PET and PET/CT in Small Cell Lung Cancer

By Neeta Pandit-Taskar, M.D., and Steven M Larson, M.D.

LEARNING OBJECTIVES
- Describe the fundamental approach of imaging use in small cell lung cancer
- Summarize the usefulness of PET or PET/CT imaging compared with conventional methods
- Explain the role of FDG-PET or PET/CT in evaluation of SCLC
- Describe the potential role of PET or PET/CT in management of SCLC

Upon completion of this activity, participants should be able to:

- Describe the fundamental approach of imaging use in small cell lung cancer
- Summarize the usefulness of PET or PET/CT imaging compared with conventional methods
- Explain the role of FDG-PET or PET/CT in evaluation of SCLC
- Describe the potential role of PET or PET/CT in management of SCLC

PET and PET/CT: Internal Medicine and Nuclear Medicine Issues

PET is a diagnostic imaging modality that produces images of glucose metabolism in the body. It is based on the detection of positrons emitted by short-lived radioisotopes, which are injected into the patient. PET has become a standard imaging tool in the evaluation of small cell lung cancer (SCLC) due to its high sensitivity and specificity. PET/CT combines PET imaging with computed tomography (CT) to provide anatomical and functional information.

PET provides information about the metabolic activity of tissues, which can distinguish between normal and abnormal tissues. In SCLC, PET has been shown to be useful in staging, treatment planning, and surveillance. PET/CT, on the other hand, offers improved spatial resolution and allows for better target definition.

PET has been shown to detect small foci of tumor not visible on CT scans, which can be crucial for treatment planning. It is particularly useful in detecting metastatic disease, as it can image the liver, bone, and other organs simultaneously.

PET/CT can also help determine the response to therapy, as changes in tumor metabolism can be monitored over time. This is particularly important in SCLC, as the disease is characterized by rapid growth and frequent recurrence.

In summary, PET and PET/CT play a significant role in the management of SCLC, providing important information for diagnosis, staging, treatment planning, and follow-up.

References:

PET/CT in Small Cell Lung Cancer

PET/CT has been shown to be more accurate than CT alone in detecting metastatic disease, especially in the liver and bone. It can also help in identifying the extent of primary tumor involvement, which is crucial for treatment planning.

PET/CT is particularly useful in patients with limited disease, as it can detect small foci of disease that may not be visible on CT. This can help in choosing the appropriate chemotherapy regimen and in determining the optimal radiation field.

PET/CT can also help in assessing the response to therapy, as changes in tumor metabolism can be monitored over time. This is important in SCLC, as the disease is characterized by rapid growth and frequent recurrence.

In summary, PET/CT is a valuable tool in the management of SCLC, providing important information for diagnosis, staging, treatment planning, and follow-up.

References:
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als. Staging is based on biopsy confirmation, 
thus major surgery, and must be aug- 
mented by standard workup including chest 
radiography, CT scanning, thoracoscopy/ 
thoracoscopy, MR imaging, bone scans, 
and bone marrow biopsy.

Imaging plays a critical role not only in 
initial staging but also in staging by establishing 
the correct extent of disease. Chest x-ray is use- 
ful for screening, while lesions are also detect- 
ed on CT scans performed for evaluation of symptoms. CT scanning has an established 
role in initial diagnosis, allowing chest x-ray to make a 
differentiation of benign from malignant disease.
CT scanning allows easier, more accurate 
localization of FDG-avid foci.

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<th>SURVIVAL CURVES FOR PET+ AND PET– PATIENTS</th>
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<td>Time (months)</td>
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Figure 3. Kaplan Meier curve for the PET+ and PET– patients. There is statistically significant difference between number of patients surviv- ing in the PET and in the PET– group (p = 0.0108, log rank test).

**DISCUSSIONS IN PET IMAGING**

Established limiting disease by excluding extrathoracic disease would indicate treatment with radiation and chemotherapy as opposed to only chemotherapy for extensive disease. Accurate PET/CT scanning in the evaluation of thoracic disease is also important in distinguishing an appro- priate radiation port. Since CT assessment is based on the extent of disease, PET/CT could be more sensitive than CT scans in a small number of cases. A study by Schumacher et al that evaluated FDG-PET could be more sensitive for evaluation of bone metastases than bone scan in three of 10 patients with bone disease and were found to be needed to firmly establish this conclusion.

**BENEFITS IN STAGING**

FDG-PET scanning is now routinely used in SCLC for staging, restaging, and assess- ment of therapy. It is highly sensitive and accu- rate in distinguishing benign from malignant lesions for evaluation of mediastinal nodes and in staging of mediastinal disease. It is useful in distinguishing N0/N1 disease from N2/N3 dis- ease and helps in optimizing invasive procedures such as mediastinoscopy and thoracotomy by identifying N3 disease. It has also been found to be more cost-effective for follow-up and has prognostic value in imaging lung cancer patients on treatment.

