PET/CT in Oncology

Positron emission tomography (PET) is a molecular imaging method that provides complementary information to anatomic imaging by CT or MRI.

Fluorine-18-deoxyglucose (FDG) PET/CT is valuable for:
- Detection of selected primary tumors,
- Detection of distant metastases, and the
- Detection of tumor recurrence.

PET/CT is used for monitoring response to therapy and, because PET changes are relatively rapid compared to tumor size, clinicians may modify the course of treatment relatively soon after initiation of therapy.

PET Applications for Initial Treatment Strategy

PET/CT is used in the initial diagnosis of primary tumors of selected cancers. This includes the work-up of solitary pulmonary nodules, which are common incidental findings on CT. PET is often able to identify metabolically active nodules that are suspicious for malignancy, but it is important to realize that false positive results can occur in a variety of inflammatory and granulomatous processes. False negative PET scans may occur in some malignant nodules, particularly indolent, slow growing tumors. A negative PET scan does not exclude malignancy in a nodule.
and continued CT follow-up may still be required. As a general rule, pulmonary nodules must be at least 8 mm in
diameter for meaningful evaluation because PET imaging does not have sufficient resolution to successfully image
nodules that are smaller than this.

PET/CT using contrast enhanced diagnostic CT is critical for the initial evaluation of head and neck tumors, where
the complexity of the surrounding anatomy, together with relatively high rates of physiological uptake in tissues
such as brown fat, salivary glands, vocal cords, and skeletal muscle, pose challenges to the accuracy of diagnosis
and staging.

FDG-PET is commonly employed in the initial assessment of a wide variety of common malignancies, but PET
imaging may not demonstrate small tumor foci. In the breast, for example, FDG is taken up relatively rapidly into
dense breast tissue and the image contrast is not sufficient to detect small (<5 mm) tumors. Therefore, the
sensitivity of detection of breast lesions <5 mm has been reported to be 53%, although those >20 mm are detected
with a sensitivity of 92%. FDG-PET is not recommended for staging of axillary lymph nodes in breast cancer
because PET is not sensitive enough to detect micrometastases in lymph nodes that are not pathologically enlarged.
This is a general principle of PET imaging. For example, in melanoma patients, FDG-PET detected 100% of lymph
node metastases ≥10 mm, 83% of metastases 610 mm, and 23% of metastases ≥5 mm. It is also important to
realize that inflammatory reactive lymph nodes may show increased FDG uptake, so biopsy of PET-positive lymph
nodes is sometimes needed to confirm the presence of malignancy.

There is a relatively short list of tumors for which PET imaging is generally not useful. In prostate cancer, FDG-PET
is not sufficiently accurate because these tumors are often not FDG avid. Intense excretion of tracer by the kidneys
similarly makes evaluation of bladder and renal cancers very difficult.
Figure 2. PET/CT scan performed for evaluation of a new lung nodule. (A) PET scan shows moderately intense uptake in the nodule (solid arrow), indicating metabolic activity and incidental uptake in metabolically active brown fat (dotted arrows). (B) CT scan showing lung nodule (arrow) (C) Fused PET/CT image showing alignment of metabolic activity with nodule seen on CT. However, subsequent tissue sampling revealed that this was cryptococcal infection, not malignancy.

The inclusion of PET/CT in the diagnostic work-up of patients increases the accuracy of staging and leads to more appropriate management. For example, in lung cancer, PET/CT has been shown to have additional value over PET alone for the detection of extrathoracic metastases, such as those in the intestine, liver, adrenal gland, or skeleton. With more accurate staging, fewer patients undergo futile operations and the overall costs of caring for lung cancer patients is lower. In addition, PET imaging is useful for planning for radiation therapy because it can distinguish between tumor and surrounding reactive normal tissue.

PET has been shown to be sensitive for the detection of nodal and extranodal manifestations of both Hodgkins and non-Hodgkins lymphoma and has become an important modality for the development of treatment strategy. PET/CT is also commonly used for the detection of metastatic disease in a number of other primary cancers, including colorectal and esophageal cancers and melanoma.
PET Applications for Subsequent Treatment Strategy

The response detected by PET/CT is generally apparent much sooner than tumor shrinkage. Therefore, PET/CT has been used to assess response early in therapy to allow clinicians to modify their treatment strategy for non-responding patients. For example, in patients with esophageal cancer, a metabolic response detected by PET at two weeks was predictive of treatment outcome. In patients with Stage IV non-small cell lung cancer, a 65% decrease in FDG uptake relative to baseline was observed after two cycles of chemotherapy in responding patients. In lymphoma patients, PET/CT is more accurate than anatomic imaging for assessing treatment response, identifying patients with residual disease, and predicting therapeutic outcome. PET-negative scans after the first cycle of chemotherapy predicts outcome in diffuse large cell and Hodgkin’s lymphoma and a sustained complete response (with a median follow-up of 28 months). In patients with advanced head and neck cancers, a response to chemoradiotherapy was detected at 8 weeks by PET/CT with a sensitivity of 100%, compared to 26% for CT alone.

In esophageal cancer, a decrease of $\geq 50\%$ in FDG uptake is associated with significantly longer disease-free survival. PET/CT is also useful for monitoring response to chemotherapy in advanced colorectal cancers, and for the detection of recurrence in surgically treated patients.

PET/CT is well-suited to differentiating between residual tumor and post-therapy changes because the latter show little or no FDG uptake, while CT alone cannot differentiate between these two possibilities. For example, in head and neck cancers, PET/CT was shown to be more sensitive (88100%) and specific (75100%) than CT (3890% and 3885%, respectively) for the detection of recurrent or residual disease. In patients with squamous cell carcinoma of the esophagus, PET/CT detected recurrence with a sensitivity of 93%, specificity of 76%, and accuracy of 87%.

