Lung Cancer

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KEYWORDS

• Positron emission tomography • Lung cancer • Radiotherapy • Chemotherapy • CT scanning

KEY POINTS

- Undiagnosed ^{18}F-fluorodeoxyglucose–avid pulmonary nodules generally require further evaluation.
- PET-assisted staging of the mediastinum is much more accurate than computed tomography–based evaluation.
- PET imaging before planned surgery for apparently resectable lung cancer reduces the futile thoracotomy rate.
- Almost one-third of patients with apparent stage III non–small cell lung cancer will be found to have disease too advanced for curative radiation therapy after PET staging.
- PET-assisted radiation therapy planning greatly increases the accuracy of target volumes used in curative radiation therapy.

POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY IMAGING IN THE MANAGEMENT OF LUNG CANCER

Rational decision-making in oncology is dependent on high-quality data regarding the biological characteristics, location, and extent of malignancy. Although pathologic sampling of the presumed primary or suspected metastatic disease provides critical diagnostic information about tumor type and grade, economic and physical (morbidity) factors mandate noninvasive evaluation of the extent of disease. Medical imaging is pivotal in providing this information. Although computed tomography (CT) or MRI can provide detailed anatomic information, ^{18}F-fluorodeoxyglucose–positron emission tomography (FDG-PET) supplements this with metabolic data to generally improve both the sensitivity and specificity of staging. With the development of hybrid PET/CT and, more recently, PET/MRI, detailed anatomic and metabolic characterization of disease has become feasible in a single efficient and data-rich procedure.

It is important to recognize that imaging studies are not therapies in themselves and impact patient outcomes only insofar as they influence treatment choice and delivery. Patient survival and other oncological end-points are dependent on the efficacy of the therapy chosen, which relate to its delivery, the nature of the malignancy, and host factors. Traditionally, treatment choice has been based on disease stage, but increasingly molecular and genomic characterization of tumors is also guiding targeted approaches. Incorrect characterization of cancer, either of its biology or extent, can lead to errors of management that harm patients through the delivery of inappropriate therapy or incorrect amounts of an otherwise appropriate therapy. In this article, we consider the impact of PET imaging with FDG on the management of

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patients with non–small cell lung cancer (NSCLC). There is, perhaps, no other malignancy, that better epitomizes the value of FDG-PET/CT to patients for diagnosis, lesion characterization, staging, treatment selection, targeting of therapy, response assessment, and evaluation of relapse.

LUNG NODULE CHARACTERIZATION

As CT scans are increasingly performed for investigation of a range of diseases and, in some patients, as a screening procedure, the incidental detection of pulmonary nodules is becoming more common. FDG-PET can play a key role in characterizing many of these nodules. The Fleischner Society does not currently recommend FDG-PET/CT scanning of patients with nodules smaller than 8 mm.[1] These recommendations recognize that lesions smaller than twice the theoretic spatial resolution of the scanner (as defined by a parameter termed the full-width-at-half-maximum or FWHM) are subject to partial volume effect. Additionally, the effects of respiratory motion on lesion detectability are also exaggerated for small lesions. The net effect of partial volume averaging and lesion motion is an underestimation of the true activity in a lesion, thereby limiting the ability of PET to accurately exclude malignancy. Follow-up monitoring of these lesions for growth is advocated for this purpose.

As nodules increase in size, the risk of malignancy also increases and the hazards of an observational strategy are heightened by potentially allowing greater opportunity for metastatic spread. Accordingly, immediate characterization of such nodules is desirable. Although biopsy is the definitive method for this purpose, not all lesions are amenable to biopsy and, depending on the method used, can have significant associated morbidity and cost. Relatively early studies using stand-alone FDG-PET scanning of larger pulmonary nodules indicated the nodules without significant FDG-avidity can be safely observed with careful follow-up due to a relatively high negative predictive value.[2] The positive predictive value of FDG scans in indicating the presence of a lung cancer will depend on the relative pretest likelihoods of lung cancer or of another active pulmonary pathology being present. This reflects the fact that FDG is actively concentrated in both malignant and inflammatory cells. Factors that influence the a priori likelihood of malignancy as the etiology of an FDG-avid nodule include the patient's smoking history, ethnicity, and sex; the presence of a prior tumor; and the regional prevalence of tuberculosis or endemic granulomatous conditions, such as histoplasmosis.[3,4]

Although the intensity of FDG uptake as measured by the maximum standardized uptake value (SUVmax) has been suggested to be an indicator of tumor aggressiveness,[5] the relationship between this parameter and prognosis is not necessarily seen for all types of treatment.[6] Nevertheless, FDG uptake in the primary tumor mass does appear to influence the likelihood of nodal involvement.[7,8] The significance of a high SUV also may vary depending on histopathological subtype.[9] Despite its potential utility for characterization of disease biology, FDG uptake intensity does not currently determine the therapeutic approach to proven lung cancers in most centers. Nevertheless, in the exceptional cases in which biopsy is considered extremely risky to a patient with a high pretest probability of lung cancer, a pragmatic approach can be taken where FDG-avid lesions are treated as malignant, without an apparent adverse outcome.[10] Application of probabilistic models suggests that when the likelihood of malignancy is more than 85%, empiric treatment of lung nodules may be appropriate without recourse to biopsy in such patients.[11] PET also can help target biopsies to the most informative anatomic sites in patients found to have metastatic disease.

STAGING OF KNOWN NON–SMALL CELL LUNG CANCER

The most powerful adverse prognostic parameter in patients with NSCLC is the presence of metastatic disease (M status). Stage IV disease is defined by the presence of distant metastases (M1) and is independent of N-stage and T-stage because these cease to have independent prognostic significance in this setting. In the absence of distant metastases (M0), nodal (N) status (a surrogate for the later development of distant metastatic disease) becomes relevant to both treatment choices and prognosis. Finally, it is only in the absence of unresectable regional nodal disease (N2-3) that the resectability of the primary tumor itself (T status) becomes relevant. TNM staging reflects a surgical orientation to the management of lung cancer and in an era of multidisciplinary care of NSCLC, MNT-staging may be conceptually more appropriate. Although conventional imaging paradigms are focused on providing optimal assessment of T-stage, the major advantage of FDG-PET is its ability to more accurately define M-stage and N-stage. This information has the potential to significantly influence treatment choices and thereby influence patient outcomes. Accordingly, discussion of the advantages of FDG-PET/CT in staging NSCLC focuses on an MNT-staging paradigm.