The Role of Percutaneous Image-Guided Thermal Ablation for the Treatment of Pulmonary Malignancies

**OBJECTIVE.** Image-guided thermal ablation is a minimally invasive treatment option for patients with primary and secondary pulmonary malignancies. Modalities include radiofrequency ablation, microwave ablation, and cryoablation.

**CONCLUSION.** Although no large randomized studies exist comparing ablation to surgery or radiotherapy, numerous studies have reported safety and efficacy for the treatment of both primary and metastatic disease in select patients. Future studies will refine patient selection, procedural technique, and assessment for local recurrence and will evaluate long-term survival.

A variety of image-guided thermal ablation techniques exist for patients with non–small cell lung carcinoma (NSCLC) and oligometastatic disease. Many of these patients are not surgical candidates, so thermal ablation techniques—including radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation—have been explored, showing safety, efficacy, and good local disease control while preserving the lung parenchyma [1–8]. For patients with stage I or II NSCLC, surgical resection provides the best curative option, with 5-year survival rates of 50–75% [9]. However, only one-third of patients may meet the criteria for lobar or sublobar resection [10]. For the remaining patients, ablative therapies have proved useful [3, 11–14]. Additionally, the lungs are the second most common site of metastatic disease [15]. In selected patients with a limited number of tumors that can be ablated with adequate margins or those who present with residual or recurrent disease after having undergone other treatments, percutaneous thermal ablation plays a role in disease management. Over the past 2 decades, ablation has played an important role in the treatment of both primary and secondary pulmonary malignancies, providing an effective therapy, which can also provide potential cure in select cases.

**Mechanism of Action and Local Efficacy**

The unique characteristics of pulmonary parenchyma facilitate thermal ablation, including heat insulation and low electrical conductivity. These characteristics permit a larger volume of tissue to be ablated for a given energy than in other tissues in the body [16]. With RFA, an electrode from a generator causes frictional heating, elevating tissue temperature to 60–100°C. This creates a necrotic zone covering both the tumor and margin of normal parenchyma [17]. However, this thermal energy can be limited by the heat-sink effect of adjacent blood vessels and airways [1]. Several groups have reported that the presence of vessels or bronchi greater than 3 mm in diameter within the ablation zone are predictors of incomplete local treatment [18, 19]. Pathologic analyses of 354 NSCLC cases (adenocarcinoma and squamous cell carcinoma) have revealed that 8 and 6 mm margins, respectively, are needed to cover 95% of microscopic disease extension [20]. Thus to obtain adequate margins, the ablation zone must exceed the tumor size [21]. RFA therefore performs best for lesions smaller than 2 cm, with rates of complete ablation ranging from 78% to 96% with a mean follow-up of 1 year [3, 14, 18, 22, 23]. Lower success rates are seen with tumors 2–3 cm in diameter [3, 18, 22, 23]. More specifically, a ratio of RFA-induced ground-glass opacity (GGO) to tumor area of greater than 4 (bidimensional area on axial images) is correlated with a significantly higher rate of complete ablation than a ratio of less than or equal to 4 [3].

MWA uses microwaves to cause friction between water molecules, generating hyperthermia [24]. Unlike RFA, during which only one probe is activated at a time, MWA enables
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simultaneous energy delivery with multiple probes, thus permitting larger ablation zones than RFA. In animal studies, investigators have reported lung ablation zones as large as 54.8 ± 8.5 mm (mean ± SD) [25]. Clinically, Wolf et al. [4] reported MWA results in 50 patients with pulmonary tumors up to 5 cm. The authors reported an overall recurrence rate of 26% and a tumor size of larger than 3 cm being predictive of recurrent disease.

Cryoablation uses compressed argon gas to generate subzero temperatures with ice-ball formation. When temperatures are less than −40°C, protein denaturation, cell rupture, and ischemia occur [26]. Unlike heat-based ablation, cryoablation does not create GGO intraprocedurally; instead, the ice ball is used to estimate the ablated margin. Hinsaw et al. [27] examined the temperature isotherms and associated ablation zone size seen with cryoablation in an in vivo porcine lung model. They identified the −20°C isotherm as the zone of coagulative necrosis, with a mean ablation zone diameter of 2.4 ± 0.2 cm [27]. Most ablation protocols call for three freeze-thaw cycles to achieve tissue necrosis [27, 28].

