Ablation of Pulmonary Malignancy: Current Status
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Since the first reported use of radiofrequency ablation of the lung in 2000, the field of image-guided lung ablation has received a considerable amount of attention. Survival studies have demonstrated the potential utility of thermal ablation in the treatment of patients with early-stage primary and limited secondary pulmonary tumors with promising results. Diagnostic imaging studies have advanced the understanding of the expected immediate postablation appearance of treated lesions, leading the way for early detection of local tumor progression. These survival studies and the expected imaging follow-up of these patients are reviewed herein.

Abbreviations: FDG = [18F] fluorodeoxyglucose, NSCLC = non-small-cell lung cancer, PET = positron emission tomography, RF = radiofrequency, RT = radiation therapy

SINCE the first report of radiofrequency (RF) ablation of pulmonary tumors in 2000, multiple publications have confirmed the feasibility, safety, and effectiveness of RF ablation of lung malignancy (1). These successes have spurred interest in the use of other ablative technologies such as microwave ablation and cryoablation for treatment of thoracic malignancies (2,3). Currently, thoracic ablative therapy has a role in three broad scenarios: treatment of primary lung cancer, treatment of lung metastases, and palliation of painful chest wall masses, the latter of which is beyond the scope of this review (4,5).

PRIMARY LUNG CANCER

Primary lung cancer remains the leading cause of cancer-related mortality in the United States, with non–small-cell lung cancers (NSCLCs) constituting the most common histologies (6). Small-cell lung cancer, although it comprises as many as 15% of lung cancers overall, is a more aggressive subtype, with patients usually presenting with lymph node involvement or metastatic disease at the time of diagnosis. Systemic chemotherapy is therefore considered the mainstay, with a small subset of patients qualifying for local salvage therapies. In comparison, NSCLC is slower-growing, allowing local therapies to be tailored with a curative intent. Therefore, the majority of literature addressing treatment of early-stage primary lung cancer refers to NSCLC. This review will similarly be focused on NSCLC.

Since the publication of a prospective, multiinstitutional randomized trial by the Lung Cancer Study Group in 1995 (7) comparing lobectomy and sublobar resections in T1 N0 disease, lobectomy has been considered the standard of care in view of the lower rate of local recurrence compared with sublobar resection. Sublobar resection was deemed appropriate for only those with inadequate pulmonary reserve to undergo lobectomy (7). This trial (7) has current broader implications as it would seem to suggest that, compared with lobectomy, all local therapies—sublobar resection, RF ablation, or radiation therapy (RT)—may be inferior and should be reserved for patients unable to undergo anatomic lobectomy.

Although sublobar resection is still currently limited to patients without adequate pulmonary reserve to undergo lobectomy, the superiority of lobectomy versus sublobar resection is being challenged by several more modern studies. Review of literature suggests that sublobar resection, especially in tumors less than 2 cm in diameter, confers patients with stage IA NSCLC a similar overall and cancer-free survival (8). A recent nonrandomized multicenter study (9) compared patients with stage IA disease (all lobectomy candidates) and found no difference in survival even if these patients underwent sublobar resection. Overall 5-year survival rate in the sublobar resection group was 89.6%, whereas the overall 5-year survival rate in the lobectomy group was 89.1%, leading the authors to conclude that sublobar resection can be a viable option for patients with tumors smaller than 2 cm even if they have the pulmonary reserve to undergo lobectomy (9). Currently, a National Cancer Institute–sponsored randomized study (Cancer and Leukemia Group B study 140503) is underway in hopes of clarifying this disparity.
Sublobar resection can be further divided into anatomic segmentectomy and nonanatomic wedge resection. Anatomic segmentectomy is thought to be more complete as it requires identification and removal of the segmental bronchus and artery as well as removal of segmental lymph node drainage and intrapulmonary lymph nodes. Critics of wedge resection argue that incomplete lymph node identification and resection may lead to increased local recurrence as well as pathologic understaging. Indeed, some studies (10) suggest a decreased locoregional recurrence (16% vs 55%) and improved cancer-related survival in the segmentectomy group versus the wedge resection group, at 71% and 48%, respectively (10). The outcome of the continuing debate as to the most appropriate surgical therapy for early-stage lung cancer will unquestionably have a tremendous impact on other local therapies such as RF ablation and RT.

