Navigation Bronchoscopy-Guided Radiofrequency Ablation for Nonsurgical Peripheral Pulmonary Tumors

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Established Facts

- Radiofrequency ablation (RFA) is a promising alternative treatment method for early-stage lung cancer in patients who are poor surgical candidates or have exhausted their maximum amount of radiation therapy. It can also be used for oligometastasis from distant cancer or as a therapy for the local control of tumors.
- RFA has been widely utilized via a percutaneous approach into a variety of organs. In the lung, percutaneous RFA is associated with severe complications, including pneumothorax, hemothorax, broncho-pleural fistulas, and pleural effusions.

Novel Insights

- A bronchoscopic flexible RFA catheter can significantly decrease the severity and frequency of complications compared to percutaneous RFA.
- Navigation bronchoscopy-guided RFA is safe, efficacious, and feasible for poor surgical candidates with stage IA lung cancer or lung metastasis.

Keywords

Radiofrequency ablation · Navigation bronchoscopy · Lung cancer

Abstract

We have recently developed a flexible catheter electrode used for bronchoscopic radiofrequency ablation (RFA). Two patients with nonsurgical stage IA peripheral lung cancer

and 1 with lung metastasis underwent treatment with flexible catheter RFA utilizing navigation bronchoscopy. Chest computed tomography (CT) and positron emission tomography/CT (PET/CT) were performed before and after RFA to assess the ablation response of the patients. One patient's tumor had no prior PET uptake and therefore no follow-up

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PET was obtained. The first and the third patient obtained partial response to RFA, and the second patient obtained complete response 3 months after RFA. The first patient developed progressive disease 6 months after RFA. The second and the third patient achieved one-year progression-free survival. No significant complications occurred in the 3 patients. Navigation bronchoscopy-guided RFA is a safe and feasible procedure for poor surgical candidates with stage IA lung cancer or lung metastasis.

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Introduction

Surgical resection remains the recommended treatment approach for patients with early-stage, non-small cell lung cancer and some pulmonary metastases [1–3]. However, not all patients are eligible for surgical resection due to comorbidities or other contraindications. Stereotactic body radiotherapy and radiofrequency ablation (RFA) are recommended for patients medically inoperable as local therapy [4, 5]. Stereotactic body radiotherapy is an effective, noninvasive treatment modality but is limited by respiratory movements, requirements for multiple treatments, cost, and the complication of radiation pneumonitis. RFA is a promising alternative treatment method with overall survival data appearing to be similar to sublobar resection and radiotherapy [6–8]. RFA has been widely used via a percutaneous method, and complications including pneumothorax, hemothorax, bronchopleural fistula, and pleural effusions are very common ranging from 15.2 to 55.6% [9]. Bronchoscopic RFA offers the chance to potentially decrease these severe complications [10]. Koizumi et al. [11] reported bronchoscopy-guided RFA to be a safe and effective procedure for medically inoperable patients. Navigational bronchoscopy techniques have allowed accurate access to peripheral pulmonary lesions for biopsy. The same techniques can be utilized for accurate placement of therapeutic tools as well as ablation catheters [12, 13]. We present 3 cases utilizing navigational peripheral bronchoscopic RFA for ablation of tumor.

Methods

Three patients diagnosed with pulmonary tumors (2 lung tumors and 1 metastasis) by bronchoscopy underwent bronchoscopic RFA. The patients were either medically unsuitable for surgery or refused consent for thoracic surgery. Chest thin-slice computed tomography (CT) and positron emission tomography/CT

(PET/CT) were performed prior to RFA. Electromagnetic navigation bronchoscopy (superDimension/inReach system; Medtronic, Minneapolis, MN, USA) or virtual bronchoscopic navigation (VBN; DirectPath; Olympus, Tokyo, Japan) were used for navigational assistance and performed as previously described [14, 15]. Bronchoscopic RFA was performed under general anesthesia and a dispersive electrode was placed on the lower back of the patient. When the bronchoscopic peripheral catheter (extended working channel [EWC], inReach system; Medtronic, or guide sheath [GS], K-201; Olympus) reached the lesion with navigation assistance, a radial endobronchial ultrasound probe (UM-S20-20R or UM-S20-17S; Olympus) was inserted via the peripheral catheter. Combined with fluoroscopy, the radial endobronchial ultrasound probe was used to confirm the position of the EWC/GS in relation to the tumor. A flexible electrode connected to a radiofrequency generator (S500; Medsphere, Shanghai, China) (Fig. 1a) was introduced into the tumor through EWC/GS under fluoroscopic guidance.

