepatectomy</th> </tr> </thead> <tbody> <tr> <td>1 year</td> <td>71%</td> <td>69%</td> </tr> <tr> <td>2 years</td> <td>57%</td> <td>56%</td> </tr> <tr> <td>3 years</td> <td>14%</td> <td>23%</td> </tr> </tbody> </table> <p>Mean disease-free interval</p> <ul style="list-style-type: none"> MW group: 11.3 months Hepatectomy group: 1.3 months p = 0.47 <p>During the follow-up period there were 9 deaths among the 14 patients treated with microwave ablation, 6 of whom died due to hepatic failure. In the hepatic resection group there were 12 deaths among 16 patients with 7 dying from hepatic failure.</p> <p>Surgical parameters</p> <table border="1" data-bbox="94 1115 699 1446"> <thead> <tr> <th></th> <th>MW</th> <th>Resection</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>Blood loss (ml)</td> <td>360 ± 230</td> <td>910 ± 490</td> <td>0.027</td> </tr> <tr> <td>Blood transfused (ml)</td> <td>0</td> <td>540 ± 690</td> <td>0.080</td> </tr> <tr> <td>Patients requiring transfusion (%)</td> <td>0</td> <td>38</td> <td>0.035</td> </tr> <tr> <td>Operation time (min)</td> <td>180 ± 20</td> <td>200 ± 50</td> <td>0.20</td> </tr> <tr> <td>Length of stay (days)</td> <td>20 ± 7</td> <td>25 ± 12</td> <td>0.23</td> </tr> </tbody> </table> <p>Biochemical markers</p> <p>Carcinoembryonic antigen levels decreased significantly 4 weeks after surgery in both groups.</p> <p>MW: 18.5 ± 21.6 ng/ml to 5.8 ± 6.3 ng/ml (p < 0.05)</p> <p>Hepatectomy: 13.5 ± 11.4 ng/ml to 4.1 ± 3.9 ng/ml (p < 0.01)</p>		Microwave	Hepatectomy	1 year	71%	69%	2 years	57%	56%	3 years	14%	23%		MW	Resection	p	Blood loss (ml)	360 ± 230	910 ± 490	0.027	Blood transfused (ml)	0	540 ± 690	0.080	Patients requiring transfusion (%)	0	38	0.035	Operation time (min)	180 ± 20	200 ± 50	0.20	Length of stay (days)	20 ± 7	25 ± 12	0.23	<p>Operative complications</p> <p>There were no intraoperative deaths in either group.</p> <p>Post-operative complications</p> <table border="1" data-bbox="865 415 1446 793"> <thead> <tr> <th></th> <th>MW (n = 14)</th> <th>Resection (n = 16)</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>Internal obstruction</td> <td>0</td> <td>1</td> <td>NS</td> </tr> <tr> <td>Bile duct fistula</td> <td>1*</td> <td>1*</td> <td>N/S</td> </tr> <tr> <td>Hepatic abscess</td> <td>1*</td> <td>0</td> <td>N/S</td> </tr> <tr> <td>Wound infection</td> <td>0</td> <td>1*</td> <td>N/S</td> </tr> </tbody> </table> <p>*Patient was treated by antibiotics.</p>		MW (n = 14)	Resection (n = 16)	p	Internal obstruction	0	1	NS	Bile duct fistula	1*	1*	N/S	Hepatic abscess	1*	0	N/S	Wound infection	0	1*	N/S
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Abbreviations used: MW, microwave; W, Watts.																																																									

Study 2 Correa-Gallego C (2014)

Details

Study type	Retrospective matched-cohort comparative study
Country	USA
Recruitment period	MWA: 2008 - 2011 RFA: 2001 - 2010
Study population and number	n=134 (67 MWA versus 67 RFA) patients with colorectal liver metastases
Age and sex	MWA: median 56 years; gender not reported RFA: median 55 years; gender not reported
Patient selection criteria	Patients who had undergone MWA or RFA for colorectal liver metastases.
Technique	All patients underwent open operative ablations. MWAs were performed with an Evident Microwave System, including a Valleylab microwave generator (915 MHz/45 W) and Evident microwave surgical antennas. RFAs were performed with a Covidien RFA system, AngioDynamics RITA system, or Boston Scientific system. The duration of ablations was determined by the surgeon at the time of the ablation depending on the characteristics of the target lesion and the suggested protocol by the manufacturer. Intraoperative ultrasound guidance for probe placement and ablation monitoring was used at the practitioner's discretion.
Follow-up	MWA: median 18 months RFA: median 31 months
Conflict of interest/source of funding	Not reported.

Analysis

Follow-up issues:

- Follow-up was significantly shorter for MWA (median 18 months versus 31 months, $p < 0.001$).
- All but 1 patient were seen at least once in follow-up within 4 weeks after discharge from the hospital.

Study design issues:

- Tumours in both groups were matched on size, use of chemotherapy, and clinical risk score.

Study population issues:

- MWA and RFA groups were comparable by age, gender, median number of tumours treated, proximity to major vessels, and postoperative complication rates.

Other issues: None.

Key efficacy and safety findings

Efficacy	Safety
<p>Number of patients analysed: 67 MWA versus 67 RFA</p> <p>Recurrence</p> <p>Ablation-site recurrence rate</p> <ul style="list-style-type: none"> • MWA: 6% (at median 18 months) • RFA: 20% (at median 31 months) <p>p<0.001</p> <p>Kaplan-Meier estimates of ablation-site recurrence at 2 years:</p> <ul style="list-style-type: none"> • MWA: 7% • RFA: 18% <p>p=0.01</p> <p>MWA (HR 0.25 [95 % CI 0.08–0.75]; p = 0.01) was associated with lower local recurrence on stratified univariate and multivariate Cox regression.</p>	<p>Post-procedural complications were seen in 25 % of patients. Morbidity rates were similar between the 2 groups (27% versus 24%, p = 0.8).</p> <p>Only 3 of the 16 patients who had an ablation without a liver resection developed a complication (2 in the RFA and 1 in the MWA groups). None of these could be directly attributed to the ablation (2 wound infections, and a ureteral leak related to primary tumour resection).</p> <p>In the patients who had an ablation combined with a resection (88% of patients), the most common complications were wound infections (16 %), intra-abdominal fluid collections (8%), and pleural effusions (4%).</p>
Abbreviations used: CI, confidence interval; HR, hazard ratio; MWA, microwave ablation	

Study 3 Liu Y (2013)

Details

Study type	Non-randomised comparative study
Country	China
Recruitment period	2003-2009
Study population and number	n= 89 (35 MWA versus 54 RFA) patients with liver metastases
Age and sex	Mean 53 years; 61% (54/89) male
Patient selection criteria	All patients were not amenable or refused to receive surgical resection. Less than 5 lesions in each patient, maximum diameter of 5 cm or less, and primary lesions under control after complete resection. Exclusion criteria: patients with extrahepatic metastases or vascular invasion.
Technique	MWA and RFA were performed with the patient under intravenous conscious sedation and additional local anaesthesia. MWA: an ECO-100C (ECO Microwave electronic institute) microwave generator and a FORSEA MTC-3C (Qinghai Microwave electronic institute) microwave system with a frequency of 2450 MHz and a power output of 0-150 W were used. The choice of system was at the discretion of the operator. RFA: the RF 2000 (Radiotherapeutics) system was used before September 2004 and the Elektrotom Hitt 106 (Berchtold) system was used after September 2004.
Follow-up	Mean 32 months
Conflict of interest/source of funding	The authors declared no conflicts of interest.

Analysis

Follow-up issues:

- Retrospective study.
- At the time of analysis, 55% (49/89) of patients were dead. The main cause of death was hepatic tumour progression in 65% (58/89) of patients.

Study design issues:

- The choice of MWA or RFA was at the discretion of each primary physician.

Study population issues:

- 81% (72/89) of patients had been previously treated by post-ablation systemic chemotherapy.
- Primary lesions included colorectal (43%), nasopharyngeal carcinoma (21%), breast cancer (11%), ovarian cancer (9%), lung cancer (9%) and gastric cancer (7%).

Other issues: None.

Key efficacy and safety findings

Efficacy	Safety																																			
<p>Number of patients analysed: 89 (35 MWA versus 54 RFA)</p> <p>Complete ablation rate (assessed 1 month after the procedure)</p> <ul style="list-style-type: none"> MWA: 94% (58/62) of tumours RFA: 84% (59/70) of tumours p=0.094 <p>The complete ablation rate of tumours of 3 cm or less was significantly higher than that of tumours greater than 3 cm, all groups considered (94% and 67% respectively, p=0.001).</p> <p>Recurrence</p> <p><u>Univariate analysis of factors associated with recurrence</u></p> <p>Local recurrence was defined as a new lesion that appeared in or adjacent to the successfully treated nodule or an enlargement of the treated nodule.</p> <ul style="list-style-type: none"> MWA: 9% (3/35) RFA: 20% (11/54) p=0.072 <p>Other factors such as age, sex, type of primary lesions, stage of primary lesions and tumour size were analysed but none of them showed a significant association with local recurrence.</p> <p>Distant recurrence was defined by the presence of intrahepatic new tumours nodules.</p> <ul style="list-style-type: none"> MWA: 43% (15/35) RFA: 56% (30/54) p=0.242 <p><u>Multivariate analysis of factors to predict recurrence</u></p> <table border="1" data-bbox="94 1150 837 1438"> <thead> <tr> <th>Dependent variable</th> <th>Prognostic factor</th> <th>Regression coefficient</th> <th>Standard error</th> <th>p value</th> </tr> </thead> <tbody> <tr> <td>Overall recurrence</td> <td>Chemotherapy>6 cycles</td> <td>-1.824</td> <td>0.753</td> <td>0.015</td> </tr> <tr> <td>Distant recurrence</td> <td>Disease-free interval greater than 12 months</td> <td>-1.044</td> <td>0.480</td> <td>0.030</td> </tr> <tr> <td>Local recurrence</td> <td>Ablation modality</td> <td>1.180</td> <td>0.610</td> <td>0.053</td> </tr> </tbody> </table> <p>Overall survival rate</p> <table border="1" data-bbox="94 1507 837 1619"> <thead> <tr> <th></th> <th>1-year</th> <th>2-year</th> <th>3-year</th> <th>5-year</th> </tr> </thead> <tbody> <tr> <td>MWA</td> <td>82%</td> <td>67%</td> <td>56%</td> <td>44%</td> </tr> <tr> <td>RFA</td> <td>87%</td> <td>55%</td> <td>44%</td> <td>32%</td> </tr> </tbody> </table> <p>No significant difference between the MWA and the RFA group with respect to overall survival (p=0.438)</p>	Dependent variable	Prognostic factor	Regression coefficient	Standard error	p value	Overall recurrence	Chemotherapy>6 cycles	-1.824	0.753	0.015	Distant recurrence	Disease-free interval greater than 12 months	-1.044	0.480	0.030	Local recurrence	Ablation modality	1.180	0.610	0.053		1-year	2-year	3-year	5-year	MWA	82%	67%	56%	44%	RFA	87%	55%	44%	32%	<p>No procedure-related mortality was reported.</p> <p>Major complications were reported in 1% (1/89) of patients. Low to moderate fever which resolved within 7 days: 23% (20/89).</p> <p>One patient treated by RFA developed a subcapsular haematoma which resolved within 1 month.</p>
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Study 4 Engstrand J (2014)

