

## REVIEW

# Role of positron emission tomography in lung cancer

K A Miles

*Southernex Imaging & Queensland University of Technology, The Wesley PET Centre, Department of Radiology, The Wesley Hospital, Auchenflower, Queensland, Australia*

*Corresponding address: K. A. Miles, Southernex Imaging & Queensland University of Technology, The Wesley PET Centre, Department of Radiology, The Wesley Hospital, Chasely Street, Auchenflower, Queensland 4066, Australia. E-mail: ken.miles@wesley.com.au*

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### Abstract

The ability to demonstrate tumour foci that are undetected by conventional imaging has resulted in the emergence of positron emission tomography (PET) as a valuable clinical tool in oncology. This article describes the technique and indications for fluorine-18 labelled fluorodeoxyglucose ( $^{18}\text{FDG}$ )-PET in lung cancer, demonstrating the high accuracy and cost-effectiveness of  $^{18}\text{FDG}$ -PET in the characterisation of solitary pulmonary nodules and in the pre-operative staging of non-small cell lung cancer. Emerging roles in determination of prognosis, radiotherapy planning, therapy monitoring and diagnosis of recurrence are illustrated.

**Keywords:** *Positron emission tomography; lung neoplasms; diagnostic methods.*

### Introduction

After many years of application in research, positron emission tomography (PET) is now emerging as a valuable clinical tool, particularly in the field of oncological imaging. This transition has resulted largely from the development of one particular PET radiotracer, fluorine-18 labelled fluorodeoxyglucose ( $^{18}\text{FDG}$ ). The relatively long half-life of Fluorine-18 (110 min) has meant that PET units no longer require their own cyclotron for isotope production as Fluorine-18 from one cyclotron can be transported to several PET scanners at sites remote from the production facility. Furthermore, Fluorine-18 imaging is not associated with the high count rates obtained with other shorter-lived isotopes, allowing lower cost sodium iodide (NaI) detector systems to be used in preference to Bismuth Germanate (BGO). NaI detector systems also benefit from greater energy resolution, allowing superior rejection of scattered photons and thereby enhancing imaging quality for whole body studies.

$^{18}\text{FDG}$  demonstrates high uptake in many cancers, including lung cancer. Uptake results from increased

expression of hexokinase and of Glut-1 glucose transporters on the cell surface. Both of these metabolic changes result from oncogene mutations with the tumour cells, most notably the p53 gene-mutation, which occurs commonly in lung cancer. It is important to realise that the detection of a tumour focus on  $^{18}\text{FDG}$ -PET is determined by the degree of metabolic change rather than the size of the lesion (Fig. 1). The high glucose metabolic rate of tumours as compared to normal tissues allows tumour foci as small as 3 mm to be commonly identified by PET.

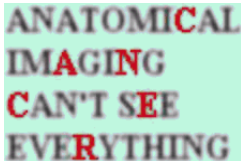
Lung cancer is an important indication for PET imaging<sup>[1,2]</sup>, accounting for approximately one quarter of the patients examined at the Wesley PET Centre. This article describes the technique and indications for PET in lung cancer and reports on its accuracy and cost-effectiveness.

### Technique

After a six-hour fast to ensure low blood glucose levels, patients are injected with 185–370 MBq  $^{18}\text{FDG}$  and

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imaging of the chest, abdomen and pelvis is performed one hour later. The brain is not routinely imaged, as detection of small cerebral metastases is unreliable, due to masking by the high uptake seen in normal cerebral cortices. A dedicated PET system (NaI or BGO) should be used, because the low sensitivity of coincidence gamma camera systems results in failure to detect small nodal metastases<sup>[3]</sup>. Attenuation correction is essential to optimise the detection and localisation of deep lesions. Image reconstruction should employ iterative (OSEM) techniques to further enhance the quality of final images. Tumour uptake can be quantified by measurement of the standardised uptake value (SUV).

<p>ANATOMICAL IMAGING CAN'T SEE EVERYTHING</p>	
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**Figure 1** An illustration of how the detection of small tumours by PET is not determined by spatial resolution. The text on the left is displayed with high spatial resolution but is unable to detect the hidden message 'CANCER'. Even though the text on the right is blurred (low resolution), the hidden message is revealed by labelling the letters that are functionally different (i.e. they carry the hidden message).

