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Original Article

Role of Local Thermal Intervention as A treatment Option for Patients with Metastatic Liver Tumors

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Abstract

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Background: The liver remains a common site of metastases. Surgical resection was previously considered the mainstay for the treatment of hepatic metastases [HMs]. Currently, local ablation provides potential benefits for the treatment of such metastases with comparable results.

The aim of the work: This study aimed to evaluate the effect of different local thermal ablation interventions in the management of metastatic liver tumors

Patients and Methods: Our research included a total of 58 cases with 120 nodules who underwent local thermal ablation for the treatment of metastatic liver lesions. Microwave ablation [MWA] was employed for 22 cases, while radiofrequency ablation [RFA] was employed for 34 cases; two cases underwent both RFA and MWA. Technical assessment of ablation was performed using contrast-enhanced CT, dynamic MRI with DWI, or PET-CT scans conducted 4–6 weeks post-procedure to evaluate treatment response, defined by the absence of contrast enhancement at the ablation site. Follow-up was done for all cases at 3 and 6 months to evaluate recurrence rate, local tumor progression, disease-free interval, and 1-year survival.

Results: The technical effectiveness was 82.5% [48 / 58] on a per-case basis and 87.7% [100 / 114 lesions] on a per-tumor basis. The intrahepatic recurrence rate was 24.14% [14 / 58] after 3 months and 20.69% [12 / 58] after 6 months. The median follow-up was 14 months [range 10-18 months], and the 1-year survival rate was 87.8%.

Conclusion: RFA and MWA are very promising, minimally invasive interventions for treating secondary malignant hepatic tumors. Their application as local ablative therapies significantly enhances the role of interventional radiologists in the multidisciplinary management of oncologic cases..

Keywords: Liver Metastases; Thermal Ablation; Microwave; Radiofrequency.



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INTRODUCTION

The liver is considered the most frequent spot of metastatic lesions, particularly those originating from colorectal carcinoma [CRC] ^[1].

Numerous therapeutic options are established to address metastatic liver tumors ^[2]. Surgical interventions are still considered the gold standard for the treatment of metastatic liver lesions ^[3,4].

Although, many cases are non-operable for surgical resection ^[5]. Different interventional approaches for the treatment of unresectable liver tumors have become widely accessible ^[6].

Two main treatment strategies are available for liver malignancies: first, trans-arterial procedures involving embolic agents, chemotherapy, or radioactive substances; second, percutaneous thermal ablation methods such as radiofrequency ablation [RFA], microwave ablation [MWA], laser-induced interstitial thermotherapy [LITT], irreversible electroporation [IRE], and cryotherapy ^[7].

Percutaneous ablative procedures are employed for the treatment of small volume disease [small lesion size or lesions number < 5], whereas trans-arterial procedures are employed for the treatment of large volume diffuse disease [large lesion size or multiple lesions >5] ^[8].

Percutaneous thermal ablation has many advantages, including a wide range of therapeutic responses from a curative choice with the ability to completely ablate lesions to debulking of tumor load, thus allowing cases to become surgical candidates. Local ablation stands out from surgical resection by offering a more cost-effective approach, with fewer complications and significantly shorter recovery times ^[9].

Percutaneous local ablative interventions, such as MWA and RFA, induce cytotoxicity in liver lesions by heating the tissue, leading to acute coagulative necrosis and tumor cell death ^[10].

The extent of tumor cell cytotoxicity is determined by the temperature achieved during the heating process, which is influenced by the microwave or radiofrequency energy applied through the electrode. Temperatures exceeding 60°C cause protein denaturation and result in rapid cell death. In contrast, temperatures between 42°C and 60°C cause irreversible cell damage through mechanisms such as microvascular thrombosis, ischemia, and hypoxia ^[10].

THE AIM OF THE WORK

This research aimed to evaluate the impact of different local thermal ablative therapies [radiofrequency and microwave] in the management of metastatic liver tumors.

PATIENTS AND METHODS

This prospective research was carried out in the National Liver Institute – Menoufia University from October 2021 to October 2023 for 85 cases with 120 metastatic liver lesions treated by local ablation RFA and MWA.