Details

Study type	Retrospective comparative study
Country	Sweden
Recruitment period	2009–2012 (MWA) and 2008-2013 (resection and palliative care)
Study population and number	n=81 (20 MWA ± local resection versus 36 liver resection versus 25 palliative care) patients with colorectal liver metastases.
Age and sex	Range 42-83 years; 58% (47/81) male
Patient selection criteria	MWA: patients for whom primary curative-intended treatment was precluded by absence of a tumour-free future liver remnant due to the extent of segmental engagement, patients for whom the whole liver could be rendered macroscopically tumour-free by the procedure, lesions of less than 35 mm. Resection group: patients selected from all patients diagnosed with colorectal liver metastases in Stockholm county in 2008 who had a follow-up of 5 years. Palliative oncologic treatment: patients of less than 85 years, having less than 20 metastases with a maximum size of 30 mm or more and no unresectable extrahepatic disease.
Technique	MWA: performed via laparotomy using Acculis MTA (angiodynamics) device. Local resection was combined to MWA for tumours engaging the liver surface. Antibiotic prophylaxis before the procedure was used in all patients. Patients received chemotherapy as neo-adjuvant, adjuvant or palliative treatment.
Follow-up	MWA: Median 25 months Resection and palliative care groups: 5 years
Conflict of interest/source of funding	The authors reported no conflicts of interest.

Analysis

Follow-up issues:

- All patients had follow-up with CT or US 1 month after the procedure, every 3 months for 1 year and 6-monthly thereafter.
- In case of tumour recurrence, patients re-treated with MWA and/or resection if they were suitable.

Study design issues:

- The clinical outcomes of the patients treated by MWA were compared with the clinical outcomes of 2 historic cohorts (1 that was treated by resection and 1 that received palliative treatment).

Study population issues:

- Ratio synchronous/metachronous detection of tumour different between groups: 18/2 for MWA; 17/19 for resection and 15/10 for palliative ($p < 0.05$ for MWA group versus palliative group).
- Median (range) number of tumours different between groups: 9 (5-22) for MWA; 2 (1-15) for resection and 5 (1-16) for palliative ($p < 0.05$ for MWA group versus palliative group).

Other issues:

- In 60% (12/20) of patients, MWA was performed at the same time as the primary cancer operation.
- In 20% (4/20), local resections were performed at the same time.
- In 1 patient, the intra-operative finding that the bulk of metastatic disease was in the right lobe prompted a change in the management plan to clearing the tumour in the left lobe with MWA followed by a right-sided hemi-hepatectomy as a second procedure.

Key efficacy and safety findings

Efficacy				Safety		
Number of patients analysed: 81 (20 MWA ± local resection versus 36 liver resection versus 25 palliative care)				No perioperative mortality was reported in the patients treated by MWA.		
Treatment results (MWA group)				Complications (Clavien-Dindo classification): 60% (12/20)		
	Alive (n=10)		Deceased (n=10)			
Median follow-up (range, months)	30 (18-54)		21 (9-31)			
Disease-free	5					
Recurrence						
85% (17/20) had recurrent hepatic disease in the form of new lesions.						
Survival						
	MWA	Liver resection	Palliative			
4-year survival	41%	70%	4%			
Significant survival benefit in MWA group compared against palliative group.						
Results of multivariate analysis of factors to predict survival showed that only treatment modality (MWA versus palliative treatment) was a significant predictor of survival: HR 0.56, 96% CI 0.33-0.96, p<0.05.						
Operative characteristics (MWA group)						
Median length of stay: 10 days (range 2-24)						
Abbreviations used: CT, computed tomography; MWA, microwave ablation; US, ultrasound.						

Study 5 Tanaka K (2006) - included in 2011 overview**Details**

Study type	Non-randomised controlled study
Country	Japan
Recruitment period	1992–2004
Study population and number	n=53 (16 MWA and liver resection, 37 liver resection alone) patients with multiple, bilobar colorectal liver metastases. Mean diameter = 5.1cm.
Age and sex	Mean 60 years; 62% (33/53) male
Patient selection criteria	Patients with 5 or more lesions in a bilobar distribution.
Technique	All procedures via laparotomy. MWA at 70 W for 45 seconds (repeated 4 or 5 times per lesion).
Follow-up	Median 20 months
Conflict of interest/source of funding	Not reported.

Analysis**Follow-up issues:**

- Retrospective study.
- No loss to follow-up.

Study design issues:

- Patients were selected for combined MWA plus resection where resection alone could not retain sufficient vascularised hepatic parenchyma to support hepatic function.
- Thirty patients received neoadjuvant chemotherapy.
- Some patients in each group underwent a second planned hepatectomy ± MWA, making evaluation of outcomes difficult.

Study population issues: Groups were matched at baseline in terms of demographics and most clinical characteristics, however those receiving combined ablation and resection had significantly more metastases, were more likely to have had neoadjuvant chemotherapy, but less likely to have had a major hepatectomy.

Other issues: Some discrepancy between text and tables in terms of length of follow-up for survival outcomes.

Key efficacy and safety findings

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<p>Number of patients analysed: 53 (16 MWA and liver resection, 37 liver resection alone)</p> <p>Survival</p> <p>Hepatic recurrence-free survival</p> <table border="1"> <thead> <tr> <th></th> <th>MWA + resection</th> <th>Resection</th> </tr> </thead> <tbody> <tr> <td>1 year</td> <td>56%</td> <td>55%</td> </tr> <tr> <td>3 years</td> <td>39%</td> <td>42%</td> </tr> <tr> <td>5 years</td> <td>39%</td> <td>35%</td> </tr> </tbody> </table> <p>(p=0.86)</p> <p>Overall survival</p> <table border="1"> <thead> <tr> <th></th> <th>MWA + resection</th> <th>Resection</th> </tr> </thead> <tbody> <tr> <td>1 year</td> <td>80%</td> <td>87%</td> </tr> <tr> <td>3 years</td> <td>51%</td> <td>49%</td> </tr> <tr> <td>5 years</td> <td>17%</td> <td>44%</td> </tr> </tbody> </table> <p>(p=0.43)</p> <p>Treatment procedure (combined resection plus MWA compared against resection alone) did not influence overall survival on multivariate analysis.</p> <p>Disease-free survival</p> <table border="1"> <thead> <tr> <th></th> <th>MWA + resection</th> <th>Resection</th> </tr> </thead> <tbody> <tr> <td>1 year</td> <td>33%</td> <td>26%</td> </tr> <tr> <td>3 years</td> <td>17%</td> <td>11%</td> </tr> </tbody> </table> <p>(p=0.54) overall.</p> <p>Operative characteristics</p> <p>Group mean ± standard deviation – first treatment</p> <table border="1"> <thead> <tr> <th></th> <th>MWA + resection</th> <th>Resection</th> </tr> </thead> <tbody> <tr> <td>Blood loss (ml)</td> <td>386±515</td> <td>379±475</td> </tr> <tr> <td>Length of stay (days)</td> <td>23±14</td> <td>22±10</td> </tr> </tbody> </table> <p>Measurement of significance not reported.</p>		MWA + resection	Resection	1 year	56%	55%	3 years	39%	42%	5 years	39%	35%		MWA + resection	Resection	1 year	80%	87%	3 years	51%	49%	5 years	17%	44%		MWA + resection	Resection	1 year	33%	26%	3 years	17%	11%		MWA + resection	Resection	Blood loss (ml)	386±515	379±475	Length of stay (days)	23±14	22±10	<p>Complications</p> <p>No death within 60 days reported in either group.</p> <p>Rates of complications for first treatment</p> <table border="1"> <thead> <tr> <th></th> <th>MWA + resection</th> <th>Resection</th> </tr> </thead> <tbody> <tr> <td>Infection</td> <td>3% (1/37)</td> <td>13% (2/16)</td> </tr> <tr> <td>Biliary fistula</td> <td>3% (1/37)</td> <td>6% (1/16)</td> </tr> <tr> <td>Bleeding</td> <td>0% (0/37)</td> <td>6% (1/16)</td> </tr> <tr> <td>Hyper-bilirubinemia</td> <td>3% (1/37)</td> <td>0% (0/16)</td> </tr> <tr> <td>Intestinal obstruction</td> <td>8% (3/37)</td> <td>0% (0/16)</td> </tr> </tbody> </table> <p>(measurement of significance not reported)</p>		MWA + resection	Resection	Infection	3% (1/37)	13% (2/16)	Biliary fistula	3% (1/37)	6% (1/16)	Bleeding	0% (0/37)	6% (1/16)	Hyper-bilirubinemia	3% (1/37)	0% (0/16)	Intestinal obstruction	8% (3/37)	0% (0/16)
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	MWA + resection	Resection																																																											
1 year	33%	26%																																																											
3 years	17%	11%																																																											
	MWA + resection	Resection																																																											
Blood loss (ml)	386±515	379±475																																																											
Length of stay (days)	23±14	22±10																																																											
	MWA + resection	Resection																																																											
Infection	3% (1/37)	13% (2/16)																																																											
Biliary fistula	3% (1/37)	6% (1/16)																																																											
Bleeding	0% (0/37)	6% (1/16)																																																											
Hyper-bilirubinemia	3% (1/37)	0% (0/16)																																																											
Intestinal obstruction	8% (3/37)	0% (0/16)																																																											
Abbreviations used: MWA, microwave ablation; US, ultrasound; W, Watts.																																																													