Irreversible electroporation, which uses electrical pulses to generate high electrical fields (1500 V/cm²), was developed as a non–thermal ablation technique. This technique causes cellular apoptosis by creating cell membrane pores and resultant cell lysis. However, in the multicenter phase II trial of 23 patients with metastatic disease, Ricke et al. [29] reported local progression in 61% of treated patients. They postulated that the high local recurrence was likely because of conductivity differences between the tumor tissue and normal lung parenchyma. Given these results, irreversible electroporation requires refinement before becoming an effective ablative modality for pulmonary malignancies.

Imaging and Response

CT is the preferred image guidance modality for thermal ablation because it provides excellent contrast between the tumor tissue and normal aerated lung. CT provides multiplanar imaging, which facilitates accurate and quick probe placement [30]. In fact, operators who have access to multiplanar imaging have been shown to better distinguish between margin- and lesion-centered probe placement than operators who have access to axial images alone [31]. Cone-beam CT has been used for lung ablation because it facilitates ablation approaches from any angle; however, it lacks real-time imaging capability. This can be an issue in the setting of moving target lesions [32].

CT is also the modality of choice for follow-up after ablation. After ablation, the targeted lesion is replaced by a central area of increased radiographic density that is surrounded by GGO [11], which may overestimate the actual pathologic margins of RFA [33] and cryoablation [28]. An ablation margin surrounding the target lesion of less than 4.5 mm or an incomplete margin has been correlated with local tumor progression [34]. GGO margins of less than 3 mm have been associated with tumor progression as well [35]. During the initial postablation period (<2 months), this dense opacification and surrounding GGO serve as the new “baseline” postablation image [21, 36]. Any increase in the size of this lesion on follow-up should be considered local progression.

The evolution of the imaging appearance of the ablation zone varies depending on the thermal ablation modality. Palussière et al. [37] described the involution pattern seen after RFA of 350 treated lesions with CT follow-up up to 12 months. Although they reported five different imaging patterns, they concluded that none of these patterns can be used to exclude local tumor progression. RFA-treated lesions show a relatively slow rate of involutions, with a 40% decrease in size at 15 months after treatment [38]. Similar postablation imaging findings have been described after MWA [4] (Fig. 1). Cryoablated lesions, however, show faster involution on CT follow-up so that local tumor progression can be visualized as early as 6 months after treatment [39]. CT enhancement patterns after both RFA and cryoablation have not shown correlation with local progression [6, 39]. CT is therefore primarily used to examine morphologic changes to the ablation zone. However, detecting local progression at follow-up using CT alone remains difficult. Beland et al. [40] found that in 79 patients with NSCLC treated using RFA, local progression was seen in only 1.5% at 6 months, increasing to 10.1% at 1 year and 28% at 2 years. De Baère et al. [13] retrospectively examined the records and images of 566 patients with metastatic disease treated with RFA and reported rates of local tumor progression of 10.4% at 1 year and 18.1% at 4 years.

To overcome the limitations of CT’s morphologic assessment of local recurrence, PET/CT follow-up has been explored (Table 1). Yoo et al. [41] examined the role of PET/CT in 30 patients with stage I NSCLC treated with RFA. They reported that imaging 6 months after RFA more accurately reflected outcomes at 1 year than imaging performed immediately after RFA [41]. Suzawa et al. [33] studied the utility of PET/CT in the follow-up of 143 patients treated with RFA. Local tumor progression was seen in 20.4% of tumors with a median follow-up of 24 months, and PET’s diagnostic performance exceeded that of CT at all follow-up imaging time points. However, for up to 3 months after ablation, PET/CT

| TABLE 1: Modification of the Response Evaluation Criteria in Solid Tumors (RECIST) as Presented by Herrera et al. [96]a |

<table>
<thead>
<tr>
<th>Response</th>
<th>CT Mass Size (RECIST)</th>
<th>CT Mass Quality</th>
<th>PETb</th>
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<tbody>
<tr>
<td>Complete (2 of the criteria)</td>
<td>Lesion disappearance (scar) or &lt;25% of original size</td>
<td>Cyst cavity formation, low density</td>
<td>SUV &lt; 2.5</td>
</tr>
<tr>
<td>Partial (1 of the criteria)</td>
<td>&gt;30% Decrease in sum LD of target lesions²</td>
<td>Mass central necrosis or central cavity with liquid density</td>
<td>Decreased SUV or area of FDG uptake</td>
</tr>
<tr>
<td>Stable lesion (1 of the criteria)</td>
<td>&lt;30% Decrease in sum LD of target lesions²</td>
<td>Mass solid appearance, no central necrosis or cavity</td>
<td>Unchanged SUV or area of FDG uptake</td>
</tr>
<tr>
<td>Progression (2 of the criteria)</td>
<td>Increase &gt;20% in sum LD of target lesions²</td>
<td>Solid mass, invasion adjacent structures</td>
<td>Higher SUV or larger area of FDG uptake</td>
</tr>
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Note—Modified from the RECIST criteria [97, 98]. SUV = standardized uptake value. Sum LD = sum of largest diameter of all target lesions.


