Original Article

Microwave ablation for colorectal cancer metastasis to the liver: a single-center retrospective analysis

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Background: The purpose of this study is to evaluate the safety and intermediate-term efficacy of percutaneous microwave (MW) ablation for the treatment of colorectal liver metastases (CRLM) at a single institution.

Methods: A retrospective review was performed of all CRLM treated with MW ablation from 3/2011 to 7/2020 (102 tumors; 72 procedures; 57 patients). Mean age was 60 years (range, 36–88) and mean tumor size was 1.8 cm (range, 0.5–5.0 cm). The patient population included 19 patients with extra-hepatic disease. Chemotherapy (pre- and/or post-ablation) was given in 98% of patients. Forty-five sessions were preceded by other focal CRLM treatments including resection, ablation, radiation, and radioembolization. Kaplan-Meier curves were used to estimate local tumor progression-free survival (LTPFS), disease-free survival (DFS), and overall survival (OS) and multivariate analysis (Cox Proportional Hazards model) was used to test predictors of OS.

Results: Technical success (complete ablation) was 100% and median follow-up was 42 months (range, 1–112). There was a 4% major complication rate and an overall complication rate of 8%. Local tumor progression (LTP) rate during the entire study period was 4/98 (4%), in which 2 were retreated with MW ablation for a secondary LTP-rate of 2%. LTP-free survival at 1, 3, and 5 years was 93%, 58%, and 39% and median LTP-free survival was 48 months. OS at 1, 3, and 5 years was 96%, 66%, 47% and median OS was 52 months. There were no statistically significant predictors of OS.

Conclusions: MW ablation of hepatic colorectal liver metastases appears safe with excellent local tumor control and prolonged survival compared to historical controls in selected patients. Further comparative studies with other local treatment strategies appear indicated.

Keywords: Colorectal cancer; ablation; hepatic metastasis; treatment of metastasis; liver targeted therapy

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Introduction

Colorectal cancer is the second leading cause of cancer death worldwide (1). Approximately 50% of colorectal cancer patients will eventually develop liver metastases (CRLM) (2), and surgery is the primary curative treatment option when feasible. If patients are able to undergo surgical resection, 5-year overall survival (OS) rates are approximately 31–60% in carefully selected patients (3,4). Unfortunately, less than 20% of patients with CRLM are candidates for resection due to co-morbidities or the number, size, and distribution of tumors (5,6).

Percutaneous thermal ablation remains a potentially curative option for some patients with CRLM who are not surgical candidates (7). Radiofrequency (RF) ablation is the most widely used ablative modality for CRLM, and long-term studies have shown improved survival with low rates of complications. However, most RF studies demonstrate a high rate of local tumor progression (LTP) and an inability to treat larger tumors, likely due to small ablation zones resulting in inadequate margins (8-14). More recently, microwave (MW) ablation has gained popularity for the treatment of liver tumors due to a number of technological advantages, including higher applied temperatures, multiple probe synergy, less susceptibility to the heat-sink effect, larger ablation zones, possibly improved local tumor control, and some data which suggests equivalent OS to surgical resection (15-20). However, most hepatic MW literature is for hepatocellular carcinoma, and the clinical experience with MW for CRLM is limited to just a few studies (18,21-23). These reports are quite heterogenous and include a mixture of percutaneous and intraoperative cases, are limited to the use of single probe devices, or use MW systems not approved for human use worldwide (14,21-26).

The purpose of this single-center single-arm retrospective study is to report the technical and intermediate-term oncological outcomes and complications after percutaneous MW ablation of CRLM from our multi-disciplinary tertiary care oncologic practice.

Methods

Institutional review board approval was obtained to deidentify a clinical database for research purposes, and a waiver of informed consent was granted for this retrospective study (University of Wisconsin-Madison Health Sciences IRB; ID: 2012-0519). There was no industry support for this publication.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/jgo-21-159).

Patient selection

All patients who underwent percutaneous MW ablation for CRLM between March 2011 and July 2020 at a single academic medical center were included. Treatment decisions were made by a multidisciplinary team of radiologists, medical oncologists, and oncologic and transplant surgeons at a consensus conference. The decision to treat was based upon age, comorbidities, tumor size, location and histology, treatment status, proximity of non-target anatomy, and patient preference. In general, patients that underwent MW ablation were technically unresectable or were otherwise poor surgical candidates due to co-morbidities, anatomic location of tumors, or recent prior surgery. MW has been the thermal modality of choice at the study institution since 2011 and was performed by one of seven radiologists with 1–25 years of percutaneous ablation experience.

