REVIEW ARTICLE

CURRENT CONCEPTS

Positron-Emission Tomography and Assessment of Cancer Therapy

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Positron-emission tomography (PET) is a noninvasive imaging technique that exploits the unique decay physics of positron-emitting isotopes. The isotopes of oxygen, carbon, nitrogen, and fluorine have been used in the development of diagnostically useful biologic compounds that are available for PET imaging in order to provide a functional or metabolic assessment of normal tissues or disease conditions.

The past few years have seen a tremendous expansion of clinical applications of PET, particularly in oncology, mostly with the use of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) as the PET tracer. PET with ^{18}F-FDG is now being used in the evaluation of several neoplasms, both before and after therapy, as well as in the planning of radiotherapy in various cancers, such as tumors of the lung and of the head and neck. Its use in the assessment of cancer after therapy, including restaging tumors and monitoring tumor response, is the focus of this article.

Oncologic PET Tracers

Several radiotracers have been used in oncologic applications of PET.[1] Table 1 shows the breadth of these molecular probes that provide insight into physiologic features, extending from glucose consumption (assessed by ^{18}F-FDG) to cell hypoxia (assessed by ^{18}F-fluoromisonidazole).[2,3] Of these radiotracers, ^{18}F-FDG is by far the most commonly used in oncologic PET and is the only oncologic PET tracer approved by the Food and Drug Administration for routine clinical use.

The uptake of ^{18}F-FDG is substantially increased in most types of cancer as compared with its uptake in most normal organs or tissues.[1] A notable exception is prostate cancer, in which ^{18}F-FDG uptake has been found to be variable and unpredictable, a factor that limits the use of PET in the staging and restaging of this disease.[4] In contrast, moderate-to-high uptake is seen in most lung, colorectal, esophageal, stomach, head and neck, cervical, ovarian, and breast cancers and in melanoma and most types of lymphoma. Variable uptake is observed in thyroid, testicular, hepatocellular, renal, and bladder cancers and in sarcomas and neuroendocrine tumors. Increased tumoral uptake of ^{18}F-FDG reflects elevated glucose consumption by tumor cells, as evidenced by the overexpression of glucose transporter proteins at the cells' surface and increased levels of active hexokinase demonstrated in many tumors.[5] The degree of tumoral ^{18}F-FDG uptake is often expressed with the use of a semiquantitative measure, the standardized uptake value.

Although ^{18}F-FDG is an exquisite tumor-localizing tracer, it is not tumor-specific. The uptake of ^{18}F-FDG reflects glucose use in essentially any tissue; its increased uptake in tumors is a result of increased and inefficient use of glucose. Other benign processes associated with cells that have increased glucose use, such as inflammatory cells or hyperplastic bone marrow or thymic cells, also have en-

Table 1. Selected Tracers for Use in Oncologic PET.*

Tracer	Biologic Analogue	Mechanism of Uptake in Tumor Cells	Measured Effect	Application or Potential Application
^{18}F-fluorodeoxyglucose	Glucose	Facilitated diffusion by glucose transporters, phosphorylation by hexokinase with subsequent "metabolic trapping"	Aerobic and anaerobic glycolysis, glucose consumption or metabolism	Diagnosis, staging, restaging, monitoring response of various cancer types
^{11}C-thymidine ^{18}F-fluorothymidine	Thymidine	Facilitated diffusion and active transport by nucleoside transporters, phosphorylation by thymidine kinase with subsequent incorporation into DNA (with ^{11}C-thymidine) or metabolic trapping (with ^{18}F-fluorothymidine)	DNA synthesis, tumor-cell proliferation	Diagnosis, staging, restaging, monitoring response of various cancer types
^{11}C-methionine	Methionine	Active transport by amino acid transporter system A with subsequent incorporation into protein	Protein synthesis, tumor-cell proliferation	Diagnosis, staging, restaging, monitoring response of various cancer types
^{11}C-choline ^{18}F-fluorocholine	Choline	Active or passive transport with subsequent phosphorylation and synthesis of phosphatidylcholine cell membrane phospholipid	Cell-membrane metabolism, tumor-cell proliferation	Staging, restaging, monitoring response of various cancer types
^{11}C-tyrosine ^{18}F-fluorotyrosine ^{18}F-fluoroethyltyrosine	Tyrosine	Active transport by amino acid transport system L	Natural amino acid transport	Staging, restaging, monitoring response of various cancer types
^{18}F-fluorodihydroxyphenylalanine	Phenylalanine	Active transport by natural amino acid transport system	Dopamine synthesis, natural amino acid transport	Staging, restaging, monitoring response of neuroendocrine and brain tumors
^{18}F-fluoromisonidazole	NA	Diffusion into hypoxic cell, reduction and trapping caused by decreased oxygen concentration	Tissue hypoxia	Identification of hypoxic tumor cells
^{18}F-fluoro-17-β-estradiol	Estradiol	Binding to estrogen receptors	Estrogen-receptor status	In vivo assessment of estrogen-receptor density, monitoring response of estrogen-receptor–positive breast cancer
^{18}F-annexin V	Annexin V	Binding to externalized phosphatidylserine on apoptotic cells	Apoptotic cell death	In vivo detection of tumor-cell apoptosis, monitoring treatment response of various cancer types
^{18}F-fluorouracil	Uracil	Binding to thymidylate synthetase and hepatic catabolism in liver to β-fluoroalanine with subsequent accumulation in tumor	Accumulation of 5-fluorouracil in tumor	Prediction of tumor response to 5-fluorouracil (e.g., colorectal cancer)
^{11}C-acetate	Acetate	Incorporation into cell-membrane lipids	Lipid synthesis	Staging, restaging, monitoring response of various cancer types

