REVIEW ARTICLE

Modern diagnostic and therapeutic interventional radiology in lung cancer

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ABSTRACT Imaging has an important role in the multidisciplinary management of primary lung cancer. This article reviews the current state-of-the-art imaging modalities used for the evaluation, staging and post-treatment follow-up and surveillance of lung cancers, and image-guided percutaneous techniques for biopsy to confirm the diagnosis and for local therapy in non-surgical candidates.

KEY WORDS Lung neoplasms; computed tomography (CT); positron emission tomography (PET)/CT; magnetic resonance (MR) ; biopsy; ablation

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Introduction

Imaging has an important role in the multidisciplinary management of primary lung cancer, and is necessary to establish the diagnosis; localise, characterise and stage the tumour; map relevant nodal, vascular and bronchial anatomy for treatment planning; and for surveillance of treatment efficacy and development of metachronous tumours. Image-guided treatment of primary lung cancers can be performed in select cases. This article reviews the imaging modalities currently used for the evaluation of lung cancers, and discusses image-guided percutaneous interventional techniques for histopathologic diagnosis and local tumour treatment. Lung cancer screening is beyond the scope of this article.

Imaging modalities

Computed tomography (CT) is the imaging modality of choice for the initial evaluation of suspected or proven lung cancers. Positron emission tomography (PET)/CT is the most accurate imaging modality for the staging of primary lung cancers. Magnetic resonance (MR) imaging is useful for evaluation of superior sulcus (Pancoast) tumours and suspected malignant invasion of the chest wall, mediastinum or spine. The current recommended imaging required for lung cancer staging is CT scan of the thorax and PET/CT from skull base to mid-thigh (1).

Computed tomography

Advanced CT scanners permit a high-resolution, comprehensive evaluation of the entire chest in a single breath-hold lasting several seconds with an improved radiation dose profile to generate an isotropic dataset that allows detailed anatomical assessment as well as functional assessment of lung cancers. Radiation dose reduction is achieved by utilising automatic tube current modulation and iterative reconstruction techniques, which enable a CT examination to be performed either at a reduced dose with a similar image quality or at the same dose with improved image quality (2,3). Improved detection of small lung tumours is achieved by rapid acquisition and new visualisation techniques. Rapid acquisition reduces respiratory and cardiac motion artefacts that allow more accurate depiction of lung nodules, especially in the lung bases and in the para-cardiac lung. New visualisation techniques, such as maximum intensity projection, volume rendering, stereographic display and computer-aided detection, enhance lung cancer detection and enable the reader to differentiate small lung nodules from vessels (4). Isotropic dataset acquisition permits easy multiplanar reconstructions, including high-resolution angiograms and three-dimensional reconstruction of vascular and bronchial anatomy, for surgical or percutaneous interventional planning.

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Staging

Despite recent advances in CT technology, lung cancer staging with CT remains suboptimal but is routinely performed because it remains excellent for local staging of T1 and T2 tumours, is able to delineate T3 and T4 tumours, guides selection of the most appropriate lymph nodes and the invasive technique for nodal sampling, and allows triage of patients to non-surgical therapy when unequivocal distant metastases are present. Limitations of CT for staging include accurate detection of early mediastinal and chest wall invasion, mediastinal staging and detection of small extrathoracic metastases. With regards to local tumour extent, differentiation between absent, minimal and gross T3 and T4 disease is of critical clinical significance as it determines whether the tumour is completely resectable and the surgical approach (5). The utility of thin-section CT has not significantly improved the detection of malignant invasion of the parietal pleura. One study of 90 patients using a 4-detector CT showed sensitivity, specificity and accuracy of 42%, 100% and 83%, respectively, for the detection of chest wall invasion (6). Another small study using a 4-detector CT showed the use of multiplanar reconstructions can improve the sensitivity, specificity and accuracy of CT to 86%, 96% and 95%, respectively, for the detection of chest wall invasion (7). With regards to malignant nodal involvement, a recent meta-analysis showed a pooled sensitivity and specificity of 55% and 81%, respectively, for the detection of malignant mediastinal lymph nodes when a widely accepted definition of normal-sized lymph nodes of a short-axis diameter of ≤1 cm on a transverse CT scan image is used to differentiate benign from malignant lymph nodes (8). These results show that nodal size criterion alone is insufficient for the accurate detection of nodal metastases because metastases to normal-sized lymph nodes are missed and enlarged lymph nodes can be reactive or hyperplastic in aetiology. Recent studies suggest that evaluation of nodal morphology and CT enhancement pattern can improve the accuracy of CT for the detection of nodal metastases in lung cancer (9,10). With regards to distant metastases, CT is inferior to PET/CT for detection of extrapulmonary metastases with an accuracy of 88% compared to 97% with PET/CT (11). To our knowledge, there has been no study that examined the accuracy of CT for lung cancer staging using CT scanners with more than 16-detector rows.

Post-treatment evaluation and surveillance

There is currently no consensus on the optimal follow-up and surveillance programme for patients with proven lung cancers. CT has been recommended for the routine evaluation and surveillance of patients who have undergone therapy with curative-intent for non-small cell lung cancer (NSCLC), but routine imaging surveillance is not recommended in asymptomatic patients with advanced lung cancer who are not undergoing therapy (12-14). CT evaluation of response to treatment is usually dependent on morphologic changes in tumour and nodes. However, morphology is not a good indicator of early response to treatment and a positive response can be manifested as a delayed reduction in size or paradoxical increase in size (15). CT can be effective for post-treatment surveillance with one study showing CT detected 93% of new lung cancers and 61% of recurrences in a cohort of over 1,000 patients after resection of early-stage NSCLC (16).

