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Safety and efficacy of microwave ablation for lung cancer adjacent to the interlobar fissure

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Abstract

Background: This retrospective study aimed to assess the safety and efficacy of microwave ablation for lung tumors adjacent to the interlobar fissures.

Methods: From May 2020 to April 2021, 59 patients with 66 lung tumors (mean diameter, 16.9 ± 7.7 mm; range, 6–30 mm) adjacent to the interlobar fissures who underwent microwave ablation at our institution were identified and included in this study. Based on the relationship between the tumor and the interlobar fissure, tumors can be categorized into close to the fissure, causing the fissure, and involving the fissure. The complete ablation rate, local progression-free survival, complications, and associated factors were analyzed.

Results: All 66 histologically proven tumors were treated using computed tomography-guided microwave ablation. The complete ablation rate was 95.5%. Local progression-free survival at 3, 6, 9, and 12 months were 89.4%, 83.3%, 74.2%, and 63.6%, respectively. The complications included pneumothorax (34.8%), pleural effusion (24.2%), cavity (18.2%), and pulmonary infection (7.6%). There were statistical differences in the incidence of pneumothorax, cavity, and delayed complications between the groups with and without antenna punctures through the fissure.

Conclusions: Microwave ablation is a safe and effective treatment for lung tumor adjacent to the interlobar fissure. Antenna puncturing though the interlobar fissure may be a potential risk factor for pneumothorax, cavity, and delayed complications.

KEYWORDS
complication, interlobar fissure, lung cancer, microwave ablation

INTRODUCTION

Lung cancer is the second most common cancer globally and has the highest mortality among malignant diseases.[1] Based on pathology, lung cancer is categorized into non–small cell lung cancer (NSCLC) and small cell lung cancer. NSCLC is the commonest, accounting for 85% of all cancer cases.[2] Surgical resection is commonly acknowledged as the first-line treatment for early-stage primary lung cancer. However, ∼60% of lung cancer cannot be resected surgically owing to reasons such as poor cardiopulmonary function or advanced age.[3] Stereotactic body radiation therapy is a good regimen for most patients with lung cancer who cannot undergo surgical resection, but it also has limitations.[4–6] Therefore, several novel local treatment approaches have been developed, including image-guided thermal ablation (IGTA) therapy. IGTA, a precise, minimally invasive technique, has been used to treat early-stage lung cancer. The number of patients with lung cancer treated using IGTA each year is rapidly increasing.[7–10]

The scientific guarantor of this publication is Xin Ye.

FIGURE 1 The relationship between the tumors (white arrows) and the fissures was defined as follows: (a) close to the fissure, (b) causing the fissure, and (c) involving the fissure.

IGTA includes radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation, and laser ablation. Compared with other technologies, MWA has several advantages in the treatment of lung tumors, such as faster ablations (shorter procedure time), larger ablation zones, less sensitivity of tissue type to high temperatures, and less "heat sink" impact on perivascular tissues.[11–13] Based on previous studies, we consider that tumors located at a distance of <5 mm from the pleura, including subpleural and interlobular fissure, should be studied further. The increasing difficulties in puncture and the limitations of ablation directly affect local efficacy and exacerbate the complications. However, only a few studies with small sample sizes have reported the issues associated with ablation of subpleural lung tumors and biopsy of pulmonary interlobar fissure tumors.[14–16] To the best of our knowledge, this is the first study to assess the technical safety, efficacy, and complications of computed tomography (CT)-guided percutaneous MWA of lung tumors adjacent to the interlobar fissures and analyze the aspects involved.

METHODS

Patients

In our database, 289 patients with primary lung cancer who received MWA were enrolled between May 2020 and April 2021. Tumors within 5 mm of the interlobar fissure at any distance were characterized as adjacent to the interlobar fissure. The inclusion criteria were: (i) a distance of ≤5 mm between the tumor and the interlobar fissure, (ii) single tumor of <30 mm, and (iii) patients who refused or were not candidates for surgical resection. The exclusion criteria were: (i) poorly controlled infection, (ii) severe coagulation dysfunction, (iii) severe lung dysfunction, (iv) an ≤Eastern Cooperative Oncology Group performance score of >3, (v) chest wall muscle involvement, and (vi) massive pleural effusion resulting in atelectasis. This study eventually comprised 59 patients (35 men and 24 women, mean age, 60.5 ± 12.27 years) with 66 lung tumors.

