SUPPLEMENT

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NCCN Task Force Report: PET/CT Scanning in Cancer

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This educational activity is designed to meet the educational needs of both specialists in nuclear medicine and radiology and medical, surgical, and radiation oncologists and primary care physicians who impact decisions on the use of PET in the treatment of cancer patients.

Educational Objectives

After completion of this CME activity, physicians should be able to:

- Describe the technology and science of PET and its general relevance to cancer care
- Describe broadly clinical applications of PET in cancer care, including diagnosis, staging, monitoring/surveillance, and evaluation
- Describe the relevance of PET scanning and potential contribution of the imaging technology alone and, where appropriate, in combination with other imaging technologies in the management of patients diagnosed with breast cancer, colon cancer, rectal cancer, non-Hodgkin's lymphoma, non small cell lung cancer, and thyroid cancer
- Provide specific recommendation regarding the appropriate use and application of PET scanning with breast cancer, colon cancer, rectal cancer, non-Hodgkin's lymphoma, non-small cell lung cancer, and thyroid cancer.

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Supplement

NCCN Task Force Report: Positron Emission Tomography (PET)/Computed Tomography (CT) Scanning in Cancer

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NCCN Clinical Practice Guidelines in Oncology, positron emission tomography (PET), computed tomography (CT), PET/CT, ^{18}F-FDG, radiography, oncology, diagnosis, treatment, lymphoma, lung cancer, colorectal cancer, breast cancer, standard uptake value, fluorodeoxyglucose

Abstract

The use of positron emission tomography (PET) is increasing rapidly in the United States, with the most common use of PET scanning related to oncology. It is especially useful in the staging and management of lymphoma, lung cancer, and colorectal cancer, according to a panel of expert radiologists, surgeons, radiation oncologists, nuclear medicine physicians, medical oncologists, and general internists convened in November 2006 by the National Comprehensive Cancer Network. The Task Force was charged with reviewing existing data and developing clinical recommendations for the use of PET scans in the evaluation and management of breast cancer, colon cancer, non-small cell lung cancer, and lymphoma. This report summarizes the proceedings of this meeting, including discussions of the background of PET, possible future developments, and the role of PET in oncology. (*JNCCN* 2007;5(Suppl 1):S1–S22)

The use of positron emission tomography (PET scanning) is increasing rapidly in the United States. The most common use of PET scanning is related to oncology, especially in staging and managing lymphoma, lung cancer, and colorectal cancer (Figure 1).

In November 2006, the National Comprehensive Cancer Network (NCCN) gathered a panel of expert radiologists, surgeons, radiation oncologists, nuclear medicine physicians, medical oncologists, and general internists to review the existing data and develop clinical recommendations for using PET scans in evaluating and managing breast cancer, colon cancer, non-small cell lung cancer (NSCLC), and lymphoma. Because of time constraints, the PET Task force limited its review to these four most common oncologic indications. However, PET scan has a role in most other types of cancers, which are reviewed on an annual basis by the NCCN Guideline Panels for individual malignancies. (For further information, please go on-line to the NCCN Clinical Practice Guidelines in Oncology at www.nccn.org.) This supplement summarizes the proceedings of this meeting. The term *PET scan* refers to either a PET scan or PET/computed tomography (CT) scan, unless otherwise specified. In addition, the PET radiotracer used is ^{18}F-fluorodeoxyglucose (^{18}F-FDG), unless otherwise specified.

What is PET and How Does It Work?

Imaging can be broadly subdivided into anatomic and molecular, with molecular imaging defined as the "in vivo characterization and measurement of biologic processes at the cellular and molecular level." PET is considered the prototypical molecular imaging technique, with PET/CT providing combined anatomic and molecular imaging.

PET imaging is based on a unique chemical process involving the collision between an electron and a positron arising from a positron-emitting radioisotope, leading to a process known as annihilation that produces two 511-KeV photons emitted at 180°. These photons can be simultaneously detected with a PET scanner, which consists of multiple stationary detectors that encircle the body.

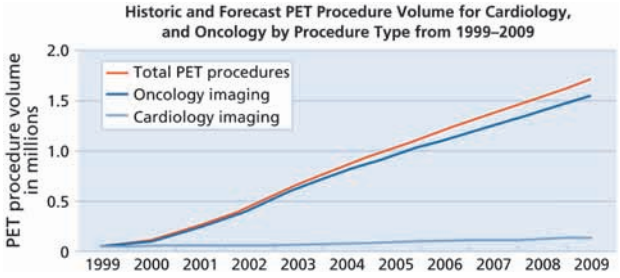

Figure 1 Growth of clinical PET.

Fluorine-18 (^{18}F) incorporated into fluorodeoxyglucose (FDG) is the most common tracer used clinically, with a half-life of approximately 110 minutes. Substitution of fluorine for a hydroxyl group blocks metabolism of the tracer. The level of FDG uptake reflects the rate of trapping of phosphorylated FDG (FDG-6P) and thus the rate of glycolysis (Figure 2). PET scans can be performed with multiple tracers (Table 1) to provide information on blood flow, receptor expression, and metabolism.

FDG uptake is increased in most malignant tissue and in various benign pathologies, such as inflammatory conditions, trauma, infection, and granulomatous diseases. For example, sarcoidosis causes false-positive PET scans. Benign neoplasms and hyperplastic and dysplastic tissue may also accumulate FDG. Because of the variability of FDG in normal tissue and benign conditions, physicians interpreting the scans must be familiar with the normal pattern of distribution and the benign causes of FDG accumulation to accurately interpret the data.

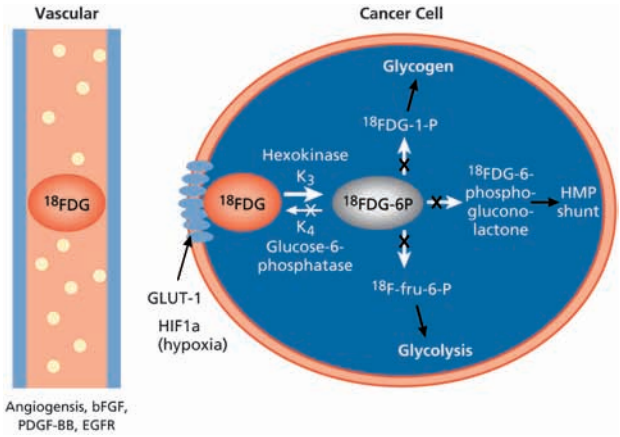

Figure 2 FDG uptake in a cancer cell.

Source: Data from Macheda ML, Rogers S, Best JD. Molecular and cellular regulation of glucose transporter (GLUT) proteins in cancer. J Cell Physiol 2005;202:654–662; and Bos R, van Diest PJ, de Jong JS, et al. Hypoxia-inducible factor-1alpha is associated with angiogenesis, and expression of bFGF, PDGF-BB, and EGFR in invasive breast cancer. Histopathology 2005;46:31–36.

Patient preparation is critical, with the major goals of minimizing tracer uptake in normal issues (e.g., myocardium and skeletal muscle) while maintaining uptake in target tissues (neoplastic disease). The preparation should include, but not be limited to:

1. Pregnancy testing when appropriate.
2. Fasting instruction and no oral or intravenous fluids containing sugar or dextrose (4–6 hours) to maintain normal glycemia and insulinemia.
3. Hydration to reduce accumulated urinary tracer activity in the collecting system and bladder.
4. A focused history regarding diabetes, recent exercise, dates of diagnosis and treatments, medications, and recent trauma or infections.

The oncologic applications of PET scanning are based on increased FDG uptake by tumor tissue. Glucose metabolism is the culmination of many different molecular pathways, and interrupting any of these components can result in glycolysis interruption and a change in the PET scan. Although genetic arrays can be considered multiple biomarkers of the myriad underlying metabolic pathways and may identify targets for intervention, PET scans can be considered a type of downstream imaging from biomarkers, reflecting the final common pathway of glucose metabolism, and they can provide real-time monitoring of treatment response.

Cyclotrons that produce ^{18}F and PET scanners have evolved over the past several decades, and current equipment is smaller and easier to use. Mini cyclotrons now available are highly computerized and can be operated by radiopharmacists or technicians. Mini-cyclotrons can make short-lived isotopes, such as ^{18}fluorine, ^{11}carbon, ^{15}oxygen, or ^{13}nitrogen. These radionuclides can be incorporated into metabolically important substrates through automated synthesis devices.

In the United States, an estimated 55% of PET scanners are PET/CT scanners, and approximately 100% of scanners purchased in the past year have been PET/CT. The original impetus for combining PET/CT scans was to improve attenuation correction and throughput associated with the CT scan. However, PET/CT scans provide more specific anatomic correlation than PET alone,

Table 1 Clinically Used Positron-Emitting Isotopes and Positron-Containing Tracers

Positron Isotopes	Half-life	Postitron Tracers	Use
F-18	109.7 min	NaF	Bone imaging
		FDG	Metabolism
N-13	9.96 min	Ammonia	Perfusion
O-15	2.07 min	$H_2{}^{15}O$	Perfusion
		$C^{15}O$	Blood volume
		$^{15}O_2$	Metabolism
		$C^{15}O_2$	Blood flow
C-11	20.4 min	All carbons	Numerous
Rb82	1.30 min	In saline	Perfusion

and this technology has been widely adopted. A rapid conversion to PET/CT has clearly occurred, and this technique is emerging as the new standard.

Most literature has focused on PET rather than PET/CT scans, and the incremental value of the combined scan is only now being rigorously tested.[1–5] Nevertheless, most clinicians feel comfortable extrapolating data from PET scans to PET/CT scans. Studies have shown that, in some specific clinical situations, the combined image can further clarify the anatomic location of the PET tracer, improve specificity, and thus reduce false-positive results.

The CT portion of a PET/CT scan is used for attenuation correction and anatomic localization. A diagnostic quality CT scan similar to that obtained for diagnostic CT-only scans is not necessary to accomplish these tasks, and the CT component of a PET/CT scan is often a low-dose CT scan to minimize patient radiation exposure. Additionally, contrast is not used because it complicates the use of the CT scan for attenuation correction of the PET scan if appropriate algorithms are not used to correct for the high density of some contrast material. Sometimes patients have already undergone a diagnostic CT scan before being referred for a PET/CT. For example, patients who are potential candidates for liver resection will typically undergo an initial diagnostic CT to evaluate the vascular anatomy of the liver, and then be referred for PET/CT to evaluate for extrahepatic metastases. Another common situation is a patient with a history of malignancy who is being followed up with serial CT scans and is undergoing a PET scan to follow-up the CT scan findings. In these situations, the low-dose CT incorporated into the PET/CT is adequate.

This implies that if a diagnostic CT scan is indicated, patients must undergo a separate scan. In most current PET/CT scanners, the CT component is comparable to stand-alone CT devices and capable of providing a high-quality diagnostic CT. Therefore, in some institutions, when patients require a diagnostic CT at the same time as PET/CT, it can be performed immediately after the PET/CT with the same CT scanner using normal CT scan technique and contrast.

Standardized Uptake Value

Aberrant glucose metabolism FDG uptake in malignant tissues and therefore alterations in glucose metabolism may reflect response to treatment. In this sense, FDG can be construed as a biomarker.[6,7] Various different techniques for assessing the uptake of the tracer attempt to control for background uptake in the blood pool and surrounding tissues, including very sophisticated kinetic studies providing a quantitative analysis. However, a semiquantitative technique, the standardized uptake value (SUV), is most commonly used because of its relative simplicity. The SUV is calculated using the following formula:

$$\frac{\text{Activity per unit volume}}{\text{Injected Activity/Body Weight}}$$

The use of SUV is an area of active research, with the number of citations rapidly increasing for many different tumor types; currently more than 1000 citations are available for SUV values and tumor response.

The SUV is most useful if it reflects the uptake localized to the tumor and not the surrounding tissues. Maximum SUV is a better parameter than the average SUV because of the heterogeneity of the

tumor. From a purely visual perspective, the SUV reflects everything in the field of view, regardless of whether the FDG is incorporated into the tumor cell. Therefore, the clinical usefulness is probably greatest when the SUV is very high, where the uptake is clearly related to phosphorylated FDG (FDG-6P) uptake in the tumor rather than background uptake. Because of this background, changes in SUV may not be adequate to assess response in tumors with low pretherapy uptake or high normal uptake. For example, the brain has a high SUV because it is an obligate user of glucose and the kidneys have a high SUV because they routinely clear FDG.