The most common indication for sublobar resection in primary lung cancer is inadequate pulmonary reserve to tolerate lobectomy. It is in this subset of patients that RF ablation has been increasingly used. A recent multicenter trial (11) demonstrated no significant difference in pulmonary function on multiple follow-up visits after pulmonary RF ablation. In fact, there has been at least one report of successful pulmonary RF ablation in a patient with only a single lung (12). To date, our group has successfully performed RF ablation in the solitary lung of six patients who had undergone pneumonectomies previously (unpublished data). However, beyond those patients with limited lung function, pulmonary RF ablation may be used for patients deemed to be at high risk for surgery (for reasons other than pulmonary reserve) as well as for those patients who refuse surgery.

### RF Ablation

Since RF ablation was initially reported for treatment of lung tumors in 2000, many groups have published outcomes, and selected results are summarized in Table 1 (11,13–22). A recent prospective, intent-to-treat multicenter clinical trial, the Radiofrequency Ablation of Pulmonary Tumors Response Evaluation trial (11), showed that, in 106 patients with 183 primary or secondary lung tumors smaller than 3.5 cm treated with RF ablation, cancer-specific survival rates for patients with NSCLC were 92% at 1 year and 73% at 2 years (11). Another study (18), which reported a 5-year follow-up, noted overall survival rates for NSCLC of 78% at 1 year and 27% at 5 years. For most studies, inclusion criteria were limited to those patients unfit for surgery, RT, or chemotherapy, leading many authors to suggest the need for a randomized controlled trial comparing standard treatment versus RF ablation to assess possible benefits.

Rates of local tumor progression and survival for lesions treated with RF ablation have been linked to pretreatment tumor size and location (18). Pretreatment tumor size of 3 cm or less (ie, stage IA disease) is associated with higher rates of complete tumor necrosis and local progression–free survival. Akeboshi et al (13) demonstrated that a complete tumor necrosis rate of 69% can be achieved with tumors smaller than 3 cm, whereas a complete necrosis rate of only 39% was achieved in those larger than 3 cm. This correlates with median

### Table 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Tumor Type</th>
<th>Mean Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akeboshi et al (13)</td>
<td>44 tumors in 31 pts.</td>
<td>NSCLC, n = 13; metastatic, n = 41</td>
<td>9.3 mo, PET and contrast CT</td>
</tr>
<tr>
<td>Ambrogi et al (14)</td>
<td>64 lesions in 54 pts.</td>
<td>NSCLC, n = 40; metastasis, n = 24</td>
<td>23.7 mo</td>
</tr>
<tr>
<td>Belfiore et al (15)</td>
<td>33</td>
<td>NSCLC, n = 33</td>
<td>Follow-up CT 6 mo (n = 29) and 1 y (n = 10); 19 also had cytohistopathologic assessment with CT-guided biopsy at 6 mo CT after 48 h and 2, 4, 6, 9, and 12 mo 21.8 mo</td>
</tr>
<tr>
<td>de Baere et al (16)</td>
<td>100 tumors in 60 pts.</td>
<td>NSCLC stage I</td>
<td>—</td>
</tr>
<tr>
<td>Hiraki et al (17)</td>
<td>183 tumors in 106 pts.</td>
<td>NSCLC, n = 33; metastasis (colorectal), n = 53; metastasis (other), n = 20</td>
<td>Followed up to 2 y</td>
</tr>
<tr>
<td>Lencioni et al (11)</td>
<td>189 tumors in 153 pts.</td>
<td>Symptomatic patients for palliation, n = 21; NSCLC, n = 75; metastasis, n = 57</td>
<td>Up to 5 y, CT and PET</td>
</tr>
<tr>
<td>Simon et al (18)</td>
<td>36 tumors in 30 pts.</td>
<td>NSCLC, n = 18; metastasis, n = 11; mesothelioma, n = 1</td>
<td>2–26 mo follow-up</td>
</tr>
<tr>
<td>VanSonnenberg et al (19)</td>
<td>155 tumors in 71 pts.</td>
<td>Colorectal metastasis</td>
<td>CT and PET, 4–42 mo</td>
</tr>
<tr>
<td>Yamakado et al (20)</td>
<td>99 tumors in 35 pts.</td>
<td>NSCLC, n = 3; metastatic, n = 96</td>
<td>7.1 mo</td>
</tr>
</tbody>
</table>

