

Part II: NCCN Practice Guidelines Narrative Summary PET and PET/CT

NCCN guidelines were reviewed on 3/25/2013 for utilization of ¹⁸F-fluorodeoxyglucose (FDG) PET and PET/CT (available at:

http://www.nccn.org/professionals/physician_gls/f_guidelines.asp). This narrative summary lists all of the practice guidelines, and describes the specific indications for PET and PET/CT. The NCCN terminology corresponds to the terminology used by CMS (i.e., diagnosis/staging = initial treatment strategy; restaging / treatment response / recurrence = subsequent treatment strategy; surveillance not recognized by CMS as an indication).

- 1. Acute Lymphocytic Leukemia (V.2.2012): No PET
- 2. Acute Myeloid Leukemia (v.2.2013): No PET
- 3. Anal cancer (v.2.2012)
 Initial staging of anal canal (not anal marginal): Consider PET/CT scan (staging).
- 4. Bladder cancer (v.1.2013): No PET.

Note: Bone scan recommended for staging if alkaline phosphatase elevated or symptoms, and in patients with metastatic disease.

5. Bone cancer (v.2.2013)

- a. Chondrosarcoma: No PET.
- b. Chordoma: consider PET scan and/or bone scan (staging)
- c. Ewing sarcoma: PET scan and/or bone scan (staging); consider PET scan or bone scan (restaging); consider PET scan or bone scan (surveillance).
- d. Osteosarcoma: PET scan and/or bone scan (staging); consider PET scan, consider bone scan (restaging); consider PET scan (category 2B) and/or bone scan, (surveillance).

6. Breast cancer (v.2.2013)

- a. Invasive breast cancer:
 - 1. Stage I, II or operable III: PET or PET/CT scanning not recommended
 - 2. Stage IIIA (T3, N1, M0) or IIIB: FDG PET/CT optional (Category 2B)



FDG PET/CT can be performed at the same time as diagnostic CT. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.

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 (staging)

If FDG PET/CT is performed and clearly indicates bone metastases, on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.

- 3. 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)
- 4. Recurrent/Stage IV: FDG PET/CT is considered optional (Category 2B) (staging and restaging). Same disclaimers as for Stage IIIA and B

b. Inflammatory breast cancer

1. Stage T4d, No-N3, M0: FDG PET/CT

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If FDG PET/CT is performed and clearly indicates bone metastases, on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.

7. Central Nervous System Cancers (v.1.2013)

- a. Anaplastic gliomas/Glioblasoma: Consider MR spectroscopy, MR perfusion, or brain PET to rule out radiation necrosis (recurrence).
- b. Metastatic lesions: Consider FDG PET if 2-3 or multiple lesions and no primary has been found (diagnosis).
- c. Primary CNS lymphoma: Consider body FDG-PET scan (Category 2B) (diagnosis).

Body PET scan may replace CT, bone marrow, and testicular ultrasound, but data for its use in Primary CNS lymphoma (PCNSL) is lacking.

For full primary CNS lymphoma staging guidelines, refer to Abrey LE, Batchelor TT, Ferreri AJM, et al. Report of an international workshop to standardize



- baseline evaluation and response criteria for primary CNS lymphoma. J Clin Oncol 2005;23:5034-5043.
- d. Patient diagnosed with cancer or patient with newly discovered abnormality suspicious for spinal metastasis: Systemic imaging (i.e. PET, MRI, CT, bone scan) (diagnosis).

8. Cervical Cancer (v.2.2013)

- a. Initial staging:
 - a. Imaging (optional for ≤IB1) including chest x-ray, CT or PET/CT scan, or MRI as indicated (staging).
 - b. Para-aortic lymph nodes positive by surgical staging: chest CT or PET/CT scan (staging).
 - c. Incidental findings of invasive cancer at simple hysterectomy, Stage IA1 with LVSI or Stage > IA2: CT or PET/CT scan
- b. Surveillance: Imaging (CXR, CT, PET, PET/CT, MRI) as indicated based on symptoms or examination findings suspicious for recurrence (recurrence, 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.
- c. For radiation treatment planning: in patients who are not surgically staged, FDG PET imaging is useful to help define the nodal volume of coverage.

