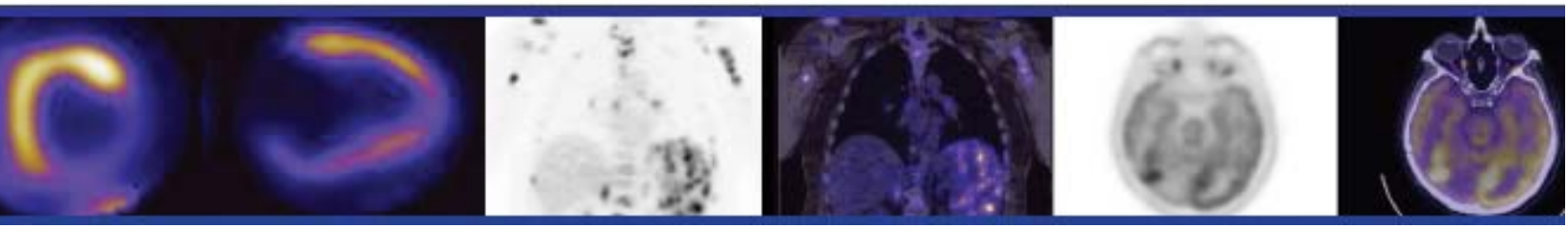
PET PROS

PET Professional Resources and Outreach Source



^{18}F-fluorodeoxyglucose (FDG) PET and PET/CT
Practice Guidelines in Oncology

A summary of the recommendations and practice guidelines of professional groups

April 2013

The recommendations and practice guidelines of professional organizations regarding the use of ^{18}F-fluorodeoxyglucose (FDG) PET and PET/CT in oncology are summarized on the following pages for the nine indications approved by the Centers for Medicare and Medicaid Services (CMS). The summary is intended to serve as an educational tool for referring physicians, as well as nuclear medicine physicians and radiologists. The summary may not include all published guidelines. Practice guidelines are revised and updated periodically, and new guidelines are written. Readers are advised to check the websites of professional organizations as well as published literature for current information.

EXECUTIVE SUMMARY

Practice guidelines from the SNM, National Comprehensive Cancer Network (NCCN), and other professional groups are summarized for nine major cancer types:

HEAD/NECK CANCER

1. Detection of occult primary tumor site in patients presenting with metastatic disease.
2. Initial staging of patients with suspected advanced stage disease.
3. Detection of residual disease after initial treatment.

THYROID CANCER

1. Detection of residual or recurrent thyroid cancer when serum thyroglobulin is elevated and radioiodine scan is negative
2. Assessment of disease extent in patients with poorly differentiated thyroid cancers and invasive Hurthle cell carcinomas.
3. Evaluation of treatment response following systemic or local therapy of metastatic or locally invasive disease.

BREAST CANCER

1. Initial staging of patients with locally advanced or metastatic breast cancer when conventional staging studies (e.g., CT or bone scan) are equivocal or suspicious.
2. Follow-up or surveillance patients with breast cancer when conventional studies (e.g., CT or bone scan) are equivocal or suspicious.

LUNG CANCER

1. Characterization of an indeterminate pulmonary nodule which is at least 8-10 mm in diameter.
2. Initial staging in patients with non-small cell lung cancer and selected patients with small cell lung cancer.
3. Delineation of gross-tumor volume in patients receiving radiation therapy.

ESOPHAGEAL CANCER

1. Initial staging (primarily to assess resectability).
2. Restaging after neoadjuvant chemotherapy and/or radiation.
3. Assessment of treatment response following definitive chemoradiation.
4. Delineation of gross tumor volume in patients receiving radiation therapy.

COLORECAL CANCER

1. Preoperative evaluation of patients with potentially resectable metastatic disease.
2. Determining location of tumors when rising CEA level suggests recurrence.

CERVICAL CANCER

1. Initial treatment planning assistance, including determination of extrapelvic / systemic spread.
2. Detection of residual or recurrent disease following initial treatment which may be potentially resectable / curable.
3. Suggested for use in radiation treatment planning (to help define nodal volume of coverage)

MELANOMA

1. Detection and localization of potential extranodal metastatic lesions in initial evaluation of patients with advanced stage disease.
2. Evaluation of the extent of metastatic disease burden in patients with recurrent disease following treatment.
3. Post-treatment screening for recurrent / metastatic disease in patients with advanced stage disease.

LYMPHOMA

1. Routine pre-treatment staging of patients with HD and many NHL subtypes.

2. Routine restaging / assessment of treatment response after chemotherapy and/or radiation therapy.

PRACTICE GUIDELINES -- HEAD/NECK CANCER (EXCLUDING THYROID OR CNS MALIGNANCIES)

Approximately 53,640 new cases of oral cavity, pharyngeal, and laryngeal cancers occurred in 2013, which account for about 3% of new cancer cases in the United States. An estimated 11,520 deaths from head and neck cancers occurred during the same time period. Squamous cell carcinoma or a variant is the histologic type in over 90% of these tumors. Alcohol and tobacco abuse are common etiologic factors in cancers of the oral cavity, oropharynx, hypopharynx and larynx. Patients with head/neck cancer are at risk for developing second primary neoplasms of the head/neck, lung, and esophagus. (Excerpted from NCCN practice guidelines, as cited below.)

The applications of -FDG PET and PET/CT in head and neck cancer include:

1. Detection of occult primary tumor site in patients presenting with metastatic disease.
2. Initial staging of patients with suspected advanced stage disease.
3. Detection of residual disease after initial treatment.

PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in patients with head/neck cancer (excluding thyroid or CNS malignancies) for:

1. Development of initial treatment strategy.
2. Development of subsequent treatment strategy
   (Medicare National Coverage Determinations Manual, Section 220.6, available at https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf)

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with head and neck cancer are listed below:

SNM, 2008

Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008 Mar;49(3):480-508. (http://jnm.snmjournals.org/cgi/content/full/49/3/480)

1. Identification of unknown primary tumors if conventional imaging tests are negative.
2. Local (lymph node) staging in addition to CT or MRI.

3. Detection of distant metastases in patients with advanced stage disease (might be beneficial)
4. Detection of potential recurrence in addition to conventional imaging

National Comprehensive Cancer Network, 2013

NCCN Clinical Practice Guidelines in Oncology™
Head and Neck Cancers v. 1.2013
(http://www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf)

1. Occult primary: PET/CT scan as indicated (before exam under anesthesia).
2. Initial staging of cancer of the oral cavity, oropharynx, hypopharynx, glottic larynx, and supraglottic larynx: Consider PET/CT for stage III-IV disease.
3. Initial staging of mucosal melanoma: Consider PET/CT scan to rule out metastatic disease.
4. Initial staging of cancer of the nasopharynx: Imaging for distant metastases (chest, liver, bone) for WHO class 2-3/N2-3 disease (may include PET scan and/or CT).
5. Post-treatment evaluation of cancers of the head and neck (minimum 12 weeks): PET/CT (suggest full dose CT with IV contrast). If PET/CT is performed and negative for suspicion of persistent cancer, further cross sectional imaging is optional.

American Head and Neck Society, 1995, edited in 2013

The American Head and Neck Society Clinical Practice Guidelines were developed in **1995** by the Practice Guidelines Committee. Dr. Jesus Medina, then Chairman of the Clinical Practice Guidelines Task Force compiled and edited them for publication. The AHNS encourages you to use the newer guidelines available at the **National Comprehensive Cancer Network (NCCN)** http://www.ahns.info/resources/)

1. Identification of occult primary tumors in patients presenting with cervical nodal metastases, especially in difficult cases where no obvious mass was seen clinically or on either CT or MRI.

PRACTICE GUIDELINES -- DIFFERENTIATED THYROID CANCER

Thyroid carcinoma is relatively uncommon. Approximately 60,220 new cases of thyroid cancers occurred in 2013 in the United States. An estimated 8,250 deaths from thyroid cancers occurred during the same time period. For the U.S. population, the lifetime risk of being diagnosed with thyroid carcinoma is less than 1%. Differentiated thyroid cancers (including papillary, follicular and Hurthle cell tumors) account for the vast majority (94%) of thyroid cancers treated in the U.S. (Excerpted from NCCN guidelines listed below)

The applications of FDG PET and PET/CT in thyroid cancer include:

1. Detection of residual or recurrent thyroid cancer when serum thyroglobulin is elevated and radioiodine scan is negative

2. Assessment of disease extent in patients with poorly differentiated thyroid cancers and invasive Hurthle cell carcinomas.
3. Evaluation of treatment response following systemic or local therapy of metastatic or locally invasive disease.

PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in patients with thyroid carcinoma subsequent treatment strategy of recurrent or residual thyroid cancer of follicular cell origin in patients who have been previously treated by thyroidectomy and radioiodine ablation and have serum thyroglobulin > 10ng/ml with negative I-131 whole body scan.
(Medicare National Coverage Determinations Manual, Section 220.6, available at) https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf)

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with thyroid cancer are listed below:

SNM, 2008

Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman 1. GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008 Mar;49(3):480-508. http://jnm.snmjournals.org/cgi/reprint/49/3/480.pdf
1. FDG PET should routinely be performed on patients previously treated for well-differentiated (follicular or papillary) thyroid cancer when the findings of ^{131}I whole-body scintigraphy are negative and the thyroglobulin serum marker is greater than 10 ng/mL.

National Comprehensive Cancer Network, 201

NCCN Clinical Practice Guidelines in Oncology™
Thyroid Carcinoma v. 1.2013
(http://www.nccn.org/professionals/physician_gls/PDF/thyroid.pdf)

1. Papillary Carcinoma: Consider non-radioiodine imaging if Tg > 2-5 ng/mL and I-131 imaging negative (e.g. neck ultrasound, neck CT, chest CT, FDG PET/CT).
2. Follicular Carcinoma: Consider non-radioiodine imaging if Tg > 2-5 ng/mL and I-131 imaging negative (e.g. neck ultrasound, neck CT, chest CT, FDG PET/CT).
3. Hurthle Cell Carcinoma: Consider non-radioiodine imaging if Tg > 2-5 ng/mL and I-131 imaging negative (e.g. neck ultrasound, neck CT, chest CT, FDG PET/CT).
4. Anaplastic Carcinoma: Consider FDG PET +/- CT scan.

American Thyroid Association, 2009

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2009; 19(11):1167-1214.

Available at:
http://thyroidguidelines.net/sites/thyroidguidelines.net/files/file/ATA_DTC_Guidelines_2009.pdf

1. In patients with differentiated thyroid carcinoma, routine preoperative PET scanning is not recommended.
2. In patients with elevated Tg but negative post-treatment scan following an empiric RAI dose (100-200 mCi of I-131), FDG PET ± CT scanning should be considered, especially in patients with un-stimulated serum Tg levels >10–20 ng/mL or in those with aggressive histologies, in order to localize metastatic lesions that may require treatment or continued close observation. Tg-positive, RAI negative patients with no structural evidence of disease can be followed with serial structural imaging studies and serial Tg measurements, with both performed more frequently if the Tg level is rising. When and how often to repeat FDG PET ± CT imaging in this setting is less certain.
3. FDG PET or PET/CT scanning may be employed as part of initial staging in poorly differentiated thyroid cancers and invasive Hurthle cell carcinomas (especially those with other evidence of disease on imaging or because of elevated serum Tg levels), as a prognostic tool in patients with metastatic disease to identify those patients at highest risk for rapid disease progression and disease-specific mortality, and as an evaluation of post-treatment response following systemic or local therapy of metastatic or locally invasive disease.
4. The sensitivity of FDG PET scanning may be marginally improved with TSH stimulation (especially in patients with low Tg values), but the clinical benefit of identifying these additional small foci is yet to be proven.

