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CT-guided microwave ablation of hepatic malignancies via transpulmonary approach without ancillary techniques

Driss Raissi¹, Sreeja Sanampudi², Qian Yu², Michael Winkler²

¹Department of Radiology Surgery, Medicine, and Obstetrics and Gynecology, University of Kentucky College of Medicine, ²Department of Radiology, University of Kentucky, Lexington, Kentucky, United States.



***Corresponding author:**

Driss Raissi,
Department of Radiology
Surgery, Medicine, and
Obstetrics and Gynecology,
University of Kentucky College
of Medicine, Lexington,
Kentucky, United States.

driss.raissi@uky.edu

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ABSTRACT

Objectives: The objectives of the study were to determine the safety and efficacy of computed tomography (CT)-guided transpulmonary percutaneous microwave ablation (MWA) for hepatic malignancies without the use of ancillary techniques.

Material and Methods: A retrospective review was performed on patients who underwent MWA for hepatic malignancy between January 2014 and February 2020 at a single tertiary center. Imaging was reviewed for each procedure to identify MWA showing transpleural transgression on CT scans. For these patients, demographics, ablation data, pulmonary complication rate, and predictors of pneumothorax were analyzed.

Results: A total of 71 consecutive sessions (62.1 ± 11.3 years, 79% of males) of MWA were performed to treat 71 tumors (1.90 ± 0.96 cm) via transpulmonary approach under CT guidance. Technical success was achieved in all cases immediately after the procedure. At 1-month follow-up, 65/69 (94.2%) patients had no residual disease (two patients were lost to follow-up). Pulmonary complications occurred in 26/71 (36.6%) sessions, and 15/26 (57.7%) were minor requiring no intervention. Pneumothorax occurred in 14/71 (19.7%) sessions, and the rate of major pneumothorax requiring chest tube was 8/71 (11.3%). Lesions on the left side of the liver (segments I–IV) and intra-procedural probe adjustment were found to be independent predictors of developing major pneumothorax ($P = 0.007$ and 0.028 , respectively). There were no reported pulmonary complications at the 1-month follow-up.

Conclusion: CT-guided transpulmonary MWA is safe and effective in treating hepatic malignancies. Although it is associated with the risk of developing pulmonary complications, patients underwent successful ablation of their hepatic malignancies without life-threatening complications and mortality.

Keywords: Computed tomography, Hepatic malignancy, Liver tumor, Microwave ablation, Percutaneous thermal ablation, Pneumothorax, Transpulmonary, Transthoracic

INTRODUCTION

Microwave ablation (MWA) has been universally acknowledged for its therapeutic efficacy in treating early-stage hepatocellular carcinoma (HCC) and metastatic liver lesions.^[1] Interventionalists take great caution in pre-procedural planning of tumors located within the superior segments, particularly the hepatic dome, given the high likelihood of pleural/lung transgression by the MWA probe.^[2] Multiple maneuvers can be performed to avoid the need for transpleural/transpulmonary approach, such as hydrodissection and iatrogenic

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pneumothorax.^[2-4] However, these techniques often necessitate additional interventions and can be associated with increased risk of minor complications.^[2,5] Given the increased risk of pulmonary morbidity, the choice of transpulmonary approach is still a matter of debate. The purpose of this study is to evaluate the feasibility and safety of transpulmonary computed tomography (CT)-guided MWA of hepatic malignancies using the latest generation of single probe high-power MWA system.

MATERIAL AND METHODS

Patient's selection

Following approval by our Institutional Review Board, a retrospective review was performed for patients who underwent MWA for primary or metastatic liver cancers at a single tertiary center between March 2015 and February 2020. The following inclusion criteria were adopted to screen a total of 409 patients who underwent MWA during this time frame: (1) Age >18 years; (2) patient received MWA for hepatic malignancy; (3) Emprint™ MWA System (Covidien, Boulder, Colorado, USA), (4) visualization of the probe's transpleural transgression on intraoperative CT scans, and (5) sessions with no more than 1 transpulmonary/transpleural pass. Dynamic contrast-enhanced cross-sectional imaging (CT or magnetic resonance imaging [MRI]) was used to determine the size and location of liver lesions 2–4 weeks before the procedure. Only patients that would have required ancillary maneuvers such as iatrogenic pneumothorax or hydropneumothorax were selected to undergo MWA through transpulmonary approach. Patients with lesions that could be treated without traversing pleura were not included in the study. MWA was performed by four interventional radiologists with at least 5 years of experience.