* NA denotes not applicable.

hanced ^{18}F-FDG uptake. Thus, increased ^{18}F-FDG uptake is usually observed in infectious and inflammatory processes, inflammatory changes after surgery or irradiation, and thymic or bone marrow hyperplasia after treatment. Recognition of these imaging pitfalls with ^{18}F-FDG is essential in the assessment of patients after therapy with the use of this tracer.

PET VS. CONVENTIONAL RADIOLOGIC IMAGING

In the assessment of cancer, perhaps the most fundamental difference between PET and the various conventional radiologic imaging techniques, such as computed tomography (CT) and conventional magnetic resonance imaging, is that the former assesses functional or metabolic characteristics of the tumor, whereas the latter predominantly assess the tumor's anatomical or morphologic features — for example, density, size, and shape. Because of the largely nonspecific nature of these morphologic features, differentiation between malignant and benign processes is generally inferior to metabolic assessment by PET. Furthermore, PET sometimes detects clinically relevant changes even when no changes or minimal ones are detected by morphologic imaging. In many circumstances, this feature permits a more accurate assessment after treatment and enables early detection of cancerous lesions.

APPLICATIONS IN ASSESSMENT OF CANCER AFTER THERAPY

Although PET has been used in cancer research for more than two decades, its clinical application in oncology has only recently found widespread use. This development has been facilitated by the availability of newer, second-generation PET scanners with a larger field of view than that of the first-generation scanners and improved resolution and sensitivity, as well as by the recent introduction of systems that combine a PET scanner and a CT scanner in a single instrument (PET–CT). An additional factor of equal or greater importance is the decision by the Centers for Medicare and Medicaid Services (CMS) to approve reimbursement for several oncologic clinical indications for PET, including the staging and restaging of non–small-cell lung, esophageal, colorectal, breast, and head and neck cancers, as well as lymphoma and melanoma; the monitoring of the response to treatment of breast cancer; and recently, the staging of cervical cancer. Furthermore, the CMS announced its intent to provide coverage for PET for essentially all cancers and indications that are currently not covered in cases in which PET is performed under the conditions of specifically defined prospective clinical trials or a prospective registry, such as the National Oncologic PET Registry (www.cancerpetregistry.org) ("coverage with evidence development").

Although the decision by the CMS to approve a particular indication continues to be made on an indication-by-indication basis for each cancer type, the CMS broadly categorizes current indications into diagnosis, staging, restaging, and the monitoring of response to treatment. According to the CMS, PET for monitoring tumor response is performed during the planned course of therapy, whereas restaging is performed after the completion of treatment in order to detect residual tumor or suspected recurrence or to determine the extent of a known recurrence. Although these definitions may be arbitrary, they can help to separate CMS-approved indications for the use of clinical PET from those not yet approved.

MONITORING RESPONSE TO TREATMENT

The purpose of PET for monitoring is to provide an early and yet accurate assessment of the response to multicourse treatment with the ultimate goal of tailoring therapy according to the information provided. Thus, patients who demonstrate an early response on PET can continue treatment, whereas a change in treatment should be contemplated for those in whom such a response is lacking. The only currently approved clinical indication for PET in monitoring the response to treatment is in breast cancer.

Studies performed in patients with breast cancer demonstrated a relatively rapid decline in the standardized uptake value of ^{18}F-FDG in responding tumors after just one cycle of chemotherapy or chemohormonal therapy, whereas nonresponding tumors showed an increase, no change, or only a small decline in ^{18}F-FDG uptake.[6-8] In these studies, an early response to treatment as shown on PET has generally correlated well with the ultimate response seen in clinical, radiographic, or pathological findings a few weeks or months later.[6-8]

A variety of other neoplasms — such as lymphomas and esophageal, stomach, colorectal, head and neck, and non–small-cell lung cancers