New developments

Recent advances in CT technology have allowed investigation of novel methods for the evaluation of lung cancers including nodule volumetry, nodule perfusion analysis, dual-energy applications and computer-aided detection. Quantitative analysis of lung nodules by assessment of a nodule's volume can be performed using semi-automated or automated segmentation tools that allow assessment of nodule stability or progression over time. The rate of growth of a nodule is a predictor of the likelihood of malignancy, and volumetric analysis can be used to predict tumour response to treatment (17). CT perfusion analysis of nodules may allow better characterisation of the nodule in order to determine likelihood of malignancy as well as earlier determination of treatment response compared to morphologic change in size (18,19). The likelihood of malignancy is considered low when contrast uptake is below 30 Hounsfield units (HU) (20). Dual-energy CT is a technique that allows differentiation of iodine from other materials, such as soft tissue and bone, due to iodine's stronger photoelectric absorption (21). This method allows visualisation of the degree and pattern of enhancement within a mass following contrast-enhanced CT. One study showed that the degree of enhancement within a pulmonary nodule can be used to differentiate benign from malignant tumours with a sensitivity, specificity and accuracy of 92%, 70% and 82%, respectively (22). In another study, moderate correlation was found between the maximum iodine attenuation and SUV_{max} in thoracic nodes in patients with NSCLC, but poor correlation in those patients with small cell lung cancer (23). The authors suggest that moderate correlation in NSCLC could be explained by moderate specificity of PET for determination of malignant nodes, and the difference in correlation seen with NSCLC compared to SCLC due to differing tumour biology such as angiogenic ability.

Positron emission tomography

Solitary pulmonary nodule

PET with F-18 deoxyglucose (FDG) is a useful technique

for the characterisation of pulmonary nodules to distinguish between benign and malignant lesions. Two meta-analyses showed the sensitivity and specificity of FDG-PET for the diagnosis of malignant pulmonary nodules were about 96% and 80%, respectively (24,25). The significance of a PET-positive result is dependent on the clinical context and the prevalence of granulomatous and infectious disease, which are recognised causes of false positive PET results. False negative results can occur in small (<10 mm) nodules due to partial volume effect or the effect of respiratory blurring, or in some subtypes of lung malignancy with a low intrinsic FDG avidity, such as adenocarcinoma in situ. On a practical level, a PET-positive study often implies that biopsy or intervention is warranted to obtain pathological confirmation (26), while a PET-negative study may allow conservative approach and avoidance of unnecessary invasive procedures (27). There is evidence that the use of FDG-PET is cost-effective in the management of solitary pulmonary nodules (28,29).

Staging

PET is the most accurate imaging modality for the assessment of nodal and distant metastases from lung cancer, which is vital for treatment planning. PET has been found to be more accurate than CT in the staging of mediastinal nodal disease in many clinicopathological studies, including two meta-analyses that showed the sensitivity and specificity of PET was 79-85% and 90-91%, respectively, compared to 60-61% and 77-79% for CT (30,31). The accuracy of nodal assessment is further increased with PET/CT, which has an excellent negative predictive value of 91% in the mediastinal assessment of early-stage disease (32,33). Despite the high accuracy of PET/CT in nodal staging, there remains a significant false positive rate that is more common with larger (>1 cm) nodes, which is often due to reactive or granulomatous nodal disease (34). With the increased availability of minimally invasive mediastinal nodal sampling procedures, such as endobronchial ultrasound and endoscopic ultrasound, it is imperative to obtain pathological confirmation of PET-positive nodes before denying surgery to patients with potentially curable disease (35,36). PET is the imaging modality of choice in the assessment for distant metastases of lung cancer due to its whole body imaging capability and high tumour to background contrast which allows superior detection of both osseous and soft tissue metastases (37-39). There is a significant incidence of unrecognised distant metastatic disease when staging with conventional CT and bone scintigraphy. One study showed distant metastases were only identified with PET in 7.5%, 18% and 24% of stage I, stage II and stage III disease, respectively (40). Up to 20% of patients who are thought to be operable when staged with conventional imaging are found to be inoperable following PET and, therefore, PET is considered essential prior to curative treatment to avoid unnecessary futile surgical intervention (41,42). PET/CT has been shown to be superior to standalone PET or CT in the detection of distant disease mainly due to the ability of PET/CT to obtain anatomical correlation to reduce false positive PET interpretation of physiologic uptake in normal structures (43). A recent meta-analysis showed PET/CT was significantly superior to PET, MR imaging and bone scintigraphy for the detection of bony metastases with a pooled PET/CT sensitivity and specificity of 92% and 98%, respectively (44). Given the high background FDG uptake in the brain, FDG-PET is not the optimal imaging modality for the exclusion of cerebral metastases, which should be evaluated by MR imaging when clinically indicated (45). The availability of both functional and structural information on PET/CT also facilitates the selection of stage critical lesions for biopsy to allow pathological confirmation. The use of PET and PET/CT is cost-effective in the staging of NSCLC (46-48) with a recent randomised clinical trial showing cost savings of 899 Euro per patient and 4,495 Euro per avoided thoracotomy (49). There is also a strong correlation between PET-stage and survival in both surgical and radical radiotherapy candidates which suggests that PET provides prognostically significant information (50,51).

