

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of microwave ablation for the treatment of metastases in the liver

Microwave ablation is a process that uses the heat from microwave energy to kill cells. When it is used in the treatment of liver cancer that has spread from other parts of the body, the energy is applied directly to the tumour through a special needle.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making 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 overview was prepared in November 2006

Procedure name

- Microwave ablation for secondary liver metastases.

Specialty societies

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

Description

Indications

Liver metastases from primary cancers in other organs, most commonly colorectal cancer.

Current treatment and alternatives

Most patients with metastatic liver disease from colorectal primaries have inoperable lesions. However, for patients with operable colorectal liver metastases, surgical resection could offer the possibility of 5-year survival rates of 25–39%. Metastatic disease from other primaries may also be operable. Most patients are not candidates for surgical resection because of the number or distribution of tumours, and/or the presence of extra-hepatic metastases. A number of non-resective therapies have been developed, and can be used with palliative and sometimes curative intent, including hepatic artery infusion chemotherapy (HAIC), trans-arterial chemoembolisation, percutaneous ethanol injection, cryoablation, laser-induced ablation and radiofrequency ablation.

What the procedure involves

Microwave ablation is a technique that destroys tumours by heating cells, resulting in localised areas of necrosis and tissue destruction. Ablation is a term encompassing both coagulation and destruction of tumour tissue and the surrounding liver tissue. Several types of microwave needle electrodes and generators are available.

The needle electrodes are advanced into the liver tumour(s) either during laparotomy or laparoscopy, or percutaneously under image guidance. They are attached to a generator, and the targeted tumour(s) are ablated. Multiple pulses of energy may be delivered during one session and multiple needle electrodes can be used to treat larger tumours.

The procedure can be performed under local or general anaesthesia.

Efficacy

The key efficacy outcomes for assessment of this procedure as identified by Specialist Advisers, include survival at 3 and 5 years.

Data on the efficacy of microwave ablation for liver metastases were available from one randomised controlled trial and 3 case series. Statistical methods employed to calculate survival varied between studies, making comparison difficult.

Survival

One randomised controlled trial of 30 patients (14 undergoing microwave ablation) reported that the mean survival was 27 months following microwave ablation and 25 months following hepatectomy ($p=0.83$)¹. Disease-free survival was also similar between the groups, being 11.3 and 13.3 months respectively ($p=0.47$)¹.

One case series reported that the mean survival period following microwave ablation was 22 months, and disease-free survival to final follow up (25

months) was achieved in 35 % (26/74) of patients². A second case series of 22 patients with liver metastases treated with microwave ablation found that there was no tumour recurrence during 17 months follow up in 32% (7/22) of patients, and 72% (16/22) survived to 17 months follow up³. A third case series of 74 patients reported that the number of tumours present at baseline ($p=0.03$), the grade of tumour differentiation ($p=0.03$), and recurrence of tumour or development of a new tumours during follow up ($p=0.04$) were all independent predictors of survival in multivariate analysis².

Surgical parameters

One randomised controlled trial reported that there was a statistically significant difference in the volume of operative blood loss during microwave ablation 360 (± 230) ml, and hepatectomy 910 (± 490) ml ($p=0.027$)¹. Also the number of patients requiring a transfusion was significantly lower, 0 and 38 respectively ($p=0.035$). However, there was no significant difference in the mean operative time, or hospital length of stay between the groups¹.

Safety

Reduced pain levels compared to other interventions, complication rates of liver abscess formation, and other 30 day morbidity and mortality were the key safety outcomes identified by Specialist Advisers.

One randomised controlled trial of 30 patients (14 undergoing microwave ablation) reported that there were no intraoperative deaths in either group¹. Two case series of 74² and 22³ patients reported that there were no severe complications following microwave ablation procedures.

Among the patients in the microwave ablation arm of a randomised controlled trial and in one case series the rate of bile duct fistula was reported to be 7% (1/14)¹ and (2/29)⁴. Similarly, the rate of hepatic abscess formation following microwave ablation was 7% (1/14)¹ and (2/29)⁴.