Microwave ablation procedure

Procedures were performed in a dedicated interventional computed tomography (CT) suite (Optima 580 W; GE Healthcare, Waukesha, WI, USA) under general anesthesia. After 2018, high frequency jet ventilation (HFJV) became the anesthesia standard due to decreased hepatic motion (27). Ultrasound was used by default for antenna placement (US; LOGIQ E9 or E10, GE Healthcare). When the lesion was not visibly by US, CT fluoroscopy guidance was used.

A 2.45-GHz, multiprobe, gas-cooled MW ablation system was used for all cases (NeuWave Microwave Ablation System, Ethicon Inc., Madison, WI, USA). The treatment duration and power were determined by the operating physician based on tumor size, proximity to vulnerable structures (particularly central bile ducts and adjacent bowel loops), and real-time monitoring. Procedures were monitored primarily by US to ensure that the visible zone of gas encompassed the tumor and a target ablative margin of 5–10 mm. At procedure completion, a contrast-enhanced CT was performed to determine technical success and complications. If residual tumor or an inadequate margin was suspected, repeat ablation was performed in the same session.

Data collection

Data was collected from an institutional database, electronic medical record, and image storage system (McKesson, Alpharetta, GA, USA). Images, dictations, and clinic notes were reviewed for procedural data, oncologic outcomes, and complications. All procedural and follow-up metrics were reported using established criteria (28). Technical success (ablation zone encompasses target tumor plus an ablative margin) was determined on the immediate post-procedure CT (28), and technique efficacy on the first scan ~1-month post-ablation (28). Other metrics reported included: location and pathology of the primary tumor, pre-ablation CEA, tumor size and number, chemotherapy, *KRAS*/*BRAF* status, metastases, prior CRLM interventions, complications, LTP, LTP-free survival (LTPFS), disease-free survival (DFS), and OS, which was defined from the date of the first MW to the date of death or date that the patient was last known to be alive (28).

Complications

Peri-procedural complications were monitored and recorded during an overnight observation. Delayed complications were evaluated with follow-up imaging and clinic visits. Complications were categorized according to the Society of Interventional Radiology (SIR) classification system for complications by outcome (29).

Statistical analysis

The Kaplan-Meier method was used for survival analyses, which included LTPFS, DFS, and OS. Multivariate analysis was performed using the Cox Proportional Hazards model to test predictors of shortened OS (30). LTPFS was defined as the time period from ablation until radiologic evidence of recurrence or latest imaging follow-up (28). Patients that did not have follow-up imaging were excluded from the calculation of technique efficacy and LTP rate. DFS was defined as the time period from ablation to evidence of new disease or latest imaging follow-up (first session was used for patients with multiple sessions) (28). Patients with extrahepatic disease present at the time of ablation were excluded from DFS. Cox model P values were derived using two-sided Wald tests, where the null hypothesis, H_0: $\beta=0$, was tested against the alternative, H_1: $\beta\neq0$, for each coefficient. $P<0.05$ was considered significant for all statistical results. All analyses were performed using R (V 4.0.3).

Results

The study population consisted of 102 consecutive CRLM treated in 57 patients (22 female, 35 male) during 72 sessions (*Table 1*). The mean patient age was 60±12 years (range, 36–88). Mean tumor diameter was 1.8±1.0 cm (median: 1.6 cm; range, 0.5–5.0). Tumors treated in a single session ranged from 1–6: one tumor (n=56), two (n=8), three (n=4), four (n=3), and six (n=1). Extrahepatic disease was present in 19 patients at the time of ablation, including lung metastases (n=11), lymph nodes (n=3), and multiple sites of metastasis (n=5). In five procedures, the primary tumor had not yet been resected but was planned for a later date. Ten sessions were part of a prospective multi-stage treatment plan in which the ablation was followed by surgical resection of remaining liver disease.

Chemotherapy was given to 98% of patients: 88% prior to ablation and 74% after. Thirty patients (53%) had prior liver-directed therapies including hepatic resection, ablation, SBRT, and radioembolization. Ninety-nine tumors were adenocarcinomas (97%), two were squamous cell (2%), and one was composite adeno-/squamous/neuro-endocrine (1%). Twenty-four patients had a *KRAS* mutatation, two had a *BRAF* mutation, and *KRAS*/*BRAF* testing was not performed in 28 patients.

