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Thermal Ablation of Lung Tumors

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Abstract

Lung cancer remains the leading cause of cancer death in the United States, accounting for an estimated 29% of cancer deaths in 2009.¹ Pneumonectomy or lobectomy with hilar and mediastinal lymph node sampling is the gold standard treatment and offers the best option for cure of stage 1/2 nonsmall cell lung cancer (NSCLC).² Unfortunately, only 15% of patients present with stage 1/2 disease, and many of these patients do not meet the pulmonary physiologic guidelines for lobar resection.³ In addition to lung cancer, pulmonary metastases are present in 25% to 30% of patients dying from all types of cancer.⁴ For some patients with oligometastatic pulmonary disease, metastectomy is associated with an improvement in survival.⁵ External beam radiation traditionally has been offered as the alternative to surgical resection for NSCLC or pulmonary metastatic disease. Unfortunately, the 5-year survival following radiation for stage 1 and 2 NSCLC remains low at 15% to 20%, with local recurrence being the most common mode of failure.^{6,7} Thermal ablation offers an intriguing therapeutic option to increase local tumor control and survival in patients with early stage NSCLC or with limited metastatic disease from nonlung primaries who are not surgical candidates because of poor cardiopulmonary reserve, anatomic constraints limiting resection, failure of traditional therapies, or refusal of operative approaches.

Thermal ablation has been shown to be effective in treating tumors in bone, kidney, and liver.^{8–11} Most preclinical and clinical trials have focused on demonstrating the feasibility of three modalities for pulmonary thermal ablation, namely radiofrequency (RF) ablation, microwave (MW) ablation, and cryoablation. This article discusses the unique challenges of performing thermal ablation in lung tissue and reviews the current literature regarding RF, MW, and cryoablation in the lung.

Keywords

Ablation; Lung; Cancer; Thermal

THERMAL ABLATION IN LUNG TISSUE

Clinical success in thermal ablation depends upon the unique characteristics of the tissue being ablated. A major obstacle for all thermal ablation techniques is the heat sink effect, which describes how bloodflow or airflow through or adjacent to the target tissue can offset

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the applied cooling or heating, thus limiting intended tissue damage. Experimental studies with RF ablation in liver demonstrated that perfusion-mediated cooling was responsible for the smaller ablation diameters obtained in in vivo versus in vitro experiments.¹² Proximity to vessels larger than 3 mm also has been associated with increased risk of local tumor progression.¹³ Thermal heat sink effects are particularly important in lung ablation, as the lungs are exposed to 100% of right heart blood flow. In addition to vascular perfusion, the lungs are uniquely composed of air-filled spaces that are constantly ventilated, resulting in a second type of heat sink analogous to an air-cooled radiator.¹⁴

A second factor influencing thermal ablation is the thermal conductivity of the tissue being ablated. Thermal conductivity is lower in lung than in other tissues, such as bone, liver, and kidney due to its high percentage of air by volume.¹⁵ Lower thermal conductivity of aerated lung would be expected to limit heat transfer into tissues adjacent to solid pulmonary masses, and if true, this could prevent adequate ablation of infiltrative margins or satellite tumors at the periphery of lung lesions. Although surrounding air-filled lung may restrict heat transfer into the partially aerated peripheral portion of lesions, it may also effectively insulate the interior of lesions and create improved tumor damage via an oven- or freezer-type effect.^{16,17} This has been demonstrated by animal data showing an increase in ablation zone size in implanted tumors in lung when compared with kidney.¹⁸ A histologic study of NSCLC showed that treatment margins of 8 mm for adenocarcinoma and 6 mm for squamous cell carcinoma are necessary to cover 95% of microscopic disease.¹⁹ The dichotomy of decreased transfer of heat to the periphery of lesions and the insulating effect of aerated lung can be an important consideration in choosing which lesions to treat and with what thermal ablation modality.

