

Radiofrequency ablation of lung tumours – new perspective in treatment of lung neoplasms

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Background. Percutaneous radiofrequency ablation (RFA) is a minimally invasive technique used to treat solid tumours. Because of its ability to produce large volume of coagulation necrosis in controlled fashion this technique has been progressively tested as a possible treatment of lung malignancies. Recent clinical studies have shown that RFA enables successful treatment of relatively small lung malignancies with high rate of complete response and acceptable morbidity and have suggested that the technique could represent a viable alternate or complementary method for patients with non-small cell lung cancer or lung metastases of favourable histotypes who are not candidates for surgical resection.

Conclusions. Initial intentional studies as well as the clinical experience of Institute of Radiology in Clinical Center Ljubljana, although limited, indicated that RFA is mostly well tolerated by patients and also, that it can result in complete necrosis of targeted lesion. Pneumothorax is most common procedure related complication, occurring in up to 40% of cases, with approx. half of them requiring drainage.

Key words: lung neoplasms – surgery; catheter ablation

Introduction

Image-guided percutaneous radiofrequency ablation (RFA) is a minimally invasive technique for the treatment of solid tumours that has only been introduced recently into every day clinical practice. Now it is considered to be a feasible treatment option for patients with primary hepatocellular carcinoma or limited metastatic liver

disease.^{1,2} With the improvement of the technology RFA is now being evaluated for in other types of tumours, including lung neoplasms.

As being well known, the lung is the most common site of primary cancer worldwide and is also a common site for metastatic disease. Many of these patients and also the patients with otherwise resectable tumours are not operable due to associated conditions such as age, poor cardiovascular and/or respiratory function and/or other serious coexisting health conditions or because of the size and location of the tumour itself. For all these patients (e.g. patients with limited lung tumours not eligible for surgical resection) radiofrequency ablation seems to be a good treatment option.³⁻⁸

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RFA

In principle RFA is caused by high-frequency current from radiofrequency generator passed between the needle electrode placed in the tumour and a large electrode on patient's skin. Electrodes create an alternating electric field which induces marked agitation of ions resulting in frictional heating of the surrounding tissue, which results in irreversible damage.^{3,5,6,9,10} Experimental studies in animals showed a well defined area of coagulation 72 hours after RFA, surrounded by a zone of hyperaemia that gradually resolves.

The technique found to be especially suitable for lung tumours since the air in surrounding alveoli acts as insulation, helping to concentrate the energy in the lesion. The disadvantage of the method is, however, that the technique is suitable only for patients with solitary or small number of lung lesions since each tumour or metastasis need to be treated individually.³

Detailed diagnostic workup, including chest CT, is essential to determine the exact number, site and position of target tumour(s). The treatment procedure is CT guided. During the procedure the needle electrode is positioned in the tumour, using the workflow of stereotactic biopsy of lung lesions.³ It is important to select the entry site on the skin that allows the shortest and most vertical path for the needle, avoiding blood vessels, interlobar fissures and bullae. Image reconstructions and multiple planes help us to ensure the correct placement of the electrode needle within the tumour, which is a crucial point of the procedure. The ablation device has 9 flexible hooks, deployed from the trocar tip, some use cooled tip electrodes. The power output of the radiofrequency generator and duration of the ablation are programmed according to tumour volume and continuously monitored by a computer. At the end of procedure the

track ablation is carried out to reduce the risk of seeding tumour cells.³

The important limitation for the procedure is the size of the tumour. Since we need to ablate all viable tumour tissue and an adequate tumour-free margin which is 1 cm, it is clear, that largest, a 5 cm ablation device can be used to treat tumours up to 3 cm in diameter and not more.¹¹ One cm margin is necessary to assure that all possible microscopic invasions around the periphery of a tumour have been eradicated.

