

# Major Complications After Lung Microwave Ablation: A Single-Center Experience on 204 Sessions

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**Background.** The purpose of this study is to retrospectively evaluate the incidence of and risk factors for major complications after microwave ablation (MWA) of lung tumors.

**Methods.** From January 2011 to May 2013 in 184 consecutive patients (67 women and 117 men; mean age, 61.5 years; range, 19 to 85 years), 204 sessions of MWA were performed on 253 lung tumor lesions. Records were reviewed to evaluate prevalence of major complications and risk factors, which were analyzed using univariate and multivariate analyses.

**Results.** Major complications developed after 42 sessions (20.6%), including 32 cases (15.7%) of pneumothorax requiring chest tube placement which that were associated with emphysema ( $p = 0.001$ ); 6 cases (2.9%) of pleural effusions requiring chest tube placement, which were associated with a distance of less than 1 cm from chest wall to target tumor ( $p = 0.014$ ); 6 cases

(2.9%) of pneumonia which that were associated with target tumor maximal diameter ( $p = 0.040$ ); number of pleural punctures ( $p = 0.001$ ) and ablation time ( $p = 0.006$ ); and 1 case (0.5%) of pulmonary abscess. Two cases (1.0%) of the large pneumothorax occurred at the same time with extensive subcutaneous emphysema, including 1 case (0.5%) caused by bronchopleural fistula. Death related to the procedures occurred after 1 session (0.5%).

**Conclusions.** As a relatively practical and safe modality, lung tumor MWA can induce serious complications. Enough attention should be paid to patients with emphysema, subpleural, or large target tumor, but the indications for lung MWA need not be limited as most major complications were easily managed.

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Most patients with primary or metastatic lung cancer are unresectable because of poor physiologic or oncologic conditions. This prompted the development of lung ablation techniques. The most widely used technique is radiofrequency ablation (RFA) [1–9]. Compared with RFA, microwave ablation (MWA) is a less studied but promising modality that may improve the efficacy of thermal ablation in the lung [10–14]. It offers all the benefits of RFA as well as some other advantages such as enlarged ablation zones, reduced procedure times, and decreased heat-sink effects [15, 16]. In spite of being a minimally invasive procedure just as RFA, MWA can also lead to some major complications which have been rarely reported systemically. The purpose of this retrospective study was to evaluate the incidence of and risk factors for major complications after MWA of lung tumors.

## Patients and Methods

### Patients

The Institutional Review Board at Medical College of Shandong University approved this retrospective study. Local ethics committee approval and written informed consent from all patients were obtained before the procedure, although informed consent was waived for our retrospective study. We searched the Provincial Hospital Affiliated to Shandong University database to identify patients who underwent lung MWA. From January 2011 to May 2013, 204 sessions of MWA were performed on 253 lung lesions of 184 consecutive patients (67 women and 117 men) with a mean age of  $61.5 \pm 13.4$  (range, 19 to 85) years. The patient backgrounds and tumor characteristics were summarized in Table 1.

All tumors were diagnosed with direct or indirect pathologic evidence. The patients were not candidates for surgery because of previous pulmonary resection, poor cardiopulmonary status, multiple tumors, or other reasons after discussion with thoracic surgeons. The patients refusing surgery were also considered candidates. The patients who were considered unsuitable for MWA included the following: patients with 6 or more lesions in

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Table 1. Patient, Tumor and Procedural Characteristics and Results of Statistical Analysis to Determine Risk Factors for Major Complications With a Morbidity of More Than 1%

