Image-guided Biopsy: What the Interventional Radiologist Needs to Know about PET/CT

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Positron emission tomography (PET)/computed tomography (CT) with fluorine 18 fluorodeoxyglucose (FDG) is increasingly used in evaluation of oncology patients. Because PET/CT can demonstrate malignancy before morphologic changes are evident, application of PET/CT information to image-guided biopsy can facilitate early histologic diagnosis and staging. However, because FDG uptake is not specific to cancer, PET/CT findings may raise questions about whether uptake in a lesion is an indication for biopsy. To properly select patients for image-guided biopsy, interventional radiologists should be familiar with the biologic significance of FDG uptake and various causes of false-positive uptake. PET/CT images may also become a source of confusion in the interpretation of biopsy results. Various causes of false-positive and false-negative FDG uptake need to be considered, especially when there is a discrepancy between biopsy results and PET/CT findings. False-negative FDG uptake can result from cancers that are too small to be observed or not FDG avid. False-positive FDG uptake can be due to underlying inflammation from recent treatment. Conversely, complete resolution of FDG uptake in a treated lesion does not necessarily indicate absence of viable cells. When questions about PET/CT findings arise in the context of image-guided biopsy, discussion with experienced nuclear imaging physicians is essential.

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Introduction

Integrated positron emission tomography (PET) and computed tomography (CT) performed with fluorine 18 ($^{18}$F) fluorodeoxyglucose (FDG) is one of the functional imaging modalities used to visualize glucose metabolism in living human tissues. Given its high sensitivity in detection of malignancy, FDG PET/CT is increasingly being used in evaluation of oncology patients. Accordingly, interventional radiologists are encouraged to be familiar with interpretation of PET/CT images and to understand the advantages and limitations of this modality. First, because PET/CT can demonstrate malignancy even before morphologic changes are evident, the application of PET/CT information to image-guided biopsy can contribute to early histologic diagnosis and staging of malignancies. Second, because PET/CT can demonstrate viable malignant tissue in masses that contain nonmalignant tissue, such as those with necrosis or fibrosis, the metabolic information provided by PET/CT could potentially improve the diagnostic accuracy of image-guided biopsy. Third, with the increasing ubiquity of PET/CT scanners, the number of biopsy requests based on PET/CT findings is increasing because of the ability of PET/CT to demonstrate malignancies that are not visible on anatomic images. Finally, because FDG uptake is not specific to cancer, FDG uptake can be seen in many noncancerous disorders including inflammation or infection. Similarly to malignant cells, inflammatory cells such as activated lymphocytes, neutrophils, and macrophages exhibit increased expression of GLUT and high intracellular levels of hexokinase (4,5). Increased affinity of GLUT to deoxyglucose is also observed in these cells, presumably because of the presence of various cytokines and growth factors (6).

Mechanism of Cancer Imaging with FDG PET/CT

A basic knowledge of the mechanism of cancer imaging with FDG PET/CT is essential for accurate interpretation of PET/CT images and biopsy results in conjunction with PET/CT findings. FDG, which is an analog of glucose, is transported into cells by glucose transporters (GLUTs) and phosphorylated by hexokinase. It then becomes metabolically trapped and accumulates within the cells at a rate proportional to glucose utilization (1) (Fig 1). FDG preferentially accumulates in cancers because of their increased glucose metabolism. This metabolic alteration is mainly the result of increased expression of GLUT and hexokinase in cancer cells (2,3). Although a wide range of FDG uptake is observed in different cancers in accordance with differences in GLUT and hexokinase expression, FDG PET/CT generally has high sensitivity for detection of various cancers. However, increased glucose metabolism is not specific to cancer. FDG uptake can be seen in many noncancerous disorders including inflammation or infection. Similarly to malignant cells, inflammatory cells such as activated lymphocytes, neutrophils, and macrophages exhibit increased expression of GLUT and high intracellular levels of hexokinase (4,5). Increased affinity of GLUT to deoxyglucose is also observed in these cells, presumably because of the presence of various cytokines and growth factors (6).