SUV values have been investigated in various malignancies to assess diagnosis, prognosis, and therapy monitoring. For example, a high SUV score may be associated with a poor prognosis, warranting more aggressive treatment. RTOG-0235 is a clinical trial enrolling 250 patients with NSCLC to determine whether SUV measured shortly after definitive chemoradiotherapy can predict long-term survival or local disease control. However, how specific SUV numbers can be used in managing individual patients is still unclear.

Training and credentialing are extremely important aspects of PET imaging. These issues are summarized in Table 2.

Future of PET

Although FDG has been the standard tracer for oncologic applications of PET, many additional tracers are being developed. One of the areas of active research is the development of radiolabeled thymidine analogues that specifically evaluate proliferation. 3′-deoxy-3′-^{18}F-fluorothymidine (^{18}F-FLT) is the most common example[8] and is anticipated to become broadly commercially available over the next 3 to 5 years.

Imaging of HER2 is another area of active interest, creating the potential for virtual immunohistology, which could be used for early assessment of tumor response to costly therapies such as trastuzumab.[9] Additionally, the increasing understanding of the signaling pathways and their disruption has spurred the development of a broadening array of targeted drugs.

Table 2 Summary of PET-CT on-the-job training. The ACR considers this training a minimum for supervising and interpreting anatomic localization in the setting of PET-CT, but it does not meet the training prescribed in its current ACR Practice Guideline for Performing and Interpreting Diagnostic Computed Tomography (CT). The SNM considers this training sufficient for supervising and interpreting the CT scan performed with PET regardless of the protocol used.

Training	ABMS Board Certification	PET-CT Interpretations (supervised)	†CT Interpretations (supervised)	PET-CT CME	CT CME
Nuclear Medicine	ABNM	150	500	8 hours	100 hours
*Diagnostic Radiologist (recent CT)	ABR	150		35 hours	
*Nuclear Radiologist (recent CT)	ABR	150		8 hours	
*Radiologist (recent CT)	ABR & ABNM	150		8 hours	
Diagnostic Radiologist (no recent CT)	ABR	150	500	35 hours	100 hours
‡Other Physicians	Neither ABR nor ABNM	150	Per ACR guidelines for CT	35 hours	Per ACR guidelines for CT

*Radiologist/nuclear radiologist with recent experience in body CT (100 body CT cases/yr for the past 5 years).
†CT cases should include a reasonable distribution of head and neck, chest, abdomen and pelvis.
‡Who comply with ACR Guidelines for Interpretation of CT and nuclear medicine studies.

Source: Reprinted by permission of the Society of Nuclear Medicine from Coleman RE, Delbeke E, Guiberteau MJ, et al. Concurrent PET/CT with an integrated imaging system: intersociety dialogue from the Joint Working Group of the American College of Radiology, the Society of Nuclear Medicine, and the Society of Computed Body Tomography and Magnetic Resonance. J Nucl Med 2005;46:1225–1239.

Examples include tyrosine kinase inhibitors to bcr-abl (imatinib) and Kit (gefitinib). Radiotracers to identify these targets are also in development and early animal studies have shown high concentrations within tumors.[10]

Radiolabeled antibodies, where the antibodies bind to the surface of the tumor cell, offer another approach to PET imaging. Molecular imaging with radiolabeled antibodies potentially could be used to predict response to therapy or even eliminate the need for a biopsy in certain situations, if the technique proves to be sufficiently sensitive and specific. Quantitative PET (i.e., SUV) can also provide information on the distribution of tracer and provide superior contrast compared with other radioimaging techniques.

Interpretation of molecular imaging is still somewhat uncertain. For example, a positive PET scan that becomes negative after targeted therapy suggests either effective treatment or tumor cells that have lost the target or quiescent tumor cells that are now in the G0 cell-cycle phase. Studies to validate these biomarkers are problematic. Although other laboratory biomarkers can be potentially studied in large clinical trials, the cost of PET scans makes this approach prohibitive. Hopefully, PET biomarkers will be included as exploratory end points in drug trials of targeted therapies.

Role of PET or PET/CT in Oncology: Research Issues

Investigating the clinical role of a diagnostic test such as PET imaging requires several steps. Initially, the diagnostic performance of the test must be assessed, with initial studies focusing on whether the test is reproducible and safe. The next level of assessment involves the clinical assessment of the patient; this determines whether PET can accurately distinguish individuals with disease from those without disease or accurately determine the extent of disease. For this analysis, performing blinded assessment of the PET studies without any prior knowledge of the results of other studies is essential. Finally, assessing how the results of the PET scan impact patient management and improve health outcomes is important. Health outcomes include not only survival but also quality of life, toxicity, and symptom relief. These types of studies are underrepresented in the PET literature.

Hillner et al.[11] studied a prospective cohort of 248 patients undergoing PET scans at one university center to determine the impact of PET scans on patient management. Before and after PET, a questionnaire was administered to solicit information regarding each physician's preceding actions, intended management, and probability estimates. Physicians changed their intended management in 60% of patients. If the pre-PET intended plan involved more testing or biopsies, the results of the PET scan resulted in a change in management in 79% of patients. Finally, in 32% of cases, physicians changed to a treatment from a nontreatment strategy. The authors concluded that physicians often changed their treatment management based on results of the PET scan. However, the possibility also exists that physicians are overconfident in the diagnostic performance of PET and may use the results of a PET scan as the final arbiter of treatment after other imaging options have been exhausted. For example, PET scans could be associated with cost savings if the PET scan is performed earlier in the imaging hierarchy so that other imaging techniques are avoided.

Therefore, the optimal uses of PET scans in relation to other imaging strategies must be further defined. Efficacy and cost savings are possible if PET is used more selectively before surgical procedures or if it can replace other imaging procedures. PET may also result in a reduction in toxicity if the results can more specifically determine the extent of disease and thus the extent of radiation therapy.

PET scans can be cost-saving when the results are used to deselect patients for surgery. In one study, 188 patients with suspected NSCLC planning to undergo thoracotomy were randomized to undergo workup with or without PET scans.[12] The primary outcome measure was futile thoracotomy defined as the presence of benign disease, explorative thoracotomy, pathologic stage IIIA–N2/IIIB, or postoperative relapse or death within 12 months of randomization. Among patients who did not undergo PET scan, 41% underwent a futile thoracotomy, compared with only 21% who did undergo a PET scan. The authors concluded that adding PET to conventional workup prevented unnecessary surgery in 1 of 5 patients with suspected NSCLC.

In another study of 51 patients with potentially resectable liver metastases, clinical management decisions were recorded after conventional workup and then after a subsequent PET scan.[13] Discordance between the results of the conventional workup and the PET scan were then compared with the final histologic diagnosis. PET changed clinical management

decisions in 20% (n = 10) of patients, including 8 patients who were potentially deselected for exploratory surgery.

Aside from the surgical setting, no completed randomized studies have examined the role of PET in the overall hierarchy of imaging strategies. Prospective trials can be used to determine the accuracy of a biomarker used for staging, prediction, or response to therapy. However, validating the role of a biomarker such as a PET scan in patient care is problematic. Ideally, this would involve a trial randomizing patients to either undergo a PET scan or not. Such a randomized trial has not yet been conducted; physician resistance to this design may exist based on preconceptions about the value of a PET scan and potential ethical issues.

Trials in which all participants undergo PET scanning with randomization to treatment based on the results of a biomarker are more common. Several ongoing randomized studies have incorporated PET scans as an intermediate outcome. Another possible research design involves performing the PET scan but blinding the results to subsequent treatment, which remains the primary outcome. The secondary outcome of the trial is to then compare the results of the PET scan with the treatment outcome. This design has been incorporated into several cooperative group studies.

PET and Breast Cancer

Diagnosis

Although PET has high sensitivity and specificity for breast lesions greater than 1 cm, it has poor sensitivity for small nonpalpable lesions or ductal carcinoma in situ (DCIS). This limited sensitivity may be related to background uptake in breast tissue and, specifically, to the underlying tumor biology. For example, DCIS is often less vascular and less glycolytic than invasive breast cancer, and therefore usually has low FDG uptake levels even when large. Lobular carcinoma in situ (LCIS) and low-grade lobular carcinoma also have low uptake. Interest has been shown in improving the underlying technology using dedicated breast PET scanners for primary detection of breast cancer, but these devices are still in the early stages of testing.

Staging

Regional Nodal PET scans have been extensively studied as a technique to assess the axillary lymph nodes in patients with breast cancer, and early studies showed sensitivities from 85% to 100% and specificities from 75% to 96%. However, these early studies included high numbers of patients with advanced disease with a high pre-test likelihood of axillary node involvement, thus improving the diagnostic performance of PET. A more recent large multicenter clinical trial suggests a lower sensitivity and specificity. Wahl et al.[14] evaluated 360 patients with newly diagnosed breast cancer who underwent PET for axillary staging. PET scans were evaluated by 3 readers and the results compared with axillary node pathology. The mean sensitivity, specificity, and positive and negative predictive values were 61%, 80%, 62%, and 70%, respectively. The false-negative axillae had fewer and smaller lymph nodes (mean number of involved nodes, 2.7) compared with the true-positive axillae (mean number of involved nodes, 5.1). An SUV of 1.8 had a positive predictive value of 90% but a sensitivity of only 32%. The authors concluded that FDG-PET is not recommended for routine axillary staging of newly diagnosed breast cancer.

PET has also been compared with sentinel lymph node biopsy (SLNB). These studies, which have included 15 to 80 patients, have reported very low sensitivity (20%–44%), but high specificity (94%–100%) compared with SNLB.[15–18] Recently, Veronesi et al.[19] published a larger case series of 236 patients with breast cancer and clinically negative axillae who underwent both PET and SNLB. This larger study reported similar statistics: the sensitivity of FDG PET was 37%, whereas the specificity and positive predictive value were high at 96% and 88%, respectively. These results suggest that FDG-PET should not be used for axillary staging of early-stage breast cancer.

Some studies suggest that a preoperative PET scan can be used as a triage technique for subsequent axillary dissection in patients at high risk for axillary involvement. Patients with a positive PET scan for axillary node involvement could progress directly to an axillary dissection and forego SLNB. Gil-Rendo et al.[20] investigated this approach, performing SNLB only in patients with a negative FDG-PET scan. The use of PET to select the method of axillary lymph node evaluation with SLNB or formal axillary lymph node dissection must also be considered in the context of clinical axillary examination results and the potential results of fine needle aspiration or core needle biopsy of suspicious axillary nodes.[21]

PET scans of the axilla have also been used in patients with symptomatic or advanced axillary disease for various reasons, such as determining the extent of disease or distinguishing radioplexopathy from locoregional recurrence. In a 1999 study of 10 patients with lymphedema or neurovascular symptoms suggestive of locoregional axillary breast cancer recurrence, Hathaway et al.[22] reported that FDG-PET was useful in further evaluating indeterminate MRI findings. In a study of 19 patients with symptoms and brachioplexopathy, Ahmad et al.[23] reported that PET was helpful in evaluating the brachial plexus if other imaging studies are normal. Of the 19 patients, 14 had abnormal uptake of FDG, whereas CT scans were normal in 6 of these. In these difficult clinical situations, results of a PET scan can be used to help direct a biopsy.

PET scans were investigated as a prognostic technique in a case series of 81 patients who underwent preoperative a PET scan of the primary and axillary regions of the breast, with both standard imaging and SUV values assessed.[24] The prognosis of the 40 patients with the highest SUV was significantly poorer than the 41 with the lowest SUV. Additionally, the combination of positive lymph nodes, as detected with PET, and a high primary SUV was shown to be a highly significant risk factor independent of the traditional TNM risk factors; the 5-year disease-free survival rate of these patients was 44% compared with 96.8% among the other patients. Mankoff et al.[25] also evaluated patients with locally advanced breast cancer to determine whether the results of PET predicted response to neoadjuvant chemotherapy. In this study of 37 patients, 21 of 24 patients with positive nodes at the end of neoadjuvant chemotherapy showed a positive FDG-PET scan before therapy, suggesting that high glucose metabolism predicts a poor response to neoadjuvant chemotherapy. Additionally, in patients with advanced nodal disease, a PET scan before neoadjuvant chemotherapy can show the extent of macroscopic disease, which can be very helpful in planning the extent of subsequent radiation therapy. Therefore, PET may be very helpful in assessing regional nodal disease in locally advanced breast cancer, but more data are needed.

