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Current perspectives on microwave ablation of liver lesions in difficult locations

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ABSTRACT

Microwave ablation (MWA) is becoming the standard of care in treating liver lesions smaller than 3 cm benefiting from a plethora of radiofrequency ablation (RFA) data in the literature. Some of the advantages of MWA compared to RFA are as follows: Faster ablations, more reproducible and predictable heating, better thermal conductivity in different liver tissue environments, and less susceptibility to heat-sink effect. Despite its many advantages, there are still concerns regarding MWA use in high-risk locations such as near portal veins, near the bile ducts, and near the heart. Some centers have historically considered these tumor locations as a contraindication to percutaneous thermal ablation. In this review, we summarize the current data on the safety of MWA of liver tumors in challenging locations. We also discuss several technical tips with examples provided.

Keywords: Microwave, Ablation, Tumor, Liver, Transplant, Metastasis, Ablation contraindication, Location

INTRODUCTION

According to the most recent update of the Barcelona Clinic Liver Cancer staging system, if a liver transplant is not an option in the treatment of hepatocellular carcinoma (HCC), the first approach should be thermal ablation for BCLS 0 stage and lesions <2 cm.[1] However, according to this recent update, resection may be preferred for larger nodules and those in high-risk locations for ablation. The most commonly used two modalities of liver ablation are radiofrequency ablation (RFA) and microwave ablation (MWA). While RFA is a well described modality for liver ablation in the literature, MWA is becoming the standard of care in HCC treatment due to its many advantages, such as predictable heating thermodynamics, absence of impendence allowing for greater penetration of MW energy through charred tissues, and rapid achievement of the target temperature.[2,3] However, there are still concerns about performing MWA for lesions in challenging locations such as subdiaphragmatic, near cardiac areas, near gallbladder, porta hepatis, and inferior vena cava (IVC). Meanwhile, there is growing literature investigating the safety of MWA of hepatic lesions located in high-risk areas.[5] This article presents an overview of the latest evidence on the outcomes of image-guided MWA therapies for liver lesions in difficult locations.

MWA OF LIVER LESIONS NEAR THE DIAPHRAGM

Subdiaphragmatic liver tumors can be difficult to target due to the variable temporal position of the tumor during the breathing cycle. Mainly, there are two concerns during the ablation of these lesions. First is the need for transpleural access, which is believed to be associated with pulmonary or diaphragm complications.[5] Second, local tumor progression (LTP) due to ineffective ablation is considered another inherent limitation. As a result of these concerns, subdiaphragmatic location is accepted as a contraindication for tumor ablation by some operators. While the existing literature suggests that MWA of subdiaphragmatic tumors is not associated with significantly higher complication rates, most of this concern is based on case reports describing diaphragmatic perforation and hernias following subdiaphragmatic tumor ablations.[6,7] Furthermore, data describing complications after transpleural approach during percutaneous liver ablation derive from RFA studies. Several RFA reports show high complication or LTP rates for these tumors compared with surgical approach.[8-10] As a stark contrast, MWA literature describes far less concerns. The largest retrospective study reporting the safety of transpleural access for MWA was published by Chieu *et al*., who reviewed 174 liver tumors. They found that most complications were minor, and the most common complication of the transpleural approach was pneumothorax.[11] In another study with 131 liver tumors that underwent computed tomography (CT)-guided transpleural MWA, tumors >3 cm were associated with higher pneumothorax risk. However, the authors did not report the number of antennas used for MWA.[12] Another large study reviewing 71 consecutive MWA sessions through transpulmonary approach under CT guidance reported technical success of 100%. The most severe complication was pneumothorax needing chest tube placement (11%), and there were no pulmonary complications at the 1-month follow-up.[13] According to their results, the most significant predictor of pneumothorax was lesional location within the left hemi-liver. In addition, some authors mention that subdiaphragmatic left-sided lesions should be performed with extra caution as access to these lesions can be more difficult as they oscillate more with respiratory or cardiac motion.