Lung RFA is painful and requires adequate pain relief with conscious sedation or general anaesthesia, although the latter seems to be connected with greater risk of pneumothorax in the ventilated patient.^{3,5,7,8,12}

International clinical experience

Initial studies as well as the clinical experience of Institute of Radiology in Clinical Center Ljubljana, although limited, indicated that RFA is mostly well tolerated by patients and also, that it can result in complete necrosis of targeted lesion. Pneumothorax is most common procedure related complication, occurring in up to 40% of cases, with approx. half of them requiring drainage.^{3,5,6,9,10}

Recently, one of the largest trials of RFA for lung tumours was completed.¹² Patients were followed up to 27 months. Patients with primary lung cancer or lung metastases 3.5 cm or less in diameter, who were not candidates for surgery, were included into this multicenter, prospective study. One hundred and six patients with 186 malignant masses were enrolled. There were 33 patients with non-small cell lung cancer, 53 with colorectal lung metastases and 20 with other primary malignancy metastasis, none of them eligible for surgery. Patients underwent CT guided RFA treatment un-

der conscious sedation. There were no procedure-related deaths, but 27 cases of pneumothorax, requiring treatment and also 4 pleural effusions, 2 pneumonias and 1 atelectasis.

At CT evaluation after 3 months post procedure, complete ablation of the tumour was observed in 173 of 186 tumours, which set the primary effectiveness rate to 93%. Overall survival rate of the primary lung cancer patients was 69% at year 1 and 49% at year 2. However, many deaths were not cancer related and when excluded, the cancer specific survival rates were 91% at year 1 and 72% at year 2, after exclusion of non-cancer related deaths.¹²

Clinical experience of Institute of Radiology in Clinical Center Ljubljana

We have treated 5 patients up-to date. In all cases the procedure was performed with intent to cure. All patients have had cito/histologically proven non-small cell lung cancer without metastatic disease. The disease was resectable in all cases but patients were inoperable due to cardiac and pulmonary disease (3 patients), extreme obesity (1 patient) and consent withdrawal (1 patient).

During pre-ablation work-up patients underwent a chest CT to determine target tumour(s) location and size and percutaneous or CT-guided fine needle biopsy to confirm the nature of the lesion. Abominal US or CT were used to search for distant metastases. All patients had solitary primary lung neoplasms without distant metastatic disease. In all cases the disease was unilateral and as such treated during single session. One patient had larger (3 x 5 cm) tumour with central necrosis while the rest were smaller, up to 3 cm in diameter, and solid.



Figure 1. Radiofrequency generator with multiple temperature displays and impedance and power monitoring.

In case of patients with history of diffuse lung disease or lung surgery lung spirometry is needed, since it is known that the tolerance is good in patients with a FEV1 of more than 1 litre but transitory respiratory insufficiency developed in about one third of patients with a FEV1 less than 1 litre.

We used general anaesthesia in 4 cases and conscious sedation in one. The first provides higher feasibility while with latter



Figure 2. Radiofrequency ablation procedure in patient with NSLC of the left lung. The flexible part of expandable needle is outside the patient while the rigid part is already placed in patient's lung. On the handle of the electrode there are clearly seen the markings (arrow), which indicate the amount of electrode array deployment from the trocar.

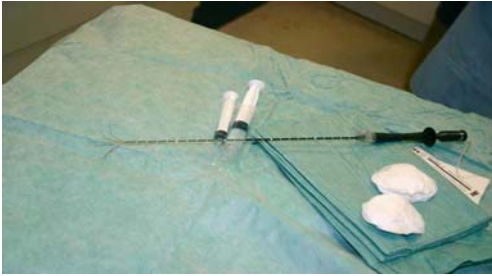


Figure 3. Radiofrequency ablation device. 15-gauge, 9-hook expandable electrode needle (StarBurst XL, RITA Medical Systems).

patient suffered from perioperative pain and the treatment needed to be interrupted twice due to pain. Duration of the procedure was 1-3 hours, mean duration was 1.5 hour.

