Percutaneous Radiofrequency Ablation of Lung Malignant Tumours: Survival, disease progression and complication rates

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Purpose

5 year survival of lung cancer is only 15% (1). The Gold standard for managing early stage non small cell lung cancer (stages 1 &2) is surgical. Only one third of these are fit for surgery at time of diagnosis. An unknown additional percentage refuses surgery for treatment of their cancers.

Lungs are the second most common site for solid organ tumour metastases. Patients with a limited number and size of pulmonary metastases who are not candidates for surgery or in whom resection, external beam radiotherapy and chemotherapy have failed may be appropriate for RFA.

Radiofrequency ablation (RFA) is a minimally invasive method of treatment that has shown promise in patients with non-small cell lung cancer (NSCLC) and pulmonary metastases from both lung and extrapulmonary primary tumours. Most commonly, RFA has been applied when surgical resection was not an option due to advanced age, coexistent medical morbidities and/or refusal of surgery.

The aim of this study was to determine the survival rate associated with RFA of inoperable +/- symptomatic lung tumours (NSCLC or metastases). We also aimed to determine the rate of progression of lung tumours post RFA. Besides we wanted to measure the morbidity associated with this novel technique by studying its immediate complications rate.

Methods and Materials

This study has been done in University College Hospital Galway. It was a retrospective cohort study. Convenience sampling was used. All adult patients referred for RFA of primary and metastatic lung tumours were included. 12 patients who underwent RFA for lung tumours in the period between 2005 and 2010 were studied. No patients were excluded. Outcome variables were: 1) Survival measured in months post date of procedure (to calculate the 6 and 12 monthly survival rates). 2) Objective response measured by change in size of lung nodules. RECIST (Response Evaluation Criteria in Solid Tumours) guidelines were used (2). These provide a standard approach to solid tumour measurement and definitions of objective assessment of change in tumour size. An initial evaluation of tumour burden would be done prior to RFA and used as a comparator for subsequent measurements. The same method (e.g. CT, CXR) is used to characterise each identified and reported lung nodule at baseline and follow-up. Table (1) provides the definitions of the criteria used to determine objective tumour response for target lung lesions. 3) The third outcome variable assessed was the rate of secondary pneumothorax due to RFA's.
Data were obtained from the Hospital electronic picture archiving and communication system (PACS) and from the Primary, Community and Continuing Care (Ireland) life register. Statistical analysis was done using Minitab 16 statistical software.

Predictor variables were age, sex, histological diagnosis, size and number of lesions treated.

Table (1): definitions of the criteria used to determine objective tumour response for target lung lesions (RECIST).

<table>
<thead>
<tr>
<th>Response Criteria</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Complete response (CR)</td>
<td>Disappearance of all target lesions</td>
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<tr>
<td>Partial response (PR)</td>
<td>At least 30% decrease in the diameter of target lesion.</td>
</tr>
<tr>
<td>Progressive disease (PD)</td>
<td>At least 20% increase in the diameter of target lesion. This has to demonstrate an absolute increase of at least 5mm.</td>
</tr>
<tr>
<td>Stable disease (SD)</td>
<td>Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.</td>
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Technique: RFA is a technique that involves placement of an electrode percutaneously into a specific location to cause focal tissue destruction with thermal energy. Tissue heating is achieved through the generation of heat by an alternating electric current in the frequency of radio waves (460-500 kHz).

An insulated radiofrequency (RF) electrode with an exposed conductive tip is connected to an RF generator and is inserted into the targeted tissue under image-guidance. The tip of the RF electrode conducts the electric current, which causes local ionic agitation and subsequent frictional heat in the tissue in a concentrated fashion, thereby creating a controlled zone of coagulation necrosis. A reference electrode (most commonly a large grounding pad) is placed on the patient’s skin in an area of good electrical conductivity (typically the thigh or the opposite chest wall) to complete the electrical circuit.

The target tissue temperature using RFA is between 50 and 100°C. At temperatures greater than 50°C, tissue coagulation results from denaturing of cellular proteins and damage to cell membranes. At temperatures above 100°C, however, tissue charring and cavitation occur, which increases tissue impedance and limits current flow, thereby reducing the effectiveness of thermal ablation.

The aim of RFA is to destroy the entire tumour, killing the malignant cells with minimal damage to surrounding normal tissue and without damaging adjacent organs. A 0.5 to 1.0 cm rim of apparently healthy lung tissue around the lesion is included in the target
because the exact tumour margin is uncertain and because microscopic disease may exist in the tissue surrounding the tumour.