Table adapted with permission from Pua et al (22).
Alternative Local Therapies

Currently, RT with or without chemotherapy represents an accepted option for local tumor control in nonsurgical candidates. A recent metaanalysis (27) suggested that 5-year overall survival rates after conventional external-beam RT range from 0% to 42%. Not unlike RF ablation, there is much interest in improving survival outcomes and efficacy. Although it is beyond the scope of this review, current interest surrounds a comparison of conventional RT versus image-guided hypofractionated RT (ie, hypofractionated stereotactic RT). Hypofractionated RT differs in the number of sessions and dose of radiation delivered at each session. Generally, the goal of RT is to deliver a total dose of 50–60 Gy to the target area. Conventional RT protocols deliver anywhere from 20 to 30 small radiation doses over a period of several weeks, whereas new hypofractionated protocols (which vary) deliver smaller numbers of large doses. With the addition of image guidance, hypofractionated stereotactic RT affords an additional advantage of allowing the operator to more accurately focus the dose, delivering a higher effective dose of the target area. Although early results for hypofractionated RT look promising, results from a prospective randomized trial are not available. Currently, one such trial, the Stereotactic Precision and Conventional RT Evaluation (28), is underway in Scandinavia.

**Primary Lung Cancer: Salvage Therapy**

Although, in primary lung cancer, RF ablation is predominantly a therapy used in unresectable stage I cancers, there are some patients with local tumor progression after initial treatment with other modalities, such as surgery, chemotherapy, or RT, for which RF ablation may also be a useful adjunct. Often, other therapies such as surgery or RT alter the remaining lung parenchyma or pleural space, making repeat resection technically difficult and leading to increased operative morbidity and mortality and high secondary recurrence rates (4). Additional RT in patients who have already received large doses is also not feasible as a result of the deterministic effects of radiation. Such patients may be optimal candidates for image-guided thermal ablative therapies that, by and large, are not limited by local anatomic alterations, previous radiation, or a biologically more aggressive tumor type (29). Although, to our knowledge, no study has looked specifically at survival benefits of thermal ablation for local tumor progression, studies reporting treatment of primary and secondary lung tumors have demonstrated its feasibility (18,30).

An interesting application of pulmonary RF ablation is in patients with sta-
ble metastatic disease receiving targeted therapy who have a single focus of tumor progression. Lung cancers, NSCLC in particular, have been found to overexpress certain genetic receptors associated with lung carcinogenesis, such as epidermal growth factor receptor (31). This discovery led to the use of epidermal growth factor receptor tyrosine kinase inhibitors, such as gefitinib and erlotinib, in patients with advanced NSCLC that does not show a response to conventional chemotherapy agents (32,33). Mitsuomdi et al (34) demonstrated that, even in patients with postsurgical recurrence, gefitinib conferred prolonged survival in patients with this specific mutation in epidermal growth factor receptor. However, recently, it has been shown that, even with this targeted therapy, some cancers develop a second mutation that confers it resistance to these epidermal growth factor receptor tyrosine kinase inhibitors (35). This conversion is evidenced by a single tumor focus increasing in size despite improvement in the other metastatic foci. This focus of tumor progression would be a target for thermal ablation as this type of local therapy is indiscriminate to tumor genetics.