Table 1 All patient, procedure, and tumor characteristics

Variable	No.	%
Total patients	57	
Female	22	39%
Male	35	61%
Total number of sessions	72	
Total number of treated tumors	102	
Location of primary tumor		
Cecum/ascending colon	15	26%
Transverse colon	2	4%
Descending colon	4	7%
Sigmoid	11	19%
Rectum	24	42%
Unspecified	1	2%
Tumor pathology		
Adenocarcinoma	99	97%
Squamous	2	2%
Adeno-/squamous/neuro-endocrine	1	1%
Tumors treated per procedure		
1	56	78%
2	8	11%
>2	7	10%
Pre-ablation CEA (ng/mL), median	3.2 (range, 0.5–382)	
>10 ng/mL	9	13%
<10 ng/mL	61	85%
Not available	2	3%
Tumor size (cm), mean ± SD	1.8±1.0 (range, 0.5–5.0)	
≤1	26	26%
1.1–2	41	40%
2.1–3	21	20%
>3	14	14%
Pre-ablation chemotherapy	49	86%
Post-ablation chemotherapy	42	74%
Both pre- and post-ablation chemotherapy	35	61%
KRAS mutant	24	42%
KRAS wild-type	15	26%
KRAS not tested	18	31%

Table 1 (*continued*)

Table 1 (*continued*)

Variable	No.	%
BRAF mutant	2	4%
BRAF wild-type	9	16%
BRAF not tested	46	81%
Primary tumor		
Resected	67	93%
Not yet resected	5	7%
Extrahepatic metastases		
None	53	74%
Lung only	11	15%
1 site (not lung)	3	4%
More than 1 site	5	7%
History of hepatic resection		
Yes	28	49%
No	29	51%
Hepatic treatment naïve	27	47%
Prior treated liver metastases (resection, radiation, ablation, Y-90)	30	53%
Number of CRLM at time of ablation		
Solitary	44	61%
Multiple	28	39%

CEA, carcinoembryonic antigen; CRLM, colorectal liver metastases.

Ablation procedure, technical success, and technique efficacy

Technical success was 100% (complete ablation at the time of the procedure). The mean treatment time was 6.9±2.6 minutes (range, 3–15) with a mean power of 68.1±10.4 Watts (range, 55–112) per tumor. Two antennas were most commonly used per tumor (range, 1–3).

Median patient follow-up was 42 months (range, 1–112) with two patients lost to follow-up before a one month CT and thus were not included in follow-up statistics. Technique efficacy (complete treatment at 1 month post-ablation) was achieved in 98/100 (98%) of tumors. These technique failures both occurred within the first 14 months of the introduction of MW. One patient had surgery (lesion not amenable to ablation) and the other had palliative chemotherapy and radiation for residual and extrahepatic disease.

Complications (Table 2)

The major complication rate was 4% (3/72), with an overall rate of 8% (6/72). There were three major procedure-related complications: Tract seeding in a patient that had a recent biopsy along a similar trajectory; bile leak and abscess which resolved with drainage; and pulmonary emboli that resolved with anti-coagulation. Minor complications included asymptomatic pneumothorax (n=2) not requiring chest tubes, and body wall arterial bleeding (n=1) contemporaneously cauterized without sequela. There were no deaths within 30 days after ablation.

Table 2 Complications after MW ablation

Complication	N
Major complications	
Bile leak treated with drain placement (Grade D)	1
Pulmonary embolism treated with anticoagulation (Grade D)	1
Tract seeding treated with systemic chemotherapy (Grade E)	1
Minor complications	
Pneumothorax treated with pleural blood patch (Grade B)	2
Muscle arterial bleeding resolved with cautery (Grade B)	1
Total (rate)	6 (8.3%)

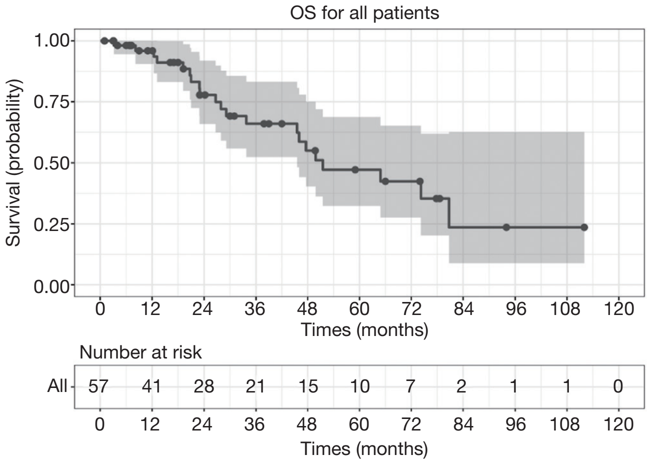

Figure 1 Overall survival Kaplan-Meier curve with 95% confidence bands.

OS

Median OS was 52 months (*Figure 1*). Survival at 1, 3, and 5 years was 96%, 66%, and 47%. For patients that died, the causes of death were progressive cancer (n=14), subdural hematoma (n=1), or unknown causes (n=6).

