NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of microwave ablation for primary hepatocellular cancer

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

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 August 2006.

Procedure names

- Microwave ablation.
- Microwave coagulation.
- Microwave resection.

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

Primary liver cancer.

The most common primary liver cancers are hepatocellular carcinoma and cholangiocarcinoma.

Current treatment and alternatives

For primary liver cancer, surgical resection may be a treatment option for some patients. However, both for primary and secondary liver cancer, 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 and radiofrequency ablation. Hepatic transplantation may be appropriate in some cases

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 are available.

The needle electrodes are advanced into the liver tumour(s) during either laparotomy, laparoscopy, or percutaneously under immage 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 the complete ablation of the tumour(s) on imaging, and survival at 3 and 5 years.

One randomised and one non-randomised controlled trial were identified comparing outcomes of microwave ablation and liver resection. Two non-randomised controlled trials compared microwave ablation with radiofrequency ablation or percutaneous ethanol injection. Three case series reported outcomes of patients after microwave ablation therapy for liver

tumours. Only one of the seven studies relates to metastatic liver disease, the other six relating to hepatocellular carcinoma.

One randomised controlled trial found that the mean overall survival time was similar among patients treated with microwave ablation and liver resection (27 and 25 months, respectively).[1] Patients who underwent microwave coagulation had significantly less operative blood loss than those who underwent hepatectomy (360 ml and 910 ml, respectively, p = 0.027). A non-randomised controlled study also found that overall survival was similar between groups of patients treated by microwave ablation and liver resection. In this study local recurrence occurred in 8% (3/38) of patients treated with microwave ablation and 8% (4/51) of patients treated by resection to 25 months follow-up.[2]

In a non-randomised controlled study comparing microwave with radiofrequency ablation, the mean disease-free survival period in patients treated by microwave ablation was reported as 15.5 months (95% confidence interval [CI] 11.3 to 20.0 months) and in those receiving radiofrequency ablation 16.5 months (95% CI 10.1 to 19.2 months). The difference was not statistically significant (p = 0.53).[3]

One non-randomised controlled trial found that 5-year overall survival was similar among patients with well-differentiated liver tumours treated by microwave ablation and percutaneous ethanol injection (70% and 78%, respectively). However, with moderately or poorly differentiated tumours the 5 years' overall survival was significantly higher in the microwave ablation group (78%) than in the percutaneous ethanol injection group (35%) (p = 0.03).[4]

One case series of patients undergoing microwave ablation therapy reported that overall survival at 5 years was 58%, and local re-growth of tumours in 8% (24/288) of patients.[6]

Safety

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

A randomised controlled trial found that there were no differences in the rates of bile duct fistula or hepatic abscess formation, or wound infection between the groups treated with microwave ablation and liver resection.[1] A non-randomised controlled trial with 25 months' follow-up also found no difference in the incidence of intra-abdominal bleeding, gastrointestinal bleeding, billiary stenosis and wound dehiscence between patients treated by microwave ablation and those treated by liver resection.[2]

Another non-randomised controlled trial reported that major complications occurred in 8% (4/49) of patients treated with microwave ablation, and 6% (3/53) of patients following radiofrequency ablation (p = 0.71).[3]

A case series reported that acute respiratory distress syndrome occurred in 19% (4/21) of patients undergoing open microwave ablation.[7]

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to microwave ablation for liver tumours. Searches were conducted via the following databases, covering the period from their commencement to 14 July 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. If 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 If no clinical outcomes were reported, or if 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 primary or secondary liver tumours.
Intervention/test	Microwave ablation by any mode of application.
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 overview

This overview is based on two randomised controlled studies, three non-randomised controlled studies, and two case series.

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

- Laparoscopic liver resection. *NICE interventional procedure guidance* no. 135 (2005) Available from www.nice.org.uk/IPG135

- Radiofrequency ablation for the treatment of colorectal metastases of the liver. *NICE interventional procedure guidance* no. 92 (2004) Available from www.nice.org.uk/IPG092

- Radiofrequency ablation of hepatocellular carcinoma . *NICE interventional procedure guidance* no. 2 (2003) Available from www.nice.org.uk/IPG002

Technology appraisals

- None.

Clinical guidelines

- None.

Public health

- None.