Radiotherapy planning

FDG-PET and PET/CT have been found to have a critical role in patient selection and target volume definition in patients with locoregionally advanced NSCLC considered for curative or radical radiotherapy. Radical radiotherapy is given with curative intent to non-surgical patients with gross locoregional tumour that can be encompassed by high-dose radiation in the absence of distant disease (52). A number of prospective studies investigating the utility of PET in the staging of potential candidates for radical radiotherapy found 25-30% of the patients were unsuitable for radical treatment owing to the presence of more advanced disease that was not shown on conventional imaging (53-55). PET-assisted radiotherapy treatment volume contouring has been found to be more accurate and significantly different from conventional treatment volumes, and a change in radiation volume was found in more than 30% of the patients (53,56,57). Survival benefit has also been shown with PET/CT-assisted radical radiotherapy. In one study, the 4-year survival of stage IIIA patients managed with PET/CT-assisted radical radiotherapy is 32%, which is superior to outcome with CT-assisted radical radiotherapy (58).

Post-treatment evaluation

A prospective study of 73 patients comparing FDG-PET with CT for the assessment of response following radical radiotherapy and chemoradiation of NSCLC showed significantly more complete

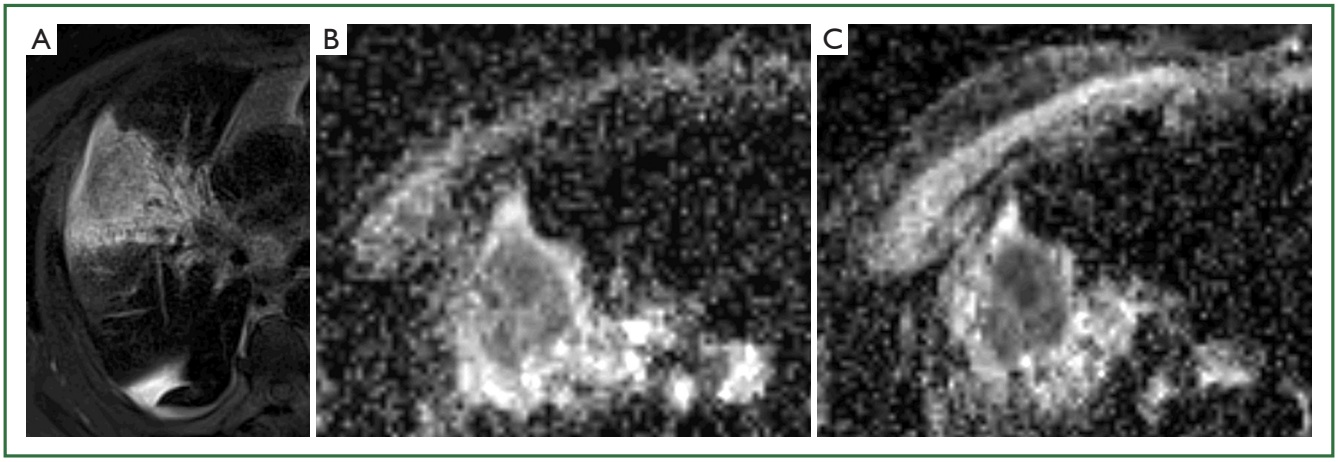

Figure 1. A 71-year-old man with Stage III NSCLC in the right upper lobe. A. Axial T2-weighted MR image shows a heterogeneous T2 hyperintense mass with surrounding atelectasis; B, C. Axial ADC diffusion images before (B) and 24 hours after (C) starting chemotherapy show reduced ADC signal intensity in tumour following treatment.

responders on PET (34 patients) than CT (10 patients). PET response was more predictive of survival duration than CT response, and is the only prognostic factor associated with survival duration on multifactor analysis (59). A more recent paper also reported a high metabolic tumour volume post definitive treatment for NSCLC was an independent poor prognostic factor (60). FDG-PET has also been found to provide prognostically significant response assessment in NSCLC patients undergoing induction chemotherapy. In a prospective study involving 31 patients with stage III unresectable disease, complete response on PET was more accurate than response on CT, and PET showed superior correlation with longer time to progression and overall survival (61). The ability of FDG-PET to provide superior prognostic information has also been reported in the setting of induction chemotherapy prior to surgical resection or chemoradiation, and there may be a role of PET in treatment selection and planning (62,63).

Magnetic resonance imaging

Modern MR techniques have overcome the principal problem of magnetic field inhomogeneities due to the numerous air-soft tissue interfaces when imaging the lung as well as artefacts associated with cardiac and respiratory movement to produce diagnostic images. The utility of MR for the diagnosis, staging, radiotherapy planning and post-treatment evaluation in lung tumours is under-utilised and has been investigated at only a few centres. The sensitivity, specificity, positive predictive value and negative predictive value of MR for the detection of lung carcinoma and non-calcified lesions greater than 5 mm are close to 100% (64). Therefore, MR can potentially be used for lung cancer screening, but to our knowledge, there are no prospective trials investigating the utility of MR for this purpose (65,66). MR imaging with diffusion-weighted imaging (DWI) can be used to predict benignity of pulmonary lesions. One prospective study of 66 patients showed DWI had a sensitivity, specificity and positive predictive value of 95%, 73% and 87%, respectively, for the diagnosis of a malignant lesion (67).