As with the liver, several investigators have attempted to overcome perfusion and ventilation heat sinks inherent to lung tissue. Ipsilateral mainstem bronchus occlusion and pulmonary artery occlusion have both been shown to significantly increase the mean volume of the ablation zone with RF ablation. Although the effect is larger with pulmonary artery occlusion, bronchial occlusion is much more practical to apply clinically.^{14,20,21}

RADIOFREQUENCY ABLATION

In RF ablation, an alternating electrical current (approximately 500 KHz) with 10 to 200 W of power is applied to the target tissue via an interstitial electrode. Two to four grounding pads on the skin surface complete the electrical circuit through the body. Current conducted through tissue adjacent to the electrode leads to ion agitation, which is converted by means of friction into heat.²² Heat generation is proportional to the current density and is attenuated exponentially with increasing distance from the electrode. As tissue is heated, predictable changes occur based on time and temperature. At temperatures between 42°C and 45°C, cells become susceptible to damage by outside agents like radiation and chemotherapy. Temperatures maintained above 46°C for a prolonged period of time (on the order of 30 to 60 minutes) cause irreversible cell damage. Between 50°C and 52°C, the time to cytotoxicity is reduced to 4 to 6 minutes. The goal of RF ablation is to achieve temperatures between 60°C and 100°C, where there is near instantaneous induction of protein coagulation with damage to cytosolic and mitochondrial enzymes and DNA–histone complexes leading to coagulative necrosis.^{23,24} Conversely, temperatures above 105°C cause boiling, desiccation, vaporization, and carbonization of tissues. The resulting impedance rise limits electrical current flow, leading to reduced coagulative necrosis volumes.²⁵ Thus, the therapeutic temperature range for RF ablation is narrow (60°C to 100°C).

Early percutaneous RF ablation technology was able to create ablation zones only 1.6 cm in diameter.²⁶ Many strategies since have been developed to increase the size of RF ablations. For example, internally cooled electrodes reduce tissue charring near the electrode and permit greater energy delivery.²⁷ When combined with pulsed power delivery, the cooled electrodes were able to increase ablation zone size to approximately 2 cm in diameter while keeping at 17-gauge profile.²⁸ Clustered, deployable, and multipolar electrode designs use a different approach by increasing the effective surface area of the electrode and distributing energy delivery over a larger volume (Fig. 1).²⁹ When compared directly, it has been shown that these designs produce potentially larger ablations than the single cooled electrode design, but often at the expense of irregular shape, protracted treatment times, or increased applicator diameter (14-gauge).³⁰ More recently, a system that exploits the aforementioned pulsing algorithm to switch power between multiple electrodes has been shown to increase ablation zone size while retaining a relatively spherical ablation shape.^{31–33}

While most studies have focused on the performance of RF devices in liver models, some have demonstrated that multitined or multiple-electrode designs may produce more effective ablations in the lung due to their ability to spread out energy delivery.³⁴ However, it also has been noted that deployable designs can be more problematic to use in lung. For example, ballotable solid tumors can be difficult to penetrate with a deployable device, and some studies have described difficulty retracting the tines after treatment.^{35,36}

Another strategy to overcome low tissue conductivity is by infusion of sodium chloride solutions into the targeted ablation zone.^{37,38} Sodium chloride is ionic and thus improves the electrical conductivity of the surrounding tissue. Infusion during treatment also prevents charring and keeps the ablated tissue hydrated, resulting in a larger zone of ablation. However, saline infusion can produce irregular and unpredictable ablations with potentially serious complications and thus is not routinely performed.³⁹

There are multiple US Food and Drug Administration (FDA)-approved RF ablation devices on the market with different performance characteristics. Examples include: the Angiodynamics 1500X RF generator with the StarBurst and Uniblate electrodes (Latham, NY, USA), the Boston Scientific RF3000 with LaVeen electrodes (Natick, MA, USA) (both of which use multitined, expandable electrodes) (Fig. 2) and the Covidien Cool-tip system (Boulder, CO, USA), which uses either a single straight electrode, cluster of three electrodes, or up to three independent, switched straight electrodes that are actively cooled during ablation (Fig. 3). Importantly, these systems were all developed for use in liver, and have been applied in lung without modification. Currently, there are no devices available for clinical use optimized for treating tumors in the lung.