Table 2 Summary of key efficacy and safety findings on microwave ablation for hepatocellular liver cancers

Abbreviations used: CT, computed tomography; GI, gastrointestinal; MRI, magnetic resonance imaging; MW, microwave; RF, radiofrequency; US, ultrasound; NS, not stated; NR, not reported

Study details	Key efficacy findings	Key safety findings	Comments
Shibata T (2005)[5] **Randomised controlled trial** Japan Study period: Mar 1999 – Dec 2000 **n = 72 (n = 36 MW coagulation, 36 liver resection)** Population: male = 69%, age = 63 years. Indications: patients with hepatocellular carcinoma confirmed histologically by needle biopsy, either a single tumour <40 mm, or up to 3 tumours with largest tumour < 30 mm in diameter Technique:Local anaesthesia **Percuatneous** microwave ablation using a generator and a 1.6 mm diameter electrode through a guiding needle. Local anaesthesia. RF ablation with a monopolar array needle electrode with 8 to 10 expandable electrode tines. Power up to 90 W Repeat RF or MW ablations were performed on patients with incomplete necrosis on CT imaging at 1 week. **Follow-up: 6 to 27 months** Conflict of interest: not stated	**Operative parameters** Outcome / MW / RF / p= Treatments per lesion: 2.4 (± 1.0) / 1.1 (± 0.46) / <0.001 Operative time (mins): 33 ± 11 / 53 ± 16 / <0.001 Intravenous analgesia required during treatment: 47% (15/32) / 31% (10/32) / NR **Local control** Analysis based on number of nodules Outcome / MW / RF / p= Complete therapeutic effect: 89% (41/46) / 96% (46/48) / 0.26 Residual lesions: 11% (5/46) / 4% (2/48) / NR Residual foci of untreated disease during follow up: 17% (8/48) / 8% (4/48) / 0.20	**Complications** Outcome / MW / RF / p= Major complication: 11% (4/32) / 3% (1/32) / 0.36 Segmental hepatic infarction (recovered with conservative therapy): 0% / 3% (1/32) / NR Liver abscess (catheter inserted): 3% (1/32) / 0% / NR Cholangitis (with intrahepatic bile duct dilation requiring antibiotics): 3% (1/32) / 0% / NR Subcutaneous abscess with skin burn: 3% (1/32) / 0% / NR Subcapular haematoma: 3% (1/32) / 0% / NR 9% (3/32) of patients in the MW group requested that treatment be stopped due to pain despite intravenous analgesics, and required general anaesthesia for repeat procedures.	No details provided of randomisation sequence generation method, however concealment of allocation by opaque envelopes. No details provided of blinding of outcome assessors One operator carried out all the procedures in both groups There were no significant differences in demographic or clinical characteristics between the treatment groups at baseline. Highly selected patient cohort. The MW system created a smaller area of ablation than RF so disparity in number of treatment sessions should be expected. Authors stated that coagulation efficacy was moderated by cooling effect of hepatic blood flow, and that 3 tumours (2 and 1 respectively) that were incompletely ablated were near hepatic or portal vein.

Abbreviations used: CT, computed tomography; GI, gastrointestinal; MRI, magnetic resonance imaging; MW, microwave; RF, radiofrequency; US, ultrasound; NS, not stated; NR, not reported

Study details	Key efficacy findings	Key safety findings	Comments
Lu M-D (2005)[3] **Non-randomised controlled trial** China Study period: Aug 1997 – July 2002 **n = 102 (n = 49 MW coagulation, 53 RF ablation)** Population: male = 85%, age = 52 years, mean tumour size 26 mm Indications: **hepatocellular carcinoma** confirmed by needle biopsy. Exclusion criteria included more than 5 tumours, tumours more than 8 cm, vascular invasion, lymph node spread/distant metastases, liver function Child–Pugh grade C Technique: both groups received local anaesthesia, with ablation undertaken under US guidance with the aim of destroying tumours with a surrounding 0.5–1.0 cm safety margin. **Percutaneous** microwave coagulation using a tissue coagulator probe through a 14 G guiding needle. For tumours greater than 2.0 cm multiple insertions were used. 60 W of energy delivered for 5 min, each nodule given two sessions within a week Percutaneous RF ablation through a delivery system with maximum 200 W output, for 5 min. Multiple electrodes inserted for tumours larger than 3.0 cm **Follow-up: 25 months** Conflict of interest: not stated	**Local control** Complete ablation (as defined by uniform hypo-attenuation in the ablated area on CT scan) was achieved in 95% (93/98) of tumours treated by MW, and 93% (67/72) treated by RF (p = 0.75) Local recurrence rates were 12% (11/93) following MW ablation and 21% (14/67) following RF ablation (p = 0.12) based on tumours that were successfully ablated **Distant recurrence** The distant recurrence rate was 69% (34/49) among patients treated by MW ablation and 76% (40/53) in those treated by RF ablation (p = 0.49) The mean time until distant recurrence was 8.2 ±6.9 months in the MW group and 7.2 ± 6.4 months in the RF group (p = 0.53) **Survival** The mean disease-free survival period in the MW group was 15.5 months (95% CI 11.3 to 20.0 months), in the RF group the period was 16.5 months (95% CI 10.1 to 19.2 months) (p = 0.53) The mean overall survival time in the MW group was 32.5 months (95% CI 27.4 to 37.7 months), in the RF group the period was 27.1 months (95% CI 22.5 to 31.8 months) (p = 0.12) There was no significant difference between the groups when only patients with tumours smaller than 3.0 cm were included in the analysis Cause of death |	MW	RF
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Tumour progression	27% (13/49)	43% (23/53)
Liver failure	12% (6/49)	19% (10/53)
Upper GI tract bleeding	8% (4/49)	6% (3/53)
Unknown	2% (2/49)	2% (1/53)		**Complications** |	MW	RF
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Discharge from puncture wounds	4% (2/49)	NR
Subcapsular haematoma (absorbed within 2 weeks)	4% (2/49)	NR
Skin burn	NR	4% (2/53)
Puncture wound infection	NR	2% (1/53)
Death	0%	0%
Total major	8% (4/49)	6% (3/53) | (p = 0.71 for difference in rate of major complications between groups)	Retrospective study. Treatment was based on availability of the coagulation device, in effect two periods of consecutive patients. Slightly different anaesthesia regimen between the treatment groups, although unlikely to have influenced outcomes. More patients in the MW group had multiple tumours, and had Child–Pugh grade B liver function. For unsuccessfully treated tumours additional MW or RF ablation was used; it is not stated in how many patients in each group this was required. Analysis of local recurrence was restricted to patients with complete ablation only. Unable to discern how many patients remained in analysis at various time points for analysis of cumulative survival.