In current clinical practice, MR imaging is primarily used for the assessment of suspected chest wall or mediastinal invasion by lung cancer due to the superior soft tissue contrast resolution of MR. Comparative studies between MR and FDG-PET/CT have shown the two techniques to be equivalent for staging NSCLC (68-70). The strength of MR is in the detection of cerebral and hepatic metastases, while PET/CT is better at nodal staging. A recent prospective study showed MR imaging with DWI was superior to PET/CT for the detection and nodal assessment of NSCLC (71). MR also allows differentiation of viable tumour from necrotic tumour and atelectasis, and is helpful in radiotherapy planning (72). Post-treatment tumour response has been investigated using MR techniques such as magnetization transfer, blood oxygen level dependent MR, and perfusion and diffusion imaging. Dynamic contrast-enhanced perfusion allows assessment of tumour angiogenesis, which has the potential to predict chemotherapy response in NSCLC patients, but its use is unproven for monitoring of anti-angiogenic therapy (73). MR perfusion can also be used for prediction of postoperative lung function (74). With regards to DWI, the apparent diffusion coefficient (ADC) measures the magnitude of diffusion of water molecules within tissue. Cell swelling or shrinkage is reflected in changes in ADC values. In general, an initial decrease in tumour ADC measurement performed within 30 days of treatment (Figure 1), and an increase in tumour ADC measurement 30 days following treatment were found to be predictive of a positive

outcome, and our own unpublished data support similar findings (75,76).

Image-guided percutaneous interventions

Image-guided percutaneous biopsy can be performed for confirmation of diagnosis and treatment planning. In non-surgical candidates, image-guided percutaneous therapy can be performed with curative-intent or for palliation, and these techniques include cryoablation, radiofrequency ablation and microwave ablation.

Percutaneous biopsy

Percutaneous needle core biopsy is a minimally invasive procedure that can be used to confirm the diagnosis of lung malignancy. The most common complications are pneumothorax and bleeding. A higher risk of pneumothorax has been reported to occur with biopsy of smaller lesions and deeper lesions. Biopsy of lesions less than 2 cm in size is associated with an 11 times greater risk of pneumothorax than lesions greater than 4 cm, and this may be explained by the prolonged procedure time required to successfully biopsy smaller lesions (77). This study also showed that the risk of a pneumothorax is negligible for lesions abutting the pleura because the needle does not need to cross aerated lung, but there is a seven-fold increase in the rate of pneumothorax for biopsy of lesions less than 2 cm from pleura and a four-fold rate for lesions greater than 2 cm (77). Hence, the authors advocated a longer oblique needle path for biopsy of sub-pleural nodules to minimise pneumothorax risk, but a different study suggested that a smaller needle-to-pleura angle increases the risk of a pneumothorax (78). Other potential factors for the higher risk of a pneumothorax when lesions less than 2 cm from the pleura are biopsied include multiple punctures and difficulty anchoring a heavy hub cutting needle. A higher risk of pneumothorax following biopsy in patients with obstructive pulmonary disease has been reported in some studies (78,79), but other studies did not find this association (77,80,81). Factors that were not associated with an increased risk of pneumothorax include biopsy of cavitary lesions, biopsy needle size and patient positioning following biopsy (77). Bleeding is the second most common complication of percutaneous lung biopsy, and the two main predisposing factors were lesion size and distance of lesion from the pleural surface. A six-fold increase in bleeding was shown for lesions less than 2 cm in size compared to those greater than 4 cm in size, and lesions greater than 2 cm from the pleura have a ten-fold bleeding risk compared to those abutting the pleural surface (77,82). The presence of a pleural effusion on the side of the biopsy was associated with a decreased risk of bleeding and was found to be an independent risk factor for bleeding following biopsy (77).

Cryoablation

Cryoablation is a percutaneous minimally invasive technique used for the treatment of lung tumours in non-surgical candidates. Cryoablation causes coagulative necrosis of tumour cells and its vasculature. During cryoablation, a 2 to 3 cm rim of normal tissue surrounding the lesion should be ablated to achieve a margin of safety. The cryoablation probe is introduced into the tumour and cooled to –40 ℃ for about 10 minutes, then thawed for 8 minutes and then cooled once again for a further 10 minutes. Ice formation around the probe disrupts cell membrane function and enzymes, and creates a relative hypertonic extracellular environment causing intracellular dehydration by osmosis. The rapid return of water into the cell during the thawing process causes cell lysis. Direct damage to small (<3 mm) vessel walls and vessel stasis supplying the tumour may also play a role in tumour destruction (83). There is limited long-term outcome data for lung tumours treated with cryoablation. A Japanese series of 20 patients with 35 treated lesions followed for a median of 28 months showed a local recurrence rate of 20% (84). Another study investigated patients with stage I NSCLC who were unsuitable for standard surgical resection, and showed a 3-year survival rate of 77%, 88% and 87% when treated with cryoablation, radiofrequency ablation (RFA) or sublobar resection, respectively (85). Although cryoablation is comparable to other ablative techniques for the management of non-surgical candidates with lung cancer, longer term follow-up data are required to determine its role in the management of lung cancers.

Radiofrequency ablation

RFA is a technique that involves the placement of an electrode into tissue to cause focal destruction with thermal energy, which is generated by friction secondary to oscillating tissue ions that occur when an alternating electric current in the frequency of 460-500 kHz (radio waves) is applied. Heating tissue to 50 ℃ for at least 5 minutes causes cells to undergo coagulative necrosis. Therapeutic RFA aims to heat tissues to 60-100 ℃, which leads to near instant cell death through protein denaturation (86). Pulmonary lesions are ideal for RFA because air in lung parenchyma surrounding the lesion provides thermal insulation to allow concentration of the applied radiofrequency (RF) energy within the lesion. Non-surgical candidates or patients who refuse surgery are potential candidates for RFA and the decision to treat with RFA should ideally be made in consultation with the interdisciplinary pulmonary tumour board. The most suitable lesions for RFA are less than 3 cm in size, and patients with stage I NSCLC are ideal candidates. Reported long-term survival rates after RFA of stage I NSCLC at 1, 2, 3, 4 and 5 years are 78%, 57%, 36%, 27% and 27%, respectively (87).