PET assessment of the internal mammary (IM) nodes has been of interest, because the presence of positive IM nodes predicts outcome and may alter treatment. Additionally, standard imaging of the IM nodes has low sensitivity. However, the accuracy of PET in this setting has not been thoroughly evaluated, partly because, unlike axillary nodes, few patients undergo pathologic verification of suspicious IM nodes.[20,21,26]

Distant Metastases Extensive staging studies are not recommended for stage I or early stage II disease because of the low yield and psychological distress associated with false-positive results.[27–29] Whole-body PET scans have been investigated for evaluating suspected distant metastases. Similar to CT scanning, such an extensive workup is not recommended in patients with early-stage disease. In one of the first studies of whole-body PET for evaluation of distant metastases, 57 patients with breast cancer and suspected disease recurrence underwent PET scans with clinical follow-up for 24 months to evaluate the accuracy of the PET diagnosis through biopsy, follow-up imaging, or other diagnostic tests.[30] The sensitivity and specificity were 93% and 79%, respectively. Bone metastases had a significantly larger proportion of false-negative results compared with nonosseous sites. In a study of 60 patients with suspected recurrence, Kamel et al.[31] reported that whole-body PET had a sensitivity of 89% and a specificity of 84%. Other studies have not focused on whole-body PET but PET focused to the probable site of occurrence. Eubank et al.[32] reported that, compared with CT scan, PET had an increased sensitivity for detecting positive internal mammary and mediastinal nodes without a loss in specificity. Unsuspected involvement is most likely in patients with greater than 3 axillary nodes at diagnosis, increasing tumor size, estrogen-receptor–negative disease, medial location of tumor, or chest wall invasion. However, the authors of this study caution that these data do not support routine evaluation of internal mammary or mediastinal nodes in patients with recurrent disease.

PET scans for suspected bony metastases must be interpreted with great caution. For example, several studies have shown that FDG uptake is low in sclerotic lesions compared with lytic lesions. In contrast, Tc-99m methylene diphosphonate (MDP) scintigraphy is more sensitive than FDG for sclerotic lesions.[33–35] Therefore, the 2 imaging techniques provide complementary information, and a PET scan cannot be considered a substitute for a bone scan (Figure 3).

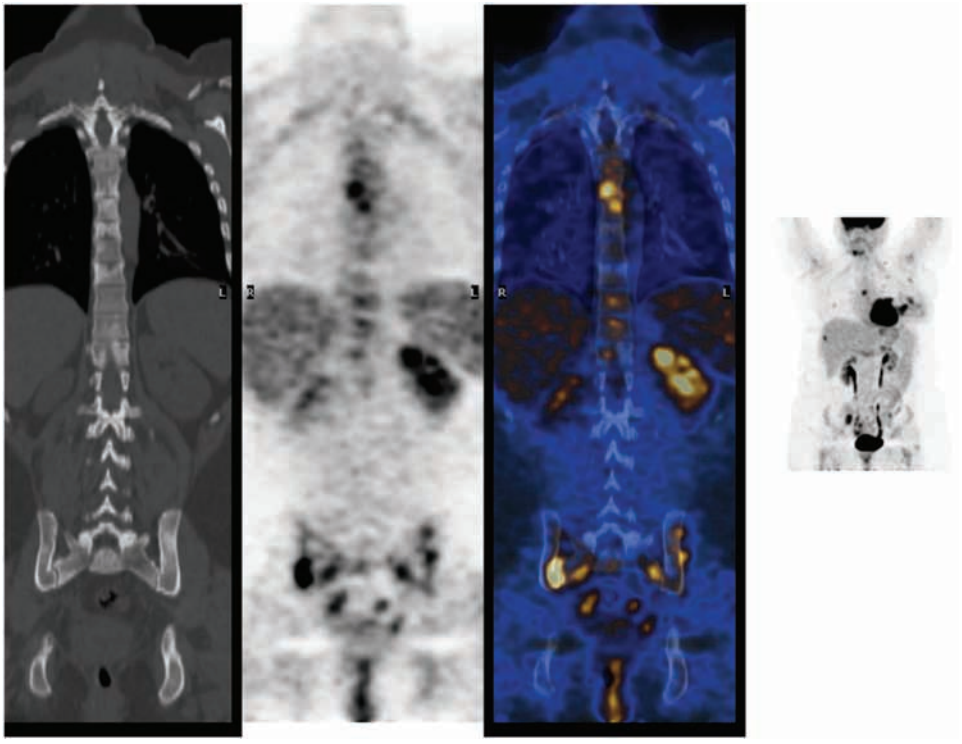

Figure 3 Comparison of bone scan and PET/CT. Note different sites of disease.

Monitoring Response to Therapy

Most research on PET as a technique to monitor response to therapy has focused on neoadjuvant chemotherapy for locally advanced breast cancer (LABC), because the pathologic end points of therapy offer a gold standard for comparison.

In a study of 22 patients undergoing neoadjuvant chemotherapy, Schelling et al.[36] reported that differences in FDG uptake distinguished nonresponding and responding tumors as early as after the first course of chemotherapy. After the first course of therapy, all responding tumors were correctly identified (sensitivity 100%, specificity 85%) through a decrease in the SUV below a 55% reduction of the baseline level. Smith et al.[37] similarly reported that SUV values could be used to provide early predictions of response to neoadjuvant therapy.

Other studies have focused on a mid-course assessment of response and generally show that a complete response is associated with a 50% to 60% reduction in baseline SUV.[38,39] However, the early decline in SUV is more striking; possibly by the mid-course of therapy, some of the nonresponding tumors will also show a reduction in SUV related to altered metabolic pathways within the tumor cells as opposed to a reduction in the number of tumor cells. Although data are still preliminary, changes in SUV may also predict disease-free and perhaps progression-free survival in patients with locally advanced disease.[39]

After completion of therapy, the persistence of PET positivity is predictive of macroscopic viable tumor. In a study of 50 patients, Kim et al.[40] reported that response rates were correlated with the reduction rates of the peak SUV. A 79% reduction in SUV was able to distinguish complete and partial response with a sensitivity and specificity of 85.2% and 82.6%, respectively. The authors conclude that if these findings can be confirmed in larger studies, PET may be a useful tool to assess the pathologic response at the completion of neoadjuvant therapy.

The clinical usefulness of PET assessment of tumor response to neoadjuvant therapy is still evolving, but PET scan results may be useful to confirm lack of response suggested by anatomic assessment. Such strategies are complicated by the routine use of sequential chemotherapy regimens in the neoadjuvant setting. PET scans might also be useful in determining the timing of breast surgery by identifying patients who are not benefiting from neoadjuvant therapy and who might benefit from more immediate surgery.

Minimal data are available on PET as a technique to assess response to treatment in patients with metastases. Two studies totaling 24 patients have been published on the application of FDG-PET to metastatic breast cancer response.[41,42] Both studies examined PET results at early and late points during the course of therapy, reporting that a 25% drop in SUV during the first cycle of therapy was associated with tumor response, whereas no significant decreases were noted in nonresponding tumors. A particularly

vexing clinical need in metastatic breast cancer is the assessment of bone metastasis response to therapy, which is poorly served with standard imaging studies such as bone scan. Promising early data in a study of 24 patients with bone-dominant breast cancer indicate that FDG-PET may be helpful in measuring bone metastasis response.[43] This application of PET to metastatic breast cancer response may have significant clinical applications, but clearly more research is needed (Figure 4).

Summary of Recommendations

A PET scan is not indicated for 1) detecting or screening of primary breast cancer, 2) staging of the primary tumor, axilla, or metastatic disease in patients with clinically early-stage disease, or 3) post-treatment disease surveillance. Promising data exist for several applications of PET scanning, but more research is needed. These applications are locoregional staging for locally-advanced breast cancer; as an early response indicator for systemic therapy, either neoadjuvant or therapy for metastatic disease; and for assessment of treatment response in metastatic disease, particularly bony disease. PET scans may be recommended as an adjunct to other imaging techniques (i.e., CT, magnetic resonance imaging [MRI], bone scan) for initial evaluation for recurrent or metastatic disease or as clinically indicated when results of other imaging tests are equivocal (e.g., the evaluation of brachial plexopathy or metastatic bone disease).

Colorectal PET

Diagnosis and Initial Staging

PET scans are infrequently used in the primary diagnosis of colorectal cancer, which is based on colonoscopy. However, colonic primaries can be identified on whole-body PET scans performed for other reasons. For example, Agress and Cooper[44] retrospectively reviewed 1750 PET scans performed to evaluate malignancy. Unexpected foci of FDG uptake were identified in 3.3% of patients, and of the abnormalities followed up with pathologic confirmation, half were malignant lesions. PET scans can also identify incidental polyps.[45] Therefore, biopsy may be recommended for incidental findings of FDG uptake localized to the bowel wall.

Initial staging of known colorectal cancers is typically performed preoperatively with CT scans complemented by intraoperative findings. However, compared with CT scan, the sensitivity and specificity of PET for detecting liver metastases are higher.[46–49] In the largest case series of 104 patients, Llamas-Elvira et al.[46] reported that PET had a 92% accuracy in detecting metastases compared with 87% for CT. PET identified 8 additional patients with liver metastases, and

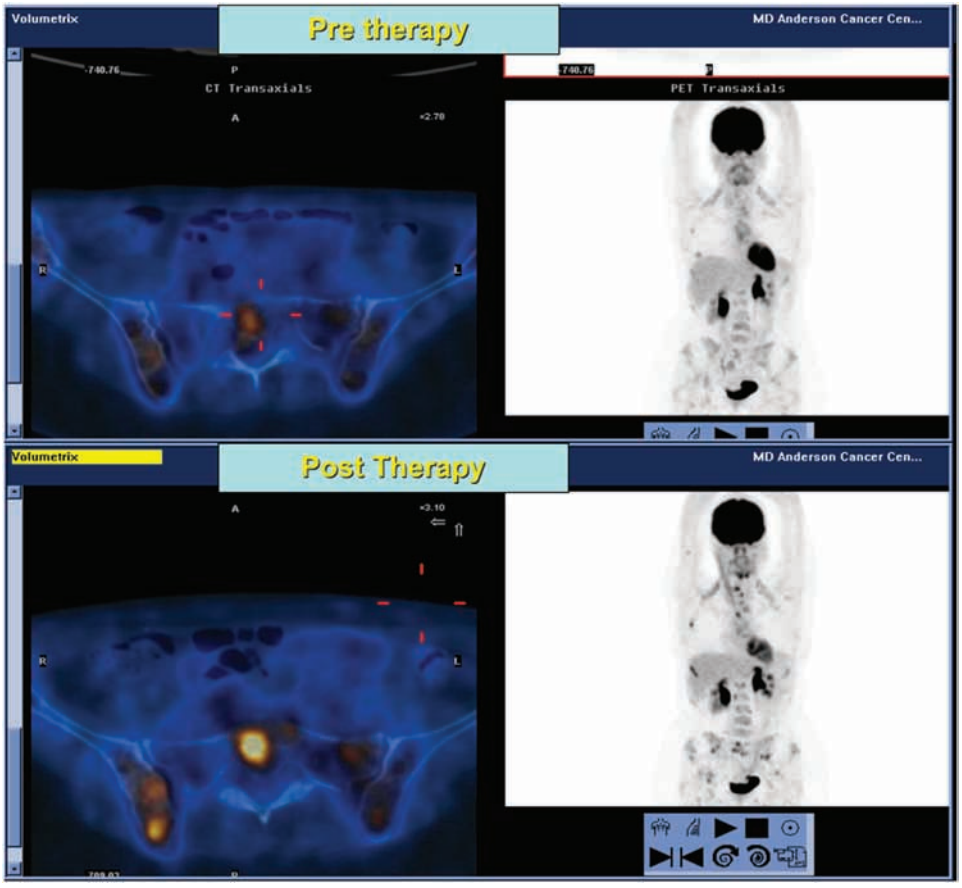

Figure 4 Demonstration of flare in the healing response. Increased metabolism is caused by therapy not worsening disease.

