PET/CT: INTRODUCTION TO
PET/CT AND CLINICAL UTILIZATION

GEETHA ASHOK, M.D.

PET/CT Imaging

✓ Positron Emission Tomography
✓ **Positron**
  - Detects two gamma rays resulting from decay of positron-511kev

✓ **Emission**
  - Photons emitted from inside subject - as opposed to “transmission” where they are generated externally.

✓ **Tomography**
  - Generates three-dimensional maps of radioactivity concentration
[18F]-Fluorodeoxyglucose (18F-FDG)

- Glucose analog that is taken up by glucose-using cells and phosphorylated by hexokinase.
- Mitochondrial hexokinase is greatly elevated in rapidly-growing cells.
- Because the oxygen atom (which is replaced by F-18) is required for the next step in glucose metabolism, no further reaction occur on FDG.
- FDG is trapped in the cells.
- Results in intense radio labeling of tissues with high glucose uptake.
- Fluorine F 18 decays by positron (β+) emission and has a half-life of 109.7 minutes. The principal photons useful for diagnostic imaging are the 511 keV gamma photons, resulting from the interaction of the emitted positron with an electron.

Standard PET/CT Protocol

- Questionnaire is administered to collect information regarding
  - Clinical History
    - Malignancy being evaluated
    - Date of diagnosis
    - Therapy and dates of therapy
    - Any relevant co-morbidities that may cause misinterpretation such as recent infections, inflammatory process, or trauma,
    - Diabetic status; serum glucose should be less than 200mg/dL and ideally less than 150 mg/dL
Procedure

• Patient fasting for 4-6 hours/ limit exercise
• Check blood glucose by a glucometer
• Start intravenous line
• Injection of 10-15 mCi of FDG
• 30-45 minutes of uptake period
• Patient has to empty urinary bladder
• Patient is positioned in scanner
• Imaging from neck to upper thigh
• First low KEV CT done followed by PET imaging
• Patient motion can lead to significant misregistration of CT and PET images
• Mismatch in lung bases due to differences in respiration may obscure nodules.

Procedure

• For typical scan protocol,
  • Emission Scan
    2-5 minutes/bed position,
    total emission time of 12-30 minutes
    for a 6 bed position scan
    plus CT Scan time from 1-3 minutes.
    (CT used for attenuation correction and fusion)
Clinical Added Benefits

- **General Added Benefits of PET/CT**
  - Detection of lesions by PET missed on CT, even with good contrast-enhanced CT
  - Contrast-enhanced CT more sensitive than noncontrast CT but still may miss early lesions, even with good parenchymal enhancement
  - CT very insensitive for detection of early lytic bone metastases; FDG PET more sensitive than traditional bone scanning for detection of osteolytic lesions
- **Detection of Lesions in CT Artifacts**
- **Improved lesion localization**
- **Biopsy Localization Information**

Physiologic vs. Pathologic FDG Activity

- Prior to PET/CT, areas of focal muscular FDG activity and brown fat were often misinterpreted as pathology
- Many structures may have intense physiologic FDG activity
- PET/CT helped differentiate physiologic from pathologic FDG activity by allowing accurate coregistration
Normal Distribution of 18F-Fluorodeoxyglucose (FDG)

<table>
<thead>
<tr>
<th>System</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>High uptake in cortex, basal ganglia, thalami, cerebellum, brainstem. Low uptake into white matter and cerebrospinal fluid.</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>Variable but homogenous uptake into left ventricular myocardium. Usually no discernible activity in the right ventricle and atria.</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
<td>Variable uptake into the stomach, small intestine, colon, and rectum.</td>
</tr>
<tr>
<td>Reticuloendothelial and lymphatic</td>
<td>Liver and spleen show low-grade diffuse activity</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Urinary excretion can cause variable appearances of the urinary tract.</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>Low activity at rest</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>Normal marrow shows uptake that is usually less than liver.</td>
</tr>
<tr>
<td>Lung</td>
<td>Low activity (regional variation)</td>
</tr>
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Lung Cancer

