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A Retrospective Comparison of Microwave Ablation vs. Radiofrequency Ablation for Colorectal Cancer Hepatic Metastases

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Abstract

Background—Microwave (MWA) and radiofrequency ablation (RFA) are the most commonly used techniques for ablating colorectal-liver metastases (CRLM). The technical and oncologic differences between these modalities are unclear.

Methods—We conducted a matched-cohort analysis of patients undergoing open MWA or RFA for CRLM at a tertiary-care center between 2008 and 2011; the primary endpoint was ablation-site recurrence. Tumors were matched by size, clinical-risk score, and arterial-intrahepatic or systemic chemotherapy use. Outcomes were compared using conditional logistic regression and stratified log-rank test.

Results—We matched 254 tumors (127 per group) from 134 patients. MWA and RFA groups were comparable by age, gender, median number of tumors treated, proximity to major vessels, and postoperative complication rates. Patients in the MWA group had lower ablation-site recurrence rates (6% vs. 20%; $P < 0.01$). Median follow-up, however, was significantly shorter in the MWA group (18 months [95% confidence interval 17–20] vs. 31 months [95% confidence interval 28–35]; $P < 0.001$). Kaplan–Meier estimates of ablation-site recurrence at 2 years were significantly lower for the lesions treated with MWA (7% vs. 18%, *P*: 0.01).

Conclusions—Ablation-site recurrences of CRLM were lower with MWA compared with RFA in this matched cohort analysis. Longer follow-up time in the MWA may increase the recurrence rate; however, actuarial local failure estimations demonstrated better local control with MWA.

Whereas complete resection is the "gold standard" for treatment of colorectal liver metastases (CRLM), thermal ablation is a valuable adjunct to resection in otherwise unresectable patients.[1,2] These include patients with multiple bilobar lesions, and those with lesions in areas of the liver not well suited for resection. Furthermore, thermal ablation allows parenchymal preservation, management of small-volume disease in patients who are otherwise unfit to tolerate larger liver resections, and repeated management of recurrences.[2]

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Cryoablation was the first ablation modality used to treat CRLM. Due to high local recurrence rates and associated morbidity, this was replaced by radiofrequency ablation (RFA). Currently, the two most common energy sources are microwave (MWA) and RFA. Theoretical benefits of MWA over RFA include larger ablation volumes, shorter duration, no charring and electrical insulation, and no heat-sink effect.[3] It has been suggested that these characteristics translate into better local control with MWA over RFA.[3,4] Studies describing these two modalities are heterogeneous, and there is a paucity of data that directly compare the two modalities and their oncologic outcomes.

We recently reported our experience with liver-tumor ablation.[1] We found an overall local-recurrence rate of 11 %. In that experience, MWA was used in a minority of cases (13 %) and no significant difference was found with RFA (used in 70 % of the cases) in terms of local-recurrence (i.e., ablation-site recurrence). Since then, MWA has been used almost exclusively. This change was prompted by ease of use and shorter ablation times with MWA. The present study analyzed our most current experience with MWA and RFA for CRLM, with a matched-cohort analysis evaluating differences in oncologic outcome between both techniques.

METHODS

After obtaining institutional review board (IRB) approval we queried our prospective hepatobiliary surgery database for patients who had undergone operative MWA of CRLM between 2008 (when we started performing MWAs) and 2011. Patients' demographics and number of tumors treated, tumor characteristics, and presentation data were obtained from this database. Subsequently, we queried the same database for patients who had undergone RFA of CRLM between 2001 and 2010 as historical controls.

We identified 73 patients who had undergone 129 MWA and 112 patients who had undergone 222 RFAs. All patients underwent open operative ablations by a hepatobiliary surgeon (no laparoscopic or interventional radiology-guided ablation were included in this analysis). We then matched the *tumors* in both groups on size (maximal diameter on cross-sectional imaging), systemic chemotherapy, or hepatic-arterial infusion (HAI) chemotherapy, and clinical-risk score (the clinical risk score predicts prognosis based on presence of positive lymphnodes with the primary tumor, disease-free interval, carcinoembryonic antigen >200, >1 liver metastasis, and size of the largest metastasis >5 cm).[1,5] This system has been shown to stratify risk of recurrence for patients in the modern chemotherapy era.[6] For evaluation of recurrence, tumor size ≥1 cm was used as a threshold based on our prior experience, which found these tumors to be at increased risk for local recurrence.[1] Postoperative outcomes, local recurrence, and survival data were abstracted from the medical records and stored on a *per tumor* basis. Local recurrence was defined as a recurrence within 1 cm of a previously ablated area noted on cross-sectional imaging performed during follow-up. This was identified by reviewing radiology reports and reexamining CT images.

