SNM PRACTICE PERFORMANCE ASSESSMENT PROJECT

Diagnostic Accuracy of
18F-FDG PET-CT in Patients with Cancer

I. OVERVIEW

This Practice Performance Assessment Project (PPAP) is designed to improve diagnostic accuracy of PET-CT with F18 2-fluoro 2-deoxy [D] glucose (FDG) in patients with newly diagnosed or suspected cancer. The objectives are: improve sensitivity for detection of malignancy in patients with cancer (fewer false negative results); improve specificity in patients without cancer (fewer false positive findings); and improve accuracy in cancer staging.

The accuracy of PET-CT in therapy evaluation and the impact on therapeutic management will be the subject of another PPAP.

Completion of this project may be used for the Part IV requirement of the American Board of Nuclear Medicine for Maintenance of Certification.

This PPAP is appropriate for physicians performing FDG PET-CT on all types of scanners except coincidence capable gamma camera, and those physicians interpreting CT done as part of PET-CT for anatomic registration as well as optimized CT for diagnosis. This PPAP may be used as an individual, center-based, or group-based project.

II. OBJECTIVES

The objectives of this PPAP are

- Improve sensitivity in patients with cancer so that >80% of exams will be positive for malignancy
- Improve specificity in patients without cancer so that >80% exams will be negative in the absence of malignancy.
- Improve accuracy for lymph node staging so that >50% of exams will be correct for N stage.
- Improve accuracy for detection of distant metastases so that >80% of exams will be correct for M stage.
- Improve overall staging so that >80% of patients with malignancy appropriate for localized therapy (surgery or radiation, plus or minus chemotherapy) are correctly identified

III. BACKGROUND

The accuracy of PET-CT is dependent upon higher FDG accumulation in malignant cells compared to normal cells (1). Several factors have been identified as being important determinants of FDG uptake, including overproduction of hexokinase and over expression of glucose transporter proteins in cellular membranes, especially GLUT-1, GLUT-3 and/or
The retention of FDG within the cell is also an important factor determining intracellular FDG concentration. Glucose-6-phosphatase cleaves the phosphate group from FDG-6-phosphate resulting in FDG, which can back diffuse across the cell membrane (3). It has been theorized that high concentrations of glucose-6-phosphatase may account for the low sensitivity of PET-CT in some types of cancer. Despite our understanding of cellular metabolism, FDG uptake by malignant cells is unpredictable. The utility of PET-CT imaging is empirical. Cancers that concentrate high levels of FDG suitable for imaging have been extensively described. The average sensitivity of PET across all oncology applications is 84% (4). Small tumor size (<10mm) is a major cause of false negative findings. Conversely, the specificity of PET-CT is dependent on the prevalence of infections and inflammatory conditions in patients without cancer. Granulomatous disease and other focal inflammatory conditions cause high levels of FDG uptake indistinguishable from malignancy. The average specificity of FDG PET is 88% (4). Maintaining high accuracy, therefore, depends on careful evaluation of the appropriateness of PET-CT in individual patients.

The sensitivity of PET-CT for lymph node metastases is generally lower than the sensitivity for primary tumors because the volume of metastatic disease is generally smaller, especially when PET-CT is compared to lymph node dissection or sentinel node biopsy. Sensitivity ranges from 40% to 93% for axillary nodal metastases in breast cancer, 34% to 69% for local nodal metastases in esophagus cancer, and 77% to 87% for mediastinal nodal metastases in lung cancer (5).

The interpretation of PET-CT is usually based on visual assessment of FDG uptake using a binary decision model where no discernible uptake is interpreted as normal or benign, versus increased FDG uptake, which is interpreted as likely malignant (6). This model results in high sensitivity, particularly for small lesions, at the expense of lower specificity. In order to maintain sensitivity while improving specificity, a number of quantitative approaches have been suggested. The most common method is the standardized uptake value (SUV). The SUV compares the concentration of FDG uptake in a region of interest to a computed average throughout the body. It has been proposed that a mean SUV threshold of 2.5 more accurately distinguishes benign from malignant pulmonary nodules compared to visual assessment in nodules > 1.5 cm (7). Unfortunately, SUV is dependent on many variables that are not easily controlled in a clinical setting, and limits its utility (8). It has also been recognized that the SUV of inflammatory lesions may be greater than 2.5, further limiting the value of this measurement. To overcome this limitation, it has been suggested that measuring SUV after administration of FDG at 60 minutes and again at 120 minutes can help distinguish malignant lesions from inflammatory foci, based on the observation that SUV increases in malignant lesions, and shows no change or decreases with time in benign foci (9). This approach, called dual-time point imaging has undergone refinement since its introduction, but has not been widely accepted.