All treatments were evaluated based on typical clinical features and radiological evidence, referring to expert consensus.[10] All tumors were diagnosed based on CT-guided tumor biopsy findings. Interlobar fissures were classified as left oblique, right oblique, and right horizontal fissures. Three classifications were devised based on the relationship between target lesions and interlobar fissures: lesions close to the fissures, lesions causing the fissures indentation, and lesions involving the fissures (Figure 1).

Procedure

CT (NeuViz64, Neusoft or uCT 760, United Imaging Healthcare) was used to guide the procedures. MWA was performed using the MTC-3C microwave ablation system (Vison-China Medical Devices R&D Center), ECO-100A1 microwave ablation system (ECO Medical Instrument), or KY-2450B microwave ablation system (CANYOU Medical), with a frequency of 2450 ± 50 MHz and adjustable continuous-wave output power ranging from 0 to 100 W. For the microwave antenna, the effective length was 100 to 180 mm and the outside diameter was 19G (19G antenna has the advantage of high puncture accuracy and fewer complications), with a 1.5 cm radiating tip (tapered end). The surface of the antennas was cooled using a water circulation cooling system.

Detailed ablation procedures were as previously described.[16,17] Immediately after the procedure, a chest CT scan was performed to evaluate the ablation zone and procedural complications. An additional chest radiograph was obtained 24 hours later to assess the occurrence of complications. The main complications observed were pneumothorax, post-ablation pain (measured using a numerical rating scale score), hemorrhage/hemoptysis, infection, or other syndromes. If a clinically significant pneumothorax or pleural effusion was noted during or after the procedure, immediate chest catheter was performed. For solid tumors close to the fissures, we preferred to puncture parallel to the fissure, avoiding damage to the two layers of the pleura (Figure 2).

For tumors causing and involving the fissures, we preferred to puncture vertical to the fissure, which made it easier to place the antenna in the center of the tumor and obtain an accurate ablation zone (Figure 3).