Secondary Lung Cancer

Although pulmonary metastasectomy, or surgical removal of lung metastases, is still a much-debated topic in view of the lack of randomized controlled clinical trials, it remains a widespread practice (36). The potential benefits of pulmonary metastasectomy have been reported in several retrospective studies. An international registry formed in 1991 demonstrated that complete surgical metastasectomy demonstrates 5-, 10-, and 15-year actuarial survival rates of 36%, 26%, and 22%, respectively (37). The subset of patients who experience the most benefit are those with a long disease-free interval from initial resection of the primary tumor, those without extrathoracic metastasis, and those in whom a microscopic complete resection (ie, R0 resection) can be achieved. The vast majority of patients being evaluated for pulmonary metastasectomy will be considered only if an R0 resection is attainable. Often, the possibility of an incomplete resection is considered a contraindication. However, there is new interest in sequential metastasectomy and the role of incomplete resection is being investigated, predominantly in metastatic renal and breast cancers (38,39). Vogl et al (40), while defining prognostic factors for treatment of metastatic renal cell cancer with cytokine therapy, demonstrated that even although only 10% of patients undergoing metastasectomy had “no evidence of disease” after resection, there was a significant survival benefit with concomitant metastasectomy, even incomplete.

Currently, the major role of RF ablation in pulmonary metastasis, not unlike that for primary lung cancer, is in treatment of those patients for whom surgical metastasectomy would not be ideal. A frequently treated pulmonary metastasis is colon cancer. Colon cancer is the second most common cause of cancer-related mortality in the United States, and 10%-30% of patients with colon cancer have pulmonary metastasis at presentation (41). The prevalence of colorectal metastases to the lung, as well as a recent report that suggests local control after RF ablation is independent of tumor type (29), makes colon cancer a reasonable model in which to evaluate current data. One group (42) reported initial data that show that, on 6-month follow-up computed tomography (CT) of 44 lesions treated with RF ablation, three lesions progressed, 25 were stable or smaller, and 11 were not visible.

In patients with colorectal metastasis, the Radiofrequency Ablation of Pulmonary Tumors Response Evaluation study (11) demonstrated cancer-specific survival rates of 93% at 1 year and 67% at 2 years. Simon et al (18) reported a 5-year follow-up and noted overall survival rates for colorectal metastasis of 87% at 1 year and 57% at 5 years. On univariate analysis, there was a statistically significant difference in survival associated with size of metastasis, location of metastasis, and need for repeat RF ablation for recurrence, with tumor size greater than 3 cm independently associated with overall survival on multivariate analysis (30). The authors also suggest that the apparent improved 3-year survival rate of 78% excluded patients with extrapulmonary metastasis, which may contribute to survival benefit (30).

It is worth noting that in applying ablative therapies to metastases, a “test-of-time” paradigm may be appropriate. It is known that some patients who undergo surgery for oligometastases (ie, limited-volume metastatic disease in a limited location) subsequently go on to develop new metastases. The test-of-time paradigm, initially proposed for treatment of liver metastases from colorectal cancer, suggested initial treatment by ablation. Patients who undergo successful ablations are spared surgery for the index metastases; those who subsequently develop new metastatic disease have been spared noncurative major surgery. For patients with unsuccessful ablation of the index metastases, surgery can be offered. In fact, one study (43) found that, in 53 patients with colorectal hepatic metastasis who underwent RF ablation according to this paradigm, 98% were spared surgical resection; 44% remained free of disease and 56% developed disease progression.