Abbreviations used: CT, computed tomography; GI, gastrointestinal; MRI, magnetic resonance imaging; MW, microwave; RF, radiofrequency; US, ultrasound; NS, not stated; NR, not reported

Study details	Key efficacy findings	Key safety findings	Comments
Midorikawa T (2000)[2] **Non-randomised controlled trial** Japan Study period: Jan 1994 – Feb 1999 **n = 89 (n = 38 MW coagulation, 51 liver resection)** Population: male = 72%; age = 62 years; mean tumour size 38 mm, mean number of tumours 1.7 Indications: **hepatocellular carcinoma**, confirmed by pathology Technique: **open** microwave coagulation following laparotomy, to completely ablate tumours, using a tissue coagulator probe (different probes for surface or deep tumours); 6 applications of 60 W for 30 seconds Control group underwent hepatic resection by a standard technique without hilar inflow clamping **Follow-up: 25 months** Conflict of interest: not stated	**Surgical parameters** Mean operative time was significantly shorter in the MW group (237 min) than in the resection group (385 min) (p = 0.0014) Mean surgical blood loss was significantly lower in the MW treated group (175 ml) than in the resection group (1574 ml) (p = 0.0005) **Local control** Control (was defined by adequate necrosis of the tumours and margin on CT scan). Local recurrence occurred in 8% (3/38) of patients treated by MW ablation, and 8% (4/51) of patients treated by resection **Survival** Survival curves were compared by log rank test and there were no significant differences between the groups Multivariate analysis found that survival related to the prothrombin time (p = 0.0045), operative time (p less than 0.0129), operative blood loss (p = 0.0329) and Child–Pugh classification (p = 0.0317). However, treatment modality was not an independent predictor of outcome	**Complications** Hospital mortality: Resection 6% (3/51); MW 0% (0/38) Intra-abdominal bleeding: Resection 4% (2/51); MW 0% (0/38) GI bleeding: Resection 2% (1/51); MW 0% (0/38) Liver failure: Resection 6% (3/51); MW 0% (0/38) Abdominal abscess: Resection 2% (1/51); MW 5% (2/38) Biliary fistula: Resection 4% (2/51); MW 3% (1/38) Biliary stenosis: Resection 0% (0/52); MW 5% (2/38) Wound dehiscence: Resection 2% (1/52); MW 0% (0/38) Wound infection: Resection 4% (2/51); MW 3% (1/38) None of the differences in rates of complications were significantly different between the treatment groups	There were no statistically significant differences in the demographic characteristics, number and size of tumours or incidence of underlying cirrhosis between the groups. Biochemical measures of hepatic function differed between the groups. There were more patients with Child–Pugh grade A and fewer with grade B in the resection group than in the MR coagulation group (p = 0.0001). Absolute survival data were not provided. No description was provided for treatment allocation. All analyses were based on number of patients rather than tumours treated. No details were provided of operator experience. No blinding of outcome assessors.