MWA OF LIVER LESIONS NEAR THE HEART

Similar to ablating near the diaphragm, percutaneous ablation of liver lesions near the heart is often avoided due to concern for direct cardiac injury or cardiac arrhythmia. A publication by Carberry *et al*. retrospectively compared MWA cases performed with ablation zones ending within 5 mm of the myocardium against a control group. There was no significant difference in the ablation zone size, the number of ablation probes used or duration or wattage used during the procedure, the number of cardiovascular events, and rates of LTP.[14] Another study by Sanampudi *et al*. reviewed 17 liver lesion cases with ablation zones located 5 mm or less to the heart and reported no cardiac complications.[15] However, an animal study investigating MWA of lesions close to the heart in porcine models demonstrated that MWA within 5 mm of the pericardium was associated with an increased risk of cardiac arrhythmias and thermal injury to the cardiac tissue.[16] They have also observed spontaneous resolution of arrhythmias once ablation was terminated.[14]

Nearly of authors of these studies agree that subdiaphragmatic and near-cardiac liver lesion ablations can be challenging as it requires high level of expertise and diligence. Possible contributing factors are limited visualization, breathing motion, ventilator related settings, and, ultimately, a greater challenge with antenna placement for subdiaphragmatic tumors than those located more centrally.[17] Another possibility is that these tumors may have been undertreated due to fear of damaging the diaphragm, lungs, or pericardium.[8] To the contrary, the movement of the heart during systole and diastole, as well as the movement of the lungs and diaphragm with breathing, can serve as a protective mechanism in decreasing cardiac and diaphragmatic thermal injury, as it has been shown that thermal injury occurs as a compounding effect on gross morphology in porcine models during lung MWA.

Carberry *et al*. commented that MWA of hepatic dome lesions located near the heart could be treated using craniocaudal CT gantry angulation, which can help delineate the ablation antenna trajectory while correcting for diaphragmatic angulation to see the trajectory in one plane. Another proposed maneuver is taking into account the epicardial fat pad during needle placement to use as protective natural barrier to slow energy diffusion toward the pericardium since adipose tissue is a known poor conductor of MW energy.[15] Other techniques include artificial pleural effusion and iatrogenic pneumothorax. Contrast and saline mixture can be instilled into the pleural space to isolate the ablation site and diaphragm. Similar to the fluid, air can be injected into pleural space to create iatrogenic pneumothorax to minimize lung injury during ablation.[15] An example of subdiaphragmatic and subcardiac lesion ablation is demonstrated in [Figure 1].

MWA OF LIVER LESIONS NEAR HEPATIC VEINS AND IVC

The superior thermodynamics of MWA has spurred a debate regarding treatment strategies of liver tumors near large vascular structures. Perivascular locations defined as lesions immediately adjacent to vessels >3 mm, have been associated with higher LTP rates; an aggressive approach may be needed for adequate coverage. The overarching goal of thermal ablation is to effectively treat the tumor with an ablative margin to minimize the risk of LTP. Meanwhile, the concern of thrombosis of the adjacent hepatic vessels can result in serious liver injury.[18] However, data on hepatic vascular injury after thermal ablation is limited.[19] Some studies showed that vessel size, vessel-antenna distance, and hepatic vessel type can all be factors associated with risk of vascular occlusion after thermal ablation. Nevertheless, these conclusions were derived from phantom or non-tumor porcine models.

Caval blood flow is also subject to transmitted backpressure from the heart throughout the cardiac cycle, resulting in a substantially faster and more pulsatile flow pattern as compared to the portal veins.[20] Chieng *et al.*'s study showed that greater vessel size causes a higher heat-sink effect, increasing the risk of incomplete ablation and higher recurrence rates.[20,21] As previously discussed, MWA of liver tumors has shown very promising results for lesions adjacent to large liver vasculature such as the hepatic veins and IVC.[22] An example of liver lesion near the IVC is shown in [Figure 2].

