Diagnostic and Interventional Imaging (2016) **97**, 1019—1024

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Percutaneous thermal ablation of primary lung cancer

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KEYWORDS
Lung cancer;
Non-small-cell lung cancer;
Radiofrequency ablation;
Microwave ablation;
Cryoablation

Abstract Percutaneous ablation of small-size non-small-cell lung cancer (NSCLC) has demonstrated feasibility and safety in nonsurgical candidates. Radiofrequency ablation (RFA), the most commonly used technique, has an 80—90% reported rate of complete ablation, with the best results obtained in tumors less than 2—3 cm in diameter. The highest one-, three-, and five-year overall survival rates reported in NSCLC following RFA are 97.7%, 72.9%, and 55.7% respectively. Tumor size, tumor stage, and underlying comorbidities are the main predictors of survival. Other ablation techniques such as microwave or cryoablation may help overcome the limitations of RFA in the future, particularly for large tumors or those close to large vessels. Stereotactic ablative radiotherapy (SABR) has its own complications and carries the risk of fiducial placement requiring multiple lung punctures. SABR has also demonstrated significant efficacy in treating small-size lung tumors and should be compared to percutaneous ablation.

Surgical resection is the current standard of care for patients with stage I or II non-small-cell lung cancer (NSCLC). Even in the early stages of the disease, however, a subset of patients with NSCLC is ineligible for surgery due to severe medical comorbidities, primarily associated with deterioration in lung function curtailing the necessary resection. Minimally invasive therapy has been developed to give these nonsurgical candidates a curative treatment option, including stereotactic ablative radiotherapy (SABR), percutaneous

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http://dx.doi.org/10.1016/j.diii.2016.08.016
2211-5684/

image-guided ablation including radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation, and irreversible electroporation (IRE). RFA has been the primary technique used and reported for thermal ablation of the lung, with numerous publications and a large volume of data. MWA, IRE, and cryoablation are more recent treatment options.

Rationale

The local efficacy of RFA in destroying lung tumors has been shown in animals when RFA has been applied to VX2 lung tumor models to demonstrate the feasibility of ablation and the possibility of complete ablation [1]. More recently, histological evidence of complete tumor destruction after a single session of RFA has been provided for nine patients for whom percutaneous RFA was performed before surgical resection of the lung metastases [2].

The lung provides a unique environment for RFA under computed tomography (CT) guidance. Firstly, there is an excellent contrast ratio between the targeted tumor tissue, aerated lung, and metal of the needle, making it possible to provide multiplanar imaging for accurate assessment of needle placement and electrode deployment. Secondly, site-specific differences within lung tumors facilitate energy deposition due to the heat insulation and low electric conductivity provided by the aerated lung around the tumor. It has been demonstrated that a certain amount of RF current produces a larger volume of ablation in the lung than in subcutaneous tissue or the kidney [3].

Treatment and image guidance

CT is currently the most accurate image-guidance technique for lung RFA, with real-time CT enabling quick needle placement and making the procedure more comfortable for the operator. A shorter procedure time has been reported for cone-beam CT (CBCT) [4] but it does not enable rapid acquisition/reconstruction and can be problematic when a moving target tumor is displaced by the needle or a pneumothorax. Multiplanar reconstruction is required to assess the appropriate needle positioning relative to tumor margins in all planes. When the needle was deemed to be centered on axial CT image, multiplanar and volume-rendered analysis reclassified the needle position from centered to marginal or from marginal to outside in 44% of RF procedures [5]. When using needles with expandable electrodes, puncturing the tumor with the electrode shaft is not necessary for small tumors provided that the deployed arrays are encompassing the tumor, with one array through the tumor and an ablation volume containing the tumor. A carbon dioxide injection between the parietal and visceral pleura can be used to separate a sub-pleural tumor from the parietal pleura or mediastinum to avoid collateral damage during ablation of sub-pleural tumors.

Usually, the lungs are treated separately a few weeks apart to avoid life-threatening complications from bilateral adverse events, such as bilateral massive hemorrhage or pneumothorax. Single-session bilateral treatment has been reported in patients who completed treatment of the first lung with no CT-depicted complications.

The use of conscious sedation was associated with peri-procedural pain in 29% of cases with 3% of treatments being interrupted due to pain [6], and stopped due to intractable coughing in 5/30 patients [7]. The technique's feasibility under general anesthesia is reported to be as high as 97% [8].

Local efficacy

A review of 17 reports of lung RFA, including primary lung tumors and lung metastases, demonstrated a 90% median reported rate of complete ablation, although the figures range from 38% to 97% [9]. Tumors of less than 2 cm can be completely ablated in 78—96% of cases according to several reports with extended imaging follow-up [8,10—14], while lower success rates are reported for larger tumors [8,10—12]. The ablation safety margins are key to success. A ratio of RFA-induced ground glass opacity to tumor area of 4 or more is correlated with a significantly higher rate of 96% complete ablation versus 81% when this ratio is below 4 [8]. The ROC analysis constructed from recurrences, according to ground glass opacity minimal width after ablation, confirmed the ablation zone's usefulness as a predictor of recurrence, with an estimated cutoff of 4.5 mm for a specificity of 100% (i.e. no local recurrence). When using an expandable multi-tined needle array, finally, a diameter of electrode array at least 10 mm larger than the target tumor has been reported as a predictor of success with less than 10% local recurrence for arrays at least 10 mm larger and approximately 30% local recurrence when the array was less than 10 mm larger than the target tumor [15]. The aforementioned results clearly show the need for oversizing the ablation zone relative to tumor volume in order to obtain safety margins that guarantee success. It is known from pathologic evaluation of 354 cases of NSCLC that a 5 mm margin covers 80% of the microscopic extension for adenocarcinoma and 91% for squamous cell carcinoma, and that to take into account 95% of the microscopic extension, margins of 8 mm and 6 mm must be chosen for adenocarcinoma and squamous cell carcinoma respectively [16].

One of the drawbacks of monopolar RFA is that only one probe can be activated at one time, and so overlapping ablation zones with subsequent probe placement are needed to create a larger ablation volume. Microwave ablation offers the advantage of simultaneous energy delivery through several probes activated at the same time, if needed. A single MWA probe covered a slightly larger ablation volume when compared to RFA in an animal study that demonstrated a mean ablation diameter of 32.7 ± 12.8 mm perpendicular to the feeding point of the MWA antenna [17]. In this study, simultaneous activation of three antenna provided an ablation zone measuring 54.8 ± 8.5 mm perpendicular to the feeding point [17]. 50 patients, including 30 with NSCLC, received 66 microwave ablation sessions for tumors up to 5 cm (mean size $3.5\,\text{cm} \pm 1.6$) including multiple antenna in 47% of tumors larger than 2 cm (two antennae were used in 5% of cases, three antennae in 27%, four antennae in 9%, and multi-probe loop antenna in 6%) [18]. The overall local recurrence rate was 26%, but a diameter larger than 3 cm remains a predictive factor for recurrent disease ($P = 0.01$). One difficulty of MWA is that a single system