Inclusion and Exclusion Criteria: cases with primary lesion were successfully treated after complete resection or systemic chemotherapy, cases with non-operable hepatic metastases [HMs], cases with no detectable extra-HMs, cases with HMs number were five or less, and tumor size of single lesion was 5cm or less are included in our research.

Cases with non-treatable extra-HMs or evidence of vascular invasion, or cases with HMs number more than five and size single lesion more than 5 cm were excluded from the research.

Pre-ablation Assessment:

All cases underwent pre-ablation assessments including a case medical history, physical examination, laboratory investigation [coagulation profile, tumor markers], and review of previous imaging of case and preablation ultrasound evaluation to assess tumor size, location, number, accessibility and best guidance approach.

Ablation intervention

Anesthesia:

It was performed for all the cases with conscious sedation and analgesia.

Sterilization:

Cleaning of skin by iodized alcohol and betadine

Local anesthesia:

Additional local anesthesia using lidocaine was done to skin and SC tissue along needle path.

Equipment:

For MWA, a microwave generator operating at 2450 MHz with a variable power output ranging from 0 to 150 W was utilized. A cooled-shaft electrode [14 G, 15 cm] was advanced into the lesion, with its tip positioned 1 cm beyond the nodule's deep margin. Ablation duration was tailored based on ultrasound visualization, specifically when the hyperechoic zone encompassed the tumor along with a 1.0 cm circumferential safety margin.

For RFA, grounding was established using one or more skin-placed grounding pads. A radiofrequency system [RF 2000; Radio Therapeutics] was employed. After central needle placement within the lesion, the electrode hooks were deployed inside the nodule. Power delivery began at 10 W, with a gradual increase of 10 W/min until reaching 90 W. Ablation continued until a significant rise in tissue impedance was noted, with the procedural aim of generating a hyperechoic zone extending more than 1.0 cm beyond the tumor margins.

Track ablation: After ablation, the electrode was removed with cauterization of the tract.

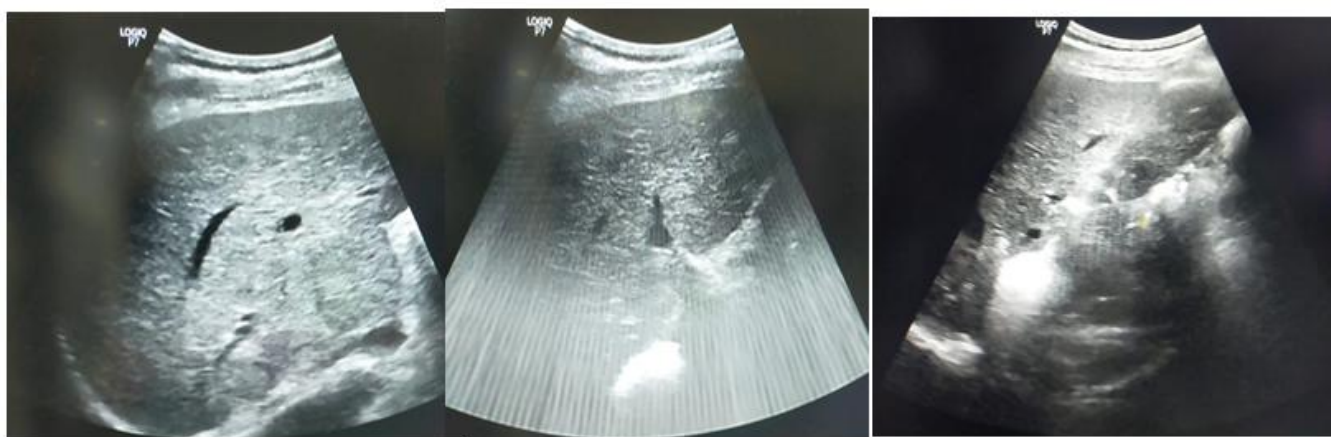


Figure [1] illustrates a target hepatic focal lesion seen between the inferior vena cava and right posterior portal vein branch, needle within hepatic focal lesion during RFA procedure, completion of procedure with complete vaporization of entire lesion

