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ScienceDirect
EJSO 36 (2010) 264–268
EJSO the Journal of Cancer Surgery
www.ejso.com

Microwave ablation for unresectable hepatic tumours: Clinical results using a novel microwave probe and generator

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Accepted 5 October 2009
Available online 31 October 2009

Abstract

Background: Microwave ablation is an in situ method of tumour destruction used to treat patients with unresectable liver tumours. A new microwave generator and probe, designed to deliver high energy into solid tumours quickly has been developed at our institution. We report the results of its use in patients with unresectable liver tumours treated by a single surgeon in a single institution.
Methods: Thirty-one patients with 89 unresectable liver tumours were recruited into the study and underwent microwave ablation in a single procedure.
Results: There were no post-operative complications. At a median of 24 months post ablation, 15 patients were alive with 7 patients disease free. At a median of 26 months, 8 patients were alive with tumour recurrence but only 1 with local recurrence. The remaining 7 patients with recurrence were found to have new disease at locations remote from the ablation site. Fourteen patients died of disease progression at a median survival of 15 months, with only 1 patient with local and remote tumour recurrence. Of the total numbers of tumours treated ($n = 89$), a local tumour recurrence rate of 2% was observed. Overall median survival was 29 months with 3 year survival of 40%.
Discussion: Microwave tissue ablation using this novel generator and probe has a low local recurrence and complication rate. Overall survival is comparable to alternative ablation modalities and its ability to treat, even large tumours, with a single insertion of the probe makes it an extremely attractive treatment option.

Keywords: Microwave ablation; Liver tumours; Radiofrequency; Cryotherapy; Hepatocellular carcinoma; Colorectal metastases

Introduction

For patients presenting with primary and secondary liver tumours hepatic resection is currently the only potentially curative treatment. Such surgery is associated with a 5 year survival of 25–30% and a median survival of 25 months.[1] Regrettably, 75–80% of patients with these tumours are not amenable to surgical resection due to a variety of factors such as extra-hepatic disease, tumour number or location or poor physiological reserve. Patients with primary hepatocellular carcinoma (HCC) are frequently considered unresectable as the hepatic functional reserve is often poor due to underlying liver cirrhosis/hepatitis, thus making resection of large volumes of liver parenchyma unfeasible. This large cohort of unresectable and currently incurable patients has stimulated the expansion of ablation techniques whereby the tumours are destroyed in situ either by heating (radiofrequency or microwave) or by cooling (cryotherapy). At this institution a novel microwave applicator used to destroy liver tumours in patients deemed inoperable has been developed.

Technical data

Microwave energy was generated using a magnetron at a frequency of 2.45 GHz and delivered using a 6.4 mm interstitial probe (Microsulis Medical Ltd, Denmead, UK). Microwave Tissue Ablation (MTA) uses electromagnetic energy at a high frequency, thus causing heating by constantly re-aligning polar molecules to the continuously

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doi:10.1016/j.ejso.2009.10.006

fluctuating wave.[2] The purpose of this study was to report on the initial clinical experience of microwave ablation with particular reference to local recurrence and survival rates.

Methods

Patient selection

A total of 31 consecutive patients were recruited into this study over a 4 year period (Table 1). After local ethical approval, all patients with primary or secondary liver tumours, deemed unsuitable for hepatic resection were recruited and treated with a curative intent. All patients with metastases had previously undergone excision of the primary tumour prior to the resection/ablation. All patients with colorectal liver metastases ($n = 24$) had neo-adjuvant chemotherapy, usually in the form of oxaliplatin ± 5FU. Patient suitability for microwave ablation and/or hepatic resection was determined at the hepatobiliary cancer multidisciplinary team meeting following clinical assessment and results of cross-sectional imaging (MRI/CT).

Ablation technique

All patients underwent MTA treatment at laparotomy except the patient with a hepatic parathyroid metastasis who was treated laparoscopically. The microwave equipment was set to deliver energy at a variety of powers ranging from 45 to 150 watts at the discretion of the surgical team. All ablations were carried out under real time Intra-operative Ultrasound (IOUS) monitoring with the aid of a Consultant Radiologist.