RFA in combination with conventional radiotherapy has been used to treat inoperable lung tumours because hypoxic cells in the centre of tumour respond poorly to radiotherapy alone. A study showed cumulative survival rates of 50% and 39% at 2 and 5 years, respectively, following combined RFA and conventional radiotherapy for stage I NSCLC (88), and dual therapy achieves better local tumour control and patient survival compared to radiotherapy alone (89). Furthermore, RFA can be used to treat small slow growing pulmonary metastases (90) and to palliate patients with larger tumours that cause chest pain, dyspnoea, cough or haemoptysis (87). RFA of larger tumours often requires multiple overlapping ablations to ensure satisfactory tumour coverage, and recurrence rates tend to be higher in larger tumours than with smaller tumours (87,89).

Microwave ablation

Microwave ablation (MWA) represents the most recent addition to the growing armamentarium of minimally invasive thermal ablation therapies for the nonsurgical treatment of lung malignancies (91). Microwaves are electromagnetic waves with a frequency range that extends from 300 MHz to 300 GHz. However, microwave generators for clinical use operate at frequencies of 915 MHz or 2.45 GHz (92). Microwaves agitate water molecules, which are small electric dipoles, in the target tissue, and they spin between 2 and 5 billion times per second in an attempt to follow the rapidly alternating electric field (92,93). This leads to heat generation through friction. Conduction and convection allow further tissue heating beyond the directly agitated water molecules (94). Temperatures thus generated, usually in excess of 100 ℃, lead to almost instantaneous irreversible cell damage. The centrifugally growing coagulation necrosis around the active tip of the microwave antenna is spherically shaped. It should ideally encompass the target tumour and a circumferentially surrounding safety margin (Figure 2). This safety margin, ideally at least 6 mm in thickness, is necessary to destroy tumour cell nests and satellite foci in the immediate periphery of the tumour not perceivable on cross-sectional imaging. A smaller safety margin carries a higher risk for local recurrence (95).

Advantages of MWA over RFA

There are several advantages of microwave over RF energy. RF heating requires an electrical conduction path and is, therefore, less effective in areas of low electrical conductivity and high baseline impedance, such as lung parenchyma. This results in heating of the target tissue only immediately adjacent to the RF electrode (96,97). Microwaves are capable of propagating through many types of tissue and effectively heating them, even those with low electrical conductivity, high impedance or low thermal conductivity (98). Unlike RF and laser, microwaves can penetrate through the charred or desiccated tissues that build up around all hyperthermic ablation applicators which result in limited power delivery for non-microwave energy systems (99). Multiple microwave antennae can be simultaneously powered to maximise the ablation volume when placed in close proximity to each other, or when widely spaced, to simultaneously ablate several tumours, such as multiple pulmonary metastases (95). Larger and more homogeneous ablation volumes can be achieved with MWA because the rapid heating with MWA results in less susceptibility to heat sink effect (92). Further advantages of MWA over RFA include no requirement for grounding pads which avoids potential pad site burns, and implanted cardiac devices are less prone to malfunction (100,101).

Detailed histopathological assessment of microwave ablated lesions has confirmed the concentric layered ablation zones post RFA described by Clasen *et al.* (102). The central inner necrosis is surrounded by an intermediate zone of equally irreversibly destroyed tissue corresponding to the safety margin strived for. The outer zone of ground glass opacity encompasses a haemorrhagic ring, which in turn is surrounded by oedema and a lymphocytic infiltrate (103). In these outermost layers, there was only partial thermal cell destruction seen with RFA (102). Vital histochemical nicotinamide adenine dinucleotide staining of resected lung tumours which have undergone intra-operative MWA immediately prior to resection confirmed cellular death (because of a lack of mitochondrial enzymatic activity) in a much larger ablation zone (104). No viable cells could be detected within five of the six ablation zones; uniform cellular death was shown to extend through sharp well-demarcated transition zones separating viable and nonviable ablated cells (104).

Patient selection and method

Patients selected for MWA are usually deemed medically inoperable. Exclusion criteria for MWA include uncontrolled primary tumour, radiologic evidence of lymph node metastases, extrathoracic spread, infiltration of the chest wall, mediastinal structures, main bronchi or main pulmonary arteries, sepsis and irreversible coagulopathy (94,105). Patients who have undergone prior surgery (including pneumonectomy), chemotherapy or radiotherapy are usually not excluded. Some patients may have resectable tumours, but have declined surgery. The patient is positioned in the CT scanner that allows the shortest and safest access route to the tumour. Crossing of fissures should be avoided whenever possible. The skin is prepped and draped as usual, and local anaesthetic is infiltrated along the needle tract. A short cut into the skin allows for a smooth passage of the antenna. Under visual guidance, preferably CT fluoroscopy, the antenna is advanced in a stepwise manner into the tumour. Calcified pleural plaques and cartilage