Biologic Significance of FDG Uptake Relevant to Biopsy

Both in vitro and in vivo studies have shown that, across a wide range of tumor types, the extent of FDG uptake in a tumor is positively correlated with the number of viable tumor cells in the tumor (5,7). Therefore, if the FDG uptake is not uniform in a tumor, a higher biopsy yield would be expected in the area with higher FDG uptake. Notably, FDG uptake is seen not only in parts of the tumor with viable cancer cells but also in macrophages infiltrating the marginal areas of necrosis and in the newly formed granulation tissue around the tumor (8). However, these nonmalignant elements that exhibit FDG uptake compose only a small part of the tumor.
However, FDG uptake does not necessarily correlate with the number of viable tumor cells after intervention or treatment. Mild to moderate FDG activity may be detected after open biopsy or resection owing to tissue regeneration or inflammation (9). The acute cellular response to irradiation or chemotherapy can increase tracer uptake as the result of increased glucose utilization by tumor cells in response to the “shock” of treatment in the early posttreatment phase (10). In addition, residual FDG uptake after treatment can be caused by a secondary inflammatory reaction (11). During or soon after certain chemotherapies, the FDG uptake in tumors can decline to a greater extent than the actual number of viable tumor cells (the “stunning” effect) (12).

Therefore, it is generally suggested that use of FDG PET/CT be delayed until several weeks after treatments such as chemotherapy or irradiation. The precise length of time required after treatment to optimally assess the tumor response has not yet been fully determined.

**Physiologic Distribution of FDG Uptake**

Intense physiologic FDG activity is seen in organs dependent on glucose metabolism, such as the brain or nonfasting myocardium. Because FDG is excreted in the urine, intense FDG activity is also seen in the renal collecting system, ureters, and bladder. In all other organs, physiologic tracer activity is typically distributed at low levels in recognizable anatomic structures and is rarely misinterpreted as a pathologic process.

However, some sites of physiologic FDG uptake can potentially mimic a pathologic process. Such sites include FDG activity in a renal calyx or in a communicating renal cyst (vs small primary or secondary renal malignancies) (Fig 2), isolated activity in a kinked ureter (vs retroperitoneal lymph node disease), focal uptake in the small or large bowel (vs peritoneal metastatic implants or mesenteric lymph node disease), and normal ovarian activity in premenopausal women (vs pelvic lymph node disease) (13). Awareness of these sites of physiologic FDG uptake that can mimic disease and correlation of FDG PET data with anatomic imaging are important to avoid misinterpretation of the results and unnecessary biopsies.
Normal Variations in FDG Uptake

**Brown Adipose Tissue.**—Brown adipose tissue can show intense FDG uptake from elevated glycolytic metabolism. FDG-avid foci located in brown adipose tissue appear as regions of fat-attenuation tissue located in the neck, supraclavicular area, shoulder, or axilla. These foci can mimic metastatic lymph nodes, particularly when they are focal and asymmetric (Fig 3). Paravertebral (vs rib metastasis) or mediastinal (vs metastatic lymph nodes) brown adipose tissue can also be misleading.

**Thymus.**—Physiologic uptake in the thymus can be seen in children and young adults. The region of uptake is typically triangular, a finding that corresponds to the bilobed configuration of the thymus (Fig 4) (14). Patients with thymic rebound hyperplasia after a recent stress event such as chemotherapy or corticosteroid therapy can demonstrate moderate to high FDG uptake in the thymus. This should not be confused with pathologic uptake from lymphoma or from residual or recurrent disease in patients with lymphoma after chemotherapy (15).

**Myocardium.**—FDG activity in the myocardium can vary depending on the patient’s fasting state. During fasting, the myocardium shifts from a dominantly glycolytic metabolism to a fatty acid metabolism, resulting in myocardial FDG uptake profiles that range from uniform and intense to virtually absent. The transition may not be entirely uniform, and cardiac activity can be irregular in distribution. This phenomenon could be misinterpreted as FDG-avid mediastinal lymph nodes or pulmonary masses (13).