MWA

MWA was performed using the Emprint™ MWA system (Covidien, Boulder, Colorado, USA), with a generator using a frequency of 2450 MHz, maximum power of 100 W, and a single 14-gauge water-cooled dipole antenna.

All patients underwent MWA under general anesthesia. Initial non-contrast CT images were obtained (Somatom Aera, Siemens, Erlangen, Germany). The abdomen was prepped using standard antiseptic technique. A microwave probe was advanced into the location of the liver lesion under CT guidance. Adequate positioning of the probe was confirmed with single slice non-contrast CT images. The pre-calculated ablation zone included an ablative tumor-free margin of at least 1.0 cm. Ablation time and power were recorded. Following ablation of the lesion, standard tract ablation was performed at the end of the procedure with probe removal. An example of transpulmonary MWA is shown in [Figure 1].

No additional maneuvers such as hydrodissection and/or artificial pneumo-/hydrothorax were performed.

Chest and upper abdominal CT scans were obtained immediately after the procedure to evaluate for immediate complications. Serial chest X-rays were performed at 1 and 3 h after the procedure to exclude lung-related complications. Post-operative complications were classified into major and minor according to the Society of Interventional Radiology (SIR) adverse events criteria. All patients were admitted to the interventional radiology inpatient service for overnight observation and discharged the following day if the stay was uneventful. A pain control regimen with intravenous patient-controlled analgesia was provided and supervised by a dedicated pain team.

Post-MWA evaluation

All patients were instructed to return to the clinic for follow-up within 4–6 weeks postoperatively. CT or MRI scans of the abdomen and chest were performed to evaluate post-ablation response. The mRECIST criteria were used to assess for treatment response.^[6] Partial ablations were managed with further ablative treatments.

Variables of interest

The following patient demographics were identified for patients with transpleural/transpulmonary approach: Gender, age, smoking status (defined as history or current use of inhaled tobacco products), and history of chronic medical conditions (including chronic obstructive pulmonary disease and underlying cirrhosis and etiology). In addition, the following tumor characteristics and procedural information

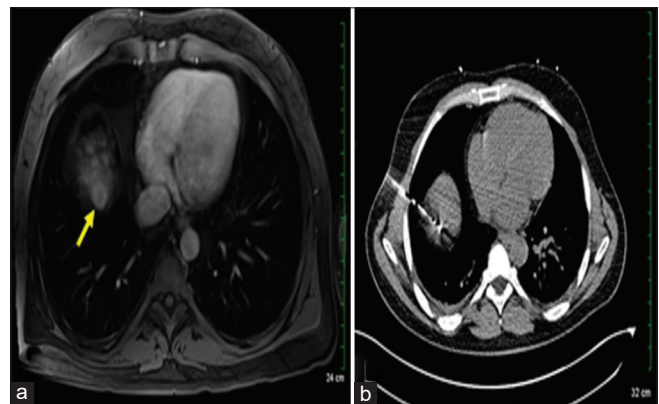


Figure 1: Computed tomography (CT)-guided transpulmonary microwave ablation (MWA) in a 51-year-old male with hepatocellular carcinoma in the hepatic dome. (a) Pre-procedural contrast-enhanced T1-weighted magnetic resonance imaging shows the targeted lesion measuring 1.9 cm (yellow arrow). (b) Intraprocedural CT image showing MWA needles transgressing the lung parenchyma and targeting the hepatic lesion.

were identified and recorded: Indication for ablation, type of tumor, tumor location (right hemi-liver: Segments V, VI, VII, and VIII; left hemi-liver: I, II, III, and IV), tumor size, intraprocedural probe adjustment, active ablation time per session, complications, and complete response rate immediately post-procedure and at 1-month follow-up. Intraprocedural probe adjustment is defined as repositioning of a MWA probe after the initial ablation has been performed to provide larger overlapping ablation zones to account for large lesions or a suboptimal initial ablation without exiting the transpulmonary/transpleural access site.

Complications were categorized as major and minor based on the SIR guidelines.^[7]

Statistical analysis

All statistical analyses were performed with STATA (v.15.1). Clinically relevant variables that were associated with $P < 0.10$ on univariate analysis were introduced into a multivariate logistic regression analysis to assess for factors predicting pneumothorax. $P < 0.05$ is considered statistically significant. Only sessions with a single transpulmonary/transpleural stick were included in the analysis.