— also have a rapid and significant decline in ^{18}F-FDG uptake in tumors that ultimately respond to treatment by clinical, radiographic, or histopathological assessment, whereas no such decline is observed in nonresponding tumors.[9-17] Perhaps more important, several studies of these tumor types have shown a good correlation between the early decline in ^{18}F-FDG uptake and the outcome of patients, as measured by either progression-free or overall survival.[10-13,16,17] For example, Weber et al. have shown that patients with gastroesophageal cancer who had a reduction of 35 percent or more in the standardized uptake value of ^{18}F-FDG two weeks after the first cycle of chemotherapy had a significantly longer time to either progression or recurrence of disease and longer overall survival than those with a reduction of less than 35 percent in ^{18}F-FDG uptake.[12] Statistically significant differences in progression-free survival were also found between patients with lymphoma who had "normalization" of ^{18}F-FDG uptake one week after the first cycle of chemotherapy and those with persistent tumoral ^{18}F-FDG uptake,[10] suggesting that PET may be able to predict response as early as one to three weeks after the first cycle of therapy in various cancer types.[10,12,13,16]

Despite the intriguing and often persuasive findings of several studies investigating PET for monitoring the response during the course of therapy, no published reports have clearly demonstrated that PET results were used to alter treatment. The absence of such studies may have contributed to the current lack of CMS coverage for this indication in other types of cancer. Therefore, clinical trials are needed to demonstrate the beneficial effect of early PET scanning on the treatment of patients and the ultimate outcomes. Until such effect is clearly shown, this application of PET remains experimental or exploratory.

RESTAGING

To date, restaging with the use of PET is approved in the clinical setting for breast, colorectal, esophageal, head and neck, and non–small-cell lung cancers, as well as for melanoma and lymphoma. PET restaging is also approved for suspected recurrent thyroid cancer of follicular-cell origin after thyroidectomy and radioiodine ablation in patients with a negative ^{131}I whole-body scan and an elevated level of serum thyroglobulin.

Table 2 shows the typical time points for restaging with the use of PET in these cancer types, along with the dominant contribution of PET in each. Figures 1 and 2 show the use of PET in the restaging of tumors in breast and cervical cancer (see additional figures in the Supplementary Appendix, available with the full text of this article at www.nejm.org).

A comprehensive review of studies reported from 1993 to 2000 regarding the diagnostic performance of PET in restaging found that in the detection of persistent or recurrent disease (both locoregional and distant), PET had a sensitivity of about 80 to 95 percent, a specificity of 75 to 90 percent, and an accuracy of 80 to 90 percent for the tumor types listed in Table 2.[47] More recent studies generally indicate that restaging with the use of PET is more accurate than it was before 2000, owing to the increasing use of higher-resolution PET scanners and PET–CT systems.[48-54] The use of PET–CT results in a significant improvement in the diagnostic accuracy of PET, principally because the more accurate anatomical localization of the PET findings by the concurrently performed CT leads to fewer false positive PET interpretations caused by variability between patients in physiologic ^{18}F-FDG uptake.[49]

A detailed review of the various studies pertaining to the use of PET in the restaging of various cancer types is beyond the scope of this article.[18-47,55] Therefore, we will focus on highlighting issues that are likely to be most relevant to both specialists and nonspecialists.

REQUIREMENT FOR PRETREATMENT PET BEFORE RESTAGING PET

The majority of patients undergoing restaging with PET did not undergo PET before treatment (i.e., baseline) to document the "^{18}F-FDG avidity" of their untreated tumor, either because of cost or because such scans were not thought to contribute to the initial diagnosis or staging. Since a very high percentage of the tumor types that are approved by the CMS for restaging with PET are consistently ^{18}F-FDG–avid,[1] baseline PET might be considered only for tumor types with less predictable avidity, such as marginal-zone lymphoma. PET should not be performed for staging or restaging of tumor subtypes that are known not to be ^{18}F-FDG–avid.[56]

APPROPRIATE TIME POINT FOR RESTAGING WITH PET

The appropriate time point for restaging with PET at the conclusion of therapy for the detection of residual or recurrent tumors varies with the

Table 2. Timing and Role of Restaging with PET.

Cancer Type	Timing of Restaging with PET	Dominant Contributions of PET
Non–small-cell lung cancer[18-21]	2–6 Mo after completion of chemoradiotherapy; 1–2 mo after surgery	Differentiation between persistent or recurrent tumor and fibrosis in patients with residual chest radiographic abnormalities
	When recurrence is suspected on the basis of clinical or biochemical findings or by conventional imaging	Selection of biopsy sites for confirmation of suspected recurrence Determination of actual extent of recurrence (locoregional and distant)
Breast cancer[22-25]	When recurrence is suspected on the basis of clinical or biochemical findings or by conventional imaging	Determination of actual extent of recurrence Differentiation between metastatic and benign brachial plexopathy
Colorectal cancer[26-31]	When recurrence is suspected on the basis of clinical or biochemical findings or by conventional imaging	Detection of recurrence suspected by elevation of carcinoembryonic antigen by distinguishing of viable tumor from fibrosis after therapy Determination of actual extent of recurrent disease (isolated vs. disseminated) and resectability of liver metastases
Esophageal cancer[32,33]	When recurrence is suspected on the basis of clinical or biochemical findings or by conventional imaging	More accurate diagnosis of regional and distant recurrence than with conventional imaging (less accurate for perianastomotic recurrence)
Head and neck cancer[34-38]	2–6 Mo after completion of chemoradiotherapy; 1–2 mo after surgery	More accurate assessment of response to therapy and earlier detection of persistent or recurrent disease (locoregional and distant) than with conventional imaging
	When recurrence is suspected on the basis of clinical or biochemical findings or by conventional imaging	Determination of actual extent of recurrence
Lymphoma[39-42]	3–4 Wk after completion of therapy; 2–3 mo or more after external-beam radiation	Differentiation between viable tumor and necrosis or fibrosis in patients with a residual mass and more accurate differentiation between complete and partial responses than with conventional imaging
	When recurrence is suspected on the basis of clinical or biochemical findings or by conventional imaging	Determination of actual extent of lymphoma recurrence
Melanoma[43,44]	When recurrence is suspected on the basis of clinical or biochemical findings or by conventional imaging	More accurate diagnosis of locoregional and distant recurrence than with conventional imaging, except for lung metastases (less sensitive than CT)
Follicular thyroid cancer[45,46]	When serum thyroglobulin is elevated (>10 ng per milliliter) and whole-body ^{131}I scan is negative	Detection of residual or recurrent disease (locoregional or distant) Identification of patients for potentially curative surgery vs. palliative treatment