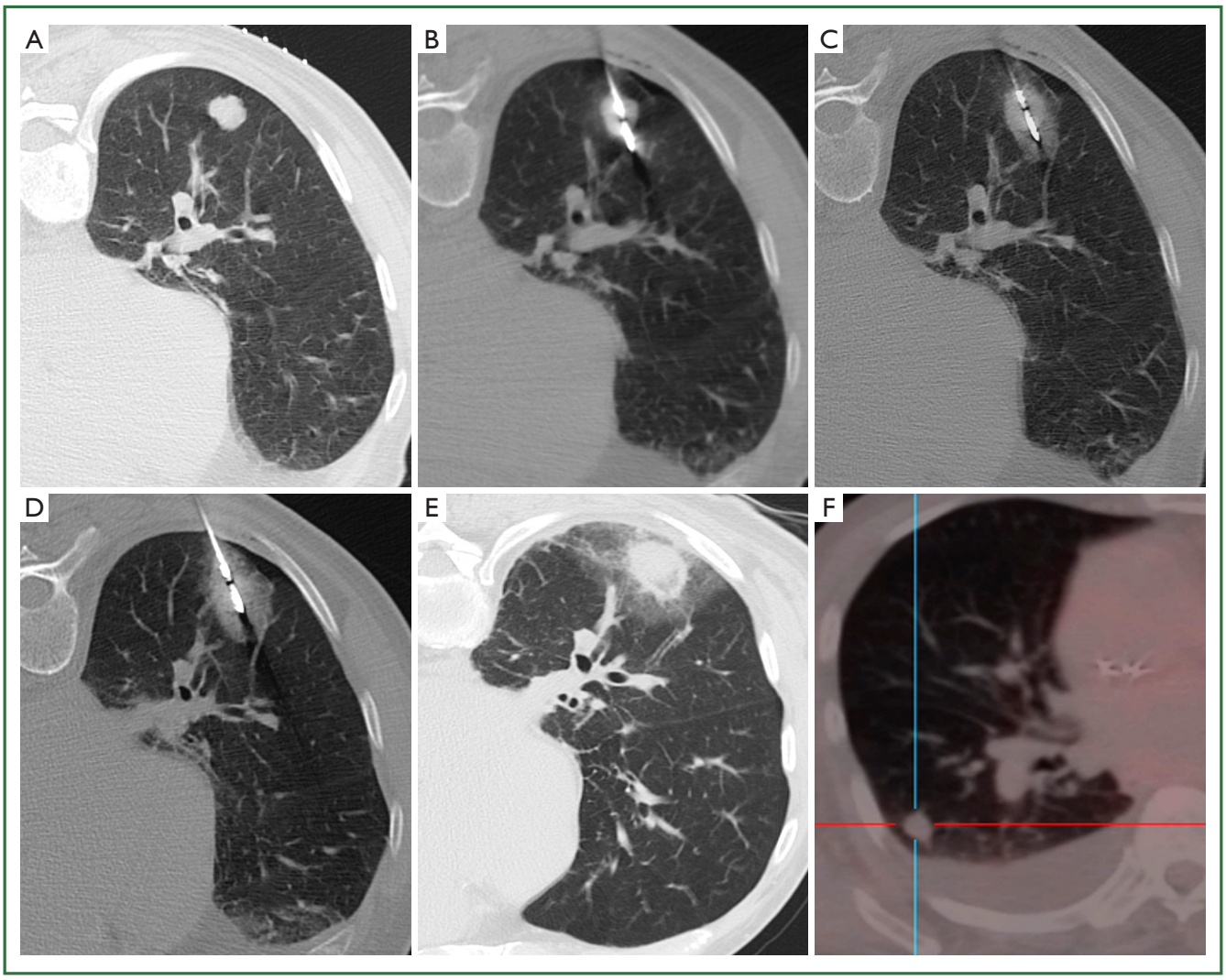

Figure 2. A 70-year-old man with cardiomyopathy and new solitary melanoma metastasis to the right lower lobe. A. Prone axial CT image shows a lobulated 1.6 cm tumour; B. The feed point of the microwave antenna is positioned within the centre of the tumour; C, D. At 5 minutes following the start of ablation (C), there is ground glass opacity forming mainly on the far edge of the tumour, and at 10 minutes (D), a 3-10 mm circumferential rim of ground glass opacity has formed around the tumour; E. At 3 hours following ablation, there is marked (>1 cm) circumferential ground glass opacity around the tumour; F. Axial FDG-PET/CT image 6 months following MWA shows complete lack of FDG uptake at the site of tumour, indicating eradication of tumour. New cardiac-related pleural effusion is present.

should be avoided because the fragile microwave antenna is at risk of fracture if forced through rigid tissue (106). Conscious sedation or general anaesthesia can be used with no difference in complications and outcome between the two modalities (107). Single ablation duration depends on tumour size, location and power capacity of the generator, but usually does not exceed 20 minutes. It is advisable to perform a limited CT scan during the ablation cycle to identify any displacement of the antenna from its original position or early complications. Only a few centres routinely administer prophylactic antibiotics for the procedure (108). Immediate post-procedural recovery includes continuous monitoring for pulse and oxygen saturation, and blood pressure measurements taken every 15-20 minutes. Other observations are performed as per the hospital's policy. A baseline chest radiograph is performed 3 to 4 hours following the ablation. In most centres, patients are hospitalised after the procedure and discharged the following day provided no complications have occurred. In principle, the procedure can be performed on an outpatient basis, but it is recommended to observe them overnight because of the potential for delayed complications.