Study 6 Hompes R (2010) - included in 2011 overview**Details**

Study type	Matched-cohort comparative study
Country	Belgium
Recruitment period	2008
Study population and number	n=19 (6 MWA, 13 RFA) patients with liver metastases without underlying liver disease.
Age and sex	Median 61 years; 47% (9/19) male
Patient selection criteria	Tumours smaller than 3 cm.
Technique	US guidance MWA either laparoscopically or percutaneously with 40W energy delivered for 10 minutes (combined with hepatectomy in 1 patient).
Follow-up	Median 6 months
Conflict of interest/source of funding	The authors reported no conflicts of interest.

Analysis**Follow-up issues:**

- Patient accrual method not reported.
- No loss to follow-up in the MWA group.

Study design issues:

- Tumours matched for size and location, no other characteristics were considered.
- Concomitant treatment not standardised between groups.

Study population issues: No comparison of groups at baseline.

Other issues:

- A larger ablation diameter represented better outcome.
- Period of follow up for CT scan evaluation was not reported although measurements were taken at 1 week and 3 months.
- Few clinical outcomes were reported.

Key efficacy and safety findings

Efficacy	Safety																																				
<p>Number of patients analysed: 19 (6 MWA versus 13 RFA)</p> <p>Recurrence</p> <p>Biopsy-proven local recurrence occurred in 1 out of 6 patients in the microwave ablation group at 6-month follow-up. There was no local recurrence in the RFA group.</p> <p>Tumour response</p> <p>CT scan demonstrated that tumour destruction was complete in all patients undergoing MWA at 1-week follow-up.</p> <p>CT scan transverse tumour/margin diameter: median (range) (length of follow-up not reported).</p> <table border="1" data-bbox="94 604 958 714"> <thead> <tr> <th></th> <th>MWA</th> <th>RFA</th> <th>p value</th> </tr> </thead> <tbody> <tr> <td>Baseline (tumour diameter)</td> <td>12 mm (6 to 18)</td> <td>12 mm (7 to 24)</td> <td>> 0.792</td> </tr> <tr> <td>Post-operative (ablation diameter)</td> <td>18.5 mm (12 to 64)</td> <td>34 mm (16 to 41)</td> <td>0.003</td> </tr> </tbody> </table> <p>(measurement of significance between groups at each time point)</p> <p>CT scan antero-posterior diameter: median (range)</p> <table border="1" data-bbox="94 787 938 896"> <thead> <tr> <th></th> <th>MWA</th> <th>RFA</th> <th>p value</th> </tr> </thead> <tbody> <tr> <td>Baseline (tumour diameter)</td> <td>12 mm (6 to 24)</td> <td>12 mm (7 to 17)</td> <td>> 0.792</td> </tr> <tr> <td>Post-operative (ablation diameter)</td> <td>26 mm (14 to 60)</td> <td>35 mm (28 to 40)</td> <td>0.046</td> </tr> </tbody> </table> <p>(measurement of significance between groups at each time point)</p> <p>CT scan cranio-caudal diameter: median (range)</p> <table border="1" data-bbox="94 1003 943 1113"> <thead> <tr> <th></th> <th>MWA</th> <th>RFA</th> <th>p value</th> </tr> </thead> <tbody> <tr> <td>Baseline (tumour diameter)</td> <td>10.5 mm (6 to 20)</td> <td>11 mm (8 to 20)</td> <td>> 0.792</td> </tr> <tr> <td>Post-operative (ablation diameter)</td> <td>20 mm (10 to 73)</td> <td>32 mm (20 to 45)</td> <td>0.025</td> </tr> </tbody> </table> <p>(measurement of significance between groups at each time point)</p>		MWA	RFA	p value	Baseline (tumour diameter)	12 mm (6 to 18)	12 mm (7 to 24)	> 0.792	Post-operative (ablation diameter)	18.5 mm (12 to 64)	34 mm (16 to 41)	0.003		MWA	RFA	p value	Baseline (tumour diameter)	12 mm (6 to 24)	12 mm (7 to 17)	> 0.792	Post-operative (ablation diameter)	26 mm (14 to 60)	35 mm (28 to 40)	0.046		MWA	RFA	p value	Baseline (tumour diameter)	10.5 mm (6 to 20)	11 mm (8 to 20)	> 0.792	Post-operative (ablation diameter)	20 mm (10 to 73)	32 mm (20 to 45)	0.025	<p>No perioperative mortality was reported.</p> <p>Haemobilia (resolved with conservative treatment) was reported in 1 of 6 patients in the microwave ablation group.</p>
	MWA	RFA	p value																																		
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Abbreviations used: CT, computed tomography; MWA, microwave ablation; RFA, radiofrequency ablation; US, ultrasound; W, Watts																																					

Study 7 Yu J (2015)

Details

Study type	Prospective case series
Country	China
Recruitment period	2005-2012
Study population and number	n= 1249 (307 with liver metastases) consecutive patients with primary or metastatic liver tumours.
Age and sex	Mean 59 years; 76% (952/1249) male
Patient selection criteria	Single lesion of 8 cm or smaller; 3 or fewer lesions with a maximum diameter of 4 cm or less in an ablation procedure; absence of portal vein thrombosis or extrahepatic metastases; a normal serum total bilirubin level or one that is less than 60 µmol/L; a normal albumin level or a level that is not less than 25 g/L; platelet count no less than 50x10 ⁹ /mm ³ and prothrombin activity no less than 50 %. The patients had Eastern Cooperative Oncology Group performance status of 0–2 to tolerate the procedure.
Technique	2 cooled-shaft microwave systems (KY-2000, Kangyou Medical) with frequencies of 2,450 MHz and 915 MHz, respectively, were used as well as 2 generators, both capable of producing 100 Watts of power.
Follow-up	Median 20.3 months
Conflict of interest/source of funding	The authors reported no conflict of interest. The study has been supported by 3 grants from the public sector.

Analysis

Follow-up issues:

- One to three days after the last course of a defined ablation protocol, contrast-enhanced imaging was performed to evaluate the treatment efficacy. If complete ablation was achieved, then routine contrast-enhanced imaging and serum tumour markers were repeated at 1 month and 3 months after MWA and then at 6-month intervals.

Study design issues: None.

Study population issues:

- Of patients with metastases primary locations were gastrointestinal = 387, breast = 47, lung = 44, pancreatic = 38, extrahepatic cholangiocarcinoma = 37, ovarian cancer = 26, other = 74.

Other issues:

- Technique effectiveness was defined as complete local necrosis 1 month after MWA treatment.
- Only outcomes relating to patients with liver metastases (not hepatocellular or other primary liver tumours) were extracted.

Key efficacy and safety findings

Efficacy	Safety								
Number of patients analysed: 307 with liver metastases Local tumour progression (LTP) occurrence rate 73% (20/27) LTPs occurred within 1 year, 24% (6/27) occurred between 1 year and 2 years, and only one developed after 2 years. <table border="1" data-bbox="87 1554 451 1711"> <thead> <tr> <th>Follow-up</th> <th>LTP rate</th> </tr> </thead> <tbody> <tr> <td>1 year</td> <td>10%</td> </tr> <tr> <td>2 years</td> <td>15%</td> </tr> <tr> <td>3 years</td> <td>17%</td> </tr> </tbody> </table>	Follow-up	LTP rate	1 year	10%	2 years	15%	3 years	17%	The paper did not provide details of any complications.
Follow-up	LTP rate								
1 year	10%								
2 years	15%								
3 years	17%								
Abbreviations used: LTP, local tumour progression; MWA, microwave ablation.									

Study 8 Groeschl R T (2014)

Details

Study type	Case series
Country	USA (4 centres)
Recruitment period	2003 - 2011
Study population and number	n= 450 consecutive patients with primary or metastatic liver tumours treated by 473 procedures (334 for liver metastases) for a total of 875 tumours
Age and sex	Median 60 years; 62% (293/473) male (data reported for n=473 procedures)
Patient selection criteria	Cirrhotic patients with HCC for whom the risk of hepatectomy was considered unsafe, extensive bilobar metastatic disease where R0 resection was neither safe nor feasible, patients who had undergone previous major liver resection and the anatomy of recurrence in the remnant liver precludes resection, and percutaneous MWA for patients whose comorbid conditions precluded an operation.
Technique	Covidien Evident equipment was used.
Follow-up	Median 18 months
Conflict of interest/source of funding	One of the authors had an active consulting agreement with Covidien, Bard and Baxter, and received unrelated research support from Microsulis. Two of the authors had also an active consulting agreement with Covidien.

Analysis

Follow-up issues:

- Incomplete ablations were identified immediately after the procedure with CT or magnetic resonance imaging.
- Most patients had a quarterly follow-up for 1 year and then were followed biannually thereafter.

Study design issues:

- Some patients underwent concurrent hepatectomy at the time of ablation.
- A small number of patients underwent 2 ablation procedures.