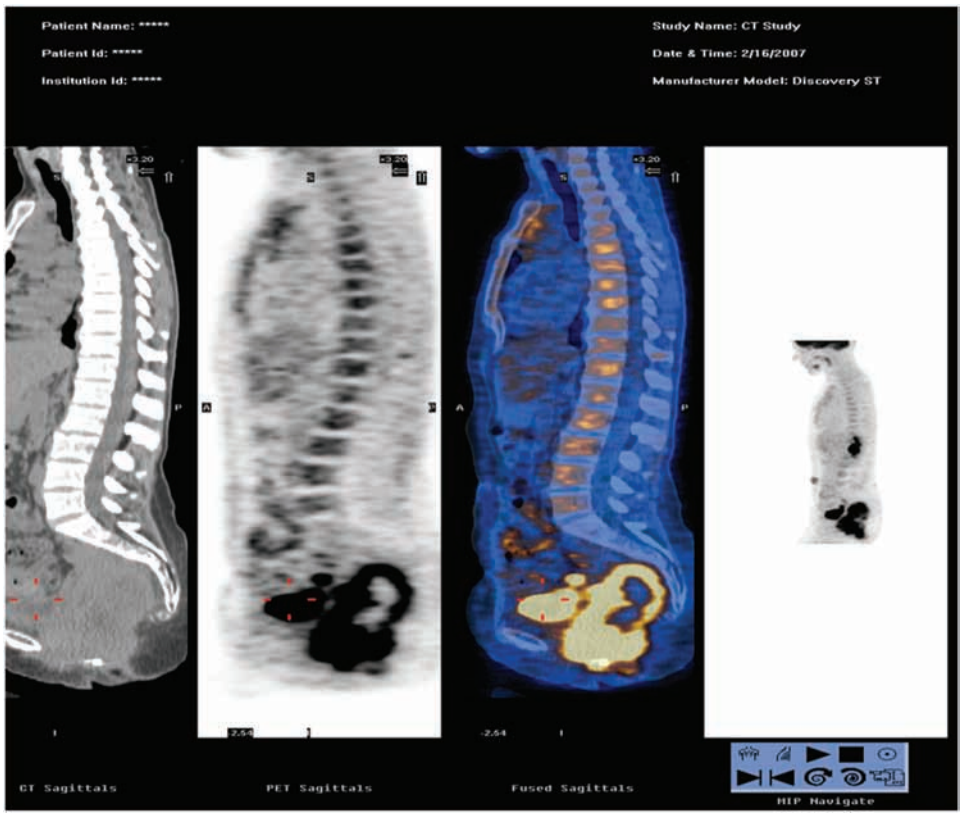

Figure 5 Demonstration of large presacral local recurrence with central area of necrosis.

preoperative PET results modified the scope of surgery in 11.54% of patients.

Detection of Recurrent Colorectal Cancer

A major role of PET scans in the management of colorectal disease is the detection of recurrence, complementing monitoring of carcinoembryonic antigen (CEA) levels, CT scanning, and colonoscopy. Although various organizations have developed practice guidelines recommending the frequency of follow-up tests, PET has not been recommended as a routine surveillance technique for recurrent colorectal cancer.[50] However, the alternative techniques (i.e., CEA, CT scans, and colonoscopy) have limitations. For example, only approximately two thirds of patients with suspected recurrence have elevated CEA levels. Additionally, the CEA level does not provide any information on location of recurrence. A CT scan is suboptimal for detecting metastases in the peritoneum, mesentery, and lymph nodes. Additionally, CT scans may not adequately distinguish between post-treatment changes and recurrence.

No studies have specifically evaluated PET as a routine surveillance technique, but many have looked at PET as a technique to assess suspected recurrence. A meta-analysis by Huebner et al.[51] in 2000 included 11 studies investigating the role PET to detect cancer recurrence. The pooled 577 patients represent a mix of those with suspected or documented recurrence. PET had a sensitivity of 97% and specificity of 75% in detecting recurrence, resulting in a management change in 29% of patients. Although the sensitivity of PET for detecting recurrence is typically reported between 90% and 95%, the sensitivity of CT scan is rarely reported to be more than 90%.

Several studies have looked at PET specifically as a technique to evaluate local recurrence. The largest study was reported by Schiepers et al.,[52] who studied 75 patients with suspected recurrent local or distant colorectal disease. The accuracy of PET was 95% compared with a 65% accuracy for CT scans. If surgical resection of recurrent disease is contemplated, these results suggest that a preoperative PET scan can further define the extent of disease and either help determine if the patient is a surgical candidate or assist in defining the extent of surgery (Figure 5). Several studies have compared the diagnostic performance of PET with other anatomic imaging techniques, such as various types of CT scans, MRI, or ultrasound, for detecting liver metastases, with PET consistently shown to have a higher sensitivity.[53,54]

Isolated liver metastases are common in colon cancer. Because hepatic resection is the only curative therapy, accurate noninvasive detection of extrahepatic disease plays a pivotal role in selecting surgical candidates. Several studies have examined PET scanning as

a technique to identify surgical candidates. The diagnostic performance of PET and CT scans were assessed through sites of extrahepatic metastases in a series of 155 patients.[55] The sensitivity of PET was greater than CT for all locations except the lungs, where the two had similar sensitivities. The specificity of PET was greater than CT at all sites except the abdomen. A diagnostic CT scan of the liver is essential in surgical candidates to evaluate the vasculature. A low-dose CT without the contrast component of a PET/CT scan is not adequate to evaluate liver vasculature. Evaluating liver vasculature requires a diagnostic CT with intravenous contrast, whether performed as the CT component of a PET/CT scan or separately.

Another common indication for a PET scan is in evaluating patients with a rising CEA but otherwise normal workup. Pooling the results of 169 patients represented in 4 studies suggests that when the conventional workup is negative (including CT scan), PET identifies tumor in 84% of patients, leading to surgical resection in 26%.[55–58] In general, PET will detect unsuspected metastases in 25% of patients and, depending on the study, will impact management in about 20% to 58%.[59] For example, in one study of 52 patients with suspected recurrence, the PET scan changed the surgical management in 28%, helped plan surgery in approximately one third, and helped avoid unnecessary surgery in two thirds.[60] Studies concluding that PET scans are cost-effective cite the impact of PET results on rates of surgery.

The next step in evaluating the impact of PET on management is to examine survival data. Currently, only retrospective studies are available. Strasberg et al.[61] presented the survival results of 43 patients whose liver resections for colorectal metastases were guided by the results of PET scan. Surgery was cancelled based on the results of PET scan in 6 patients. The estimated 3-year overall survival was 77% compared with the 40% survival rates reported in series using only CT for operative assessment. The authors concluded that preoperative PET is associated with a decrease in recurrence rate from deselecting patients with extrahepatic disease not found on conventional imaging. In a subsequent article focusing on 5-year survival, Fernandez et al.[62] reported that patients staged with PET scans had a 58% survival rate compared with 30% for those staged with CT scans alone.

Response to Therapy

Therapies for colorectal cancer include radiation therapy, chemotherapy, and regional liver therapy. Minimal data are available on PET for monitoring response to radiation therapy. Interpretation is complicated by the associated inflammatory changes in the radiation field, but current studies suggest that if a baseline PET scan is available, changes can be assessed in as soon as 2 months by focusing on the original site of increased uptake within the pattern of diffuse uptake associated with inflammation.

Small studies suggest that PET scans can identify tumors that are not responsive to 5-fluorouracil–based chemotherapy after 1 month of therapy.[63] Guillem et al.[64] showed that FDG-PET imaging performed before and 4 and 5 weeks after completion of preoperative radiation and 5-fluorouracil–based chemotherapy had the potential to assess pathologic response. Subsequently, these same authors showed that FDG-PET imaging could predict long-term outcome after a median follow-up of 42 months. The mean percent decrease in SUV max was 69% for patients free from recurrence and 37% for patients with recurrence.

PET scans have been used to evaluate the response to regional therapy where distinguishing necrosis from viable tumors is frequently an issue. For example, small studies have examined various regional therapies, such as chemoembolization, radioactive spheres, and radiofrequency ablation, and all have suggested that PET can identify residual and recurrent tumor, and potentially direct further therapy. CT scan is limited in this role because the rim of regenerating tissue enhances and can create false-positive results.[65–68]

Summary of Recommendations

For staging, PET is not routinely indicated unless initial studies are suggestive but not conclusive for metastatic disease. PET scans are indicated for evaluating a rising CEA level or a patient with suspicious symptoms, unless a CT scan has already identified metastatic disease. PET scans are not indicated for routine surveillance for colon cancer recurrence.

PET scans are not routinely indicated for restaging patients after nonsurgical treatment of metastatic disease unless curative resection is considered. However, they are indicated for preoperative evaluation in surgical resection of metastases (i.e., lung or liver). A diagnostic CT is also required to evaluate liver vascularity; a PET/CT scan alone is inadequate. Conversely, PET

scans are not routinely indicated to monitor response to chemotherapy or radiation therapy.

Lymphoma

Although lymphoma accounts for only 4% of cancers diagnosed annually, its diagnosis, staging, and management requires frequent imaging such that lymphoma may account for more than approximately 50% of the PET scans performed at a referral institution. However, imaging of lymphoma is challenging because its appearances are diverse with potential involvement of almost all organs. Additionally, lymphoma can mimic the appearance of almost all other neoplasms. Finally, the glucose uptake of a lymphoma within a given patient may be heterogeneous, presumably representing different clones of cells with different patterns of glucose metabolism; however, significant heterogeneity may suggest important differences in biologic behavior.[69]

Initial Staging

Routine staging of lymphoma, including both Hodgkin and non-Hodgkin's lymphoma, involves a CT scan with contrast to the neck and pelvis and a PET scan. Although a gallium scan was typically part of the pretreatment workup of lymphoma, gallium scans have been largely replaced by PET scans. Various studies have reported that a PET scan can contribute to staging by upstaging disease, but this rarely results in a treatment change.[70,71] Although the actual impact on treatment might be uncertain, particularly if disease is upstaged from stage III to stage IV, the consistent message from these studies is that PET scan more typically upstages disease rather than downstages. PET scans may also help identify extranodal disease. For example, PET may identify bone involvement not detected with CT scan, typically upstaging disease from stage III to stage IV.

Although a clinical role of the initial PET scan is to provide a baseline for subsequent evaluation, controversy is ongoing about this indication. For some types of lymphoma, such as Hodgkin disease, the initial PET scan is almost always positive, and if treatment response is based on a normal PET scan, then an initial PET scan is not routinely needed. Additionally, unlike other malignancies, a high correlation exists between the CT scan (i.e., anatomic image) and PET scan (i.e., functional image), and therefore the interpretation of a positive PET scan in the setting of a negative CT scan is uncertain. Thus, if a CT scan after therapy is negative, residual FDG uptake in a site of initial disease is of uncertain significance. The need for a baseline PET scan may also vary with histologic subtype and stage of disease. For example, a baseline PET scan may not be required for advanced stage follicular lymphoma if the recommended treatment was observation, whereas it would be recommended if treatment was recommended.

PET scan also has been evaluated as a technique to assess bone marrow involvement. A meta-analysis including 587 patients with lymphoma pooled from 13 studies showed that, compared with biopsy, PET had a moderate sensitivity of 51% and a specificity of 91%. These results suggest that PET cannot replace bone marrow biopsies. In general, PET is not commonly used to assess bone marrow involvement, although its results will be reported as an incidental finding potentially used to direct biopsy.[72]

Limited data are available on PET as a routine method of surveillance. Although no survival advantage has been documented, PET scan may be helpful in the small subset of patients with unusual sites of disease, such as bone, subcutaneous tissue, or skin, in which follow-up with other imaging techniques is limited.

PET Scans and Lymphoma Histology

Several studies have shown that the intensity of FDG uptake is associated with aggressive disease. In one study of 97 patients with non-Hodgkin's lymphoma who were either treatment-naïve or undergoing initial evaluation for relapsed disease, all cases of indolent lymphoma that had an SUV less than or equal to 13 and an SUV greater than 10 excluded indolent lymphoma with a specificity of 81%. The authors concluded that this information may be helpful if discordance is seen between biopsy and clinical behavior.[69] Because of the overlap in SUV values across the histologies, a PET scan cannot replace a biopsy but may be particularly useful in guiding biopsies. For example, unless otherwise instructed, a surgeon may biopsy the most convenient node available, but a PET scan can specifically target a lymph node with the highest SUV.

PET scans also have been investigated as a technique to detect malignant transformation of chronic lymphocytic lymphoma, such as Richter's transformation. For example, an SUV greater than 5 has been considered highly suggestive of Richter's transformation. In a retrospective study of 37 patients with CLL, 10 of 11 (91%) with Richter's transformation had an SUV uptake greater than 5.[73]

Response Criteria and Prognosis

In 1999, an international workshop developed standard response criteria for lymphoma based on clinical radiologic and pathologic (i.e., bone marrow criteria) findings.[74] The radiologic response was typically evaluated with CT scan. One category of response was *complete response uncertain* (CRu), which reflects the inability of CT to distinguish among viable tumor, necrosis, or fibrosis in residual masses.