Animal models first were used to investigate RF ablation in normal lung tissue to develop treatment algorithms for people.⁴⁰ Human ablate-and-resect studies also were performed and, although early results were mixed, they demonstrated that RF ablation was feasible for lung tumors, ultimately leading to clinical use.^{19,41} A systematic review published in 2008 summarized the literature regarding RF ablation. Among the 17 studies included in the review, the median complete necrosis rate was 90% (range: 38% to 97%) with 1-, 2- and 3-year survival rates of 63% to 85%, 55% to 65%, and 15%–46%, respectively.⁴² The only prospective single-arm multicenter intent-to-treat clinical trial of RF ablation in 106 patients (33 non-small cell lung cancer, 53 colorectal cancer metastases, 20 other metastases) found promising overall and cancer-specific survival rates in these patients.⁴³ A summary of lung RF ablation studies is listed in Table 1.^{34,43–51}

There are several factors that determine the likelihood of a successful ablation, but similar to other organ systems, tumor size is one of the most important considerations.^{44,49,50} Tumors

less than 3.0 cm tend to be associated with complete necrosis in most cases, with less than 50% complete necrosis in tumors from 3.0 to 5.0 cm, and a low likelihood of successful ablation in tumors greater than 5.0 cm. Importantly, these studies illustrate that complete necrosis has a positive effect on survival and should be the goal of any ablative treatment.⁴⁹

One advantage of RF ablation over surgical resection and radiation therapy is repeatability. The minimally invasive nature of percutaneous ablation allows for multiple treatment sessions on a given tumor or patient with relatively low complication risk. In fact, it has been shown that repeat treatment of local tumor progression after the primary treatment can improve survival.³⁴ In contrast, particularly in patients with a limited pulmonary reserve, repeat surgery is often not possible, and radio-therapy is associated with a maximum tolerated dose, which limits repeat treatment. Thus, all patients with local tumor progression should be considered for retreatment unless there is evidence of regional or distant disease.

When radiation therapy is a viable treatment option, RF ablation and external beam radiation appear to be synergistic.⁵² RF ablation is most effective in the center of relatively avascular tumors, while external beam radiation and stereotactic radiosurgery are most effective at the periphery of the tumor where there is high oxygen content and a hyperthermic rim around the ablation zone. Combining the two therapies has been shown to increase survival, at no additional toxicity, as compared with radiation therapy alone, and this technique should be considered for larger tumors.⁵³

In summary, RF ablation has been shown to be a suitable means of local tumor control for selected small tumors in patients with NSCLC or pulmonary metastatic disease. Pulmonary function, as measured by forced expiratory volume in the first second of respiration (FEV₁) and forced vital capacity (FVC), is well preserved following ablation, giving it a significant advantage in patients with limited pulmonary reserve.⁴³ Despite these promising results, RF ablation continues to be plagued by modest rates of local tumor progression, particularly in tumors greater than 3 cm and in the vicinity of larger heat sinks. Further investigation will be required to continue to improve the efficacy of this promising technique and the associated adjuvant techniques.

MW ABLATION

MW ablation is a less studied, but promising modality that may improve the efficacy of percutaneous thermal ablation in the lung. MW ablation involves the application of electromagnetic waves at frequencies of typically 915 and 2450 MHz. The alternating waves cause polar water molecules to rotate rapidly, converting the applied energy into heat and elevating tissue temperatures to cytotoxic levels.⁵⁴ As discussed previously, limitations of RF ablation include a small zone of active heating,²² low energy delivery in high-impedance aerated or charred/desiccated tissue, and the heat sink effect.^{21,55,56} In these regards MW ablation has several theoretical advantages over RF ablation. MW energy is deposited over a larger active heating zone and produces higher temperatures more quickly than is possible with RF ablation. Additionally, the electromagnetic waves associated with MW are not limited by lower thermal conductivity of lung, or the increased impedance of charred tissues.^{55,57,58} MW energy also has been shown to effectively treat perivascular tissue and coagulate large vessels, with improved efficacy near heat-sinks.^{59,60} Finally, multiple MW antennae can be placed and activated simultaneously, which increases ablation zone size even more than bronchial or vascular occlusion in the lung.^{60,61} The performance of MW ablation is highly system dependent, and factors such as system frequency, total energy delivery, and relative phase of the alternating fields produced by each antenna can greatly affect the resulting ablation zone size. In evaluating these systems, delivered power is the most important factor for determining ablation zone size. To date, many systems have been