- **Epidemiology**
  - Lung cancer is the leading cause of cancer-related deaths for both men and women.
  - An estimated 170,000 new cases of lung cancer and an estimated 150,000 deaths from lung cancer will occur in the United States.
  - Most of those people will be from minority groups.
  - Direct medical cost for treatment of lung cancer is approximately $5 billion annually.
  - Smoking is responsible for 87 percent of lung cancer deaths.
Classification of lung cancer

- **Histologic Classification of Non-small Cell Lung Cancer**
  - Squamous cell (epidermoid) carcinoma
    - spindle cell variant
  - Adenocarcinoma
    - acinar
    - papillary
    - bronchoalveolar
    - solid tumor with mucin
  - Large cell carcinoma
    - giant cell
    - clear cell
  - Adenosquamous carcinoma
  - Undifferentiated carcinoma
  - **Small cell lung cancer**

FDG Uptake in Lung Cancer

- Lung cancer is very FDG-avid. This uptake becomes even more conspicuous as there is relatively low uptake in the surrounding aerated lung as opposed to other soft tissues. Non-aerated lung may have about three times the activity of aerated lung. As lung tissue is less "dense", an area of atelectasis would have relatively higher uptake per volume of tissue compared to surrounding normal lung. This would hold true for a lung nodule as well. Therefore nodules should not be compared to surrounding aerated lung, but rather to other solid soft tissue to assess for relatively increased uptake. Comparison typically can be made with mediastinal soft tissues or blood pool.
Possible false negatives on FDG-PET

1. Histologic types of lung cancer with variable uptake:
   - Pulmonary carcinoid
     - Atypical carcinoid tumors are more likely to be FDG-avid than typical carcinoid tumors
   - Bronchioloaveolar cell cancer
     - Solid components of BAC on CT are more likely to be FDG-avid.
   - *Should not be used to exclude these specific types*

Possible false negatives on FDG pet

- **Necrosis**
  - An area of necrosis within a tumor will show little FDG activity
  - Typically there is an FDG-avid rim however, which can be easily detected.
  - Can help direct area of tumor to biopsy
  - Directing a biopsy to the most FDG-avid portion of the lesion may improve the diagnostic yield and avoid a false positive biopsy result
Possible false negatives

3. Size
- Less than 8 mm
- 95% sensitivity > 8mm
- Limited resolution of PET scanner
- Unreliable evaluation due to partial voluming "dilution" effect on degree of uptake

4. Other lesions
- Granulomatous disease is a common cause of false positive single pulmonary nodule.
- Fungal granulomas due to coccidiomycosis, histoplasmosis, and aspergillosis are particularly in endemic areas.
- Granulomas due to tuberculosis.
- Sarcoidosis often has a characteristic pattern, but it can cause false positives.
- Active infections
- Post infectious nodules

SUV

SUV Criteria
- Standardized Uptake Value takes into account the differences between normalizing for body weight, for lean body mass, or for surface area.

SUV calculation: \[ \text{SUV} = \frac{\text{mCi/ml (decay corrected) in tissue}}{\text{mCi of tracer injected/body weight (grams)}} \]
- "Cut off" value between benign and malignant single pulmonary nodules is in the range 2.0-2.5.
- Value decreases for smaller lesions due to partial volume effects
- Indirect comparison can be made to the mediastinal blood pool (generally in the range of 2.5).
- A positive nodule will demonstrate uptake greater than the mediastinal blood pool.
- Using this internal control can help avoid errors in the SUV calculation
- Quantified SUV facilitates comparison with the mediastinal blood pool on the display
Solitary Pulmonary Nodules

- **Terminology**
  - Solitary pulmonary nodule (SPN)
  - Opacity in the lung parenchyma measuring up to 3 cm with no associated mediastinal adenopathy or atelectasis

