

Radiofrequency Thermal Ablation in the Treatment of Lung Malignancies

COSMO GADALETA¹, ANNAMARIA CATINO¹ and VITTORIO MATTIOLI²

¹*Interventional Radiology Operative Unit and*

²*Critical Area Department, Oncology Institute, Bari, Italy*

Abstract. *Background:* Radiofrequency ablation (RFA) is an advanced, minimally invasive technique used to treat several types of neoplasm. Its application in the treatment of lung tumors has received great interest. *Patients and Methods:* Fifty-four patients with 10 unresectable primary lung tumors and 83 lung metastases from various solid tumors were treated with percutaneous RFA. *Results:* The procedure was performed under CT scan guidance and general anaesthesia. The rate of complete necrosis of the treated neoplasms was 95%, while the most frequent complication was pneumothorax, requiring pleural drainage in 12% of sessions. CT scan and MRI with gadolinium have shown to be accurate and useful in assessing the therapeutic efficacy of lung RFA. *Conclusion:* Lung RFA is a very promising technique, minimally invasive and well-tolerated in the majority of patients; further investigation is required in order to define the optimal role of lung RFA in the multidisciplinary therapy of lung malignancies.

Among the new image-guided percutaneous techniques which are based on hyperthermic energy, radiofrequency thermal ablation (RFA) has recently received much attention as minimally invasive approach for the local treatment of solid neoplasms (1).

Medium-frequency electromagnetic waves of 480 kHz produce ionic agitation and frictional heat within the tissue surrounding the tip of the needle, leading to irreparable cellular damage and coagulative necrosis (1).

Lung tumors seem to be good targets for RFA because the surrounding air in the adjacent normal lung parenchyma provides an insulating effect, concentrating the RF energy within the tumor tissue (2).

Correspondence to: Dr. Cosmo Gadaleta, Interventional Radiology Operative Unit, Oncology Institute Bari-Italy, Via Hahnemann, 10 – 70126, Bari, Italy. Tel: +39 0 805555674, Fax: +39 0 805555677, e-mail: c.gadaleta@infinito.it

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In addition, experimental studies have reported that RFA of lung tumors results in the greatest coagulation diameter, depending on a variety of tissue-specific characteristics (3).

After the first experience reported by Dupuy *et al.* (4), many studies have been published on lung RFA (5-8); despite the differences with regard to various approaches (*i.e.*, percutaneous or thoracotomic), type of device, patient characteristics and duration of follow-up, the technique can be considered safe, feasible and well-tolerated by patients.

Patients and Methods

From February 2002 to June 2006, 54 patients with 93 lung neoplasms (9 with primary NSCLC and 45 with metastases from other solid tumors) underwent lung RFA.

Lung lesions were subclassified as follows: paramediastinal, those in contact with mediastinal structures (without infiltration) or less than 1 cm from them, including fibrous pericardium, major vessels, cardiac pedicle, trachea and bronchi; central-parenchymal, those fully surrounded by pulmonary aerated parenchyma, more than 1 cm from the mediastinal structures and visceral pleura; subpleural, those in direct contact (without infiltration), or distant less than 1 cm from the pleura.

Patients were considered unresectable due to technical or anatomic/functional contraindications, or in case of refusal of surgery. Main inclusion/exclusion criteria are summarized in Table I.

The technique was performed under general anaesthesia with intubation by a double-lumen tube used for all patients. After CT scan centering, percutaneous lung RFA was performed using a 17-gauge monopolar, cooled electrode needle, with lengths ranging between 10 and 15 cm, depending on the depth of the lesion to be treated. The exposed part of the needle (*i.e.*, the non-insulated portion) was between 1 and 3 cm. Selection of the exposed tip length of the needle was based on the diameter of the lesion (36), choosing a needle size always greater than the area to be treated. The wattage/current setting is selected automatically by the system and is based on the amount of water within any specific tissue (*i.e.*, the amount of free-ions present). The system adjusts itself according to the level of resistance and impedance. A maximum treatment time of 12 min has been found to ensure complete necrotic coagulation of the tumor volume according to the corresponding diameter of the exposed part of the needle. The system alternates between "on" (active) and "off" (inactive) modes. Long periods (30-40 sec) of inactivity by the machine and short

Table I. Inclusion and exclusion criteria.**Inclusion criteria:**

- Age between 18 and 80 years
- Histological proof of lung tumor
- Unresectable lung metastases, mono or bilateral (3 nodules at most, <10 cm)
- Unresectable primary lung tumors (NSCLC), with single or multiple lesions, monolateral, <10 cm
- ECOG Performance Status 0-1
- Written informed consent

Exclusion criteria:

- Neoplastic lesions infiltrating the wall of the main bronchial branches and/or big vessels and/or interstitial mediastinal tissue
- Extrapulmonary disease
- Suppurative neoplasms
- SCLC and bronchioalveolar carcinoma
- Pleural effusion
- Severe impairment in coagulative tests

periods (5-7 sec) of activity (*i.e.*, with readings by the system of >100 Ohm) indicate that the scheduled volume of the nodule has been ablated.