Patients who are not candidates for surgery on the basis of age, underlying lung disease, or other medical co morbidities and those who refuse surgery are candidates for treatment with RFA. The decision to use RFA rather than another modality is determined in a multidisciplinary meeting that includes Respiratory physicians, Cardio-thoracic surgeons and medical and radiation oncologists.

Biopsy proof of malignancy should be obtained prior to treatment. An informed consent is also obtained. At our hospital, all lung RFA treatments are performed using CT fluoroscopy for image-guidance. The patients will be treated under conscious sedation (using fentanyl and midazolam) or general anaesthesia. A staff nurse monitors heart rate, blood pressure, and pulse oximetry during the procedure. Chest x-rays to detect and monitor pneumothorax and other complications were obtained after the procedure.

**Results**

17 lung malignant nodules in 12 patients were treated with radiofrequency ablation during the period of Nov. 2005 and April 2010. Of them, 9 (67%) were females and 3 (33%) were males. The mean age of study population was 65.8 years (95% confidence interval 60.08 - 71.45). Histology of lung lesions revealed 7 (58%) cases of metastatic colorectal cancer, 2 (17%) cases of metastatic breast cancer, 1 (8%) case of metastatic oesophageal cancer and 2 (17%) cases of primary non-small cell lung cancer (NSCLC).

The number of pulmonary tumours ranged from 1-3 per patient (6 patients had a single tumour, 5 patients had 2 tumours and one patient had 3 pulmonary tumours). The median size of target pulmonary nodules was 20 mm. (95% confidence interval 18 - 29 mm.). The largest nodule treated was 79 mm in size in a patient with metastatic colorectal Ca. No more than one nodule was treated per single session. The median energy level applied during RFA was 40 Watts (95% confidence interval 40 - 69 Watts). The mean duration of RFA session was 30 minutes (95% confidence interval 18.5 - 41.5 minutes).

The 6 months survival rate was 88.4%. The one year survival rate was 58.9%. The mean time to first follow-up CT chest was 12 weeks (95% confidence interval 8.7 - 13.4 weeks).

The mean difference in the size of pulmonary nodules was an overall increase of 2.9 mm (95% confidence interval -5.96 - 0.08). This was not a statistically significant difference indicating a tendency for lung nodules treated with RFA not to change in size within the 12 week follow-up period in this study. Summarising this using RECIST showed 52.9% had stable disease (SD), 5.9% had partial response (PR) and 41.2% had progressive disease (PR).
6 RFA's (35.5%) resulted in a pneumothorax. Only one patient (5.8 %) needed chest drain insertion for 48 hours with complete resolution of pneumothorax. Two of the pneumothoraces needed simple aspiration during the procedure. The remaining 3 (50%) patients with pneumothoraces needed no specific treatment.

Overall, Radiofrequency thermal ablation is an interesting technique. Indeed surgery remains the standard treatment for patients with localised primary lung cancer and metastatic resectable lesions, although only a small percentage of these patients are candidates for surgery because of co-morbidity, poor cardio-respiratory reserve. Therefore, the use of RFA in such patients is attractive especially when considering the generally poor outcome of such patients if they underwent chemo-radiotherapy in addition to the short hospital stay post-RFA.

This study demonstrates good 6 and 12 months survival rates for patients with primary or metastatic lung tumours treated with RFA. It also demonstrated that only 41% of treated patients did show evidence of disease progression during the follow-up period. One of the study limitations was the retrospective design.

Convenience sampling and the small number of subjects studied will reduce the generalisability of this study results. Missing data were compensated for during the statistical analysis.

Estimating the true beneficial effect of RFA is difficult as a routine biopsy of lung malignant nodules, the gold standard, in the follow up period, to look for any residual viable malignant cells, is not a common practice. That is why we had to rely on change of size of lung nodules only during follow-up. The radiological follow-up period in our study was relatively short (12 weeks). Longer periods of follow up with serial CT imaging of the thorax at fixed intervals would be very helpful in detecting evidence of continued growth of pulmonary nodules.

Our study result of an average increase in the size of RFA treated lung nodules within the 12 weeks follow-up period correlates well with previous studies that demonstrated a tendency for lung nodules to increase in size post RFA (due to ground-glass opacification or hemorrhage around the treated lesion). On longer follow-up, these tend to get smaller or stay stable. If a significant increase in nodule size is noted, this might indicate disease progression.

Images for this section:
Table 1: Table showing baseline characteristics for all RFA treated malignant lung nodules

Fig. 1: Kaplan Meier Survival post RFA
**Fig. 2:** Tumour response to RFA during follow up (time 0, 1, 3, 6 & 12 months).
Conclusion

Radiofrequency ablation is a relatively safe procedure that could be administered multiple times. It is associated with good survival benefit and with a reasonably low rate of pneumothorax requiring drainage.

References


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