Although it is hard to directly compare RF ablation with surgical metastasectomy given that there exists longer follow-up after surgical metastasectomy, RF ablation remains a viable option in those patients who cannot undergo surgery for technical factors based on tumor location, earlier radiation, or medical contraindication to surgery.

Other Ablative Technologies

The efficacy and safety data that have emerged for pulmonary RF ablation serve as a benchmark for performance of newer ablative technologies such as microwave ablation and cryoablation.

Early studies of microwave ablation suggest that this technique may be less hindered by pretreatment tumor size, which is the limitation with RF ablation. Animal models comparing effective ablation zones of microwave ablation versus RF ablation (that use similarly sized applicator probes/antennas) indicate that ablative diameter and cross-sectional area were 25% and 50% larger with microwave ablation versus RF ablation (44). Wolf et al (45) suggested that microwave ablation of primary and metastatic tumors in patients deemed to have medically inoperable disease may confer a survival benefit versus RF ablation in tumors larger than 3 cm. Their report was unable to find a significant difference in survival between index tumor sizes smaller or larger than 3 cm, although residual enhancing tumor was found more frequently at follow-up in treated tumors that were larger than 3
cm (45). In this study of CT-guided microwave ablation of 50 patients (82 masses), actuarial survival rates at 1, 2, and 3 years after ablation were 65%, 55%, and 45%, respectively. Cancer-specific survival rates at 1, 2, and 3 years after ablation were 83%, 73%, and 61%, respectively.

The possible advantages of microwave ablation versus RF ablation are thought to be related to inherent properties of the target tissue as well as the different mechanisms by which microwave and RF achieve tissue ablation. As RF ablation is dependent on thermal conductivity, air-filled spaces in the ventilated lung adjacent to tumors tend to limit the size of the ablation, which is a potential cause of local tumor progression at the periphery of the ablated lesion (46). Microwave propagation is thought not to be similarly hindered and may therefore be more effective in achieving a complete ablation. In addition to advantages of increased zones of heating, microwave ablation has the ability to be specifically tuned to maximize energy deposition depending on the dielectric properties of the target tissue. Durick and colleagues (47) have demonstrated in a porcine model that a triaxial microwave ablation system, when tuned for lung parenchyma, is able to produce a larger zone of coagulation than current one-antenna microwave systems. The same group (48) has since reported that the properties of lung tumors are similar to those of solid organs, suggesting optimal tuning is yet to be elucidated and that different tissue resonances might be necessary to treat solid lung tumors and the aerated margin that surrounds them. Although early work with microwave ablation suggests that its advantage versus RF ablation includes increased intratumoral temperatures and larger ablation volumes, many of these advantages are theoretical or have been seen only in animal models (49). More studies are needed to determine how best to exploit the properties of this technology for better tumor ablation.

As previously mentioned, a major limitation of RF ablation has been related to complications and difficulties encountered when treating tumors neighboring blood vessels, the mediastinum, and chest wall (50). Although advanced separation techniques such as single-lung ventilation and creation of an artificial pneumothorax have been reported, these techniques are not feasible in all patients (51,52). Cryoablation, to the contrary, has been shown to be associated with low procedural morbidity rates when used near mediastinal structures (53). In fact, very early studies (54) demonstrated that the collagen architecture of central bronchi is preserved after cryoablation. A recent investigation (55) evaluated 35 tumors in 20 patients after cryoablation with CT every 3 months. The mean follow-up time was 21 months, with a reported 1-year survival rate of 89.4% and a 20% local tumor progression rate. Although few large reported studies exist with long-term follow-up of patients after cryoablation, this modality may permit safer thermal ablation of tumors adjacent to central structures, in contrast to heat-related ablative therapies.