Association of American Clinical Endocrinologists, 2001

Thyroid Carcinoma Task Force. AACE/AAES Medical/Surgical Guidelines For Clinical Practice: Management Of Thyroid Carcinoma. Endocr Pract 2001;7(3):202-220. Available at https://www.aace.com/files/thyroid-carcinoma.pdf

If the source of a high Tg level remains uncertain, additional imaging studies should be considered. Many clinicians perform a levothyroxine-withdrawal scan after administration of therapeutic doses of ^{131}I (100 to 300 mCi), particularly when the only recent radioiodine scan has been performed with low doses of ^{131}I or ^{123}I. Additional isotopic scans may be of benefit: WBS with ^{201}Tl, ^{99m}Tc sestamibi, or tetrofosmin, ^{111}In pentetreotide, and positron emission tomographic (PET) scanning with fluorodeoxyglucose. Image quality and resolution with fluorodeoxyglucose, a positron emitter, may prove to be superior to ^{201}Tl, sestamibi, and tetrofosmin. Probably best nonspecific imaging modality.

PRACTICE GUIDLINES -- BREAST CANCER

The American Cancer Society estimated that 234,280 new cases of invasive breast cancer would be diagnosed and 40,030 would die of breast cancer in the United States in 2013. Breast cancer is the most common malignancy in women in the United States and is

second only to lung cancer as a cause of cancer death. The incidence of breast cancer has increased steadily in the United States over the past few decades, but breast cancer mortality appears to be declining, suggesting a benefit from early detection and more effective treatment. (Excerpted from NCCN practice guidelines, as cited below.)

The applications of FDG PET and PET/CT in breast cancer include:

1. Initial staging of patients with locally advanced or metastatic breast cancer when conventional staging studies (e.g., CT or bone scan) are equivocal or suspicious.
2. Follow-up or surveillance patients with breast cancer when conventional studies (e.g., CT or bone scan) are equivocal or suspicious.

PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in female and male patients with breast cancer for:

1. Development of initial treatment strategy (***NOTE*** CMS exceptions / limitations for initial treatment strategy: non-covered for initial diagnosis and/or staging of axillary lymph nodes; covered for initial staging of metastatic disease and all other indications).
2. Development of subsequent treatment strategy.
   (Medicare National Coverage Determinations Manual, Section 220.6, available at https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf)

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with breast cancer are listed below:

SNM, 2008

Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of FDG PET in oncology. J Nucl Med. 2008 Mar;49(3):480-508. Available at:
http://jnm.snmjournals.org/cgi/reprint/49/3/480.pdf
FDG PET should routinely be added to the conventional work-up in detecting metastatic or recurrent breast cancer in those patients clinically suspected of metastasis or recurrence.

National Comprehensive Cancer Network, 2013

NCCN Clinical Practice Guidelines in Oncology™
Thyroid Carcinoma
v.2.2013(http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf)

The consensus of the NCCN panel is that FDG PET/CT is most helpful in situations where standard imaging results are equivocal or suspicious. However, limited studies support a potential role for FDG PET/CT to detect regional nodal involvement as well as distant metastases in locally advanced breast cancer including T3N1M0 disease. The NCCN panel suggests that bone scan may be omitted if FDG PET/CT is clearly positive

for bone metastases. Equivocal or suspicious sites identified by PET/CT scanning should be biopsied for confirmation whenever possible and the site of disease would impact the course of treatment.

1. The NCCN panel recommends *against* the use of PET or PET/CT scanning for staging of patients with clinical stage I, IIA, or IIB breast cancer. This recommendation against the use of PET is supported by the high false negative rate in detection of small (<1 cm) and/or low grade lesions, the low sensitivity for detection of axillary nodal metastases, the low prior probability of these patients having detectable metastatic disease, and the high rate of false positive scans.

2. For patients with clinical stage IIIA or IIIB breast cancer, additional staging studies (which may include CT chest +/- abdomen +/- pelvis, bone scan, abdominal MRI or FDG PET) could be considered. FDG PET/CT is this setting is considered "optional" (Category 2B). FDG PET/CT is considered most helpful in situations where standard imaging results are equivocal or suspicious. FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastasis in locally advanced breast cancer when used in addition to standard imaging studies. FDG PET can be considered at the same time as diagnostic CT.

3. For patients with Recurrent/Stage IV breast cancer, FDG PET/CT is considered optional (Category 2B). The routine use of PET or PET/CT scanning should generally be discouraged for the evaluation of metastatic disease except in situations where other staging studies are equivocal or suspicious. Even in those situations, biopsy of equivocal or suspicious sites is more likely to provide useful information. If FDG PET/CT clearly indicates bone metastases, bone scan or fluoride PET/CT may not be needed.

4.After lumpectomy or mastectomy and surgical axillary staging with > 4 positive axillary nodes: Consider imaging for systemic staging, including diagnostic CT or MRI, bone scan, and optional FDG PET/CT (Category 2B)

5. In follow-up or surveillance of patients with breast cancer, the use of PET or PET/CT scanning should generally be discouraged for the evaluation of metastatic disease except in those clinical situations where other staging studies are equivocal or suspicious. Even in these situations, biopsy of equivocal or suspicious sites is more likely to provide useful information.