We used a 150 W generator (Figure 1) and 15-gauge ablation needles. The ablation procedure was CT-guided (Figure 2)

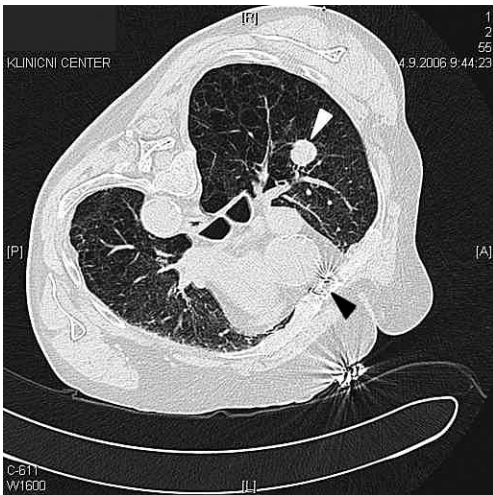


Figure 4a. Lung tumour treated with radiofrequency ablation. Pre-treatment CT shows the focal mass of about 2 cm in diameter in right upper lobe (white arrow). In the parenchyma there are numerous larger and smaller emphysematic bullae – this patient was not a surgical candidate due to severe emphysema, COPD and cardiac condition – note artefacts after sternotomy for CABG (black arrow) and a cardiac pacemaker.

and handled with 9-hook expandable electrode needle (StarBurst XL, RITA Medical Systems) which was flexible and stiff (Figure 3). They enabled direct temperature measurement throughout the tissue to prevent any electrode in multi-tined configuration from exceeding 110⁰ C.

The radiofrequency generator had multiple temperature displays as well as impedance and power monitoring. The generator was programmed on the “average temperature” mode and the target temperature was set at 90⁰. Ablation protocols, appropriate for lungs, were used, since lung parenchyma is different from e.g. liver in terms of energy deposition, electrical conductivity, heat diffusion and heat convection. The ablation procedure was terminated by coagulating the needle track to prevent tumour cell dissemination along the needle path.

After completion of the procedure a single expiratory scan is obtained throughout the thorax to detect pneumothorax and other possible complications (parenchymal changes, haemorrhage, pleural effusion). We put the patient into the needle

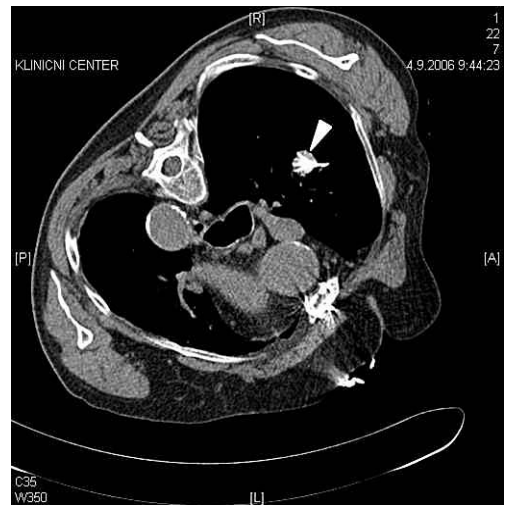


Figure 4b. Lung tumour treated with radiofrequency ablation. CT obtained after electrode placement confirm proper deployment (arrow).



Figure 4c. Lung tumour treated with radiofrequency ablation. CT after completed ablation procedure shows ground glass density area (between black arrows) encompassing the native tumour as well as a safety margin of surrounding lung parenchyma. In addition, a small asyptomatic pneumothorax (white arrow) was detected at the end of procedure.

site dependent position which helps reduce air leak and post-procedural pneumothorax and possibly prevents transbronchial spread of induced alveolar haemorrhage.

There were no major procedure-related complication in our patients, in general the procedure was well tolerated. Pneumothorax requiring catheter drainage occurred in only one case. Productive cough with brown sputum lasting about one week was observed in one patient (Figures 4a, 4b, 4c).

All patients received antibioprophylaxis with broad spectrum antibiotic administered intravenously immediately before ablation. Antibiotics were given orally after 24 hours and prolonged over 7 days.