Characteristics	No. (%) of 204 Procedures or Mean ± SD	No Chest Tube for Pneumothorax (n = 172) <sup>a</sup>	Chest Tube for Pneumothorax (n = 32)	p Value for Univariate (Multivariate) Analysis	No Chest Tube for Pleural Effusion (n = 198) <sup>b</sup>	Chest Tube for Pleural Effusion (n = 6)	p Value	No Pneumonia (n = 198)	Pneumonia (n = 6)	p Value
Patient characteristics:										
Gender (female/male)	72(35.3)/132(64.7)	67/105	5/27	0.011(0.056)	70/128	2/4	1.000	71/127	1/5	0.427
Age (years)	61.5 ± 13.5	61.4 ± 13.3	62.5 ± 14.6	0.663(0.310)	61.6 ± 13.3	59.5 ± 19.2	0.707	61.6 ± 13.6	61.0 ± 7.5	0.920
Emphysema (no/yes)	157(77.0)/47(23.0)	140/32	17/15	0.0005(0.001)	154/44	3/3	0.137	153/45	4/2	0.623
Diabetes (no/yes)	168(82.4)/36(17.6)	145/27	23/9	0.090(0.123)	164/34	4/2	0.286	163/35	5/1	1.000
Hypertension (no/yes)	142(69.6)/62(30.4)	118/54	24/8	0.470(0.159)	139/59	3/3	0.371	139/59	3/3	0.371
Smoking index (≤100/>100)	103(50.5)/101(49.5)	89/83	14/18	0.406(0.973)	100/98	3/3	1.000	100/98	3/3	1.000
Previous radiotherapy (no/yes)	199(97.5)/5(2.5)	167/5	32/0	10.000(0.434)	194/4	5/1	0.140	194/4	5/1	0.140
Previous pulmonary surgery (no/yes)	194(95.1)/10(4.9)	165/7	29/3	0.194(0.075)	188/10	6/0	1.000	188/10	6/0	1.000
Previous chemotherapy (no/yes)	138(67.6)/66(32.4)	118/54	20/12	0.498(0.070)	134/64	4/2	1.000	136/62	2/4	0.088
Tumor characteristics:										
Origin (primary/metastasis)	148(72.5)/56(27.5)	125/47	23/9	0.926(0.149)	143/55	5/1	1.000	144/54	4/2	0.667
Maximal diameter (cm)	3.29 ± 1.93	3.34 ± 1.99	2.99 ± 1.59	0.348(0.373)	3.27 ± 1.92	4.08 ± 2.54	0.308	3.24 ± 1.91	4.88 ± 2.07	0.040
No. of treated tumors	1.24 ± 0.63	1.22 ± 0.62	1.31 ± 0.64	0.464(0.209)	1.24 ± 0.63	1.17 ± 0.41	0.779	1.22 ± 0.60	1.83 ± 1.17	0.256
Lower lung field involved (no/yes)	133(65.2)/71(34.8)	110/62	23/9	0.388(0.519)	130/68	3/3	0.421	130/68	3/3	0.421
Distance from chest wall (≤1/≥1 cm)	40(19.6)/164(80.4)	35/137	5/27	0.537(0.653)	36/162	4/2	0.014	39/159	1/5	1.000
Procedural characteristics:										
Approach (anterior/posterior) <sup>c</sup>	91(44.6)/105(51.5)	76/90	15/15	0.670(0.793)	87/104	4/1	0.185	89/101	2/4	0.688
No. of pleural punctures	2.87 ± 1.65	2.82 ± 1.69	3.13 ± 1.45	0.339(0.289)	2.86 ± 1.66	3.17 ± 1.72	0.654	2.80 ± 1.61	5.00 ± 1.79	0.001
Length of lung tissue traversed by antennas (cm)	5.93 ± 4.78	5.88 ± 4.87	6.17 ± 4.33	0.753(0.733)	5.97 ± 4.83	4.58 ± 2.73	0.486	5.88 ± 4.81	7.50 ± 3.83	0.415
Ablation time (minutes)	12.78 ± 11.13	12.66 ± 11.19	13.41 ± 10.99	0.730(0.530)	12.63 ± 10.92	17.83 ± 17.38	0.498	12.41 ± 10.86	25.00 ± 14.14	0.006

<sup>a</sup> With or without pneumothorax. <sup>b</sup> With or without pleural effusion. <sup>c</sup> Eight sessions with lateral approach were not admitted.

a hemithorax; patients with a lesion immediately adjacent to major vessels, hilum, major bronchus, or mediastinum; patients with bleeding diatheses; patients with extrapulmonary lesions that would hardly be controlled; patients with a Zubrod performance status of 2 or more; and patients with active inflammation or infection.