Impact of tumor characteristics on survival (Table 3, Figure 2)

Multivariate analysis demonstrated no statistically significant predictors of OS. Although not significant, a slight association between history of hepatic resection (P=0.06) and reduced hazard of death was observed. There also was a slight association observed between presence of extrahepatic disease (P=0.07) and LTP (P=0.07) independently increasing hazard of death. The size of the tumor (>3 *vs.* <3 cm), number of tumors (solitary *vs.* multiple), *KRAS* status, and CEA were not associated with a shortened OS.

Disease progression and DFS

The overall DFS at 1, 3, and 5 years was 34%, 21%, 10% and median DFS was 8 months (*Figure 3*). New CRLM remote from the ablation site occurred in 52% (24/46; 11 patients excluded with lack of follow-up and/or liver disease present at time of ablation). Extrahepatic disease occurred or progressed in 55% (30/55; 2 patients excluded due to lack of follow-up). Sites of extrahepatic disease: pulmonary nodules and thoracic lymph nodes (n=16), abdominal/pelvic masses (n=8), abdominal/pelvic lymph nodes (n=5), brain metastasis (n=1).

LTP, management of LTP, and LTP free survival (LTPFS)

The LTP rate was 4/98 (4%) per tumor and 4/53 (8%) per patient (*Table 4*, *Figure 4*; note: 4 patients were excluded due to lack of technique efficacy and/or follow-up) . One of four patients with LTP was identified within 1-year post-ablation, two within 2 years, and one at 4 years. Two were retreated with MW for a secondary LTP-rate of 2% (*Figure 5*). The tumors not re-treated with MW were treated with surgery or palliative chemotherapy due to the inability for repeat ablation (n=1) and concomitant detection of multifocal disease (n=1). LTPFS rate at 1, 3, and 5 years was 93%, 58%, and 39% and median LTPFS was 48 months (*Figure 4*). Two of three non-adenocarcinoma patients had recurrences: combined local/intrahepatic/distant tumor progression (n=1) and intrahepatic/distant tumor progression (n=1).

Table 3 Results of multivariate analysis for predictors of overall survival

Predictor	No. of patients	Hazard ratio [95% CI]	P value
Sex			
Male	35	1.1 [0.2, 5.2]	0.92
Female	22		
Age (years)		1.0 [0.9, 1.1]	0.81
Prior liver resection			
Yes	28	0.3 [0.1, 1.1]	0.06
No	29		
No. of CRLM present			
Single	34	0.3 [0.1, 1.3]	0.12
Multiple	23		
Size of tumor		1.8 [0.7, 4.7]	0.22
CEA (ng/mL)			
>10 ng/mL	8	1.4 [0.4, 5.4]	0.61
<10 ng/mL	47		
KRAS mutation			
Wild-type	15	1.4 [0.3, 5.4]	0.65
Mutant	24		
Extrahepatic disease			
Yes	15	4.0 [0.9, 17.3]	0.07
No	42		
LTP			
Yes	4	0.1 [0.0, 1.2]	0.07
No	53		

Tumor size is the largest tumor in the procedure for those with multiple tumors treated. See OS curves (Figure 4). CI, 95% confidence interval; OS, overall survival.

Discussion

Treating hepatic colorectal metastases with thermal ablation is not new, but the vast predominance of available data is from centers in which radiofrequency is the dominant ablation modality. Microwave is a newer technology that creates larger, hotter, and faster ablation zones when compared to RF (15-19). However, there is a paucity of MW data for treating CRLM, and it remains unclear as to whether the physical advantages of microwave result in improved patient outcomes. Prior MW studies have been performed with a mixture of laparoscopic and percutaneous approaches, CT and/or US guidance, single rather than multiple probe systems, and with devices that are not approved for worldwide use (14,21-26,31). The results of this study demonstrate that percutaneous ultrasound-guided MW ablation for selected colorectal liver metastases is