Follow up examinations are usually performed at month 1, 3 and 6 after the procedure and at 3-month or 6-month intervals thereafter. However the compliance of the patients was low. One of our patient had 6 month disease free interval while in second

we observed tumour recurrence at month 9 follow up. The rest were lost to follow up.

Conclusions

RFA is a new, minimally invasive procedure that shows promise for the treatment of primary and secondary lung cancer. Results of recent clinical studies have shown that it can provide effective and reproducible tumour destruction with acceptable morbidity but no survival benefit associated with the use of RFA of lung malignancies has been demonstrated so far.

Owing to small number of treated cases and short follow-up period, no definite conclusion concerning the potential clinical role can currently be drawn. For this reason additional clinical trials are required to further evaluate the place of the method in the management of primary tumours and metastases in lung, either alone or with respect to additional chemotherapy or radiotherapy.

Nevertheless, with continued improvement in technology and increasing clinical experience RFA could represent a viable alternate or complementary treatment for patients with NSCLC or lung metastases who are not candidates for surgical resection.

References

1. Lencioni R, Cioni D, Crocetti L, Franchini C, Pina CD, Lera J, et al. Early-stage hepatocellular carcinoma in patients with cirrhosis: Long-term results of percutaneous image-guided radiofrequency ablation. *Radiology* 2005; **234**: 961-67.
2. Berber E, Pelley R, Siperstein AE. Predictors of survival after radiofrequency thermal ablation of colorectal metastases to the liver: a prospective study. *J Clin Oncol* 2005; **23**: 1358-54.
3. Lencioni R, Crocetti L, Cioni R, Mussi A, Fontanini G, Ambrogi M, et al. Radiofrequency of lung malignancies: where do we stand? *Cardiovasc Intervent Radiol* 2004; **27**: 581-90.

4. Fernando HC, De Hoyos A, Landreneau RJ, Gilbert S, Gooding WE, Buenaventura PO, et al. Radiofrequency ablation for the treatment of non-small cell lung cancer in marginal surgical candidates. *J Thorac Cardiovasc Surg* 2005; **129**: 639-44.
5. Herrera LJ, Fernando HC, Perry Y, Gooding WE, Buenaventura PO, Christie NA, et al. Radiofrequency ablation of pulmonary malignant tumors in nonsurgical candidates. *J Thorac Cardiovasc Surg* 2003; **125**: 787-8.
6. Lee JM, Jin GY, Goldberg SN, Lee YC, Chung GH, Han YM, et al. Percutaneous radiofrequency ablation for inoperable non-small cell lung cancer and metastases: preliminary report. *Radiology* 2004; **230**: 125-34.
7. King J, Glenn D, Clark W, Zhao J, Steinke K, Clingan P, et al. Percutaneous radiofrequency ablation of pulmonary metastases in patients with colorectal cancer. *Br J Surg* 2004; **91**: 217-23.
8. Steinke K, Glenn D, King J, Clark W, Zhao J, Clingan P, et al. Percutaneous imaging-guided radiofrequency ablation in patients with colorectal pulmonary metastases: 1-year follow-up. *Ann Surg Oncol* 2004; **11**: 207-12.
9. Schaefer O, Lohrmann C, Langer M. CT-guided radiofrequency ablation of a bronchogenic carcinoma. *Br J Radiol* 2003; **76**: 268-70
10. Steinke K, Habicht JM, Thomsen S, Soler M, Jacob AL. CT-guided radiofrequency ablation of a pulmonary metastasis followed by surgical resection. *Cardiovasc Intervent Radiol* 2002; **25**: 543-6.
11. Steinke K, Glenn D, King J, Morris DL. Percutaneous pulmonary radiofrequency ablation: difficulty achieving complete ablations in big lung lesions. *Br J Radiol* 2003; **76**: 742-5.
12. Lencioni R. Radiofrequency ablation of lung tumours. *Controversies and consensus in imaging and intervention* 2006; **3**: 16-7.