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**Figure 2.** Isolated calyceal FDG activity in a 54-year-old man with a history of lung cancer. (a, b) Axial PET/CT (a) and coronal maximum intensity projection PET (b) images show an isolated focus of FDG activity in the upper pole of the right kidney. No correlative abnormality was seen at corresponding nonenhanced CT. (c) On a contrast material–enhanced CT image obtained during attempted CT-guided biopsy, the site of FDG uptake in the upper pole corresponds to the posterior renal calyx. The dependent location of the upper pole calyx in the supine patient likely resulted in isolated pooling of the urinary tracer.
Figure 4. Physiologic FDG uptake in the thymus in a 21-year-old woman with a history of sigmoid colon cancer. (a) Axial PET/CT image shows diffuse homogeneous FDG uptake in the retrosternal region. (b) On a coronal PET image, the uptake is bilobed and triangular, a finding typical of physiologic thymic uptake.

Figure 3. FDG uptake in brown adipose tissue in the supraclavicular region after four cycles of chemotherapy in a 57-year-old man with a history of stage III lymphoma involving axillary and inguinal lymph nodes. (a) Coronal PET image shows foci of FDG uptake in bilateral supraclavicular regions (arrows), a finding that suggests possible new involvement of the supraclavicular lymph nodes. (b) Corresponding CT image shows fat attenuation in the supraclavicular regions of FDG uptake, a finding suggestive of hypermetabolic brown adipose tissue.

Spleen.—Diffuse FDG uptake in the spleen in patients with lymphoma in a pretreatment setting is a relatively reliable indication of lymphomatous involvement (16). However, diffuse uptake in the spleen could also represent a physiologic reaction to extrasplicenic infection, granulocyte colony-stimulating factor therapy, or anemia resulting in extramedullary hematopoiesis within the spleen (16). Therefore, the patient’s medical history is crucial in identifying the nature of diffuse FDG uptake in the spleen and avoiding confusion with benign or malignant causes.

Skeletal Muscle.—Skeletal muscle under active contraction or heavy use or injected with exogenous insulin can demonstrate elevated FDG accumulation. Focal asymmetric muscle uptake resulting from asymmetric strain caused by disease or surgery can mimic a pathologic process (Fig 5) (13). FDG uptake can be present in diaphragmatic crura in hyperventilating patients with chronic obstructive pulmonary disease; this finding can be confused with celiac or perigastic lymph node disease (17).
Figure 5. Focal asymmetric FDG uptake in a left paravertebral muscle in a patient with a history of extensive neck dissection for a malignant salivary gland tumor. (a) Axial PET/CT image shows an isolated focus of FDG activity in the left paravertebral region (white arrow). FDG uptake is also noted in the left sternocleidomastoid muscle (asterisk) and left pharyngeal muscle (black arrow). (b) CT image from biopsy of the left paravertebral region shows no malignancy; instead, fragments of skeletal muscle were found. The FDG uptake in the left paravertebral muscle was considered to be caused by asymmetric strain from the surgery.

Bone Marrow.—Diffuse extensive FDG uptake in the bone marrow is observed after administration of granulocyte colony-stimulating factor or chemotherapy. This phenomenon can be misinterpreted as diffuse malignant marrow infiltration, particularly when the marrow activity is nonuniform in distribution because of radiation therapy or a superimposing disease process such as a vertebral hemangioma (18,19).

Figure 6. FDG-avid cavitary granulomatous lesion mimicking malignancy in a 62-year-old active smoker with a history of rheumatoid arthritis. Axial PET/CT (a) and corresponding PET (b) images show an FDG-avid cavitary mass in the right upper lung. CT-guided biopsy of the mass demonstrated granulomatous inflammation related to rheumatoid arthritis.
Benign Pathologic FDG Uptake
Due to Infection and Inflammation

Because glycolytic metabolism is elevated in activated inflammatory cells, nonmalignant inflammatory conditions are associated with increased FDG uptake. Certain infectious processes may be difficult to differentiate from malignancy because of their morphology. Pneumonia or granulomatous infection with central necrosis or cavitation, abscesses, or pancreatitis with a pseudocyst may appear indistinguishable from a centrally necrotic or cavitating neoplasm (Fig 6). Fistulous or sinus tracts can exhibit focal areas of FDG uptake secondary to inflammation and may be mistaken for a metastasis or primary bowel neoplasm.