A single insertion was performed for lesions with a diameter less than or equal to 2.8 cm, and treatment session lasted 12 min. Larger lesions (>3 cm) were divided into sectors, and each sector was treated as if it was a 2-cm lesion, with the exposed part of the needle.

The sectors overlapped to ensure full ablation of the entire nodule. All lesions were treated in one session, both multiple and large lesions, even if long treatment sessions were required.

Repeated CT scans were performed during the procedure, with a collimation of 5 mm, in order to select the optimal access path of the needle, to detect and manage possible acute complications, and, finally, to monitor the treatment-related structural changes of the lesion.

All patients received antibiotic prophylaxis. The assessment of treatment efficacy included a contrast-enhanced CT scan and NMR with gadolinium; it was based on the absence of contrast-enhancement in the treated area and, on the possible presence of cavitation.

Results

Ninety-three lung neoplasms in 54 patients underwent RFA, while 67 sessions of treatment were carried out.

With a median follow-up of 18 months, complete ablation of the entire lesion was achieved in 88 out of 93 cases (95%). Local recurrence only in the treated area was observed in 2 cases (2%), whereas 5 cases showed relapse both in treated area and/or other distant sites. Among the 5 patients who relapsed in the treated area, 3 had nodules larger than 3.5 cm.

The major complication was pneumothorax, requiring chest-tube placement in 8 out of 67 (12%) sessions.

One case of bronchopleural fistula was observed, resolved after a prolonged pleural drainage; other side-effects, considered to be moderate and easily manageable, were cough with rust-coloured spitting (18/67: 28% of sessions), minimal pleural effusion (20/67: 30%), thoracic pain (15/67: 23%), transient dyspnoea (8/67: 12%) and moderate-grade fever lasting more than 3 days (10/67: 15%). No treatment-related death occurred.

Immediately after treatment, CT images showed wrinkling of the edges of the lesion with unchanged diameter and partial emptying, likely due to vaporization of tissue; in addition, multiple concentric rings with various densitometric characteristics were visible in the pulmonary parenchyma around the lesion.

This appearance, so-called "cockade phenomenon", was most evident 48-72 h after treatment.

CT scans obtained after 30 days and revealed progressively less definition of the lesion, and ultimately a core of hyperdense scar tissue surrounded by a thin hyperdense ring with a distance from the nucleus that was inversely correlated to the size of the nodule.

In case of complete ablation, the treated nodules appeared enlarged, most likely due to central necrosis and cavitation surrounded by reparative fibrosis, without contrast-enhancement.

NMR, obtained during the follow-up, usually showed a central hypointense area, surrounded by a homogeneous hyperintense ring likely due to hyperemia and inflammatory phenomena.

Discussion

Lung RFA was demonstrated to be safe and feasible; the percutaneous approach and imaging guidance made this procedure suitable for patients considered unfit for standard surgical resection. The usually short hospital stay and the good tolerability contributed to RFA being well accepted by patients, resulting in a favourable impact on quality of life. Pneumothorax was the most serious complication; in our experience it occurred in 12% of sessions.

The technique was extremely promising also with respect to the efficacy; in our experience it was possible to obtain a high rate of complete ablation in the treated nodules (95%).

In agreement with other authors (8), we think that in case of lesions larger than 3.5 cm it is difficult to achieve complete necrosis; nevertheless, when the subdivision of the lesion in overlapped sectors is required, the use of repeated CT scan during the procedure could improve the technical results, due to the capability of monitoring even the slightest repositioning of the electrode-needle.

Lung RFA produces a typical radiological appearance which resembles a "cockade", so-called due to the formation of concentric layers surrounding the ablated lesion, most

likely corresponding to histopathological changes and related to thermal gradients between the tumoral nodule and the surrounding parenchyma (5).

CT scan is the most widely used imaging technique to evaluate lung tumors treated with RFA, able to detect changes in contrast-enhancement, as well as the presence of cavitation (5-7, 9-12). In addition, NMR with gadolinium could be potentially useful to evaluate the therapeutic efficacy of lung RFA, by providing information about tumoral density and composition, as well as to accurately determine the extent of tissue necrosis (5-7, 13). Notwithstanding the need for more standardized methods, we consider CT scan and NMR with gadolinium reliable techniques for radiologic assessment of treatment efficacy and follow-up of lung neoplasms submitted to RFA.

Further well-designed and long-term clinical trials are warranted to: 1) identify which subgroups of patients are ideal candidates for this procedure, 2) determine the optimal combination of lung RFA with other antineoplastic therapies, and finally 3) establish the impact of lung RFA on patient survival with respect to standard therapy.

In conclusion, the current experience on lung RFA suggests that this procedure could represent an important tool in the multidisciplinary approach to unresectable lung tumors.

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