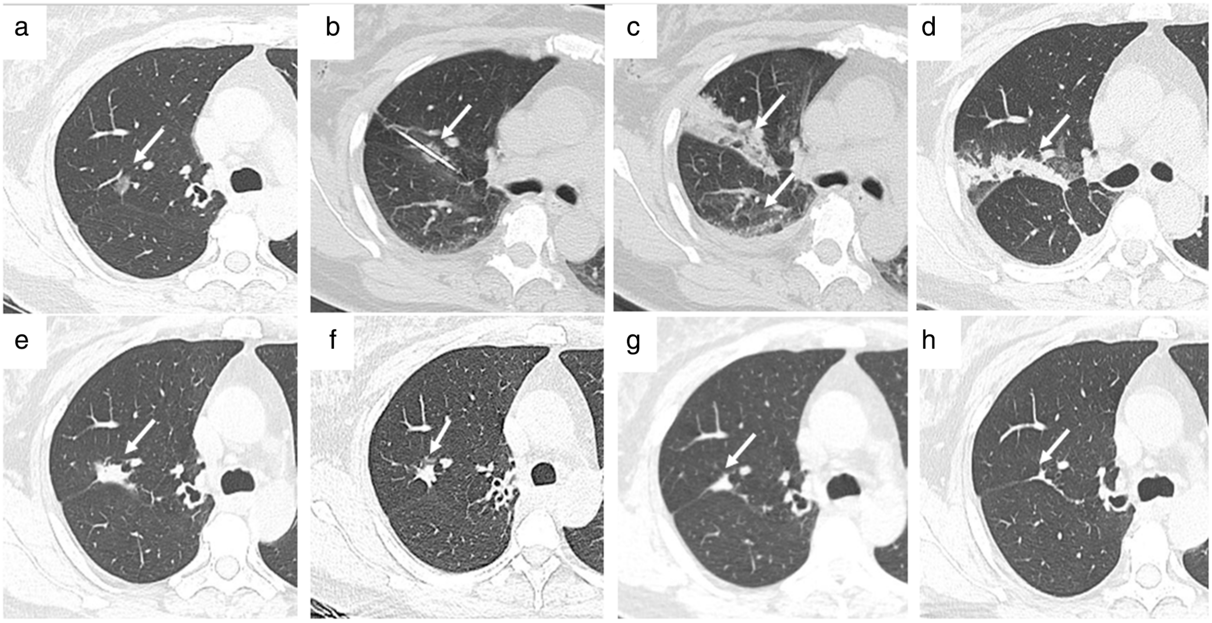

FIGURE 2 The antenna did not pierce through the fissure. (a) A pure GGO close to the right oblique fissure. (b) The antenna did not pierce through the fissure (parallel direction). (c) Immediate post- procedure (bleeding and pleural effusion). (d) 24 hour post-procedure. (e) One month post-procedure. (f) Three months post-procedure. (g) Six months post-procedure. (h) One year post-procedure.

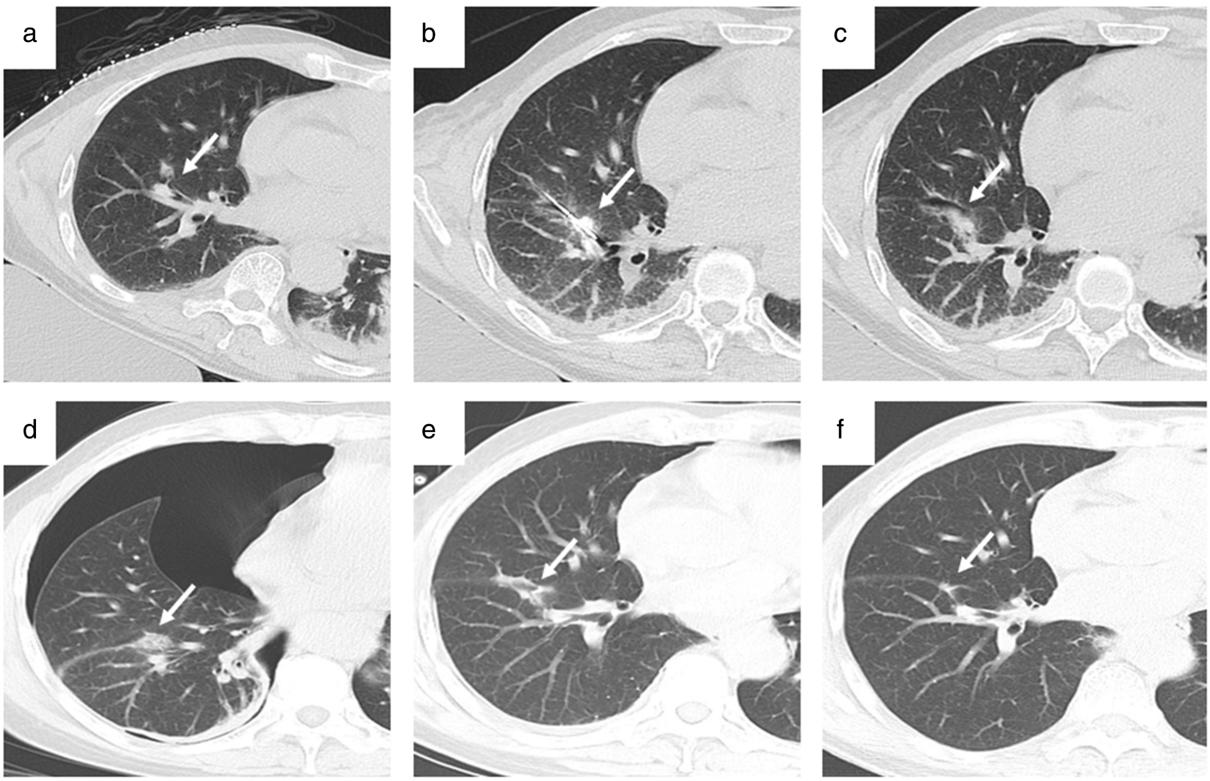

FIGURE 3 The antenna pierced through the fissure. (a) A pure GGO close to the right horizontal fissure. (b) The antenna pierced through the fissure. (c) Immediate post-procedure (pleural effusion). (d) 24 hour post-procedure. (e) 72 hour after chest drainage. (f) Six months post-procedure.