An inflammatory reaction associated with normal wound healing demonstrates mild to moderate FDG uptake. Therefore, postoperative or postinterventional wounds (Fig 7), including sites of ostomy (Fig 8), anastomosis, or biopsy, can be focally FDG avid and should not be confused with residual tumor, recurrence, or tract seeding. Talc pleurodesis can be associated with intense FDG uptake at the sites of talc deposits in the pleura, even years after the procedure. These sites can mimic pleural metastases (Fig 9). A history of talc pleurodesis and the characteristic CT appearance of high-attenuation foci along the pleura corresponding to the sites of FDG uptake can suggest talc-related pleural disease.

Healing fractures demonstrate increased FDG uptake even months after the injury. FDG uptake at sites of rib fractures, acute vertebral body fractures, or insufficiency fractures of the sacrum can be misinterpreted as osseous metastases. Clinical correlation with a previous injury and careful review of CT or correlative images are important for determining the cause of FDG uptake in these osseous structures. Benign extraarticular inflammatory disorders that affect surrounding joint tissue, such as tendinopathy, enthesopathy, or bursitis, are associated with focal FDG uptake (20). These conditions can mimic metastasis to the soft tissue around the joint.

**Figure 7.** FDG uptake in the groin related to surgical changes from multiple hernia repairs in a 65-year-old man with a history of surgery for rectal cancer. Axial PET/CT (a) and contrast-enhanced CT (b) images show an enhancing soft-tissue mass with FDG uptake in the left groin. CT-guided biopsy of the mass demonstrated chronic granulomatous inflammation.

**Figure 8.** FDG uptake at a recent tracheostomy site in a 60-year-old man with a history of advanced oropharyngeal cancer. Axial PET/CT image shows FDG uptake in soft tissue around a tracheostomy tube, a finding thought to be due to an inflammatory reaction associated with normal wound healing.
FDG uptake in lymph nodes secondary to inflammatory changes can pose an interpretive challenge and may be impossible to distinguish from malignancy with PET/CT alone. Active granulomatous disease such as tuberculosis or sarcoidosis can cause intense FDG uptake. The inflammatory response of regional lymph nodes to infection or recent instrumentation is a common source of elevated FDG uptake in noncancerous lymph nodes (19). Intense FDG uptake arising from persistent inflammation can be observed in lymph nodes in the region of prior surgery. Therefore, during biopsy of FDG-avid lymph nodes, knowledge of the pertinent clinical history is essential to reasonably interpret the biopsy results.

**FDG Uptake in Benign Tumors**

Some benign tumors are associated with FDG uptake, which can be intense across a range of malignancies. Table 1 shows representative FDG-avid benign tumors or tumorlike conditions. Benign salivary gland tumors such as pleomorphic adenoma or Warthin tumor (Fig 10) are associated with fairly intense focal FDG uptake. Benign thyroid nodules such as follicular adenoma or hyperplastic nodules can be FDG avid (21). However, incidental focal FDG uptake in the thyroid gland is highly concerning for and suggestive of malignancy (22); a tissue diagnosis is usually required in such cases.

