Percutaneous ablation for lung tumours

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by Dr N Macias-Rodriguez
Thoracic imaging fellow

Ms J Beeson
Ablation CNS

Dr P Dalal
Consultant radiologist

The Lung Tumour Ablation Centre, Harefield Hospital, Middlesex
email: p.dalal@rbht.nhs.uk

Introduction
Primary lung cancer remains a very commonly diagnosed malignancy in adults and a major cause of cancer related deaths. In patients with primary non-small cell lung carcinoma (NSCLC), surgical resection remains the gold-standard therapy, however, curative surgery can only be offered in up to 20% of patients. The advantages of surgery in patients with metastatic lung disease have also been demonstrated, but more recently the debate over whether surgery truly affects prognosis has been reopened.

Medically inoperable patients with early stage primary disease have traditionally been treated with conventional external beam radiotherapy. However, the reported outcomes from this treatment have been poor. More recently, the emergence of stereotactic radiotherapy has improved outcomes (with lower toxicity than conventional techniques).

Percutaneous tumour ablation originally gained acceptance in the treatment of hepatic and renal tumours. Over the last decade, its use has progressively become more common in the treatment of lung tumours. Several ablative techniques have been developed including: ethanol ablation, laser ablation, radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation (CA) and irreversible electroporesis (IRE). The most commonly used and evidence based technique for lung tumour ablation in the UK is RFA.

Percutaneous ablation for lung tumours
Since the first report of the use of RFA in lung tumours at the turn of the century, RFA has gained an increased acceptance as an alternative to radiotherapy in selected non-operable cases principally owing to its efficacy, safety and low cost. The principle of action of this treatment hinges on electrical current flow (created by a voltage difference between two points around the tumour) heating the tumour and thereby producing coagulation necrosis and irreversible cell death. Impaired efficacy of RFA has been reported as a consequence of heat sink effect (dissipation of heat from lung parenchyma due to surrounding circulating blood or air).

Microwave and cryoablation are alternative thermal ablative techniques that may offer some advantages over RFA.

FIGURE 1
68-year-old female with lung cancer in the left upper lobe (figure 1A). This lesion was successfully treated with percutaneous CT-guided radiofrequency ablation. The two-month post-procedure scan demonstrates that the ablation zone is bigger than the original tumour (figure 2B) as would be expected. Over successive images the ablation zone shrinks consistent with completely treated tumour (figure 1C-H). Cavitation within the ablation zone is frequently seen, as a consequence of the tumour destruction (figure 1D).
although direct comparison between the techniques has yet to be reported. Microwave ablation utilises high frequency electromagnetic waves to induce kinetic energy in water molecules to produce tissue heating effects. This technique has been reported to create high temperatures in short periods of time and is less susceptible to the heat sink effect. Cryoablation produces cellular damage during cycles of tissue freezing and thawing. It is less destructive to collagenous tissue architecture and can be particularly beneficial when treating lesions adjacent to the tracheobronchial tree and mediastinum.

Irreversible electroporesis is a non-thermal ablative technique which uses direct electrical pulses to create permanent nanoscale defects (pores) in cell membranes that eventually lead to cell death. Precise probe positioning is fundamental for treatment success with IRE to avoid inhomogeneous deposition of the energy in the tumour. This technique does not suffer from the heat sink effect and is also reported to cause little or no collateral damage to adjacent structures.

The procedure (RFA)
Currently available RFA systems consist of three components: a generator (the source of electromagnetic energy); active electrodes (placed into the target tissue and depositing the energy); and grounding pads (to dissipate the return current). Generally in these patients, after formal consent, a low dose pre-procedure non-contrast CT scan is performed to confirm the final treatment plan. The patients are treated under conscious sedation or general anaesthetic. The probes are usually placed into the tumour using CT fluoroscopic guidance. Probe placement under direct vision has also been successfully used intra-operatively. Treatment is commenced and repeated (including repositioning of needles) until the entire planned treatment zone has been ablated. A post-procedure CT scan is performed to both confirm complete ablation and identify any complications.

Post procedure follow-up and imaging review
Computed tomography (CT)
CT scanning during and immediately after successful ablation can demonstrate a perilesional ground glass ‘halo’. It is important that this extends at least 5-10mm beyond the visualised border of the lesion to achieve a complete ablation. The ‘halo’ may not be seen in patients with emphysema, in which case surrogate markers need to be used to judge success (eg temperature and impedance changes).

The post-procedure ‘halo’ typically resolves within the first month after treatment. Normal post-ablation changes can include an increase in size of the ablation zone for one to three months or enlargement of loco-regional lymph nodes. These findings usually stabilise or decrease in size within six months.

