Cancer Imaging (2006) **6,** 1–3
DOI: 10.1102/1470-7330.2006.0004

CI

e-med
www.e-med.org.uk

ARTICLE

Staging of non-small cell lung cancer (NSCLC)

S C Rankin

Guy's and St Thomas Foundation Trust, London, UK

Corresponding address: S C Rankin, Guy's and St Thomas Foundation Trust, London, UK
E-mail: sheila.rankin@gstt.nhs.uk

Date accepted for publication 21 November 2005

Abstract

Staging of non-small lung cancer (NSCLC) uses the TNM classification and is undertaken to identify those patients who are surgical candidates, either initially or after chemo-radiotherapy, and to differentiate patients who will be treated radically from those requiring palliation and to plan radiotherapy fields. Computed tomography and magnetic resonance imaging (MRI) are used in staging and provide anatomical information but have well known limitations in differentiating reactive from malignant nodes, 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}F]fluorodeoxyglucose 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.

Keywords: *Non-small cell lung cancer; staging; CT; MRI; FDG-PET.*

Primary tumour (T status)

The primary tumour is usually easy to define on computed tomography (CT) and [2-^{18}F]fluorodeoxyglucose positron emission tomography (FDG-PET). Increased uptake on PET is also seen in tuberculosis, aspergillomas, rheumatoid nodules and amyloid. False negatives occur in small tumours, bronchoalveolar cell carcinoma and carcinoid[1].

T3 tumours include tumours of any size with direct extension into the chest wall, diaphragm, mediastinal pleura or pericardium (Tables 1 and 2). 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 magnetic resonance imaging (MRI) both being inaccurate in differentiating contiguity from subtle invasion[2–5] with a reported sensitivity of 55% and specificity of 89% in predicting T3 or T4 disease. 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%[5], and it is better than CT for superior sulcus (Pancoast) tumours and can identify involvement of the inferior branches of the brachial plexus (C7, T1), vascular infiltration and invasion of the spinal canal or vertebral body.

FDG-PET alone is worse than CT but the combination of PET/CT will improve things but is unlikely to make it any more accurate than CT alone.

Nodal status (N)

Using CT and MRI, size is the only criteria 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%). In a meta-analysis of CT accuracy for assessment of mediastinal lymph nodes, Dales *et al.*[6] reported a sensitivity, specificity, and overall accuracy of 79%, 78%, and 80%, respectively, with similar results for MRI.

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[7]. The initial 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%)[8,9]. Combining FDG-PET and CT is better than CT alone with a very high negative predictive value (NPV) for staging N2 and N3 disease (95% overall and 99% for individual nodes) and therefore some authors would suggest a negative CT and negative FDG-PET would obviate the need for mediastinoscopy prior to surgery in patients with resectable tumours[10] (Table 3). However, recent studies have found the NPV of PET decreases to 17% in patients with central tumours and mediastinoscopy should still be performed in those patients. 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[11] performed mediastinoscopy on patients who were node negative on CT and found that 20% had N2 disease. Endoscopic ultrasound (EUS) with fine needle aspiration allows sampling of posterior mediastinal nodes and has produced some excellent results with reported sensitivity, specificity and NPV of 92%, 100% and 94%[12]. Fine needle aspiration of scalene nodes may also be helpful in assessing occult N3 disease.

Metastatic disease (M status)

The commonest sites for metastatic disease in NSCLC in post mortem studies 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%)[13]. However, small (<3 cm), non-functioning adrenal adenomas are a common finding and both CT and MRI can be helpful in evaluating these using either the CT on unenhanced scans or chemical shift imaging[14,15]. 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[16].

Conclusion

Initial staging will usually be with CT, with MRI reserved for problem areas. FDG-PET is used to stage the mediastinum, with nodes that are positive biopsied prior to thoracotomy, and for the assessment of distant metastases (Table 3). The development of PET/CT may change the staging algorithm. Clinician surveys have suggested that FDG-PET influences or changes management in 39%–67% of patients[17,18].

Table 1 Staging of NSCLC

T1	Tumour <3 cm, surrounded by lung or visceral pleura. Involves lobar bronchus (not main bronchus)
T2	Tumour >3 cm. Involves main bronchus >2 cm from carina. Invades visceral pleura. Associated with atelectasis (not whole lung)
T3	Tumour any size. Invades chest wall, diaphragm, mediastinal pleura or is less than 2 cm from carina. Atelectasis of whole lung
T4	Tumour any size invades vertebral body, heart, great vessels, trachea, or mediastinum. Separate nodule of tumour in same lobe. Malignant pleural effusion
N0	No regional nodes
N1	Ipsilateral peribronchial or hilar nodes. Intrapulmonary nodes
N2	Ipsilateral mediastinal or subcarinal nodes
N3	Contralateral mediastinal or hilar nodes and ipsilateral or contralateral scalene or supraclavicular nodes
M0	No metastases
M1	Distant metastases