Other complications reported following microwave ablation of liver metastases include minor to moderate pleural effusions in 9% (7/74) of patients, and slight subcapsular bleeding in 3% (2/74) of patients which resolved without transfusion². One case series reporting on a mixed cohort of patients with either liver metastases (7 lesions) or hepatocellular carcinoma (27 lesions) reported fever in 13% (6/24) of patients, and subcutaneous haematoma in 8% (2/24)⁵.

One case series of 79 patients (29 with liver metastases) reported that there were no statistically significant differences in clinical or demographic characteristics between patients who did or did not develop complications following microwave ablation⁴.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to microwave ablation for the treatment of metastases in the liver. Searches were conducted via the following databases, covering the period from their commencement to 02/11/2006: Medline, 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.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these 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, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with liver metastases from other primary cancers
Intervention/test	Microwave ablation of tumours
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy. Relevant outcomes are identified by specialist advisors in the efficacy and safety section above
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 overview

This overview is based on one randomised controlled trial¹ and four case series^{2,3,4,5}.

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.

Existing reviews on this procedure

There were no published reviews identified at the time of the literature search.

Related NICE guidance

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

Interventional procedures:

IPG 092 Radiofrequency ablation for the treatment of colorectal metastases in the liver

<http://www.nice.org.uk/download.aspx?o=IPG092guidance&template=download.aspx>

IPG XXX Microwave ablation of hepatocellular carcinoma (post consultation)

http://www.nice.org.uk/ipcat.aspx?o=IP_370

Technology appraisals:

None

Clinical guidelines:

None

Public health:

None

Table 2 Summary of key efficacy and safety findings on microwave ablation for the treatment of metastases in the liver