Abbreviations used: CT, computed tomography; GI, gastrointestinal; MRI, magnetic resonance imaging; MW, microwave; RF, radiofrequency; US, ultrasound; NS, not stated; NR, not reported

Study details	Key efficacy findings	Key safety findings	Comments
Seki T (1999)[4] **Non-randomised controlled trial** Japan Study period: Sept 1990 – Mar 1997 **n = 90 (n = 48 MW coagulation, 52 percutaneous ethanol injection)** Population: male = 88%, age = 62 years, mean tumour size 17 mm Indications: solitary **hepatocellular carcinoma**, stage I on CT or MRI imaging, with histological grade of differentiation confirmed by biopsy Technique: local anaesthesia in all patients **Percutaneous** microwave coagulation under US guidance using a 2.9 mm electrode through a 13 G guiding needle. 80 W of energy delivered for 1 min, given 2–4 times to different sites Control group underwent percutaneous ethanol injection therapy (PEIT) with 2–4 ml of ethanol mixed with lidocaine into the tumour and 2 or 3 sites in the vicinity For both groups repeat treatment given for recurrences less than 2.0 cm (mean number of treatment 1.6 sessions) **Follow-up: 12–72 months** Conflict of interest: not stated	**Local control** Complete necrosis and more than 5 mm margin (evaluated by CT scan) was achieved in 94% (45/48) of tumours treated by MW and 62% (26/42) treated by PEIT In patients with well-differentiated tumours there was no difference in the pattern of location of recurrence between the two treatment groups In patients with moderately or poorly differentiated tumours there were more recurrences at the site of initial treatment or in the same liver segment in patients treated with PEIT and more recurrences in other segments in patients treated by MW coagulation (p = 0.03) 94% (15/16) of recurrences were successfully ablated with MW coagulation, and 73% (11/15) successfully ablated by repeat PEIT **Survival** 5-year overall survival well-differentiated tumour: MW 70%, PEIT 78%, p = N/S (0.85) moderately/poorly differentiated tumour: MW 78%, PEIT 35%, p = 0.03 4-year cancer-free survival well-differentiated tumour: MW 37%, PEIT 39%, p = N/S (0.37) moderately/poorly differentiated tumour: MW 30%, PEIT 18%, p = N/S (0.17)	**Complications** There were no clinically serious side effects associated with either treatment modality. Almost all patients in the PEIT group had transient pain during injection, and half of the MW coagulation group experienced some pain, although none refused to continue treatment	Patients who were either inoperable due to impaired liver function or who requested a percutaneous treatment. There were no differences between treatment groups at baseline in demographic characteristics, tumour size, liver status or biochemical markers. No patients were lost to follow-up. Patients chose treatment modality after discussion with clinician. Only qualitative description of safety outcomes. Analysis divided by subgroups with well-differentiated tumours (Edmonson's grade I or I–II) or medium or poorly differentiated (Edmonson's grade II or above). Initial intention was to subdivide into three groups on grade of differentiation, but two groups aggregated a posteriori due to inadequate sample in one group. Not stated how many patients in each group had reached 5 years of follow-up.

Abbreviations used: CT, computed tomography; GI, gastrointestinal; MRI, magnetic resonance imaging; MW, microwave; RF, radiofrequency; US, ultrasound; NS, not stated; NR, not reported

Study details	Key efficacy findings	Key safety findings	Comments
Liang P (2005)[6] **Case series** China Study period: May 1994 – Oct 2002 **n = 288** Population: male = 90%, age = 55 years, mean tumour size 38 mm, single tumour n = 180, multiple tumours, n = 108. Well-differentiated tumours = 30%, moderately differentiated = 47%, poorly differentiated = 23%. Cirrhosis = 90%. Child–Pugh grade A = 19%, Child–Pugh grade B = 74%, Child–Pugh grade C = 7% Indications: patients with **hepatocellular carcinoma**, confirmed by biopsy. Exclusion criteria included more than 5 tumours, tumours more than 8 cm, no portal vein thrombosis or extrahepatic metastases, prothrombin time less than 25 s Technique: general anaesthesia. **Percutaneous** microwave coagulation using an applicator through a 16 G guiding needle. For tumours greater than 1.7 cm multiple insertions were used. 60 W of energy delivered for 5 min. **Follow-up: 31 months** Conflict of interest: no financial relationship to disclose	**Recurrence** Local regrowth of a lesion occurred in 8% (24/288) of patients. New tumours occurred in 9% (25/288) of patients in the same liver segment, and in 12% (34/288) in different segments New extrahepatic tumours occurred in 6% (17/288) of patients **Survival** The cumulative survival was 93% at 1 year, 82% at 2 years, 72% at 3 years, 63% at 4 years, and 51% at 5 years (n = 30 patients were followed up for 5 years or more) 30% (86/288) of patients died of hepatocellular carcinoma and complications, and 2% (7/288) died of non-hepatic disease Multivariate analysis found that survival related to the number of tumours (single vs. multiple) at baseline (p=0.005), tumour size (p less than 0.001), and Child–Pugh classification (p = 0.01)	Not reported	Analysis based on consecutive patients, bar 12/300 who were lost to follow-up. Microwave coagulation was one of five treatment modalities offered at the centre. Patient selection criteria were not specified, experienced surgeons made choice of treatment option. For unsuccessfully treated tumours or recurrence additional MW ablation was used in 62 patients. Microwave ablation with curative intent in the majority of patients. Retrospective study. Authors stated that they had considerable experience with microwave ablation.