Follow-up and outcomes

A routine chest CT was performed the next day. Most minor complications did not necessitate treatment. However, major complications can result in hospitalization, incapacity, or even death, and they should be treated at the earliest. Thoracic drainage should be used to actively close a considerable quantity of pneumothorax, effusion, and hydropneumothorax. Hemothorax was a relatively rare complication. Multi-phase CT should be recommended to observe whether there was active hemorrhagic point and vascular interventional embolization could be further performed.[10,18] Hemothorax drainage should be performed more than 48 hours after the procedure to ensure that the vessels are thoroughly destroyed and hemostasis is achieved. Anti-infection treatment should be vigorously administered in the ablation area for severe cavities, consolidation, and bronchiectasis, and the frequency of chest CT review should be appropriately increased for early diagnosis of associated infections.[19]

Response criteria

One month later, all patients were required to undergo a chest-enhanced CT scan to assess local efficacy.[10,11] The ground glass opacity (GGO) would display three circumstances when compared with the pre-procedure chest CT: (i) complete ablation, (ii) residual lesion, and (iii) off-target. Solid and subsolid nodules need to be determined by local enhancement on chest-enhanced CT: (i) a complete absence of enhancement in the ablation area was defined as technical success, (ii) irregular enhancement in the ablation area was defined as a residual or recurrent tumor, (iii) the absence of contact between the ablation zone and the target lesion was defined as off-target.[20] Next, the patients were instructed to undergo a chest-enhanced CT every 3 months for a year after the procedure. Local progression-free survival (LPFS) was used to describe the absence of progression of the treated lesion.

Statistical analysis

Pearson χ^2 and Fisher's bilateral tests were used. For continuous variables, Mann–Whitney U tests were used. For statistical analysis, SPSS version 20.0 was used. p values <0.05 were considered statistically significant. All data used in this study were recorded for future reference.

RESULTS

Patients and procedure details

A total of 59 patients (35 men and 24 women) with 66 interlobar fissure lung tumors underwent microwave ablation. The mean age of the patients was 60.5 ± 12 years. All tumors were pathologically diagnosed. The counts of tumors near the left oblique and the right horizontal fissures were 24 cases and 28 cases, and the proportions were 36.4% and 42.4%, respectively. Subsolid tumors, including pure and mixed GGOs, accounted for 47 cases and a proportion of 71.2%. The proportion of solid tumors was 28.8%. During the procedure, the antenna pierced through the interlobar fissure in 19 cases (28.8%) of the 66 sessions. All sessions underwent an adequate pre-procedure evaluation to ensure complete ablation. The baseline characteristics of the patients are shown in Table 1.

TABLE 1 Baseline characteristics of the study patients and lung tumors

Characteristics	No. (%) or mean ± SD
No. of patients	59
No. of lung tumors	66
Age (years)	60.5 ± 12
Sex	35/24
Male	35 (59.3)
Female	24 (40.7)
Tumor size	
≤10 mm	23 (34.8)
10–20 mm	30 (45.5)
20–30 mm	13 (19.7)
Tumor location	
Left oblique fissure	24 (36.4)
Right oblique fissure	14 (21.2)
Right horizontal fissure	28 (42.4)
Relationship to fissure	
Close to fissure	28 (42.4)
Causing fissure	27 (40.9)
Involving the fissure	11 (16.7)
Tumor density	
Solid	19 (28.8)
Subsolid	47 (71.2)
Puncture direction	
Not through the fissure	47 (71.2)
Through the fissure	19 (28.8)