### Table 1. Applications of FDG PET Covered by the Center for Medicare and Medicaid Services (CMS)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Initial Treatment Strategy</th>
<th>Subsequent Treatment Strategy</th>
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<tbody>
<tr>
<td>Colorectal</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Esophageal</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Head and neck (not thyroid, CNS)</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Lymphoma</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Non-small cell lung</td>
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<td>Ovarian</td>
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<td>Yes</td>
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<td>Brain</td>
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<td>Small-cell lung</td>
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<td>Soft tissue sarcoma</td>
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<tr>
<td>Pancreatic</td>
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<td>Testes</td>
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<tr>
<td>Breast (male and female)</td>
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<td>Melanoma</td>
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<td>Yes</td>
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<td>Myeloma</td>
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<td>All other solid tumors</td>
<td>Yes</td>
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<tr>
<td>All other cancers not listed here</td>
<td>Possible³</td>
<td>Possible³</td>
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<tr>
<td>Solitary pulmonary nodule</td>
<td>Yes</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Formerly "diagnosis" and "staging"; †Formerly "restaging" and "monitoring treatment response"  
¹One FDG-PET for biopsy-proven cervical cancer if needed to determine location and/or extent of tumor  
²For evaluation of selected known brain tumors; not for detection of primary or metastatic brain tumors  
³Only with evidence development paradigm requiring completion of a pre- and post-scan form by the referring physician;  
⁴Not for initial diagnosis or staging of axillary lymph nodes;  
⁵Not for initial staging of regional lymph nodes;  
⁶After treatment with thyroidectomy and radiiodine ablation, with serum thyroglobulin <10 ng/mL and negative $^{131}$I whole-body scan

**PET/CT Examination Procedure**

All current PET scans at the MGH are performed on a hybrid PET/CT scanner. The PET scan requires the use of a very low dose CT acquisition to allow attenuation correction and anatomic localization. If desired, standard diagnostic CT imaging can be performed at the conclusion of PET imaging as part of the same examination, and can...
be acquired using intravenous contrast. All MGH Imaging hybrid PET scanners have 64 slice CT scanners that provide high quality images comparable to those done on any other CT device. If a patient needs both diagnostic CT imaging and PET imaging, the diagnostic CT scans should be scheduled as part of the PET/CT study. Acquiring diagnostic CT scans at the same sitting as the PET study allows better image registration, improving diagnostic confidence, and optimizes patient convenience. If recent diagnostic CT images have been performed, the PET/CT scan can be scheduled using only low dose attenuation-correction CT, without acquiring any diagnostic CT images.

Patients are routinely asked to fast for 4-6 hours prior to the examination. Water is permitted but no sweetened beverages. Diabetic patients should fast for 4 hours before the study, and should eat and take their insulin just prior to fasting. If the patient is on an IV, there should be no glucose in the IV solution in the hours preceding the scan. This is necessary to minimize the amount of insulin circulating in the blood and maximize FDG uptake into the metabolically active cells. All patients will have a blood glucose level measured before the scan. In a diabetic patient, a blood glucose level below 200 mg/100ml is acceptable. Above that level, the scan will be performed only if the referring physician does not believe that it is possible for the patient to lower his or her glucose level.

Patients receive an injection of 18F-FDG about an hour before the start of imaging to allow time for metabolic uptake of the tracer. During the wait time, physical activity or repetitive movement should be avoided to minimize uptake into the muscles.

The examination starts with low radiation-dose non-contrast transmission CT scan, which provides data to correct for attenuation for the PET scan. Immediately after that, the PET scan is performed while the patient remains in the same position. Depending on the size of the patient, the PET scan takes about 25-35 minutes for a routine whole-body scan, which entails imaging of the neck, chest, abdomen, and pelvis. After the PET scan is complete, intravenous contrast is administered to the patient for a standard diagnostic CT scan, if this is performed.

The radiation exposure for a PET/CT scan is about 1.4 mSv for a whole body low-dose attenuation correction scan, 16.2 mSv for a whole body (neck/chest/abdomen/pelvis) diagnostic CT scan, and about 16 mSv from the injection of 18F (15 mCi in an average sized patient). 18F has a half-life of 109 minutes and is effectively fully decayed within a few hours of administration.

PET/CT Image Interpretation
All PET/CT studies at the MGH are interpreted by a nuclear medicine specialist and a radiologist specializing in the relevant anatomy. Initial interpretations are performed separately and multidisciplinary conferences are performed twice each day. This approach results in a coherent interpretation, in which a review of the CT findings can initiate a second look by a nuclear medicine specialist, or vice versa. For example, small diffuse tumors can be overlooked in a CT examination but readily seen by PET.

While multidisciplinary interpretations can result in more accurate diagnoses, final reports may not be available the same day as the PET/CT examination and it is not possible to perform "wet reads". If necessary, there may be an expedited review without a multidisciplinary conference. However, Mass General Imaging recommends that patients do not schedule a PET/CT on the same day as an office examination.

Scheduling
Appointments can be scheduled by calling 617-724-9729 or through the Radiology Order Entry system, http://mghroe/. PET/CT is available at the main campus and at the Mass General Imaging Center in Chelsea. A PET scan can be requested without a diagnostic CT (a low-dose CT will be necessary for attenuation correction). This can be appropriate if a diagnostic CT has been performed recently.
Further Information
For more information about PET/CT, please contact, Edwin L. Palmer, MD, Director, Clinical Nuclear Medicine and Molecular Imaging, Mass General Hospital, 617-726-8350.

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References


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