Abbreviations used: CT, computed tomography; GI, gastrointestinal; MRI, magnetic resonance imaging; MW, microwave; RF, radiofrequency; US, ultrasound; NS, not stated; NR, not reported

Study details	Key efficacy findings	Key safety findings	Comments
Ajisaka H (2005)[7] **Case series** Japan Study period: Jan 1999 – Apr 2003 **n = 21** Population: male = 81%, age = 64 years, tumour size 10–70 mm, mean number of tumours = 2.28. Cirrhosis = 100% (from hepatitis virus) Indications: patients with **hepatocellular carcinoma**, who were unfit for systematic hepatectomy due to poor liver function Technique: **open** microwave coagulation. Applications of 60–80 W for 30–45 seconds **Follow-up: not stated** Conflict of Interest: not stated	None stated	**Complications** Postoperative bleeding occurred in 5% (1/21) of patients Acute respiratory distress syndrome (ARDS) occurred in 19% (4/21) of patients The was no incidence of sepsis in this study cohort	Diagnosis of ARDS was based on American–European consensus conference on ARDS criteria. All baseline demographic and clinical characteristics were similar in the group that developed ARDS and in the group that did not except for a higher hepaplastin test in the ARDS group (p = 0.0352). There was no significant difference with regard to the mean irradiation dose between those who developed ARDS (35 380 J) and those who did not (36 600 J). 6 of 17 patients who did not develop ARDS received potassium canrenoate, or spironolactone until the fourth postoperative day; none of the 4 patients who developed ARDS received an aldosterone antagonist (p = N/S). Follow-up period was not stated. However, cumulative water balance and sodium administration were measured for 4 postoperative days. There is a discrepancy between the text and the figure for the significance of the difference in postoperative water balance on day 4, potentially due to rounding.

Validity and generalisability of the studies

- All but one of the studies included in the overview relate to hepatocellular carcinoma, which indeed is rarely operable. However, some patients could benefit from liver transplantation. The most common presentation of liver cancer is metastatic liver disease. A number of the studies listed in appendix A describe experience treating liver metastases from distant primaries, including colorectal and breast cancer.
- Neither treatment intent nor eligibility for surgical resection were adequately stated in presented evidence.
- All the studies summarised in this overview are from either Japan or China. Smaller case series studies from the UK are included in Appendix A.
- Studies employed a variety of approaches for microwave coagulation – open, laparoscopic or percutaneous.
- Some studies used local anaesthesia, some general.
- Some studies excluded patients with large or multiple liver tumours, making comparison between studies difficult.

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 D Breen, Dr G Poston.

- 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, billiary peritonitis, bowel perforation, adjacent vessel thrombosis, and the potential for collateral thermal injury.
- The procedure is often carried out percutaneously by hepato-biliary interventional radiologists.

- Practitioners require experience in ultrasound and image 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

- No UK studies have been included in the overview data extraction table. Devices and techniques employed in other regions may not be similar to those used locally.
- Microwave ablation devices have received a CE mark and are being trialled in the UK outside formal research protocols on the basis of equivalence to radiofrequency ablation.