Treatment assessment and follow up

Initial follow up imaging [4-6 wks. Post procedure]: A triphasic CT research [140 kVp, 220 mAs, 1.5-2 ml/body weight of nonionic contrast] or dynamic MRI with DWI research or whole body PET CT were performed to evaluate the presence of residual tumor at the target lesion and any early complications. Non-enhancement of the ablated zone in the confine the tumor area and lack of peripheral irregular enhancement were considered complete ablation of the target lesion

Regular follow-up imaging: All cases have under gone follow up

using contrast-enhanced CT or MRI of the abdomen or PET CT every 3–6months. Technical effectiveness was defined as the proportion of target nodules exhibiting complete necrosis on initial post-ablation imaging, excluding any de novo lesions. We defined De novo lesions as new tumor foci appearing within the ablation zone on the first post-treatment imaging research, which are distinct from residual viable tumor tissue and represent entirely new sites of disease rather than incomplete treatment of the original nodule. Local recurrence referred to nodular or irregular enhancement at the margin of a previously successfully ablated lesion. Near local recurrence denoted new tumor foci immediately adjacent to the ablation zone. Distant recurrence encompassed new lesions appearing remotely from the treated site.

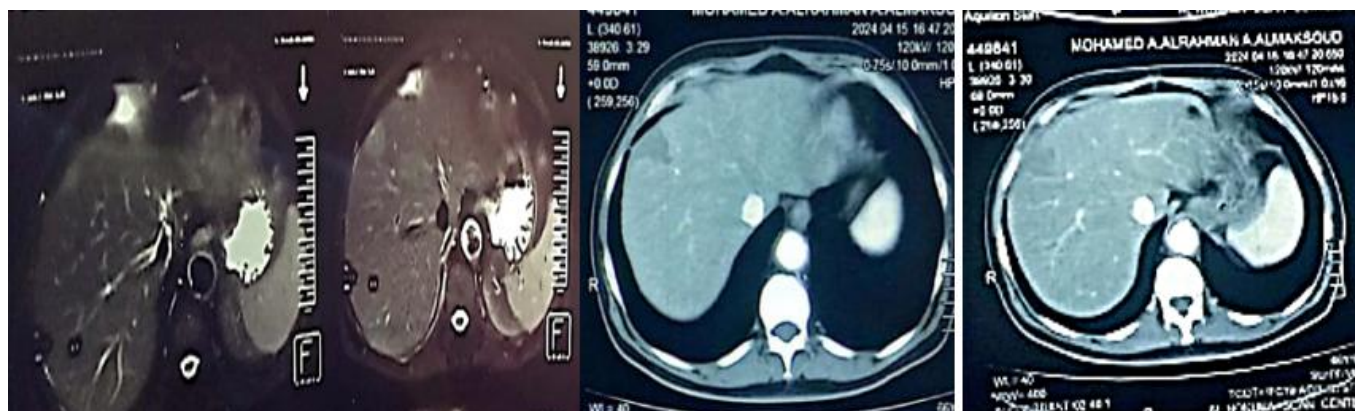


Figure [2]: MRT2WI preablation reveals right lobe segment VIII hepatic focal lesion and CECT post ablation reveals adequate ablation of target hepatic focal lesion.

Ethical Consideration: Written consent was taken from all cases before enrollment in the research. This research was conducted in accordance with the Research Ethics Review Committee of the National Liver Institute and was approved by the Institutional Review Board at National Liver Institute, Menoufia University at January 2024 [IRB: NLI IRB 00014014].

Statistical Analysis:

Categorical data were analyzed using either the Chi-squared test or Fisher's exact test, as appropriate. Univariate logistic regression was employed to identify independent prognostic factors associated with recurrence. A P-value < 0.05 was considered statistically significant. All statistical analyses were conducted using R Software version 4.1.2 [R Foundation for Statistical Computing, Vienna, Austria]. Kaplan-Meier survival curves were generated to illustrate survival outcomes.