American Society of Breast Surgeons

As of 2012, practice guidelines exist for breast ultrasound and MRI but there are no practice guidelines for PET or PET/CT at this time. (http://www.breastsurgeons.org)

PRACTICE GUIDELINE -- LUNG CANCER

Lung cancer is the leading cause of cancer death in the United States. An estimated 228,190 new cases (118,080 in men and 110,110 in women) of lung and bronchial cancer were projected to be diagnosed in 2013, and 159,480 deaths (87,260 in men, 72,270 in women) were estimated to occur due to this disease. Only about 15.6% of all lung cancer patients are alive 5 years or more after diagnosis. The primary risk factor for lung cancer is smoking tobacco, which accounts for more than 85-90% of all lung cancer-related deaths. (Excerpted from NCCN practice guidelines, as cited below.)

The applications of FDG PET and PET/CT in lung cancer include:

1. Characterization of an indeterminate pulmonary nodule which is at least 8-10 mm in diameter.
2. Initial staging in patients with non-small cell lung cancer and selected patients with small cell lung cancer.
3. Delineation of gross-tumor volume in patients receiving radiation therapy.

PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) for:

1. Characterization of solitary pulmonary nodules.
2. Development of initial treatment strategy and subsequent treatment strategy in patients with NSCLC.
   Development of initial treatment strategy and subsequent treatment strategy in patients with SCLC.

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with lung cancer are listed below.

SNM, 2008

Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008 Mar;49(3):480-508. http://jnm.snmjournals.org/cgi/reprint/49/3/480.pdf

1. FDG PET should routinely be obtained in the diagnostic work-up of patients with a solitary pulmonary nodule.
2. PET should routinely be added to the conventional work-up of patients with non small cell lung cancer.

National Comprehensive Cancer Network, 2013

NCCN Clinical Practice Guidelines in Oncology™
Non-Small Cell Lung Carcinoma v.2.2013
(http://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf)

1. Diagnosis: Nodule suspicious for lung cancer: FDG avidity on PET imaging: >8mm solid non-calcified nodule: Consider PET/CT
A positive PET result is defined as a SUV in the lung nodule greater than the mediastinal blood pool.
A positive PET scan finding can be caused by infection or inflammation, including absence of lung cancer with localized infection, presence of lung cancer with associated infection, and presence of lung cancer with related inflammation (nodal, parenchymal, pleural).
A false negative PET scan can be caused by a small nodule, low cellular density (nonsolid nodule or ground glass opacity (GGO)), or low tumor avidity for FDG (eg adenocarcinoma in situ, previously known as bronchoalveolar carcinoma, carcinoid tumor.
Patients with a suspicion of lung cancer after PET/CT require histologic confirmation before any nonsurgical therapy.

2. Initial staging: The NCCN panel believes that PET or PET/CT plays a role in the accurate staging of NSCLC of all stages. However, the panel cautions that positive PET scan findings need pathologic or other radiologic confirmation and, if PET scan is positive in the mediastinum, lymph node status needs pathologic confirmation.

3. Restaging after induction therapy is difficult to interpret, but CT +/- PET should be performed to exclude disease progression or interval developing of metastatic disease.

4. PET is not indicated for routine surveillance of NSCLC patients who are clinically felt to be NED.

5. Radiation treatment planning should be performed by IV contrast-enhanced CT scans obtained in the treatment position. PET/CT significantly improves targeting accuracy, especially for patients with significant atelectasis and when IV contrast is contraindicated. The ideal is to obtain PET/CT in the treatment position. PET/CT significantly improves targeting accuracy, especially for patients with significant atelectasis and when IV contrast is contraindicated.

NCCN Clinical Practice Guidelines in Oncology™
Small Cell Lung Carcinoma v.2.2013
(http://www.nccn.org/professionals/physician_gls/PDF/sclc.pdf)

1. Initial staging of small cell lung carcinoma and high grade/large cell neuroendocrine carcinoma: PET/CT is recommended in the initial evaluation / staging of patients with small cell lung cancer if limited stage is suspected. Pathologic confirmation is

recommended for lesions detected by PET/CT that would potentially alter stage (i.e., those which would "upstage" the patient and thus alter treatment planning).2. PET/CT has replaced bone scan in NCCN guidelines; bone scan is now only recommended if PET/CT is not available.

2. PET/CT is not recommended for routine follow-up after initial therapy.

3. PET/CT is suggested for radiation treatment planning purposes.

4. Low and intermediate grade neuroendocrine carcinomas (e.g., carcinoid tumor): PET scan is considered optional (staging). PET is undergoing evaluation in clinical trials and should only be considered as a supplement and not a replacement to other studies.

American College of Chest Physicians, 2007

Alberts WM. *Chest* 2007;132;1-19 Clinical Practice Guidelines (2nd Edition) Executive Summary: ACCP Evidence-Based Diagnosis and Management of Lung Cancer (http://journal.publications.chestnet.org/data/Journals/CHEST/22061/zcb10907000001.pdf)

Pulmonary Nodules

1. In patients with a low to moderate test probability of malignancy (5% - 60%) and an indeterminate SPN that measures at least 8-10 mm in diameter, FDG PET should be performed to characterize the nodule.
2. In patients with an SPN that has a high pretest probability of malignancy (>60%), or patients with a nodule that measures <8-10 mm in diameter, FDG PET should not be performed to characterize the nodule.
3. In surgical candidates with an indeterminate SPN that measures at least 8-10 mm in diameter, surgical diagnosis is preferred when the clinical probability of malignancy is moderate to high (> 60%), when the nodule is hypermetabolic by FDG PET imaging, and when the fully informed patient prefers undergoing definitive diagnostic procedure.