MWA OF LIVER LESIONS NEAR PORTAL VEIN

Portal veins have slower blood flow due to drainage into high-resistance hepatic sinuses. This relatively sluggish flow is exacerbated in patients with cirrhosis and portal hypertension, with even higher sinus pressures and slower hepatofugal flow. This state of relative blood flow stasis is less effective at dissipating heat, resulting in vessel occlusion as a consequence of thermal heat ablation. A study by Chiang *et al.* demonstrates that portal vein occlusion significantly correlates with smaller vessel diameter (<3.2 mm).[23] In comparison, hepatic veins thermal injury is only significant with much smaller vessel diameter (<1.5 mm) than the portal venous system. The reason behind the higher occlusion rate of portal veins compared to hepatic veins could be due to differences in the flow's pattern and velocity. Hepatic veins were found to be more resistant to thermal induced occlusion, with vessels larger than 1.5 mm in diameter being relatively protected from occlusion. This increased rate of likelihood of portal vein occlusion as compared with hepatic vein occlusion within the ablation zone (39.7% versus 15.0%) using equivalent size distributions is similar to the results of previous *in vivo* studies.[20] Meloni *et al.* reported that 3/21 (14%) liver ablations showed diffuse endothelial damage of portal vein after MWA in an *in vivo* porcine model.[24] A study investigating the safety of MWA lesions near porta hepatis among 65 patients found that CT-guided MWA is an effective and safe treatment for tumors adjacent to the porta hepatis, particularly for lesions <3 cm.[25]

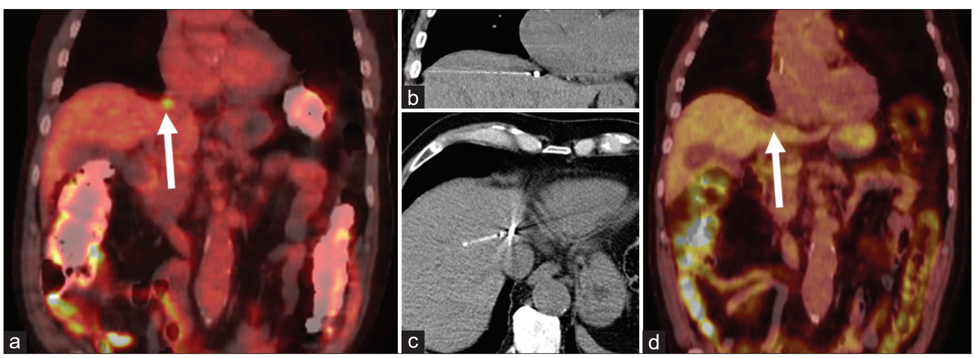

Figure 1: A 67-year-old male with alcoholic cirrhosis found to have LIRADS-5 lesion in hepatic segment VIII. (a) Pre-procedure coronal PET – computed tomography (CT) shows 1 cm increased FDG uptake in segment VIII near the heart (arrow). (b) CT-guided microwave ablation ablation of the tumor. The antenna tip abuts the diaphragm just under the heart. (c) Post-ablation 1-month follow-up PET-CT shows no more FDG uptake within the lesion (arrow).

Figure 2: A 63-year-old female with NASH cirrhosis found to have LIRADS-5 lesion in hepatic segment VII. (a) Axial contrast-enhanced late arterial phase computed tomography (CT) images demonstrates a 2.6-cm arterially enhancing hepatocellular carcinoma (arrow) in segment VII near the IVC (arrowhead). (b) Axial CT image from the microwave ablation procedure shows probe directed to IVC (arrowhead). The tip is directed at the IVC. (c) Contrast-enhanced magnetic resonance imaging at 1-month shows ablation cavity (arrow) without residual disease and patent IVC (arrowhead).

In an animal study investigating the effect of portal venous blood flow variation during MWA in a blood-perfused bovine liver model, Dodd *et al*. found no significant change of the average portal venous flow (60 vs. 100 mL/min per 100 g) throughout the ablation cycle. This was interpreted as follows; the size of the MWA zone is not affected by venous blood flow rates.[26]

In the same study, it was also found that the size of the ablation zone was highly variable when using RFA for liver ablation, with an opposite relationship to the rate of portal venous blood flow. These findings highly suggest that MWA has a more predictable thermodynamics, as it is less affected by heat sink, especially for lesions near portal veins; therefore, one would expect improved LTP rates with MWA as compared to RFA in percutaneous ablation of liver tumors. An example of liver lesion near the portal vein is shown in [Figure 3].