underpowered and produce small ablation zones. The reason for this is primarily due to the inability to handle the waste heating of the antenna shaft. This heating is caused by power loss and reflected power related to impedance mismatches at the tissue/antenna interface. This is being addressed with improved cooling of the antenna shaft and better antenna design. The antenna cooling can be accomplished in several ways. The most common technique is to use water cooling similar to RF ablation systems. However, because of the higher energies and temperatures associated with MW ablation, this technique is limited. Another technique is the use of gas cooling, which is based upon the same principle as cryoablation. Because of the increased cooling power, this technique is associated with more effective cooling of the antenna shaft, allowing much higher delivered power. Further development in shaft cooling is critical to optimizing the advantages of MW ablation.

There have been several early clinical studies of MW ablation for lung tumors in people, which have shown promising rates of local control even with tumors larger than 3 cm.^{62,63} The only clinically available FDA-approved MW ablation system with clinical data to date is the Evident system produced by Covidien (Boulder, CO, USA) (Fig. 4), but there are several other systems in development and likely to be available soon. Thus far, MW ablation has demonstrated higher pneumothorax rates than those reported in the RF ablation literature, which may be related to the large antenna size and may improve with the development of smaller antenna.⁶³

Although no studies have been performed in people to compare the relative effectiveness of MW ablation and RF ablation in lung, there have been several promising studies performed in animal models. In particular, one study looked at a prototype 17 gauge internally cooled MW antennae and showed that it produced ablation zones that were 25% larger in diameter and 50% larger in cross-sectional area than the ablation zones achieved with a similarly configured internally cooled RF ablation electrode (Fig. 5).⁵⁷

The current body of literature regarding clinical MW ablation in lung is limited,^{63,64} but given the limitations of RF ablation regarding lung impedance, charring, and the heat sink effect, more investigation in people is warranted to determine whether the theoretical and experimental advantages of MW ablation can produce improved local control and patient survival in patients with lung tumors.

CRYOABLATION

Cryoablation causes cellular damage through a complex combination of cellular events during tissue freezing and thawing. As the temperature decreases, tissues are damaged by failed metabolism, extracellular crystallization causing cell dehydration, and finally and most severely by intracellular ice crystal formation disrupting organelles and cell membranes. Additionally, postfreezing damage occurs during thawing as ice crystals coalesce into larger crystals that disrupt cell membranes. Finally, these changes result in vascular thrombosis and stasis in the postfreezing period.⁶⁵ Given the complex nature of cellular damage that occurs with cryoablation, the protocol for lung, with its low thermal conductivity, can be expected to be somewhat different than for other tissues.^{15,66} Cryoablation possesses several properties that make it an attractive option as a thermal ablation technique. The first advantage is visualization of the ablation zone (Fig. 6). Radiologic-pathologic studies have shown that the ice ball visualized on computed tomography (CT) scans correlates well with the pathologic zone of ablation.⁶⁷ Second, as pulmonary fluid fills the alveolar spaces after the first freeze and thaw cycle, thermal conductivity increases 20-fold.⁶⁶ It is possible that this results in more rapid freezing and expanded ablation zones on subsequent freezing cycles.⁶⁶ Third, cryoablation preserves the

collagenous architecture of the tissue being ablated, which may be particularly beneficial in treating lesions adjacent to the tracheobronchial tree and mediastinum.⁶⁸

In the largest clinical series to date, pulmonary cryoablation was performed on 187 patients (165 primary lung, 22 metastatic), many with advanced stage disease who had failed traditional therapies. Higher technical success rates were achieved in patients with tumors less than 4 cm in diameter and peripheral tumors. Follow-up was too short to determine postprocedure survival. Of note, pulmonary cryoablation was associated with a low pneumothorax rate (12%), no procedure-related mortality, and improved quality of life scores in patients 1 week following the procedure.⁶⁹ Another study with follow-up found local tumor progression in 35% of patients, with a median time to progression of 9 months.⁷⁰ Like RF ablation, cryoablation is limited by the poor thermal conductivity of lung, but the ability to use numerous cryoprobes simultaneously, preservation of the collagenous tissue in airways, and a highly visible ablation zone are all advantages over heat-based therapies, particularly for larger tumors and tumors near mediastinal structures.