RESULTS

Case's characteristics data: The study included 58 cases [24 males and 34 females], with 120 nodules that had undergone percutaneous thermal ablation treatment for HMs. Primary lesions were colorectal in 28 cases, breast in 10 case, pancreatic in 8 case, gastrointestinal stromal tumor [GIST] in 6 case, cancer cervix in 2 cases, lung in 2 cases and Renal cell carcinoma in 2 cases. 22/58 cases were treated by MWA, whereas 34/58 cases were treated by RFA and two cases have undergone both RFA and MWA ablation as shown in Table [1].

Technical effectiveness: initial imaging 4-6 weeks post procedure to detect completely ablated lesions Vs non-ablated lesion. The complete ablation rate on a per case basis was 82.5% [48 /58] and on a per tumor basis 87.7% [100 / 114 nodules] as shown in Table [2].

Survival after ablation was assessed over a median follow-up of 12 months [IQR 10–18]. By Kaplan–Meier analysis [Fig.3], the median

overall survival [OS] was 23 months, and the estimated probability of surviving to one year post-ablation was 87.8 % [95 % CI 78.8–97.7 %]. Progression-free survival had a median of 9 months. Table 3, 4

Intrahepatic Recurrence: The overall recurrence rate was 24.14 % [14/ 58] for the after 3 Months post ablation and 20.69% [12 / 58] after 6 Months post ablation. Univariate analysis was conducted to evaluate the impact of various factors—such as age, sex, ablation modality, number of lesions, and technical success—on recurrence rates, as presented in Table 5. While MWA was associated with a lower recurrence rate compared to RFA, the difference did not reach statistical significance [P = 0.240], also recurrence rate was affected by number of

lesions with higher recurrence rate in lesions more than 2 lesion compared to one lesion, no significant difference [P value 0.151], technical success was one of important factors that influence recurrence with significant higher recurrence rate with incomplete ablation Vs complete ablation [P value 0.022]. During the first year after treatment, six cases died, and four more deaths occurred thereafter. The principal cause of death was progression of the primary malignancy, particularly in pancreatic and colorectal primaries; other fatalities were attributable to chemotherapy complications in colorectal cancer and to local hepatic tumor progression in a case of cervical cancer.

Table [1]: Demographic and clinical data of the studied cases

All cases N=58		
Age [years]	Median [IQR]	50.5 [45-65.25]
Sex	Male	24 [41.38]
	Female	34 [58.62]
Type of primary lesions	Breast	10 [17.24]
	Cancer cervix	2 [3.45]
	CRM	28 [48.27]
	GIST	6 [10.34]
	Lung	2 [3.45]
	Pancreas	8 [13.79]
	RCC	2 [3.45]
Primary treatment	Surgery	50 [86.21]
	Chemotherapy	6 [10.34]
	No	2 [3.45]
Number of lesions	1	26 [44.83]
	2	20 [34.48]
	3	12 [20.69]
Ablation modality	MWA	22 [37.93]
	RFA	34 [58.62]
	MWA + RFA	2 [3.45]

Data are expressed as Median [IQR] or Number of cases [%]. MWA, microwave ablation; RFA, radiofrequency ablation. GIST: Gastrointestinal stromal tumor. RCC: Renal cell carcinoma

Table [2]: Results of ablation 4-6 weeks post

All lesions [N=120]		
Tumor necrosis	Complete	100 [87.71]
	Residual	8 [6.67]
	Viable	6 [5.00]
	Denovo	6

Technical effectiveness was 87.72% [100 of 114]

Table [3]: Time-to-event outcomes

All cases [N=58]	
Time to progression [months]	5 [4-5]
Time free interval [months]	9 [5-16]
Follow-up period [months]	12[10-18]