Complications of Thermal Ablation

A recent retrospective study (50) performed to evaluate the risks and frequency of overall complications after 112 RF ablation sessions in 57 patients reported a 50% rate of postprocedural minor complications and an 8% rate of postprocedural major complications. Minor complications included pneumothorax not requiring a chest tube (13%), subcutaneous emphysema (16%), and hemoptysis (9%). Major complications included fever greater than 38.5°C (5%), abscess (5%), pneumothorax requiring chest tube (3.5%), and air embolism (n = 1). Pain and pleural effusion, occurring in 46% and 13% of sessions, respectively, were considered side effects (50).

Pneumothorax is a relatively common complication after pulmonary RF ablation. Rates of postprocedural pneumothorax after RF ablation were as high as 83% in earlier studies and as low as 9% in more recent studies (15,56). Rates of pneumothorax for microwave ablation and cryoablation have been reported as high as 39% and 12%–50%, respectively (45,53,55). Risk factors associated with the development of pneumothorax have been studied by multiple groups. Pneumothorax appears to be more frequent after treatment of central tumors and in patients with no history of previous lung surgery. Concomitant emphysema, larger tumor size, number of electrode passes, and electrode size have not been found to cause increased risk (50,57,58).

Additional more common complications include cough, hemoptysis, fever, pleural effusion, and skin injury. Hemoptysis occurs in as few as 3% of cases (56). Death from massive hemoptysis is rare and was reported after open RF ablation of a central tumor in a patient who also received brachytherapy (59). Although not definitively investigated, it is postulated that cryoablation may carry an increased risk of hemoptysis. Of two studies reporting complications after cryoablation (53,55), hemoptysis was reported in 36% and 62% of procedures.

As the use of pulmonary thermal ablation continues to increase, operators must be aware of potential, less well known complications. One such complication is thermal nerve damage leading to neuropathy. Thermal ablation near nerves carries risk for nerve injury, and similarly, nerve damage also occurs with surgery or radiation treatment of tumors near nerves. When the ablated tumor is near the chest wall, the most frequent injury is an intercostal nerve injury that may cause paresthesias; pleuritic pain may also be seen in treatment of juxta-pleural lesions. The natural history of such an injury is variable. Over time, symptoms may improve. Antiseizure medications such as pregabalin or gabapentin may help. An artificial pneumothorax at the chest wall can sometimes be created to protect the intercostal nerve (60). Other thoracic nerves that can be jeopardized by thermal ablation of adjacent tumors include the phrenic nerve and brachial plexus. Phrenic nerve injury is a known complication of cardiac surgery and is increasingly recognized as a potential complication of cardiac ablation for atrial fibrillation. Our group (61) reported two cases of phrenic nerve injury secondary to thermal ablation of lung tumors resulting in postprocedural dyspnea and diaphragmatic paralysis. An additional case was described in the same report (61) of successful ablation of a right upper lobe mass abutting the superior vena cava, in the expected location of the phrenic nerve course, with separation techniques involving the creation of an artificial pneumothorax. As the role of ablation is expanded and treatment of patients with a history of radiation or paramediastinal lesions increases, awareness of anatomy and the appropriate preprocedural planning is important.

It should be stressed that complications of ablation are not limited to those...
caused by ablation or by trauma secondary to probe/antenna insertion. Risks of brachial plexus injuries from poor patient positioning and padding, as well as potential thermal injuries from poor grounding pad placement during RF ablation, underscore the importance of caution throughout the entire process, not just the actual ablation.

Recently, microbubble formation has been seen during pulmonary RF ablation (62,63). Rose et al (62) initially interrogated the carotid arteries with use of Doppler US of three patients undergoing pulmonary RF ablation. This group demonstrated that all three patients had detectable microbubbles, but none resulted in neurologic deficit or CT changes on immediate post-RF ablation head CT. This study has since been followed by that of Yamamoto et al (63), who evaluated 20 patients after pulmonary RF ablation with pre- and postprocedural magnetic resonance (MR) imaging with diffusion-weighting imaging. Of the 20 patients, 17 received US evaluation, only three of whom had detectable microemboli. This apparent discrepancy with the study of Rose et al (62) was explained as differences in lower generating frequency, leading these authors (63) to suggest that the possibility of microbubble formation is associated with higher maximum power. These authors also report no changes in diffusion-weighting imaging or fluid-attenuated inversion recovery sequences at 24 hours after RF ablation, which are infarction-sensitive sequences on MR imaging. Both these studies suggest that, although microbubble formation is a possibility, initial reports would suggest no clinical sequela.