type of therapy administered. Thus, PET may be performed within four weeks after the completion of chemotherapy, chemoimmunotherapy, or chemohormonal therapy. In contrast, PET is generally not performed until two to three months after radiation or chemoradiation or one to two months after surgery (as in the case of lung or head and neck cancers), because acute inflammatory changes that are commonly seen in the first few weeks after radiation or surgery can result in false positive PET scans.[18-21,34-38] It should be noted, however, that false positive PET findings within the first one to two months after surgery are generally located at the site of the recent surgery; PET evaluation of distant metastatic disease should be reliable even during this time. In addition, findings obtained on CT and knowledge of the radiation therapy port are likely to be particularly helpful in interpreting PET scans in patients with lung and head and neck cancers and will often lead to a decrease in the false positive interpretations of PET.

VIABLE TUMOR VS. NECROSIS OR FIBROSIS IN RESIDUAL MASSES

An important contribution of restaging with PET among patients without any other clinical or biochemical evidence of disease is the possibility of distinguishing between viable tumors and necrosis or fibrosis in residual masses that may be present after treatment.[39-42,57] This feature appears most relevant in patients with lymphoma or testicular cancer but could be important in other cancers, such as those of the head and neck.[37,57]

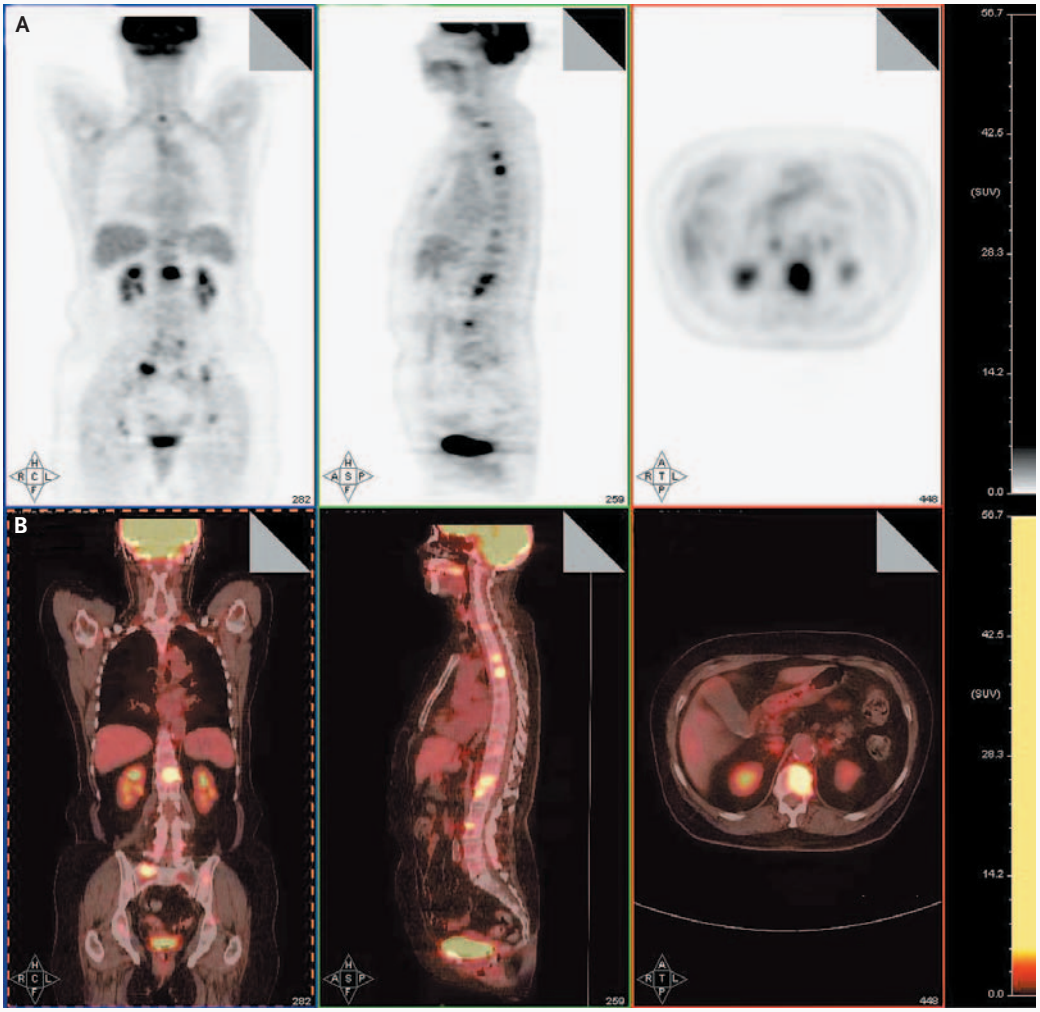

Figure 1. Detection of Recurrent Breast Carcinoma on PET–CT with ^{18}F-FDG.

The 74-year-old woman in this image had stage IV inflammatory breast cancer and had completed six cycles of doxorubicin and cyclophosphamide in October 2004. PET–CT and contrast-enhanced CT scans obtained at that time were negative. The patient was then given trastuzumab and was doing well clinically. PET–CT was performed for restaging in August 2005. Coronal, sagittal, and axial views on PET (Panel A) and on integrated PET–CT (Panel B) show disease recurrence with widespread bony metastases.