References

1. Shibata T, Niinobu T, Ogata N et al. (2000) Microwave coagulation therapy for multiple hepatic metastases from colorectal carcinoma. *Cancer* 89: 276–84.
2. Midorikawa T, Kumada K, Kikuchi H et al. (2000) Microwave coagulation therapy for hepatocellular carcinoma. *Journal of Hepato-Biliary-Pancreatic Surgery* 7: 252–9.
3. Lu MD, Xu HX, Xie XY et al. (2005) Percutaneous microwave and radiofrequency ablation for hepatocellular carcinoma: a retrospective comparative study. *Journal of Gastroenterology* 40: 1054–60.
4. Seki T, Wakabayashi M, Nakagawa T et al. (1999) Percutaneous microwave coagulation therapy for patients with small hepatocellular carcinoma: comparison with percutaneous ethanol injection therapy. *Cancer* 85: 1694–02.
5. Shibata T, Iimuro Y, Yamamoto Y et al (2002) Small Hepatocellular Carcinoma: comparison of Radio-frequency Ablation and Percutaneous Microwave Coagulation therapy. *Radiology* 223: 331–7.
6. Liang P, Dong B, Yu X et al. (2005) Prognostic factors for survival in patients with hepatocellular carcinoma after percutaneous microwave ablation. *Radiology* 235: 299–307.
7. Ajisaka H, Miwa K. (2005) Acute respiratory distress syndrome is a serious complication of microwave coagulation therapy for liver tumors. *American Journal of Surgery* 189: 730–3.

Appendix A: Additional papers on microwave ablation for hepatocellular liver cancers 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 T, Shinzawa H, Wakabayashi H et al. (2000) Value of laparoscopic microwave coagulation therapy for hepatocellular carcinoma in relation to tumor size and location. *Endoscopy* 32: 598–603	Case series n = 43 Follow-up = 17 months	The rate of complete necrosis was significantly higher for tumours less than 40 mm	Larger series included in table 2.
Aramaki M, Kawano K, Ohno T et al. (2004) Microwave coagulation therapy for unresectable hepatocellular carcinoma. *Hepato-Gastroenterology* 51: 1784–7	Case series n = 24 Follow-up = 1–60 months	Local recurrence at the margin of treated tumour in 1 patient and 15 recurrences in different segments	Larger series included in table 2.
Asahara T, Nakahara H, Fukuda T et al. (1998) Percutaneous microwave coagulation therapy for hepatocellular carcinoma. *Hiroshima Journal of Medical Sciences* 47: 151–5	Case series n = 19 Follow-up = 1–36 months	For single tumours < 3 cm MW coagulation comparable with hepatectomy in overall and disease-free survival	Larger series included in table 2.
Dong B, Liang P, Yu X et al. (2003) Percutaneous sonographically guided microwave coagulation therapy for hepatocellular carcinoma: results in 234 patients. *AJR American Journal of Roentgenology* 180: 1547–55	Case series n = 234 Follow-up = 28 months	6-year cumulative survival 57%	Same patients as included in Liang (2005) described in table 2.
Hamazoe R, Hirooka Y, Ohtani S et al. (1995) Intraoperative microwave tissue coagulation as treatment for patients with nonresectable hepatocellular carcinoma. *Cancer* 75: 794–800	Case series n = 8 Follow-up = 4–24 months	Recurrence in 3 of 8 patients treated	Larger series included in table 2.
Hyodoh H, Hyodoh K, Takahashi K et al. (1998) Microwave coagulation therapy on hepatomas: CT and MR appearance after therapy. *Journal of Magnetic Resonance Imaging* 1998; 8: 451–8	Case series n = 17 Follow-up = 10 months	All treated lesions reduced in volume	Larger series included in table 2.
Ido K, Isoda N, Kawamoto C et al. (1997) Laparoscopic microwave coagulation therapy for solitary hepatocellular carcinoma performed under laparoscopic ultrasonography. *Gastrointestinal Endoscopy* 45:415–20	Case series n = 18 Follow-up = 17 months	No serious complications during MW ablation procedure	Larger series included in table 2.
Ishida T, Murakami T, Shibata T et al. (2002) Percutaneous microwave tumor coagulation for hepatocellular carcinomas with interruption of segmental hepatic blood flow. *Journal of Vascular & Interventional Radiology* 13(2 Pt 1): 185–91	RCT n = 31 Follow-up = 2–33 months	Complete necrosis in all patients. Recurrence in 2 of 31 patients	Study comparing two MW coagulation techniques.
Ishikawa M, Ikeyama S, Sasaki K et al. (2000) Intraoperative microwave coagulation therapy for large hepatic tumors. *Journal of Hepato-Biliary-Pancreatic Surgery* 7: 587–91	Study paper not obtainable		
Itamoto T, Katayama K, Fukuda S et al. (2001) Percutaneous microwave coagulation therapy for primary or recurrent hepatocellular carcinoma: long-term results. *Hepato-Gastroenterology* 48: 1401–5.	Case series n = 33 Follow-up = to 5 years	Overall survival was 49% at 5 years for patients with primary hepatocellular carcinoma.	Larger series included in table 2
Ito T, Niiyama G, Kawanaka M et al. (1999) Laparoscopic microwave coagulation for the treatment of hepatocellular carcinoma. *Digestive Endoscopy* 11: 137–43	Case series n = 14 Follow-up = 18 months	Recurrence occurred in 4 of 22 patients treated	Larger series included in table 2.
Jiao LR, Habib NA. (2003) Experimental study of large-volume microwave ablation in the liver (*British Journal of Surgery* 2002; 89: 1003–1007) [comment]. *British Journal of Surgery* 90: 122	Study paper not obtainable		
Kawamoto C, Ido K, Isoda N et al. (2005) Long-term outcomes for patients with solitary hepatocellular carcinoma treated by	Case series n = 69	Overall 5 years survival was 63%; among patients with	Larger series included in table 2.