Study population issues:

- Some patients were treated by neoadjuvant or adjuvant chemotherapy.
- The 'other' cancer category included a wide range of malignancies, the most common of which were breast (n=14), cholangiocarcinoma (n=10) and melanoma (n=8).

Other issues:

- Tumour recurrence was defined as 'local' if within 1 cm of the ablation site.
- Only outcomes relating to patients with liver metastases (not hepatocellular tumours) were extracted.

Key efficacy and safety findings

Efficacy				Safety
Number of patients analysed: 334 procedures for liver metastases				Complications were not specifically attributed to the type of tumour.
Recurrence and survival				
	CLM (n=198 procedures)	NLM (n=61 procedures)	Other (n=75 procedures)	
Local recurrence	5% (21/393*)	3% (6/191*)	7% (7/96*)	
Recurrence-free survival				
Median (months)	24.5	33.0	24.9	
3-year	34%	36%	31%	
5 year	9%	11%	9%	
Overall survival				
Median (months)	32.1	91.9	25.5	
3-year	45%	70%	48%	
5 year	17%	54%	23%	
*Completed ablated lesions.				
Abbreviations used: CLM, colorectal liver metastases, CT, computed tomography; HCC, hepatocellular carcinoma; MWA, microwave ablation; NLM, neuroendocrine liver metastases.				

Study 9 Liang P (2009) - included in 2011 overview**Details**

Study type	Case series
Country	China
Recruitment period	1994-2007
Study population and number	n=1136 (257 with metastases) patients with primary or metastatic liver tumours. Of patients with metastases primary locations were colorectal = 86, breast = 49, gastrointestinal = 47, lung = 30, other = 45.
Age and sex	Mean 54 years; 79% (902/1136) male
Patient selection criteria	Patients with tumours of less than 8 cm, and 7 or fewer lesions in total.
Technique	General anaesthetic and ultrasound guidance. Percutaneous MWA with single probe used for lesions < of less than 1.7cm. Ablation at 60 W for 300 seconds.
Follow-up	Not reported
Conflict of interest/source of funding	Authors reported no conflict of interest.

Analysis**Follow-up issues:**

- Patients selected for treatment with MWA rather than other treatment option by an MDT panel.
- 21 of 1157 patients lost to follow-up.
- Prospective follow-up at 1 and 3 months and then 3–6 monthly.

Study design issues:

Two different MWA systems were used during the data collection period; a cooled shaft version was introduced in 2005.

Study population issues: Patient demographics and clinical characteristics relate to the study population as a whole and not specifically patients with metastases.

Other issues: Only outcomes relating to patients with liver metastases (not hepatocellular) were extracted.

Key efficacy and safety findings

Efficacy	Safety															
Number of patients analysed: 1136 (257 with metastases) Efficacy outcomes were not reported.	Major complications Major complications were classified as those leading to substantial morbidity and disability, increasing the level of care required, or that resulted in admission or prolonged hospital stay. <table border="1" data-bbox="771 1386 1429 1711"> <thead> <tr> <th>Outcome</th> <th>Rate</th> <th>Treatment</th> </tr> </thead> <tbody> <tr> <td>Skin burn requiring resection</td> <td><1% (1/257)</td> <td>Full-thickness resection and suture</td> </tr> <tr> <td>Pleural effusion</td> <td>1.6% (4/257)</td> <td>Aspiration or drainage</td> </tr> <tr> <td>Liver abscess</td> <td><1% (2/257)</td> <td>Aspiration or drainage</td> </tr> <tr> <td>Biloma</td> <td><1% (1/257)</td> <td>Drainage</td> </tr> </tbody> </table>	Outcome	Rate	Treatment	Skin burn requiring resection	<1% (1/257)	Full-thickness resection and suture	Pleural effusion	1.6% (4/257)	Aspiration or drainage	Liver abscess	<1% (2/257)	Aspiration or drainage	Biloma	<1% (1/257)	Drainage
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Abbreviations used: MDT, multidisciplinary team; MWA, microwave ablation; W, Watts.																

Study 10 Livraghi T (2012)

Details

Study type	Case series
Country	Italy (14 centres)
Recruitment period	2008-2011
Study population and number	n=736 (187 with metastases) patients with primary or metastatic liver tumours.
Age and sex	Not reported.
Patient selection criteria	Inclusion criteria: disease limited to the liver, operable nodules up to 2 cm, nonoperable nodules between 2 and 5 cm, fewer than 3 lesions at initial presentation, and no substantial coagulopathy. The decision to treat lesions larger than 5 cm in diameter or more than three in number was left to the discretion of the individual treatment centre. MWA also was used as down-staging or bridging therapy to liver transplantation in cirrhotic patients with HCC. MWA was contraindicated when lesions were abutting the main biliary ducts or the bowel in patients with previous abdominal surgery, or when pneumobilia was present.
Technique	MWA was performed using a 2.45-MHz generator (AMICA-GEN) delivering energy through a 14- or 16-gauge internally cooled coaxial antenna (AMICA PROBE). According to the tumour size, a single microwave energy application was delivered to the patient, ranging from 60 to 100 W net power at the applicator end, for 5–15 min. Generally, the intended ablation margin was at least 0.5 cm. Contrast-enhanced ultrasound evaluation was usually performed immediately after treatment to verify treatment success.
Follow-up	Not reported.
Conflict of interest/source of funding	The authors declared no conflict of interest.

Analysis

Follow-up issues:

- Patients were evaluated clinically and with contrast material-enhanced computed tomography or magnetic resonance at 1 month after ablation and every 3–4 months thereafter. When indicated, in case of possible complications, these imaging examinations were performed immediately after symptom onset.

Study design issues:

- Retrospective study.
- The analgesia regimen and the prophylactic antibiotic administration were left to the discretion of the investigators.

Study population issues: None.

Other issues: Only outcomes relating to patients with liver metastases (not hepatocellular or other primary liver tumours) were extracted.

Key efficacy and safety findings

Efficacy	Safety																					
<p>Number of patients analysed: 187 with metastases</p> <p>No efficacy outcomes reported.</p>	<p>No death was reported.</p> <p>Major complications: 3% (6/187) Event that, if left untreated, could be life-threatening, lead to substantial morbidity and disability or resulted in prolonged hospital stay of 1 week or more.</p> <table border="1" data-bbox="867 432 1500 785"> <thead> <tr> <th>Outcome</th> <th>Rate</th> <th>Treatment</th> </tr> </thead> <tbody> <tr> <td>Haemothorax, hepatic haematoma</td> <td>1/187</td> <td>Medical therapy</td> </tr> <tr> <td>Biliary stenosis, jaundice</td> <td>1/187</td> <td>Surgical repair</td> </tr> <tr> <td>Peritoneal haemorrhage</td> <td>1/187</td> <td>Blood transfusion</td> </tr> <tr> <td>Hepatic abscess</td> <td>1/187</td> <td>Drainage</td> </tr> <tr> <td>Pneumothorax</td> <td>1/187</td> <td>Drainage</td> </tr> <tr> <td>Tumoral seeding</td> <td>1/187</td> <td>Surgical repair</td> </tr> </tbody> </table> <p>The case of seeding was the only delayed complication.</p> <p>Minor complications: not attributed to cancer diagnosis.</p>	Outcome	Rate	Treatment	Haemothorax, hepatic haematoma	1/187	Medical therapy	Biliary stenosis, jaundice	1/187	Surgical repair	Peritoneal haemorrhage	1/187	Blood transfusion	Hepatic abscess	1/187	Drainage	Pneumothorax	1/187	Drainage	Tumoral seeding	1/187	Surgical repair
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Tumoral seeding	1/187	Surgical repair																				
<p>Abbreviations used: HCC, hepatocellular carcinoma; MWA, microwave ablation.</p>																						

Study 11 Shady W (2014) [conference abstract only]**Details**

Study type	Case series
Country	USA
Recruitment period	2008-2013
Study population and number	n= 26 patients with colorectal liver metastases
Age and sex	Age not reported; 54% (14/26) male
Patient selection criteria	Patients with colorectal liver metastasis of 5 cm or less with no more than 3 liver tumours at the time of ablation.
Technique	MWA
Follow-up	Median 8.5 months
Conflict of interest/source of funding	Not reported.

Analysis**Follow-up issues:**

- Technique effectiveness was assessed on CT 4-8 weeks after ablation. Scans were repeated every 2-4 months to assess for tumour progression.

Study design issues:

- Retrospective review of a clinical ablation database in 1 centre.

Study population issues:

- Median lesion size: 1.8 cm (range 0.7-3.6).

Other issues: None.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 26 Efficacy findings from conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview.	<ul style="list-style-type: none"> • Pneumothorax: 8% (2/26), treated by thoracostomy. • Asymptomatic left portal vein thrombosis with segmental liver infarction: 1/26 • Transient deterioration of pulmonary function in an asthmatic patient who had simultaneous lung ablation: 1/26
Abbreviations used: CT computed tomography; MWA, microwave ablation.	

Efficacy

Survival

An RCT of 30 patients with multiple colorectal liver metastases reported that the 1-year, 2-year and 3-year survival rates were 71%, 57% and 14% respectively in patients treated by microwave ablation (MWA), and 69%, 56% and 23% respectively in patients treated by liver resection. Mean overall survival was 27 months in patients treated by MWA and 25 months in patients treated by liver resection ($p = 0.83$); mean disease-free survival was 11 months and 13 months respectively ($p=0.47$).¹

A non-randomised comparative study of 89 patients treated by MWA ($n=35$) or radiofrequency ablation (RFA; $n=54$) reported overall survival rates at follow-up of 1, 2, 3 and 5 years of 82%, 67%, 56% and 44% respectively for MWA and 87%, 55%, 44% and 32% respectively for RFA (no significant difference between groups).³

A retrospective comparative study of 81 patients (20 patients treated by MWA with or without local resection, 36 patients treated by liver resection, and 25 patients treated palliatively) reported 4-year survival rates of 41% in the whole MWA group, 70% in the liver resection group and 4% in the palliative treatment group (significant survival benefit reported in patients treated by MWA compared with the palliative treatment group). The same study reported that 50% (10/20) of patients treated by MWA were still alive at a median follow-up of 30 months and 25% (5/20) were disease-free.⁴

A non-randomised controlled study of 53 patients with liver metastases reported overall survival rates at follow-up of 1 year, 3 years and 5 years of 80%, 51% and 17% in patients treated by MWA plus resection and of 87%, 49% and 44% in patients treated by resection alone ($p=0.43$ for the overall comparison). Disease-free survival was 33% at 1-year follow-up and 17% at 3-year follow-up in the MWA plus resection group, and 26% at 1 year and 11% at 3 years in the patients treated by resection alone ($p=0.54$ for the overall comparison)⁵.