SOLITARY PULMONARY NODULE

- Significant overlap in FDG activity between benign and malignant nodules
- SUV > 2.5 has sensitivity/ specificity 90-100%, 69-95% for detection of malignancy
- Detection depends largely on size
- Lower resolution limit 6-8 mm
- Partial volume averaging of small nodules can produce falsely low SUV
- Bronchioloalveolar carcinoma has multifocal form that is often detected with FDG PET
- Overall, BAC tends to have lower FDG uptake than other pulmonary malignancies
SOLITARY PULMONARY NODULE

**False positives**
Focal hypermetabolic uptake unrelated to malignancy
most common include infection, inflammatory reaction, granuloma, hamartoma

**False Negatives**
Malignant subcentimeter nodules may not be detected on FDG PET
Hypometabolic tumors: BAC, carcinoid lesions post-therapy (“stunned tumor”)
Ground glass nodules often false negative due to size and association with BAC

**PET provides prognostic information for malignant nodules**

- May be more accurate than pathology in predicting recurrence free survival

- Low stage tumor with high SUV often has poor prognosis
- MAX SUV is $>\text{or equal to } 9.68\%$, 2 year survival
- MAX SUV $<\text{or equal to } 9; 96\%$ 2 year survival
Diagnostic Checklist

- Continued CT follow up in PET negative SPN
- If nodule has features of BAC, a negative PET does not rule out malignancy
- Predictive value of stability in size over time of a SPN is only 65%.

Sensitivity and Specificity

- FDG-PET is very sensitive though not very specific
- Sensitivity of 96.8 and specificity of 77.8 in accuracy to differentiate malignant and benign lesions. Negative FDG-PET significantly reduces the chance that a lesion is malignant
- This decreases with smaller lesions in the 5-7 mm range, continue follow up
- May be adequate to obviate further clinical work up or continue non-invasive follow up
- FDG avidity of bronchioloaveolar cell cancer is reduced
- Nodules adjacent to heart and in lung bases may be obscured due to motion on pet imaging
LUNG CANCER

- Therapy planning is determined by stage. Accurate staging is very important since it has such a major impact on both therapy and prognosis and FDG-PET plays an important role in selection of therapy.
- Stage IA and IB can often be treated with surgery alone. Adjuvant chemotherapy can be considered in stage IB.
- Stage II is treated with a combination of surgery and chemotherapy or radiotherapy.
- Stage IIIA patients typically have preoperative chemotherapy or radiotherapy. Neoadjuvant therapy can be used to shrink the tumor prior to resection.
- Stage IIIB and IV patients are generally considered incurable and are treated with palliative therapy. Some selected stage IIIB patients may be considered for an aggressive combined therapy approach.
- Stage IV patients with a single brain metastasis are a special case; a highly selected group of these patients are considered for curative resection.

Lymph Node Stations

- Precise lymph node localization is useful for staging as well as for communication with the bronchoscopist or surgeon. A numbering system has been adopted to describe the various lymph node locations.
- Lymph node stations are designated with a single digit, 1-9, within the mediastinum.
  - N2 nodes are ipsilateral to the tumor.
  - N3 nodes are contralateral to the tumor in the TNM classification.
- Lymph node stations 10-14 correspond to N1 nodes
  - These nodes lie distal to the mediastinal pleural reflections.
  - An "R" or an "L" can be appended to right or left of midline.
Advantages of FDG-PET in Lymph Node Staging

- FDG-PET has the ability to identify positive nodes that are smaller than the standard CT pathologic enlargement criteria of one centimeter as well as identify larger size nodes that are negative.
- PET imaging with anatomically fused images is advantageous in being able to identify the exact location of mediastinal nodes near the midline.