Abbreviations used: MW –microwave HR – Hazard ratio, CI – Confidence interval, CT – Computed tomography, HCC – hepatocellular carcinoma.																																																			
Study details	Key efficacy findings	Key safety findings	Comments																																																
<p>Shibata T (2000)¹</p> <p>Randomised controlled trial</p> <p>Japan</p> <p>Study period: Dec 1990 – Aug 1997</p> <p>n = 30 (n = 14 MW coagulation, 16 liver resection)</p> <p>Population: male = 53%, age = 61 years, mean number of tumours = 5.3, mean tumour size 30 mm</p> <p>Indications: patients with primary colorectal carcinoma, and multiple but fewer than 10 metastatic liver tumours (at least one confirmed histologically), largest tumour < 80 mm, and no signs of cirrhosis or chronic hepatitis</p> <p>Technique: open microwave coagulation following laparotomy using a tissue coagulator for a net period between 2 and 20 min at between 60 W and 100 W</p> <p>Hepatic resection including lobectomy, segmentectomy, subsegmentectomy, and/or wedge resection depending on number, location and size of tumours</p> <p>Follow-up: not stated, imaging follow-up at every 3 months</p> <p>Conflict of interest: not stated</p>	<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> <p>Survival</p> <p>The mean survival time was 27 months in the MW group and 25 months in the hepatectomy group (p = 0.83). The mean disease-free interval was 11.3 and 13.3 months, respectively (p N/S 0.47)</p> <p>During the follow up period there were 9 deaths among 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"> <thead> <tr> <th></th> <th>MW</th> <th>Hepatectomy</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>N/S</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>N/S</td> </tr> <tr> <td>Length of stay (days)</td> <td>20 ± 7</td> <td>25 ± 12</td> <td>N/S</td> </tr> <tr> <td></td> <td></td> <td></td> <td>0.23</td> </tr> </tbody> </table>		MW	Hepatectomy	p	Blood loss (ml)	360 ± 230	910 ± 490	0.027	Blood transfused (ml)	0	540 ± 690	N/S	Patients requiring transfusion (%)	0	38	0.035	Operation time (min)	180 ± 20	200 ± 50	N/S	Length of stay (days)	20 ± 7	25 ± 12	N/S				0.23	<p>Operative complications</p> <p>There were no intraoperative deaths in either group</p> <p>Postoperative complications</p> <table border="1"> <thead> <tr> <th></th> <th>MW (n = 14)</th> <th>Hepat (n = 16)</th> <th>p =</th> </tr> </thead> <tbody> <tr> <td>Internal obstruction</td> <td>0</td> <td>1</td> <td>N/S</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>Hepatic function as determined by serum bilirubin and prothrombin time recovered to preoperative normal levels within 2 weeks in both groups</p>		MW (n = 14)	Hepat (n = 16)	p =	Internal obstruction	0	1	N/S	Bile duct fistula	1	1	N/S	Hepatic abscess	1	0	N/S	Wound infection	0	1	N/S	<p>There were no significant differences in clinical or demographic characteristics between the groups at baseline.</p> <p>Randomisation was by computer generated sequence without stratification.</p> <p>No details were provided of blinding.</p> <p>25% (10/40) of patients dropped out during the surgery phase, outcomes for these patients were not compared.</p> <p>No clear reporting of follow-up period and completeness. Cumulative survival calculated by Kaplan–Meier method.</p> <p>No details given of concomitant treatment.</p> <p>MW intervention characteristics differed for treatment of superficial and deeply seated tumours.</p> <p>Authors issued caution in applying microwave coagulation to tumours near a large branch of a bile duct.</p>
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<p>Liang P (2003)²</p> <p>Case series</p> <p>China</p> <p>Study period: Jul 1995 – Mar 2002</p> <p>n = 74</p> <p>Population: male = 59%, age = 27 to 81 years, mean largest tumour size 31 mm. Primary cancer colorectal n=28, gastric / cardiac n=12, lung n=11, breast n=11, other n=11. All patients had undergone resection of primary tumours 5 to 74 months prior to MW ablation. Well differentiated n=9, moderately differentiated n=33, poorly differentiate n=32.</p> <p>Indications: patients with liver metastases confirmed histologically. Patients were not treated surgically due to multiple lesions in multiple segments (78%) or refused surgery 9"25).</p> <p>Technique: Percutaneous microwave coagulation using an electrode through a 14G needle under sonographic guidance. Power range 10 W and 80 W. a mean of 2.6 punctures and 4.6 applications per tumour. Under IV anaesthesia.</p> <p>77% (57/74) of patients had concomitant chemotherapy.</p> <p>Mean follow-up = 25 months</p> <p>Conflict of interest: supported by a grant from a national foundation</p>	<p>Survival</p> <p>The mean survival time was 22.1 months (\pm 13.8 months). The disease-free survival throughout the follow up period was achieved in 35% (26/74) patients.</p> <p>Cumulative survival was 91% at 1 year falling to 29% at five years (absolute figures not stated).</p> <p>Prognostic factors for survival</p> <p>Univariate analysis was undertaken to evaluate whether the following factors were predictive of survival. Sex age, location of primary, tumour differentiation grade, number of tumours, size of tumours, change in tumour size at 3 months follow up, and local recurrence or new metastases occurring.</p> <p>The following variables were found to be predictive of survival. Number of metastases ($p < 0.001$) tumour size ($p = 0.03$) recurrence or new tumour ($p < 0.001$), and degree of differentiation ($p = 0.01$).</p> <p>Multivariate analysis showed that three factors were independent predictors of survival. The number of tumours ($p = 0.03$) HR 1.94 (95% CI 1.06 to 3.53), tumour differentiation grade ($p = 0.02$) HR 0.46 (95%CI 0.23 to 0.91), and recurrence or new tumour development ($p = 0.04$) HR 3.58 (95% CI 1.02 to 12.64).