Efficacy

Sixty-two lesions were totally ablated. One incompletely ablated tumor was ablated again 1 week after the procedure, resulting in complete ablation. The final statistical complete ablation rate was 63 (95.5%). The other two patients did not receive any treatment because the lesions were stable after a follow-up observation. In lung tumors measuring <30 mm, the tumor characteristics, including tumor location, relationship to fissure, tumor density, and puncture direction, were insignificantly related to technique efficacy. At 3, 6, 9, and 12 months, the overall LPFS rates were 89.4%, 83.3%, 74.2%, and 63.6%, respectively. The short-duration follow-up of LPFS is shown in Table 2. During the follow-up period, 15 patients were treated with targeted therapy or chemotherapy and one patient received immunotherapy.

Side effects and complications

There was no ablation-related death in all patients. Major complications were observed in 18.2% (12/66) of the cases, including seven pneumothorax cases requiring chest drainage and five cavity cases requiring continuous anti-infective

TABLE 2 Technique efficacy and short-duration follow-up of LPFS

Characteristics	Complete ablation Rate (%)	*p*	3 months LPFS rate (%)	6 months LPFS rate (%)	9 months LPFS rate (%)	12 months LPFS rate (%)
Total	63 (95.5)		89	83	74	63
Tumor size		**0.084**				
≤10 mm	22 (95.7)		87	83	78	65
10–20 mm	30 (100)		97	93	76	66
20–30 mm	11 (84.6)		77	62	61	63
Tumor location		**0.118**				
Left oblique fissure	24 (100)		96	96	87	66
Right oblique fissure	14 (100)		100	86	78	71
Right horizontal fissure	25 (89.3)		79	71	60	57
Relationship to fissure		**0.348**				
Close to fissure (<5 mm)	27 (96.4)		89	89	82	75
Causing fissure	25 (92.6)		89	74	70	59
Involving the fissure	11 (100)		91	91	63	45
Tumor density		**>0.999**				
Solid tumors	18 (94.7)		84	68	63	42
Subsolid tumors	45 (95.7)		92	89	83	72
Puncture direction		**0.551**				
Not through the fissure	44 (93.6)		89	89	79	68
Through the fissure	19 (100)		89	68	63	52

Note: The statistical *p* values are in bold. Abbreviation: LPFS, local progression-free survival.

therapy. The incidence of complications and associated factors are shown in Table 3.

There was a statistical difference ($p < 0.05$) in the occurrence of major complications between the groups who were punctured through the fissures and those who were not punctured through the fissures. The overall incidence rates of pneumothorax and pleural effusion were 34.8% and 24.2%, respectively, which were not as high as expected. The group with punctures through the fissures had four (6.1%) delayed complications, including a severe hydropneumothorax and infection more than 1 month after the treatment. Cavity was observed in 12 cases (18.2%), with 5 cases having infections. A significantly higher incidence of pneumothorax and cavity was found in the group of punctures through the fissures. During the follow-up, cavities were found to heal into a scar within 6 to 12 months of systematic anti-infective therapy, without subsequent damage (Figure 4), which was consistent with previous reports.[21]

DISCUSSION

The MWA technique is based on placing a microwave antenna in the tumor area through the percutaneous puncture. Special sites, such as subpleura, pericardium, and interlobar fissure, increase the difficulty in puncturing and aggravate the post-procedure complications.[22,23] Imprecise punctures or severe complications may directly affect the prognosis.[23] This study analyzed the MWA of lung tumors adjacent to interlobar fissures from continuous medical records in a single institution, observing a complete ablation rate of 87.1%. At 3, 6, 9, and 12 months, the LPFS rates were 86%, 77%, 75%, and 64%, respectively. Interlobar fissures are anatomic fissures where the pleura extend into the interlobar region, allowing each lobe to expand or collapse independent of the others. From the hila outward, the visceral pleura adheres to the lung parenchyma and lines the transverse and oblique fissures.[24] The interlobar fissures mainly include left oblique, right oblique, and right horizontal fissures.[25] Many studies have shown that punctures through the interlobar fissure increase the risk of complications. Based on a single-center study of 875 biopsies, Ruud et al.[19] concluded that insertion through the interlobar fissure can cause clinically significant post-biopsy pneumothorax and chest drainage. An et al.[26] analyzed 665 lung biopsies based on propensity score matching analysis and concluded that biopsy puncture through the interlobar fissure was a risk factor for pneumothorax and recommended that biopsy should avoid traversing interlobar fissure as far as possible. Elshafee et al.[27] found similar results in a retrospective analysis of 311 lung biopsies. In addition, Tsai et al.[28] also found that using laser angle guide assembly could significantly reduce the incidence of pneumothorax by improving puncture accuracy and reducing puncture times of pulmonary