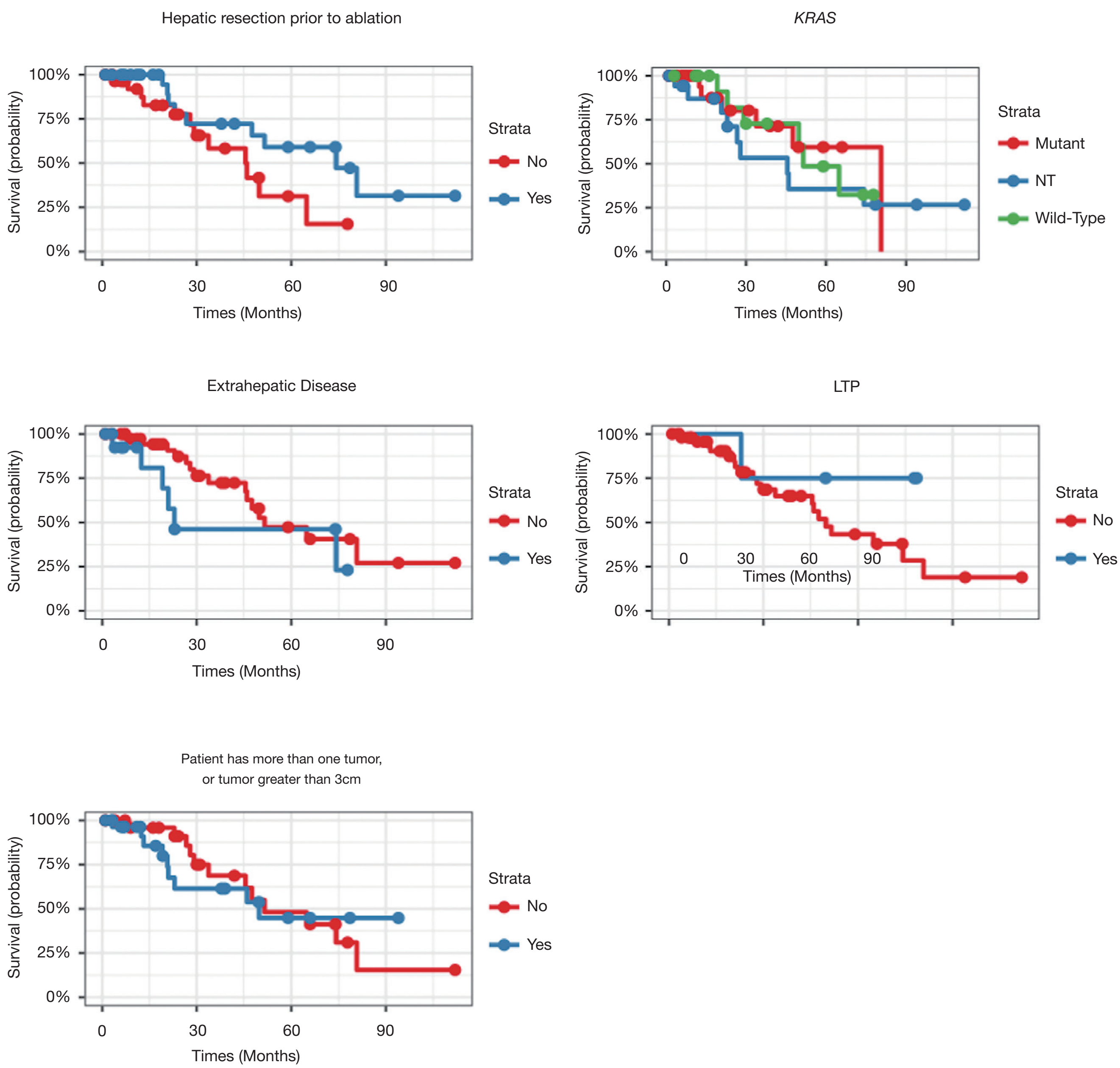

Figure 2 Overall survival Kaplan-Meier analysis for predicting factors that influence OS. OS, overall survival.

associated with few serious complications, high rates of local tumor control, and prolonged survival in selected patients.

The effectiveness of an ablation modality to destroy a targeted tumor is best described by LTP. The LTP rate was low in this study (4% per tumor and 8% per patient) and there was no obvious correlation between LTP and tumor size, genetic mutations, or original site of disease (*Table 4*). Other recent studies of MW for CRLM report LTP rates ranging from 24–38% (23,31,32). Comparatively, LTP rates for RF range from 6–51% (8-10,23,33-36) and 11–25% for cryoablation (37,38) (*Table 5*). One matched cohort study suggests that LTP is lower for MW than for RF (6 *vs.* 20%, P=0.01) (21), however patients in that study were treated during open liver surgery, a much different procedure than the percutaneous approach described herein.

Several technical reasons that could contribute to the low reported LTP rates include experienced operators at a high-volume ablation center, careful patient selection, the use of ultrasound to precisely place probes and monitor the ablation, a multiprobe MW system that produces thermal and electrical synergy, and immediate post-ablation CT with re-ablation of positive or close margins (8,16,40-43). The relative contribution of each of these factors to the overall results is unknown but it is possible that the use of multiple antennas played a significant role. For example, in this study 80% of tumors were treated with multiple antennas and LTP was 4.1%. In a different study with tumors of similar size (1.7 cm), only 22% of tumors were treated with 2+ antennas and the LTP rate was 38% (23). Notably, all four patients with LTP in this study occurred within the first four years of this study, suggesting that there may be a learning curve for MW (43,44). It is important to consider that image-guided percutaneous ablation is a nascent treatment strategy that is currently highly reliant on individual physician experience and skill. There are several important emerging technological advances that will likely improve the consistency of outcomes across centers as well as continue to improve LTPFS (45-48). For example, semi-automated post-ablation margin analysis tools are becoming available, and these technologies can notify physicians of inadequate ablation margins at the time of the procedure (45-48). Given the known critical role that ablative margins play in LTPFS, retreatment of inadequate margins based on objective imaging criteria is likely to improve patient outcomes.