Non-small cell lung cancer

1. PET to evaluate for mediastinal and extrathoracic staging should be considered in patients with clinical 1A lung cancer being treated with curative intent.
2. Patients with clinical IB-IIIB lung cancer being treated with curative intent should undergo PET (where available) for mediastinal and extrathoracic staging.
3. Patients with abnormal clinical evaluations should undergo imaging for extrathoracic metastases. Site-specific symptoms warrant directed evaluation of that site with the most appropriate study (*e.g.*, head CT/MRI plus either whole body PET or bone scan plus abdominal CT).
4. Routine imaging for extrathoracic metastases (*e.g.*, head CT/MRI plus either whole-body PET or bone scan plus abdominal CT) should be performed in patients with clinical stage IIIA and IIIB disease (even if they have a negative clinical evaluation).

Special treatment issues

1. In patients with a Pancoast tumor being considered for curative resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) is recommended. Involvement of mediastinal nodes and/or metastatic disease represents a contraindication to resection.
2. In patients with a clinical T4N0-1M0 NSCLC being considered for curative resection, it is recommend that invasive mediastinal staging, and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) be undertaken.
3. In patients with two synchronous primary NSCLCs being considered for curative surgical resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended. Involvement of mediastinal nodes and/or metastatic disease represents a contraindication to resection.
4. In patients with an isolated brain metastasis from NSCLC being considered for curative resection of a stage I or II lung primary tumor, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended.
5. In patients with an isolated adrenal metastasis from NSCLC being considered for curative intent surgical resection, invasive mediastinal staging, and extrathoracic imaging (head CT/MRI plus either whole body PET or abdominal CT plus bone scan) are recommended.
6. In patients with a NSCLC invading the chest wall who are being considered for curative intent surgical resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended.

Bronchoalveolar cancer

For patients whose CT scans show ground-glass attenuation or pneumonic consolidation (suggesting BAC), PET scan results are often false negative, and therefore we recommend that a negative PET scan result be followed by additional diagnostic testing to exclude the presence of cancer.

Small cell lung cancer

PET scanning is not recommended in the routine staging of SCLC.

Surveillance

In lung cancer patients following curative intent therapy, use of blood tests, PET scanning, sputum cytology, tumor markers, and fluorescence bronchoscopy is not currently recommended for surveillance.

PRACTICE GUIDELINES -- ESOPHAGEAL CANCER

Upper gastrointestinal tract cancers originating in the esophagus, gastroesophageal junction, and stomach constitute a major health problem around the world. An estimated 39,590 new cases of and 26,200 deaths from upper GI cancers (esophagus and stomach) were projected to occur in the United States in 2013. In western Hemisphere countries, the most common site of esophageal cancer is in the lower third of the esophagus where it often involves the gastroesophageal junction. (Excerpted from NCCN practice guidelines, as cited below.)

The applications of FDG PET and PET/CT in esophageal cancer include:

1. Initial staging (primarily to assess resectability).
2. Restaging after neoadjuvant chemotherapy and/or radiation.
3. Assessment of treatment response following definitive chemoradiation.
4. Delineation of gross tumor volume in patients receiving radiation therapy.

PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in patients with esophageal cancer for:

1. Development of initial treatment strategy.
2. Development of subsequent treatment strategy.
   (Medicare National Coverage Determinations Manual, Section 220.6, available at https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf))

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with lung cancer are listed below:

SNM, 2008

Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008 Mar;49(3):480-508. http://jnm.snmjournals.org/cgi/reprint/49/3/480.pdf
PET should routinely be used as an additional tool for staging esophageal cancer. The panel found moderate evidence that the use of FDG PET will likely improve important health-care outcomes and concluded that the use of FDG PET is beneficial, mostly by avoiding futile surgeries.

National Comprehensive Cancer Network, 2013

NCCN Clinical Practice Guidelines in Oncology™
Esophageal Carcinoma v.1.2013
(http://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf)

1. Staging studies are utilized to select patients for surgery, to exclude metastatic disease, and to identify and quantify lymph node involvement. Clinical staging using endoscopic ultrasound (EUS), chest and abdomen CT scan (with oral and IV contrast) and, if no evidence of M1 disease on CT), PET/CT should be performed before surgery to assess resectability. PET/CT has been shown to improve lymph node staging and detection of

stage IV esophageal cancer. It was also shown to be independent predictor of overall survival in patients with non-metastatic esophageal cancer.

2. For patients receiving preoperative / neoadjuvant chemotherapy or radiation, PET/CT should be considered before surgery as it has been found to be useful in predicting treatment responses to such therapy (Category 2B). However, PET scans should not be used for the selection of patients to surgery following preoperative chemoradiation. If performed, PET/CT should at least 5-6 weeks after completion of preoperative therapy.

3. For patients receiving definitive chemoradiation therapy, PET/CT is indicated to assess treatment response (Category 2B), done at least 5-6 weeks following completion of treatment.

4. For radiation treatment planning, the gross tumor volume should include the primary tumor and involved regional lymph nodes as identified by imaging studies such as CT scan, barium swallow, EUS, and PET/CT scans.

PRACTICE GUIDELINES -- COLORECTAL CANCER

Colorectal cancer is the fourth most frequently diagnosed cancer and the second leading cause of cancer death in the United States. In 2013, an estimated 102,480 new cases of colon cancer and approximately 40,340 cases of rectal cancer occurred. During the same year, it is estimated that 50,830 people will have died from colon and rectal cancer combined. Despite these statistics, the incidence is decreasing and mortality from colorectal cancer has decreased ~35% since 1990, possibly because of earlier diagnosis through screening and better treatment modalities. (Excerpted from NCCN practice guidelines, as cited below.)

The applications of FDG PET and PET/CT in colorectal cancer include:

1. Preoperative evaluation of patients with potentially resectable metastatic disease.
2. Determining location of tumors when rising CEA level suggests recurrence.

PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in patients with colorectal cancer for:

1. Development of initial treatment strategy.
2. Development of subsequent treatment strategy.
   (Medicare National Coverage Determinations Manual, Section 220.6, available at https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf)

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with lung cancer are listed below:

SNM, 2008

Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008 Mar;49(3):480-508. http://jnm.snmjournals.org/cgi/reprint/49/3/480.pdf
1. FDG PET should be used routinely in addition to conventional imaging in the preoperative diagnostic work-up of patients with potentially resectable hepatic metastases from colorectal cancer. The panel found moderate evidence that the use of PET will likely improve important health-care outcomes and concluded that PET is beneficial, mostly by avoiding futile surgeries.

National Comprehensive Cancer Network, 2013

NCCN Clinical Practice Guidelines in Oncology™
Colon Cancerv.3.2013; Rectal Cancer
v.4.2013(http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf;
http://www.nccn.org/professionals/physician_gls/PDF/rectal.pdf)

1. In the initial staging of colorectal cancer that is felt to be non-metastatic / appropriate for resection, PET/CT does not supplant a contrast-enhanced diagnostic CT scan and is not routinely indicated. If abnormalities are seen on CT or MRI scan that are considered to be suspicious but inconclusive for metastases, then a PET/CT scan may be considered for further delineation of the abnormality if such delineation will change management. Patients with clearly unresectable metastatic disease should not have baseline PET/CT scans.

2. PET/CT should not be used to assess response to chemotherapy, because a PET/CT scan can become transiently negative following chemotherapy (e.g., in the presence of necrotic lesions) and false positive PET/CT results can occur in the presence of tissue inflammation following surgery or infection.

3. Routine use of PET/CT to monitor for disease recurrence (i.e., general surveillance) is not recommended. In patients with suspected or proven metastatic synchronous adenocarcinoma, PET/CT scan is recommended only in the scenario of potentially surgically curable M1 disease for the purpose of identifying unrecognized metastatic disease that would preclude the possibility of surgical management. In patients with documented metachronous metastases by CT, MRI and/or biopsy which is potentially resectable, PET/CT may be considered for the purpose of identifying unrecognized metastatic disease that would preclude the possibility of surgical management. Patients with clearly unresectable metastatic disease should not have baseline PET/CT scans.

4. In the setting of elevated CEA level, contrast-enhanced CT is typically the imaging modality of first choice but PET/CT may be considered, especially if CT fails to identify a site of disease to account for elevated CEA level.

PET PROS
PET Professional Resources and Outreach Source

PRACTICE GUIDELINES -- CERVICAL CANCER

In 2013, an estimated 12,340 new cases of cancer of the cervix will be diagnosed and approximately 4, 030 patients will die from their disease. Cervical cancer rates are decreasing among women in the United States, however, cervical cancer remains a major world health problem for women. It is the third most common cancer in women worldwide; 78% of cases occur in developing countries where cervical cancer is the second most frequent cause of cancer death in women. (Excerpted from NCCN practice guidelines, as cited below.)

The applications of FDG PET and PET/CT in cervical cancer include:

1. Initial treatment planning assistance, including determination of extrapelvic / systemic spread.
2. Detection of residual or recurrent disease following initial treatment which may be potentially resectable / curable.
3. Suggested for use in radiation treatment planning (to help define nodal volume of coverage)

FDG PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in patients with cervical cancer for:

1. Development of initial treatment strategy following initial diagnosis (**NOTE:** use of PET for initial diagnosis of cervical cancer is excluded from coverage).
2. Development of subsequent treatment strategy.
   (Medicare National Coverage Determinations Manual, Section 220.6, available at https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf)

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with cervical cancer are listed below:

National Comprehensive Cancer Network, 2013

NCCN Clinical Practice Guidelines in Oncology™
Cervical Cancer v.2.2013
(http://www.nccn.org/professionals/physician_gls/PDF/cervical.pdf)

1. Radiologic staging is optional for patients with stage IB1 or smaller tumors.

2. For patients with stage IB2 or greater tumors, radiologic imaging studies (including FDG PET/CT) are recommended. FDG PET/CT can be done to rule out extrapelvic disease prior to deciding on how to treat these patients.

3. If para-aortic lymph nodes are found positive during surgical staging, patients should undergo further screening with chest CT or combined FDG PET/CT scan.

4. Incidental findings of invasive cancer at simple hysterectomy, Stage IA1 with LVSI or Stage > IA2: CT or PET/CT scan is recommended.

5. For surveillance: A single PET/CT performed at 3-6 months after chemo-radiation for locally advanced cervical cancer can be used to identify early or asymptomatic persistence/recurrence. Other imaging studies (such as CXR, CT scan, MRI, and subsequent PET/CT) may also be used to assess or follow recurrence when clinically indicated but are not recommended for routine surveillance.

6. For radiation treatment planning: in patients who are not surgically staged, FDG PET imaging is useful to help define the nodal volume of coverage.

PRACTICE GUIDELINES -- MELANOMA

In 2013, an estimated 76,690 new cases of melanoma will be diagnosed and 9,480 patients were estimated to die of the disease in the United States.. The figures for new cases may represent a substantial underestimation because many superficial and in situ melanomas treated in the outpatient setting are not recorded. The incidence of melanoma continues to increase dramatically. Melanoma is increasing in men more rapidly than any other malignancy and is increasing in women more rapidly than any other malignancy except lung cancer. (Excerpted from NCCN practice guidelines as cited below.)

The applications of FDG PET and PET/CT in melanoma include the following:

1. Detection and localization of potential extranodal metastatic lesions in initial evaluation of patients with advanced stage disease.
2. Evaluation of the extent of metastatic disease burden in patients with recurrent disease following treatment.
3. Post-treatment screening for recurrent / metastatic disease in patients with advanced stage disease.