Prediction of the true nature of the residual mass on the basis of the PET scan helps avoid the administration of unnecessary toxic therapy to patients with a nonviable mass and allows the early administration of salvage therapy to patients with persistent tumors. However, it is important to note that the decision to administer salvage therapy should be made after the positive PET finding has been confirmed by biopsy. This is one of the most promising uses of PET and is very likely to become routine practice in the near future.

Largely because of the superior differentiation between viable tumor and necrosis or fibrosis in residual masses, PET that is performed in patients with aggressive lymphoma at the conclusion of treatment provides a more accurate response classification than does assessment by CT (Fig. 3).[41] These findings are likely to alter the response guidelines that are currently based on conventional imaging.

DETECTION OF RECURRENCE IN ASYMPTOMATIC PATIENTS

Several studies have persuasively demonstrated that tumor restaging with PET can detect and localize disease recurrence among patients who have no

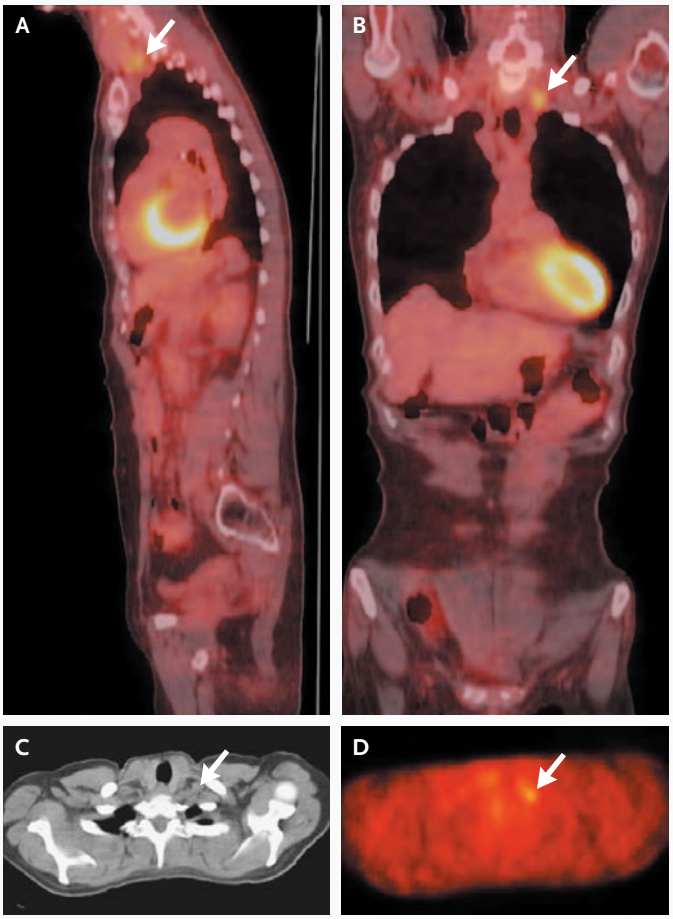

Figure 2. Detection of Recurrent Cervical Carcinoma on PET–CT with ^{18}F-FDG.

The 36-year-old woman in this image underwent concurrent radiation therapy and chemotherapy for stage IIB squamous-cell cervical carcinoma in November 2003. A para-aortic nodal recurrence was found and treated with additional radiation therapy and chemotherapy in July 2004, and a cervical recurrence was found and treated with additional chemotherapy in November 2004. PET–CT was performed for restaging in January 2005. A sagittal view (Panel A) and coronal view (Panel B) on PET–CT, as well as axial CT (Panel C) and PET (Panel D) images, show increased uptake of ^{18}F-FDG in a nonpalpable, left supraclavicular lymph node of under 1 cm (arrows). Metastasis was confirmed by biopsy. (Images are courtesy of Mallinckrodt Institute of Radiology, St. Louis.)