</p>	<p>Complications</p> <p>No severe complications were reported.</p> <table border="1"> <thead> <tr> <th>Outcome</th> <th>Rate (n=74)</th> </tr> </thead> <tbody> <tr> <td>Local pain</td> <td>91% (67/74)</td> </tr> <tr> <td>Minor to moderate pleural effusion</td> <td>9% (7/74)</td> </tr> <tr> <td>Slight subcapsular bleeding (assessed by ultrasound) resolved without transfusion</td> <td>3% (2/74)</td> </tr> <tr> <td>Skin burns, where lesion protruded beyond liver capsule</td> <td>4% (3/74)</td> </tr> </tbody> </table>	Outcome	Rate (n=74)	Local pain	91% (67/74)	Minor to moderate pleural effusion	9% (7/74)	Slight subcapsular bleeding (assessed by ultrasound) resolved without transfusion	3% (2/74)	Skin burns, where lesion protruded beyond liver capsule	4% (3/74)	<p>Consecutive patients treated at one institution</p> <p>Difficult to assess the specific efficacy of MW ablation when combined with chemotherapy management.</p> <p>Cox multivariate analysis used to determine factors predictive of survival. No details provided of sequence of adding univariate factors into the model.</p> <p>Good description of proportion of patients available at each follow up point.</p> <p>Authors advocate the use of a 10mm margin around the tumour during ablation.</p> <p>No details provided of loss to follow up.</p>
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<p>Shimada S (1998)⁴</p> <p>Case series</p> <p>Japan</p> <p>Study period: 1990 to 1995</p> <p>n = 71 (29 metastatic)</p> <p>Population: male = 72, age = 60 years. Mean tumour size (maximum) = 32mm. Child Pugh score A = 100%</p> <p>Indications: patients with liver tumours, either HCC or secondary metastases (groups not further quantified)</p> <p>Technique: In patients with metastases either open or percutaneous microwave coagulation was employed using various electrodes. Power 60 to 100 W for 60 seconds, with transcatheter cooling of the bile duct. A mean of 15 applications per patient were delivered. Mode of anaesthesia not stated.</p> <p>Most patients had previously received chemotherapy or resection except 5 patients with metastases for whom this was the initial therapy.</p> <p>Follow-up = 11 to 55 months</p> <p>Conflict of interest: Not stated</p>	<p>No efficacy outcomes reported</p>	<p>Complications</p> <table border="0"> <tr> <td>Outcome</td> <td>Rate (n=29)</td> </tr> <tr> <td>Overall</td> <td>21% (6/29)</td> </tr> <tr> <td>Abscess (resolved following percutaneous drainage)</td> <td>7% (2/29)</td> </tr> <tr> <td>Biliary fistula (treated by drainage tube period required not stated)</td> <td>7% (2/29)</td> </tr> <tr> <td>Bleeding (treated either by sponges or transarterial embolisation)</td> <td>7% (2/29)</td> </tr> </table> <p>There were no statistically significant differences in clinical or demographic characteristics between the patients with metastatic tumours that did or did not develop complications.</p> <p>There was no statistically significant difference in the incidence of complications between patients with HCC and those with metastases.</p>	Outcome	Rate (n=29)	Overall	21% (6/29)	Abscess (resolved following percutaneous drainage)	7% (2/29)	Biliary fistula (treated by drainage tube period required not stated)	7% (2/29)	Bleeding (treated either by sponges or transarterial embolisation)	7% (2/29)	<p>A mixed tumour cohort. Population and technique details provided in column one and complication in column three relate to patients with metastases.</p> <p>Location of cancer primaries was not stated for all patients, only those in whom complications occurred.</p> <p>Method of case selection or accrual were not stated.</p> <p>Not all outcomes reported separately for patients with liver metastases.</p> <p>Deep tumours were selected to be treated by the percutaneous technique.</p> <p>No analysis was undertaken to compare the complication rate between the open and the percutaneous technique in patients with metastases.</p>
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<p>Morikawa (2002)³</p> <p>Case series</p> <p>Japan</p> <p>Study period: Jan 2000 to May 2001</p> <p>n = 30 (22 metastatic)</p> <p>Population: male = 27%, age = 60 years. Primary cancer colorectal n=12, stomach n=4, breast n=4, ovarian n=1, leiomyosarcoma n=1.</p> <p>Indications: patients with liver tumours, either HCC or secondary metastases (not further defined)</p> <p>Technique: Percutaneous microwave coagulation using an electrode through a 14G needle under MR guidance. Power 60 W for 3x60 seconds. Multiple applications per lesion sometimes used. Under local or general anaesthesia. 4 patients received repeat treatments.</p> <p>Adjunctive chemo or immunotherapy given on clinical need. 4 patients had no adjunctive therapy</p> <p>Mean follow-up = 17 months</p> <p>Conflict of interest: Not stated</p>	<p>Survival</p> <p>There was no recurrence to final follow up in 32% (7/22) of patients with secondary liver metastases. IN each of these cases the tumour size was <30 mm.</p> <p>28% (6/22) of patients died during follow up.</p>	<p>Complications</p> <p>There we no major complications (massive bleeding or pneumothorax) reported across all patients treated.</p>	<p>Consecutive cases treated.</p> <p>Filter used to allow MRI monitoring of procedure.</p> <p>Largely a technical description of procedure with minimal clinical information provided.</p> <p>Not all outcomes reported separately for patients with liver metastases.</p> <p>Authors state that the 12 to 28 month follow up does is not sufficient to demonstrate therapeutic effects.</p>