bPET scan was used selectively in lesions with unclear response by CT imaging.

cTumors treated with radiofrequency ablation.
can be confounded by inflammatory changes in both the treated tissues and mediastinum [40]. Split-dose PET/CT has been developed to aid in target localization and evaluation of treatment effectiveness intraprocedurally [42, 43] (Figs. 2 and 3).

Clinical Outcomes
Non–Small Cell Lung Carcinoma
An early study by Simon et al. [44] reported a median overall survival (OS) of 29 months (95% CI, 20–38 months) in 75 patients with NSCLC, with 1- and 5-year survival rates of 78% and 27%. They found improved survival in patients with lower stage disease and lesions less than 3 cm in diameter [44]. Ambroggi et al. [45] and Huang et al. [46] reported similar 5-year survival rates of 25% in patients with stage I NSCLC. Huang et al. reported a local progression rate of 23.7%, with a significantly increased rate of local progression in patients with lesions larger than 4 cm. More recent studies have reported improved survival, which is likely a combination of multiple factors, including technical refinements, better patient selection, and the use of targeted systemic therapies [30]. Palussière et al. [37] reported a 5-year OS rate of 58.1% and disease-free survival rate of 27.9% in 87 patients with NSCLC after thermal ablation. On multivariate analysis, tumor size larger than 2 cm was an independent prognostic factor for disease-free survival [37]. Dupuy et al. [47] reported the outcomes of the American College of Surgeons Oncology Group trial of 51 patients with stage IA NSCLC tumors less than 3 cm in diameter. These authors reported 1- and 2-year OS rates of 86.3% and 69.8%, with 2-year survival rates increasing to 83% for patients with lesions less than 2 cm [47]. Similar results were seen by Hiraki et al. [48] and Liu et al. [49] in patients with stage I NSCLC. Both groups reported 1-year OS rates ranging from 90% to 94% and 3-year OS rates ranging from 74% to 79%. In addition to baseline tumor characteristics, patient comorbidities are predictive of survival. In 82 patients with NSCLC treated with RFA, Simon et al. [50] reported that 40 patients died; however, only 19 patients died due to disease progression. On multivariate Cox regression analyses, the Charlson comorbidity index (CCI), a measure of comorbidities, was strongly predictive of OS. A CCI of greater than 5 (mean OS, 10.43 months) was associated with significantly increased mortality versus a score of 1–2 (mean OS, 55.5 months) or 3–4 (mean OS, 36.62 months). No significant difference in survival was seen between CCI scores of 1–2 and 3–4 [50].

Long-term data after MWA for the treatment of NSCLC are limited. Wolf et al. [4] reported outcomes after MWA of NSCLC in 30 patients. With a mean follow-up of 10 months, Wolf et al. found a local recurrence rate of 26%, which was significantly increased in lesions larger than 3 cm on logistic regression analysis. OS rates ranged from 65% at 1 year to 45% at 3 years, which were not associated with tumor size [4]. Lu et al. [51] reported 1- and 3-year OS rates of 75% and 29.2% after MWA in 48 patients with NSCLC of various stages (I–IV). A significantly increased risk of local progression was seen for lesions larger than 4 cm. Belfiore et al. [52] reported 1- and 3-year cancer-specific survival (CSS) of 69% and 49% after MWA in 44 patients with lung cancer of various disease stages. A formal survival analysis was omitted due to cohort heterogeneity. In 47 patients with stage I NSCLC treated with MWA, Yang et al. [53] reported local control rates of 96% and 48% at 1 and 5 years after MWA. Median CSS and OS were 47.4 and 33.8 months, with significantly improved survival in patients with lesions less than 3.5 cm. Zheng et al. [54] studied outcomes in 183 patients (138 of whom had primary lung cancer) treated with MWA. The local progression rate was 19.1%, with an increased risk of progression seen in patients with lesions larger than 3 cm and in the setting of emphysema on multivariate analysis [54]. The authors reported a median progression-free survival (PFS) and CSS of 16.5 and 29.0 months. Tumor stage and diameter greater than 3 cm were independent risk factors for CSS on multivariate analysis. A recent retrospective study by Healey et al. [55] examined outcomes of 108 patients (82 NSCLCs) who underwent MWA with a median follow-up of 14.1 months. The authors found significantly higher rates of technical success with lesions less than 3 cm in diameter. The median time to tumor recurrence was 62 months, with recurrence rates ranging from 22% at 1 year to 44% at 3 years. Significantly lower rates of recurrence were seen with lesions less than 3 cm. The median OS was 27.1 months, with 1- and 3-year OS rates of 78% and 39%.