Complications

Complications resulting from ablation procedures should be

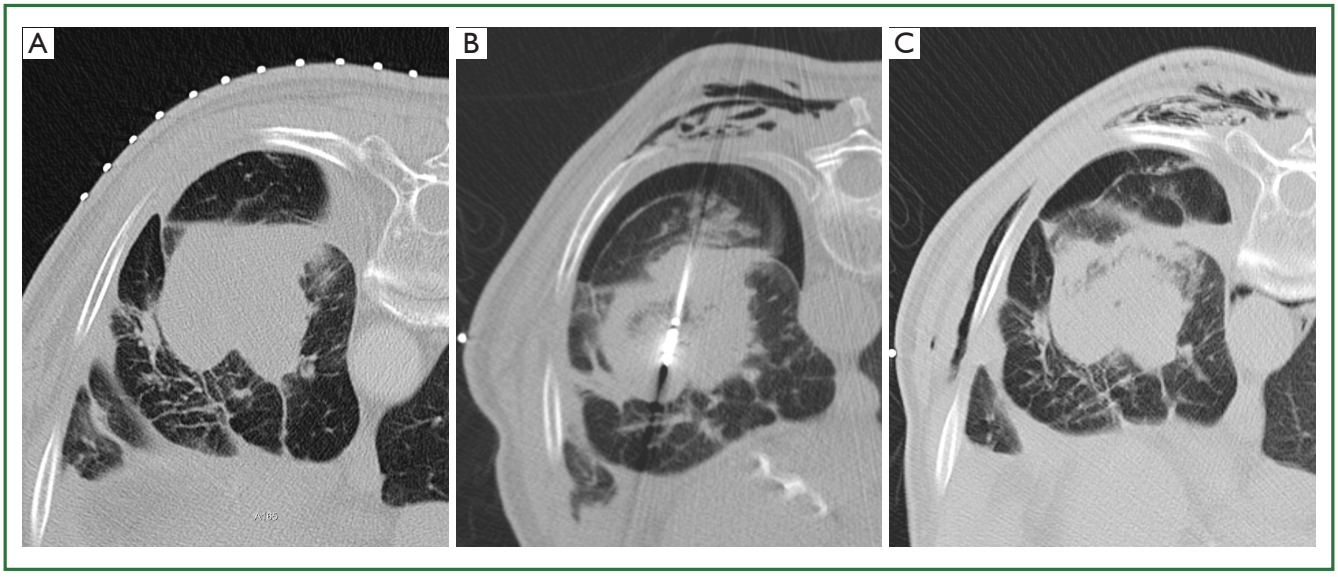

Figure 3. A 72-year-old man with incomplete response to external beam radiation to left lower lobe NSCLC, who presented for salvage MWA. He had an intractable cough throughout the procedure. A. Prone axial CT image shows a 5.5 cm mass before MWA; B. Prone axial CT during the procedure shows a small pneumothorax and surgical emphysema developing around the antenna entry site; C. Prone axial CT at the end of the procedure shows the pneumothorax has remained similar in size, but there is increased surgical emphysema.

classified in accordance with the Common Terminology Criteria for Adverse Events (CTCAE) (109). The complication rate from MWA varies and can be expected to be higher in patients who have poor underlying pulmonary reserve. Pneumothorax is the most common immediate complication with a reported incidence of up to 43% (110), but less than one-third of these patients require a chest tube (105,110,111). Post-ablation syndrome, defined as a constellation of productive cough with or without minor haemoptysis, residual soreness in the treated area, and fever occurring several days after ablation, is reported in 2% of cases (105). Small pleural effusions not requiring thoracentesis occur in around a quarter of ablations. Cavitary changes are reported in up to 43% of ablated tumours, 14% of which display air-fluid levels that usually involute spontaneously (105). Infective complications (abscess, pneumonia) are rare (105,110). Chest wall emphysema occurs in approximately 20% of cases (unpublished author's experience) and is usually concurrent with a pneumothorax (Figure 3). Ablated tumours abutting the visceral pleura result in pleural thickening in over one-third of cases (105), and prolonged pleural retractions occur in a small proportion of these cases. Up to 15% of patients require hospitalisation after MWA primarily due to pneumothoraces (105).

There is scarce comparable long-term outcome data for the effectiveness of MWA in lung cancer owing to the relatively recent addition of MWA to the armamentarium of minimally invasive hyperthermal treatment modalities; different MWA protocols that use different ablation systems operating at different frequencies with different shaft cooling mechanisms, different antennae size and different active tip lengths; and heterogeneous patient population treated, including treatment-naïve primary lung cancer, locally recurrent primary lung cancer following prior therapy, synchronous or metachronous lung cancers, and pulmonary metastases. Two recent publications using the same MWA device and with similar protocols showed promising short to mid-term results. In a homogeneous patient population of early stage NSCLC, the local control rate was 88% and 75% at a median follow-up of 6 months and 1 year, respectively (110,111).

Post-treatment evaluation

CT is the imaging modality of choice for follow-up despite additional radiation exposure. A common post-ablation surveillance protocol is to perform a CT study the day following ablation to assess for complications, and this study can be used as a reference for comparison with subsequent studies, which are performed at 3 , 6 and 12 months during the first year, and at 6-monthly intervals thereafter (110). A thin (<5 mm) symmetric circumferential rim of peripheral enhancement is seen up to 6 months following ablation and is considered a sign of benign reactive enhancement. Irregular focal soft-tissue enhancement of >15 HU is, however, considered to be a sign of residual or recurrent disease (105). The initial size of the ablation zone is supposed to be much larger than the treated tumour as it encompasses the surrounding safety margin. Continuous shrinkage thereafter should occur and this usually leaves a small focus of atelectasis (Figure 4) or scar. FDG-PET imaging is considered to be more sensitive for detecting early

