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Imaging follow-up of RF ablation of lung tumours

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Abstract

Imaging is important in the decision-making process of how to treat a lung tumour, which ideally should be a multi-disciplinary team decision. Imaging is important during radiofrequency ablation (RFA) treatment with regard to optimal placement of the electrode, the immediate post-treatment criteria and very early detection of complications of the procedure. Imaging is very important in the treatment follow-up. In lung RFA, as in many other interventional procedures, the traditional morphological imaging techniques to evaluate treatment response have difficulties and functional imaging techniques may potentially be more useful. However, larger studies showing this impact have not yet been performed.

Keywords: *Radiofrequency ablation; lung tumour; imaging; lung cancer; pulmonary metastases.*

Introduction

Although surgical resection is the preferred treatment at the early stages and confers the best outcome, only a quarter of patients are diagnosed in the early stages of non-small lung cancer (NSCLC). Lobectomy is considered the standard of care in T1 N0 NSCLC due to a low rate of local recurrence compared with sublobar resection[1]. Other studies, however, have demonstrated that the 5-year survival rate in the sublobar resection group was equal to lobectomy[2,3]. The most common indication for sublobar resection in primary lung cancer is inadequate pulmonary reserve or comorbidities that contraindicate lobectomy.

Alternative local therapies such as radiofrequency ablation (RFA) and stereotactic radiation therapy may be attractive in this group of patients. The procedural mortality rate after RFA is 0.2% vs 1% after surgery[4] and lung function does not deteriorate with repeated procedures when RFA is performed. It has been demonstrated that lung function was similar before and after RFA[5,6].

Several retrospective studies have demonstrated a survival benefit after resection of pulmonary metastases[7–10]. In general, patients whose primary tumour is under control, with no extra pulmonary metastases, and who have a small pulmonary metastatic burden will benefit the most from surgical resection[11]. Currently, the major role of RFA in pulmonary metastases is the treatment of patients for whom surgical metastectomy would be ideal, but in whom comorbidities or technical issues render RFA more attractive.

Conventional treatment of inoperable or non-resectable lung tumours with systemic chemotherapy and conventional external beam radiation therapy has not been satisfactory in terms of survival outcomes[2].

In general, tumours of up to 3 cm in diameter and located in the periphery of the lung are the ideal candidates for RFA. The rate of complete ablation in tumours larger than 3 cm in diameter has been shown to be poor in several studies[13–16]. Biologic tissues heated to greater than $50°C$ for more than 5 min undergo coagulation necrosis. A temperature of $60–105°C$ is preferred for RFA. The area of coagulation is related to the strength of the radiofrequency energy, the current-carrying time, the diameter and shape of the electrode, and the composition of the surrounding tissues[17].

Both before, during and especially after RFA of a lung tumour, imaging is challenging, and this review focuses on some of these problems.

Pre-procedure management

Proper pre-procedural staging is important in patients with NSCLC or lung metastases as it will determine the best modality for treatment. Staging should include chest and abdominal computed tomography (CT) together with positron emission tomography (PET)/CT. Histopathological or cytological confirmation of the tumour should be performed. The decision of how to treat a lung tumour should ideally be made by a multi-disciplinary team.

RFA is performed with either a combination of local anaesthesia and conscious sedation or with general anaesthesia. The most frequently used imaging modality during RFA in lung tumours is CT. The patient is placed supine or prone in the CT scanner and the shortest, most vertical path that avoids bullae, interlobular fissures or pulmonary vessels is chosen. Tumour contact with a vessel of more than 3 mm in diameter is thought to create a heat sink effect that may render coagulation less successful. The relationship of the needle with the tumour must be assessed in 3 planes using image reconstructions. When expandable needles with multiple tines are used, it is important to assess the correct placement of the deployed tines before starting the ablation (Fig. 1).

Post-procedure management

In pathologic evaluation of microscopic tumour extension from NSCLC, Giraud et al.[18] found that 95% of microscopic extension of primary NSCLC would be encompassed in a margin of 8 mm for adenocarcinoma and 6 mm for squamous cell carcinoma. An RFA-induced area with ground glass is depicted in the RF ablated area immediately after the process and is easily seen on CT (Fig. 2). The ground glass area around the tumour represents inflammation and should be considered a safety margin of pulmonary parenchyma that has been covered by treatment. So the target diameter of an ablation must ideally be at least 1 cm larger than the diameter of the tumour that undergoes treatment[19,20]. Anderson et al.[19] proposed ground glass as an early indicator of treatment success after percutaneous RFA, and demonstrated that the point on the tumour surface where there is no ground glass margin is likely to be the site of future recurrence.

Tumour size and location has been linked to the rates of local tumour progression for lesions treated with RFA[13]. A tumour size of less than 3 cm is associated with higher rates of complete tumour necrosis[13,21].