EVALUATION OF TREATMENT RESPONSE

Follow-up imaging after pulmonary ablation is more challenging than resection, because a both a residual mass and an ablation zone are present. In addition, ablation incites an inflammatory/cytotoxic response in adjacent normal lung tissue that appears as ground glass opacity or frank consolidation that initially increases the apparent size of the tumor. In fact, the size of the ground glass opacity surrounding the ablated lesion on immediate postablation imaging has been shown to be predictive of an effective ablation (see Fig. 6). One study with RF ablation suggested that a ground glass margin of at least 5 mm was required to ensure complete ablation.⁷¹ Other investigators found that a postablation area of ground glass opacity four times the area of the ablated lesion is predictive of complete ablation.⁷² The ablation zone may start to decrease in size as early as 2 to 3 weeks following ablation as tissue repair progresses, but may continue to evolve over months to years (see Fig. 6). Cavitation has been reported in up to 30% of patients following MW and RF ablation and is associated with effective ablation and further complicates interpretation of postablation imaging (see Fig. 3).

Given the apparent increase in lesion volume following ablation, the authors' follow-up protocol includes a postablation CT scan within 1 month of the procedure (to serve as a new baseline) and then contrast-enhanced CT at 3-month intervals to determine treatment response. Tumor morphology, volume, and contrast enhancement can be followed over time, and the authors consider tumors that are stable or decreasing in size and do not demonstrate more than 10 hounsfield units of contrast enhancement to be completely ablated. This method of evaluation has limitations, since some patients with incomplete treatment are not discovered until late in the follow-up period.⁷³

To increase the sensitivity of detecting early recurrence some centers employ CT densitometry protocols where contrast is given, and sequential series of images are obtained at 0, 45, 180 and 300 seconds following contrast enhancement. This technique is not widely used, because it is cumbersome and not well suited to follow multiple lesions or to determine progression in complex lesions with cavitation. Positron emission tomography (PET)-CT also has been employed following ablation and can be advantageous, since it is not limited to an anatomic evaluation. Fluorodeoxy-glucose (FDG) uptake should decrease in tumors as early as 2 months following ablation and nodules with a percent reduction in FDG uptake less than 60%, or an absolute SUV of 3.0 or greater at 2 months should be considered incompletely ablated and further treatment may be required.^{74,75} Finally, diffusion weighted imaging (DWI) can identify differences in completely and incompletely

ablated tumors, but the clinical utility of this technique is yet to be determined.⁷⁶ At this time, most clinicians follow patients with CT and use PET-CT as a problem-solving technique.

COMPLICATIONS

Although the complication rate varies and can be expected to be higher in patients who have poor underlying pulmonary reserve, a minor complication rate of approximately 50% and a major complication rate of approximately 8% can be expected. Minor complications seen after RF ablation can include: pleural effusion, pneumo-thorax, subcutaneous emphysema, fever, and hemoptysis, while major complications include pneumothorax requiring chest tube placement, air embolism, and pulmonary abscess.⁷⁷ Pneumothorax is the most common complication following all modalities of thermal ablation (Fig. 7). A median pneumothorax rate of 28% (range 4.5 to 61.1%) was reported for RF ablation in a recent meta-analysis with approximately 11% (range 3.3 to 38.9%) of these requiring chest tube placement.⁴² In RF ablation, the risk of pneumothorax has been shown to be greater in patients in whom multiple lesions are treated, in patients without history of previous lung surgery, and in patients with a longer pleura-to-lesion distance.⁷⁸ In MW ablation, pneumothorax rates up to 39% have been reported.⁶³ This relatively high pneumothorax rate may be secondary to the larger, 14.5-gauge antenna currently available. Conversely, pneumothorax rates as low as 12% have been reported with cryoablation.⁷⁰