The formation of micro-bubbles from evaporated tissue water was visualised as a hyper-echogenic image (this became termed the 'thermal cloud'); treatment was considered complete when this thermal cloud overlapped the entire tumour by a 1 cm margin. Following completion of the treatment the ultrasound image changed to a hypoechoic one of similar dimensions to the initial image (Fig. 1).

Temperature monitoring probes (thermocouples) were used in some cases to ensure cytotoxic temperatures (~55 °C) were achieved at the lesion margins. All tumours were treated with a single insertion of the applicator with treatment times varying between 2 and 4 min. On withdrawal of the probe, the track was heated at low power in an attempt to reduce any chance of tumour seeding and to aid haemostasis. Sixteen patients underwent a concomitant liver resection and 15 MTA only. All patients in this study had at least one tumour ablated although the maximum was 10. Peri- and post-operatively, patients were treated in a similar manner to those undergoing standard hepatic surgery.

Follow up

After discharge, all patients underwent 3-monthly cross-sectional imaging in the first year after surgery and subsequently 6 monthly imaging. The cross-sectional data was interpreted by two Consultant Gastrointestinal Radiologists. The success of MTA was assessed by a number of criteria; post-operative complications, early post-operative deaths (30-day mortality), local disease control (with particular emphasis being placed on the outcome of treatment to the larger lesions), disease free and overall survival. Unsuccessful local disease control was defined as tumour recurrence at the site of previous ablation and determined by appearances on cross-sectional imaging. Remote recurrence was defined as either new intra-hepatic tumour but distant to the previous ablation site or extra-hepatic disease.

Results

Morbidity and mortality

A total of 89 lesions were treated with MTA in 31 patients. The mean tumour diameter ablated was 20 mm

Table 1
Patient demographics.

	$N = 31$		
Age (mean)	61 (range 36–78)		
Gender			
Male	18		
Female	13		
Tumour type	No. Patients	No. of tumours	Size range
Colorectal mets.	24	76	2–50 mm
HCC	4	7	10–30 mm
Other			
PTH metastasis	1	1	40 mm
Carcinoid	1	1	10 mm
Choroid Melanoma mets.	1	4	9–28 mm
Numbers treated	31	89	
Mean size		20 mm (range 2–50 mm)	
Concomitant liver resection	16		

*PTH-Parathyroid metastasis.

Figure 1. The hypoechoic lesion post ablation. Arrows show the extent of the ablation with the diamond illustrating the acoustic shadow cast by the treatment.

and the largest tumour treated was 50 mm in diameter. MTA was well tolerated with none of the patients experiencing any of the post-operative complications reported following other alternative ablative modalities (bile leaks, abscess formation, pleural effusions, sepsis or haemorrhage from the probe track). Two patients died within 30 days of the surgery following myocardial infarctions; one at day 5 and another at day 30.

Survival and recurrence rate

During the follow up period of four years, a total of 15 patients were alive and 7 patients were disease free at a median of 24 months post ablation (range 12–33 months) (Fig. 2). Eight patients were alive with tumour recurrence at a median of 26 months post ablation (range 12–40 months). Of these 8 patients with tumour recurrence, only 1 (3%) had demonstrable local recurrence as determined by cross-sectional imaging. The remaining 7 with hepatic tumour recurrence were noted to have new disease at sites remote from the ablation site. Three of these patients were noted to have developed extra-hepatic disease. During the follow up period, 14 patients died of disease progression, with a median survival in this group of 15 months post ablation (range 9–42 months). One of these patients died at 9 months post ablation and had local and remote tumour recurrence. Of the total numbers of tumours treated ($n = 89$), a local tumour recurrence rate of 2% was observed in the four years of this study. Of the all the patients treated ($n = 31$) with MTA, only 2 had demonstrable evidence of local recurrence, a patient based recurrence rate of 6%. Including the two early post-operative deaths, the overall survival in all patients was a median of 29 months and the 3 year survival was 40% (Fig. 3).