Combination scanning with PET and CT has added a new dimension to cancer imaging, and the number of sites with PET/CT has grown rapidly in the last two years. The combina- tion scanner allows faster imaging by predict- ing the need for slower transmission images and by avoiding the need to acquire PET images. CT images provide an anatomic map and are used for attenuation correction. Combined PET/CT images provide a more accu- rate fusion of images and overcomes the draw- backs of time-consuming retroprospective fusion through CT and PET images. PET/CT images can help iden- tify such candidates by accurate staging that complements the information of CT scanning and can localize detected tumor sites for surgical biopsy or in cases with carcino- noid or other mixed histology tumors. FDG- PET imaging can provide more precise information for staging and precise thoracic versus extrathoracic staging, leading to better identification of patients who are eligible for surgery. Establishment of limited disease is vital for determining the extent of thoracic disease outside the thoracic cavity. Bone metastases may be present in 25% to 41% of patients and in 9% to 13% as a single site of metastatic involvement. While large studies evaluating PET imaging for bone lesions in SCLC are lacking, some studies have found higher sensitivity of FDG-PET than CT scans. FDG-PET can detect bone metastases in 47% of patients with SCLC. FDG-PET can be particularly useful in detecting bone metastases in patients with SCLC. FDG-PET has been shown to be highly sensitive in detection of recurrent disease. FDG-PET has been shown to be of prognos- tic value in SCLC. We evaluated scans in 62 patients with SCLC. In 54 scans that were done for residual or recurrent disease, there was avid uptake of tracer by the tumors. FDG-PET showed high sensitivity in detection of recur- rent and residual disease. We correlated PET positivity and SUV as predictors of outcome. All patients with negative scans had better long-term survival as compared with the PET-positive cases. Limited disease patients showed a greater statistically significant differ- ence in survival than extensive disease patients.

In another study by Blum et al, PET/CT (complete remission) was shown to confer longer median time to progression (13.7 months) as compared with patients with no CR (9.7 months). We feel that FDG-PET can help in cases in which evaluation of residual disease is equiva- lent by other methods due to therapy effect and can provide prognostic information so that further therapies can be suitably managed.

**CHANGE IN MANAGEMENT**

PET imaging has played an important role in management of many cancers. In various cancers, it has been used to assess early...
nodes, skeleton, brain, bone, liver, and aden- a. Staging is based on biopsy confirmation, rather than major surgery, and must be aug- mented by standard workup including chest radiography, CT scanning, thoracoscopy/ mediastinoscopy, MR imaging, bone scans, and bone marrow biopsy. Imaging plays a critical role not only in ini- tial staging but also in staging by establishing the correct extent of disease. Chest x-ray is useful for screening, while lesions are also detect- ed on CT scans performed for evaluation of symptoms. CT scanning has an established role in initial diagnosis and staging in the chest and mediastinum. Diagnosis of lymph node involvement by CT scans is considered reason- ably accurate, except that diagnosis is based on the size of lesions, and nodes that are not sig- nificantly enlarged are categorized as benign. The accuracy for detection of metastatic lymph node involvement in the mediastinum is reported to be between 50% and 82%.3 Tumor recurrence and residual disease post- treatment are often difficult to diagnose by other methods due to therapy effect and can be more sensitive for evaluation of bone metastasis than bone scans in 103 of 10 patients with bone disease. FDG-PET can help identify active sites by their tracer avidness even if the lymph nodes are not enlarged.

Various radiopharmaceuticals, including thallium-201 chloride and indium-111 octreotide, have been used for evaluation of SCLC.4,5FDG PET uses a physiolog- ical method for evaluation of tumor that is based on increased metabolic activity and uptake of glucose by tumor cells. It has the ability to detect active sites of tumor tissue and plays an established role in diagnosis and staging of many cancers.

FDG-PET scanning is now routinely used in NSCLC for staging, restaging, and assess- ment of therapy. It is highly sensitive and accu- rate in distinguishing benign from malignant lesions for evaluation of mediastinal nodes and in staging of mediastinal disease. It is useful in distinguishing N2/N3 disease from N2/N3 dis- ease and helps in obviating invasive procedures such as mediastinoscopy and thoracotomy by identifying N3 disease. It has also been found to be more cost-effective for follow-up and has prognostic value in imaging lung cancer patients on treatment.6

Combination scanning with PET and CT has added a new dimension to cancer imaging, and the number of sites with PET/CT has grown rapidly in the last two years. The combina- tion scanner allows faster imaging by preclud- ing the need for slower transmission images and provides additional information with PET images. CT images provide an anatomic map and are used for attenuation correction. Combined PET/CT scans allow more accu- rate fusion of images and overcomes the draw- backs of time-consuming retrospective fusion through multiplanar reconstructions. Imaging can help iden- tify such candidates by accurate staging that complements the information of CT scanning and locates restaged undetected tumors sites for surgical biopsy or in cases with carci- noid or other mixed histology tumors. FDG- PET imaging can provide more accurate and close proximity of vasculature and nodal stations, and of adrenal lesions and liver by accurate localization of FDG-avid foci.