RESULTS

Baseline characteristics

A total of 71 consecutive sessions of CT-guided percutaneous MWA were performed using transpulmonary/transpleural transgression with the MWA probe [Table 1]. Sixty sessions were performed to treat primary hepatic malignancies (53 cases of HCC and two cases of cholangiocarcinoma); 16 were intended to treat metastatic lesions. A total of 71 tumors with an average diameter of 1.90 ± 0.96 cm were ablated as evidenced on immediate post-procedural CT scan. Most lesions were located in the right liver segments (58/71, 81.7%, segments V, VI, VII, and VIII). The mean age of this population was 62.1 ± 11.3 years with a male-to-female ratio of 55:16. The percentages of a smoker, chronic obstructive pulmonary disease (COPD), and cirrhosis were 38/71 (53.5%), 20/71 (28.2%), and 49/71 (69.0%), respectively. Hepatitis C (19/49, 38.8%) and non-alcoholic steatosis cirrhosis (NASH, 19/49, 38.8%) were the most common underlying etiologies of cirrhosis. Twelve of the 69 patients were listed for transplant, and two of these patients underwent transplant within the short-term follow-up period of 4–6 weeks.

Complications

Post-procedural pulmonary complications occurred in 26/71 (36.6%) sessions. More than half were minor, requiring no additional intervention (15/26, 57.7%). Pneumothorax was the most commonly encountered complication (14/71,

Table 1: Patient and tumor characteristics, treatment efficacy, complications, and follow-up data.

Sample size	76 sessions
Male: female	55:16
Age	62.1±11.3 years
Indication of ablation	
Primary: HCC or cholangiocarcinoma	55
HCC	53
Cholangiocarcinoma	2
Metastasis	16
Colorectal	15
Carcinoid	1
Location (per tumor analysis)	
I, II, III, IV	13/71 (18.3%)
V, VI, VII, VIII	58/71 (81.7%)
Size	1.90±0.96 cm
Smoker	38/71 (53.5%)
COPD	20/71 (28.2%)
Cirrhosis	49/71 (69.0%)
Hepatitis C	19/49 (38.8%)
Alcohol	6/49 (12.2%)
NASH	19/49 (38.8%)
Mixed	2/49 (4.1%)
Others	2/49 (4.1%)
Unknown	1/49 (1.85%)
Average ablation time	10.0±7.3 min
Total complication	26/71 (36.6%)
Pneumothorax	14/71 (19.7%)
Major pneumothorax	8/71 (11.3%)
Pleural effusion	10/71 (14.1%)
Atelectasis	8/71 (11.3%)
Hemothorax	2/71 (2.8%)
Complete response rate at 1-month follow-up	65/69 (94.2%)
HCC: Hepatocellular carcinoma, COPD: Chronic obstructive pulmonary disease	

19.7%), followed by pleural effusion (10/71, 14.1%), atelectasis (8/71, 11.3%), and hemothorax (2/71, 2.8%). Major pneumothorax occurred in 8/71 (11.3%) sessions. These patients were successfully treated with chest tube placement and were clinically unremarkable during their initial post-operational follow-up in the clinic. There was a 100% survival rate at 30-day post-procedure follow-up.

During 23/71 sessions, probe adjustment within the vicinity of the target lesion was performed to enlarge the ablation without exiting the initial transpulmonary/transpleural stick site. When probes were adjusted intraprocedurally, 6/23 (26.1%) sessions developed major pneumothorax compared to 2/48 (4.17%) sessions without probe adjustment.

Major pneumothorax occurred in 3/58 (5.2%) of the sessions involving right hemi-liver (segments V, VI, VII, and VIII) compared to 5/13 (38.5%) sessions involving left hemi-liver (I, II, III, and IV). According to the logistic regression analysis, tumor location ($P = 0.007$) and intraprocedural

probe adjustment ($P = 0.028$) were statistically significant predictors of major pneumothorax [Table 2].

When both major and minor pneumothoraces were considered, they occurred in 8/23 (34.8%) sessions in which probe's position was adjusted and 6/48 (12.5%) without adjustment. Nine out of 58 (15.5%) ablations on the right and 5/13 (38.5%) on the left developed pneumothorax, respectively. Tumor location and intraprocedural probe adjustment were not on multivariate analysis [Table 3, $P = 0.12$ and 0.053].

In the two patients who underwent liver transplants within a 4–6 weeks follow-up period, there was no evidence of diaphragmatic injury or scarring reported during the transplant surgery.

No statistical significance was found between the following variables and the development of pneumothorax: Cirrhosis, smoking status, COPD, ablation time, and tumor diameter. Although a large population of the patients in this study had underlying cirrhosis as comorbidity, cirrhosis in itself was not found to be a predictor of increased morbidity.

Outcomes

Complete ablation without residual disease was achieved in 65/69 (94.3%) sessions at 1-month post-ablation

follow-up imaging [Table 1]; two patients were lost to follow-up. All patients with residual disease underwent repeat successful ablation. No tract seeding (hepatic or pulmonary) or diaphragmatic hernia was reported during follow-up.