FDG PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in patients with melanoma for:

1. Development of initial treatment strategy (***EXCEPTION***: not covered for the initial staging of regional lymph nodes).
2. Development of subsequent treatment strategy.
   (Medicare National Coverage Determinations Manual, Section 220.6, available at https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf))

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with melanoma are listed below:

National Comprehensive Cancer Network, 2013
NCCN Clinical Practice Guidelines in Oncology™

Melanoma v.2.2013
(http://www.nccn.org/professionals/physician_gls/PDF/melanoma.pdf)

1. Initial staging of Stage 0 or Stage IA melanoma: routine imaging studies are not recommended in the absence of adverse features. In the presence of adverse features (>= 0.75 mm thick, Clark level IV, lymphovascular invasion, positive deep margins) imaging (CT, PET/CT, MRI) is indicated only to evaluate specific signs or symptoms.
2. Initial staging of Stage IB, IIA, IIB, IIC melanoma: routine imaging studies (CT, PET/CT, MRI) are not recommended and should only be performed to evaluate specific signs or symptoms.
3. Initial staging of Stage III melanoma: consider imaging (CXR, CT, PET/CT, MRI) for baseline staging and to evaluate specific signs or symptoms.
4. Initial staging of Stage IV melanoma: encourage CT C/A/P, brain MRI, and/or PET/CT for baseline imaging and to evaluate specific signs or symptoms.
5. Routine follow-up of Stage IA - IIA melanoma (NED): routine imaging to screen for asymptomatic recurrence / metastasis not recommended
6. Routine follow-up of Stage IIB - IV melanoma (NED): consider CXR, CT and/or PET/CT every 3-12 months to screen for recurrent / metastatic disease; routine imaging to screen for asymptomatic recurrence / metastasis is not recommended after 5 years.
7. Local, satellite, in-transit or nodal recurrence: tissue sampling preferred; consider CT, PET, and/or MRI for staging and to evaluate specific signs or symptoms.
8. Distant metastatic disease: tissue sampling preferred; encourage CT C/A/P, brain MRI, and/or PET/CT for baseline imaging and to evaluate specific signs or symptoms.
9. NCCN general comment: PET/CT can help to characterize lesions found to be indeterminate on CT scan and can image areas of the body not studied by routine body CT scans (e.g., arms and legs).

American Society of Plastic Surgeons, 2007

Evidence-based Clinical Practice Guideline: Treatment of Cutaneous Melanoma
(http://www.plasticsurgery.org/Documents/medical-professionals/health-policy/evidence-practice/Evidence-based-Clinical-Practice-Guideline-Treatment-of-Cutaneous-Melanoma.pdf)
Patients with advanced-stage disease who have abnormal findings on screening tests, patient history, or physical examination are ideal candidates for directed radiologic examinations, including a chest x-ray, abdominal CT scan, and PET scan to identify possible sites of metastasis.

PRACTICE GUIDELINES -- LYMPHOMA

In 2013, an estimated 79,030 new cases of lymphoma (Hodgkin: 9,290, Non-Hodgkin: 69,740) will be diagnosed and 20,200 patients (Hoidgkin: 1,180, Non-Hodgkin:19,020) were estimated to die of the disease in the United States. Non-Hodgkin's lymphomas (NHL) are a heterogeneous group of lymphoproliferative disorders originating in B-

lymphocytes (80-85% of cases), T-lymphocytes (15-20% of cases), or natural killer cells. NHL is the seventh leading site of new cancer cases among men and women, accounting for 4% of new cancer cases and 3% of cancer related deaths. Hodgkin's disease/lymphoma (HD/HL) is less common than NHL but is curable in at least 80% of patients. (Excerpted from NCCN practice guidelines as cited below.)

The applications of FDG PET and PET/CT in lymphoma include:

1. Routine pre-treatment staging of patients with HD and many NHL subtypes.
2. Routine restaging / assessment of treatment response after chemotherapy and/or radiation therapy.

PET and PET/CT are approved by the Centers for Medicare and Medicaid Services (CMS) in patients with lymphoma for:

1. Development of initial treatment strategy.
2. Development of subsequent treatment strategy.
   (Medicare National Coverage Determinations Manual, Section 220.6, available at https://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf))

Professional organizations with practice guidelines or recommendations that include PET or PET/CT in patients with lymphoma are listed below:

SNM, 2008

Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008 Mar;49(3):480-508. http://jnm.snmjournals.org/cgi/reprint/49/3/480.pdf

1. FDG PET should routinely be obtained in addition to the conventional work-up in the pretreatment staging of lymphoma. FDG PET is considered more valuable in Hodgkin's disease (HD) and early stage aggressive non-Hodgkin's lymphoma (NHL) and less useful in indolent NHL. Therefore, depending on clinical circumstances, physicians may decide to modify this recommendation.
2. FDG PET may be added to bone marrow biopsy for staging bone marrow infiltration in the staging of lymphoma.
3. FDG PET should routinely be added to the conventional work-up for restaging or detecting recurrence (of HD and NHL) in patients who were treated with curative intent. The greatest benefit is more accurate detection of the extent of disease, including better differentiation of necrotic or scar tissue from active disease in patients with a residual mass. However, if the FDG PET findings are positive, further confirmation by biopsy is mandatory.
4. The panel concluded against the use of FDG PET in the routine follow-up of asymptomatic patients with HD or NHL.