Because studies have reported that PET scan results have prognostic value, interest was shown in incorporating PET imaging into response criteria.[75–78] For example, Juweid et al.[79] assessed response using the international criteria in conjunction with PET scan results in 54 patients with aggressive non-Hodgkin's lymphoma after 4 to 6 cycles of chemotherapy and compared response with progression-free survival. PET scans were considered positive or negative based on visual assessment; in the lung, scans were considered positive if the uptake exceeded that of the mediastinal blood pool structures. Using the CT-based international criteria alone, 17 patients experienced a complete response and 7 a CRu. In contrast, when PET results were incorporated, 35 patients experienced a complete response and no patients experienced a CRu. Therefore, a negative PET scan even in the presence of a residual mass is interpreted as a complete response. In this study, results of the PET scan recategorized patients with a CRu to either a complete response or partial response, essentially eliminating the CRu category except for the small subset of patients with indeterminate bone marrow.

In 2007, the International Working Group for non-Hodgkin's lymphoma published 2 documents establishing the role of PET scans in assessing lymphoma tumor response. One document developed guidelines for performing and interpreting PET imaging to assess treatment response, whereas the second proposed revised response criteria.[80,81] Specifically, the revised response criteria have eliminated the category of CRu, and the categories of complete response, partial response, and stable disease are based partly on the results of PET scans (Table 3).

Interim Restaging

As an interim restaging technique, a PET scan after a few cycles of chemotherapy could provide early detection of treatment failure, prompting a switch to more aggressive therapy. For example, in patients whose tumors respond to chemotherapy, an estimated 80% to 90% of the effect of chemotherapy on tumor FDG uptake occurs within the first 7 days after initiation of therapy. Various studies have examined interim PET as a prognostic indicator, concluding that the results of an interim PET scan are strong and independent predictors of progression-free survival in Hodgkin disease and non-Hodgkin's lymphoma.[82–84]

Study results suggest that therapy does not need to be changed when the PET scan is negative, but a separate trial is needed to determine whether a positive PET scan should prompt an alternative therapy and whether this alternative therapy can improve outcomes. A trial design to test these outcomes would include a PET scan as an interim staging technique. Patients with a negative PET scan would continue on therapy, whereas those with a positive PET scan may undergo biopsy confirmation considering the rate of false-positive PET scan results. Patients with a positive biopsy can then be randomized to either continue initial therapy or be switched to an alternate therapy. Ideally, treatment outcomes would be improved in patients switching to alternative therapy.

Summary of Recommendations

In staging, PET scans serve as a baseline for lymphomas that are potentially curative (i.e., diffuse large B-cell lymphoma [DLBCL], Hodgkin disease). The PET scan serves as a baseline when assessing treatment response. Scans rule out systemic disease in clinically localized lymphoma (i.e., early-stage Hodgkin lymphoma, DLBCL, Hodgkin disease, follicular lymphoma, and mantle zone lymphoma), and are used to assess lymphoma when transformation is suspected.

PET scans can be useful for evaluating residual masses. At the end of therapy, a positive PET scan is associated with a poor disease-free survival. However, because of false-positives, biopsy is necessary for deciding on aggressive therapeutic interventions.

For evaluating treatment response, PET scans have a limited role if the diagnostic CT is normal. PET scans have been incorporated into treatment for aggressive non-Hodgkin's lymphoma and Hodgkin lymphoma, and PET scans also are used to direct

Table 3 Response Definitions for Clinical Trials*

Response	Definition	Nodal Masses	Spleen, Liver	Bone Marrow
CR	Disappearance of all evidence of disease	a) FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative	Not palpable, nodules disappeared	Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunohisto-chemistry should be negative
		b) Variably FDG-avid or PET negative; regression to normal size on CT		
PR	Regression of measurable disease and no new sites	≥ 50% decrease in SPD of up to 6 largest dominant masses; no increase in size of other nodes	≥ 50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen	Irrelevant if positive prior to therapy; cell type should be specified
		a) FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site		
		b) Variably FDG-avid or PET negative; regression on CT		
SD	Failure to attain CR/PR or PD	a) FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET		
		b) Variably FDG-avid or PET negative; no change in size of previous lesions on CT		
Relapsed disease or PD	Any new lesion or increase by ≥ 50% of previously involved sites from nadir	Appearance of a new lesion(s) > 1.5 cm in any axis, ≥ 50% increase in longest diameter of a previously identified node > 1 cm in short axis	> 50% increase from nadir in the SPD of any previous lesions	New or recurrent involvement
		Lesions PET positive if FDG-avid lymphoma or PET positive prior to therapy		

Abbreviations: CR, complete remission; CT, computed tomography; FDG, [^{18}F] fluorodeoxyglucose; PD, progressive disease; PET, positron emission tomography; PR, partial remission; SD, stable disease; SPD, sum of the product of the diameters.
*Adapted with permission from Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol 2007;25:582.

biopsy of most suspicious areas based on SUV. Because of the high false-positive rate (outside of a clinical trial), PET scans are not routinely indicated in the interim evaluation for prognostication and are not used for routine follow-up of node-based disease. However, PET may be beneficial in selecting patients with unusual sites of disease, such as bone, where PET is superior to CT, and for distinguishing between indolent and aggressive non-Hodgkin's lymphoma based on SUV value (Figure 6).

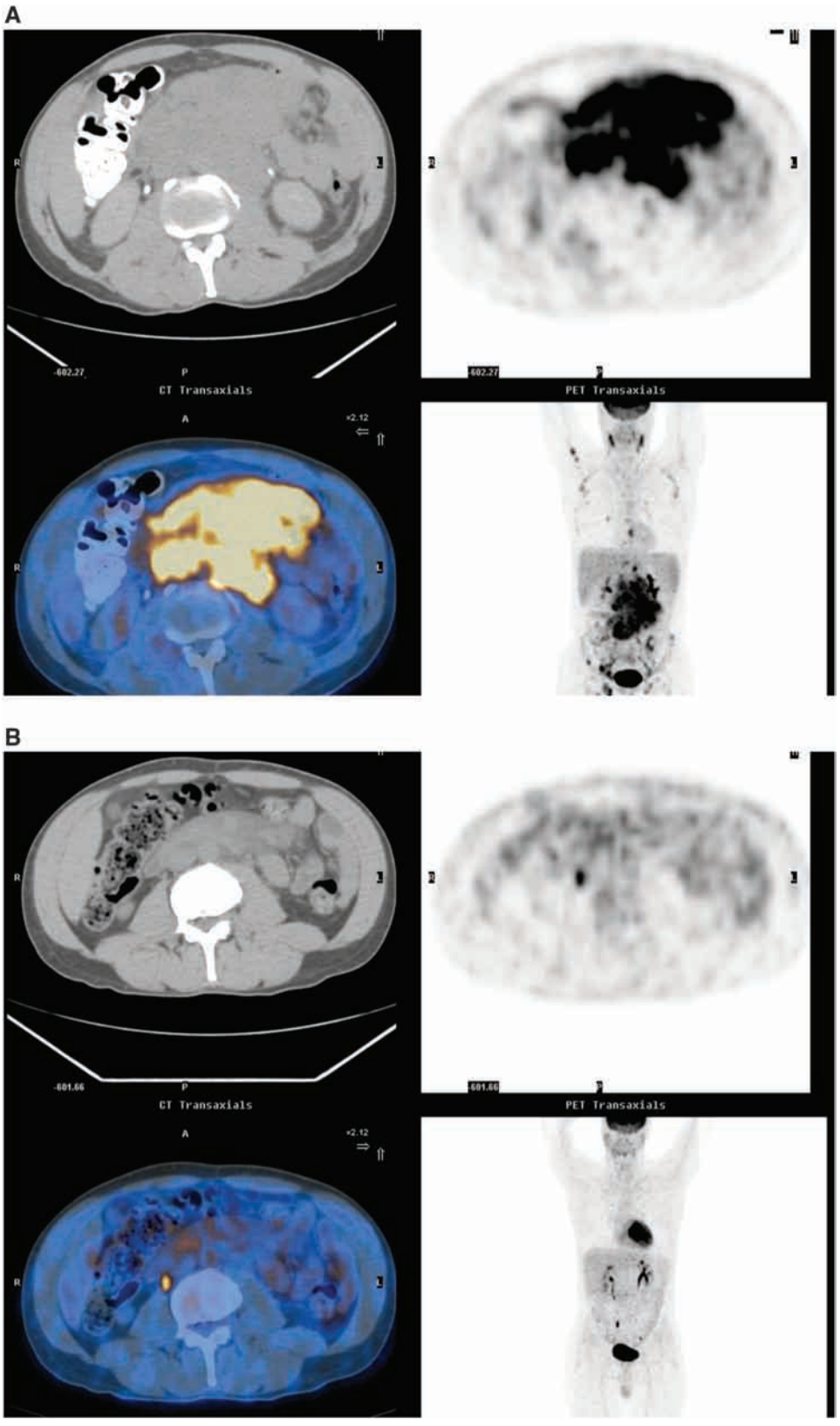

Figure 6 Pre- (A) and post-therapy (B) PET/CT in a lymphoma patient expected to have a good outcome.

NSCLC

Diagnosis/Staging

An established indication for PET scans is to evaluate solitary pulmonary nodules. In a patient with several pulmonary nodules, a PET scan also can identify the most metabolically active lesion and help direct biopsy.

CT scans are among the initial imaging studies typically used to stage lung cancer and specifically evaluate the mediastinal lymph nodes. However, when using mediastinoscopy as the gold standard, CT scans have a sensitivity of 71.0%, a specificity of 87.7%, and an overall accuracy of 82.1%.[85] CT scans only evaluate the size of the lymph nodes, and lymph nodes may be enlarged in lung cancer because of postobstructive pneumonitis, leading to false-positive results. However, many studies have reported that PET has improved diagnostic accuracy compared with CT, and now PET is routinely recommended as part of the workup of NSCLC. For example, in a meta-analysis of 13 international studies, 12 reported greater accuracy of PET in evaluating the mediastinal nodes.[86] The estimate of overall sensitivity was 83%, whereas specificity ranged from 79% to 100%. For CT, the sensitivity and

specificity ranged from 50% to 97% and 58% to 94%, respectively.

Herder et al.[87] investigated whether initial PET might simplify staging in a trial randomizing 465 patients with newly diagnosed lung cancer to undergo conventional workup or an initial PET scan. The primary outcome was the number of noninvasive tests to determine clinical TNM staging. The results suggested that initial PET was not associated with a reduction in the overall number of diagnostic tests (n = 7.9), but it maintained quality of TNM staging with a reduction in the number of mediastinoscopies.

The roles of CT and PET raise issues about which test should be performed first to provide the most efficient and cost-effective workup. At presentation, 10% to 15% of patients have stage I disease, 20% have stage II disease, 30% have stage III disease, and 40% have stage IV. Therefore, a CT scan may identify distant metastases, frequently liver lesions, in 40% of patients. These patients do not require a PET scan.

Current guidelines recommend PET scans for all tumor stages after CT scan, except for patients with multiple metastases; in this situation a PET scan is not needed.[88] PET scans are recommended also in patients with solitary metastases who are potential candidates for surgical resection to rule out additional metastases. Essentially, a PET scan is recommended in the 60% of patients without multiple distant metastases in whom the results could change either surgical candidacy or extent of surgery.

In many instances, patients present initially with an upper respiratory infection. A chest radiograph is then performed and the patient started on antibiotics. If the symptoms do not resolve, another chest radiograph is performed. If the radiograph is suspicious for lung cancer, a chest CT scan is performed and the results of the scan ultimately prompt referral to an oncologist. The availability of combined PET/CT scans may modify this hierarchy if the repeat chest radiograph is highly suspicious for lung cancer. Because most patients will need a PET scan as part of the initial workup, it may be efficient to follow up the abnormal chest radiograph with a PET/CT scan if the CT scan is of diagnostic quality. Another issue is whether the CT component of PET/CT is performed with a breath hold. For example, because of respiratory motion, small parenchymal lung lesions can be missed on CT acquired during shallow breathing, but phase of the breath hold may impact the alignment of the PET/CT. In a consecutive case series of 142 patients who underwent PET/CT with shallow breathing and a separate breath-hold CT scan, Allen-Auerbach et al.[89] showed that the breath-hold CT scan identified an additional 125 parenchymal nodules. Different breathing protocols for PET/CT are currently being investigated for thoracic PET/CT scans.[90,91]

Restaging

PET has been used as a restaging technique after chemotherapy or radiation therapy. Cerfolio et al.[92] reported on a prospective case series of 93 patients with N2 disease who underwent initial staging with mediastinoscopy, PET/CT, and CT scans. Patients were then restaged with the same imaging techniques 4 to 12 weeks after induction chemoradiation and results were compared with pathologic staging. The repeat PET/CT missed residual N2 disease in 20% of patients, and false-positive results were seen in 25%. However, results of PET/CT were more accurate than CT scan. In addition, a reduction in the SUV value of 75% or more suggested a complete response, whereas a reduction of 55% or more suggested a partial response. The authors concluded that, although PET/CT is superior to CT, a biopsy to confirm the PET/CT may be required, depending on the clinical situation and treatment goals. As an example, a PET/CT might show a shrinking tumor but an SUV reduced by 55% or less. The clinical choices are then to assume that residual disease is present and recommend additional therapy or obtain biopsy results to direct treatment. Some physicians argue that a biopsy might not be recommended in medically inoperable patients, whereas others counter that the morbidity of biopsy might outweigh the morbidity of additional treatment. The biopsy technique (e.g., fine needle aspiration, mediastinoscopy) is another variable that should be considered, because some may be more difficult to perform in patients who underwent prior radiotherapy.[93] The timing of the repeat PET scan is another issue, because in the setting of radiation therapy and associated inflammation, the SUV may not drop for several months.