#### *Ablation Protocol*

All procedures were performed with patients under local anesthesia and moderate sedation. The microwave ablation therapeutic instrument (MTC-3C, Nanjing Qinghai Research Institute of Microwave Electric, China) we used could produce 0 to 100 W of power at a frequency of  $2,450 \pm 50$  MHz. Under the guidance of computed tomographic (CT) fluoroscopy (Lightspeed16; GE Healthcare, Waukesha, WI), a microwave antenna (14G outside diameter, 100 to 180-mm length, using water circulation cooling system) was placed into the tumor. One antenna was used for tumors 3 cm or less in maximum diameter and 2 antennae for greater than 3 cm. Ablation was performed with a power of 60 to 80 W for 4 to 8 minutes per site. Antennae were placed sequentially at 1 to 8 different sites in the tumor according to the tumor size and shape. Antenna track ablation was routinely performed at the end of the procedure to prevent needle track implantation. To prevent infection and postablation syndrome, cefazolin and dexamethasone were administered prophylactically before and for 2 days after ablation.

#### *Pneumothorax or Pleural Effusion Management*

If there was pneumothorax or pleural effusion detected by routine physical and imaging examination, the patient was monitored until it stabilized. A patient whose pneumothorax or pleural effusion was enlarging or exceeded 35% to 40%, or who became dyspneic or developed diminishing oxygen saturation was treated with chest tube placement.

#### *Follow-Up*

The follow-up protocol included routine physical examination and laboratory tests during the hospital stay. At 24 hours from the procedure, each patient underwent non-enhanced chest CT scans to evaluate early complications. All patients were followed up at 1, 3, 6, and 12 months, and thereafter at 6-month intervals with chest enhanced CT images.

#### *Complication Assessment and Recorded Variables*

Complications were evaluated on the basis of MWA procedures by reviewing medical records and CT images. Major complications were defined as those events leading to substantial morbidity and disability, increasing the level of care, or resulting in hospital admission or substantially lengthening hospital stay. This included any case in which an interventional drainage procedure was required. All these were in accordance with the classification proposed by the Society of Interventional Radiology [17].

To find underlying factors influencing major complications, the following factors were assessed: (1) patient

characteristics as gender, age, absence or presence of pulmonary emphysema, hypertension and diabetes, smoking index, history of pulmonary surgery, pulmonary external-beam radiotherapy and chemotherapy; (2) tumor characteristics as primary or secondary origin, maximal diameter, lower lung field involved or not, distance from chest wall ( $<1$  or  $\geq 1$  cm); (3) procedural characteristics such as puncture approach (anteroposterior), number of pleural punctures ( $<3$  or  $\geq 3$ ), length of lung tissue traversed by antennas, or ablation time. Emphysema was defined as low-attenuation areas with disrupted vasculature but without discernible surrounding walls in the pulmonary parenchyma on the basis of CT.

#### *Statistical Analysis*

Data were expressed as mean  $\pm$  standard deviation. Risk factors affecting major complications that were found in more than 1% of procedures were assessed using a  $\chi^2$  test for categorical variables and an independent-samples *t* test for continuous variables. If a categorical variable was not fit for the  $\chi^2$  test because 1 or more cells in crosstab had an expected count less than 5, the 2-sided Fisher exact test was adopted. Then the factors affecting major complications that were found in more than 10 events were analyzed again with multivariate analysis using binary logistic regression. A *p* value of less than 0.05 was considered to be statistically significant. All statistical analyses were performed with SPSS 17.0 for window software package (SPSS, Inc, Chicago, IL).

## Results

#### *Major Complications*

In the 204 treatment sessions, major complications developed after 42 sessions (20.6%), including 32 cases (15.7%) of pneumothorax requiring chest tube, 6 cases (2.9%) of pleural effusions requiring chest tube, 6 cases (2.9%) of pneumonia, and 1 case (0.5%) of pulmonary abscess. Two of them had large pleural effusion and pneumonia sequentially. One of them had large pneumothorax and large pleural effusion sequentially. Two cases (1.0%) of the large pneumothorax occurred at the same time with large subcutaneous emphysema, including 1 case (0.5%) caused by bronchopleural fistula. No delayed major complication was detected during the follow-up period.

The 6 patients who developed pneumonia after lung ablation received  $18.7 \pm 7.8$  (range, 12 to 34) days of further treatment for this complication and were discharged without obvious sequelae. The patient who developed pulmonary abscess was a 63-year-old man with a smoking index of 1,500 and pulmonary emphysema. Twenty-one days after MWA for a squamous cell carcinoma focus in the right upper lung lobe with a maximal diameter of 4 cm, the patient came up with high fever and enhanced CT scanning revealed the abscess. The abscess eventually recovered after about 3 weeks of drainage and antibiotic treatment. Both of the 2 patients with large subcutaneous emphysema had emphysema

and large pneumothorax. One of the 2 patients suffered from intractable pneumothorax resulting from the development of a bronchopleural fistula. In that case, air leakage persisted after pleurodesis with video-assisted thoracoscope, until he died of brain metastasis 7 months later.