Although the long-term studies on cryoablation of NSCLC are limited, the initial studies have yielded promising results. Yamachi et al. [56] used cryoablation to treat 34 NSCLC stage I tumors and reported a median survival of 68 months and a 2-year OS rate of 88%; these results are comparable to results seen with RFA. Moore et al. [57] reported a 5-year OS rate of 67.8% and a local recurrence rate of 14.9% in 45 patients with T1 NSCLC. A recent study by McDevitt et al. [58] of 25 patients with NSCLC found a median OS of 43 months (95% CI, 30–57 months) with a median PFS of 15 months (95% CI, 8.7–20 months).

Thermal ablation has a role in the setting of advanced disease or as salvage therapy. Kodama et al. [59] examined RFA of 51 recurrent NSCLCs that were initially treated with surgery and reported a 1-year survival rate of 97.7% and a 5-year survival rate of 55.7%. The authors found that tumor size less than 3 cm predicts prognosis, with 1- and 3-year survival rates of 100% and 79.8% for tumors greater than 3 cm versus 83.3% and 31.3% for smaller tumors [59]. In patients with stage III or IV NSCLC, Lee et al. [60] found longer median OS in patients treated with RFA and chemotherapy (n = 24) than in those treated with chemotherapy alone (n = 18) (42 vs 29 months, respectively; p < 0.03). Ablation has also been used in patients with a solitary lung after pneumonectomy, a population with few treatment options for new or recurrent disease and limited pulmonary reserve. Hess et al. [12] and Sofocleous et al. [61] have shown acceptable morbidity and safety of ablation in treating these patients. Sofocleous et al. [61] caution that postablation pneumonitis may be a concern in these patients and may be mitigated with periprocedural steroid administration.

Metastatic Disease
Thermal ablation plays a role in the management of metastatic disease in selected patients with limited disease burden that can be ablated with margins. In general, this group includes patients with up to four lesions per lung and with lesions smaller than 3.5 cm [6, 62–65]. Given the clinical course of metastatic disease, the therapies should be repeatable and associated with limited effects on pulmonary function [5, 63, 66]. The Radiofrequency Ablation of Pulmonary Tumors Response Evaluation (RAPTURE) trial in 53 patients with metastatic colorectal carcinoma (CRC) reported 1- and 2-year OS rates of 89% and 66% [14]. De Baere et al. [13] reported the largest series of pulmonary metastases (566 patients with 1037 metastases) treated with RFA. The authors reported a
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The median OS of 62 months and 1- and 5-year OS rates of 92.4% and 51.5% for the entire cohort. On multivariate analysis, the location of the primary tumor, disease-free interval, tumor size greater than 2 cm, and presence of more than three metastases were associated with OS. Several studies have reported similar 1- and 3-year OS rates [67, 68]. Most series evaluating RFA for metastatic disease report local progression rates of 10–30%, especially for lesions larger than 3 cm [14, 18, 63, 69–71]. Omae et al. [72] reported long-term follow-up in 123 patients with lung oligometastases treated with RFA. The authors found a 5-year OS rate and recurrence-free survival rate of 62% and 25% [72].

MWA has also been explored for the treatment of pulmonary metastatic disease. Vogl et al. [5] reported outcomes of MWA in 80 patients with metastatic disease. The authors found a rate of local recurrence of 26%, with treatment success significantly related to tumor size less than 3 cm and to peripheral lesions rather than central lesions. The 1- and 2-year survival rates were 91.3% and 75%. In a follow-up study in 57 patients with 91 metastatic lesions [73], local progression was seen in 33% of patients, with a median time to local progression of 22.6 ± 12.4 months. On regression analysis, the shape of the primary lesion and energy deployed per unit of tumor volume (< 26.7 J/mm³) were associated with disease progression. In a more recent comparison study, Vogl et al. [74] examined the role of MWA (n = 47 patients) and RFA (n = 41 patients) in the treatment of CRC metastases. These authors reported significantly improved local control rates with MWA over RFA and no significant difference in OS or PFS [74]. However, these studies did not perform histopathologic analysis of ablation zones, via biopsy or resection, to validate technical success.