National Comprehensive Cancer Network, 2013

NCCN Clinical Practice Guidelines in Oncology™

Hodgkin Lymphoma v.1.2013 and Non-Hodgkin's Lymphoma v.1.2013 (http://www.nccn.org/professionals/physician_gls/PDF/hodgkins.pdf and http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf)

NHL:

a. CLL/SLL
   PET/CT is generally not useful in CLL/SLL but can assist in directing nodal biopsy if Richter's transformation is suspected.
b. Follicular lymphoma, grade 1-2.
   a. Initial staging: PET/CT scan considered "useful in selected cases".
   b. Restaging after completion of treatment: imaging should be performed whenever there are clinical indications.
   If PET/CT is used in follow-up, progressive disease should be histologically documented (e.g., biopsy) to rule out transformation
c. Non-gastric MALT lymphoma, marginal zone lymphoma (nodal, splenic),
   a. Initial staging: PET/CT scan considered "useful in selected cases".
d. Mantle cell lymphoma
   a. Initial staging: PET/CT scan considered "useful under certain circumstances".
e. Diffuse large B-cell lymphoma
   a. Initial staging: PET/CT scan considered "essential".
   b. Restaging after completion of treatment: repeat all positive studies.
   Biopsy of PET-positive sites is recommended before changing course of treatment.
   The optimum timing of PET/CT is unknown; however, waiting a minimum of 8 weeks to repeat PET/CT is suggested. False positives may occur due to post-treatment changes.
   c. PET/CT scan at early/interim restaging (following 2-4 cycles of chemotherapy) can lead to increased false positives and should be carefully considered in select cases.
f. Burkitt lymphoma
   a. Initial staging: PET/CT scan considered "useful in selected cases" because it is unlikely to alter therapy.
   Initiation therapy should not be delayed in order to obtain a PET/CT scan.
g. Lymphoblastic lymphoma
   a. Initial staging: PET/CT scan considered "useful in selected cases".
   Initiation therapy should not be delayed in order to obtain a PET/CT scan.
h. AIDS-related B-cell lymphoma
   Initial staging: PET/CT scan considered "essential".
i. Primary Cutaneous B-Cell Lymphoma
   a. Initial staging: PET/CT scan considered "useful in selected cases".
j. Peripheral T-cell Lymphoma

   a. Initial staging: Chest/Abdomen/Pelvis CT with contrast of diagnostic quality and/or PET/CT scan considered "essential".
   b. Interim restaging for ALCL and ALK+: repeat all positive studies. If PET/CT is positive, re-biopsy before changing the course of treatment.
   c. Restaging after completion of treatment: repeat all positive studies. If PET/CT is positive, re-biopsy before changing the course of treatment.

k. Mycosis Fungoides/Sezary Syndrome
   Initial staging: PET/CT scan considered "useful in selected cases".
l. Adult T-cell leukemia/lymphoma (ATLL)
   a. Initial staging: PET/CT scan considered "useful in selected cases".
   b. Restaging after completion of treatment: the use of PET or PET/CT has not been evaluated in response assessment of ATLL.
m. Extranodal NK/T-cell lymphoma, nasal type:
   a. Initial staging: PET is considered essential
   b. Post RT evaluation: repeat initial imaging of CT, MRI, or PET/CT scan. The role of PET is not well established post-RT evaluation
n. Post Transplant Lymphoproliferative Disorder
   Initial staging: PET/CT scan considered "useful in selected cases".
o. T-cell prolymphocytic leukemia
   Initial staging: PET/CT scan considered "useful in selected cases"
p. Hairy cell leukemia: No PET
q. For radiation therapy planning, incorporating PET enhances field determination
r. Revised response criteria for NHL have include PET

HD:

a. Initial staging: PET/CT scan is considered "essential" during initial staging. A separate diagnostic CT scan need not be performed if it was done as part of the integrated PET/CT scan.
b. Early / Interim Restaging: Recent studies have shown the prognostic value of early interim PET/CT scans (after 2-4 cycles of standard dose chemotherapy) in patients with advanced or extranodal disease. The significance of early interim PET/CT scans in patients with early stage disease is unclear for many clinical scenarios. All measures of response should be considered in the context of management decisions.
c. Restaging after completion of chemotherapy: PET/CT scan is recommended to assess treatment response and/or to characterize residual masses at the end of treatment.
   Reference to Deauville PET criteria
   Deauville 3 should have short interval follow-up including PET/CT.
d. Restaging after radiation therapy: PET/CT is recommended, typically 3 months following completion of radiation.

e. Surveillance: PET/CT should not be done routinely for surveillance due to risk for false positives. Management decisions should not be based on PET alone; clinical or pathological correlation is needed.
f. Radiation therapy planning is enhanced by PET and MRI. NCCN endorses International Harmonization revised response criteria (Cheson et al., J Clin Oncol 2007;25:579-86) for interpreting post-treatment PET images in HD.

International Harmonization Project in Lymphoma, 2008

Juweid ME, Stroobants S, Hoekstra OS, Mottaghy FM, Dietlein M, Guermazi A, Wiseman GA, Kostakoglu L, Schneidhauer K, Buck A, Naumann R, Spaepen K, Hicks RJ, Weber WA, Reske SN, Schwaiger M, Schwartz LH, Zijlstra JM, Siegel BA, Cheson BD. Subcommittee of International Harmonization Project in lymphoma. J Clin Oncol 2007;25:571-578

1. PET scanning after completion of therapy should be performed at least 3 weeks and preferably at 6-8 weeks, after chemotherapy or chemoimmunotherapy, and 8-12 weeks after radiation or chemoradiotherapy. The role of PET for response assessment of aggressive NHL subtypes other than diffuse large B cell lymphoma (DLBCL) and indolent and mantle-cell lymphomas, is less clear. Pretreatment PET is not obligatory for assessment of response after treatment of patients with HL, DLBCL, follicular lymphoma, or mantle-cell lymphoma because these lymphomas routinely are FDG-avid. In contrast, pretreatment PET is mandatory for variably FDG-avid lymphomas, if PET is used to assess their response to treatment.

2. PET or PET/CT scanning during treatment of patients with HL and aggressive NHL appears to be justified if the information provided by the scan clearly will be used to alter management.