Univariate analysis suggested the following; that male patients ( $p = 0.011$ ) and emphysema ( $p = 0.0005$ ) predisposed patients to chest tube placement for pneumothorax; a distance of less than 1 cm from chest wall to target tumor predisposed patients to chest tube placement for pleural effusion ( $p = 0.014$ ); and longer target tumor maximal diameter ( $p = 0.040$ ), more pleural punctures ( $p = 0.001$ ), and longer ablation time ( $p = 0.006$ ) were associated with higher pneumonia rates. Further multivariate analyses indicated the relevance between emphysema and chest tube placement for pneumothorax ( $p = 0.001$ ) (Table 1).

#### *Procedure-Related Death*

Death related to the procedures occurred after 1 session (0.5%). The 70-year-old man was admitted to undergo MWA for a lung adenocarcinoma lesion with a maximum diameter of 7.1 cm located in the left upper lobe. He had suffered from diabetes for 11 years and had a history of cerebral infarction without sequelae; 2 cycles of pemetrexed combined with cisplatin followed with 2 months of gefitinib, which resulted in progressive disease and general fatigue. Eighteen hours after the procedure, the patient exhibited progressive dyspnea and chest X-ray showed a large pneumothorax with a good-sized pleural effusion. Chest tube placement and thoracic drainage alleviated the respiratory failure, but the patient died of sudden ventricular fibrillation 41 hours after the procedure.

#### *Efficacy*

After the first procedure of ablation, complete necrosis was observed in 131 of 137 (95.6%) lesions with maximum diameter of 3 cm or less, 80 of 89 (89.9%) lesions with a maximum diameter of greater than 3 cm and 5 cm or less, and 18 of 27 (66.7%) lesions with a maximum diameter of greater than 5 cm at CT performed at the end of the procedure and confirmed 1 month after ablation.

#### **Comment**

In this study, pneumothorax requiring drainage occurred in 15.7% of procedures. The rates were 1.3% to 60% (median = 13.4%) in a metaanalysis for lung RFA in 2008 [1], and 1.8% to 23.7% (17.5%, 398 of 2,280 totally) in recent studies for lung RFA with patient series of more than 100 [2-9]. In the few reports for lung MWA, the rates were 0% to 14.3% (7.7%, 26 of 338 totally) [10-14]. The rate in this study is similar to those reported for lung RFA, but much higher than those for lung MWA. All of the 5 reports concerning MWA did not provide rate of emphysema in patients. Maybe it was the low emphysema rates that led to low pneumothorax rates, especially in Thomas' report that studied pulmonary metastases with a chest tube

placement or manual evacuation rate of 3.8% (5 of 130) [12].

There were no previous studies analyzing factors influencing pneumothorax after lung MWA and chest tube placement for pneumothorax after lung MWA or RFA, but there were some reports analyzing factors influencing pneumothorax after lung RFA [2, 4, 5, 7, 18, 19]. The most generally received risk factor was emphysema. In this study, emphysema was a factor significantly influencing chest tube placement for pneumothorax. In addition, it was reported that the presence of emphysema significantly increased the risk of lung abscess [4]. Therefore, great attention should be paid to patients with emphysema in case of severe complications.

Pleural effusion represented the next most common complication following pneumothorax and occurred during or after 11.6 to 18.8% (15.3%, 105 of 686 totally) of previously reported procedures [2, 6, 9, 19]. Of the 5 previous studies on lung MWA [10-14], only 1 reported self-limiting minor pleural effusion with a rate of 20.7% (17 of 82) [11]. Generally speaking, most patients with pleural effusion were clinically asymptomatic and rarely required drainage [2]. But 2.9% of procedures required drainage for pleural effusion in this study. Hiraki and colleagues reported that cluster electrode, decreased distance to the nearest pleura, and decreased length of the aerated lung traversed by the electrode resulted in a significantly higher incidence of pleural effusion [19]. This is in accordance with the report of Tajiri et al. who concluded that higher pleural temperature was associated with the occurrence of pleural effusion [18]. In our series of patients, the fact that patients with target tumor located less than 1 cm from chest wall were more prone to chest tube placement for pleural effusion partly corroborated the studies of the above two authors [18, 19].