After the procedure is completed a CT scan of the chest is obtained to detect pneumothorax, pleural fluid collection and haemorrhage. The procedure-related
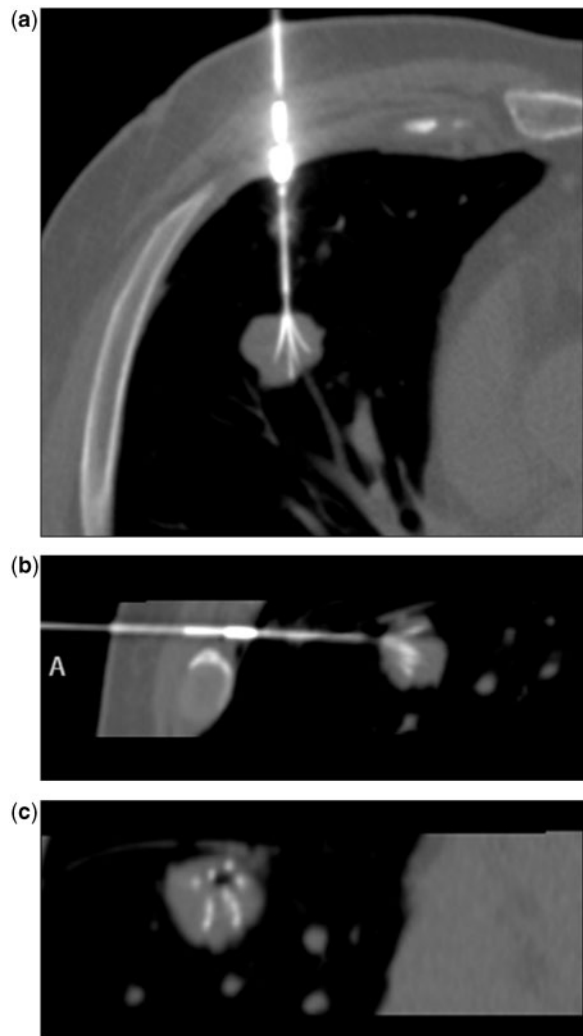
Figure 1 **RFA ablation is most often performed using CT as the modality of choice for guidance of placement of the RFA electrode. The relationship of the electrode needle with the tumour must be assessed in 3 planes: (a) axial, (b) sagittal, (c) coronal, and when needles with multiple tines are used, it is crucial to check the correct placement of the deployed tines before starting the ablation.**

mortality rate is as low as 0.21% when 2905 ablations are considered[4]. The prevalence of pneumothorax (Fig. 2) was 28.3%, with 14.4% (range 0.0–63.2%) requiring aspiration or a chest drain[4]. Pleural effusions are often seen. However, the incidence of pleural effusions that need to be drained is in the order of 1 and 7%[22–24]. Immediate self-limiting parenchymal haemorrhage occurs in 7–8% of the procedures[19]. Other complications reported are haemoptysis[4], which usually does not require intervention, and infections[10,13]. Although the production of air micro-embolisms that pass from the pulmonary vein to the systemic circulation has been described, this phenomenon probably does not cause cerebral ischemia[17].

Figure 2 **Post-procedure imaging ensuring that the tumour is surrounded by a circumferential area of ground glass of 1 cm is ideal, as areas of an ablated tumour with a small rim of ground glass are associated with future recurrent disease. In this case a sufficient area of ground glass is displayed. Note that a small pneumothorax is also visualized.**