Hemoptysis is a common occurrence after pulmonary ablation, but is usually low volume and self-limited. When the hemoptysis is large volume, it can be a potentially fatal event. Large-volume hemoptysis has been reported to occur in a median of 11.1% (range 3.3% to 18.2%) of patients undergoing RF ablation.⁴² There has been one reported fatality following RF ablation secondary to hemoptysis; however, this patient also received brachytherapy.⁷⁹ Patients undergoing cryoablation may be at increased risk for hemoptysis, as higher rates have been reported in lung cryoablation literature, but once again, it is generally self-limited.^{69,70}

Less commonly reported complications following ablation include thermal damage to the phrenic nerve, intercostal nerves and brachial plexus (see Fig. 7). When damaged during cryoablation, the associated symptoms tend to resolve over time. When treating lesions near the chest wall or mediastinum, an intentional pneumo-thorax to act as a thermal or electrical insulator can be considered to protect the intercostal or phrenic nerve.^{80,81}

Microbubbles generated during thermal ablation procedures can be seen in the pulmonary veins and even the carotid artery. Although a cause of alarm when first described, this finding does not appear to be associated with adverse outcomes.^{82,83} Patients undergoing thermal ablation are also at risk for air embolism and tumor track seeding similar to what is seen with needle lung biopsy.^{42,84}

With MW ablation, there have been several reports of severe skin burns, possibly requiring skin grafting.⁶³ This is likely related to either shaft heating caused by inadequate cooling, or propagation of the MW energy along the shaft with multiple antenna ablations, resulting in nontarget tissue ablation. This issue should be addressed with the development of improved shaft cooling paradigms on future systems. An awareness of the potential complications of each of the thermal ablation modalities is an important part of preprocedural patient selection and treatment planning.

SUMMARY

The 5-year survival of all stages of NSCLC remains bleak, having only increased from 13% to 16% over the past 30 years.¹ RF ablation, MW ablation, and cryoablation are each intriguing possibilities with some track record in patients with NSCLC and pulmonary metastatic disease who are poor surgical candidates. If ablation is going to be a viable treatment for these patients, local control has to be optimized, and appropriate patient selection is key.⁷³ Further studies will need to address optimization of ablation protocols and should include prospective randomized trials comparing these three ablation modalities and other techniques to determine the most effective means of local tumor control in this population of patients.

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Fig. 1.

55-year-old woman with history of metastatic colorectal cancer. History of previous liver ablation, now with a new left lower lobe pulmonary metastasis. (A) 9 mm left lower lobe colorectal metastasis (*arrow*). (B) A single Cool-tip electrode was positioned, but it was somewhat eccentric in the nodule and the ground glass opacity associated with the radiofrequency ablation only partially enveloped the nodule (*arrow*), suggesting that a complete treatment was not accomplished. (C) 6 months later, the nodule had increased in size, and it was determined that there was local tumor progression (*arrow*). (D) For the retreatment, a Cool-tip cluster electrode was used to increase the power deposition, and a better technical result was achieved. (E) However, the increased invasiveness resulted in a large hemothorax that required chest tube placement and prolongation of her hospitalization stay. (F) 2-year follow-up computed tomography scan shows a small residual scar (*arrow*), but no evidence of local tumor progression.

Fig. 2.
A deployable array electrode positioned within a right lower lobe nonsmall cell lung cancer. Note that the increased surface area associated with this electrode allows greater power deposition, but decreased control and increased invasiveness. (*Courtesy of Ricardo Lencioni, MD, Pisa, Italy.*)

Fig. 3.

51-year-old man with history of metastatic colorectal carcinoma s/p hepatic and pulmonary resection, including right pneumonectomy, referred for radiofrequency (RF) ablation of a single left lower lobe metastasis. (A) 1 cm peripheral pulmonary nodule in left lower lobe (*arrow*), with no large adjacent vessels. (B) A single Cool-tip electrode was placed centrally in the tumor for the ablation (*arrow*). (C) Immediately following RF ablation, there was ground glass opacity entirely encompassing the lesion (*arrow*), consistent with a technically successful ablation. Note the small pneumothorax that resolved without treatment. (D) 4-month follow-up computed tomography (CT) demonstrates cavitation of the nodule (*arrow*), a favorable prognostic sign. (E) 14-month follow-up positron emission tomography/CT scan demonstrates parenchymal scarring, but no significant radiotracer uptake, consistent with a successful ablation.