Staging - Distant metastases

- One of the most important roles for FDG-PET
- Common sites
  - adrenal glands, liver, bones
- Stage IV - palliative chemotherapy is indicated.
- Direct biopsy site to confirm the highest stage of disease expediting the work up
- FDG-PET scan can reveal a distant site of disease that can be biopsied. This often can obviate the need to biopsy the primary lesion.
- Biopsy based on an FDG-PET scan can make the diagnostic workup more effective.
Staging of lung cancer

- Detection of disease
- Identify occult mets-adrenal
- Detects bone mets with equal sensitivity to and greater specificity than bone scintigraphy
- 100% PPV and high NPV for mediastinal node mets
- Brain mets overlooked due to high background FDG activity
- Necrotic mets may be negative

Staging-influence on management

- Pet more sensitive for supraclavicular lymph nodes—inoperable/tissue diagnosis needed
- Pet >90% NPV for nodal disease; if negative mediastinal nodes thoracotomy without mediastinoscopy
Staging--prognosis

- SUV>5 poor prognosis; significant increase in postop relapse in early stage lung cancer
- Intense BM uptake-poor outcome

Response to treatment

- Decrease in FDG avidity of malignant lesion by 60% following 2-3 cycles of chemotherapy—may indicate good response and predictive of improved survival
- After surgery or radiotherapy, PET for differentiating scar from residual or recurrent tumor—2 months after surgery and 4-6 months after radiotherapy
Radiation Therapy

- Effects seen within the radiation port with well defined borders
- Typically low level FDG uptake
- Usually returns to normal after six months but can persist for longer
- There can be increase uptake in both the lung and the chest wall
- Focal increased or increasing uptake within the radiation port is suspicious for recurrence especially if associated with mass
- Mild to moderate uptake in a region corresponding to typical radiation changes does not suggest recurrence.

Post Therapy

- **Post Operative Changes**
  - Inflammatory
  - Anatomic
- **Post Radiation Changes**
  - Significant and often dose limiting side effect of external beam radiation therapy
  - Uptake can often be quite intense
  - Pattern of uptake may be more helpful in differentiating benign and malignant uptake
- **Radiation Pneumonitis**
  - A common occurrence following thoracic radiation
  - Can pose a diagnostic problem on both anatomic and functional images
  - Occurs in the involved portion of the lung due to associated inflammation
  - Can make early detection of recurrent cancer a problem
Staging small cell lung cancer

• Patients with limited disease
• Pts with extensive disease
• PET USED FOR PLEURAL TUMOR INVOLVEMENT-benign vs malignant

LUNG CANCER

• Diagnosis, staging, and restaging of non-small cell lung cancer is one of the most promising and powerful applications of FDG-PET.
• Use of FDG-PET in the appropriate setting can significantly affect patient outcome
• More accurate staging with FDG-PET can help guide and ensure the most appropriate therapy
• Degree of FDG uptake may provide valuable prognostic information
• Knowledge of the limitations of FDG-PET/CT will help to provide the most accurate interpretation
LYMPHOMA

- Baseline PET/CT scan for staging.
- For assessment of early response during therapy - after one cycle, few cycles or at midtherapy ---- change in therapy.
- Predict response, progression free survival and overall survival.

LYMPHOMA

- Evaluation after completion of chemotherapy and/or radiotherapy.
- Residual masses seen on CT/MRI - maybe fibrosis vs viable tumor cells.
COLORECTAL CANCER

• EVALUATION OF ELEVATED SERUM CEA LEVEL.
• PREOPERATIVE STAGING OF RECURRENT CRC
• CHARACTERIZATION OF EQUIVOCAL LESIONS ON PET IMAGING
• THERAPY MONITORING

OTHER CANCERS

• PETCT UTILIZED IN BREAST CANCER, MELANOMA, ESOPHAGEAL CANCER….
• CASE PRESENTATIONS
DEMENTIA

• EVALUATION OF NEURODEGENERATIVE DISEASES
  • ALZHEIMER’S DISEASE
  • FRONTOTEMPORAL DISEASE
  • DEMENTIA WITH LEWY BODIES
  • DEMENTIA IN PARKINSON’S DISEASE
• PATTERN SEEN IN ALZHEIMER’S DISEASE

CONCLUSION

• PETCT USEFUL TOOL IN MANAGEMENT OF PTS WITH CANCER
• WORK UP OF DEMENTIA
• CARDIOLOGY