After initial assessment with PET, patients can be followed up with CT to assess the emergence of a new mass. Changes in a CT scan may then prompt repeat PET scan. Although PET is clearly superior to CT in identifying the presence of scarring, distinguishing between radiation effect, pneumonitis, and residual tumor requires an experienced radiologist.

Restaging most clearly impacts treatment of patients with stage III disease.[88] For example, patients with stage III disease most frequently experience local relapses at 3 to 15 months, and results of PET scan may suggest alternative therapy if patients were originally treated with radiation therapy alone. Restaging after completion of neoadjuvant therapy also may impact surgical decisions. Residual tumor in the mediastinum may direct treatment to definitive chemoradiation. Additionally, the identification of a distant metastasis may deselect patients for resection of the primary tumor. However, because individual physicians and institutions vary in how they determine surgical candidacy after neoadjuvant therapy, the role of PET in this setting varies.

The role of restaging in patients with stage IV disease is more controversial because of the uncertain impact on treatment decisions. Additionally, a CT scan may be adequate to identify distant metastases. Although PET may be more sensitive in detecting subtle metastases, this discovery is unlikely to influence treatment. One exception may be a patient with a solitary metastasis that has been surgically resected, rendering the patient disease-free, at which point many clinicians would recommend a PET scan to verify the disease-free status.

Currently, PET scan is not recommended as a primary surveillance method in treated patients, but is recommended when follow-up CT scans identify a suspicious lesion.

Response to Therapy/Monitoring Therapy

Several studies have examined the role of PET in determining response to neoadjuvant therapy. Pottgen et al.[94] studied 50 consecutive patients with locally advanced lung cancer who underwent induction therapy with either chemotherapy alone or chemoradiation. Patients underwent a PET scan before and after induction. The PET scans were evaluated according to lesion volume and SUV, and were compared with the pathology found at subsequent surgical excision. The authors reported that changes in the SUV in PET/CT scans before and after three chemotherapy cycles or later have prognostic value and allow prediction of histopathologic response in the primary tumor and mediastinal lymph nodes. A retrospective review of 56 patients with lung cancer treated with neoadjuvant therapy also focused on changes in SUV as a predictor of response.[95] Patients underwent PET scan both before and after neoadjuvant therapy, followed by complete resection of the cancer. The change in SUV had a near-linear relationship to the percent of nonviable tumor cells in the resected tumor, and was much better correlated to the pathology than the CT scan results. Specifically, when the SUV decreased by 80% or more, complete response was likely. These studies focused on the results of PET scan after the completion of adjuvant therapy.

Additional interest has been expressed in using PET scans as an interim assessment of treatment response. In this setting, positive PET scans or minimal changes in the SUV could prompt a treatment change. In a prospective study of 57 patients with advanced lung cancer who underwent PET scan before and after the first cycle of therapy,[96] a 25% reduction in SUV was considered a metabolic response. Median time to progression and overall survival were significantly longer for tumors with a metabolic response compared with those without (163 vs. 54 days and 252 days vs. 151 days, respectively). The authors concluded that metabolic response can be used to identify patients with nonresponding tumors to avoid the morbidity of ineffective therapy. However, the PET results were not used to direct therapy.

Summary of Recommendations for NSCLC

PET scans are recommended in 1) diagnosis in patients with 1 to 2 solitary pulmonary nodules and 2) in staging as part of the initial evaluation in all patients, except those with multiple distant metastases. In addition, an initial PET/CT may eliminate the need for a CT of the chest and upper abdomen. PET scans are also recommended in 3) restaging, both for stage III disease, 2 to 3 months after neoadjuvant therapy or before surgery, and for stage IV disease with solitary metastasis 2 to 3 months after treatment; and 4) for surveillance in patients with symptoms suggesting recurrence (Figure 7). PET scans are not recommended for restaging patients with stage I or II disease.

Summary

The role of PET or PET/CT scans in oncology is rapidly evolving, with well-defined roles in the common malignancies of breast, lung, colorectal cancer, and lymphoma. The role of PET scans is most established for certain indications in lymphoma, colorectal cancer, and lung cancer. For example, common indications for PET scans in lymphoma include a baseline study

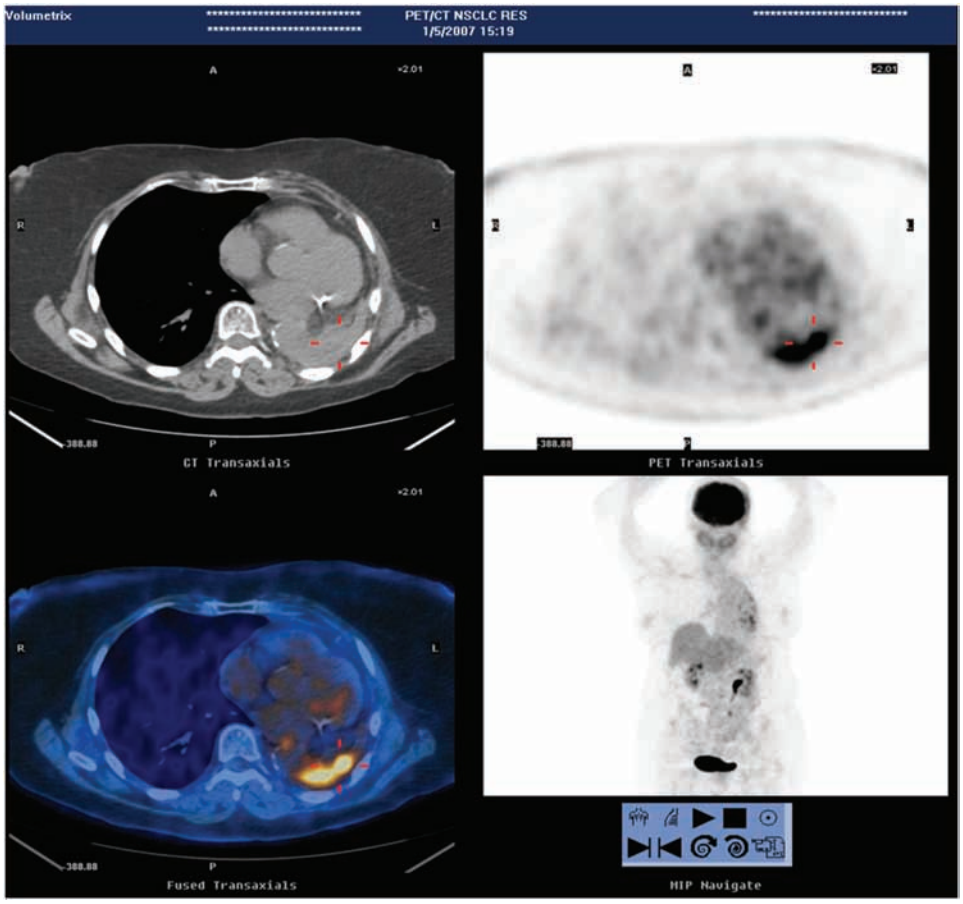

Figure 7 Biopsy-proven infection, not tumor, in follow-up of patient with history of non-small cell lung cancer.

for staging patients with diffuse large B-cell lymphoma or Hodgkin disease, followed by a study at the end of therapy to assess treatment response. Lymphoma is the only disease for which PET scan is routinely used to assess tumor response. In patients with colorectal cancer, PET scans have an established role in evaluating surgical candidacy of patients with isolated liver metastases or evaluating possible recurrence in patients with a rising CEA. In lung cancer, PET scans have been used to further evaluate solitary pulmonary nodules and for staging all patients with known lung cancer. PET scans are also routinely used for restaging tumors in patients with stage III or stage IV disease with solitary metastasis. PET scans are not routinely recommended in breast cancer, but may be valuable as an adjunct to the initial evaluation of suspected recurrent or metastatic disease. Emerging applications of PET scans focus on the role of SUV values to detect tumor response. For example, in patients with lymphoma, a high SUV value can be used to direct biopsy. SUV values also may be helpful in assessing response to breast cancer therapy.

Researching the role of PET in the overall hierarchy of imaging options in patients with cancer presents various challenges. Although published literature on PET has focused on its diagnostic performance, less literature is available on the impact on patient management. One key outcome is the elimination of other tests if PET scans were performed earlier in the imaging hierarchy. However, a PET scan is often the last imaging test performed. The ultimate patient outcome would focus on whether a PET scan changed the management of a patient and improved survival. Ideally, this would involve a trial randomizing patients to either undergo a PET scan or not. Such a trial has not yet been conducted, and there may be physician resistance to this design based on preconceived notions about the value of a PET scan.

PET/CT imaging has been rapidly adopted nationally, and although a large body of data do not exist demonstrating the incremental value of a PET/CT scan compared with a PET scan, radiologists have appreciated the additional anatomic detail provided by the CT scan. PET/CT scans have created questions about the most efficient imaging strategy for patients who may benefit from a separate diagnostic CT scan. In some institutions, this scan can be performed concurrently with the PET/CT scan. In other situations, the diagnostic CT scan is performed before the PET/CT scan, and the CT component can be a low-dose CT.

Future directions of PET imaging include various new imaging agents that target different cellular and signaling pathways. ^{18}F-FLT, which may be used to

assess proliferation, is probably the closest to clinical application.