Ablation Technique

Microwave ablations were performed with an Evident™ Microwave System, including a Valleylab microwave generator (915 MHz/45 W) and Evident™ microwave surgical antennas. RFAs were performed with a Covidien RFA system, AngioDynamics RITA system, or Boston Scientific system. The duration of ablations was determined by the surgeon at the time of the ablation depending on the characteristics of the target lesion and the suggested protocol by the manufacturer (e.g., using the Evident MWA surgical antenna system, two probes placed in parallel at 1.5-cm distance from each other, provide an ablation length and height of 4.5 and 4.2 cm respectively). Intraoperative ultrasound guidance for probe placement and ablation monitoring was used at the practitioner's discretion. There were no image-guided percutaneous ablations included in our study.

Follow-up: Statistical Analyses

Patient's follow-up was dictated clinically. All but one patient were seen at least once in follow-up within 4 weeks after discharge from the hospital. Complications that developed during this period were prospectively recorded into the MSKCC Surgical secondary-events program (SSE) as previously reported. This program uses a classification similar to the Dindo–Clavien system.[7,8] Cross-sectional imaging was obtained at variable times, typically two to three times yearly initially and then annually if disease was stable during the first 2–3 years. Ablation zone size was defined as the largest ablation diameter estimated on postablation cross-sectional imaging. Local recurrence was defined as recurrence of tumor in an area of previously documented complete ablation and compared between the two matched cohorts using conditional logistic regression and stratified log-rank test. To account for a potential learning curve affecting the outcome of the RFA cohort in the initial years of its application, we compared local recurrence for MWA patients with that of patients in the RFA cohort included in the most recent half of the study. The association with other independent variables was evaluated with stratified Cox regression using local recurrence as a time-dependent variable. All analyses were performed on Stata v12.0 (StataCorp LP. College Station, TX).

RESULTS

From 2001 to 2011, we performed ablations on 351 tumors (222 RFA and 129 MWA). Microwave was introduced in 2008. From 2008 to 2011, the percentage of microwave ablations increased from 20 % in 2008 to 98 % in 2010. We successfully matched 134 patients who underwent a total of 254 ablations (127 by each method). Beyond our matching criteria (tumor size, clinical risk score, and use of chemotherapy), the two cohorts were adequately balanced in terms of age, nodal status of the primary tumor, as well as the sizes of ablation achieved, and the proportion of ablations that were performed in combination with formal resections. The majority of patients (90 %) received preoperative systemic chemotherapy, and a similar proportion of patients in both arms had HAI therapy (54 and 46 %, for RFA and MWA respectively). Baseline characteristics are detailed on Table 1.

Postprocedural complications were seen in 25 % of patients. Morbidity rates were similar between the two groups (27 vs. 24 % for MWA and RFA, respectively. $P = 0.8$). Only 3 of the 16 patients who had an ablation without a liver resection developed a complication (2 in the RFA and 1 in the MWA groups). None of these could be directly attributed to the ablation (2 wound infections, and a ureteral leak related to primary tumor resection). In the patients who had an ablation combined with a resection (88 % of patients evaluated), the most common complications were wound infections (16 %), intra-abdominal fluid collections (8 %), and pleural effusions (4 %).

Ablation-site recurrence was seen in 19 %. Patients who underwent MWA had lower recurrence rates than those who underwent RFA (6 vs. 20 %, $P < 0.01$). While follow-up time was significantly shorter for MWA (18 months [95 % confidence interval (CI) 17–20] vs. 31 months [95 % CI 28–35]; $P < 0.001$), it was above the median time to local recurrence in both arms (13 months [IQR 8–21]). Neither arm has reached median local recurrence-free survival, but the local-recurrence rate remained lower for patients undergoing MWA on stratified log-rank test ($P = 0.01$; Fig. 1). The recurrence rate for patients undergoing RFA in first half of the study time (2001–2005) was higher than for patients in the second half (33 vs. 15 %; $P = 0.04$). Excluding these patients ($n = 36$), the difference in local recurrence rates between the MWA and RFA groups remained significant (6 vs. 15 %; $P = 0.04$).