Cryoablation has also been shown to be safe and effective in the treatment of pulmonary metastases, although survival data are limited [75]. Yamauchi et al. [76] reported a local progression rate of 26% with significantly improved PFS with tumors less than 15 mm in 24 patients with metastatic CRC treated with cryoablation. The 1- and 3-year OS rates were 91% and 59.6% and the 1- and 3-year PFS rates were 90.8% and 59%. McDevitt et al. [58] found a mean time to local progression of 10 months, with a median OS of 22 months across tumor types treated with cryoablation. A tumor diameter of greater than 3 cm was associated with local progression. Early results from the Evaluating Cryoablation of Metastatic Lung/Pleural Tumors in Patients—Safety and Efficacy (ECLIPSE) trial [77] of 40 patients with 60 lesions are currently being analyzed. The multicenter prospective cohort includes patients with colon (40%), renal (23%), and sarcoma (8%) primaries. The authors report a local control rate at 1 year of 94.2% and a 1-year OS rate of 97.5%. The investigators concluded that these initial results compare favorably with those of other ablation modalities including RFA and MWA [77]. Taken in conjunction with the results of other studies, these results indicate that thermal ablation performs best in tumors less than 3 cm, similar to findings seen with NSCLC.

Comparative Studies

There are limited comparative studies of thermal ablation with other treatment modalities, including surgical resection and stereotactic beam RT. Kim et al. [78] compared the outcomes of patients with stage I NSCLC treated with RFA (n = 8) versus those treated with surgical resection (n = 14). Although the rates of local recurrence were higher in the patients treated with RFA, OS was similar for the two groups [78]. Lee et al. [60] compared survival in patients with stage I and II NSCLC who were treated with RFA (n = 16) versus those who were treated with surgery (n = 13). Although the patients in the RFA group were significantly older than those in the surgery group, there was no significant difference in OS between the RFA and surgery groups (28.2 and 33.8 months, respectively; p = 0.43) [60]. Zemlyak et al. [79] studied 64 patients with biopsy-proven stage I NSCLC unfit for standard resection. The patients underwent sublobar resection (n = 25), RFA (n = 12), or cryoablation (n = 27). No significant difference in 3-year OS (sublobar resection, 87.1%; RFA, 87.5%; cryoablation, 77%) or in 3-year CSS (sublobar resection, 90.6%; RFA, 97.5%; cryoablation, 90.2%) was seen.

Using the database from the National Cancer Institute’s Surveillance, Epidemiology, and End Results program, Kwan et al. [80] examined survival in 1897 patients with early-stage NSCLC who underwent surgical resection or ablation. After propensity score matching was performed, OS and CSS were not significantly different. Alexander et al. [81] compared 56 patients with stage I NSCLC treated with RFA and 28 patients with stage I NSCLC treated with sublobar resection. The 1-, 2-, and 3-year survival rates were 100%, 95%, and 83%, respectively, for the patients who underwent surgery and 91%, 73%, and 55% for those who underwent RFA; there was a significant increase in survival in patients who underwent resection compared with those who underwent RFA [81].

There are limited data comparing ablation with stereotactic beam RT in the treatment of NSCLC. Ochiai et al. [82] compared outcomes after RFA (n = 48) and stereotactic beam RT (n = 47) in patients with solitary tumors less than 5 cm. The authors reported similar 3-year local control and OS rates between the two modalities: 9.6% and 86.4% for RFA and 7.0% and 79.6% for stereotactic beam RT, with no significant difference between the treatments. However, less than half the patients who underwent stereotactic beam RT had pathologically proven NSCLC [82]. In a pooled analysis of 31 stereotactic beam RT (n = 2767 patients) and 18 RFA (n = 328 patients) studies, Bilal et al. [83] reported that stereotactic beam RT showed lower local progression rates than RFA (3.5–14.5% vs 23.7–43%). OS rates were similar between the two treatments, but 5-year OS rates favored stereotactic beam RT over RFA (47% vs 20.1–27%) [83].

In the treatment of patients with metastatic disease, RFA compares favorably with surgical resection with reported 5-year OS rates of 27–70% [84–86]. Large studies detailing the outcomes of stereotactic beam RT in patients with metastatic disease are limited. Fode and Hoyer [87] examined 321 patients with oligometastatic disease treated with stereotactic beam RT. The authors found a median OS of 2.4 years (95% CI, 2.3–2.7 years), with 1- and 5-year OS rates of 80% and 23%. In both primary disease and metastatic disease and unlike surgical resection or stereotactic beam RT, thermal ablation techniques can be repeated with limited changes to pulmonary function [5, 47]. This capability is of particular benefit in the setting of recurrent or residual disease.