MWA OF LIVER LESIONS NEAR GALLBLADDER

Ablation of tumors near the gallbladder can be challenging due to risk of gallbladder perforation or induction of thermal cholecystitis. Although gallbladder complications are rarely life-threatening, they can cause a decreased quality of life. Therefore, ablating liver tumors in close proximity to the gallbladder remain controversial. Gallbladder complications from tumor ablation near the gallbladder have been reported in animal studies.[27] However, retrospective human studies have shown that MWA performed, near the gallbladder is safe with temperature monitoring, and that efficacy can be enhanced by adjuvant ethanol ablation. In a retrospective study, they combined ethanol ablation and MWA in the treatment of lesions near the gallbladder. During the procedure, they monitored the temperature using a thermocouple placed near the gallbladder wall.[28] Their immediate technical success was 96.5%, with no major complications. LTP was reported at 3% with a median follow-up of 30.1 months. Huang *et al*.'s reported a study, where 77 tumors were ablated using temperature control during the ablation procedure, these lesions were located 0–1 cm near the gallbladder. When the temperature reached 56 °C, microwave energy emission was discontinued and, then, restarted when the temperature dropped to 45 °C. In addition to thermal monitoring, they performed concomitant ethanol injection into the tumor. The authors of this study recommend thermal monitoring, which could be time-consuming. An example of liver lesion near the gallbladder is shown in [Figure 4].

DISCUSSION

Microwave energy causes tissue heating through the oscillation of water molecules by applying an alternating electromagnetic current. The arrival of second-generation MWA devices over the past decade produced devices with higher power outputs, greater efficiency in power delivery at the antenna tip, and an improved safety profile with the development of a more sophisticated internal cooling system, field control, and wave length control of the delivered MW energy. MWA can achieve higher temperatures and create larger ablation zones faster than RFA. Microwave technique also has the advantage of conducting multiprobe ablations without the known RF limitation of having electromagnetic interference when using several probes. Furthermore, MWA has been shown to give more predictable ablation zones with overall greater consistency across different tissues.

Given the mentioned benefits, MWA has largely supplanted RFA for liver tumor ablation in many clinical practices but still have inherited many of its conventionally accepted concerns and limitations without much direct evidence. The higher power output of MWA has led to some hesitancy in its use under certain circumstances, some of which we have reviewed in this article. Still, there is little ongoing investigation into whether these concerns are even warranted.[9]

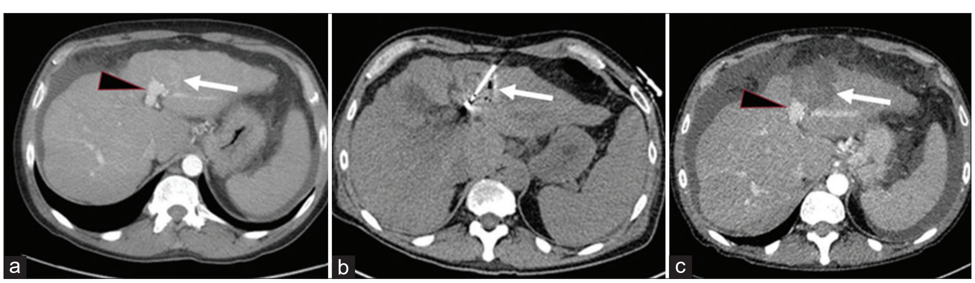

Figure 3: A 73-year-old male with alcoholic cirrhosis found to have LIRADS -4 lesion in hepatic segment III. (a) Axial contrast-enhanced late arterial phase computed tomography (CT) images demonstrate a 2.6-cm arterially enhancing hepatocellular carcinoma (arrow) in segment III near the portal confluence (arrowhead). (b) Axial CT image from the microwave ablation procedure shows probe directed toward the portal vein (arrow). (c) Axial contrast-enhanced image performed 1-month post-ablation shows no evidence of residual tumor (arrow) and patency of the adjacent portal vein (arrowhead).