Positron emission tomography (PETCT)
The destruction of the neoplastic cells reduces FDG uptake, producing a photopenic area on the PETCT image. Heat generated in the vicinity of the tumour as a result of ablation leads to local hyperaemia and inflammation, which can result in a homogeneous, predominantly low-grade FDG uptake in the periphery of the ablated tumour. The utility of PETCT to follow up patients has been widely reported; Deandreis et al stated that PETCT revealed a higher number of treatment failures than chest CT. In addition, Yoo et al concluded that six-month post-RFA PETCT findings correlate better with clinical outcome at one year than if earlier scans are performed.

Magnetic resonance imaging (MRI)
There are limited reports of the MRI appearances after percutaneous ablation of lung tumours. In our experience, central low signal intensity on T2-weighted imaging is usually associated with complete ablation. Peri-tumoural high signal corresponds to peripheral changes related to pulmonary congestion and inflammatory change in the surrounding lung.

Outcomes
Several studies have reported satisfactory results in the use of percutaneous radiofrequency ablation treatments in lung cancer patients, both primary and metastatic, positively affecting their prognosis.

Simon et al reported their survival rates in 75 patients with Stage I NSCLC. These were, for one to five years, 78%, 57%, 36%, 27% and 27%, respectively. Furthermore, the RAPTURE group of investigators reported overall survival in 33 patients with Stage I and II NSCLC as 70% at one year.
More recently, Zemlyak et al prospectively compared sublobar resection, RFA and CA in 64 NSCLC patients. They reported three-year survival for the surgical, RFA and CA groups was 87.1%, 87.5%, and 77%, respectively, which was not statistically different. The three-year cancer-specific and cancer-free survival rates, respectively, for the surgical, RFA, and CA groups were 90.6% and 60.8% versus 87.5% and 50% versus 90.2% and 45.6%, which were also not found to be statistically different. Though their patients were not randomised but instead clinically selected for each treatment, the authors showed that ablation can avail outcomes close to those of surgical resection.

Reported risk factors for local tumour recurrence in patients treated with RFA include: tumour size (>3cm), male gender, central tumour location, contact with a blood vessel (especially proximity to vessels larger than 3mm), contact with a bronchus and an estimated ratio of the ablation volume to the tumour volume of <3cm. However, it should be remembered that, owing to its low toxicity, RFA can be relatively easily repeated in cases of local recurrence or progression.

Ablative techniques have also been combined with more traditional cancer treatments. In lung tumours, the central hypoxic cells (mainly in necrotic tumours) can be resistant to radiotherapy; nonetheless these cells are susceptible to heat. For this reason, researchers have investigated potential synergistic actions between radiotherapy and RFA and have reported better survival using both treatments than either treatment on its own. However, at the time of writing no didactic studies have been completed to adequately investigate this.

Complications

The overall 30-day procedure specific mortality for CT-guided RFA has been reported to be up to 2.6%. The commonest reported complication is pneumothorax with an incidence of approximately 30%, with 5-15% of these requiring intercostal drainage. Zhu et al identified four risk factors for complications: greater than two lesions ablated; bilateral distribution of lesions; total ablation time of two hours or more; and length of probe trajectory greater than 3cm.

Complications rates have generally been translated between RFA and other techniques as few comparative studies have been reported. However, Carrafiello et al in a study of 29 patients reported an overall lower complication rate with MWA compared to RFA, with pneumothorax remaining the most common complication. In addition, cardiac arrhythmias have been reported to be induced during IRE as a result of the increase in cell membrane permeability caused by this technique. This may be avoided by ECG synchronisation.

Conclusion

Since the earliest reports of the use of lung tumour ablation, the technique has matured and has been considerably refined. In addition, the appearance of other energy delivery systems such as MWA, CA or IRE has opened new horizons. These treatments in experienced hands have been shown to have excellent outcomes. Further studies are required to augment our knowledge and help find the true role of ablation in lung cancer management.

References

10. Lu Q, Cao W, Huang L, Wen Y, Liu T, Cheng Q, Han Y, Li X. CT-guided percutaneous microwave ablation of pulmonary malignancies; results

**FIGURE 3**

69-year-old man with lung cancer in the right upper lobe (figure 3A). This patient was successfully treated with percutaneous CT-guided cryoablation. Notice the iceball formation during the ablation (arrow figure 3B). This finding suggests complete ablation of the lesion. Notice also the post-ablation changes three-months post-procedure (figure 3C).