A case series of 450 patients with primary or metastatic liver tumours reported overall survival rates at follow-up of 3 years and 5 years of 45% and 17% respectively in patients with colorectal liver metastases, of 70% and 54% in patients with neuroendocrine liver metastases, and of 48% and 23% in the patients with other liver metastases. The same study also reported median overall survival of 32 months in patients with colorectal liver metastases, 92 months in patients with neuroendocrine liver metastases and 25 months in patients with other liver metastases.⁸

Recurrence

A retrospective matched-cohort comparative study of 134 patients treated by MWA ($n=67$) or RFA ($n=67$) reported recurrence rates at the site of ablation of

6% in the MWA group at a median follow-up of 18 months and 20% in the RFA group at a median follow-up of 31 months ($p < 0.001$). The same study reported ablation-site recurrence rates at 2-year follow-up of 7% for MWA and 18% for RFA ($p = 0.01$).²

The non-randomised comparative study of 89 patients reported local recurrence in 9% (3/35) of patients in the MWA group and in 20% (11/54) of patients in the RFA group at a mean follow-up of 32 months ($p = 0.072$). Distant recurrence (defined by the presence of intrahepatic new tumours nodules) was reported in 43% (15/35) of patients in the MWA group and in 56% (30/54) of patients in the RFA group ($p = 0.242$).³

The retrospective comparative study of 81 patients reported recurrence of new lesions in 85% (17/20) of patients treated by MWA at a median follow-up of 25 months⁴.

In the non-randomised controlled study of 53 patients, there was no significant difference in hepatic recurrence-free survival between the patients treated by MWA plus resection and the patients treated by resection only; rates were 56% at 1-year follow-up and 39% at 3 years and 5 years in the MWA plus resection group, and 55%, 42% and 35% respectively in the resection-only group ($p = 0.86$ for the overall comparison)⁵.

The matched-cohort comparative study of 19 patients reported local recurrence in 1 patient out of 6 treated by MWA and in none treated by RFA (no further details provided)⁶.

The case series of 450 patients (334 procedures for liver metastases) reported local recurrence in 5% (34/680) of completely ablated lesions. The same study reported median recurrence-free survival lengths of 24 months in patients with colorectal liver metastases, 33 months in patients with neuroendocrine liver metastases and 25 months in patients with other liver metastases. Recurrence-free survival rates at 3-year and 5-year follow-up were 34% and 9% respectively in patients with colorectal liver metastases, 36% and 11% in patients with neuroendocrine liver metastases, and 31% and 9% in patients with other liver metastases⁸.

Tumour response

The non-randomised comparative study of 89 patients reported complete ablation rates at 1 month after the procedure in 94% (58/62) of tumours in the MWA group and in 84% (59/70) of tumours in the RFA group ($p = 0.094$).³

A prospective case series of 1249 patients with primary or metastatic liver tumours (307 with liver metastases) reported local tumour progression rates of 10% at 1-year follow-up, 15% at 2 years and 17% at 3-year follow-up; 73% (20/27) occurred within 1 year, 24% (6/27) between 1 and 2 years and 1 developed after 2 years⁷.

Safety

Mortality

There were no procedure-related deaths following MWA reported in an RCT of 30 patients¹ or in 4 comparative studies of 89, 81, 53 and 19 patients³⁻⁶.

Peritoneal haemorrhage

Peritoneal haemorrhage was reported in 1 patient in a case series of 736 patients (187 with metastases) treated by MWA; the patient was treated by blood transfusion (no further details provided)¹⁰.

Haemobilia

Haemobilia was reported in 1 patient out of 6 treated by MWA in the matched-cohort comparative study of 19 patients treated by MWA or RFA; this was managed conservatively (no further details provided)⁶.

Hepatic abscess

Hepatic abscess was reported in 1 patient out of 14 treated by MWA in the RCT of 30 patients treated by MWA or RFA; this was treated by antibiotics (no further details provided).¹

Multiple liver abscesses were reported in 1 patient out of 20 treated by MWA in the retrospective comparative study of 81 patients; the abscesses were drained percutaneously and treated by antibiotics.⁴

Liver abscess was reported in 2 patients with liver metastases in a case series of 1136 patients (257 with metastases) treated by MWA; these were treated by aspiration or drainage (no further details provided)⁹.

Hepatic abscess was reported in 1 patient in the case series of 736 patients (187 with metastases): this was treated by drainage (no further details provided)¹⁰.

Fistula

Bile duct fistula was reported in 1 patient out of 14 treated by MWA in the RCT of 30 patients; this was treated by antibiotics (no further details provided).¹

Biliary fistula was reported in 1 patient out of 37 treated by MWA plus resection, and in 1 patient out of 16 treated by resection alone in the non-randomised controlled study of 53 patients (measurement of significance and length of follow-up not reported)⁵.

Biloma

Biloma was reported in 1 patient with liver metastases in the case series of 1136 patients (257 with metastases); this was treated by drainage (no further details provided)⁹.

Jaundice

Jaundice caused by biliary stenosis was reported in 1 patient in the case series of 736 patients (187 with metastases); this was repaired surgically (no further details provided)¹⁰.

Hyperbilirubinemia was reported in 1 patient out of 37 treated by MWA plus resection in the non-randomised controlled study of 53 patients (no further details reported).⁵

Left portal vein thrombosis

Asymptomatic left portal vein thrombosis with segmental liver infarction was reported in 1 patient in a case series of 26 patients with colorectal liver metastases treated by MWA (no further details provided)¹¹.

Respiratory problems

Respiratory problems were reported in 15% (3/20) of patients treated by MWA in the retrospective comparative study of 81 patients; they were treated by non-invasive ventilation support and were reported to be mainly associated with complications from the colorectal surgery (no further details reported).⁴

Transient deterioration of pulmonary function was reported in 1 patient who was asthmatic and who had a simultaneous lung ablation in the case series of 26 patients (no further details reported)¹¹.

Pneumothorax

Pneumothorax was reported in 1 patient in the case series of 736 patients (187 with metastases); this was treated by drainage (no further details provided)¹⁰.

Pneumothorax was reported in 8% (2/26) of patients in the case series of 26 patients; this was treated by thoracostomy¹¹.

Pleural effusion

Pleural effusion was reported in 1 patient out of 20 treated by MWA in the retrospective comparative study of 81 patients; it was treated by percutaneous drainage.⁴

Pleural effusion was reported in 2% (4/257) of patients with liver metastases in the case series of 1136 patients (257 with metastases); this was treated by aspiration or drainage (no further details provided)⁹.

Haemothorax

Haemothorax with intrahepatic haematoma was reported in 1 patient in the case series of 736 patients (187 with metastases); this was treated by drainage (no further details provided)¹⁰.

Skin burn

Skin burn was reported in 1 patient with liver metastases in the case series of 1136 patients (257 with metastases); this was treated by full-thickness resection and suture (no further details provided)⁹.

Infection

Infection was reported in 1 patient out of 37 treated by MWA plus resection in the non-randomised controlled study of 53 patients (no further details reported)⁵.

Ileus

Intestinal obstruction was reported in 8% (3/37) of patients treated by MWA plus resection in the non-randomised controlled study of 53 patients (no further details reported).⁵

Tumour seeding

Tumour seeding was reported in 1 patient in the case series of 736 patients (187 with metastases); this was treated surgically (no further details provided)¹⁰.

Validity and generalisability of the studies

- Only 1 RCT¹ is included in table 2 and this RCT was already included in the previous overview.
- 5 comparative studies²⁻⁶ are now included in table 2. Three^{2, 4, 6} of them included a matched comparative group.
- 1 conference abstract¹¹ has been included for data reporting on safety events.
- Most studies also included patients with primary liver cancer and metastases, and results not always reported separately for these groups.
- Some studies report outcomes per patient and some per tumour, making comparison between studies difficult.

Existing assessments of this procedure

- A health technology assessment of the clinical effectiveness and cost-effectiveness of ablative therapies in the management of liver metastases: systematic review and economic evaluation was published by the National Institute for Health Research in 2014¹². It states:
 - ‘There is currently limited high-quality research evidence upon which to base any firm decisions regarding ablative therapies for liver metastases.

Further trials should compare ablative therapies with surgery, in particular. A RCT would provide the most appropriate design for undertaking any further evaluation and should include a full economic evaluation, but the group to be randomised needs careful selection.'

- A Cochrane review¹³ on microwave coagulation for liver metastases was published by The Cochrane Collaboration in 2013. It states:

'Evidence is insufficient to allow assessment of the effect of microwave coagulation versus conventional liver surgery in liver metastases. Microwave coagulation cannot be recommended outside randomized clinical trials.'
- An assessment¹⁴ of microwave ablation for hepatic metastases was published by the American College of surgeons in 2012. It states:

'The evidence base for microwave ablation for the treatment of hepatic metastases is limited. There are very few studies and these are small and may be typically characterized as 'phase II clinical trials' designed to evaluate the short-term therapeutic effect of microwave ablation in patients who suffer from the target disease; they confirm the safety outcomes established in smaller pilot studies. Much larger randomized clinical trials need to be conducted to determine whether an MWA is, in terms of safety and effectiveness, either equivalent to or superior to other treatment modalities. It is only after larger trials are run and assessed that it will be possible to determine whether MWA has a place in the treatment of patients with hepatic metastases and which types would benefit most.'