### Table 1

**Benign Tumors or Tumorlike Conditions Associated with FDG Uptake**

<table>
<thead>
<tr>
<th>Neck</th>
<th>Abdomen</th>
<th>Bone</th>
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<tr>
<td>Thyroid adenoma</td>
<td>Adrenal hyperplasia</td>
<td>Fibrous dysplasia</td>
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<tr>
<td>Hyperplastic thyroid nodule</td>
<td>Adrenal adenoma</td>
<td>Giant cell tumor</td>
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<td>Pleomorphic adenoma</td>
<td>Pheochromocytoma</td>
<td>Paget disease</td>
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<td>Warthin tumor</td>
<td>Myelolipoma</td>
<td>Nonossifying fibroma</td>
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<td>Eosinophilic granuloma</td>
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<td>Aneurysmal bone cyst</td>
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<td>Enchondroma</td>
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<td></td>
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<td>Myositis ossificans</td>
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**Figure 9.** FDG uptake in a talc deposit within the pleura in a 65-year-old man with right upper lobe non–small cell lung cancer. (a) Axial PET/CT image shows curvilinear intense FDG uptake along the liver surface. (b) Corresponding nonenhanced CT image shows a plaquelike region of high attenuation (arrow) along the liver surface. CT-guided biopsy of the high-attenuation region demonstrated chronic inflammation of the pleura, a finding consistent with pleurodesis. The patient underwent talc pleurodesis 9 years earlier.
Figure 10. FDG uptake in a Warthin tumor in a 61-year-old man with a history of lung cancer. Axial PET/CT (a) and nonenhanced CT (b) images show a nodule with FDG uptake in the left parotid gland. The nodule is hyperattenuating relative to the surrounding parotid gland parenchyma. Ultrasonography (US)-guided biopsy of the nodule demonstrated that it was a Warthin tumor.

PET/CT-related Artifacts

FDG PET has been reported to allow reliable differentiation between benign and malignant adrenal tumors (23). However, benign adrenal lesions such as adenomas, hyperplasia, or pheochromocytomas can occasionally produce false-positive FDG uptake. Benign bone tumors or tumorlike conditions such as fibrous dysplasia, giant cell tumor, nonossifying fibroma, or myositis ossificans can demonstrate increased FDG uptake. Careful review of anatomic images and knowledge of benign tumors with FDG uptake are important because these tumors or tumorlike conditions usually do not warrant biopsy.

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<table>
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<th>Table 2</th>
<th>PET/CT-related Artifacts and Their Causes</th>
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| Misregistration | Respiration  
Patient motion  
Bowel motility  
Bladder distention |
| Attenuation-correction artifact | Metallic objects*  
High-attenuation cement in vertebroplasty-treated vertebrae  
Contrast media |

*For example, dental implants, injection ports, and orthopedic prostheses.

Table 2: PET/CT-related Artifacts and Their Causes

| Misregistration | Respiration  
Patient motion  
Bowel motility  
Bladder distention |
| Attenuation-correction artifact | Metallic objects*  
High-attenuation cement in vertebroplasty-treated vertebrae  
Contrast media |

*For example, dental implants, injection ports, and orthopedic prostheses.

PET/CT-related Artifacts

Because PET/CT uses CT image data for attenuation correction of PET images, some unique image artifacts can be introduced during PET/CT. The representative artifacts are misregistration and attenuation-correction artifacts related to high-attenuation material (Table 2).

Misregistration involves the superimposition of FDG activity on inappropriate anatomic structures seen at concurrent CT. Because of the sequential—not simultaneous—acquisition of CT and PET images, respiration, patient motion, bowel motility, or distention of the bladder can cause an erroneously shifted focus of FDG uptake on PET/CT images (Fig 11). These misregistered foci of FDG uptake can potentially result in false-positive or false-negative findings on PET/CT images and can potentially guide an operator to an erroneous target for biopsy. Review of the CT images is usually sufficient to confirm an anatomic abnormality onto which the FDG uptake would have been superimposed on PET/CT images. Awareness of the potential for misregistration and its causes is important to ensure accurate interpretation of PET/CT images.