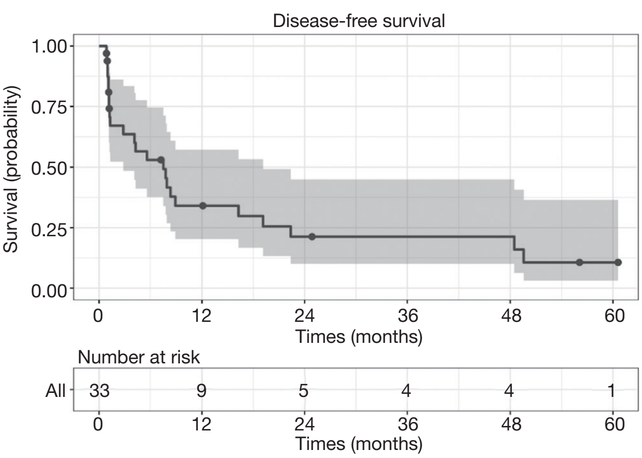

Figure 3 Disease-free survival Kaplan-Meier curve with 95% confidence bands.

The overall and progression-free survival in this study cohort appeared highly favorable with a median OS of 52 months and 3- and 5-year survival rates of 66% and 47%. These results appear to be approaching hepatic resection (49-53) and is concordant with a recently published matched cohort study in which MW ablation and hepatic resection have comparable OS rates (20). By way of comparison, prior CRLM MW studies report a median survival of 28–48 months (20,31,32) and a 33% (31) 5-year survival, and radiofrequency ablation has a reported 18–48% (8-10,34,36,39) 5-year survival rate (*Table 5*).

Table 4 LTP tumor characteristics

	Time to LTP (mo.)	Size (cm)	Number of antennas	Pathology	Genetic mutations?	Prior liver resection?	Prior chemotherapy?	Extra-hepatic disease?
Tumor 1	15	1.6	2	Adenocarcinoma	KRAS: mutant; BRAF: wild-type	n	y	n
Tumor 2	6	2.3	3	Composite tumor: squamous cell carcinoma with adenocarcinoma and neuroendocrine features	n/a	n	y	y
Tumor 3	14	2.1	2	Adenocarcinoma	KRAS: wild-type; BRAF: n/a	n	y	y
Tumor 4	50	3.5	3	Adenocarcinoma	n/a	y	y	n

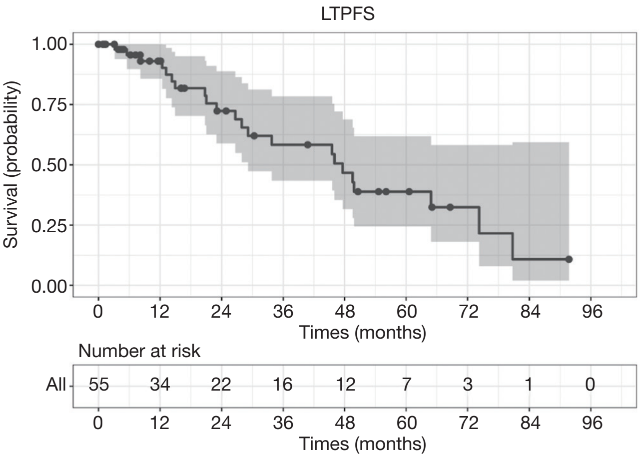

Figure 4 Local tumor progression free survival Kaplan-Meier curve with 95% confidence bands.

However, more definitive conclusions are not possible given that the patients in this study were selected by a multidisciplinary team for tumor size and location, and often had undergone the test-of-time for tumor biology by undergoing several prior lines of chemotherapy and local CRLM treatments (i.e., SBRT, Y90 or hepatic resection). A large percentage of patients in this cohort were also treated as part of a staged multi-treatment regimen which may have given patients a survival advantage as opposed to waiting for metachronous disease and then treating for salvage. This may account for the unexpected finding of potential improvements in survival for patients that received hepatic resection before ablation. Overall, one of the most important factors effecting patient survival in this study may be that 98% of patients received modern chemotherapy, with most receiving pre- and post-ablation treatment (54). Studies from earlier time points likely had higher proportions of patients treated with less effective chemotherapy, so survival comparisons across studies are interesting but limited.