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Laparoscopic liver resection. NICE interventional procedure guidance 135 (2005). Available from <http://www.nice.org.uk/guidance/ipg135>

- Radiofrequency-assisted liver resection. NICE interventional procedure guidance 211 (2007). Available from <http://www.nice.org.uk/guidance/ipg211>
- Microwave ablation for hepatocellular carcinoma. NICE interventional procedure guidance 214 (2007). Available from <http://www.nice.org.uk/guidance/ipg214>
- Radiofrequency ablation for the treatment of colorectal liver metastases. NICE interventional procedure guidance 327 (2009). Available from <http://www.nice.org.uk/guidance/ipg327>
- Cryotherapy for the treatment of liver metastases. NICE interventional procedure guidance 369 (2010). Available from <http://www.nice.org.uk/guidance/ipg369>
- Selective internal radiation therapy for non-resectable colorectal metastases in the liver. NICE interventional procedure guidance 401 (2011). Available from <http://www.nice.org.uk/guidance/ipg401>
- Irreversible electroporation for treating liver metastases. NICE interventional procedure guidance 445 (2013). Available from <http://www.nice.org.uk/guidance/ipg445>
- Chemosaturation via percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic liver cancer. NICE interventional procedure guidance 488 (2014). Available from <http://www.nice.org.uk/guidance/ipg488>

NICE guidelines

- Colorectal cancer. NICE guideline CG131 (2011). Available from <http://www.nice.org.uk/guidance/cg131/>

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Four

Specialist Advisor Questionnaires for microwave ablation for treating liver metastases were submitted and can be found on the [NICE website](#).

Patient commentators' opinions

NICE's Public Involvement Programme sent 20 questionnaires to 1 NHS trust for distribution to patients who had the procedure (or their carers). NICE received 5 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Issues for consideration by IPAC

- Data have been included for metastases from all primary sites.
- Studies including microwave ablation by any approach (laparoscopic/open/percutaneous) have been included as in previous guidance, and many studies include a mixture of these approaches.
- Ongoing trial:
 - NCT01867918 A Randomized Study With Palliative Chemotherapy With or Without Local Treatment of Liver Metastases in Patients With Colo-rectal Cancer (LOTCOL study). Location: Norway. Recruiting. Enrolment: 80 patients. Estimated completion date: December 2017.

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4. Engstrand J, Nilsson H, Jansson A et al. (2014) A multiple microwave ablation strategy in patients with initially unresectable colorectal cancer liver metastases - A safety and feasibility study of a new concept. *European Journal of Surgical Oncology* 40:1488-1493.
5. Tanaka K, Shimada H, Nagano Y et al. (2006) Outcome after hepatic resection versus combined resection and microwave ablation for multiple bilobar colorectal metastases to the liver. *Surgery* 139:263-273.
6. Hompes R, Fieuws S, Aerts R et al. (2010) Results of single-probe microwave ablation of metastatic liver cancer. *European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology* 36:725-730.
7. Yu J, Liang P, Yu XL et al. (2015) Local tumour progression after ultrasound-guided microwave ablation of liver malignancies: risk factors analysis of 2529 tumours. *European Radiology* 25:1119-1126.
8. Groeschl RT, Pilgrim CH, Hanna EM et al. (2014) Microwave ablation for hepatic malignancies: a multiinstitutional analysis. *Annals of Surgery* 259:1195-1200.
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13. Bala MM, Riemsma RP, Wolff R et al. (2013) Microwave coagulation for liver metastases. [Review]. *Cochrane Database of Systematic Reviews* 2013, Issue 10. Art. No.: CD010163. DOI: 10.1002/14651858.CD010163.pub2.
14. Horizon Scanning in Surgery: Application to Surgical Education and Practice. Microwave ablation for hepatic metastases. Prepared by the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical for the American College of Surgeons. December 2012.

Appendix A: Additional papers on microwave ablation for treating liver metastases

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Abe H, Kurumi Y, Naka S et al. (2005) Open-configuration MR-guided microwave thermocoagulation therapy for metastatic liver tumors from breast cancer. <i>Breast Cancer</i> 12: 26–31	n = 8 Follow-up = 26 months	No major complications; 5 patients alive with new metastatic foci	Larger series included in table 2.
Ahmad F, Strickland AD, Wright GM et al. (2005) Laparoscopic microwave tissue ablation of hepatic metastasis from a parathyroid carcinoma. <i>European Journal of Surgical Oncology</i> 31: 321–2	n = 1 Follow-up = 15 months	No local or distal recurrence at final follow-up	Larger series included in table 2.
Alexander ES, Wolf FJ, Machan JT et al. (2015) Microwave ablation of focal hepatic malignancies regardless of size: A 9-year retrospective study of 64 patients. <i>European Journal of Radiology</i> 84:1083-1090.	Retrospective case series n= 64 (25 hepatocellular carcinoma, 27 metastatic colorectal cancer, 12 other cancers) Follow-up = not reported	At 1 year, Kaplan-Meier analysis predicted a likelihood of local recurrence of 40% in hepatocellular carcinoma patients, 46% in colorectal cancer metastases patients, and 71% in patients with other metastases. Median cancer specific survivals for patients were 38.3 months for hepatocellular carcinoma patients, 36.3 months for colorectal cancer metastases, and 13.9 months for other histological-types. Complications occurred in 23.4% (15/64) of sessions.	Larger studies already included in table 2. The complications were not reported specifically for the treatment of liver metastases.

Eng OS, Tsang AT, Moore D et al. (2015) Outcomes of microwave ablation for colorectal cancer liver metastases: A single center experience. <i>Journal of Surgical Oncology</i> .111 (4) 410-413.	n = 33 Follow-up = 531 days	Intraoperative microwave ablation is a safe and effective modality for use in the treatment of colorectal cancer liver metastases in tumours as large as 5.5 cm.	Larger series included in table 2.
Groeschl RT, Wong RK, Quebbeman EJ et al. (2013) Recurrence after microwave ablation of liver malignancies: a single institution experience. <i>HPB</i> 15:365-371.	n = 72 patients with 83 tumours (59 liver metastases tumours) Follow-up = 16 months	MWA is safe and feasible for local control of liver tumours.	Larger series included in table 2.
Hakime A, Tselikas L, Otmazguine Y et al. (2015) Artificial Ascites for Pain Relief During Microwave Ablation of Subcapsular Liver Tumors. <i>Cardiovasc Intervent Radiol</i> .	n = 41(20 MWA without artificial ascites versus 21 MWA with artificial ascites)	Artificial ascites prevents immediate post-procedural pain, which re-appears intensively 4 days later.	Only efficacy outcome reported was pain.
Hatzidakis A, Zervakis N, and Krokidis M. (2013) Fatal arterial hemorrhage after microwave ablation of multiple liver metastases: The lessons learned. <i>Interventional Medicine and Applied Science</i> .5 (3) 140-143.	n = 1 Follow-up = 5 days	The patient died 5 days after the procedure of liver failure.	Larger series included in table 2.
Iannitti DA, Martin RC, Simon CJ et al. (2007) Hepatic tumor ablation with clustered microwave antennae: the US Phase II trial. <i>HPB</i> 9:120-124.	n = 87 (64 with metastases) 224 tumours Follow-up: 19 months	Microwave ablation is a safe and effective technology for hepatic tumour ablation.	Larger series included in table 2.
Idani H, Narusue M, Kin H et al. (2001) Hepatic resection for liver metastasis of sigmoid colon cancer after incomplete percutaneous microwave coagulation therapy. <i>Hepato-Gastroenterology</i> 48: 244–6	n = 1 Follow-up = 22 months	Incomplete necrosis required surgical resection	Larger series included in table 2. Follow up treatment of resection in case of failed microwave coagulation
Ierardi AM, Floridi C, Fontana F et al. (2013) Microwave ablation of liver metastases to overcome the limitations of radiofrequency ablation. <i>Radiologia Medica</i> 118:949-961.	n = 25 Follow-up = 12 months	Percutaneous MWA of liver metastases >3 cm or located near vessels (>3 mm) can be considered a valid and safe option, probably preferable to RFA. Further studies are required to confirm these encouraging initial results.	Larger series included in table 2.
Jagad RB, Koshariya M, Kawamoto J et al (2008) Laparoscopic microwave ablation of liver tumors: our experience. <i>Hepato-Gastroenterology</i> 55	n = 57 (46 with metastases) Follow-up = 21 months	Laparoscopic microwave ablation is a feasible and safe alternative to open microwave ablation of the liver tumors. It carries all the advantage of minimal invasive surgery. In experienced hands,	Larger series included in table 2.

(81) 27-32		microwave ablation using laparoscopic technique can be done safely and effectively	
Jiao D, Qian L, Zhang Y et al (2010) Microwave ablation treatment of liver cancer with 2,450-MHz cooled-shaft antenna: an experimental and clinical study. Journal of Cancer Research & Clinical Oncology 136 (10) 1507-1516	n = 60 (20 with metastases) Follow-up = 17 months	Effective local tumour control was achieved during one microwave ablation session	Larger series included in table 2.
Kitchin D, Lubner M, Ziemlewicz T et al. (2014) Microwave ablation of malignant hepatic tumours: Intraperitoneal fluid instillation prevents collateral damage and allows more aggressive case selection. International Journal of Hyperthermia.30 (5) 299-305.	n= 87 (28 with liver metastases) Follow-up = at least 1 month	Intraperitoneal fluid administration is a safe and effective method of protecting non-target structures during percutaneous hepatic microwave ablation. While hydrodisplacement for bowel protection allows more aggressive case selection, these cases were associated with higher rates of local tumour progression.	Larger series included in table 2.
Leung U, Kuk D, D'Angelica M et al. (2015) Long-term outcomes following microwave ablation for liver malignancies. British Journal of Surgery 102:85-91.	n = 176 with 416 tumours (81% colorectal liver metastases tumours) Follow-up = 20 months	MWA of liver malignancies, either combined or not combined with liver resection, and selective regional and systemic therapy resulted in good long-term survival. Local recurrence rates were low after treatment of tumours smaller than 3 cm in diameter, and those remote from vessels.	Larger series included in table 2.
Li M, Yu X, Liang P et al. (2015) Ultrasound-guided percutaneous microwave ablation for hepatic malignancy adjacent to the gallbladder. International Journal of Hyperthermia 31:579-587.	Comparative study n=64 liver metastases (18 liver metastases adjacent to the gallbladder versus 46 liver metastases not adjacent to the gall bladder) Follow-up =mean 30 months	Complete ablation: 88% (56/64) Local progression: 25% (16/64) Under strict temperature monitoring, US-guided percutaneous MW ablation assisted with ethanol injection appears to be safe and can achieve a high rate of complete ablation for the treatment of hepatic malignant tumours adjacent to the gallbladder	Larger studies or studies with longer follow-up already included in table 2. The complications were not reported specifically for the treatment of liver metastases.