DISCUSSION

Gervais *et al.* illustrated the safety and efficacy of CT-guided transpleural approach during percutaneous liver biopsy,^[8] which shortens the distance between the skin and the hepatic lesions, allowing for easier needle placement and avoiding excessive cephalocaudal angulation of the needle. Most reported data on transpleural approach involving percutaneous hepatic ablation originates from radiofrequency ablation (RFA) studies. In a case series of seven patients, complete ablation was achieved in all cases with no local tumor progression during follow-up (7–14 months). In a cohort of 37 patients, the local tumor progression rate was 6/37 (16.2%).^[9] According to a study in which 91.7% of hepatic lesions were treated with transpulmonary RFA, no local tumor progression occurred during a mean follow-up time of 8 months.^[10] The present study focuses on transpulmonary CT-guided MWA of hepatic lesions. The complete ablation rate at 1-month follow-up is 94.6%, consistent with the previous literature.^[11] All residual

Table 2: Univariate and multivariate analyses to show the relationship of different factors and major pneumothorax.

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Cirrhosis	1.40	0.258–7.53	0.70			
Smoking	0.48	0.105–2.18	0.342			
COPD	0.331	0.0380–2.88	0.316			
Location (left vs. right)	3.39	1.51–7.58	0.003	3.34	1.39–8.04	0.007
Ablation time \geq 10 min	3	0.559–16.1	0.2			
Tumor diameter \geq 2.5 cm	0.469	0.0531–4.15	0.496			
Intraprocedural adjustment	8.12	1.49–44.2	0.015	7.91	1.25–49.9	0.028

COPD: Chronic obstructive pulmonary disease

Table 3: Univariate and multivariate analyses showing the relationship between different variables and pneumothorax likelihood (including both major and minor).

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Cirrhosis	0.520	0.156–1.74	0.288			
Smoking	0.839	0.260–2.70	0.768			
COPD	1.56	0.449–5.39	0.486			
Location (left vs. right)	1.84	0.951–3.57	0.07	1.72	0.865–3.43	0.12
Ablation time \geq 10 min	0.857	0.263–2.79	0.798			
Tumor diameter \geq 2.5 cm	0.220	0.0263–1.84	0.162			
Intraprocedural adjustment	3.73	1.11–12.54	0.033	3.41	0.99–11.8	0.053

COPD: Chronic obstructive pulmonary disease

diseases diagnosed on imaging at 1-month follow-up were successfully retreated with subsequent ablation.

A major concern of transpulmonary/transpleural liver lesion thermal ablation is the risk of pulmonary complications. According to a retrospective study of 174 liver tumors, transpleural approach is an independent factor of complications for subdiaphragmatic hepatic lesions.^[12] However, the majority of complications were rather minor, ranging from 26.5% to 50%, with a major complication rate of up to 28.6%, and no intractable pneumothorax has been reported.^[9,13-15] The pulmonary function tests of patients who underwent transpulmonary RFA of liver lesions at 1-month follow-up were unremarkable, regardless of the occurrence of minor and major complications.^[13] No overt loss of lung function was seen during follow-up which is consistent with reported literature and the fact that no significant ablation of lung parenchyma is performed. Results from the present study are consistent with prior reported data: The cumulative pulmonary complication rate was 36.8% with a major complication rate of 14.5%.

In the era of RFA and older generation MWA systems, multiple probes were often used to achieve an adequate ablation zone.^[16-19] Increased number of probes crossing the lung/pleura correlates with an increased risk of post-procedural pneumothorax.^[20] The high-power MWA system in the present study was FDA approved in 2014. Benefits of this new MWA system include higher intratumoral temperatures, shorter procedure completion times, and use of a single probe system.^[21] All 71 sessions from the present study were performed with a single transpulmonary stick.

Given that our study is designed as a retrospective case series without a control group, we used the reported lung biopsy literature data as another surrogate control for comparison. Heerink *et al.* looked at complication rates of CT-guided transthoracic lung biopsy concerning both core biopsy and fine-needle aspiration, and in both cases, pneumothorax was the most common complication occurring at rates of 25.3% and 18.8%, respectively.^[22] The pooled overall pneumothorax rate following pulmonary core biopsy was 38.8% (34.3–43.5%), based on a meta-analysis of 32 articles and 8133 procedures.^[22] In comparison, the pneumothorax rate of the present study is surprisingly lower (19.7%). Although our MWA probe has a larger gauge size (14 gauge) compared to 18–20-gauge size needles used in core biopsies, the complication rate of pneumothorax was found to be lower in the current study.^[22] Additional factors predicting pneumothorax during lung biopsy include smoking status and COPD.^[23,24] However, in the present study, smoking status and COPD were not statistically significant predictors of pneumothorax [Tables 2 and 3], but rather, intraprocedural probe adjustment was associated with a higher risk of developing major pneumothorax ($P = 0.028$). Probes are often adjusted during