RFA was initiated at an output power of 20 W with fluoroscopic monitoring and increased 5 W every minute until the temperature reached 100°C. Tissue impedance and temperature were measured continuously by the generator and the output power stops automatically when the tissue impedance reaches 500Ω. One to three milliliter of 2% lidocaine was injected into the lateral aperture of the electrode to alleviate the airway irritation from thermal stimulation and potentially increase the ablated area during RFA [16, 17]. A chest CT scan was performed within 72 h, after 1 month, and every 3 months after the procedure. PET/CT was performed 3 months after RFA to assess the treatment response. Tumor response was evaluated 3 months after the treatment using modified Response Evaluation Criteria in Solid Tumors criteria [18]. All procedures were performed by an experienced bronchoscopist (J.S.). Patients provided written informed consent for the treatment and for their medical data to be used.

There are 3 types of flexible electrodes available (Fig. 1b–e). The electrode EB-01 is a needle electrode with the outer diameter and exposure length of 1.4 and 15 mm, respectively. Electrodes EB-02 and EB-03 consist of a cannula with 9 deployable electrodes that open “flower-like” up to a diameter of 20 and 30 mm, respectively, and the outer diameters of the cannula are 1.4 and 1.8 mm, respectively.

Case Report

Case 1

A 62-year-old male was admitted with abnormal findings on chest imaging. A chest CT scan showed a 13.3 × 11.7 mm lesion in the right lower lobe without any enlarged hilar or mediastinal lymph nodes. PET/CT showed hypermetabolism of the lesion with the maximal standard uptake value (SUV_{max}) of 3.7. Bronchoscopy biopsy demonstrated squamous cell carcinoma with a wildtype epidermal growth factor receptor. The patient had severe dilated cardiomyopathy with a low ejection fraction and was considered medically inoperable. Electromagnetic navigation bronchoscopy-guided bronchoscopic RFA was performed. The electrode EB-01 was used, and RFA continued 5 min with the total output power of 20 W. Twenty-four hours after the procedure, the patient presented chest pain and fever. This resolved with conservative treatment of pain and fever. PET/CT 3 months after treatment demonstrated a reduced tumor size, and the SUV decreased

Fig. 1. Radiofrequency ablation (RFA) generator and RFA flexible electrodes. RFA generator (a); flexible electrode (b); tip of the electrode EB-01 (c); tip of the electrode EB-02 (d); tip of the electrode EB-03 (e).

to normal range ($SUV_{max} = 1.9$). The patient was classified as having obtained partial response (PR) after the treatment. Unfortunately, the lesion demonstrated progression of size on chest CT images at 6 months of follow-up. The procedure and image data of the patient are shown in Figure 2 (1a–j). After progression, percutaneous RFA was performed. Six months after percutaneous RFA, the PET/CT demonstrated no fluorodeoxyglucose uptake of the tumor.

Case 2

A 65-year-old male was admitted with abnormal chest CT imaging demonstrating a 14.8×10.1 mm nodule in the left upper lobe without hilar or mediastinal lymphadenopathy. PET-CT demonstrated hypermetabolism of the nodule with a SUV_{max} of 9.5. Bronchoscopy examination revealed squamous cell carcinoma without epidermal growth factor receptor mutation. The patient had a history of prior renal transplantation and large B-cell lymphoma and refused thoracic surgery. VBN-guided bronchoscopic RFA was performed with the electrode EB-02. The electrode was inserted first into the more distal portion of the tumor and ablation with 20 W initiated. The ablation continued for 3 min 40 s. The electrode was withdrawn 5 mm proximal, and a second ablation began. The second ablation continued 10 min with the output power increas-

ing from 20 to 40 W. PET/CT at 3 months revealed no uptake of the tumor. The patient obtained complete response after the treatment and is 1 year out of therapy with no evidence of disease. The procedure and image data of the patient are displayed in Figure 2 (2a–j).

Case 3

A 66-year-old male with a history of right radical nephrectomy for renal clear cell carcinoma presented to our hospital with abnormal findings on imaging. Chest CT showed a 21.8×11.9 mm nodule in the right lower lobe without hilar or mediastinal lymph node enlargement. PET-CT showed no hypermetabolism of the nodule. Despite the negative PET, given the pre-test probability of malignancy, we proceeded with biopsy. Bronchoscopic examination revealed lung metastasis of his prior renal cell cancer. The patient declined thoracic resection, and VBN-guided bronchoscopic RFA was performed. The ablation was 6 min 40 s long using an electrode EB-02 with the output power starting at 20 W and increasing to 50 W. The patient obtained PR after treatment and has been followed-up for 1 year by now with the CT abnormality almost gone on follow-up imaging. The procedure and image data of the patient are shown in Figure 3.