Metallic objects attenuate more photons under CT x-ray energy than under PET energy. Therefore, CT-based attenuation correction overestimates the attenuation caused by a metallic object...
Figure 11. Respiratory motion artifact. (a) Attenuation-corrected axial PET/CT image shows focal FDG uptake within a scar in the left lung base. (b) Attenuation-corrected coronal PET image shows a focus of FDG uptake in an area of photopenia between the left lung and kidney. (c) Non–attenuation-corrected coronal PET image shows pooling of FDG in the left upper pole renal calyx. No focal FDG uptake is seen in the left lung base. These findings confirm that the FDG uptake within the lung base scar in a represents a respiratory motion artifact.

and produces artifactually increased FDG activity at that site on PET/CT images. This artifact may mimic a lesion at the site of a metallic object or lead to false-negative interpretation of a true lesion as an artifact. Similarly, oral or intravenous contrast medium can produce false-positive FDG uptake because its high attenuation can cause overcorrection of attenuation data from CT (Fig 12). Movement of contrast medium during the interval between PET and CT image acquisition may further complicate confirmation of the artifact. Careful review of the non–attenuation-corrected PET images is important to differentiate true uptake from the artifact.

Applications of PET/CT Findings to Biopsy
One inherent advantage of FDG PET/CT is early detection of malignancies before changes in morphology are evident, and application of PET/
Lesions with Nonuniform FDG Uptake
Some neoplasms, especially large ones, may demonstrate nonuniform FDG uptake; the difference in intensity of FDG uptake within the mass may be significant. These neoplasms can be mostly necrotic and contain metabolically active tumor cells in only a small portion of the total mass. In this situation, PET/CT findings can be applied to target the metabolically active part of the lesion or the area with greater or the greatest FDG uptake (Fig 13). This practice can minimize the sampling error from biopsying areas with necrosis or fibrosis that are metabolically less active or even inactive.

Multiple Lesions with Varying FDG Uptake
In patients with multiple lesions that could potentially be targeted, the lesions may exhibit a wide range of FDG uptake intensities. PET/CT allows identification of lesions with the highest FDG uptake, and sampling one of the lesions with the highest FDG uptake can potentially increase the...
diagnostic yield (Fig 14). In addition, PET/CT allows identification of the FDG-avid lesion that is most accessible for biopsy among multiple lesions with similar FDG uptake (Fig 15). Biopsy of the most accessible lesion can minimize the sampling error and reduce the chance of complications associated with the procedure.

Lesions Difficult to Target because of Underlying Anatomic Alterations
Some lesions are located in regions with anatomic alterations resulting from treatment, such as surgery or irradiation, or from a disease process, such as atelectasis or lung consolidation. These lesions are often difficult to target because of their poor delineation at anatomic imaging. PET/CT findings can guide an operator to the metabolically active area within the lesion for accurate targeting in these situations (Fig 16).

Lesions with Few or No Morphologic Changes at Anatomic Imaging
Some lesions detected with PET/CT exhibit few or no morphologic changes at CT or other anatomic imaging. These lesions can be difficult to target under the guidance of anatomic imaging alone. Corresponding PET/CT findings can suggest the area to biopsy under CT guidance (Fig 17). However, full PET/CT guidance may be needed to accurately target these lesions.
Figure 15. Multiple FDG-avid lesions with different levels of accessibility for biopsy in a 62-year-old man with multiple pulmonary nodules. (a) Axial CT image (lung window) shows multiple nodules in the right lung. Biopsy of one of the nodules was initially requested for tissue diagnosis. (b) Coronal maximum intensity projection PET image obtained after CT shows multiple foci of FDG uptake in the right lung and right lower ribs (arrows) and at the level of the diaphragm near the midline (arrowheads). (c) Axial PET/CT image at the level of the diaphragm shows an FDG-avid internal mammary lymph node. This node appeared to be the most easily accessible for biopsy. Immunohistochemical analysis of tissue from CT-guided biopsy of that node demonstrated adenocarcinoma, a finding consistent with a metastasis from primary lung cancer.

Figure 16. Local recurrence in a 75-year-old man with a history of radiation therapy for lung cancer in the left upper lobe. (a) Axial contrast-enhanced CT image shows prominent paraspinal soft tissue on the left (arrow). It is difficult to assess the presence of recurrent disease because of underlying changes due to irradiation. (b) PET/CT image shows a metabolically active area in paraspinal soft tissue, a finding suggestive of local recurrence. CT-guided biopsy of the FDG-avid area showed poorly differentiated squamous cell carcinoma, a finding compatible with local recurrence.
Figure 17. Metastatic lung cancer in the acetabulum detected with FDG PET with no morphologic changes observable at CT. (a) Axial PET image at the level of the pelvis shows a focus of FDG uptake in the region of the posterior right acetabulum. (b) Nonenhanced CT image shows no morphologic changes in the posterior right acetabulum. (c) PET/CT image shows a focus of FDG uptake in the lateral aspect of the posterior right acetabulum. CT-guided biopsy of the area of FDG uptake in the acetabulum demonstrated adenocarcinoma, a finding compatible with metastatic lung cancer.