Follow-up imaging

Accurately monitoring treatment response and early identification of residual or recurrent disease are critical for optimizing the effect of treatment. The crucial question for imaging follow-up is whether there is residual or recurrent viable tumour[23,24]. Response Evaluation Criteria In Solid Tumour (RECIST)[25] is a widely accepted system that allows objective measurement of treatment response to chemotherapy. This system is based on changes in the diameter of the lesion either by CT or magnetic resonance imaging (MRI). When RFA of lung tumours is considered, the RECIST system is suboptimal to evaluate a response, as it cannot differentiate viable from non-viable tumour or adjacent devitalized tissue[25]. As the purpose of an appropriate RFA ablation of a lung tumour is to cause a coagulation necrosis larger than the initial lung tumour, measurement of diameter is not appropriate[26]. Contrast enhancement of the lesion can also be monitored, however hyperaemia and inflammation in the ablation zone may mask contrast enhancement of underlying residual tumour as reported by Anderson et al.[19] This group suggests that both size and enhancement of the ablated zone should be analysed to fully assess for residual tumour. As the tumour ideally becomes larger after a successful ablation, it has been recommended that a new baseline CT scan is performed 1 or 3 months after the ablation procedure[5,26]. In Fig. 3
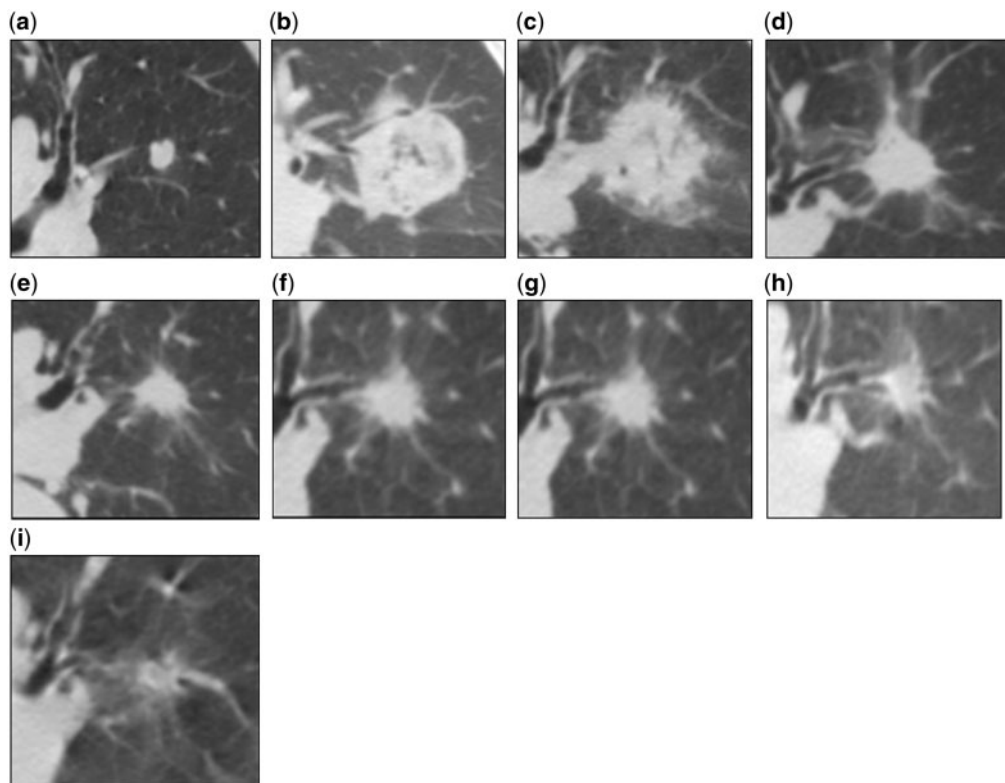
Figure 3 **The tumour size assessed by CT is larger than the volume of the tumour before ablation for a long time period. Most authors recommend a 1- or a 3-months baseline scan to follow up the success of treatment. From this time point the tumour size on CT has to decrease if the ablation is successful as in this case.**
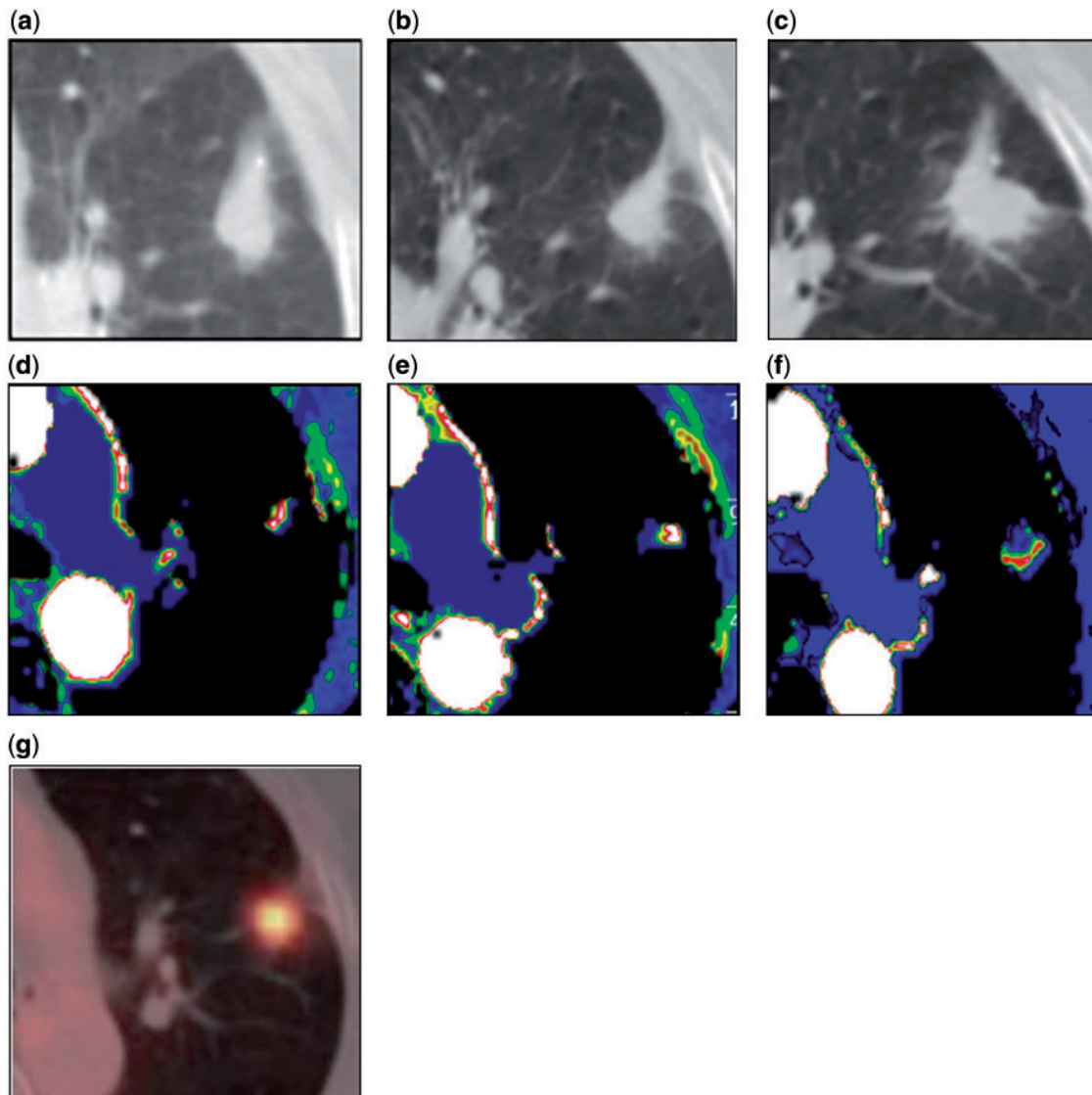
Figure 4 **This figure illustrates a patient with recurrent disease 24 months after ablation shown by traditional morphological measurements suggesting growth of a part of the tumour (c), perfusion CT (f) and PET/CT (g) and histopathology. The perfusion CT at 12 months (d) already indicates areas of perfusion probably indicative of recurrent disease, the amount of perfusion increased at the 18-month scan (e) and at the 24-month scan (f). No tumour growth is seen on the CT scans at 12 months (a) and 18 months (b). The perfusion CT (d–f) is displayed as the 5-mm slice in which most perfusion is shown.**