Table [4]: Overall survival outcomes for all cases

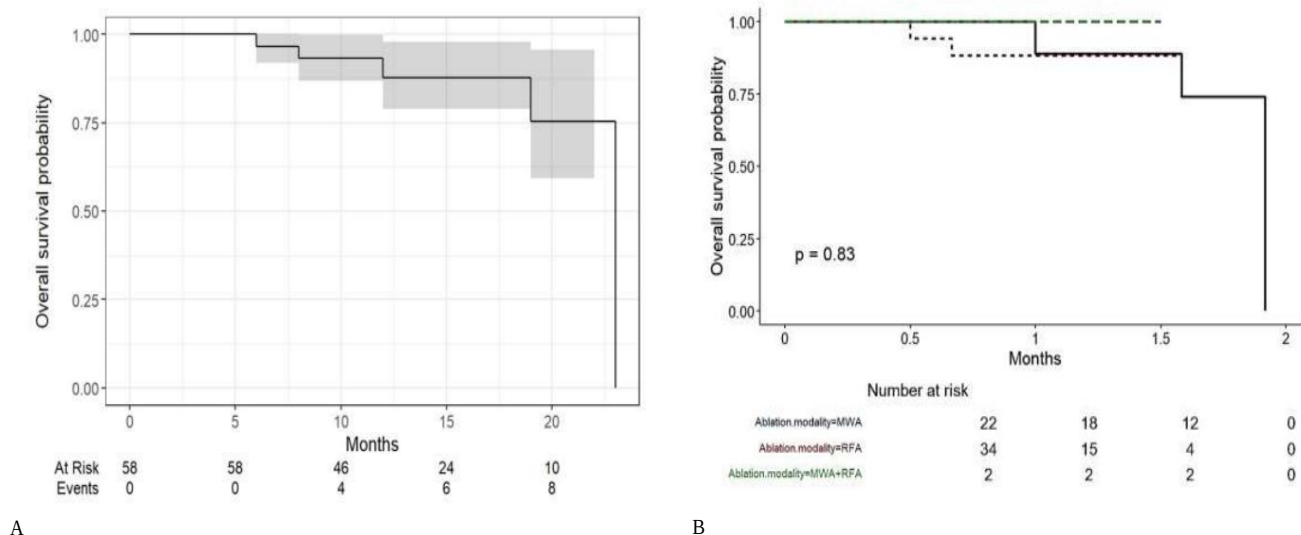
Outcome	Estimate [95 % CI]
1-Year Survival Probability	87.8 % [78.8 % – 97.7 %]
Median Survival Time [months]	23 [NA, NA]

CI – confidence interval; NA – not available

Table [5]: Univariate analysis of factors associated with local recurrence after 6 months

	Odds ratio	95% Confidence interval	P value
Age	0.98	0.93-0.1.04	0.552
Sex [male vs. female]	1.39	0.38-5.13	0.616
Lesion number [vs. 1]			
2	0.40	0.05-2.00	0.295
3	2.08	1.05-7.20	0.151
Ablation modality [RFA vs. MWA]	2.57	1.23-6.63	0.240
Technical success [incomplete Vs complete ablation]	4.78	1.92-15.08	0.022*
Denovo lesions	10.25	1.71-83.81	0.014*

Univariate analysis was carried out to assess the influence of factors including age, sex, de novo lesion, and ablation modality. We found an increased odds of recurrence after 6 months with the presence of de novo lesions [odds ratio =10.25, P<0.05]

**Figure [3]:** Kaplan-Meier curve for [A] survival rate after ablation and [B] after ablation by type of ablation.

DISCUSSION

This research involved 58 cases with 120 HMs treated with percutaneous RFA and MWA. The median OS was 12 months, with a 1-year survival rate of 87.78%, primarily due to progression of the primary disease. None of the cases with breast cancer or GIST died during the follow-up. The complete ablation rate was 82.5% per case and 87.7% per lesion.

Recurrence rates were observed at 3 and 6 months, with univariate analysis showing higher recurrence associated with incomplete ablation and a greater number of lesions. The median liver imaging follow-up was 14 months, and the 1-year local tumor progression rate was 23.4%. Tumor progression was significantly influenced by the ablation modality, primary treatment, and disease-free interval, with MWA showing better outcomes compared to RFA.

Survival

In agreement with our findings, **Vogl and colleagues** ^[11] stated median OS of 32.1 months in CRLM cases treated with MWA and a 1-year OS of 82.7%.