laparoscopic microwave coagulation. *Cancer* 103: 985–993	Follow-up = 54 months	moderately or poorly differentiated cancer it was 39%	
Kojima Y, Suzuki S, Sakaguchi T et al. (2000) Portal vein thrombosis caused by microwave coagulation therapy for hepatocellular carcinoma: report of a case. *Surgery Today* 30: 844–8	Case report n = 1 Follow-up = 12 months	Adverse event reported of portal vein thrombosis successfully treated with fibrinolytic therapy	Larger series included in table 2.
Liang JD, Yang PM, Huang GT et al. (2004) Percutaneous microwave coagulation therapy under ultrasound guidance for small hepatocellular carcinoma. *Journal of the Formosan Medical Association* 103: 908–13	Study paper not obtainable		
Liang P, Dong B, Yu X et al. (2005) Sonography-guided percutaneous microwave ablation of high-grade dysplastic nodules in cirrhotic liver. *AJR American Journal of Roentgenology* 184: 1657–60	Case series n = 30 Follow-up = 45 months	Five patients died during follow-up period, 3 from hepatocellular carcinoma	Larger series included in table 2.
Lu MD, Chen JW, Xie XY et al. (2001) Hepatocellular carcinoma: US-guided percutaneous microwave coagulation therapy. *Radiology* 221: 167–72	Case series n = 50 Follow-up = 18 months	Disease-free survival was 41% at 2 years, and overall survival 73% at 3 years	Larger series included in table 2.
Morimoto O, Nagano H, Sakon M et al. (2002) Liver abscess formation after microwave coagulation therapy applied for hepatic metastases from surgically excised bile duct cancer: report of a case. *Surgery Today* 32: 454–7	Case report n = 1 Follow-up = 1 month	Fever following MW coagulation and abscess noted on CT scan	Larger series included in table 2.
Morita T. (2003) Outcomes of patients undergoing microwave coagulation therapy for liver metastases from colorectal cancer	Study paper not obtainable		
Murakami R, Yoshimatsu S, Yamashita Y et al. (1995) Treatment of hepatocellular carcinoma: value of percutaneous microwave coagulation. *AJR American Journal of Roentgenology* 164: 1159–67	Case series n = 9 Follow-up = 6 months	5 lesions controlled with no recurrence. No serious complications occurred	Larger series included in table 2.
Ohmoto K, Mimura N, Iguchi Y et al. (2003) Percutaneous microwave coagulation therapy for superficial hepatocellular carcinoma on the surface of the liver. *Hepato-Gastroenterology* 50: 1547–51	Case series n = 58 Follow-up = 32 months	4-year survival was 64% in patients with superficial tumours, and 60% in those with non-superficial tumours	Larger series included in table 2.
Okano H, Shiraki K, Inoue H et al. (2002) Laparoscopic microwave coagulation therapy for small hepatocellular carcinoma on the liver surface. *Oncology Reports* 9: 1001–4	Case series n = 6 Follow-up = 9 to 28 months	All cases showed complete necrosis; 1 local and 2 distant recurrences	Larger series included in table 2.
Poston G. A prospective, single arm, multi-centre, study to evaluate the safety/efficacy of treatment of primary/secondary liver tumours by microwave ablation	Study paper not obtainable		
Ryu M, Watanabe K, Yamamoto H. (1998) Hepatectomy with microwave tissue coagulation for hepatocellular carcinoma. *Journal of Hepato-Biliary-Pancreatic Surgery* 5: 184–91	Case series n = 99 Follow-up = 48 months	5-year survival with patients without portal tumour thrombi was 51%	Larger series included in table 2.
Sakaguchi T, Yamashita Y, Matsukawa T et al. (1998) Microwave coagulation of hepatocellular carcinoma. *Minimally Invasive Therapy & Allied Technologies: MITAT* 7: 541–6	Case series n = 60 Follow-up = ?	Overall success rate was 72% and mean disease-free period was 24 months	Larger series included in table 2.
Sato M, Watanabe Y, Ueda S et al. (1996) Microwave coagulation therapy for hepatocellular carcinoma. *Gastroenterology* 110: 1507–14	Case series n = 19 Follow-up = 4–64 months	Local recurrence in 2 patients	Larger series included in table 2.
Sato M, Watanabe Y, Kashu Y et al. (1998) Sequential percutaneous microwave	Case series n = 6	3 patients undergoing curative	Larger series included in table 2.