Future Directions

Local recurrence remains a limitation of ablative therapy. Several predictors of local recurrence have been reported including tumor size and ablation margin [13, 18, 34]. There has been interest in developing additional biomarkers of disease local recurrence and improved predictors of response. In lung cancer specifically, several oncogenic mutations have been associated with prog-
nosis [88, 89]. Sofocleous et al. [90] reported the utility of Ki-67 protein as a biomarker for response after RFA in 47 treated tumors, both primary and metastatic. Ki-67-positive tumor cells were an independent marker of local tumor progression and shorter PFS and CSS. Ziv et al. [91] reported that KRAS mutation status of an ablated lesion was a significant predictor of local recurrence that was independent of tumor size or ablation margin in 54 patients with primary adenocarcinoma. Conversely, Wei et al. [92] reported that EGFR-positive status did not adversely affect PFS or OS in 61 patients with stage IIIB or IV NSCLC treated with MWA.

The role of inflammatory cytokines and immune markers for determining prognosis in patients with lung cancer is also being explored. RFA-mediated tumor necrosis can stimulate an immune response [93]. Schneider et al. [93] examined the impact of RFA on the profile of serum inflammatory factors and immune suppressive cells in ablation in 12 patients. In patients with disease recurrence, the investigators found elevated levels of tumor necrosis factor–α, chemokine (CC motif) ligand–2, and chemokine ligand–4 and increased nitric oxide production in circulating myeloid-derived suppressor cells. The authors concluded that these factors may serve as early indicators of incomplete ablation of NSCLC.

**Conclusion**

Thermal ablation has shown safety and efficacy in the treatment of both primary and secondary lung malignancies in nonsurgical candidates. In NSCLC, after propensity score matching was performed, 2-year OS survival rates match those of surgery and stereotactic beam RT [47, 94]. Ablation also plays a role in metastatic disease, showing safety and efficacy. Across ablation modalities, lesion size is the main determinant of treatment success and survival. Furthermore, local progression remains a limitation for these therapies. Development of new tissue and corresponding surrogate image biomarkers for patient risk stratification and earlier detection of recurrence is needed. Further refinements of ablation technique including the intraprocedural development of tissue confirmation of complete tumor ablation with margins can improve local tumor control and significantly lower recurrence rates. Although ongoing prospective clinical trials comparing the efficacy of thermal ablation, stereotactic beam RT, and surgery are unlikely to mature, they could define the role of these therapies and improve patient selection for each treatment [77, 95].

**References**


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(FIGURES START ON NEXT PAGE)
Fig. 1—Successful microwave ablation (MWA) of recurrent non–small cell lung carcinoma (NSCLC) tumor or metastasis in left lower lung lobe with gradual constriction of ablation zone: This case illustrates value of locoregional therapy in general and of ablation specifically in treatment of primary lung cancer with recurrent and metastatic nodules. Over course of treatment, patient had minimal and stable pulmonary symptoms. In this 72-year-old man, initial diagnosis in 2008 was right upper lobe lung adenocarcinoma, stage IB. Patient underwent right upper lobectomy and right lower lobe wedge resection with tumor-free margins for moderately differentiated adenocarcinoma with micropapillary (60%), papillary (30%), and lepidic (10%) components. Patient received no adjuvant chemotherapy, and there was no evidence of disease for 20 months. In 2010, imaging detected new clustering of right lower lobe nodules, which were biopsy-proven adenocarcinoma and were morphologically similar to primary tumor, and no evidence of disease elsewhere. Because of undetermined staging of disease (metastatic vs second primary tumor), no systemic therapy was used, and patient was treated with image-guided radiation therapy. In 2012, imaging showed left lung nodule, and patient was diagnosed with stage IV disease treated with MWA. After MWA, new left upper lobe nodule was treated with wedge resection in January 2013. Subsequent recurrences in two right lower lobe metastases in February 2013 and right lower lobe in May 2014 were treated with MWA. Patient’s disease was stable until December 2015 when chest CT revealed increasing left lower lobe nodule, recurrent tumor 3 years after MWA, but not in area of prior MWA.