Median overall survival for the entire cohort was 55 months (IQR 25-NR), with a median follow-up time for survivors of 34 months (IQR 19–45). There was no difference between arms in median overall survival (55 months [IQR 25-NR] vs. NR [IQR 25-NR] for RFA and MWA, respectively, $P = 0.5$). Evaluation of the association of independent variables with local recurrence revealed MWA (hazard ratio [HR] 0.25 [95 % CI 0.08–0.75]; $P = 0.01$) to be associated with lower local recurrence on stratified univariate and multivariate Cox regression (Table 2).

DISCUSSION

Thermal ablation is being used with increasing frequency for management of CRLM.[3] Most of the reported literature focuses on RFA, because it is the most commonly available technique. It provides adequate oncologic outcomes and better results than cryoablation.[1,9] During the past several years, MWA has gained acceptance as a favorable alternative and in some cases a preferred choice of ablation modality. The touted reasons are mostly theoretical and practical, because no level 1 data are available that show an oncologic advantage of MWA over RFA.[10–12]

In lieu of data from randomized controlled trials, the present retrospective cohort analysis compares these two procedures in the strictest fashion possible. Matching on size, CRS, and chemotherapy is a reasonable method to create two similar groups using factors that potentially affect oncologic outcomes. This matching allowed us to evaluate the impact of the techniques themselves on outcome. Additional matching factors could not be included given the number of ablations (127 per modality) and the 19 % overall event rate. In our cohort, MWA of CRLM resulted in lower local-recurrence than RFA. Even though longer follow-up may increase the recurrence rate in the MWA group, neither of the groups had reached the median local recurrence-free survival at last follow-up, and actuarial local failure estimations demonstrated better local control with MWA. Furthermore, the median time to local-recurrence in this cohort compares to that observed in prior studies of resection for advanced CRLM and is shorter than the median follow-up for MWA, suggesting that the follow-up period may be sufficient to capture most recurrences.[13] Given the time discrepancy between the two modalities and the initial use of RFA exclusively at our institution, we compared the local recurrence rates between RFA and MWA, excluding the patients who underwent RFA in the first half of the study. This minimizes the potential for a learning curve effect negatively impacting the outcomes of RFA. While a higher local-recurrence rate was found in the initial cohort, the difference between MWA and RFA remained significant after exclusion of the patients in the early half of the study. The present study does not attempt to compare overall survival between these cohorts as there are many variables that influence this outcome and are not considered in our analysis; we focused our analysis exclusively on local recurrence rates.

In a prior experience, we found a local recurrence rate of 11 % in patients treated with any type of ablation.[1] Larger tumors had a higher risk of local-recurrence. Interestingly, so did patients who did not receive postoperative chemo-therapy and those who had cryoablation. Our prior observations reporting high local-recurrence rates with cryotherapy are in line with previously reported data.[9] No difference in local-recurrence was identified between patients who underwent RFA and those who underwent MWA in our earlier, unmatched report; however, only a small minority of patients underwent MWA in that cohort (42/315; 13 %), thus limiting the power of that comparison.

On a prospective cohort study, Martin et al. [4] evaluated the outcomes of MWA of a variety of liver neoplasms of which the majority were CRLM. The ablation-site recurrence in this subgroup was 6 %. Furthermore, they performed a matched comparison of 40 patients undergoing MWA and 40 patients undergoing RFA. Matching criteria were sex, age, histology, number and size of tumors, operative exposure, and simultaneous liver or extrahepatic resection. Even though it is unclear from their report how many patients in that matched cohort represented CRLM, MWA came out advantageous in every outcome. In this matched analysis, they report a local recurrence of 2 % for MWA compared with 17 % for RFA. A multi-institutional, phase-II study published in 2008 enrolled 87 patients with unresectable liver tumors (38 % CRLM) to undergo MWA.[14] At a mean follow-up of 19 months, these patients exhibited a local recurrence rate of 3, and 47 % were alive with no evidence of disease. These results are consistent with the present study, in which we found a recurrence rate of 7 % for MWA and a HR for local recurrence of 0.25 (95 % CI 0.08–0.75; $P = 0.01$) compared with RFA.