**BENEFITS IN STAGING**

Establishing limited disease by excluding extrathoracic disease would indicate treatment with radiation and chemotherapy as opposed to only chemotherapy for extensive disease. Accurate localization of extrathoracic disease is also important to delineating an appro- priate radiation port. Since CT assessment is based on visible disease, FDG-PET could be used with normal nodes (<1 cm) on CT, about 10% to 15% may have disease. Treatment failure may occur with these lesions if not identified. FDG- PET can help identify active tumors by their tracer avidness even if the lymph nodes are not enlarged. Recent studies have shown high sen- sitivity and specificity for PET and PET/CT in SCLC. (Figures 1 and 2).

Initial studies in a small number of patients have shown a potential role for FDG in the staging of SCLC and high uptake of the tracer in the primary tumor.7,8 Schumacher et al compared PET/CT and CT in 13 patients, showing overall benefits for PET, which detected more sites than CT led to a change in staging in seven patients (limited to extensive disease).9 PET detected all primary and metastatic sites with sensitivity as high as 97% to 100% and 83% agreement with conventional staging. In a large study, FDG-PET caused a stage migration in 14 of 120 patients, correctly upstaging 10 patients to extensive disease and downstaging four. FDG-PET was significantly superior to CT in distinguishing thoracic lymph node involvement (sensitivity 100% versus 70%, specificity 98% versus 94%) and distal lymph nodes (sensitivity 63%, specificity 92% versus 79%).10 Overall, in various studies, FDG-PET upgraded limited disease to extensive disease in 8% to 11% of patients.11,12

- **Assessment of appropriate patients for surgery.** FDG-PET/CT in SCLC is utilized for the assessment of surgery candidates. FDG-PET is likely to be more sensitive and specific in evaluation of the mediastinum, with its complex anatomy and close proximity of vasculature and nodal stations, and of adrenal lesions and liver by accurate localization of FDG-avid foci.

**SURVIVAL CURVES FOR PET+ AND PET– PATIENTS**

Figure 3. Kaplan–Meier curve for the PET+ and PET– patients. There is statistically significant difference between number of patients surviving in the PET+ and in the PET– group (p = 0.0108, log-rank test).

**RECURRENT DISEASE AND PROGNOSIS**

Many initial PET studies included patients scanned for recurrent disease or restaging. FDG-PET has been shown to be highly sensi- tive in detection of recurrent disease and restaging.13 PET has also been shown to be of prognos- tic value in SCLC. We evaluated 62 scans in 46 patients with SCLC. In 54 scans that were done for residual or recurrent disease, there was avid uptake of tracer by the tumors. PET-DG showed high sensitivity in detection of recur- rent and residual disease. We correlated PET positivity and SUV as predictors of outcome. All patients with negative scans had better long-term survival as compared with the FDG-positive cases. Limited disease patients showed a greater statistically significant differ- ence compared with limited stage disease patients.14

In another study by Bhan et al, PET-CR (complete remission) was shown to confer longer median times to progression (13.2 months) as compared with patients with no CR (9.7 months).15 We feel that FDG-PET can help in cases in which evaluation of residual disease is equiv- alent by other means due to therapy effect and can provide prognostic information so that further therapies can be suitably managed.

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PET/CT imaging allows detection of active lesions otherwise missed by other imaging modalities. It is important to ask if the higher sensitivity of FDG-PET Imaging and improved results in staging in SCLC also lead to any changes in management. Recent studies have specifically addressed this issue, and data support the use of PET, which can help achieve better targets by inclusion of lesions otherwise missed by other imaging modalities. In another study in 42 patients, PET results changed the patient’s management in 12 cases (29%), and in 18 patients (41%) changed the RT plan, which was either cancelled or modified in radiation field and volume.

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Response to initial treatment is usually good, with about 80% of patients showing a major response. About 20% of patients with limited disease can be cured with proper therapy, while others will eventually have recurrence. The overall median survival for SCLC is only 14 to 16 months, longer for those with limited disease. Chemo-therapy is the primary form of treatment for SCLC, as only a few patients with extensive disease are cured with proper therapy, while others will eventually have recurrence. The overall median survival for SCLC is only 14 to 16 months, longer for those with limited disease. Chemo-therapy is the primary form of treatment for SCLC, as only a few patients with extensive disease are cured with proper therapy, while others will eventually have recurrence. The overall median survival for SCLC is only 14 to 16 months, longer for those with limited disease. Chemo-therapy is the primary form of treatment for SCLC, as only a few patients with extensive disease are cured with proper therapy, while others will eventually have recurrence. The overall median survival for SCLC is only 14 to 16 months, longer for those with limited disease. Chemo-therapy is the primary form of treatment for SCLC, as only a few patients with extensive disease are cured with proper therapy, while others will eventually have recurrence. The overall median survival for SCLC is only 14 to 16 months, longer for those with limited disease. Chemo-therapy is the primary form of treatment for SCLC, as only a few patients with extensive disease are cured with proper therapy, while others will eventually have recurrence. The overall median survival for SCLC is only 14 to 16 months, longer for those with limited disease.