Fig. 4.

80-year-old man with multiple comorbidities, including oxygen dependence with a cavitary squamous cell carcinoma in the left lower lobe. (A) 2 cm peripheral cavitary squamous cell carcinoma in the left lower lobe (*arrow*). (B) Two microwave antennae were positioned within the tumor with one seen on this imaging plane. Note the small pneumothorax (*arrow*), which was later treated with a small-bore chest tube. (C) Due to the cavitary nature of the tumor, saline was injected into the tumor to increase the water content and thus the likelihood of heating all of the tissue. Note that after this, the tumor no longer appears cavitary (*arrow*). (D) Immediately after the ablation, confluent ground glass opacity develops around the tumor (*arrows*), indicating a combination of ablation zone and parenchymal hemorrhage. (E) 6-month follow-up computed tomography scan demonstrates a residual nodule (*arrow*), but without cavitation, and the patient is now 18 months post-ablation with no evidence of disease. (*Courtesy of Damian Dupuy, MD, Providence, Rhode Island.*)

Fig. 5. Comparison of radiofrequency (RF) and microwave (MW) in a porcine lung model. (A) The MW ablation was associated with a more rapid and larger ablation zone than the RF ablation as shown by the development of ground glass opacity on the noncontrast computed tomography (CT) images obtained during the ablation. (B) The CT findings were confirmed on pathology also. (From Brace CL, Hinshaw JL, Laeseke PF, et al. Pulmonary thermal ablation: comparison of radiofrequency and microwave devices by using gross pathologic and CT findings in a swine model. *Radiology* 2009;251:705–11; with permission.)

Fig. 6. 62-year-old woman with history of metastatic colorectal cancer. After treatment and resection, she had two residual pulmonary metastases and was referred for ablation. (A) 1.3 cm right middle lobe colorectal metastasis (*arrow*). (B) During pulmonary cryoablation, ground glass opacity develops in the lung parenchyma around the metastasis, and the higher attenuation ring (*arrow*) indicates the edge of the ice ball. One of three cryoprobes used for the ablation is visualized. (C) 1-month follow-up noncontrast computed tomography scan demonstrates expected enlargement of the apparent tumor size due to the ablation zone changes (*arrow*) and some central cavitation (*arrowhead*). (D) 4-month and (E) 12-month follow-up demonstrates progressive reduction in ablation zone size indicative of a successful ablation (*arrows*).

Fig. 7.

73-year-old woman with history of severe emphysema and nonsmall cell lung carcinoma in the right upper lobe. She was medically inoperable and therefore, initially treated with radiotherapy and had a good response. (A) 2 years after radiotherapy, she developed positron emission tomography scan-confirmed recurrent disease (*arrow*) and was not able to receive any further radiation. Therefore, she was referred for ablation. (B) Cryoablation was performed with 4 cryoprobes. Note low attenuation within tumor, right up to the aorta and mediastinum (*arrows*). (C) After the ablation, the patient developed a large and growing pneumothorax that required chest tube placement (*arrow*) and significant intraparenchymal hemorrhage (*arrowhead*), both of which contributed to significant postablation respiratory compromise. (D) Pre-ablation chest radiograph showed normal relationship of the hemidiaphragms. (E) During the ablation, the right phrenic nerve was damaged, resulting in right hemidiaphragm paralysis, confirmed with a sniff test and seen as elevation of the right hemidiaphragm on postablation chest radiograph (*arrow*). These complications all resolved over time and in approximately 2 months, the patient returned to near her previous level of function.