In a recent systematic review, 75 studies were identified that reported outcomes on thermal ablation for CRLM between 1994 and 2010.[3] Most studies reported results with RFA (36 studies), with local recurrence rates ranging between 10 and 31 %. Cryotherapy (26 studies), had the highest local recurrence rates (12–39 %), whereas studies reporting outcomes of MWA (13 studies) had the lowest (5–13 %). Because of the very wide variability in patient selection, ablation procedures, definitions of unresectability, and recurrences, etc., there was no attempt to compare directly different ablation techniques in this meta-analysis. Furthermore, these publications span a long period of time, during which the indications for resection have changed dramatically, thus making a comparison between these cohort studies, intrinsically flawed.

MWA for CRLM was introduced at our institution in 2008. The shift towards routine use of this technique over RFA was fueled by its relative ease of use and emerging data showing equivalence of both techniques. To date, no level I evidence has indicated superiority of either technique, and that situation is unlikely to change. We believe this question is well suited for a randomized, controlled trial. However, such a trial would likely require a multi-institutional collaboration to achieve statistical power. Furthermore, as more experience is gained with MWA, clinical equipoise may become an issue for some practitioners.

MWA causes coagulation necrosis by tissue heating from the agitation of water molecules that oscillate due to the microwave radiation.[11] The electromagnetic wave created by the microwave probe generates heat directly from the tissues and produces a wide homogeneous ablation zone.[10–12] Conversely, RFA generates necrosis by direct heating of the ablation probe and heat conduction through ablated tissues which limits its penetration and creates heterogeneous ablation zones. These differences provide potential explanations to the findings of our study and others that report higher success rates of MWA over RFA. On a study evaluating MWA of renal neoplasms, there were no viable cells within the ablation zone, which could explain the very low local recurrence rates.[15]

The ablation platform used during the study period was a first-generation system: ValleyLab microwave generator, 915 MHz/45 W. We now use newer systems that use higher frequencies (2.45 GHz), but the advantages of higher frequencies are unclear. To our knowledge, there are no data to compare 915 MHz and 2.45 GHz generators in humans. However, in a porcine model lower frequency microwave systems (915 MHz) achieved higher tissue temperatures and larger ablations when compared directly to higher frequency generators.[16] It is important to consider this potential difference, as this may directly impact the ability to obtain a complete ablation.

Complete ablation is critical to the oncologic safety of any type of ablation. By allowing multiple overlapping probes to be active simultaneously, MWA increases the likelihood of complete tumor eradication, particularly of larger lesions. Furthermore, MWA is less susceptible than RFA to heat-sink effect, making it a good alternative for ablation of lesions located near branches of the hepatic veins (adequate collateral drainage provided).[11] Furthermore, there is no need for the use of grounding pads for MWA. This decreases both the risk of burn injury, and potentially postoperative pain, as there is no energy conduction through the body.[12]

Its retrospective nature limits the conclusions that can be drawn from our study. Furthermore, even though our cohorts were matched, they are temporally unrelated, and it could be argued that in the last decade there have been signifi-cant changes in chemotherapy and in the indications for intervention in these patients. Additionally, perioperative chemotherapy and follow-up were determined by physician's preference and not standardized, being subject to changes across time. Some of the technical imaging details, and details of the procedures are not accounted for in our data (e.g., number of probes used, power-time curves, and specific lesion location within the liver); however, the devices were used independently by six experienced hepatobiliary surgeons following manufacture's recommendations for optimal ablations. These limitations notwithstanding, the present matched-cohort analysis is presented as an unbiased attempt to compare the two modalities. While our findings suggest a potential benefit in local recurrence rates for MWA, we believe this question is well suited for prospective evaluation.

CONCLUSIONS

Our findings suggest that MWA is associated with a decrease in local recurrence compared with RFA of CRLM. The limitations inherent to retrospective studies temper the conclusions that can be derived from this matched cohort comparison. A randomized trial or a larger, multi-institutional matched analysis could provide further evidence to answer this question.