coagulation therapy for liver tumor. *American Journal of Surgery* 175: 322–4	Follow-up = ?	MW coagulation had no recurrence	
Satoi S, Kamiyama Y, Matsui Y et al. (2005) Clinical outcome of 214 liver resections using microwave tissue coagulation. Hepato-Gastroenterology 52: 1180–5.	Case series n = 214 Follow up = 29 months	Overall survival was 91% at 1 year, 72% at 3 years and 58% at 5 years	Not all patients treated with MW ablation outcomes not reported separately
Seki S, Sakaguchi H, Iwai S et al. (2005) Five-year survival of patients with hepatocellular carcinoma treated with laparoscopic microwave coagulation therapy. *Endoscopy* 37: 1220–1225.	Study paper not obtainable		
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	Case series n = 70 Follow-up = ?	Cholangitis or liver abscess occurred in 10 patients (1.5% of treatments)	Larger series included in table 2.
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: 1130–7	Case series n = 71 Follow-up = 11–55 months	Complications occurred in 14% of patients with hepatocellular carcinoma, and 21% of those with metastatic tumours	Larger series included in table 2.
Strickland AD, Clegg PJ, Cronin NJ et al. (2005) Rapid microwave ablation of large hepatocellular carcinoma in a high-risk patient. *Asian Journal of Surgery* 28: 151–3	Case report n = 1 Follow-up = 2 years	Shrinkage of tumour from 6 cm to 4 cm and no recurrence at 2 years	Larger series included in table 2.
Xu HX, Xie XY, Lu MD et al. (2004) Ultrasound-guided percutaneous thermal ablation of hepatocellular carcinoma using microwave and radiofrequency ablation. *Clinical Radiology* 59: 53–61	NRCT n = 97 (54 MW) Follow-up = 27 months	Complete ablation in 95% of MW-treated nodules and 90% of radiofrequency-treated nodules	Same patients as included in Lu (2005) in table 2.
Yamanaka N, Tanaka T, Oriyama T et al. (1996) Microwave coagulonecrotic therapy for hepatocellular carcinoma. *World Journal of Surgery* 20: 1076–81	Study paper not obtainable		
Yamashita Y, Sakai T, Maekawa T et al. (1998) Thoracoscopic transdiaphragmatic microwave coagulation therapy for a liver tumor. *Surgical Endoscopy* 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.
CT, computed tomography; MW, microwave; NRCT, non-randomised controlled trial.			

Appendix B: Related published NICE guidance for microwave ablation for hepatocellular liver cancers

Guidance programme	Recommendation
Interventional procedures	**Laparoscopic liver resection. *NICE interventional procedure guidance* no. 135** 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. 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. **Radiofrequency ablation for the treatment of colorectal metastases of the liver. *NICE interventional procedure guidance* no. 92** 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. 1.2 Clinicians wishing to undertake radiofrequency ablation of colorectal metastases in the liver should take the following actions: • 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. • Audit and review clinical outcomes of all patients having radiofrequency ablation for the treatment of colorectal metastases in the liver. 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 on publication of further evidence. **Radiofrequency ablation of hepatocellular carcinoma . NICE interventional procedure**

	guidance no. 2 1.1 Current evidence of the safety and efficacy of radiofrequency ablation (RFA) for hepatocellular carcinoma appears adequate to support use of the procedure, provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 It is recommended that: • patient selection should be carried out by a multidisciplinary team that includes a hepatobiliary surgeon • the procedure should be monitored by CT or ultrasound.
Technology appraisals	None applicable.
Clinical guidelines	None applicable.
Public health	None applicable.

Appendix C: Literature search for microwave ablation for hepatocellular liver cancers

Database	**Version searched**	**Date searched**
Cochrane Library	2006, Issue 2	17/07/06
CRD databases (DARE and HTA)	2006, Issue 2	17/07/06
Embase	1980 to 2006 Week 27	14/07/06
Medline	1966 to July Week 1 2006	14/07/06
PreMedline	17 July 2006	18/07/06
CINAHL	1982 to July Week 1 2006	14/07/06
British Library Inside Conferences	–	14/07/06
NRR	2006 Issue 2	17/07/06
Controlled Trials Registry	–	18/07/06

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

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	211