**Planning and Follow-up Imaging**

Treatment of the oncologic patient is best performed in conjunction with other disciplines in which representatives from surgery, interventional radiology, medical oncology, as well as radiation oncology are available for consultation. In addition to a preprocedural evaluation including a thorough history and physical examination, a recent staging cross-sectional imaging examination such as CT and/or positron emission tomography (PET)/CT is important for assessing tumor characteristics such as size and/or concurrent nodal involvement, as well as proximity to neighboring structures. Proper preprocedural staging is important as it will determine the best modality for therapy, including observation. Table 2 summarizes current published 5-year survival rates in patients with stage IA lung cancer treated with lobectomy, conventional RT, and RF ablation (18,27,52–61,64–68). If an ablative procedure is contemplated, recent imaging also allows for preprocedural planning such as access trajectory, probe choice, or the use of adjunctive imaging modalities such as CT fluoroscopy or US. Histologic diagnosis is useful for treatment planning and prognosis. Although some physicians will perform a lung biopsy on the day of the ablation, preprocedural biopsy confers some advantages. Perilesional hemorrhage related to biopsy can obscure proper placement of the ablation electrode and may therefore lead to inadequate ablation. Additionally, unexpected histologic diagnoses can change the treatment plan.

In 2009, the Technology Assessment Committee of the Society of Interventional Radiology (69) published Guidelines for Research Reporting Standards for Percutaneous Thermal Ablation of Lung Neoplasms. In this report, the group reiterated the variability of the natural history of disease of primary NSCLC and metastasis and suggested that, “for this reason it may be appropriate to perform CT imaging at 3 month intervals after an early scan (1–3 months) has been obtained that documents absence of viable tumor.” Follow-up imaging usually includes a CT scan with or without a PET/CT scan, depending on the [18F] fluorodeoxyglucose (FDG) characteristics of the index tumor on preprocedural imaging. Recognition of the expected increases in apparent lesion volume/size in the postablation setting underscores the importance of obtaining an early postablation study to document a new baseline. Any increase in size, contrast enhancement, or increase in FDG uptake compared with this baseline should prompt a search for recurrence. Animal studies have suggested that repeat postablation PET scans no earlier than 4 weeks allow normal postablation inflammatory uptake of FDG to subside, allowing for more accurate diagnosis (70).

As most experience is related to therapy with RF ablation, the majority of follow-up reports are of lesions treated with this modality. Generally, a new baseline image, regardless of modality, should be obtained shortly after the procedure (ie, within a few weeks) with which future images can be compared to determine growth, enhancement, or FDG avidity.

In addition to contrast-enhanced CT, PET/CT and CT densitometry have been used in follow-up of patients after RF ablation (13,19,56,71). Immediately after ablation, ground-glass opacity surrounding the ablated lesion appears to predict ablation adequacy of RF or microwave ablation (45,71,72). One study (16) suggested that a postablation area four times larger than the initial tumor size is predictive of complete treatment. More recently, another group (73) asserted that a minimum 5-mm margin of ground-glass opacity surrounding the lesion is needed for complete tumor ablation, adding that the region that lacks

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### Table 2

**Treatment-specific 5-year Survival for Primary Lung Cancer (18,27,64–68)**

<table>
<thead>
<tr>
<th>Treatment Modality</th>
<th>5-year Survival</th>
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</thead>
<tbody>
<tr>
<td>Surgery (lobectomy, including VATS)</td>
<td>Stage IA, up to 80% survival; stage I, average 64.6% survival; stage I (VATS), 63.6% survival</td>
</tr>
<tr>
<td>*RT (conventional)</td>
<td>Stage IA, 32%; stage I, 0%–42%</td>
</tr>
<tr>
<td>*RF ablation (18)</td>
<td>Stage I, 27%†</td>
</tr>
</tbody>
</table>

