



Imaging Modalities and Image Guided Biopsy Techniques for Lung Cancer Staging and Their Staging Implications for Lung Cancer- A Review for the General Surgeon

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Abstract

Imaging modalities in thoracic oncology continue to evolve. It is important as a community surgeon to be aware of all imaging and diagnostic tools available to diagnose potential thoracic cancer. Our review intends to be a brief overview of the most recent data supporting imaging and diagnostic procedures to help make informed decision to optimize patient care. We will cover computerized tomography, positron emission tomography, magnetic resonance imaging, endobronchial ultrasound-guided transbronchial needle biopsy, and electromagnetic navigational bronchoscopy.

Keywords: Lung cancer; CT scan; PET scan; EBUS

Key Points

1. Integrated PET-CT scan gives highest diagnostic imaging yield for lung cancer staging.
2. Tissue diagnosis of suspicious areas can safely and accurately be obtained via endobronchial ultrasound- guided transbronchial needle aspiration.
3. PET-CT scan in combination with EBUS-TBNA can guide therapy.

Introduction

There are many new imaging technologies that are available to help clinicians diagnose and stage patients to determine optimal oncologic therapy. When assessing a patient for suspected lung cancer all imaging and non-invasive staging modalities should be considered or exhausted prior to surgical intervention. When a lung nodule is found on routine screening with a chest x-ray the confirmatory exam is a computerized tomography (CT) scan to further characterize the nodule as solid or ground glass appearance and to determine presence of or absence of calcium. CT scanning may also help identify enlarged mediastinal lymph nodes. Staging algorithmic call for a positron emission tomography (PET) scan to determine parenchymal and mediastinal lymph node avidity [1].

Once radiological staging has been obtained a tissue diagnosis is appropriate. We will discuss endobronchial ultrasound biopsy as an option before surgical biopsy of mediastinal lymph nodes.

Diagnostic Imaging

Computerized tomography scan

Once a lesion has been identified on plain chest radiography or low dose CT scan the next step is to obtain a high resolution computed tomography with contrast if patient's renal clearance is appropriate. This imaging allows for better characterization of the nodule such as size, contour, density, calcification, invasion of surrounding structures, and allows examination of mediastinal lymph nodes. It is important to note that the characteristics of lung nodules are not enhanced by a contrast CT scan but the contrast will better assess invasion of surrounding structures. Given the superior resolution and quicker scan time of CT imaging in the evaluation and follow up of lung nodules it has been the gold standard for lung cancer investigation [2]. Lymph nodes greater than 1 cm and subcarinal lymph nodes greater than 1.2 cm are defined as enlarged lymph nodes suspicious for malignancy warranting tissue biopsy. For nodal metastasis CT scanning was found to have a sensitivity of 57% and specificity of 89% based on detection size of 1 cm³. In order to obtain the best resolution of hilar lymph nodes, a CT with contrast is recommended or without contrast if the patient's renal function is of concern.

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Positron emission tomography scan

PET scans detect positrons emitted by low atomic weight isotopes such as the radioactive fluoride in Fluorodeoxyglucose. This is an analog of glucose which is preferentially taken up by cells with increased glycolysis such as tumor cells, inflammatory lesions and infectious lesions. PET scans can be used for determining synchronous lesions of the lungs, nodal metastasis, and distant metastasis. The degree of FDG uptake can be semi-quantitatively interpreted using a standardized uptake value (SUV) with a cutoff of 2.5 for pulmonary nodules larger than 1 cm with a sensitivity, specificity and accuracy of 91%, 47% and 79% respectively. The two caveats are that an inflammatory or an infective lesion can imitate a malignant nodule in its FDG uptake as well as the fact that some highly differentiated cancers have a relatively low metabolic and proliferation rate, hence the low specificity. For nodal metastasis PET scan imaging was reported to have a sensitivity of 84% and specificity of 89% [3]. In this same study 11% of patients had distant metastasis to abdominal organs and bones which were not detected by CT scan making PET scans the imaging of choice for metastatic disease [3]. Due to the non-specificity of PET/CT scan abnormalities biopsies are usually required to make a tissue diagnosis of lesions in question. Essentially the PET scan becomes a staging and target imaging technique for further intervention. This dilemma raises the question of whether PET scan alone can be used without biopsies for treatment planning remains controversial. Certainly, consideration of nodal patterns which are consistent with standard modes of spread (e.g. Right upper lobe lesion, right pretracheal or subcarinal node) can be thought of as highly suspicious of spread without additional biopsy especially in absence of obstructive pneumonia. An important rule to remember is that any adenopathy which renders a patient N2 or stage III warrants a biopsy to confirm this, except in the cases of truly bulky adenopathy with supporting PET uptake.

Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) can be used in lung cancer staging but Heelan et al. [4] reported no diagnostic advantage over CT scans for lymph node assessment and a higher false positive rate. A meta-analysis by Zhang et al. [5] included 90 studies where the sensitivity of MRI ranged between 52% and 93% and specificity ranged between 82% to 100% for nodal disease. In this meta-analysis the pooled per patient sensitivity for nodal disease in MRI was 74% and specificity was 90% [5]. These findings lead us to conclude that given the accessibility and the increased sensitivity and specificity for CT scan modality in lung cancer screening it remains the radiological exam of choice. The role of MRI in thoracic surgical oncology may be best suited for determination of tissue plane invasion of mediastinal tumor threatening aortic invasion and superior sulcus structures.

Combination Imaging is it better?

The combination of PET and CT scan has been studied over the past decade. This combination is thought to increase the diagnostic yield by encompassing biological uptake and radiographic appearance of cancer lesions. A study comparing PET imaging to PET-CT scan of 129 patients yielded superior accuracy for nodular size 47% to 70% and enlarged lymph node detection 56% to 78% [6]. Given these findings and those stated in the prior sections this combined modality would be encouraged in the staging processes of the lung cancer patients. CT-PET has become the standard of care in most academic centers and it is increasingly unlikely for these not to be done concurrently. Of note anatomical structures may appear

in slightly different locations because the CT scan done with PET is not a single breath study and therefore chest volume and location of structure may change in subtle manner.

Minimally Invasive Staging Techniques

Endobronchial ultrasound- guided transbronchial needle aspiration (EBUS-TBNA)

This technique was first described in 2004 as a method for mediastinal staging in lung cancer [7]. EBUS-TBNA can be used in the diagnosis of lymphoma and lung cancer. Endoscopic therapies have proven efficient and in the ACCP guidelines for lung cancer management these therapies have recently been recommended as first line before surgical intervention such as mediastinoscopy. This recommendation was made due to Yasufuku's conclusion that there is no diagnostic difference and a cost benefit with EBUS-TBNA compared to mediastinoscopy [7,8]. Patients who should undergo EBUS-TBNA according to the American College of Chest physician guidelines are those that have peripheral tumors >3 cm, central tumors, suspicion of N1 disease by lymph nodes larger than 1cm on CT scan, or PET avid hilar and mediastinal lymph nodes. Lymph node stations accessible by EBUS are 2 upper paratracheal, 3 prevascular and retrotracheal, 4 paratracheal right and left, 7 subcarinal, 10 hilar right and left, and 11 interlobar right and left lymph nodes. The accuracy of EBUS has been reported at 96.3%, sensitivity of 94.6% and a specificity of 100%. Due to its high accuracy it is becoming the preferred method of mediastinal staging. When comparing cost effectiveness EBUS has been compared to mediastinoscopy multiple times. In a recent U.S. study cost of mediastinoscopy was found to be \$2,356 compared to EBUS/TBNA at \$2,503 [9]. In comparison an Australian study reported EBUS/TBNA to be AU\$3754 and mediastinoscopy cost of AU\$8859 [10]. The Australian study seems comparable to the predominant pattern in the U.S. in which EBUS/TBNA does offer some cost savings. At this point in time we support the current recommendations of EBUS/TBNA followed by surgical staging if the former procedure turns out to be non diagnostic.

Successful lymph node biopsy is achieved when lymphocytes with typical appearance are present on the cytology wet smear. In order to obtain good sampling proper technique must be used by the surgeon who obtained the sample. Identifying the appropriate lymph node in correlation to prior diagnostic imaging studies is crucial. The node must be maintained in central view during the ultrasound imaging and the needle passed into the center of node without traversing surrounding structures. The proper use of these techniques combined with diagnostic imaging will yield the most accurate sample possible.

With any minimally invasive technique, the patient inherits risks and complications. A post operative chest x-ray may diagnose some of these complications and is recommended after any procedure. The main risk associated with any of the techniques mentioned is: 1) pneumothoraces, 2) hemothorax, 3) endobronchial bleeding, and 4) parenchymal hemorrhage. Pneumothorax can be treated with pigtail catheter insertion during or post procedure. For hemothorax that is hemodynamically stable, chest tube insertion is recommended. If hemothorax causes hemodynamic compromise due to persistent bleeding or bleeding does not subside, surgical intervention is warranted. Endobronchial bleeding may be corrected with cautery devices deployed via bronchoscopy to control bleeding. In more persistent endobronchial bleeding tamponade with bronchial blocker may be appropriate to treat or temporize until surgical intervention can be provided. Parenchymal bleeding rarely requires surgical

intervention and only usually requires supportive therapy with fluid boluses, blood transfusions and follows up CT scanning. Most of these patients should undergo observation for 24 h to monitor respiratory and hemodynamic stability.

Electromagnetic Navigational Bronchoscopy

Electromagnetic navigational bronchoscopy (ENB) is another minimally invasive diagnostic tool that is becoming more readily available. In some institutions ENB falls into the interventional pulmonologist realm of expertise. This technique can safely and accurately be done by surgeons that have access and training on this equipment. Pearlstein et al. [11] reported 86% diagnostic yield in surgeons' hands with the addition of rapid on site examination for cytopathology. As mentioned earlier a risk to any minimally invasive pulmonary procedure is a pneumothorax which during ENB was found to be 5.8%.

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