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Radiofrequency Ablation for the Treatment of Stage I Non-Small Cell Lung Neoplasm

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Lung cancer is the most common cause of cancer related mortality in the United States. Surgical resection is the standard treatment for stage I non-small cell lung cancer (NSCLC). However, many patients who have resectable cancer may have significant comorbidities precluding surgical resection. Radiofrequency ablation is an emerging modality of treatment and may be applicable in this high-risk group of patients. In this article, we review the principles of radiofrequency ablation, the common devices in use, and the results of treatment for stage I non-small cell lung neoplasm.
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Lung cancer is the most common cause of cancer-related mortality in the United States. Surgical resection is the standard treatment for stage I non-small cell lung cancer (NSCLC).[1-3] However, many patients who have resectable cancer may have significant comorbidities precluding surgical resection. In these patients, conventional external beam radiation is typically used, although the results of this treatment have been suboptimal.[4-6] Radiofrequency ablation (RFA) is a newer modality of treatment and may be applicable in this high-risk group of patients.[7] In this article, we review the principles of RFA, the common devices in use, and the results of treatment for stage I non-small cell lung neoplasm.

Principles of Radiofrequency Ablation

The use of interstitial hyperthermia to treat lung neoplasm was initially reported by Lilly and colleagues in 1983.[8] RFA is performed using a thermal energy delivery system that applies an alternating current supplied by a radiofrequency energy generator and delivered through a needle electrode.[9] The needle electrode is most commonly introduced percutaneously under computed tomography (CT) guidance into the tumor, and the tines are deployed within the tumor. The alternating current generates ionic agitation, resulting in heat that can reach 90°C. This leads to coagulative necrosis and tissue destruction in the area of the probe.

Technique and Devices for Radiofrequency Ablation

RFA is generally performed percutaneously under CT guidance, although it can also be performed with a thoracotomy as a parenchymal-sparing adjunct to lung resection, particularly in patients with limited pulmonary metastases.[10] Under CT guidance, a finder needle, typically a 22-gauge, long spinal needle, is used to determine the trajectory and placement of the active RFA probe. The tines of the RFA probe are deployed within the tumor to allow maximal distribution of the thermal energy.

There are three FDA-approved RFA devices available in the United States for ablation of soft tissue lesions. Boston Scientific (Boston, MA) manufactures one RFA system that consists of a radiofrequency generator (RF3000; Boston Scientific, Boston, MA) and LeVeen needle electrodes (LeVeen Needle Electrode; RadioTherapeutics Corporation, Sunnyvale, CA). The second

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system comprises a RF generator and the RITA Starburst XL Electrosurgical Device (Angiodynamics, Queensbury, NY). The third FDA-approved system is the Valley Laboratory RFA device (Covidien, Boulder, CO). The Valley Laboratory electrode has a proximal insulated portion and a distal, uninsulated active tip. The electrode is irrigated with a continuous infusion of ice-water, and for this reason, is sometimes referred to as a "cool-tip" electrode.

Different algorithms are currently used by the different devices to determine the length of time that the alternating current is delivered. In the multitined RITA array probe, a temperature of 90°C, measured by thermistors placed in the electrode, serves as an endpoint. In the LeVeen multitined array probe and the cool-tip probe, a sudden increase in impedance, which corresponds to a decrease in electrical conductivity due to tissue desiccation, is used as an endpoint for ablation. Once these thresholds are reached, the machines are automatically turned off.

Comparison of Devices

Hiraki and colleagues, in an interesting study, evaluated the risk factors for local progression after RFA in a series of 128 patients with 342 lung tumors; 317 were metastatic lesions, and 25 were primary lung neoplasms.[11] The authors used the LeVeen expandable array probe (Boston Scientific) in 142 lesions and a cool-tip probe or internally cooled cluster probe (Valley Laboratory, Tyco, CO) in 200 lesions. The median follow-up was 12 months; local progression was seen in 94 lesions. Multivariate analyses showed that larger tumor size and the use of an internally cooled electrode were independent risk factors for local progression. These investigators concluded that (1) a larger tumor size and the use of the cool-tip probe were independent risk factors for local progression of lung tumors and (2) RFA for smaller tumors and the use of a multitined array probe enabled favorable local control. The limitations of this study include selection bias with the use of the internally cooled electrode for larger tumors and those more central in location and the short follow-up of about a year.

Other studies, comparing the use of the internally cooled electrode versus the expandable array electrode in liver tumors, showed equal effectiveness.[12,13] However, the electrical and thermal conductivities differ between the liver and the lung, which likely accounts for differences in the efficacy of RFA. In lung tumors, the surrounding normal tissue contains air, which may provide an insulating effect. This lack of conductivity in the surrounding lung tissue may interfere with the margins of ablation and account for the increased incidence of local progression following RFA in lung tumors as compared with liver tumors. This is supported by the animal study of Nomori and colleagues. They performed RFA with an internally cooled electrode on implanted gelatin nodules that simulated lung tumors. In this study, 60% of the nodules had nonablated regions in the periphery of the nodule, and the surrounding lung tissue was rarely ablated.[14]

Assessment of Response

Clinically, the assessment of response after RFA is difficult because, unlike surgical resection, there is a scar that persists after therapy. In the literature, there is considerable variation in how response is defined and evaluated. Chest CT scans, changes in contrast enhancement, and positron emission tomography (PET) scans have all been used. Thus, the response rates reported in the literature vary considerably.

Additionally, RFA results in inflammation, and the treated lesion is actually larger in size initially because of the surrounding zone of inflammation. This slowly shrinks over time.[15] Hence, using size alone as a criterion to determine response early after RFA may not accurately determine the initial response rate. Investigators from our group at the University of Pittsburgh have described a modified Response Evaluation Criteria in Solid Tumors (RECIST) incorporating not only the size of the lesion on CT scanning, but also the density of the lesion and metabolic activity on PET scanning[16-18] (Fig. 1). This method combines the standard RECIST criteria with evaluation of lesion quality on CT scanning and PET scanning and appears to be a comprehensive method to determine response (Table 1).

Clinical Studies of Radiofrequency Ablation for Stage I Non-Small Cell Lung Neoplasm

There are few reports of RFA in the literature with an emphasis on stage I non-small cell lung cancer. When reviewing the literature, interpretation of survival results after RFA should be done after review not only of the stage of the disease (with differing prognosis) but also of the patient population being treated. In a high-risk patient population with multiple comorbidities, it is difficult to interpret survival results because of non-cancer-related deaths. Similarly, the reported incidence of progression depends on the protocol for follow-up, the imaging modalities used during follow-up, the criteria used to determine progression and, importantly, the duration of the follow-up. These factors are critical since the methods for reporting of recurrence or progression vary considerably in the literature.

Ambrogi and colleagues reported the results of RFA in 54 patients with 64 lung lesions (40 NSCLC, 24 metastases).[19] They reported a 62% complete response rate. The follow-up in this series is one of the longest in the literature with a mean follow-up of 23.7 months, range (6-50 months). The median overall survival in this cohort of patients was 28.9 months and median local progression-free interval was 24.1 months. Staging information, however, was not provided among the 40 patients with NSCLC. Lee and colleagues reported their experience with RFA in 10 patients with stage I NSCLC.[20] Of these 10 patients, only four were considered high-risk patients where surgery was contraindicated; the remainder refused surgery. Mean survival in these 10 patients was 21