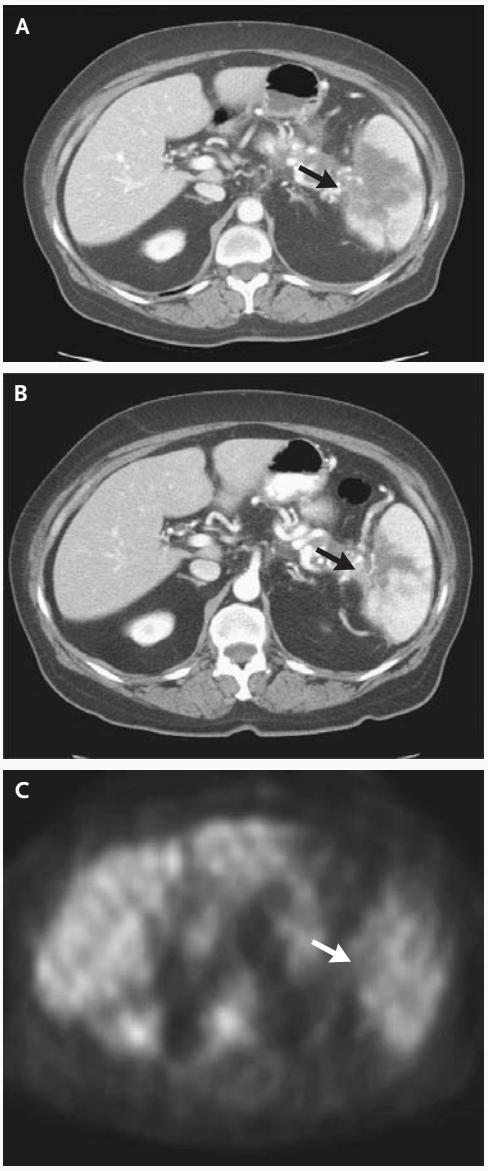

Figure 3. CT before and after Therapy and PET after Therapy in a Patient with Diffuse Large-Cell Lymphoma.

CT performed before the start of therapy shows a tumor mass in the splenic hilum (Panel A, arrow). The patient also had enlarged celiac nodes (not shown). After six cycles of therapy with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone, CT showed a 5.1-by-6.6 cm residual mass in the splenic hilum (Panel B, arrow). PET that was performed after the termination of therapy shows no evidence of increased uptake in the residual mass (Panel C, arrow), indicating that the mass shown on CT is fibrosis and not residual lymphoma. The patient had no evidence of disease at 29.5 months of follow-up. (Images are reprinted from Juweid et al.[41] with the permission of the publisher.)

symptoms or only mild ones but who have an elevated tumor marker level (e.g., among patients with colorectal cancer with elevated levels of carcinoembryonic antigen) (Fig. 4).[26-29] PET can also provide information about whether the detected disease is resectable (e.g., whether it is an isolated pelvic recurrence or involves liver metastases).[26-31] This PET application is also likely to become routine practice in the near future.