## Applications

### *Solitary pulmonary nodules*

<sup>18</sup>FDG-PET is highly accurate in the characterisation of solitary pulmonary nodules (SPN), diagnosing malignancy with reported sensitivities of 89–100% and specificities of 58–100%<sup>[1]</sup>. Thus, <sup>18</sup>FDG-PET is generally more accurate than per-cutaneous biopsy, which has lower sensitivity due to sampling error. In up to 50% of positive cases, PET also identifies sites of metastasis that have not been suspected on the basis of other imaging. Specificity values for <sup>18</sup>FDG-PET are lower in populations with a high incidence of granulomatous diseases, such as histoplasmosis, which may produce false-positive results. Other benign causes of <sup>18</sup>FDG uptake include tuberculosis, aspergillosis and pulmonary infarction. False-negative studies can occur with alveolar cell carcinoma and carcinoid tumours, and therefore follow-up imaging is recommended following a negative study for SPN. Accuracy can be improved by reporting the PET data with CT data available for comparison. Experience with <sup>18</sup>FDG-PET, along with decision tree analysis techniques, have shown that the high accuracy of PET for SPN translates to reductions in health care expenditure by avoidance of unnecessary biopsy procedures and thoracotomies<sup>[4,5]</sup>.

### *Pre-operative staging of non-small cell lung cancer*

<sup>18</sup>FDG-PET is more accurate for staging mediastinal nodes than CT (PET sensitivity 77–82%, specificity 81–98%; CT sensitivity 56–65%, specificity 44–87%). PET will identify involved nodes that are too small to be reliably diagnosed by CT, whereas the absence of <sup>18</sup>FDG uptake in nodes that are seen to be enlarged on CT indicates reactive adenopathy. Distant metastases, especially in bone or adrenal glands, are also accurately depicted by <sup>18</sup>FDG-PET. The high therapeutic impact of <sup>18</sup>FDG-PET is shown by the fact that significant changes in management occur in 32–51% of patients examined. Patients classified as stage 1 by PET demonstrate improved survival as compared to those considered to be Stage 1 on CT<sup>[6]</sup>. This improvement results from the ability of PET to identify those patients most likely to benefit from surgery. Furthermore, the high accuracy of PET has been shown to lead to savings in health care expenditure by allowing unnecessary thoracotomy to be avoided in those patients unlikely to benefit<sup>[5,7,8]</sup>.

### *Other applications in lung cancer*

Emerging roles for <sup>18</sup>FDG-PET in lung cancer include determination of prognosis, radiotherapy planning, therapy monitoring and diagnosis of recurrence. Prognostic information can be obtained from measurements of uptake with high SUV values implying a poor prognosis and a poorer response to radiotherapy<sup>[9]</sup>. The use of PET for radiotherapy planning may improve the efficacy of treatment by ensuring that tumour revealed by PET, but undetected by CT, is not excluded from the treatment volume<sup>[10]</sup>. The reduction in <sup>18</sup>FDG uptake following radiotherapy correlates with the long-term therapeutic response, and PET is more accurate than CT in predicting the down-staging that has occurred with induction chemotherapy. <sup>18</sup>FDG-PET is also useful in diagnosing recurrent tumour, particularly when CT is unable to distinguish between recurrent tumour and post-therapy fibrosis in the presence of a residual structural abnormality.

## Conclusion

There is now a substantial body of evidence supporting the use of <sup>18</sup>FDG-PET in lung cancer. The value of the technique is increasingly recognised by health purchasers. The high accuracy of <sup>18</sup>FDG-PET allows selection of the most appropriate and effective therapy for patients with lung cancer.

### Key points

- (1)  $^{18}\text{F}$ FDG-PET is accurate and cost-effective in the characterisation of SPN and in the pre-operative staging of non-small cell lung cancer.
- (2)  $^{18}\text{F}$ FDG-PET has emerging roles in determination of prognosis, radiotherapy planning, therapy monitoring and diagnosis of recurrence.

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