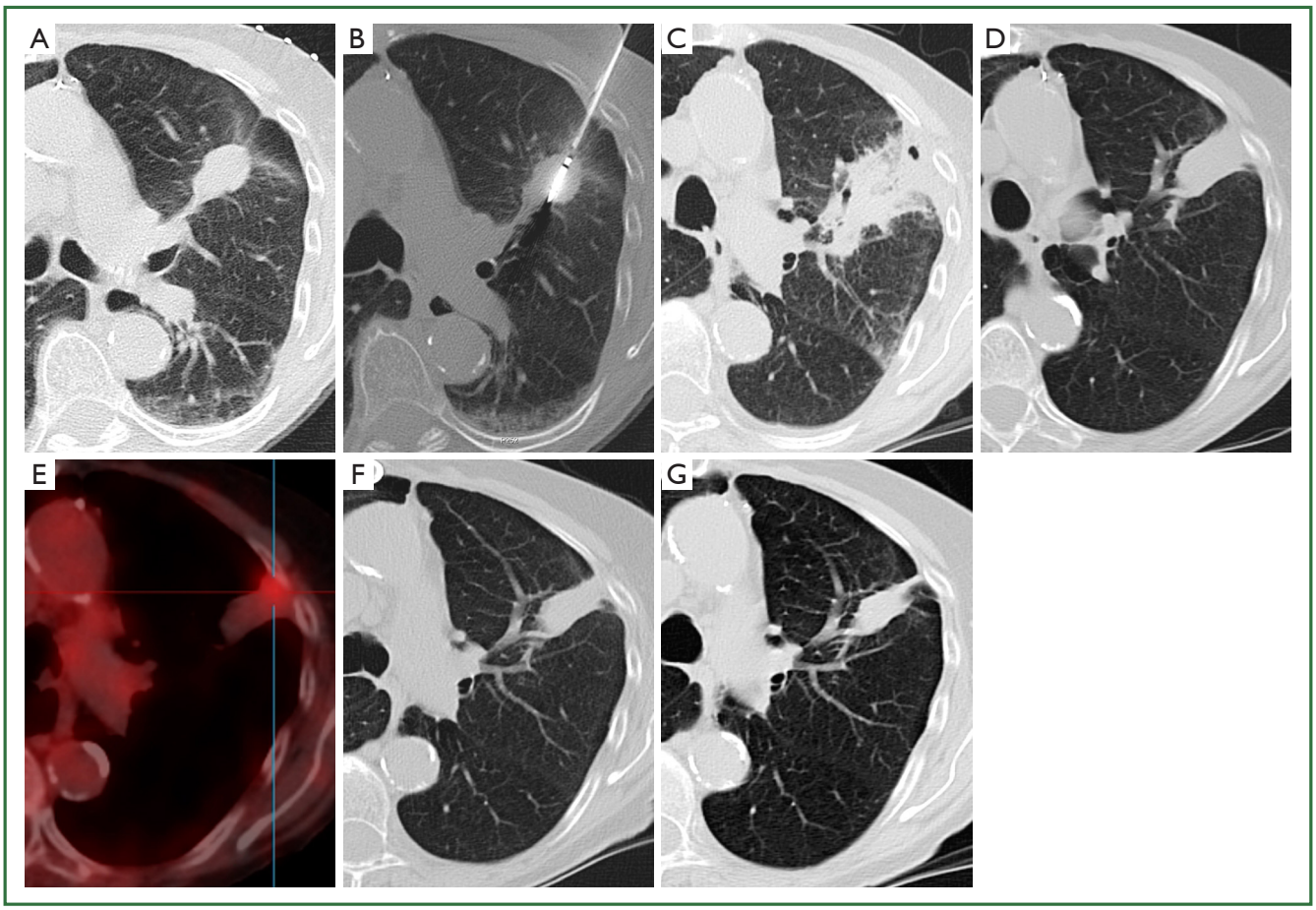

Figure 4. A 75-year-old ex-smoker with prior RFA of biopsy-proven left upper lobe NSCLC. FDG-PET 3 months following RFA was equivocal for residual tumour and repeat treatment with CT-guided MWA was performed. A. Axial CT image shows a 3 cm left upper lobe mass; B. Axial CT shows microwave antenna is positioned within the centre of the mass; C. Axial CT 24 hours following MWA shows ablation site encompasses target lesion. There is a focal pleural effusion with small cavity, and surrounding atelectasis and ground glass opacity changes; D, E. Axial CT (D) and axial fused FDG-PET/CT (E) 6 months following ablation show resolution of the ground glass opacity and shrinking of the ablation volume, but a residual broad-based pleural contact remain. FDG-PET/CT shows lack of FDG-avidity of the ablated lesion but mild sub-pleural FDG uptake, likely inflammatory; F, G. Axial CT 12 months (F) and 24 months (G) following ablation show further gradual shrinking of the ablation volume and narrowing of the pleural contact.

tumour recurrence. The specificity, however, is low in the early post-ablation period. Performing FDG-PET scans sooner than 6 months following ablation should be discouraged to ensure a low false-positive rate (112,113). In addition to the FDG uptake values, the pattern of FDG uptake is also indicative of ablation success or failure (113). Modified response evaluation criteria in solid tumours (RECIST) criteria, which incorporate both the CT and FDG-PET appearances of the lesion following ablation, are considered the most appropriate tool for follow-up assessment (114).

Conclusions

The current challenge for imaging is to exploit the advantages of each imaging modality and integrate them into a clinically useful algorithm. At present, CT and PET/CT are recommended for lung cancer staging, and MR imaging is used for evaluation of suspected T3 and T4 disease. A few recent studies suggest that MR is equivalent to FDG-PET/CT for staging NSCLC. New developments in CT, PET/CT and MR have the potential to provide improved anatomical and functional assessment of lung cancers that result in more individualized and targeted therapy. Cryoablation, RFA and MWA are promising powerful percutaneous techniques for curative-intent therapy or localised palliation of lung cancer, but available short- to mid-term data suggest MWA to be superior to RFA. However, more mid- and long-term data are required to assess for survival and cancer-free outcome following such therapies.

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