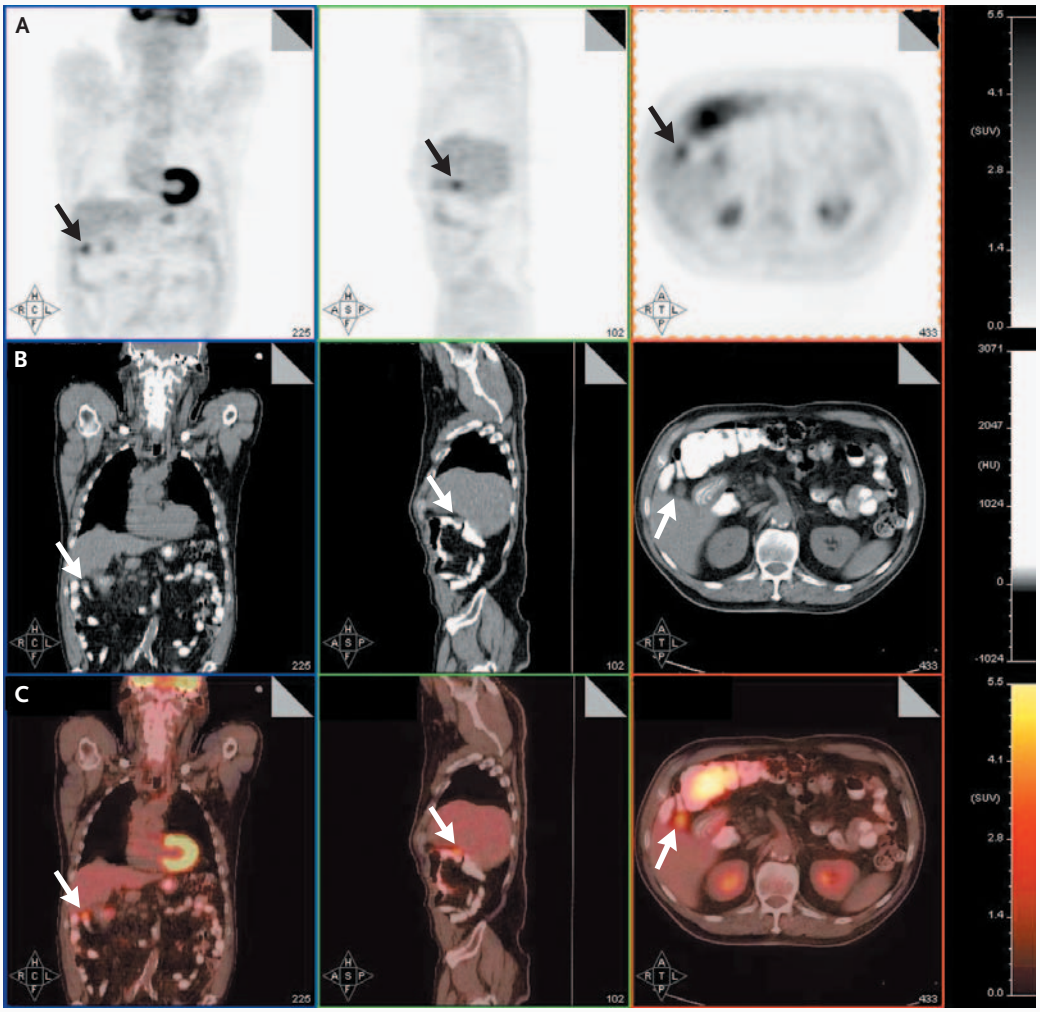

Figure 4. Detection of Occult Recurrent Colon Cancer by PET–CT with ^{18}F-FDG.

The 82-year-old man in this image presented with a slightly elevated level of carcinoembryonic antigen (3.4 ng per milliliter) one year after the completion of adjuvant chemotherapy for right-sided colon cancer. Coronal, sagittal, and axial views on PET, which was performed one month later with the use of a PET–CT scanner, show a focal area of increased uptake just below the inferior portion of the right lobe of the liver (Panel A, arrows). This mass corresponds to a new 1.2-cm soft-tissue density on CT (Panel B, arrows), as is clearly shown on the fused PET–CT images (Panel C, arrows). Three months later, the patient underwent laparotomy, which confirmed that this omental mass was recurrent colon adenocarcinoma. The tumor was successfully resected without complications.

FALSE POSITIVE FINDINGS ON RESTAGING WITH PET

Despite the generally favorable effect of restaging with PET on the treatment of patients, false positive findings occasionally present a challenge. Responsible conditions include physiologic processes such as brown fat, colonic and cyclic gynecologic activity, infectious and inflammatory processes (such as pneumonia, histoplasmosis, and sarcoidosis), and rebound thymic hyperplasia in children and young adults.

Although most infectious or inflammatory processes (i.e., most pneumonitis and granulomas) are not very ^{18}F-FDG–avid and do not usually cause a problem in the interpretation of PET scans, differentiation of these processes from residual or recurrent disease is occasionally complicated by similar uptake patterns and intensities in the processes. Careful history taking is often helpful in such instances. Furthermore, suspicion of an infectious or inflammatory process rather

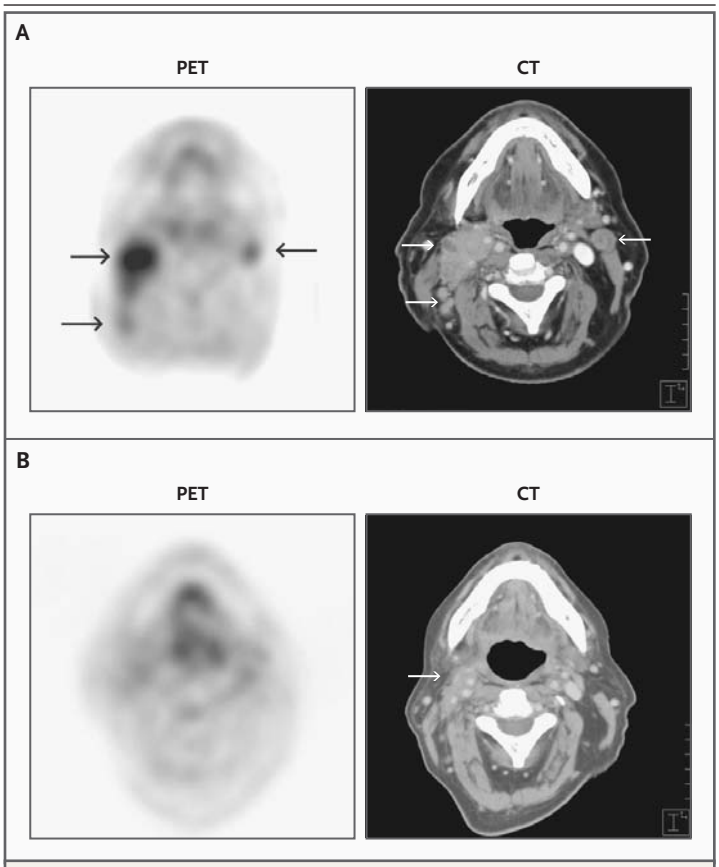

Figure 5. PET and Contrast-Enhanced CT before and after Therapy in a Patient with Base-of-Tongue Cancer (Stage I with Nodal Involvement [T1N3]).