Survival outcomes are somewhat lower compared to those stated by **Solbiati and colleagues** ^[12], who treated 179 HMs in 117 cases with colorectal cancer using RFA, achieving an estimated median survival of 36 months [95% CI, 28–52 months] and 1-, 2-, and 3-year survival rates of 93%, 69%, and 46%, respectively.

In addition, **Livraghi and colleagues** ^[13] treated 134 colorectal liver metastases [CRLM] in 88 cases using percutaneous RF ablation and achieved complete necrosis in 63% of lesions. At a median follow-up of 33 months, 44% of cases with complete response remained disease-free, and 98% were spared surgical resection.

By contrast, **Akhan and colleagues** ^[14] stated a 1-year OS rate of 94.9%, with 3- and 5-year survival rates of 52.5% and 40.6%, respectively—substantially higher than the 1-year survival rate we observed. These differences may be attributable to cohort characteristics, including tumor size and burden.

Several factors may explain this disparity: our research included fewer cases and lesions, involved both colorectal and non-colorectal primary tumors, and achieved a lower complete ablation rate [70.8% vs. 100.0%].

However, our 1-year survival rate is still comparable to earlier RFA studies focemployed on CRLM, which stated survival rates of 87–96% at one year ^[12, 15-19].

In line with our findings, **Shah and colleagues** ^[20] compared MWA and RFA for HMs and stated 1-, 2-, and 3-year local tumor progression rates of 6.8%, 11.4%, and 15.9% for MWA and 17.6%, 20.6%, and 20.6% for RFA, respectively.

In addition, **Akhan and colleagues** ^[14] stated a primary success rate of 94.4% using RFA. Furthermore, after secondary ablation of residual disease, they achieved a cumulative success rate of 98.4%.

Technical effectiveness

Similar results were observed in previous studies. **Knot and colleagues** ^[21] achieved a 100% ablation rate using MWA in 57 cases with CRLMs.

In addition, **Soliman and colleagues** ^[22] stated ablation rates of 100% for lesions adjacent to the gallbladder, 75% for perivascular lesions, and 87.5% for subcapsular lesions using microwave ablation in a cohort of 44 cases with hepatocellular carcinoma.

Martin and colleagues ^[23] achieved a 97.6% ablation rate using MWA in 83 cases with HMs. **Gwak and colleagues** ^[24] stated a 91.4% ablation rate with RFA in 35 cases with CRLM.

Intrahepatic Recurrence

Comparable recurrence rates were found in the literature, **Lorentzen T and colleagues** ^[25] stated a 9.6% local recurrence after MWA in 125 liver metastases.

In another research, **Rath and colleagues** ^[26] observed a 7.5% recurrence rate two years after RFA.

Our recurrence findings are also in agreement with **Livraghi T and colleagues** ^[27], who concluded that tumor size and number were significant factors for local recurrence. While no universal cutoff is established, most studies report optimal outcomes for ≤ 5 metastases and lesion diameters ≤ 5 cm.

Local tumor Progression

Our progression rate aligns with the findings of **Gunabushanam G and colleagues** ^[28], who stated new tumors in 58% of cases at a mean of 10 months [range 4–44 months]. Our median disease-free interval is also similar to that stated by **Vlastos G and colleagues** ^[29].

Our median disease-free interval is also similar to that stated by **Boutros and colleagues** ^[30], who concluded that MWA offers technical advantages over RFA, such as higher intratumoral temperatures, faster and larger ablation zones, and less sensitivity to the heat-sink effect.

In contrast, **Akhan and colleagues** ^[14] stated long-term disease-free survival [DFS] metrics with 1-, 3-, and 5-year DFS rates of 44%, 10.2%, and 6.7%, respectively.

Conclusion:

Local thermal ablation is a safe and effective for cases with HMs, particularly those with limited hepatic metastatic disease who are not candidates for surgical intervention. In addition, RFA and MWA can be employed for debulking tumor load, making cases eligible for surgical resection. RFA and MWA are very promising, minimally invasive interventions for treating HMs and have several advantages, including low cost, lower complication rates, reduced morbidity and mortality, and minimal hospital stay.

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