There were no clear factors that predicted LTP in this study (*Table 4*). Other studies report that a *KRAS* mutation (55-57) (42% of patients in this study), CRLM resection prior to ablation (22,23,58), tumor size greater than 3 cm (8,9,32,36,38,58), and ablative margins can influence LTP (23,36,56-59). Since there were only 4 LTP events in this study, there was not enough statistical power to confirm earlier observations of the critical nature of ablative margins on LTPFS. There was no significant predictor of decreased OS in this study but slight associations (P=0.07) were noted for patients with extrahepatic disease and LTP. Factors reported in the ablation literature that decrease OS include extrahepatic disease (8,9,39), *KRAS* mutation (55), more than one metastasis (9,31,32,34,39), CEA >10 ng/mL (31,34), and lesion size >3 cm (8,9,31,32).

The rate of serious complications reported in this study was low with only three cases requiring further intervention: a single case each of pulmonary embolus, bile leak and abscess, and tract seeding in a patient with an aggressive cell type and prior biopsy. The patient with bile leak and abscess had a prior cholecystectomy but no common bile duct interventions-a known risk factor for intrahepatic abscess post-ablation (58,60,61). Importantly, there were no cases of generalized peritoneal seeding such as those described in early trials of RF of HCC (62) or significant hepatic bleeding. The absence of these complications is likely due to the ability of all modern MW systems to perform tract ablation which was routinely performed at the study center. Overall, the types and frequency of complications in this study were mostly minor and similar to those described with RF and MW of HCC (61,63-65).

There were several limitations in this study. This is a single-center single-arm retrospective analysis in which a high number of patients received both systemic and local treatments pre- and post-ablation. This makes it challenging to attribute OS to a single intervention, and even more difficult to generalize and compare outcomes at different centers where multidisciplinary care, operator experience, patient demographics, and referral patterns may differ. Another important limitation is the rapidly evolving nature of oncologic therapies, most notably the advancement of chemotherapy regimens which makes comparison with earlier studies difficult. Finally, lack of a control group and the small sample size (57 patients) paired with a small number of events (4 LTP, 21 deaths) limits precision regarding parameter estimation within a Cox regression model and overall statistical power.

In summary, this single-center retrospective study of percutaneous ultrasound-guided MW ablation for CRLM demonstrates a high rate of technical success, few serious complications, and prolonged survival in selected patients. The low LTP rate in this study may be due to experienced operators, ultrasound guidance for probe placement and intra-procedural monitoring, and the use of multiple antennas in 80% of tumors. MW appears to be a promising