A. CT scan obtained before MWA shows 0.9 × 0.9 cm left lower lobe lung metastasis (arrow).
B. CT scan obtained during MWA. Metastasis was treated in three overlapping ablations.
C. CT scan obtained immediately after MWA shows ablation defect (arrow) that is 2.5 × 1.8 cm. Margins were assessed as 5 mm and extend to aorta.
D–F, Follow-up CT scans obtained 11 weeks (D), 7 months (E), and 1 year (F) after MWA show expected gradual constriction of ablation zone (arrows) and no evidence of local recurrence. Patient remained without disease until February 2017 when he developed bilateral lung nodules with associated rib destruction and increased pleural thickening consistent with multifocal progression of disease. Patient is currently undergoing systemic therapy for disease management.
Fig. 2—Successful microwave ablation (MWA) of recurrent biopsy-proven non–small cell lung carcinoma (NSCLC) in 83-year-old woman. Initial diagnosis in May 2007 was stage IA bronchoalveolar adenocarcinoma in right upper lobe. Wedge resections of left upper and lower lobes were performed, and malignancy was pathologically proved only in left upper lobe. Left lower lobe FDG-avid nodule remained in situ after resection. This nodule had interval enlargement and was found to be positive for adenocarcinoma in November 2007 at biopsy. This nodule was treated with radiofrequency ablation in March 2008, with no viable Ki-67–positive tumor cells detected on tissue adherent to electrodes [90]. In November 2011 patient returned with new biopsy-proven NSCLC nodule in left lower lobe. This nodule was treated with MWA.

A, Cross-sectional CT scan shows 2.8-cm recurrent NSCLC lesion (arrow) in left lower lobe.

B, Pretreatment split-dose 18F-FDG PET/CT scan shows FDG-avid lesion (arrow) with maximum standardized uptake value of 5.9. (Split-dose FDG PET/CT is technique for PET/CT-guided ablation that permits both target localization and evaluation of treatment effectiveness. During procedure, standard administered diagnostic FDG activity dose of approximately 12 mCi [444 MBq] is administered in two aliquots: 4-mCi [148-MBq] target dose or imaging dose administered 30–60 minutes before ablation and 8-mCi [296-MBq] treatment efficacy dose administered immediately after ablation. Images are obtained 30 minutes later.)

C, CT scan obtained during MWA shows microwave electrode (arrow) in tumor: two overlapping ablations of 8 minutes each were performed at 10–25 W.

D, CT scan obtained immediately after MWA shows ablation zone. All margins except medial margin are more than 5 mm. Smaller medial margin extends to aorta.

E, Split-dose FDG PET/CT scan obtained immediately after MWA shows no residual FDG avidity in area (arrow).

F, FDG PET/CT scan obtained 6 months after MWA shows expected constriction of ablated zone (arrow) and no FDG avidity.

(Fig. 2 continues on next page)
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Fig. 2 (continued)—Successful microwave ablation (MWA) of recurrent biopsy-proven non–small cell lung carcinoma (NSCLC) in 83-year-old woman. Initial diagnosis in May 2007 was stage IA bronchoalveolar adenocarcinoma in right upper lobe. Wedge resections of left upper and lower lobes were performed, and malignancy was pathologically proved only in left upper lobe. Left lower lobe FDG-avid nodule remained in situ after resection. This nodule had interval enlargement and was found to be positive for adenocarcinoma in November 2007 at biopsy. This nodule was treated with radiofrequency ablation in March 2008, with no viable Ki-67–positive tumor cells detected on tissue adherent to electrodes [90]. In November 2011 patient returned with new biopsy-proven NSCLC nodule in left lower lobe. This nodule was treated with MWA. G and H, FDG PET/CT scan (G) and corresponding CT scan (H) obtained 1 year after MWA show further constriction of ablation zone (arrows). I and J, FDG PET/CT scan (I) and corresponding CT scan (J) obtained 2 years after MWA show expected evolution of ablation zone (arrows) with no evidence of local recurrence.