TABLE 3 Incidence of complications and associated factors

Characteristics	Major complications (%)	*p*	Pneumothorax (%)	Pleural effusion (%)	Delayed complications (%)	Bleeding	Cavity	Secondary infection
Total	12 (18.2)		23 (34.8)	16 (24.2)	4 (6.1)	2 (3.0%)	12 (18.2%)	5 (7.6%)
Tumor size		**0.0872**						
≤10 mm	1 (4.3)		7 (30.4)	1 (4.3)	0	1 (4.3%)	3 (13.1%)	0
10–20 mm	7 (23.3)		9 (30)	10 (33.3)	3 (10.0)	1 (3.3%)	6 (20.0%)	3 (10.0%)
20–30 mm	4 (30.8)		7 (53.8)	5 (38.5)	1 (7.7)	0	3 (23.1%)	2 (15.4%)
Tumor location		**0.4822**						
Left oblique fissure	5 (20.8)		9 (37.5)	3 (12.5)	0	0	4 (16.7%)	2 (8.3%)
Right oblique fissure	1 (7.1)		4 (28.6)	5 (35.7)	1 (7.1)	1 (7.1%)	1 (7.1%)	1 (7.1%)
Right horizontal fissure	6 (21.4)		10 (35.7)	8 (28.6)	3 (10.7)	1 (3.6%)	7 (25.0%)	2 (7.1%)
Relationship to fissure		**0.1358**						
Close to fissure (<5 mm)	2 (7.1)		7 (25.0)	2 (7.1)	0	1 (3.6%)	3 (10.7%)	1 (3.5%)
Causing fissure	7 (25.9)		10 (37.0)	9 (33.3)	2 (7.4)	0	5 (18.5%)	2 (7.4%)
Involving the fissure	3 (27.3)		6 (54.5)	5 (45.5)	2 (18.2)	1 (9.1%)	4 (36.4%)	2 (18.2%)
Tumor density		**0.3043**						
Solid tumors	5 (26.3)		7 (36.8)	11 (57.9)	4 (21.1)	0	5 (26.3%)	3 (15.8%)
Subsolid tumors	7 (14.9)		16 (34.0)	5 (10.6)	0	2 (4.3%)	7 (14.9%)	2 (4.3%)
Puncture direction		**0.0294**						
Not through the fissure	5 (10.6)		11 (23.4)	6 (12.8)	1 (2.1)	2 (4.3%)	4 (8.5%)	3 (15.8%)
Through the fissure	7 (36.8)		12 (63.2)	10 (52.6)	3 (15.8)	0	8 (42.1%)	5 (7.6%)

Note: The statistical *p* values are in bold.

nodules adjacent to the fissures. Huang et al.[29] analyzed 610 consecutive pre-procedure CT-guided localization (POCTGL) procedures, and concluded that nodules near the interlobar fissure were one of the risk factors leading to a high incidence of pneumothorax. In these studies, complications of tumors biopsy adjacent to the interlobar fissures were higher than those of other sites.[19,29,30]

