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ARTICLE

Advances in radiological staging of non-small cell lung cancer (NSCLC)

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Abstract

Imaging plays a vital role in the management of non-small cell lung cancer including diagnosis, staging and follow-up. CT and magnetic resonance imaging (MRI) are used in staging and provide anatomical information but have well known limitations in differentiating reactive from malignant nodes, and fibrosis from active disease and in defining the extent of invasion. MRI with its superior soft tissue contrast provides optimal information on brachial plexus and central nervous system involvement. Functional imaging using 2-18 fluoro-deoxyglucose positron emission tomography is increasingly being used to provide unique information and when combined with anatomic imaging will provide better staging information for both local disease and the extent of metastases.

Primary tumour (T status)

The primary tumour is usually easy to define on CT, but 20–30% of patients present with a solitary pulmonary nodule. 2-18 Fluoro-deoxyglucose positron emission tomography (FDG–PET) will identify 95% of T1 lesions and if a SUV of greater than 2.5 is used to indicate malignancy the sensitivity, specificity and accuracy of FDG–PET are 94, 71 and 86% with PPV of 90% and NPV of 85%[1]. Increased uptake will be seen in tuberculosis, aspergillomas, rheumatoid nodules and amyloid. False negatives occur in small tumours, bronchoalveolar cell carcinoma and carcinoid[2].

T3 tumours include tumours of any size with direct extension into the chest wall, diaphragm, mediastinal pleura or pericardium. T4 tumours invade the mediastinum, great vessels, trachea, oesophagus and vertebral bodies. Chest wall and mediastinal invasion can be difficult to assess by either CT or MR, both being inaccurate in differentiating contiguity from subtle invasion[3]. Webb *et al*[4] found CT only 62% sensitive in differentiating between T3 and T4 tumours and Glazer *et al*[5] found the

sensitivity and specificity for chest wall invasion to be 87 and 59%, respectively. MRI has superior soft tissue contrast to CT and is better at identifying chest wall invasion with a reported sensitivity of 90% and specificity of 86%[6], and it is much better than CT for superior sulcus (Pancoast) tumours with an accuracy of 94% compared to that of 63% for CT[7]. MRI is very good for identification of involvement of the inferior branches of the brachial plexus (C7, T1), vascular infiltration and invasion of the spinal canal or vertebral body.

CT and MRI can identify gross invasion of the mediastinum with vascular invasion but are poor at identifying subtle changes. The sensitivity for mediastinal invasion is reported to be as low as 40–44% by CT. Glazer *et al*[8] reviewed 80 patients who had indeterminate mediastinal invasion on CT scan and found that 60% of the masses were resectable without true invasion of the mediastinum, in 22%, although there was focal invasion of the mediastinum, the lesions were still technically resectable and in only 14 (18%) was the tumour unresectable. MRI is more accurate than CT for mediastinal invasion and overall both CT and MRI are

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reasonably accurate in assessing resectability, but not for non-resectability.

Nodal status (N)

Using CT and MRI size is the only criterion used to assess malignant infiltration and nodes that have a short axis diameter greater than 1 cm are considered abnormal. The accuracy for the detection of N1 disease is similar for CT (62–88%) and MRI (68–74%). This poor accuracy is not necessarily very significant as N1 disease does not preclude surgery, although it is important in radiotherapy planning; however the results for mediastinal nodes (N2 and N3) are also poor[9]. In a meta-analysis of CT accuracy for assessment of mediastinal lymph nodes, Dales *et al*[10] reported a sensitivity, specificity, and overall accuracy of 79, 78, and 80%, respectively, with similar results for MRI.

The use of ultra small superparamagnetic iron oxide particles (USPIO) as a MRI lymph node contrast agent has been developed and does offer potential for improvement. The small iron oxide particles are injected intravenously and are taken up by the reticuloendothelial system in normal or inflamed lymph nodes. These nodes show signal drop off on T2* weighted sequences whereas metastatic nodes do not show this effect. Early studies have suggested that the use of USPIO will increase the sensitivity for MRI to 92% with a specificity of 80%[11].

FDG–PET is more accurate than CT for staging mediastinal nodes as it is dependent not on size but on metabolic activity and will identify disease in nodes less than 1 cm in size, and although the sensitivity for small nodes is slightly less than that of nodes of 1–3 cm, the overall accuracy is the same[12]. The reported sensitivity for FDG–PET in N2 or N3 disease compared to CT is 89–92% (CT 25–57%), specificity 93–99% (CT 94–98%) with a NPV for PET of 97% (CT 87%). Overall the correct stage is assessed by FDG–PET in 85–96% (CT 58–59%)[13,14]. Combining FDG–PET and CT is better than CT alone with a very high NPV for staging N2 and N3 disease (95% overall and 99% for individual nodes) and therefore some authors would suggest that a negative CT and negative FDG–PET would obviate the need for mediastinoscopy prior to surgery in patients with resectable tumours[15]. Mediastinoscopy should still be performed in those patients with a positive mediastinal FDG–PET as false positives occur in tuberculosis, histoplasmosis, sarcoidosis, and anthracosis . However, many authors feel that all patients with a potentially resectable tumour should undergo pre-operative mediastinoscopy. De Leyn[16] performed mediastinoscopy on patients who were node negative on CT and found that 20% had N2 disease. A recent study by Kernstine[17] comparing FDG–PET, CT, and MRI with USPIO for nodal disease in non-small cell lung cancer (NSCLC) found a sensitivity, specificity, and accuracy of 70, 86, 84% (PET); 65, 79, 76% (CT); and 86, 82, 83% (MRI), respectively.

These authors concluded that although PET and MRI were statistically more accurate than CT, the differences were small and no technique was either sensitive or specific enough to obviate the necessity for mediastinoscopy.

FDG–PET has been used to assess tumour response to chemo/radiotherapy in many other tumour types but there are some problems with lung cancer. Although the response of the primary tumour and the metastases to induction therapy appears accurate, Akhurst *et al*[18] found that it was inaccurate for the response in the mediastinal nodes with 33% overstaged and 15% understaged.

Metastatic disease (M status)

The commonest sites for metastatic disease in NSCLC are brain, bone, liver and adrenals (in decreasing order).

The sensitivity of CT for detecting adrenal metastases is low (41%) but the specificity is high (91%)[19]. However small (<3 cm) non-functioning adrenal adenomas are a common finding. Both CT and MRI can be helpful in evaluating adrenal masses. If the lesion has a CT number of <10 HU on an unenhanced CT scan it is benign (specificity 100%)[20] Using chemical shift, MR imaging will also differentiate benign from malignant lesions in about 85–90% of cases, benign lesions showing signal drop off on out of phase imaging (specificity 100%)[21]. FDG–PET will identify unsuspected metastases and has higher sensitivity and specificity than CT for the detection of liver, bone and extra-thoracic lymph node deposits, with the detection of extra-thoracic metastases in 11–14% of patients selected for curative surgery[22].

Conclusion

Initial staging will usually be with CT with MRI reserved for problem areas. FDG–PET is used to stage the mediastinum and for distant metastases. As it is important that patients are not deprived of appropriate surgery, nodes that are PET positive should undergo biopsy prior to thoracotomy. Clinician surveys have suggested that FDG–PET influences or changes management in 39–67% of patients[23,24].

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