Li X, Fan WJ, Zhang L et al. (2013) CT-guided percutaneous microwave ablation of liver metastases from nasopharyngeal carcinoma. <i>Journal of Vascular & Interventional Radiology</i> 24:680-684.	n = 18 Follow-up = 22 months	CT-guided MWA is safe and offers an effective treatment alternative for local tumour control in selected patients with liver metastases from nasopharyngeal carcinoma.	Larger series included in table 2.
Liang P, Dong B, Yu X et al. (2003) Prognostic factors for percutaneous microwave coagulation therapy of hepatic metastases. <i>AJR Am J Roentgenol.</i> 181:1319-1325.	n = 74 Follow-up: 25 months	The cumulative survival rates of all 74 patients were 91% at 1 year, 60% at 2 years, 46% at 3 years, 29% at 4 years, and 29% at 5 years. No severe complications occurred.	Larger series included in table 2.
Lloyd DM, Lau KN, Welsh F et al. (2011) International multicentre prospective study on microwave ablation of liver tumours: preliminary results. <i>HPB</i> 13:579-585.	n = 140 (114 MWA alone and 26 MWA+resection) Follow-up = 6 months	These multi-institution data demonstrate rapid ablation time and low morbidity and mortality rates in patients undergoing operative MWA with a high rate of multiple ablations and concomitant hepatic resection.	Larger series with longer follow-up included in table 2.
Lorentzen T, Skjoldbye BO, and Nolsoe CP. (2011) Microwave ablation of liver metastases guided by contrast-enhanced ultrasound: experience with 125 metastases in 39 patients. <i>Ultraschall in der Medizin</i> 32:492-496.	n = 39 Follow-up = 11 months	Contrast-enhanced ultrasound guided MWA of liver metastases is an efficient and safe ablation technique with several advantages compared to other ablation modalities.	Larger series included in table 2.
Martin RC, Scoggins CR, and McMasters KM. (2010) Safety and efficacy of microwave ablation of hepatic tumors: a prospective review of a 5-year experience. <i>Annals of Surgical Oncology</i> 17:171-178.	n = 100 (83 with metastases) Follow-up: 3 years	Microwave ablation of hepatic tumours is a safe and effective method for treating unresectable hepatic tumours, with a low rate of local recurrence.	Larger series included in table 2.
Mitsuzaki K, Yamashita Y, Nishiharu T et al. (1998) CT appearance of hepatic tumors after microwave coagulation therapy. <i>AJR American Journal of Roentgenology</i> 171: 1397-403	n = 63 Follow-up = not reported	Complications included abscess n = 4, haematoma n = 2, nodular dissemination n = 3, ascites n = 5 and portal vein thrombosis n = 1	Only 9 of the 63 cases had secondary metastases the other 53 had primary tumours. Outcomes were not reported separately for each group Larger series included in table 2
Ong SL, Gravante G, Metcalfe MS et al (2009) Efficacy and safety of microwave ablation for primary and secondary liver malignancies: A systematic review. <i>European Journal of</i>	n = 328 metastases Follow-up = not reported	MW ablation is a minimally invasive technique that has broadened the therapeutic option for patients with conventionally unresectable liver tumours with promising survival data. Future advances in the applicator design and treatment monitoring may further improve its efficacy and	Systematic review with no meta-analysis. Mixed patient population with HCC and liver metastases without outcomes reported

Gastroenterology and Hepatology 21 (6) 599-605		widen the indications	separately. All studies included with liver metastases populations are included elsewhere in this overview
Pathak S, Jones R, Tang JM et al. (2011) Ablative therapies for colorectal liver metastases: a systematic review. [Review]. Colorectal Disease 13:e252-e265.	n = 406 MWA patients from 13 studies Follow-up = minimum 1 year	Ablative therapies offer significantly improved survival compared with palliative chemotherapy alone with 5-year survival rates of 17-24%. Complication rates amongst commonly used techniques are low.	Systematic review with no meta-analysis.
Percivale A, Griseri G, Gastaldo A et al. (2012) Microwave assisted liver resection: clinical feasibility study and preliminary results. Minerva Chirurgica 67:415-420.	n = 10 Follow-up = not reported	This study suggests surgical advantages in terms of statement for best practice in oncologic resection of liver malignancy. It allows a complete resection obtaining a negative pathologic margin, no blood loss and need for blood transfusions factors predicting post operative morbidity and survival, and consistently reducing time of procedure and avoidance of parenchymal ischemia.	Larger series included in table 2.
Sato M, Watanabe Y, Kashu Y et al. (1998) Sequential percutaneous microwave coagulation therapy for liver tumor. American Journal of Surgery 175: 322-4	n = 6 Follow-up = not reported	3 patients undergoing curative MW coagulation had no recurrence	Larger series included in table 2.
Seki T, Wakabayashi M, Nakagawa et al (1999) Percutaneous microwave coagulation therapy for solitary metastatic liver tumours from colorectal cancer. A pilot clinical study. The American Journal of Gastroenterology 94: 322-327	n = 15 Follow-up = not reported	Percutaneous microwave coagulation therapy is a safe and effective treatment for metachronous small liver tumours that have metastasized from colorectal cancer	Larger series included in table 2.
Shibata T, Yamamoto Y, Yamamoto N et al. (2003) Cholangitis and liver abscess after percutaneous ablation therapy for liver tumors: incidence and risk factors. Journal of Vascular and Interventional Radiology: JVIR 14: 1535-1542	n = 70 Follow-up = not reported	Cholangitis or liver abscess occurred in 10 patients (1.5% of treatments)	Outcomes of patients with hepatocellular carcinoma or secondary metastases are not distinguished.
Stattner S, Jones RP, Yip VS et al. (2013) Microwave ablation with or without resection for colorectal liver	n = 43 Follow-up = 15 months	MWA is a safe and effective method of achieving disease control for small non-resectable colorectal liver metastases.	Larger series included in table 2.

metastases. European Journal of Surgical Oncology 39:844-849.		Combined resection MWA offers good medium term outcomes, comparable to that seen after 2-stage resection on an intention to treat basis and may therefore be a safe alternative.	
Tanemura H, Ohshita H, Kanno A et al. (2002) A patient with small-cell carcinoma of the stomach with long survival after percutaneous microwave coagulating therapy (PMCT) for liver metastasis. International Journal of Clinical Oncology 7: 128–32	n = 1 Follow-up = 33 months	Complete necrosis on CT scan and no recurrence to final follow-up	Larger series included in table 2.
Tropea A, Biondi A, Corsaro A et al. (2014) Combined microwave thermal ablation and liver resection for single step treatment of otherwise unresectable colorectal liver metastases; a monoinstitutional experiences. European Review for Medical and Pharmacological Sciences.18 (6-10).	n = 5 Follow-up = 12 months	Hepatic resection combined with MWA expanded indications for operative treatment of multiple bilobar liver metastasis. This procedure promise to have good long-term outcomes.	Larger series included in table 2.
Umeda T, Abe H, Kurumi Y et al. (2005) Magnetic resonance-guided percutaneous microwave coagulation therapy for liver metastases of breast cancer in a case. Breast Cancer 12: 317–21	n = 1 Follow-up = 15 months	No recurrence of metastatic tumour at final follow-up	Larger series included in table 2.
Veltri A, Gazzera C, Rotondella C et al. (2012) Image-guided microwave ablation of hepatic tumours: preliminary experience. Radiologia Medica 117:378-392.	n = 15 (9 with liver metastases) Follow-up = 8 months	MWA proved to be feasible and safe in treating advanced-stage liver tumours and represented an additional therapeutic attempt to be validated in further and larger efficacy studies.	Larger series included in table 2.
Violari EG, Petre EN, Feldman DR et al. (2015) Microwave Ablation (MWA) for the Treatment of a Solitary, Chemorefractory Testicular Cancer Liver Metastasis. Cardiovascular & Interventional Radiology 38:488-493.	n= 1 Follow-up = 35 months	After initial failure of laser, MWA of the chemorefractory liver metastasis resulted in prolonged local tumour control and rendered the patient disease-free for more than 35 months, allowing him to regain an improved quality of life.	Larger series included in table 2.
Vogl TJ, Farshid P, Naguib NN et al. (2014) Thermal ablation of liver metastases from colorectal cancer: radiofrequency, microwave and laser ablation therapies. [Review]. Radiologia Medica 119:451-461.	n = 14 studies Follow-up = 5-19 months	Reviewed literature showed a local progression rate between 3-13 % of MW ablated lesions at 5-19 months follow-up. Major complications were observed in 0-19 % of patients treated with MWA. The mean of 1-, 3- and 5-year survival rates for MWA were	Systematic review with no meta-analysis.