Abbreviations used: MW –microwave HR – Hazard ratio, CI – Confidence interval, CT – Computed tomography, HCC – hepatocellular carcinoma.													
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<p>Matsukawa T (1997)⁵</p> <p>Case series</p> <p>Japan</p> <p>Study period: Not stated</p> <p>n = 24 (27 lesions, 20 HCC and 7 metastatic)</p> <p>Population: male = 75%, age = 62 years, mean largest tumour size 31 mm. Primary cancer colorectal n=3, stomach n=2, oesophageal n=1, Cholangiocarcinoma n=1. Overall 22 of 24 patients had undergone transcatheter arterial embolisation which had failed to completely necrose the tumour.</p> <p>Indications: patients with either HCC or secondary metastases confirmed histologically. Patients were excluded if tumours were located beneath the diaphragm, or at the liver edge.</p> <p>Technique: Percutaneous microwave coagulation using an electrode through a 1.6mm needle under real time ultrasound guidance. Power 60 W for 60 seconds. 1 to 12 applications per session. Under local anaesthesia.</p> <p>Mean follow-up = 18 months</p> <p>Conflict of interest: Not stated</p>	<p>Survival</p> <p>The overall survival rate (HCC and metastatic tumours) was 83% at 1 year and 69% at 2 years.</p> <p>Tumour response</p> <p>Response was evaluated using dynamic CT, and categorised as disappeared, reduced in size and unenhanced, or enlarged.</p> <p>The tumour had dispersed in 1 of 7 of patients following MW ablation, it was reduced in 3 of 7 patients, and it was enlarged in 3 or 7. Follow up period not stated.</p>	<p>Complications (mixed HCC and metastatic tumour cohort)</p> <table> <thead> <tr> <th>Outcome</th> <th>Rate (n=24)</th> </tr> </thead> <tbody> <tr> <td>Transient mild pain</td> <td>24% (6/24)</td> </tr> <tr> <td>Fever</td> <td>13% (3/24)</td> </tr> <tr> <td>Ascites and pleural effusions</td> <td>4% (1/24)</td> </tr> <tr> <td>Subcutaneous haematomas</td> <td>8% (2/24)</td> </tr> </tbody> </table>	Outcome	Rate (n=24)	Transient mild pain	24% (6/24)	Fever	13% (3/24)	Ascites and pleural effusions	4% (1/24)	Subcutaneous haematomas	8% (2/24)	<p>No details provided of case selection criteria or case accrual method.</p> <p>Population characteristics relate to both patients with HCC and those with secondary liver metastases.</p> <p>Not all outcomes reported separately for patients with liver metastases.</p> <p>Patients were followed up every 3 to 4 months, but the time points at which outcomes were censored is not stated.</p> <p>Authors note that size of tumour is an important factor in treatment response as coagulation only occurs only 12mm from the tip of the electrode.</p>
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Validity and generalisability of the studies