Table 1

Summary of lung RF ablation studies

Study	Patient/Lesions	Pathology	Tumor Diameter (Mean and Range in cm)	Median Follow-Up (months)	Complications	Outcome/Comments
Akeoboshi et al, 2004 ³¹	31 patients/44 lesions	NSCLC, 13 Metastatic, 41	2.7 (0.7–6.0)	9.3	Ptx: 29% Ptx with chest tube: 16% Lung abscess: 6%	Complete necrosis in 69% of lesions <3 cm and 39% of lesions >3 cm
Ambrogio et al, 2006 ³²	54 patients/64 lesions	NSCLC, 40 Metastatic, 24	2.4 (1.0–5.0)	23.7	Ptx: 12.7% Ptx with chest tube: 6.4%	Complete response in 61.9%, higher (69.7%) in lesions <3 cm
Belfiore et al, 2004 ³³	33 patients/35 lesions	NSCLC, 35	3.5 (1.8–6.0)	—	Ptx: 9%, none with chest tube Pleural effusion: 9%	Pathologic follow-up at 6 months showed complete ablation: 36%, partial necrosis: 63% with: patient pain, cough, and dyspnea scores all improved at 6 and 12 months
Gadaleta et al, 2004 ³⁴	18 patients/40 lesions	NSCLC, 4; Metastatic, 14	3.0 (0.6–11)	9.2	Ptx: 16.7% Ptx with chest tube: 12.5%	Complete ablation 94%
Gilliams et al, 2007 ³⁵	37 patients/72 lesions	All metastatic	1.8 (0.4–6.6)	11.3	Major complication: 6% (ptx requiring chest tube, pleural effusion requiring drainage, tumor track seeding), Minor complication: 14% (ptx, postprocedural pain)	Recurrence in 100% of lesions >3.5 cm and 29% of lesions <3.5 cm Recurrence in 58% of lesions in direct contact with vessels and 23% in others ($p>.04$)
Hiraki et al, 2006 ³⁶	128 patients/342 lesions	NSCLC, 25 Metastatic, 317	1.7 (0.3–9.4)	12	—	Primary and secondary effectiveness rates: 72% and 84% at 1 y and 58% and 66% at 3 y Local progression: 27% of tumors (1–30 months), 52% of these were treated with repeat ablation Worse outcome with internally cooled electrode
Lee et al, 2004 ³⁷	30 patients/32 lesions	NSCLC, 27 Metastatic, 5	5.2 (0.5–12.0)	12.5	Ptx: 23% Ptx with chest tube: 7%	Complete necrosis: 100% lesions <3 cm, 38% of lesions 3–5 cm, and 8% of lesions >5 cm Survival months compared with 8.7 months with partial necrosis with complete necrosis: 19.7
Lencioni et al, 2004 ³⁰	106 patients/183 lesions	NSCLC, 33 Metastatic, 73	1.7 (0.5–3.4)	12	Ptx: 20.1% Ptx with chest tube: 19.7%	Overall survival: 70% at 1 y and 48% at 2 y in patients with NSCLC, 89% at 1 y and 66% at 2 y in patients with colorectal metastases, and 92% at 1 y and 64% at 2 y in patients with other metastases Cancer-specific survival: 92% at 1 y and 73% at 2 y in patients with NSCLC, 91% at

Study	Patient/Lesions	Pathology	Tumor Diameter (Mean and Range in cm)	Median Follow-Up (months)	Complications	Outcome/Comments
Yan et al, 2006 ³⁸	55 patients	All Colorectal Metastases	2.1 (not given)	24	Ptx: 29% Ptx with chest tube: 16% Lung abscess: 4%	1 y, and 68% at 2 y in patients with colorectal metastases Patients with other metastases: 93% at 1 y and 67% at 2 y Median survival 33 months. 1-, 2- and 3-y actuarial survival rates were 85%, 64%, and 46% Size <3 cm was significantly associated with improved survival ($p<.001$)
Yasui et al, 2004 ³⁹	35 patients/99 lesions	NSCLC, 3; Metastatic, 96	2.0 (0.3–8.0)	7.1	Ptx: 35.2% Ptx with chest tube: 4% Fever: 12%, Intraprocedural pain 29%	Probable complete ablation: 91%

Abbreviations: NSCLC, nonsmall cell lung cancer; Ptx, pneumothorax.