it is obvious that the lung lesion in a successful ablation grows during the first months and afterwards decreases in size. Different ways of interpreting contrast enhancement have been suggested[5,15,22,27,28]. One group found that the area of recurrent disease most often showed some degree of contrast enhancement. Cavitation of the tumour is seen in up to 1/3 of ablations[16]. The cavity usually resolves without further therapy. No stringent rules for the assessment of tumour response after RFA of a lung tumour exist. The features most commonly used to identify remaining viable tissue are tissue enhancement and nodular growth on serial images (Fig. 4).

In a large review[4], local recurrence was seen in 12.2% after a mean period of 13 months (range 3–45 months). So follow-up imaging is needed for a long time (Fig. 4). Although no clear follow-up program exists, most authors perform contrast-enhanced CT at 1, 3, 6, 9, 12 months and then every 6 months following RFA.

New imaging techniques may provide an opportunity for improved assessment of the post-therapy tumour bed. These techniques include diffusion-weighted MRI, CT and MR perfusion and PET[29–31]. Several retrospective[14,21,32,33] and one prospective study[25] evaluating PET/CT in the follow-up after RFA of lung tumours have been published. These studies in general suffer

from a small number of patients, methodological problems due to retrospective design, a short and inhomogeneous time of follow-up and a suboptimal standard reference. However, it seems that (1) a large decrease in the standardized uptake value in the post-RFA FDG-PET, (2) a certain pattern of FDG uptake and (3) FDG uptake in the region around the original tumour indicating inflammation, are predictors of a successful ablation. Probably FDG uptake may detect residual or recurrent disease earlier than CT.

To our knowledge, only one study[36] has evaluated diffusion-weighted MRI in a small number of patients in a retrospective design. Diffusion-weighted MRI performed 3 days after RFA showed reduced signal intensity and increased apparent diffusion coefficient values of the ablated lesions compared with pre-procedure tumour tissues.

Functional imaging probably will contribute in the work-up of treatment evaluation of lung tumour RFA (Fig. 4). However, large prospective and well-conducted studies are warranted. Other image interpretation tools such as texture analysis[37] may be useful in the follow-up of lung tumour ablation.

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