*Note.—VATS = video-assisted thoracoscopic surgery.† Mortality survival functions comparing patients with stage IA and IB in this study were not statistically significant; however, local tumor progression rates in patients with tumors less than 3 cm (stage IA) were significantly lower: 47% tumor progression–free at 5 years in index tumors less than 3 cm versus 25% in tumors greater than 3 cm.*
a ground-glass margin correlates with the site of future recurrence.

Contrast studies have also been used to determine the extent of tumor necrosis, with some authors (72) suggesting that a 10-HU increase comparing pre- and postcontrast images represents viable unablated tumor. It is recognized that, immediately after heat ablation, hyperemia and inflammation in the region may mask contrast enhancement of underlying residual tumor, leading another group (74) to suggest that evaluating the enhancement pattern in addition to the size of the ablated lesion is needed to fully assess for residual tumor.

There is an increasing number of patients who receive preprocedural PET/CT, and it seems reasonable to follow these patients with this modality in the postprocedural setting (Fig). Higaki and colleagues (75), in a study of 60 pulmonary tumors treated with ablation, attempted to clarify the optimal time point and maximum standardized uptake value for determination of recurrence. With contrast-enhanced CT as the determinant of locoregional recurrence, the cutoff maximum standardized uptake value of 1.5 at 3–9 months after RF ablation showed 77.8% sensitivity and 85.7%–90.5% specificity for recurrence (75). It is our practice to consider lesions with a maximum standardized uptake value of 3.0 or greater suspicious. Percutaneous biopsy should be considered for any suspicious findings, including new FDG activity in regions of earlier inactivity. It is important to note that it is normal to see a uniform rim of FDG activity, which represents surrounding inflammatory tissue, in the lesion even months after ablation therapy (76).

However, even in patients with loss of FDG activity after ablation, continued follow-up is necessary because recurrence is still a possibility.

**Issues Particular to Cryoablation**

During cryoablation, an ice ball, characterized by a sharply demarcated low-attenuation region (40–60 HU decrease from preprocedural attenuation on soft-tissue windows) can be seen on CT images. Unfortunately, it is difficult to visualize the ice ball in normal surrounding lung parenchyma on CT. In fact, to our knowledge, only one study (77) demonstrated that direct visualization of the ice ball is an unreliable indicator of temperature during cryoablation and therefore the region of coagulative necrosis. Therefore, imaging follow-up is critical, as it is for other ablation modalities. Usual imaging cues of recurrence, such as enhancement pattern and FDG avidity, are essential in follow-up of cryoablation-treated lesions.

**CONCLUSION**

The role of thermal ablation has evolved to the extent of acceptance in the treatment of selected patients with primary or secondary lung malignancies who are poor surgical candidates. Combining local therapies has also emerged as a possibility. Although outcomes are still early to judge, some have suggested that the use of RF ablation in combination with RT is safe and provides improved local survival versus conventional RT alone (78). Interest in the test-of-time paradigm seeks to allow patients the opportunity to undergo a less-invasive procedure with the intent of possible cure without changing survival or outcomes and, although it is unproven, it may have the potential for increased quality of life.

Although appropriate emphasis is placed on determining and improving survival data for primary lung cancer and pulmonary metastases, appropriate attention is now being placed on developing methods to adequately assess totality of immediate tumor ablation and early detection of potentially treatable residual viable or recurrent tumor. As improvements continue to be made to the various thermal ablative technologies and more experience and long-term follow-up becomes available, this field...
is poised to expand its role in the treatment of patients with pulmonary malignancies.

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