CT-guided ablation to provide larger overlapping ablation zones to account for large lesions or suboptimal initial ablation. Its manipulation during a transpulmonary approach can create air leaks through the puncture site. In addition, small lung lacerations may occur given the significant caliber of the probe and the continuous respiratory motion around the probe's axis. Thus, thoughtful pre-puncture planning may reduce the need for probe adjustment, indwelling time, thereby reducing the risk of major pneumothorax. At our institution, we limit the tidal volume from mechanical ventilation to 300–350 ml to decrease shear forces around the probe's axis and degree of lung expansion.

Another statistically significant predictor of major pneumothorax is tumor location. In the present cohort, the ablation of tumors located at the left hemi-liver had a higher risk of major pneumothorax compared to their rightside counterparts. A greater portion of the left liver is subdiaphragmatic and pericardiac. Ablating left-sided lesions can be more technically challenging as they are more subjected to respiratory and cardiac motion. Most of the pulmonary complications occurred in lesions located in segments II and VI of the left hepatic lobe.

According to a retrospective study of 117 patients and 131 liver tumors that underwent CT-guided transpleural MWA,^[15] tumor size >3 cm has been reported to be significantly associated with a higher pneumothorax rate.^[15] However, this observation should be interpreted with caution, as the authors did not elucidate the number of probes that were used during each ablation session. Greater tumor size *per se* did not correlate with increased risk of pneumothorax in the present cohort [Tables 2 and 3].

To minimize iatrogenic injury to nearby structures, a gamut of adjunctive interventions have been implemented by operators during hepatic thermal ablation.^[2] Hydrodissection, also known as artificial ascites, involves the introduction of 5% dextrose or normal saline into the intraperitoneal cavity between the liver and parietal peritoneum.^[25] In addition to the protection of surrounding structures, improved visualization during ultrasound-guided liver ablation can also be a benefit of this technique.^[26] However, the rate of post-procedural pleural effusions can be as high as 56% and can persist longer than a week.^[3] Other complications include hyperglycemia, electrolyte abnormalities, and peritonitis.^[5] While the heat-sink effect from the surrounding fluid can be a major concern for RFA, MWA would be less affected. Similar to the concept of hydrodissection, artificial hydrothorax has been attempted by injecting saline into the pleural space to enhance the visibility of lesions located near the hepatic dome.^[27] Its application is limited by the significantly decreased pulmonary function during the infusion.^[28] Less commonly, artificial pneumothorax with air or CO₂ can be used to minimize pulmonary injury during

thermal ablation.^[4,29] Moreover, operators should be cautious about patient positioning to avoid air overexpansion and air embolism.^[2] None of the aforementioned additional techniques were utilized in the present study.

The results of the present study should be interpreted with caveats. This study is a single-arm non-comparative study. A proper control group would be very challenging to design. Surgery was not an option for these patients and comparison with MWA using ancillary maneuvers such as artificial hydropneumothorax or hydrodisplacement to avoid the transpulmonary approach would have been an option, but, it would still have introduced risks of its own and it is not an accepted standard either. Randomized controlled trials may be warranted to compare clinical outcomes of transpleural versus non-transpleural MWAs using ancillary maneuvers in patients with similar baseline characteristics. Furthermore, long-term outcomes such as overall survival and progression-free survival were not analyzed. In addition to the requirement of longer follow-up time, survival analysis is further complicated by concomitant medical and locoregional therapeutic regimens. Furthermore, the borderline statistical significance of tumor location and intraprocedural probe adjustment on pneumothorax rate in general (both major and minor) could have been due to underpowering. Future studies with larger sample size or meta-analysis may yield more information on clinical predictors of pulmonary complications.

CONCLUSION

Transpulmonary CT-guided MWA is safe and effective in treating hepatic malignancies. Despite the risks of developing pulmonary complications, the majority are minor complications requiring no further interventions at par with percutaneous lung biopsy. Whereas ablation of the left hemi-liver lesions (especially segments II and IV) is associated with a higher risk of developing major pneumothorax, minimizing intraprocedural probe adjustment and careful planning can decrease this risk.

Declaration of patient consent

Institutional Review Board permission was obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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