To completely ablate the tumors, MWA requires an ablation range of 5 to 10 mm at the edge of the tumor. Additional complications may arise if the target lesion is close to the interlobar fissure because it may be subjected to puncture and thermal damages.[31] Therefore, according to studies on subpleural tumor ablation, we defined interlobar fissure tumors as cancers located within 5 mm of the fissure. Previous studies have reported that tumor size is an important factor affecting ablation efficacy. Cao et al.[14] reported a series of data on thermal ablation for 101 subpleural lung tumors. For lung cancers measuring >30 mm, the complete ablation rate was only 55.6%. For lung cancers measuring <30 mm, the complete ablation rate was 90.22%.[14]

In this study, for all 66 interlobar fissure tumors after MWA treatment, the complete ablation rate was 95.5%. The size of the 66 tumors was found to be <30 mm, and the complete ablation rate agreed with previous studies. Previous studies have reported that subpleural tumors of >30 mm were associated with increased ablation incompleteness. However, our study demonstrated that the rates of lung tumors measuring <10 mm, 10 to 20 mm, and 20 to 30 mm were 95.7%, 100%, and 84.6%, respectively, with no statistical difference between the groups. Meanwhile, no statistical difference was observed in groups of tumor location, relationship to fissure, tumor density, and puncture direction. This result suggests that MWA is an appropriate treatment for interlobar fissure lung tumors measuring <30 mm.

Basically, the interlobar fissure is just two folded layers of visceral pleura extending into the interlobar space. A puncture through the interlobar fissure means that both layers of the

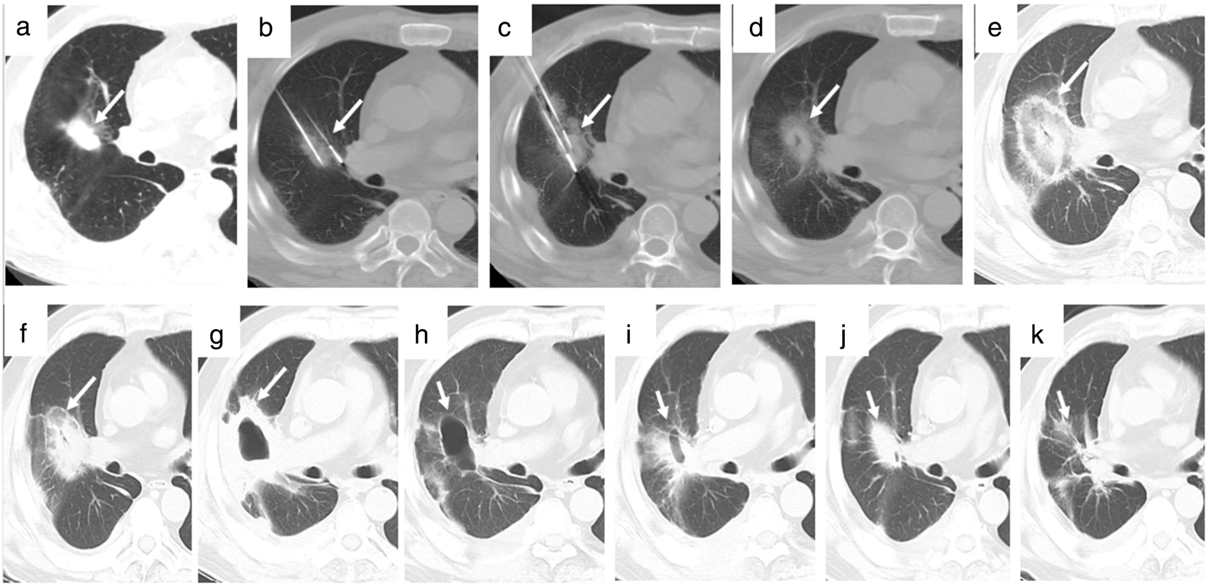

FIGURE 4 The antennas pierced through the fissure (CT follow-up of a cavity after MWA). (a) A solid tumor causing the right oblique fissure. (b) Two antennas ablate simultaneously at a power of 50 W × 5 min. (c) Adjust antennas to the other side of the tumor ablate at a power of 50 W × 5 min. (d) Immediate post-procedure. (e) 24 hour post-procedure (fried-egg sign). (f) One month post-procedure. (g) Two months post-procedure (cavitating mass). (h) Three months post-procedure (big cavity). (i) Six months post-procedure (cavity). (j) Nine months post-procedure (mass). (k) One year post-procedure (scar).