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<th>Table 3</th>
<th>Possible Diagnoses Based on Combinations of PET/CT Findings and Biopsy Results</th>
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<tr>
<td><strong>Biopsy Results</strong></td>
<td><strong>PET/CT Findings</strong></td>
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<tr>
<td>Positive</td>
<td>Malignancy</td>
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<tr>
<td>Negative</td>
<td>False-positive (benign) FDG uptake</td>
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Note.—SUV = standardized uptake value.
Pitfalls in Interpreting Biopsy Results on the Basis of PET/CT Findings

Although PET/CT can potentially help improve the diagnostic accuracy of image-guided biopsy, there are some caveats when applying metabolic information provided by PET/CT to the interpretation of biopsy results. Because FDG uptake is not specific to cancer and not all cancers can be detected with FDG PET/CT, the various causes of false-positive and false-negative FDG uptake need to be considered. This is especially true when there is a discrepancy between the biopsy result and the associated PET/CT interpretation (Table 3). Improper on-site interpretation of biopsy results on the basis of PET/CT findings can lead to sampling errors related to inadequate specimens, unnecessary additional needle passes, or radiation exposure to the patient.

False-negative FDG uptake can result from cancers that are too small to be observed or are not FDG avid. Typically, the threshold for lesion detection with PET/CT is approximately 6 mm. Lesions greater than 1 cm are routinely detected if they are FDG avid.

Some cancers inherently demonstrate low FDG uptake, including bronchoalveolar carcinoma, carcinoid tumor, marginal zone lymphoma (of which mucosa-associated lymphoid tissue lymphoma [MALToma] is a subtype) (Fig 18), low-grade hepatocellular carcinoma, renal cell carcinoma, sclerotic bone metastasis, chondrosarcoma, and low-grade sarcoma. In addition, necrotic and mucinous tumors demonstrate poor accumulation of FDG and can give false-negative results on PET/CT images. Knowledge of these malignant lesions with inherently low FDG uptake is important because false-negative uptake in these tumors can lead to cancelation of a necessary biopsy or be a source of confusion in the interpretation of biopsy results.

The SUV is defined as the concentration of tracer activity in a volume of interest divided by the injected dose per unit of body weight. It is the most common parameter used to measure tracer accumulation in PET/CT studies. The SUV allows semiquantification of FDG uptake in a lesion and may be used as a reference value to differentiate benign from malignant disease. Some authors have reported that a cutoff value of 2.5 is useful for differentiating between benign and malignant lung and nonlung lesions (24,25).
However, because of considerable overlap between the SUV results of malignant and benign lesions, the SUV is devoid of any intrinsic diagnostic value without integration into the proper clinical context and correlation with the findings at anatomic imaging. This is especially true when the SUV is just above or just below the cutoff value (Fig 19) (26). The SUV can be misleading when the lesion is small; in small cancers, the average measured SUV may be biased to lower values because of partial volume averaging (27).

In the posttreatment setting, a lesion can be falsely FDG avid because of underlying inflammation from recent treatment (eg, radiation therapy or chemotherapy), even though it may not contain any viable cells. In general, increased FDG uptake in irradiated regions resolves suffi-
Liver biopsy under real-time PET/CT guidance by using an electromagnetic needle tracking and navigation system in a 72-year-old man with a history of colon cancer. Previously acquired PET/CT images were imported into the system and coregistered with intraprocedural US images. Intraprocedural US (a) and corresponding PET/CT (b) images, which are displayed side by side on the monitor of the US unit, show a needle that is placed in an FDG-avid tumor in the lateral segment of the liver. Needle placement is guided by the expected needle path (dotted line, single arrow), which is electronically displayed on both images. The dashed line (double arrows) indicates the path that the needle has traveled within the liver. The aerated lung base on the PET/CT image (in b) is not visualized on the US image because of pleural effusion and atelectasis (in a), which developed after the PET/CT acquisition. The biopsy demonstrated adenocarcinoma, a finding compatible with metastatic colon cancer. Arrowhead in a = needle tip.