Table 2 Staging groups

Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T1	N1	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T1	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	Any T	N3	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1

Table 3 NICE guidelines (UK): February 2005

1. Patients who are staged as candidates for surgery on CT should have an FDG-PET scan to look for involved intrathoracic lymph nodes and distant metastases
2. Patients who are otherwise surgical candidates and have, on CT, limited (1–2 stations) N2/3 disease of uncertain pathological significance should have an FDG-PET scan
3. Patients who are candidates for radical radiotherapy on CT should have an FDG-PET scan
4. Patients who are staged as N0 or N1 and M0 (stages I and II) by CT and FDG-PET and are suitable for surgery should not have cytological/histological confirmation of lymph nodes before surgical resection

References

[1] Marom EM, Sarvis S, Herndon JE 2nd, Patz EF Jr. T1 lung cancers: sensitivity of diagnosis with fluorodeoxyglucose PET. Radiology 2002; 223: 453–9.

[2] Ratto GB, Piacenza G, Frola C *et al*. Chest wall involvement by lung cancer: computed tomographic detection and results of operation. Ann Thorac Surg 1991; 51: 182–8.

[3] Webb WR, Gatsonis C, Zerhouni EA *et al*. CT and MR imaging in staging non-small cell bronchogenic carcinoma: report of the Radiologic Diagnostic Oncology Group. Radiology 1991; 178: 705–13.
[4] Glazer HS, Duncan-Meyer J, Aronberg DJ, Moran JF, Levitt RG, Sagel SS. Pleural and chest wall invasion in bronchogenic carcinoma: CT evaluation. Radiology 1985; 157: 191–4.
[5] Padovani B, Mouroux J, Seksik L *et al*. Chest wall invasion by bronchogenic carcinoma: evaluation with MR imaging. Radiology 1993; 187: 33–8.
[6] Dales RE, Stark RM, Raman S. Computed tomography to stage lung cancers: approaching a controversy using meta-analysis. Am Rev Respir Dis 1990; 141: 1096–101.
[7] Gupta NC, Graeber GM, Bishop HA. Comparative efficacy of positron emission tomography with fluorodeoxyglucose in evaluation of small (<1 cm), intermediate (1–3 cm), and large (>3 cm) lymph node lesions. Chest 2000; 117: 773–8.
[8] Steinert HC, Hauser M, Allemann F *et al*. Non-small cell lung cancer: nodal staging with FDG-PET versus CT with correlative lymph node mapping and sampling. Radiology 1997; 202: 441–6.
[9] Marom EM, McAdams HP, Erasmus JJ *et al*. Staging non-small cell lung cancer with whole-body PET. Radiology 1999; 212: 803–9.
[10] Farrell MA, McAdams HP, Herndon JE, Patz EF Jr. Non-small cell lung cancer: FDG PET for nodal staging in patients with stage I disease. Radiology 2000; 215: 886–90.
[11] De Leyn P, Vansteenkiste J, Cuypers P *et al*. Role of cervical mediastinoscopy in staging of non-small cell lung cancer without enlarged mediastinal lymph nodes on CT scan. Eur J Cardiothorac Surg 1997; 12: 706–12.
[12] Eloubeidi MA, Cerfolio RJ, Chen VK, Desmond R, Syed S, Ojha B. Endoscopic ultrasound-guided fine needle aspiration of mediastinal lymph node in patients with suspected lung cancer after positron emission tomography and computed tomography scans. Ann Thorac Surg 2005; 79: 263–8.
[13] Allard P, Yankaskas BC, Fletcher RH, Parker LA, Halvorsen RA Jr. Sensitivity and specificity of computed tomography for the detection of adrenal metastatic lesions among 91 autopsied lung cancer patients. Cancer 1990; 66: 457–62.
[14] Korobkin M, Brodeur FJ, Yutzy GG *et al*. Differentiation of adrenal adenomas from nonadenomas using CT attenuation values. Am J Roentgenol 1996; 166: 531–6.
[15] McNicholas MM, Lee MJ, Mayo-Smith WW, Hahn PF, Boland GW, Mueller PR. An imaging algorithm for the differential diagnosis of adrenal adenomas and metastases. Am J Roentgenol 1995; 165: 1453–9.
[16] Weder W, Schmid RA, Bruchhaus H, Hillinger S, von Schulthess GK, Steinert HC. Detection of extrathoracic metastases by positron emission tomography in lung cancer. Ann Thorac Surg 1998; 66: 886–93.
[17] Seltzer MA, Yap CS, Silverman DH *et al*. The impact of PET on the management of lung cancer: the referring physician's perspective. J Nucl Med 2002; 43: 752–6.
[18] Kalff V, Hicks RJ, MacManus MP *et al*. Clinical impact of (18) F fluorodeoxyglucose positron emission tomography in patients with non-small-cell lung cancer: a prospective study. J Clin Oncol 2001; 19: 111–8.