pleura are pierced simultaneously, which would result in a higher rate of pneumothorax and postoperative complications. In 1452 biopsy studies, Yan et al.[15] found a higher incidence of major pneumothorax in lesions of the upper and middle lobes, which may be because of more punctures of fissures in these sites. In our study, pneumothorax occurred in 63.2% (12/19) of cases with the interlobar fissure pierced and 23.4% (11/47) of cases without the interlobar fissure pierced. The incidence rates of major complications were 10.6% (5/19) and 36.8% (7/47), respectively, with a statistical difference between the two groups ($p = 0.0294$ with Fisher's bilateral test). Yang et al.[33] reported 52 sessions of percutaneous CT-guided MWA treatment of lung GGO, accounting for 48.1% (25/52) of pneumothorax cases, of which five sessions (9.8%) required chest tube drainage.[32] There were 12 sessions (23.1%, 12/52) of pleural effusion, of which three sessions (5.7%) underwent chest tube insertion. Another study on MWA treatment of oligometastatic NSCLC observed a technical efficacy of 91.1%.[33] Moreover, 27.8% (22/79) of pneumothorax cases and 20.3% (16/79) of pleural effusion cases were observed, which is consistent with the findings of our study.

The incidence rate of cavity was 18.2% (12/66), with 7.6% (5/66) incidence of secondary infection with fungi and/or bacteria. After proper prevention and anti-infective treatment, these cavities were cured within 6 to 12 months, which was consistent with previous research.[34] Although the overall incidence insignificantly differed from previous studies,[35] we noticed a higher incidence (42.1%) of cavity in the group of punctures through the interlobar fissure. Therefore, we hypothesize that MWA puncture through the interlobar fissure might be an inducing factor for postoperative cavity formation.

In this study, 6.1% (4/66) of delayed complications were noted. More than 1 month after ablation, all four patients had severe hydropneumothorax infections, which was confirmed via imagological examination and cured after adequate drainage and anti-infection treatment. The common features of these four cases were puncture through the interlobular fissure and postoperative combination with chemotherapy or targeted therapy. Therefore, more follow-up observations and delayed anti-tumor treatment may be appropriate for these patients.[36,37]

All 66 procedures were performed using simultaneous biopsy and MWA, and pulmonary hemorrhage occurred in only 3% (2/66), which was lower than those in studies on CT-guided lung biopsy. Previous studies had demonstrated the effectiveness of ablative simultaneous biopsy therapy, and it was increasingly being used.[38–41] The lower hemorrhage rate could be because of thermal solidification resulting in blood coagulation and fewer adjustments of the antennas during the procedure.

This study has several limitations. The first is that it is retrospective. The second is that we excluded cancers measuring >30 mm from the study, which may be the reason for the high ablation completion rate and the low complication rate. Third, the number of cases included was small, and the follow-up time was short.

In conclusion, MWA therapy is a safe and effective treatment for lung tumors adjacent to interlobar fissures. For tumors measuring <30 mm, tumor size is not a factor associated with technique efficacy. Patients with antenna puncture through the interlobar fissures face significantly increased complications. Furthermore, there may be delayed complications in these patients; hence, they should receive more attention and long-term follow-up. Therefore, we believe that pre-procedure selection of correct puncture direction and intraoperative confirmation of interlobar fissure puncture are meaningful operational indicators.

AUTHOR CONTRIBUTIONS

Nan Wang was responsible for acquiring the data and drafting the manuscript. Nan Wang and Jingwen Xu were responsible for the analysis of the data. Gang Wang, Guoliang Xue, Zhichao Li, Pikun Cao, Yanting Hu, and Hongchao Cai provided and collected the clinical data. Zhigang Wei and Xin Ye was responsible for designing the experiments and supervising the study. All authors listed have made a substantial, direct, and intellectual contribution to the work and have approved it for publication.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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