- Some studies include only patients with secondary liver metastases, while some report on a mixed cohort including patients with hepatocellular carcinoma.
- All but one study report outcomes following microwave ablation via a percutaneous approach.
- Many patients received concomitant or adjunctive therapies.
- Site of primary cancer varied between studies, with colorectal cancer being the most common.

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Dr J Rose, Dr G Poston, Dr D Breen.

- Two Specialist Advisers considered the procedure to be novel and of uncertain safety and efficacy, while one thought it to be a minor variation on an existing procedure.
- Microwave liver tumour ablation aims to quickly ablate tumours in their entirety.
- Theoretical adverse events resulting from the procedure include liver abscess, intra-peritoneal haemorrhage, neoplastic seeding, biliary peritonitis, bowel perforation, and adjacent vessel thrombosis.
- The procedure is often carried out percutaneously by hepato-biliary interventional radiologists.
- Practitioners require experience in ultrasound guided procedures, and experience in other forms of thermal ablation is desirable.
- The procedure should only be undertaken in recognised tertiary hepato-biliary centres.
- Suggested audit criteria for this procedure include technical details of the treatment delivered including the power setting, ablation time, and number of needles / repeat insertions used. Other criteria might include the hospital length of stay, percentage tumour necrosis, and survival to 5 years. Complications to monitor would include the incidence of seeding, and the rate of local or extra-hepatic recurrence.

Issues for consideration by IPAC

- Solely studies from Far-Eastern countries were available
- Limited data available to establish variable efficacy depending on tumour size.

References

- 1 Shibata T, Niinobu T, Ogata N et al. (2000) Microwave coagulation therapy for multiple hepatic metastases from colorectal carcinoma. *Cancer* 89: 276-284.
- 2 Liang P, Dong B, Yu X et al. (2003) Prognostic Factors for Percutaneous Microwave Coagulation Therapy of Hepatic Metastases. *American Journal of Roentgenology* 181: 1319-1325.
- 3 Morikawa S, Inubushi T, Kurumi Y et al. (2002) MR-guided microwave thermocoagulation therapy of liver tumors: initial clinical experiences using a 0.5 T open MR system. *Journal of Magnetic Resonance Imaging* 16: 576-583.
- 4 Shimada S, Hirota M, Beppu T et al. (1998) Complications and management of microwave coagulation therapy for primary and metastatic liver tumors. *Surgery Today* 28: 1130-1137.
- 5 Matsukawa T, Yamashita Y, Arakawa A et al. (1997) Percutaneous microwave coagulation therapy in liver tumors. A 3-year experience. *Acta Radiologica* 38: 410-415.

Appendix A: Additional papers on microwave ablation for the treatment of metastases in the liver not included in summary Table 2

The following table outlines the studies that are considered potentially relevant to the 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 title	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	Case series 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	Case report n = 1 Follow-up = 15 months	No local or distal recurrence at final follow-up	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	Case report 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
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	Case series n = 63 Follow-up = ?	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
Sato M, Watanabe Y, Kashu Y et al. (1998) Sequential percutaneous microwave coagulation therapy for liver tumor. <i>American Journal of Surgery</i> 175: 322–4	Case series n = 6 Follow-up = ?	3 patients undergoing curative MW coagulation had no recurrence	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. <i>Journal of Vascular and Interventional Radiology: JVIR</i> 14: 1535–1542	Case series n = 70 Follow-up = ?	Cholangitis or liver abscess occurred in 10 patients (1.5% of treatments)	Outcomes of patients with hepatocellular carcinoma or secondary metastases are not distinguished.
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. <i>International Journal of Clinical Oncology</i> 7: 128–32	Case report n = 1 Follow-up = 33 months	Complete necrosis on CT scan and no recurrence to final follow-up	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. <i>Breast Cancer</i> 12: 317–21	Case report n = 1 Follow-up = 15 months	No recurrence of metastatic tumour at final follow-up	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	Case series 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.