Fig. 2. 1a–j Electromagnetic navigation bronchoscopy-guided bronchoscopic radiofrequency ablation (RFA) of Case 1. Chest CT before RFA (a); real-time electromagnetic navigation screen of the sensor probe nearest to the tumor (b); radial ultrasound probe image of the tumor (c); bronchoscopic RFA with the electrode EB-01 under the guidance of fluoroscopy (d); chest CT within 72 h after RFA showing that the ablation zone appeared larger than the original tumor (e); chest CT 1 month after RFA, showing a cavity in the ablation site (f); chest CT 3 months after RFA showing that the tumor decreased in size (g); chest CT 6 months after RFA showing progression (h); preoperative PET/CT (maximum standardized uptake value [SUV_{max}] 3.7) (i); PET/CT 3 months after RFA (SUV_{max} 1.9) (j). 2a–j Virtual bronchoscopic navigation-guided bronchoscopic RFA of Case 2. Chest CT before RFA (a); virtual bronchoscopic navigation screen of the pathway (b); radial ultrasound probe image of the tumor (c); bronchoscopic RFA with the electrode EB-02 under the guidance of fluoroscopy (d); chest CT within 72 h after RFA, showing partial emptying of the ablation zone (e); chest CT 1 month after RFA, demonstrating a cavity (f); chest CT 3 months after RFA, showing linear lines and a scarring shadow (g); chest CT 1 year after RFA with a minimal residual scar (h); preoperative PET/CT (SUV_{max} 9.5) (i); PET/CT 3 months after RFA, showing no fluorodeoxyglucose uptake (j).

Discussion

RFA holds the promise of a potentially effective treatment for patients with early-stage lung cancer or lung metastasis who are not surgical candidates or decline surgical intervention [19, 20]. The 3 flexible electrodes were developed for bronchoscopic RFA and are applicable for tumor sizes up to 30 mm. The electrode EB-01, which was suitable for a lesion <15.0 mm, was used in Case 1. Though the tumor decreased in size at 3 months after broncho-

scopic RFA, there was an increase at 6 months. It is unclear if this is a direct failure of RFA, a choice of too small of a catheter, or limitations to peripheral bronchoscopy (i.e., we were tangential or not directly central within the tumor). We selected EB-02 for Case 2 as it has a larger area of energy application. We also did 2 ablations of the tumor along the long axis. Of note, this tumor had a complete response after the treatment. As Case 3 had no prior fluorodeoxyglucose uptake, we did not have the benefit of PET to follow tumor response. Patient 3 obtained a PR

Fig. 3. Virtual bronchoscopic navigation-guided bronchoscopic radiofrequency ablation (RFA) of Case 3. Chest CT before RFA (a); virtual bronchoscopic navigation screen of the pathway (b); radial ultrasound probe image of the tumor (c); bronchoscopic RFA with the electrode EB-02 under the guidance of fluoroscopy (d); chest CT within 72 h after RFA showing that the ablation zone

appeared larger than the original tumor (e); chest CT 1 month after RFA showing that the ablation zone continued to increase (f); chest CT 3 months after RFA showing that the ablation zone became smaller (g); chest CT 1 year after RFA showing that the ablation zone demonstrated linear scar lines (h).

but has been followed-up for 1 year with near resolution of the radiographic abnormality. The small size limits the re-biopsy potential of the lesion and it will be followed radiographically. As this is early data on a new technology, we are continuing to learn and adapt our techniques as the clinical scenario dictates.

Traditionally, RFA is performed percutaneously. This places obvious limits for the routine use in the lung. With a high incidence rate of complications such as pneumothorax, hemothorax, and bronchopleural fistulas, there has been appropriate concern [6, 9, 21, 22]. In addition to complications, some locations are anatomically difficult to reach and also carry the risk of pleural metastasis/direct spread of the tumor [23]. Bronchoscopic RFA offers the opportunity to reach difficult locations and possibly reduce the occurrence of RFA pulmonary complications. Though our sample size was small, we observed no severe complications in the 3 patients. Our study showed that bronchoscopic RFA was a safe procedure, as had been reported previously [11]. We speculate that bronchoscopic RFA has other potentially significant advantages. First, as the radiofrequency electrode was introduced into the tumor through the bronchus, the vaporization of tissue and necrosis induced by bronchoscopic RFA can directly communicate with the bronchus reducing the occurrence

of obstructive infections (i.e., postobstructive pneumonia). Second, bronchoscopic RFA offers an excellent solution to tumors invading the bronchial lumen through direct access to the tumor, especially in central and intermediate areas of the lung.

There are some obvious limitations of bronchoscopy-guided RFA and our study. As this is a case series performed by a senior bronchoscopist, its wide applicability remains to be demonstrated. Clearly, long-term follow-up and larger sample size are needed to confirm the safety and efficacy of navigation bronchoscopy-guided RFA. The current catheters have a limited heat radius, with tumors of 30 mm or small currently being suitable for treatment. Given the current limitations of navigation technology for the periphery, and the limited ability to centrally place a catheter into an eccentric lesion, RFA remains suitable for lesions with a bronchus sign on chest thin-slice CT. New bronchoscopic transparenchymal nodule access could offer a method to access lesions with no bronchus sign, and bronchoscopic RFA could be performed using this technology in the future.

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Financial Disclosure and Conflicts of Interest

The authors have no conflicts of interest to disclose.

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