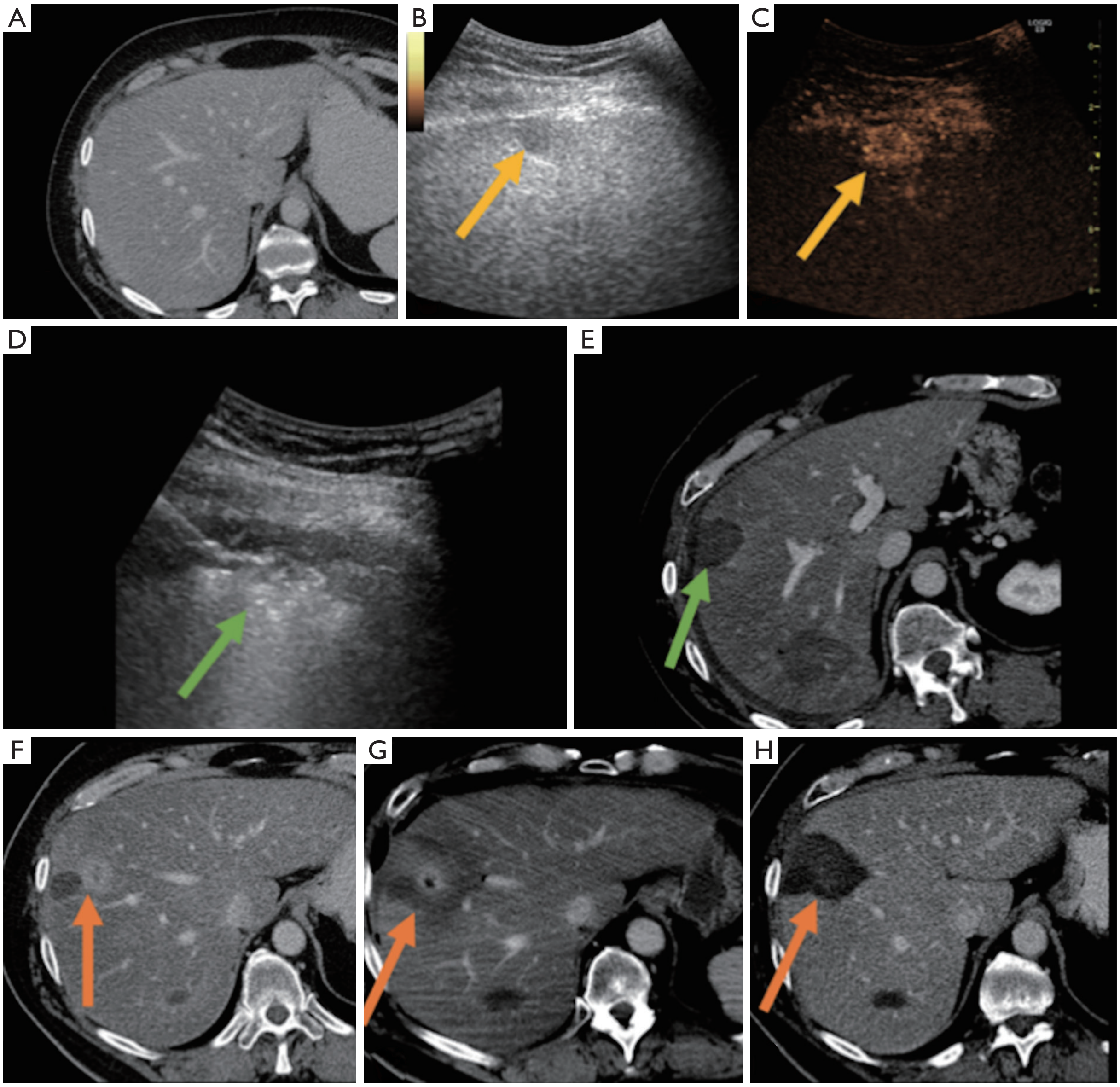

Figure 5 Example of local tumor progression with retreatment. (A) Segment VIII lesion in a 62-year-old male is radiographically occult on CT but visible by ultrasound. (B,C) US of lesion (yellow arrow) without and with US contrast. (D) Intra-procedural US demonstrating gas bubbles covering entire lesion (green arrow), and (E) post-ablation CT of lesion demonstrating appropriate coverage (green arrow). (F) New area of nodular enhancement detected along the medial ablation margin (orange arrow) 3 months post-ablation, consistent with LTP. (G) Repeat ablation shows appropriate coverage of LTP (orange arrow) without residual enhancing tissue. (H) Follow-up scan 4 months after re-treatment demonstrates no recurrence (orange arrow). LTP, local tumor progression.

Table 5 Comparison to recent published MW, cryo-, and RF percutaneous ablation studies for CRLM

Study	Year	Modality	No. of patients/ tumors	Median or mean tumor size (cm)	Median follow-up (months)	% Extrahepatic disease	% Major complications	LTP rate	Median OS (months)	3-year OS	5-year OS
Gillams and Lees (39)	2009	RF	309/(n/a)	3.5	n/a	37%	5%	n/a	5 or less tumors of ≤5 cm: 28 More than 5 tumors and/or >5 cm: 14	5 or less tumors of ≤5 cm: 40% More than 5 tumors and/or >5 cm: 13%	5 or less tumors of ≤5 cm: 18% More than 5 tumors and/or >5 cm: 3%
Sofocleous *et al.* (33)	2011	RF	56/71	1.9	22	34%	2%	51%	31	41%	n/a
Bale *et al.* (34)	2012	RF	63/189	2.0	25	0%	17%	16%	33	44%	27%
Hamada *et al.* (9)	2012	RF	84/141	2.3	27	27%	2%	28%	35	45%	21%
Solbiati *et al.* (10)	2012	RF	99/202	2.2	72	7%	1%	12%	53	69%	48%
Shady *et al.* (8)	2016	RF	162/233	2	55	31%	7%	48%	36	48%	31%
Littrup *et al.* (37)	2016	Cryo-	77/178	2.9	22[†]	n/a	n/a	11%	n/a	n/a	n/a
Glazer *et al.* (38)	2017	Cryo-	(n/a) /61	2.5[†]	(mean =30)[†]	n/a	11%[†]	25%	n/a	n/a	n/a
Shady *et al.* (23)	2018	MW	48/60	1.7	56	33%	12%	38%	n/a	n/a	n/a
		RF	62/85	1.8	29	39%	13%	40%	n/a	n/a	n/a
Urbonas *et al.* (32)	2019	MW	87/126	3.4	28	36%	n/a	34%	28	n/a	n/a
Shi *et al.* (31)	2021	MW	210/505	2.7	48	0%	2%	24%	40	53%	33%
Knott *et al.*	2021	MW	57/102	1.8	42	26%	4%	4%	52	66%	47%

[†], includes CRLM, HCC, and other non-colorectal metastases. n/a, not reported.

technology for treatment of CRLM in combination with a multidisciplinary approach which includes modern chemotherapy and a variety of liver-directed therapies, and further comparative studies appear warranted.

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