This technique, diagnostic PET/CT images acquired before the procedure and intraprocedural CT images are transferred in the Digital Imaging and Communications in Medicine format to a computer via a local area network connection. The images are fused by using Medical Image Processing, Analysis, and Visualization software (Biomedical Imaging Research Services Section, National Institutes of Health, Bethesda, Md) and used to guide an operator to the targeted area of FDG uptake.

Finally, a recently developed electromagnetic needle tracking and navigation system enables an operator to perform biopsy procedures with real-time PET/CT guidance. This system uses an ultralow electromagnetic field with position sensors placed on the patient and the needle shaft to provide real-time tracking of the position and orientation of the biopsy needle under US or CT guidance. The system also uses registration software to track the location of the needle tip and overlay the location onto cross-sectional images such as preprocedural CT images. The system can import prior PET/CT images, which are registered with preprocedural CT images to enable real-time PET/CT guidance (Fig 20).
Researchers have reported that the spatial accuracy of this technique is sufficient to display clinically relevant image guidance information during biopsy. This technique enables successful execution of procedures that are not deemed feasible with standard single-modality image guidance (32–34).

Summary
PET/CT is increasingly being used in the evaluation of oncology patients. Because FDG PET/CT can demonstrate malignancies even before morphologic changes are evident, the application of PET/CT findings to image-guided biopsy can contribute to early histologic diagnosis and staging of malignancy. In addition, PET/CT findings can potentially help improve the diagnostic accuracy of image-guided biopsy by indicating metabolically active regions within areas of necrosis, fibrosis, poor delineation arising from surgical or irradiation changes, or atelectasis. PET/CT findings are useful in selecting the most accessible lesion to biopsy from among multiple metabolically active lesions. PET/CT findings can guide an operator to a lesion targeted for biopsy with few or no morphologic changes observed at anatomic imaging.

Because FDG uptake is not specific to cancer, PET/CT findings may raise questions as to whether a lesion with FDG uptake is indicated for biopsy; the findings may also become a source of confusion in the interpretation of biopsy results. Therefore, to properly apply the metabolic information provided by PET/CT to image-guided biopsy and allow a reasonable interpretation of the biopsy results, interventional radiologists should be familiar with the biologic significance of FDG uptake relevant to biopsy, various causes of false-positive FDG uptake (physiologic FDG uptake that can potentially mimic disease, physiologically variant distributions of FDG, benign lesions such as inflammation or infection, PET/CT-related artifacts), and the potential pitfalls in interpretation of biopsy results in conjunction with PET/CT findings. As interventional radiologists take advantage of evolving nuclear functional imaging methods and the increasing availability of image-guided procedures, collaboration with nuclear medicine physicians becomes more important to achieve successful outcomes.

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Second, because PET/CT can demonstrate viable malignant tissue in masses that contain nonmalignant tissue, such as those with necrosis or fibrosis, the metabolic information provided by PET/CT could potentially improve the diagnostic accuracy of image-guided biopsy.

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Familiarity with various causes of false-positive FDG uptake is essential when performing patient selection for image-guided biopsy.

Page 1497
Because FDG uptake is not specific to cancer and not all cancers can be detected with FDG PET/CT, the various causes of false-positive and false-negative FDG uptake need to be considered. This is especially true when there is a discrepancy between the biopsy result and the associated PET/CT interpretation.

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However, because of considerable overlap between the SUV results of malignant and benign lesions, the SUV is devoid of any intrinsic diagnostic value without integration into the proper clinical context and correlation with the findings at anatomic imaging.