Both PET and CT scans performed before the start of therapy show bilateral cervical lymphadenopathy (Panel A, arrows). CT performed eight weeks after chemoradiation shows a residual soft-tissue mass in the right neck (Panel B, arrow). The post-therapy PET performed at that time was negative. The patient did not undergo neck dissection and had no evidence of disease at follow-up 30 months after therapy.

than tumor should be aroused by an increased uptake of ^{18}F-FDG at a site not previously involved with tumor, especially in association with a negative PET scan at previously involved sites and a lack of any other clinical or biochemical evidence of disease. In such circumstances, repeated PET, typically in two to four months or after a course of appropriate therapy (e.g., antibiotics), will often show an absence of or substantial decrease in uptake intensity at the site. Thus, although false positive PET findings are challenging, they are often recognized by the careful PET reader who utilizes all available clinical information and any pertinent conventional imaging. This factor reduces the potentially negative effect of such findings on the treatment of patients.

EFFECT OF RESTAGING WITH PET ON QUALITY OF LIFE IN CANCER

We are unaware of studies that specifically address the effect of restaging with PET on the quality of life of patients with cancer. However, there are several examples in which such an effect is likely to occur. Recent literature indicates that patients with head and neck cancer that was initially node-positive who have a negative PET scan two to three months after chemoradiotherapy probably can be safely observed without undergoing potentially disfiguring neck dissection (Fig. 5).[37,38]

COST-EFFECTIVENESS OF RESTAGING WITH PET

In the United States, PET is a relatively expensive imaging technique, with an estimated mean cost per scan of $1,800 to $1,900.[58,59] However, only a few studies have investigated the cost-effectiveness of restaging with PET. In one such study involving patients with recurrent colorectal cancer, restaging with PET resulted in a net savings-to-cost ratio of more than 4:1 and was more cost-effective than CT, primarily because PET identified patients with unresectable disease and thereby helped to avert futile surgeries.[59] It is also conceivable that the reportedly higher accuracy of PET, as compared with CT, in the restaging of other cancers, such as head and neck cancers, could result in cost savings because of changes in management, not infrequently resulting in the avoidance of inappropriate, costly treatments. Obviously, more research is warranted in this area. It should be emphasized, however, that obvious misuses of PET — such as periodic PET scanning in patients with no clinical or biochemical evidence of disease, even several years after initial treatment — will result in reduced cost-effectiveness and should, therefore, be avoided.

RADIATION DOSE FROM PET SCANS

The effective radiation dose from a single PET scan is relatively small, estimated to be about 10 mSv. This can be compared with up to 8 mSv for the effective dose from a chest CT. The effective dose for PET–CT (20 mSv) is twice that of a single PET scan, since a whole-body CT is performed in conjunction with PET. However, even when more than one PET or PET–CT scan is performed during follow-up of patients with certain types of cancer after therapy, the cumulative effective dose is similar to that of the same number of "dedicated" contrast-enhanced CT scans of the chest, abdo-

men, and pelvis, which often are performed during follow-up in many patients. The potential benefit from restaging with PET usually far exceeds any potential risk, particularly when the additional information provided by PET affects the patient's treatment, quality of life, or prognosis.

CONCLUSIONS

PET and PET–CT have emerged as powerful imaging tools in clinical oncology for the accurate staging and restaging of established disease, for the detection of occult tumors, and for the reliable prediction of the nature of residual masses that are difficult to evaluate with conventional imaging after therapy. PET is also being evaluated for its ability to predict response or lack of response at a very early stage in the course of treatment. The favorable experience to date is beginning to support the use of PET as a surrogate end point in trials that are aimed at testing or comparing the efficacy of new drugs or treatments. This innovation could shorten the time required to evaluate the efficacy of drugs or to determine the optimal therapeutic intervention. The indications for the use of PET in clinical oncology and cancer research are likely to expand with a move toward an assessment that is both functional and anatomical.

No potential conflict of interest relevant to this article was reported.

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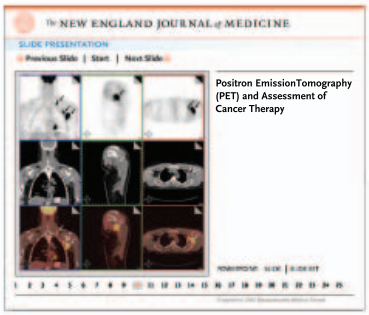

A slide presentation is available with the full text of this article at www.nejm.org. The slides show multiple examples of the uses of PET in clinical oncology.

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