Physicians who desire an in-depth review of acquisition, processing, display, and interpretative criteria are referred to practice guidelines of SNM (10) and the procedure guidelines of the American College of Radiology (ACR) (11).

This PPAP allows the physician to use PET and PET/CT studies acquired, processed, and displayed according to personal preference and local routine. The suggested learning tools allow the physician to:
• Compare different interpretative criteria, including visual and semi quantitative methods.

• Improve interpretive skills by comparing results with histology, other imaging studies, and clinical outcome.

IV. INSTRUCTIONS

Plan

Determine if this PPAP is relevant to your clinical practice. Consider how you will identify the patients to be included, and how you will collect the PET-CT data, histology, and clinical follow-up. Set a goal for completing the PPAP within a defined period of time.

Do

Select 30 patients referred for PET-CT for diagnosis of suspected malignancy or staging of known malignancy. The selection may be made from a broad cross section of patients referred for different malignancies, or based on a specific type of malignancy, depending on local interest, practice patterns and need. The role of FDG PET-CT in cancer staging has been recently reviewed (12). Recommendations on the use of FDG PET in oncology have been recently published, and include data regarding sensitivity and specificity for cancers of the breast, colon and rectum, esophagus, head and neck, lung, pancreas, and thyroid, as well as lymphoma and melanoma (5).

Ideally, patients will have had biopsy or surgery within 3 months of PET-CT. Alternatively, results of PET-CT may be compared to other imaging studies or long-term follow-up, although pre-test referral bias and post-test work-up bias limit the validity of this method. Retrospective double-blind reading of PET-CT and other imaging studies may reduce bias.

Transfer the findings and interpretation from the medical record to Form 1, or enter the information after retrospective, blind review of the studies.

Enter the clinical information and/or histologic findings from biopsy or surgery on Form 1.

Transfer the data for each patient to Form 2 to calculate accuracy for diagnosis and staging of malignancy.

Enter the overall accuracy of PET-CT on Form 2. If the overall accuracy is > 80% consider choosing another PPAP.

Study

If the overall accuracy of PET-CT is < 80%, use one or more of the following educational tools:

• Practice guidelines of SNM and ACR
• SNM LLSAP (Life-long Self Assessment Program) modules, available at www.snm.org
• SNM on-line diagnostic PET/CT and CT cases, available at www.snm.org
• Suggested reading (references 1-12)

**Act**

Apply the information learned from the educational tools to the interpretation of an additional 30 PET-CT studies.

Review the studies (do not use reports from the medical record this time), and enter the findings and interpretation on Form 1.

Transfer the data for each patient to Form 2 to calculate overall accuracy.

Compare the findings and results on Form 2 after using the suggested educational tools with the results on Form 2 before starting this PPAP.

If satisfied with the improvement, send both Forms to SNM for documentation.

If no improvement, or dissatisfied with the amount of improvement, repeat the PPAP after using additional or other educational tools.

**V. REFERENCES**


INSTRUCTIONS FOR COMPLETING FORM 1

1. Use one form for each patient.

2. Do not record negative PET-CT findings, incidental findings that are unrelated to the reason for doing the study (e.g. cysts), or findings that are clearly benign (e.g. heavily calcified nodes or nodules).

3. Enter significant PET-CT findings in the appropriate column (probably malignant, indeterminate, probably benign). Significance may be based on scintigraphic and/or radiographic findings.

4. Enter only the most significant finding for each region or organ (e.g. if PET-CT shows one mediastinal lymph node that is probably malignant, as well as other mediastinal lymph nodes that are probably benign, record only the probably malignant lymph node).

5. Significant findings should be indicated with (R) right side, (L) left side, or (B) bilateral in the appropriate column. Enter (X) if side is not relevant.