Appendix B: Related published NICE guidance for microwave ablation for the treatment of metastases in the liver

Guidance programme	Recommendation
Interventional procedures	<p>IPG 092 Radiofrequency ablation for the treatment of colorectal metastases in the liver</p> <p>1.1 Current evidence on the safety of radiofrequency ablation of colorectal metastases in the liver appears adequate. However, the evidence of its effect on survival is not yet adequate to support the use of this procedure without special arrangements for consent and for audit or research.</p> <p>1.2 Clinicians wishing to undertake radiofrequency ablation of colorectal metastases in the liver should take the following actions.</p> <p>Ensure that patients offered it understand the uncertainty about the procedure's efficacy and provide them with clear written information. Use of the Institute's Information for the Public is recommended.</p> <p>Audit and review clinical outcomes of all patients having radiofrequency ablation for the treatment of colorectal metastases in the liver</p> <p>1.3 Publication of research studies with outcome measures which include survival will be useful in reducing the current uncertainty about the efficacy of the procedure. The Institute may review the procedure upon publication of further evidence.</p> <p>IPG093 Selective internal radiation therapy for colorectal metastases of the liver</p> <p>1.1 Current evidence on the safety of selective internal radiation therapy (SIRT) for colorectal metastases in the liver appears adequate.</p>

	<p>With regard to efficacy, the procedure may reduce tumour bulk, but there is a lack of evidence of symptom relief or increased survival, and combination with other treatments makes interpretation of the published literature difficult.</p> <p>1.2 Clinicians wishing to undertake selective internal radiation therapy for colorectal metastases in the liver should take the following actions.</p> <p>Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. Use of the Institute's Information for the Public is recommended</p> <p>Audit and review clinical outcomes of all patients having selective internal radiation therapy for colorectal metastases in the liver.</p> <p>1.3 Publication of research studies with outcome measures which include survival will be useful in reducing the current uncertainty about the efficacy of the procedure. The Institute may review the procedure upon publication of further evidence.</p> <p>IPG XXX Microwave ablation of hepatocellular carcinoma (Consultation guidance)</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</p>
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	levels that should be used. Any adverse events relating to this procedure should be reported to the Medicines and Healthcare products Regulatory Agency
Technology appraisals	None applicable
Clinical guidelines	None applicable
Public health	None applicable

Appendix C: Literature search for microwave ablation for the treatment of metastases in the liver

IP: 381 Microwave ablation for the treatment of secondary liver cancer		
Database	Date searched	Version searched
Cochrane Library	02/11//06	2006, Issue 4
CRD databases (DARE & HTA)	02/11//06	2006, Issue 4
Embase	01/11/06	1980 to 2006 Week 43
Medline	01/11/06	1966 to October Week 4 2006
Premedline	01/11/06	November 01, 2006
CINAHL	01/11/06	1982 to October Week 4 2006
British Library Inside Conferences	02/11/06	-
NRR	02/11//06	2006 Issue 4
Controlled Trials Registry	02/11//06	-

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

Database: Medline		
Strategy used:		
1	(microwave\$ adj3 (ablat\$ or coagulat\$ or therap\$ or themotherap\$ or thermoablat\$)).tw.	812
2	(mct or pmct or mwa).tw.	2254
3	or/1-2	2960
4	((liver or hepat\$) adj3 (neoplasm\$ or cancer\$ or carcinoma\$ or adenocarcinom\$ or tumour\$ or tumor\$ or malignan\$ or metastas\$)).tw.	61496
5	exp Liver Neoplasms/	88114
6	or/4-5	104224
7	3 and 6	365
8	animals/	4020353
9	humans/	9581636
10	8 not (8 and 9)	3047644
11	7 not 10	342
12	limit 11 to english language	212
Comments:		