References

1. Cohade C, Osman M, Leal J, Wahl RL. Direct comparison of (18)F-FDG PET and PET/CT in patients with colorectal carcinoma. J Nucl Med 2003;44:1797–1803.
2. De Wever W, Ceyssens S, Mortelmans L, et al. Additional value of PET-CT in the staging of lung cancer: comparison with CT alone, PET alone and visual correlation of PET and CT. Eur Radiol 2007;17:23–32.
3. Lardinois D, Weder W, Hany TF, et al. Staging of non-small-cell lung cancer with integrated positron-emission tomography and computed tomography. N Engl J Med 2003;348:2500–2507.
4. Pelosi E, Messa C, Sironi S, et al. Value of integrated PET/CT for lesion localisation in cancer patients: a comparative study. Eur J Nucl Med Mol Imaging 2004;31:932–939.
5. Freudenberg LS, Antoch G, Schutt P, et al. FDG-PET/CT in re-staging of patients with lymphoma. Eur J Nucl Med Mol Imaging 2004;31:325–329.
6. Larson SM, Schwartz LH. 18F-FDG PET as a candidate for "qualified biomarker": functional assessment of treatment response in oncology. J Nucl Med 2006;47:901–903.
7. Hartwell L, Mankoff D, Paulovich A, et al. Cancer biomarkers: a systems approach. Nat Biotechnol 2006;24:905–908.
8. Mankoff DA, Shields AF, Krohn KA. PET imaging of cellular proliferation. Radiol Clin North Am 2005;43:153–167.
9. Smith-Jones PM, Solit DB, Akhurst T, et al. Imaging the pharmacodynamics of HER2 degradation in response to Hsp90 inhibitors. Nat Biotechnol 2004;22:701–706.
10. Veach DR, Namavari M, Beresten T, et al. Synthesis and in vitro examination of [^{124}I]-, [^{125}I]- and [^{131}I]-2-(4-iodophenylamino) pyrido[2,3-d]pyrimidin-7-one radiolabeled Abl kinase inhibitors. Nucl Med Biol 2005;32:313–321.
11. Hillner BE, Tunuguntla R, Fratkin M. Clinical decisions associated with positron emission tomography in a prospective cohort of patients with suspected or known cancer at one United States center. J Clin Oncol 2004;22:4147–4156.
12. van Tinteren H, Hoekstra OS, Smit EF, et al. Effectiveness of positron emission tomography in the preoperative assessment of patients with suspected non-small-cell lung cancer: the PLUS multicentre randomised trial. Lancet 2002;359:1388–1393.
13. Ruers TJ, Langenhoff BS, Neeleman N, et al. Value of positron emission tomography with [F-18]fluorodeoxyglucose in patients with colorectal liver metastases: a prospective study. J Clin Oncol 2002;20:388–395.
14. Wahl Rl, Siegel BA, Coleman RE, et al. Prospective multicenter study of axillary nodal staging by positron emission tomography in breast cancer: a report of the staging breast cancer with PET Study Group. J Clin Oncol 2004;22: 277–285.
15. Kumar R, Zhuang H, Schnall M, et al. PDG PET positive lymph nodes are highly predictive of metastasis in breast cancer. Nucl Med Commun 2006;27:231–236.
16. Fehr MK, Hornung R, Varga Z, et al. Axillary staging using positron emission tomography in breast cancer patients qualifying for sentinel lymph node biopsy. Breast J 2004;10:89–93.
17. Barranger E, Grahek D, Antoine M, et al. Evaluation of fluorodeoxyglucose positron emission tomography in the detection of axillary lymph node metastasis in patients with early-stage breast cancer. Ann Surg Oncol 2003;10:622–627.
18. Keleman PR, Lowe V, Phillips N. Positron emission tomography and sentinel node dissection in breast cancer. Clin Breast Cancer 2002;3:73–77.
19. Veronesi U, De Cicco C, Galimberti V, et al. A comparative study on the value of FDG-PET and sentinel node biopsy to identify occult axillary metastases. Ann Oncol 2007;18:473–478.
20. Gil-Rendo A, Zornoza G, Garcia-Velloso MJ, et al. Fluorodeoxyglucose positron emission tomography with sentinel node biopsy for evaluation of axillary involvement in breast cancer. Br J Surg 2006;93:707–712.
21. Zornoza G, Garcia-Velloso MJ, Sola J, et al. ^{18}F-FDG PET complemented with sentinel lymph node biopsy in the detection of axillary involvement in breast cancer. Eur J Surg Oncol 2004;30:15–19.
22. Hathaway PB, Mankoff DA, Maravilla KR, et al. Value of combined FDG PET and MR imaging in the evaluation of suspected recurrent local-regional breast cancer: preliminary experience. Radiology 1999;210:807–814.
23. Ahmad A, Barrington S, Maisey M, Rubens RD. Use of positron emission tomography in evaluation of brachial plexopathy in breast cancer patients. Br J Cancer 1999;79: 478–482.
24. Inoue T, Yutani K, Taguchi T, et al. Preoperative evaluation of prognosis in breast cancer patients by [(18)F]2-Deoxy-2-fluoro-D-glucose-positron emission tomography. J Cancer Res Clin Oncol 2004;130:273–278.
25. Mankoff DA, Dunnwald LK, Gralow JR, et al. Blood flow and metabolism in locally advanced breast cancer: relationship to response to therapy. J Nucl Med 2002;43: 500–509.
26. Bellon JR, Livingston RB, Eubank WB, et al. Evaluation of the internal mammary lymph nodes by FDG-PET in locally advanced breast cancer (LABC). Am J Clin Oncol 2004;27:407–410.
27. Norum J, Andreassen T. Screening for metastatic disease in newly diagnosed breast cancer patients. What is cost-effective? Anticancer Res 2000;20:2193–2196.
28. Puglisi F, Follador A, Minisini AM, et al. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications. Ann Oncol 2005;16:263–266.
29. Barry MC, Thornton F, Murphy M, et al. The value of metastatic screening in early primary breast cancer. Ir J Med Sci 1999;168:248–250.
30. Moon DH, Maddahi J, Silverman DH, et al. Accuracy of whole-body fluorine-18-FDG PET for the detection of

recurrent or metastatic breast carcinoma. J Nucl Med 1998; 39:431–435.

31. Kamel EM, Wyss MT, Fehr MK, et al. [18-F]-Fluorodeoxyglucose positron emission tomography in patients with suspected recurrent of breast cancer. J Cancer Res Clin Oncol 2003;129:147–153.
32. Eubank WB, Mankoff DA, Takasugi J, et al. 18fluorodeoxyglucose positron emission tomography to detect mediastinal or internal mammary metastases in breast cancer. J Clin Oncol 2001;19:3516–3523.
33. Cook GJ, Houston S, Rubens R, et al. Detection of bone metastases in breast cancer by 18FDG PET: differing metabolic activity in osteoblastic and osteolytic lesions. J Clin Oncol 1998;16:3375–3379.
34. Abe K, Sasaki M, Kuwabara Y, et al. Comparison of 18 FDG-PET with 99mTc-HMDP scintigraphy for the detection of bone metastases in patients with breast cancer. Ann Nucl Med 2005;19:573–579.
35. Fujimoto R, Higashi T, Nakamoto Y, et al. Diagnostic accuracy of bone metastases detection in cancer patients: comparison between bone scintigraphy and whole-body FDG-PET. Ann Nucl Med 2006;20:399–408.
36. Schelling M, Avril N, Nahrig J, et al. Positron emission tomography using [(18)F] fluorodeoxyglucose for monitoring primary chemotherapy in breast cancer. J Clin Oncol 2000;18:1689–1695.
37. Smith IC, Welch AE, Hutcheon AW, et al. Positron emission tomography using [(18)F] fluorodeoxy-D-glucose to predict the pathologic response of breast cancer to primary chemotherapy. J Clin Oncol 2000;18:1676–1688.
38. Mankoff DA, Dunnwald LK. Changes in glucose metabolism and blood flow following chemotherapy for breast cancer. PET Clinics 2005;1:71–82.
39. Mankoff DA, Dunnwald LK, Gralow JR, et al. Changes in blood flow and metabolism in locally advanced breast cancer treated with neoadjuvant chemotherapy. J Nucl Med 2003;44:1815–1817.
40. Kim SJ, Kim SK, Lee ES, et al. Predictive value of [18F]FDG PET for pathological response of breast cancer to neoadjuvant chemotherapy. Ann Oncol 2004;15:1352–1357.
41. Gennari A, Donatis S, Salvadori B, et al. Role of 2-[18F]-fluorodeoxyglucose (FDG) positron emission tomography (PET) in the early assessment of response to chemotherapy in metastatic breast cancer patients. Clin Breast Cancer 2000;1:156–161.
42. Dose Schwarz J, Bader M, Jenicke L, et al. Early prediction of response to chemotherapy in metastatic breast cancer using sequential 18F-FDG PET. J Nucl Med 2005;46: 1144–1150.
43. Stafford SE, Gralow JR, Schubert EK, et al. Use of serial FDG PET to measure the response of bone-dominant breast cancer to therapy. Acad Radiol 2002;9:913–921.
44. Agress H Jr, Cooper BZ. Detection of clinically unexpected malignant and premalignant tumors with whole-body FDG PET: histopathologic comparison. Radiology 2004;230:417–422.
45. Yasuda S, Fujii H, Nakahara T, et al. 18F-FDG PET detection of colonic adenomas. J Nucl Med 2001;42:989–992.
46. Llamas-Elvira JM, Rodriguez-Fernandez A, Gutierrez-Sainz J, et al. Fluorine-18 fluorodeoxyglucose PET in the preoperative staging of colorectal cancer. Eur J Nucl Med Mol Imaging 2006;Dec 29 [Epub ahead of print].
47. Kantorova I, Lipska L, Belohlavek O, et al. Routine (18)F-FDG PET preoperative staging of colorectal cancer: comparison with conventional staging and its impact on treatment decision making. J Nucl Med 2003;44:1784–1788.
48. Abdel-Nabi H, Doerr RJ, Lamonica DM, et al. Staging of primary colorectal carcinomas with fluorine-18 fluorodeoxyglucose whole-body PET: correlation with histopathologic and CT findings. Radiology 1998;206:755–760.
49. Mukai M, Sadahiro S, Yasuda S, et al. Preoperative evaluation by whole-body 18F-fluorodeoxyglucose positron emission tomography in patients with primary colorectal cancer. Oncol Rep 2000;7:85–87.
50. Desch CE, Benson AB III, Somerfield MR, et al. Colorectal cancer surveillance: 2005 update of an American Society of Clinical Oncology practice guideline. J Clin Oncol 2005;23:8512–8519. Erratum in J Clin Oncol 2006;24:1224.
51. Huebner RH, Park KC, Shepherd JE, et al. A meta-analysis of the literature for whole-body FDG PET detection of recurrent colorectal cancer. J Nucl Med 2000;41:1177–1189.
52. Schiepers C, Penninckx F, De Vadder N, et al. Contribution of PET in the diagnosis of recurrent colorectal cancer: comparison with conventional imaging. Eur J Surg Oncol 1995;21:517–522.
53. Kinkel K, Lu Y, Both M, et al. Detection of hepatic metastases from cancers of the gastrointestinal tract by using noninvasive imaging methods (US, CT, MR imaging, PET): a meta-analysis. Radiology 2002;224:748–756.
54. Bipat S, van Leeuwen MS, Comans EF, et al. Colorectal liver metastases: CT, MR imaging, and PET for diagnosis—meta-analysis. Radiology 2005;237:123–131.
55. Valk PE, Abella-Columna E, Haseman MK, et al. Whole-body PET imaging with [18F]fluorodeoxyglucose in management of recurrent colorectal cancer. Arch Surg 1999;134:503–511.
56. Flamen P, Hoekstra OS, Homans F, et al. Unexplained rising carcinoembryonic antigen (CEA) in the postoperative surveillance of colorectal cancer: the utility of positron emission tomography (PET). Eur J Cancer 2001;37:862–869.
57. Maldonado A, Sancho F, Cerdan J, et al. 16. FDG-PET in the detection of recurrence in colorectal cancer based on rising CEA level. Experience in 72 Patients. Clin Positron Imaging 2000;3:170.
58. Flanagan FL, Dehdashti F, Ogunbiyi OA, et al. Utility of FDG-PET for investigating unexplained plasma CEA elevation in patients with colorectal cancer. Ann Surg 1998;227:319–323.
59. Wiering B, Krabbe PF, Jager GJ, et al. The impact of fluor-18-deoxyglucose-positron emission tomography in the

management of colorectal liver metastases. Cancer 2005;104:2658–2670.

60. Delbeke D, Vitola JV, Sandler MP, et al. Staging recurrent metastatic colorectal carcinoma with PET. J Nucl Med 1997;38:1196–1201.

61. Strasberg SM, Dehdashti F, Siegel BA, et al. Survival of patients evaluated by FDG-PET before hepatic resection for metastatic colorectal carcinoma: a prospective database study. Ann Surg 2001;233:293–299.

62. Fernandez FG, Drebin JA, Linehan DC, et al. Five-year survival after resection of hepatic metastases from colorectal cancer in patients screened by positron emission tomography with F-18 fluorodeoxyglucose (FDG-PET). Ann Surg 2004;240:438–447.

63. Findlay M, Young H, Cunningham D, et al. Noninvasive monitoring of tumor metabolism using fluorodeoxyglucose and positron emission tomography in colorectal cancer liver metastases: correlation with tumor response to fluorouracil. J Clin Oncol 1996;14:700–708.

64. Guillem JG, Puig-La Calle J Jr, Akhurst T, et al. Prospective assessment of primary rectal cancer response to preoperative radiation and chemotherapy using 18-fluorodeoxyglucose positron emission tomography. Dis Colon Rectum 2000;43:18–24.

65. Donckier V, Van Laethem JL, Goldman S, et al. [F-18] fluorodeoxyglucose positron emission tomography as a tool for early recognition of incomplete tumor destruction after radiofrequency ablation for liver metastases. J Surg Oncol 2003;84:215–223.

66. Wong CY, Qing F, Savin M, et al. Reduction of metastatic load to liver after intraarterial hepatic yttrium-90 radioembolization as evaluated by [18F]fluorodeoxyglucose positron emission tomographic imaging. J Vasc Interv Radiol 2005;16:1101–1106.

67. Wong CY, Salem R, Qing F, et al. Metabolic response after intraarterial 90Y-glass microsphere treatment for colorectal liver metastases: comparison of quantitative and visual analyses by 18F-FDG PET. J Nucl Med 2004;45:1892–1897.

68. Barker DW, Zagoria RJ, Morton Ka, et al. Evaluation of liver metastases after radiofrequency ablation: utility of 18F-FDG PET and PET/CT. AJR Am J Roentgenol 2005;184:1096–1102.

69. Schoder H, Noy A, Gonen M, et al. Intensity of 18fluorodeoxyglucose uptake in positron emission tomography distinguishes between indolent and aggressive non-Hodgkin's lymphoma. J Clin Oncol 2005;23:4643–4651.