6. If SUV was determined, enter the value in the appropriate column.

7. Enter the appropriate information regarding histology or clinical follow-up. In the absence of histology, a finding may be considered benign if it shrinks or disappears without therapy, or size remains stable for at least two years. A finding may be considered positive if subsequent imaging findings show clear signs of malignancy (e.g. destruction or invasion or neighboring structures). All other findings should be recorded as indeterminate.

8. Make a final assessment of whether cancer is present or absent at the bottom of the form based on PET-CT, as well as histology or clinical follow-up.

9. Record T, N, M stage and overall stage (I through IV) based on PET-CT, as well as histology or clinical follow-up. Refer to the Practice Guidelines of the National Comprehensive Cancer Network (www.nccn.org) for staging information.
## Form 1
### PET-CT FINDINGS WORKSHEET

**STUDY I.D.**

**DATE OF STUDY**

**INDICATION**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Staging</th>
</tr>
</thead>
</table>

### BRAIN
- **HEAD**
- **NECK**
  - Salivary glands
  - Tonsils
  - Tongue
  - Pharynx/Larynx
  - Thyroid
  - Lymph nodes
  - Other

### THORAX
- **Breast**
- **Lung**
- **Pleura**
- **Heart**
- **Pericardium**
- **Esophagus**
- **Lymph nodes**
  - subsupraventricular
  - axillary
  - hilar
  - mediastinal
  - not otherwise specified
- **Muscle/soft tissue**
- **Other**

### ABDOMEN AND PELVIS
- **Liver**
- **Spleen**
- **Gallbladder**
- **Pancreas**
- **Stomach**
- **Small bowel**
- **Large bowel/rectum**
- **Adrenal glands**
- **Kidneys**
- **Ureters**
- **Bladder**
- **Prostate**
- **Uterus**
- **Cervix**
- **Lymph nodes**
  - abdominal
  - pelvic
  - inguinal
  - Muscle/soft tissue
- **Other**

### SKELETON
- **Skull**
- **Axial skeleton**
- **Appendicular skeleton**

### EXTREMITIES
- **Soft tissues**

### VASCULAR
- **Arterial**
- **Venous**

### PROB/MALIG
<table>
<thead>
<tr>
<th>PET/CT</th>
<th>INDETER</th>
<th>PROB/BENIGN</th>
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### MALIG
<table>
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<th>HISTOLOGY</th>
<th>INDETER</th>
<th>BENIGN</th>
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### CLINICAL FOLLOW-UP

### Cancer Present?

**YES** | **NO**

### Cancer Stage

T N M Stage:
INSTRUCTIONS FOR FORM 2

1. Transfer data from Form 1 for each patient. Aggregate results for each patient should be entered on a single row.

2. Patients referred for diagnosis of cancer:
   a. Record whether PET/CT was true positive (TP) or false negative (FN) in patients with cancer. Record whether PET/CT was true negative (TN) or false positive (FP) in patients without cancer.
   b. Record whether PET/CT was correct or incorrect regarding lymph node stage (N stage), distant metastases (M stage), and final stage.

3. Patients referred for staging:
   a. Do not record whether PET/CT was correct or incorrect regarding the presence of cancer. It is assumed that PET or PET/CT will be true positive in at least one site if patients are referred for staging.
   b. Record whether PET/CT was correct or incorrect regarding lymph node stage (N stage), distant metastases (M stage), and final stage.

4. Tabulate sensitivity, specificity, and accuracy and record on the bottom of Form 2.

5. Compare your results with the stated objectives of this PPAP.
# Form 2

**PET-CT SUMMARY DATA**

<table>
<thead>
<tr>
<th>DATE</th>
<th>MALIGNANT VS BENIGN</th>
<th>N STAGE</th>
<th>M STAGE</th>
<th>FINAL STAGE</th>
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<tbody>
<tr>
<td></td>
<td>TP</td>
<td>FN</td>
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**SENSITIVITY**  \(\frac{(TP + FN)\cdot ALL}{ALL}\)

**SPECIFICITY**  \(\frac{(TN + FP)\cdot ALL}{ALL}\)

**ACCURACY**  \(\frac{COR\cdot ALL}{ALL}\)