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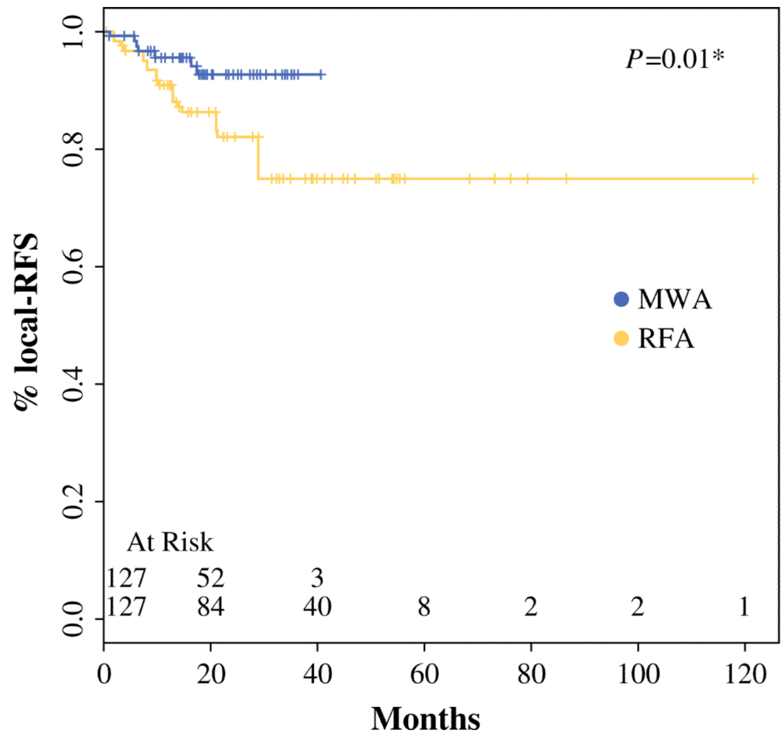

FIG. 1.

Kaplan–Meier curve illustrates the difference in local recurrence rates between patients treated with MWA and RFA.

*Stratified log-rank test. *RFS* recurrence-free survival; *MWA* microwave ablation; *RFA* radiofrequency ablation

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Table 1

Patient demographics and tumor characteristics

	RFA		Microwave		*P* value
Variable	***N***	***%***	***N***	***%***	
Total patients	67	100	67		
Age (yr), median (IQR)	56 (48–65)		55 (48–64)		0.5
Number of procedures*	75		69		
Number of treated tumors	127		127		
Tumors treated per patient (median)	1 (1–2)		1 (1–2)		0.8
1	41	61	35	52	
2	11	16	17	25	
>2	15	22	15	22	
Preoperative chemotherapy	60	90	61	91	0.9
N stage, median (IQR)	1 (1–1)		1 (1–1)		0.1
N0	25	38	16	24	
N 1–2	42	62	51	76	
Pump chemotherapy	36	54	31	46	0.5
Preablation CEA, median (IQR)	6 (3–12)		6 (3–15)		0.07
Clinical risk score					0.3
High (3, 4,5)	38	57	45	67	
Low (1, 2)	29	43	22	33	
Tumor size (cm), median (IQR)	1 (1–2)		1 (1–2)		0.09
≤1	67		78		
1.1–2	38		31		
2.1–3	15		13		
>3	7		5		
Ablation size (cm), median (IQR)	3 (3–4)		3 (3–4)		0.3
Ablation combined with resection	57 (85 %)		61 (91 %)		0.5

TABLE 2

Factors associated with local recurrence—stratified Cox

Covariate	Univariate—HR (95 % CI)	*P* value	Multivariate—HR (95 % CI)	*P* value
Age (yr)	1.06 (0.99–1.14)	0.08*		
Tumor size >1 vs. ≤1cm	1.25 (0.33–1.65)	0.7		
Ablation zone size (cm)	1.42 (0.64–3.2)	0.4		
Microwave ablation	0.25 (0.08–0.75)	0.01*	0.25 (0.6–1.0)	0.01

Clinical-risk score and perioperative chemotherapy were not included in this evaluation since they were matched for between the cohorts

*Variables included in the multivariate model