70. Bangerter M, Moog F, Buchmann I, et al. Whole-body 2-[18F]-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) for accurate staging of Hodgkin's disease. Ann Oncol 1998;9:1117–1122.

71. Young CS, Young BL, Smith SM. Staging Hodgkin's disease with 18-FDG PET. Comparison with CT and surgery. Clin Positron Imaging 1998;1:161–164.

72. Pakos EE, Fotopoulos AD, Ioannidis JP. 18F-FDG PET for evaluation of bone marrow infiltration in staging of lymphoma: a meta-analysis. J Nucl Med 2005;46:958–963.

73. Bruzzi JF, Macapinlac H, Tsimberidou AM, et al. Detection of Richter's transformation of chronic lymphocytic leukemia by PET/CT. J Nucl Med 2006;47:1267–1273.

74. Cheson BD, Horning SJ, Coiffier B, et al. Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI sponsored International Working Group. J Clin Oncol 1999;17:1244. Erratum in J Clin Oncol 2000;18:2351.

75. Reske SN. PET and restaging of malignant lymphoma including residual masses and relapse. Eur J Nucl Med Mol Imaging 2003;30(suppl 1):S89–S96.

76. Spaepen K, Stroobants S, Dupont P, et al. Prognostic value of positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose ([18F]FDG) after first-line chemotherapy in non-Hodgkin's lymphoma: is [18F]FDG-PET a valid alternative to conventional diagnostic methods? J Clin Oncol 2001;19:414–419.

77. Weihrauch MR, Re D, Scheidhauer K, et al. Thoracic positron emission tomography using 18F-fluorodeoxyglucose for the evaluation of residual mediastinal Hodgkin disease. Blood 2001;98:2930–2934.

78. Naumann R, Vaic A, Beuthien-Baumann B, et al. Prognostic value of positron emission tomography in the evaluation of post-treatment residual mass in patients with Hodgkin's disease and non-Hodgkin's lymphoma. Br J Haematol 2001;115:793–800.

79. Juweid ME, Wiseman GA, Vose JM, et al. Response assessment of aggressive non-Hodgkin's lymphoma by integrated International Workshop criteria and fluorine-18-fluorodeoxxyglucose positron emission tomography. J Clin Oncol 2005;23:4652–4661.

80. Juweid ME, Stroobants S, Hoekstra OS, et al. Use of positron emission tomography for response assessment of lymphoma: consensus of the Imaging Subcommittee of International Harmonization Project in lymphoma. J Clin Oncol 2007;25:571–578.

81. Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol 2007;25:579–586.

82. Hutchings M, Loft A, Hansen M, et al. FDG-PET after two cycles of chemotherapy predicts treatment failure and progression-free survival in Hodgkin lymphoma. Blood 2006;107:52–59.

83. Mikhaeel NG, Hutchings M, Fields PA, et al. FDG-PET after two to three cycles of chemotherapy predicts progression-free and overall survival in high-grade non-Hodgkin lymphoma. Ann Oncol 2005;16:1514–1523.

84. Haioun C, Itti E, Rahmouni A, et al. [18F]fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) in aggressive lymphoma: an early prognostic tool for predicting patient outcome. Blood 2005;106:1376–1381.

85. Patterson GA, Ginsberg RJ, Poon PY, et al. A prospective evaluation of magnetic resonance imaging, computed tomography, and mediastinoscopy in the preoperative assessment of mediastinal node status in bronchogenic carcinoma. J Thorac Cardiovasc Surg 1987;94:679–684.

86. Alongi F, Ragusa P, Montemaggi P, Bona CM. Combining independent studies of diagnostic fluorodeoxyglucose positron-emission tomography and computed tomography in mediastinal lymph node staging for non small cell lung cancer. Tumori 2006;92:327–333.

87. Herder GJ, Kramer H, Hoekstra OS, et al. Traditional versus up-front [18F] fluorodeoxyglucose-positron emission tomography staging of non-small-cell lung cancer: a Dutch cooperative randomized study. J Clin Oncol 2006;24: 1800–1806.

88. Bruzzi JF, Munden RF. PET/CT imaging of lung cancer. J Thoracic Imaging 2006;21:123–126.

89. Allen-Auerbach M, Yeom K, Park J, et al. Standard PET/CT of the chest during shallow breathing is inadequate for comprehensive staging of lung cancer. J Nucl Med 2006;47: 298–301.

90. Gilman MD, Fischman AJ, Krishnasetty V, et al. Optimal CT breathing protocol for combined thoracic PET/CT. AJR Am J Roentgenol 2006;187:1357–1360.

91. Nehmeh SA, Erdi YE, Meirelles GS, et al. Deep-inspiration on breath-hold of PET/CT of the thorax. J Nucl Med 2007;48:22–26.

92. Cerfolio RJ, Bryant AS, Ojha B. Restaging patients with N2 (stage IIIa) non-small cell lung cancer after neoadjuvant chemoradiotherapy: a prospective study. J Thorac Cardiovasc Surg 2006;131:1229–1235.

93. Granome P, van Schil P, Cesario A. Restaging patients with N2 (stage IIIa) non-small cell lung cancer after neoadjuvant chemoradiotherapy: a closer look at redo mediastinoscopy. Letter to the Editor. J Thorac Cardiovasc Surg 2007;133: 275–276.

94. Pottgen C, Levegrun S, Theegarten D, et al. Value of 18F-fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography in non-small-cell lung cancer for prediction of pathologic response and times to relapse after neoadjuvant chemoradiotherapy. Clin Cancer Res 2006;12:97–106.

95. Cerfolio RJ, Bryant AS, Winokur TS, et al. Repeat FDG-PET after neoadjuvant therapy is a predictor of pathologic response in patients with non-small cell lung cancer. Ann Thorac Surg 2004;78:1903–1909.

96. Weber WA, Petersen V, Schmidt B, et al. Positron emission tomography in non-small-cell lung cancer: prediction of response to chemotherapy by quantita-tive assessment of glucose use. J Clin Oncol 2003;21:2651–2657.

Post-test Please circle the correct answer on the enclosed answer sheet.

1. Which of the following statements is/are TRUE regarding PET/CT scans?
   a. PET/CT imaging has rapidly diffused.
   b. PET/CT imaging dramatically increases the sensitivity of PET scans.
   c. A diagnostic CT scan is always included as part of a PET/CT scan.
   d. A PET/CT scan requires contrast media.

2. Which of the following is/are TRUE regarding preparation of the patient for a PET scan?
   a. Poor preparation can lead to uptake of tracer in normal tissue, thus complicating interpretation of the image.
   b. Adequate hydration is recommended to reduce accumulation of tracer in the urinary system.
   c. False-positive results may be related to inflammatory conditions, trauma, infection, and granulomatous disease; thus, a focused history is necessary.
   d. All are true.

3. Which statement best describes the current status of research regarding the oncologic applications of PET imaging?
   a. Numerous studies have shown that the results of PET imaging are routinely used to direct patient management.
   b. Randomized studies of PET imaging may be problematic because physicians may have preconceived ideas about the value of a PET scan.
   c. Studies have delineated the place of PET in the overall hierarchy of imaging tests used in patients with cancer.

4. Which of the following is/are FALSE regarding the role of PET scanning to assess the axillary lymph nodes in patients with breast cancer?
   a. PET scans may be considered an alternative to axillary dissection.
   b. PET scans may be used as a triage technique to select which patients would benefit from sentinel node biopsy.
   c. PET scans of the axilla are not helpful in assessing the brachial plexus.
   d. All of the above are false.

5. Which of the following is/are TRUE regarding the role of PET for detecting metastatic disease in patients with breast cancer?
   a. PET scans are not routinely recommended in patients with early-stage disease because of the low yield.
   b. PET scans are very sensitive in the detection of sclerotic bone metastases.
   c. PET scans have reasonable sensitivity for detecting distant metastases, but their routine use in patients with suspected metastases is not recommended.
   d. a and c above are true.
   e. All are true.

6. Which of the following is/are TRUE of the SUV value?
   a. In patients with breast cancer, a 50% reduction in SUV suggests a meaningful response to neoadjuvant therapy.
   b. Changes in the SUV value may not be adequate to assess tumor response if the pretherapy uptake of radiotracer was low or if there is high uptake in background tissue.
   c. In lymphoma, a high SUV value may be helpful in selecting which node to biopsy.
   d. Changes in the SUV value are particularly helpful in evaluating the response to therapy of brain metastases.
   e. a, b, c are true.
   f. All are true.

7. What is the role of PET scanning in diagnosing colorectal cancer?
   a. None.
   b. PET scans performed for other purposes may detect a colorectal cancer as an incidental finding.

8. What is/are the role(s) of PET scans in detecting recurrent colorectal cancer?
   a. PET imaging is recommended as a routine surveillance tool in patients with a history of colorectal cancer.
   b. PET imaging may help determine extent of disease and surgical candidacy in patients with a suspected local recurrence.
   c. PET imaging has a higher sensitivity than CT scans in detecting liver metastases and is also helpful for assessing extrahepatic disease in patients considered candidates for resection of isolated liver metastases.
   d. b and c are correct.
   e. All of the above are correct.

9. Which are the following is/are TRUE regarding the role of PET imaging in the management of lymphoma?
   a. Interpretation of PET scans in patients with lymphoma is challenging due to its diverse appearance and potential involvement of almost all organs.
   b. A baseline PET scan is particularly useful in patients with low-grade and indolent lymphomas.
   c. A PET scan is essential to rule out systemic disease in patients with suspected localized lymphoma.
   d. a and c are true.
   e. All are true.

10. Which of the following is/are TRUE regarding PET imaging as a technique for interim staging in patients with lymphoma?
    a. A PET scan that is negative at interim staging is a strong and independent predictor of progression-free survival in patients with Hodgkin disease and non-Hodgkin's lymphoma.
    b. Clinical trials have confirmed that a positive PET scan at interim staging should prompt a change in therapy.
    c. Both are true.
11. Which of the following is/are TRUE for PET imaging in patients with non–small cell lung cancer?
    a. PET scans are recommended in all patients with non–small cell lung cancer as part of the initial staging workup.
    b. PET restaging after completion of neoadjuvant therapy rarely impacts surgical decisions.
    c. PET is routinely recommended to restage patients with stage IV disease.
    d. None of the above are true.
12. Which of the following is/are TRUE regarding potential future roles of PET imaging?
    a. An 18F FLT radiotracer may be used to detect proliferation.
    b. Imaging of HER2 is an area of active interest, and it may be used to provide an early assessment of tumor response to trastuzumab.
    c. Molecular imaging of radiolabeled antibodies could potentially be used to predict response to therapy.
    d. All of the above are true.

Post-Test Answer Sheet

Please circle one answer per question. A score of at least 70% on the post-test is required.

1.	a	b	c	d			7.	a	b			
2.	a	b	c	d			8.	a	b	c	d	e
3.	a	b	c				9.	a	b	c	d	e
4.	a	b	c	d			10.	a	b	c		
5.	a	b	c	d	e		11.	a	b	c	d	
6.	a	b	c	d	e	f	12.	a	b	c	d	

Please evaluate the achievement of the learning objectives using a scale of 1 to 5.
(1 = Not met; 3 = Partially met; 5 = Completely met)

Describe the technology and science of PET and its general relevance to cancer care.
1 2 3 4 5

Describe broadly clinical applications of PET in cancer care, including diagnosis, staging, monitoring/surveillance, and evaluation.
1 2 3 4 5

Describe the relevance of PET scanning and potential contribution of the imaging technology alone and, where appropriate, in combination with other imaging technologies in the management of patients diagnosed with breast cancer, colon cancer, rectal cancer, non-Hodgkin's lymphoma, non-small cell lung cancer, and thyroid cancer.
1 2 3 4 5

Provide specific recommendation regarding the appropriate use and application of PET scanning with breast cancer, colon cancer, rectal cancer, non-Hodgkin's lymphoma, non-small cell lung cancer, and thyroid cancer.
1 2 3 4 5

Please indicate the extent to which you agree or disagree with the following statements:

(1 = Strongly disagree; 3 = Not sure; 5 = Strongly agree)

The material was presented in a fair and balanced manner.
1 2 3 4 5

The information presented in this monograph was pertinent to my educational needs.
1 2 3 4 5

The information presented was scientifically rigorous and up-to-date.
1 2 3 4 5

The information presented in this monograph has motivated me to modify my practice.
1 2 3 4 5

I would recommend this monograph to my colleagues.
1 2 3 4 5

NCCN Task Force Report: PET Scanning in Cancer

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