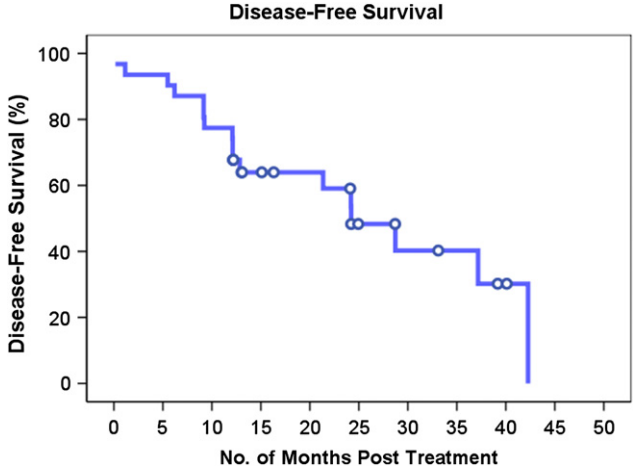

Figure 2. Overall disease free survival.

Large tumours

A sub-analysis of the 31 patients in this series revealed 22 tumours greater than 30 mm in diameter ablated in 14 patients. The mean diameter of the lesions was 35 mm (range 30–50 mm). Six patients from this sub-group were alive at a median follow up of 28 months (range 12–40 months), 3 were tumour free at median of 29 months (range 12–33 months) post ablation (Fig. 4). Of the remaining 3 patients, 1 (already mentioned above) had tumour at the ablation site along with remote hepatic disease and 2 had recurrences remote to the ablated area. Eight patients died and excluding the 2 early post-operative deaths (already mentioned earlier), the median survival in these patients was 24 months (range 12–29 months). The 3 year survival in this sub-group was comparable to the 3 year survival of all patients.

Discussion

Unresectable liver tumours present a major problem for healthcare providers. We present our experience of (MTA) using a new microwave generator and probe in an otherwise incurable cohort of patients from one surgeon working in a single institution.

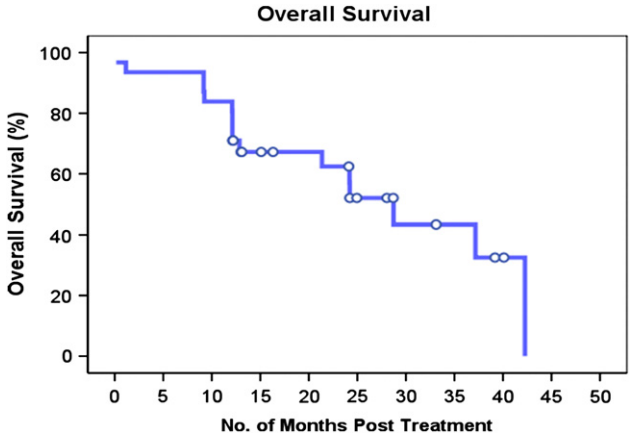

Figure 3. Overall survival.

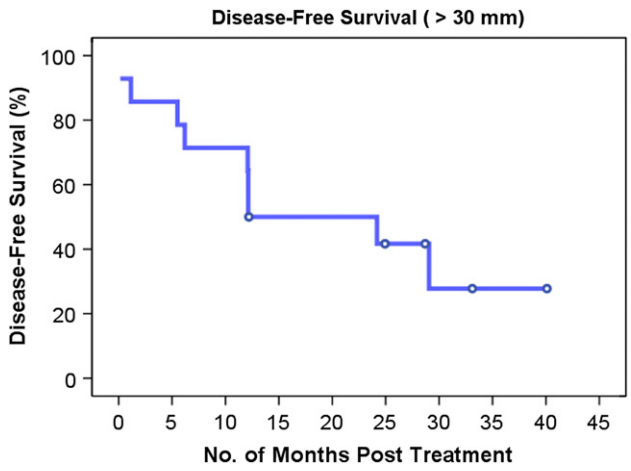

Figure 4. Disease free survival of tumours >30 mm.

Complications

MTA appeared to be a well tolerated treatment in this patient group. None of the patients in this series showed evidence of sepsis, bile duct damage, thrombocytopaenia, or significant systemic upset. This compares very favourably with studies of alternative ablative modalities which have reported complications in up to 33% of the patients treated.[3,4] In spite of the fact that some individuals underwent large volume microwave ablations, none of the patients in this study exhibited symptoms similar to that which have been described following large volume cryoablation (''cryoshock'').[5] Two patients (6%) died in the immediate post-operative period from myocardial infarctions confirmed at post-mortem. The livers of these patients were analysed and no abnormalities other than that of the ablated regions were noted. Both of these patients had documented cardiovascular disease and highlight the importance of careful patient selection for these procedures. Both patients were recruited at the beginning of the study and may reflect a learning curve often evident with new techniques. No other early post-operative deaths were encountered during the study or until the time of writing. The 30-day mortality rate observed in this study is again at least comparable to other similar studies using RF and Cryotherapy.[3,5]

Potential causes of local recurrence

Successful local disease control was evaluated using 3-monthly cross-sectional imaging post ablation interpreted by two Consultant Gastrointestinal Radiologists. Of the 89 ablations using MTA, local disease control was achieved in 87 of 89 lesions and unsuccessful in two tumours (2%).