		79, 39, 21 % respectively. The median survival in these methods was 29.5 months.	
Wang J, Liang P, Yu J et al. (2014) Clinical outcome of ultrasound-guided percutaneous microwave ablation on colorectal liver metastases. <i>Oncology Letters</i> .8 (1) 323-326).	n = 115 Follow-up = 28 months.	Ultrasound-guided percutaneous MWA is a safe and competent way to treat inoperable colorectal liver metastases.	Larger series included in table 2.
Yamashita Y, Sakai T, Maekawa T et al. (1998) Thoracoscopic transdiaphragmatic microwave coagulation therapy for a liver tumor. <i>Surgical Endoscopy</i> 12: 1254-8	n = 6 Follow-up = 4 23 months	Average length of stay was 11 days, no recurrence during follow-up period	Larger series included in table 2.
Yu MA, Liang P, Yu XL et al. (2011) Liver abscess as a complication of microwave ablation for liver metastatic cholangiocarcinoma after bilioenteric anastomosis. <i>International Journal of Hyperthermia</i> 27:503-509.	n = 5 Follow-up = 14 months	There is a high incidence of abscess formation due to multiple risk factors when MWA was used for treatment of intrahepatic metastatic cholangiocarcinoma with bilioenteric anastomosis. Understanding the causes and grasping disposal methods will help to avoid or successfully cure this major complication.	Larger series included in table 2.
Zhang X, Chen B, Hu S et al. (2008) Microwave ablation with cooled-tip electrode for liver cancer: an analysis of 160 cases. <i>Hepato-Gastroenterology</i> 55:2184-2187.	n = 160 (63 with metastases) Follow-up: not reported	Microwave ablation with this novel cooled-tip electrode is safe, minimally invasive and effective.	Larger series included in table 2.

Appendix B: Related NICE guidance for microwave ablation for treating liver metastases

Guidance	Recommendations
Interventional procedures	<p>Laparoscopic liver resection. NICE interventional procedure guidance 135 (2005).</p> <p>1.1 Current evidence on the safety and efficacy of laparoscopic liver resection appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance.</p> <p>1.2 Patient selection for laparoscopic liver resection should be carried out by a multidisciplinary team. Surgeons undertaking laparoscopic liver resection should have specialist training and expertise both in laparoscopic techniques and in the specific issues relating to liver surgery.</p> <p>Radiofrequency-assisted liver resection. NICE interventional procedure guidance 211 (2007).</p> <p>1.1 Limited evidence on the safety and efficacy of radiofrequency (RF)-assisted liver resection appears adequate to support the use of this procedure as one of the options for liver resection, provided that the normal arrangements are in place for consent, audit and clinical governance.</p> <p>Microwave ablation for hepatocellular carcinoma. NICE interventional procedure guidance 214 (2007).</p> <p>1.1 Current evidence on the safety and efficacy of microwave ablation of hepatocellular carcinoma appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance.</p> <p>1.2 Patient selection should be carried out by a multidisciplinary team that includes a hepatobiliary surgeon.</p> <p>1.3 The procedure should be performed under appropriate imaging guidance.</p> <p>1.4 A number of devices are available, and there is some uncertainty about the energy levels that should be used. Any adverse events relating to this procedure should be reported to the Medicines and Healthcare products Regulatory Agency.</p> <p>1.5 Further research on long-term survival outcomes and comparisons of microwave ablation with other ablative techniques will be useful.</p> <p>Radiofrequency ablation for the treatment of colorectal</p>

	<p>liver metastases. NICE interventional procedure guidance 327 (2009).</p> <p>1.1 Current evidence on the safety and efficacy of radiofrequency (RF) ablation for colorectal liver metastases is adequate to support the use of this procedure in patients unfit or otherwise unsuitable for hepatic resection, or in those who have previously had hepatic resection, provided that normal arrangements are in place for clinical governance, consent and audit.</p> <p>1.2 Patient selection should be carried out by a hepatobiliary cancer multidisciplinary team.</p> <p>Cryotherapy for the treatment of liver metastases. NICE interventional procedure guidance 369 (2010).</p> <p>1.1 Current evidence on the safety of cryotherapy for the treatment of liver metastases appears adequate in the context of treating patients whose condition has such a poor prognosis, but the evidence on efficacy is inadequate in quality. Therefore cryotherapy for the treatment of liver metastases should only be used with special arrangements for clinical governance, consent and audit or research.</p> <p>1.2 Clinicians wishing to undertake cryotherapy for the treatment of liver metastases should take the following actions.</p> <ul style="list-style-type: none"> • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand that other ablative treatments are available and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having cryotherapy for liver metastases (see section 3.1). <p>1.3 Patient selection and treatment should be carried out by a hepatobiliary multidisciplinary team with expertise in the use of ablative techniques.</p> <p>Selective internal radiation therapy for non-resectable colorectal metastases in the liver. NICE interventional procedure guidance 401 (2011).</p> <p>1.1 Current evidence on the safety of selective internal radiation therapy (SIRT) for non-resectable colorectal metastases in the liver is adequate.</p> <p>1.2 The evidence on its efficacy in chemotherapy-naive patients is inadequate in quantity. Clinicians should offer eligible patients who have not been previously treated by chemotherapy entry into well-designed research studies such as the FOXFIRE trial. For patients who are not eligible or who</p>
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	<p>prefer not to enter a research trial, the procedure should be used with special arrangements for clinical governance, consent and audit.</p> <p>1.3 For patients who have previously been treated with chemotherapy, there is evidence that SIRT can prolong time to progression of hepatic metastases, but more evidence is required on survival and quality of life (see section 1.7). Therefore for patients who have been previously treated with chemotherapy this procedure should be used with special arrangements for clinical governance, consent and audit.</p> <p>1.4 Clinicians undertaking the procedure for patients outside research studies should take the following actions.</p> <ul style="list-style-type: none"> • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended. • Clinicians should enter details for all patients undergoing selective internal radiation therapy for non-resectable colorectal metastases in the liver onto the UK SIRT register and review clinical outcomes locally. <p>1.5 Patients should be selected for SIRT or entry into trials by a hepatobiliary cancer multidisciplinary team including an interventional radiologist, in liaison with a colorectal cancer multidisciplinary team.</p> <p>1.6 SIRT should only be carried out by clinicians with specific training in its use and in techniques to minimise the risk of side effects of the procedure.</p> <p>1.7 The Committee considered that SIRT is a potentially beneficial treatment for patients with non-resectable colorectal metastases in the liver, but that more research and data collection are required to demonstrate its efficacy. A recommendation about research trials for chemotherapy-naïve patients is given in 1.2 above. For patients who have previously been treated with chemotherapy, comparative trials are needed to determine whether SIRT prolongs survival compared with best standard treatment, and to determine its effect on quality of life. There is also a need to identify which subgroups of patients are likely to derive clinical benefit from SIRT. Research studies should clearly describe the characteristics of treated patients, and the extent and histological details of their tumours. Outcomes should include survival and quality of life. Downstaging of metastases allowing resection or ablation should be clearly documented.</p> <p>1.8 NICE may review the procedure on publication of further evidence.</p> <p>Irreversible electroporation for treating liver metastases.</p>
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	<p>NICE interventional procedure guidance 445 (2013).</p> <p>1.1 Current evidence on the safety and efficacy of irreversible electroporation for treating liver metastases is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research. In particular, studies should report the effect of the procedure on local tumour control and patient survival.</p> <p>Chemosaturation via percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic liver cancer. NICE interventional procedure guidance 488 (2014).</p> <p>1.1 Current evidence on the efficacy of chemosaturation via percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic liver cancer ('hepatic chemosaturation') is limited in quality and quantity. With regard to safety, there is a significant incidence of serious adverse effects. Therefore, this procedure should only be performed within the context of research, which may take the form of observational studies.</p> <p>1.2 Patient selection should be done by an appropriate multidisciplinary team.</p> <p>1.3 Hepatic chemosaturation should only be carried out by clinicians with specific training in its use and in techniques to minimise the risk of adverse effects from the procedure.</p> <p>1.4 Research should document indications for treatment, details of patient selection and details of adjuvant and prior treatments. Outcome measures should include complications, survival and quality of life. Data from well-designed trials comparing the procedure against other forms of management would be particularly useful, but prospective observational studies may also be of value.</p>
NICE guidelines	<p>Colorectal cancer. NICE clinical guideline 131 (2014)</p> <p>1.3 Management of metastatic disease</p> <p>1.3.1 Patients presenting with stage IV colorectal cancer</p> <p>1.3.1.1 Prioritise treatment to control symptoms if at any point the patient has symptoms from the primary tumour. [2011]</p> <p>1.3.1.2 If both primary and metastatic tumours are considered resectable, anatomical site-specific MDTs should consider initial systemic treatment followed by surgery, after full discussion with the patient. The decision on whether the operations are done at the same time or separately should be made by the site-specialist MDTs in consultation with the patient. [2011]</p>

Appendix C: Literature search for microwave ablation for treating liver metastases

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	04/01/2016	Issue 1, 2016	32
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	04/01/2016	Issue 1, 2016	60
HTA database (Cochrane Library)	04/01/2015	Issue 1, 2016	1
MEDLINE (Ovid)	04/01/2016	1946 to November Week 3 2015	58
MEDLINE In-Process (Ovid)	04/01/2016	December 31, 2015	69
EMBASE (Ovid)	04/01/2016	1988 to 2015 Week 52	107
PubMed	05/01/2016		2
JournalTOCS	04/01/2016	-	0

Trial sources searched on

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

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

1. ((microwave* or micro-wave*) adj4 (ablat* or coagulat* or therap* or themotherap* or thermoablat*)).tw.
2. (mct or pmct or mwa or mw).tw.
3. Microwaves/tu [Therapeutic Use]
4. or/1-3

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5. ((liver or hepatic*) adj4 (secondar* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metastas*)),tw.

6. Liver Neoplasms/

7. or/5-6

8. 4 and 7

9. Animals/ not Humans/

10. 8 not 9

11. limit 10 to ed=20110430-20150408