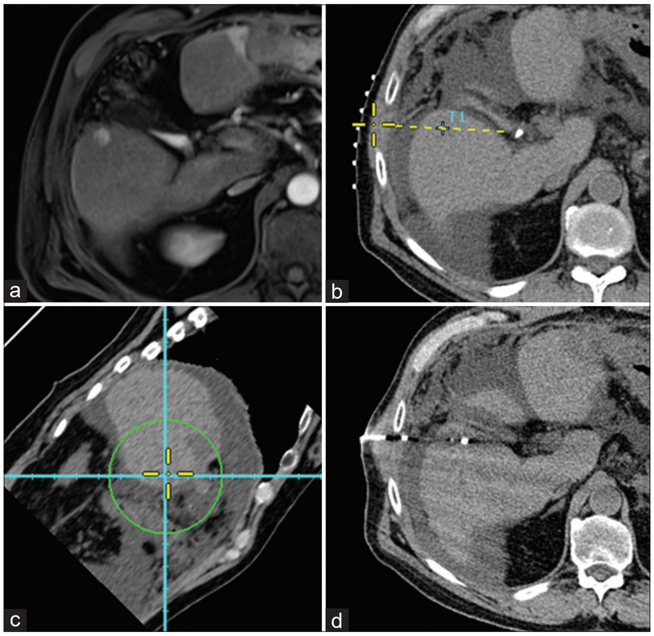

Figure 4: A 69-year-old female with cryptogenic cirrhosis found to have LIRADS-5 lesion in hepatic segment V. (a) Axial magnetic resonance imaging T1 post-contrast sequence shows a 1.2 cm enhancing target lesion with trajectory planning. (b and c) 3D computed tomography (CT)-US needle navigation (PercuNav, Philips, Andover, MA) images show. (d) Axial non-contrast CT demonstrates an microwave ablation antenna placed through a lateral percutaneous approach. The antenna was placed through the axis of the tumor.

Although literature reviewed herein support the safety of using MWA in high-risk locations such as near the heart, near the diaphragm, and near hepatic hilum, ancillary maneuvers can be performed as an added layer of safety depending on proceduralist expertise. The most commonly described ancillary maneuvers are hydrodisplacement and artificial hydropneumothorax. Both of these techniques aim to increase the distance between the ablation zone and the structure at risk for damage. Hydrodisplacement represents the administration of fluids into the surrounding adjacent third space. However, since fluids tend to move into a dependent portion, continuous administration may be required throughout the procedure to maintain the distance created by fluid as well as to provide a cooling effect during the procedure. Like fluid, air can be injected into pleural space to create an artificially induced pneumothorax or pneumoperitoneum to minimize lung or diaphragmatic injury. Another technique described in the literature was using the epicardial fat pad as a buffer zone during pericardial liver lesion ablation. However, one must note that these additional maneuvers can prolong procedural time and may cause abdominal distention and pain resulting in prolonged admissions, chest tube placement, or need for post-procedural paracentesis. Some centers use irreversible electroporation (IRE) for liver lesions in high-risk hepatic locations.[29] IRE is an emerging non-thermal ablation technique that can treat lesions near critical structures such as biliary ducts, gallbladder, and portal vein. During IRE, short pulses of high-frequency energy induce pores in the lipid bilayer of cells, causing cell death through apoptosis. However, the literature on this modality in treating liver malignancies is limited. Some advantages of this modality are the small gauge of the probes and relatively fast ablation times. However, larger ablation zones require multiple probes, which can add to procedure complexity, prolonging the procedure time and increasing bleeding risk. Canon et el. reported 59.5% 1-year recurrence-free survival rate in their prospective study, which is comparable with MWA data. They have also found that the recurrence rates tended to be higher in lesions with a diameter >4 cm.[30]

MWA seems to overcome the limitations of other percutaneous ablation modalities and is becoming the first choice for thermal-ablative therapy in HCC. Further studies are needed to support these preliminary findings.[4]

The advent of second-generation MWA devices over the past decade produced devices with higher power outputs, better heat distribution within the ablation zone, and an improved safety profile. The superiority of MWA is evident from the available literature given its ability to ablate faster, produce a larger ablation, and a far more predictable ablation zone regardless of variation in liver tissue composition or nearby vasculature.

CONCLUSION

MWA of hepatic lesions in high-risk locations seems to be relatively safe and effective in patients without the routine use of ancillary maneuvers. When hepatic lesion MWA is performed with appropriate planning and expertise, many of the historical concerns from the RFA literature did not translate into MWA ablation reported literature. A growing body of evidence continues to support the use of MWA in previously thought prohibitive locations. Further studies are still needed to validate these preliminary findings and to evaluate the extent of learning curve needed to perform these often challenging percutaneous ablations in a safe and reproducible manner.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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