The two local recurrences in our series followed treatment of tumours 18 mm and 30 mm in diameter. These lesions were situated in close proximity to major hilar vessels in both cases. A tumour diameter of 30 mm or greater and close proximity to major vascular structures are both well documented risk factors for tumour recurrence.[6-13] It is possible that the larger size of one of these tumours may be connected to its recurrence though many larger lesions were successfully treated in this series. It is however more likely that heat dissipation due to the blood flow in the nearby hilar vessels or poor probe placement are more likely explanations for these failures. Encouragingly the 3 year survival of patients with large tumours was comparable to the overall patient survival in this series. The low recurrence rate observed in our series is extremely encouraging and at least comparable to local recurrence rates reported in studies of RF, which range between 2 and 39%.[6–9] Failure of local disease control following cryotherapy is estimated to be between 9 and 44%.[10,11]

Survival

The prognosis of untreated liver cancers is poor and the patients recruited in this study were considered incurable by the current gold standard treatments. A median survival of 29 months is far superior to the best 2nd line palliative chemotherapy regimens, which report a median survival of 20 months.[14,15] The overall three year survival rate of 40% is comparable to results from similar studies of alternative ablation modalities. There is a paucity of data with respect to long term survival in RF trials. A recent review of RF ablation for unresectable liver tumours identified 6 studies which reported 3 year survival, ranging from 37%–58%.[16] The results from this study suggest that MTA is a viable treatment for this group of patients. It is however always difficult to compare data from different trials as for instance what is considered unresectable disease is subjective and is likely to vary between centres.

Mechanism of action of MTA

This trial observed tumour recurrence and patient survival rates which were comparable to those reported from similar trials using RF and Cryotherapy. However, complications rates, single insertion treatments for even large tumours and rapid treatment times are however far superior to other ablative modalities. MTA has several advantages over alternative treatment modalities which may account for these results. The mechanism by which it causes tumour destruction is integral to this. Thermal damage occurs within a microwave field radiating from the inserted probe, thereby heating an entire volume of tissue simultaneously and thus not relying on thermal conduction. This markedly reduces treatment times and the need for repeat insertions of the probe. RF and cryotherapy however, rely almost exclusively on thermal conduction to exert their cytotoxic effects. This is inefficient and time consuming in tissues with high water contents such as hepatic colorectal metastases. This may in part, along with the requirement for multiple probe insertions to treat a single tumour, explain the relatively high rates of recurrence seen with RF and cryotherapy. Research work with MTA

undertaken on porcine liver in this centre suggests that up to 80 mm ablations are possible with a single insertion.[17] RF by contrast requires a total of six overlapping deployments of the electrode to completely ablate a 40 mm tumour.[16] This ability of MTA to treat tumours with a single insertion of the probe is invaluable as accurate re-insertions are often difficult intra-operatively due to the long standing acoustic shadows which form on the IOUS post ablation. In addition, continued reinsertion of the ablation probe has potential to damage greater volumes of hepatic tissue, a feature which may be of some importance in the treatment of primary liver tumours where the background liver parenchyma is cirrhotic.

Conclusion

This study suggests MTA using a new generation of microwave generator and probe is associated with a low recurrence and complication rate. It also has the ability to rapidly treat even large tumours with a single insertion of the probe. It may have a role in the treatment of patients with unresectable liver tumours either primarily or as an adjunct to standard hepatic resection. Although the numbers of patients treated in this study are small, the initial results are encouraging and at least comparable to those achieved with alternative ablative techniques. Future developments such as percutaneously delivered MTA antennas and laparoscopic treatments may further expand the indications for this treatment.

Acknowledgments

Microsulis medical equipment, Professor Nigel Cronin, Peter Clegg (Bath University) and United Hospitals Leicester for the grant to Mr Andy Strickland.

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