Post-ablation pneumonia developed in 3 out of 338 (0.9%) lung MWA sessions previously reported [10-14]. The rates of pneumonia ranged from 0% to 12% in the metaanalysis for lung RFA in 2008 [1], and 0% to 3.9% (1.1%, 26 of 2,280 totally) in recent studies for lung RFA with patient series of more than 100 [2-9]. In this study, we obtained a similar result with a rate of 2.9%. Pneumonia is a severe complication even acting as main causes of procedure-related death [3, 4, 9]. Nomura and colleagues [3] reported that large tumor size and previous external-beam radiotherapy were risk factors for severe lung inflammation. Kashima and colleagues [4] reported that 3 out of 4 procedure-related deaths were induced by exacerbation of interstitial pneumonia, and 2 of the 3 patients had a history of receiving external-beam radiotherapy in the lung. It seems that ablation may trigger the development of radiation pneumonia. In this study, we concluded that more extent of lung tissue damaged by more punctures and ablations for larger tumor may contribute to higher pneumonia rate.

The rates of lung abscesses ranged from 0% to 2.7% (0.8%, 19 of 2,280 totally) in recent studies for lung RFA with patient series of more than 100 [2-9]. Abscess formation was not recorded in 338 lung MWA sessions previously reported [10-14]. Kashima and colleagues [4]

reported that the presence of emphysema significantly increased the risk of lung abscess, probably because decreased perfusion and ventilation made emphysematous lung parenchyma more susceptible to thermal damage and damaged lung parenchyma might serve as the nidus of infection. Only 1 lung abscess was recorded in this series and the patient was suffering from emphysema.

Bronchopleural fistula is a rare but severe complication of lung RFA [4, 20–22] and MWA [23]. Pleurodesis and endobronchial valve placement may take effect [4, 24]. Cannella and colleagues [22] suggested that minimally invasive treatment, chest tubes alone for example, was sufficient to cure bronchopleural fistula, but air leakage persisted after chest tube placement and pleurodesis till he died seven months after ablation in this study, like the case Sakurai et al. reported [21]. Large ulcers caused by lung surface burn may cause bronchopleural fistula, so avoiding excessive burn to the lung surface might be a good way.

Injuries of nerve after lung RFA, including injuries of brachial nerve, phrenic nerve or stellate ganglion, have been reported [4, 25–27]. Hemoptysis acted as side effect or minor complications in most previously reported studies [2, 6, 11], though massive hemoptysis might act as cause of procedure-related death [9]. Other major complications after lung RFA previously reported but not recorded in this study include pulmonary artery pseudoaneurysm [28], large hemothorax [4, 20], air embolism [2], needle tract seeding [29], rib fracture [30] and diaphragm injury [4]. Major complication rate in this study was 20.6% and approximated to that in the studies of Nomura and colleagues [3] and Sano and colleagues [9] (18.3% and 17.1%, respectively), but higher than that in the study of Kashima and colleagues [4] (9.8%) who did not think that pneumothorax requiring chest tube placement but not requiring pleural sclerosis was major complication.

The mortality rate was .5% in this study, resembling those of previous studies which were 0% to 2.6% for lung RFA [2–10] and no death for lung MWA [10–14]. The reported deaths were secondary to concomitant pneumonia, intractable pneumothorax, massive hemoptysis, hemothorax, pulmonary embolism, nonspecific respiratory failure or acute cardiac failure. The sudden ventricular fibrillation causing the death in this study was induced by respiratory failure. It has been reported that pulmonary function decreased after RFA and that RFA-induced severe pleuritis and ablation of a large volume of marginal parenchyma were associated with impaired pulmonary function [31]. Lung function usually recovers to preablation values after an initial reduction [32]; but before the recovery, uncontrollable respiratory failure may be induced by pneumothorax, pleural effusion or pneumonia.

In conclusion, as a relatively practical and safe modality, lung tumor MWA can induce serious complications, but the indications for lung MWA need not be limited since most major complications were easy to handle. Enough attention should be paid to patients with

emphysema, subpleural or large target tumor, especially to patients with imperfect respiratory function who need more prompt chest tube placement when a pneumothorax or an effusion develop. A patient who suffered more pleural punctures and longer ablation time for a bigger lesion may require prolonged antibiotic prophylaxis to avoid pneumonia.

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