Fig. 3—Successful microwave ablation (MWA) of lung metastases from colorectal carcinoma in 37-year-old man with history of ulcerative colitis who had undergone proctocolectomy and formation of J-pouch in 1996. In June 2010, patient was diagnosed with stage I mucinous adenocarcinoma of rectum and received adjuvant chemotherapy (folinic acid, 5-fluorouracil, oxaliplatin) and chemoradiotherapy. In April 2012, patient developed right middle lobe lung metastasis and underwent right middle lobe wedge resection. In February 2013 when patient was no longer receiving chemotherapy, follow-up imaging showed significant progression of disease in left lung with two growing nodules in left lower lobe and left upper lobe. Both lesions underwent MWA with at least 5-mm ablation margins. Tissue from ablation electrodes showed no viable tumor cells [90]. We present imaging of one of two ablated lesions. A, Pretreatment cross-sectional CT scan shows 8 × 10 mm medial left upper lobe lung metastasis (arrow). B, Fluorine-18-FDG PET/CT scan shows mildly FDG-avid lesion (arrow). C, CT scan obtained during MWA shows microwave electrode in tumor. Two overlapping ablations, 45 W for 10 minutes and 65 W for 5 minutes, were performed. (Fig. 3 continues on next page)
Successful microwave ablation (MWA) of lung metastases from colorectal carcinoma in 37-year-old man with history of ulcerative colitis who had undergone proctocolectomy and formation of J-pouch in 1996. In June 2010, patient was diagnosed with stage I mucinous adenocarcinoma of rectum and received adjuvant chemotherapy (folinic acid, 5-fluorouracil, oxaliplatin) and chemoradiotherapy. In April 2012, patient developed right middle lobe lung metastasis and underwent right middle lobe wedge resection. In February 2013 when patient was no longer receiving chemotherapy, follow-up imaging showed significant progression of disease in left lung with two growing nodules in left lower lobe and left upper lobe. Both lesions underwent MWA with at least 5-mm ablation margins. Tissue from ablation electrodes showed no viable tumor cells [90].

**D,** CT scan obtained immediately after ablation shows ablation zone (arrow) of 28 × 30 × 30 mm with minimal ablation margin of more than 10 mm.

**E,** Split-dose 18F-FDG PET/CT scan obtained after second dose shows no uptake in ablated zone (arrow); maximum standardized uptake value (SUV_{max}) is 1.0. Histopathologic analysis of tissue from ablation electrodes showed no viable tumor cells [90]. Split-dose FDG PET/CT is technique for PET/CT-guided ablation that permits both target localization and evaluation of treatment effectiveness. During procedure, standard administered diagnostic FDG activity dose of approximately 12 mCi [444 MBq] is administered in two aliquots: 4-mCi [148 MBq] target dose or imaging dose administered 30–60 minutes before ablation and 8-mCi [296 MBq] treatment efficacy dose administered immediately after ablation. Images are obtained 30 minutes later.

**F,** FDG PET/CT scan obtained 5 weeks after MWA shows hypermetabolic rim of cavitated ablation zone (arrow). Ablation zone is 2.9 × 4.1 cm with SUV_{max} of 5.5. Follow-up imaging finding of hypermetabolic rim of cavitated ablation zone was characterized as expected postablation change rather than as residual or recurrent disease. Sequential imaging follow-up with standardized uptake value (SUV) readings is helpful to detect gradual resolution. In cases of focal SUV increase in ablation zone and whenever in doubt, short-interval PET or biopsy is recommended with aim of repeat treatment.

**G,** FDG PET/CT scan obtained 4 months after MWA shows typical collapse and constriction of cavitated ablation zone (arrow), which is 1.6 × 1 cm, and decreased FDG avidity of ablation zone to SUV_{max} of 4.7.

**H,** FDG PET/CT scan obtained 7 months after MWA shows no FDG uptake in ablated area (arrow).

**I,** CT scan obtained 1 year after MWA shows constricted ablation zone (arrow).

(Fig. 3 continues on next page)
Fig. 3 (continued)—Successful microwave ablation (MWA) of lung metastases from colorectal carcinoma in 37-year-old man with history of ulcerative colitis who had undergone proctocolectomy and formation of J-pouch in 1996. In June 2010, patient was diagnosed with stage I mucinous adenocarcinoma of rectum and received adjuvant chemotherapy (folinic acid, 5-fluorouracil, oxaliplatin) and chemoradiotherapy. In April 2012, patient developed right middle lobe lung metastasis and underwent right middle lobe wedge resection. In February 2013 when patient was no longer receiving chemotherapy, follow-up imaging showed significant progression of disease in left lung with two growing nodules in left lower lobe and left upper lobe. Both lesions underwent MWA with at least 5-mm ablation margins. Tissue from ablation electrodes showed no viable tumor cells [90]. We present imaging of one of two ablated lesions. J and K, CT scans obtained 2 years (J) and 4 years (K) after MWA show ablation zone (arrows). L, FDG PET/CT scan obtained 4 years after ablation shows no FDG uptake in ablated area (arrow). After ablation of left lung metastases, patient developed right lung metastasis, which was also treated by MWA. In November 2014, patient developed pleural metastases and pleura-based metastases, which were treated with three regimens of systemic chemotherapy. Patient was alive at last follow-up in 2017.