9. Chronic Myelogenous Leukemia (v.4.2013): No PET.

10, 11. Colorectal Cancer

- a. Colon cancer (v.3.2013)
 - 1. Initial staging:
 - a. For colon cancer appropriate for resection: No PET. PET/CT is not routinely indicated and does not supplant contrasted-enhanced CT.
 - b. Suspected or proven metastatic or synchronous adenocarcinoma from large bowel (any T, any N, M1): PET/CT scan only if potentially curable M1 disease (staging).
 - 2. Recurrence:
 - a. Serial CEA elevation: consider x 2PET/CT scan (recurrence).
 - b. Documented metachronous metastases by CT, MRI, and/or biopsy: consider PET/CT scan (recurrence).
 - 3. Surveillance: No PET. PET scan is not routinely recommended.
 - 4. PET/CT should not be used to monitor progress of therapy.

b. Rectal cancer (v.4.2013)

1. Initial staging



a. For rectal cancer appropriate for resection: No PET. PET scan is not routinely indicated.

2. Recurrence:

- a. Serial CEA elevation: consider PET/CT scan x2 (recurrence).
- b. Documented metachronous metastases by CT, MRI, and/or biopsy: consider PET/CT scan (recurrence).
- 3. Surveillance: No PET. PET/CT scan is not routinely indicated.
- 4. PET/CT should not be used to monitor progress of therapy.

12. Esophageal Cancer (v.1.2013)

- a. Initial staging: PET/CT evaluation if no evidence of M1 disease (staging).
- b. Restaging: Medically fit with SCC or adenocarcinoma
 - a. Following neo-adjuvant chemo-radiation: PET/CT or PET (Category 2B), > 5-6 weeks after completion of preoperative therapy. (restaging).
 - b. Patients receiving definitive chemo-radiation: PET/CT or PET (Category 2B), > 5-6 weeks after completion of preoperative therapy (restaging).
- c. Radiation therapy planning: General radiation information: Imaging studies including PET or PET/CT when available should be reviewed. This will allow an informed determination of treatment volumes and fields borders prior to simulation.

13. Gastric Cancer (v.1.2013)

a. Initial staging: PET/CT evaluation if no evidence of M1disease (staging). b. Restaging: Medically fit/ unresectable or medically unfit patients following primary treatment: PET/CT scan as clinically indicated (restaging).

14. Head and Neck Cancers (v.1.2012)

- a. Occult primary: PET/CT scan as indicated (before exam under anesthesia)(diagnosis).
- b. Initial staging of cancer of the oral cavity, oropharynx, hypopharynx, glottic larynx, and supraglottic larynx: Consider PET/CT for stage III-IV disease (staging).
- c. Initial staging of mucosal melanoma: Consider PET/CT scan to rule out metastatic disease (staging).
- d. 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) (staging).
- e. 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 (restaging).



15. Hepatobiliary (Hepatocellular, Gallbladder, Cholangiocarcinoma) Cancers (v.2.2012):

PET/CT is not adequate for staging, staging or surveillance of hepatocellular carcinoma.

16. Hodgkin Disease/Lymphoma (v.1.2013)

- a. Initial staging: PET/CT scan is considered "essential" during initial workup. A separate diagnostic CT scan need not be performed if it was done as part of the integrated PET/CT scan (staging).
- 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 (restaging).
- 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 (treatment response, restaging).

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 (treatment response, restaging).
- 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.

17. Kidney Cancer (v.1.2013): No PET

Initial staging: Bone scan if clinically indicated.

18. Malignant Pleural Mesothelioma (v.1.2013)

a. Initial staging: PET/CT should be performed before pleurodesis (staging).

19. Melanoma (v.2.2013)

- a. Initial staging:
 - 1. Stage 0 or IA with adverse features: Imaging only to evaluate specific signs or symptoms (CT, PET/CT, MRI) (staging).
 - 2. Stage IB, Stage II: Imaging (CT, PET/CT, MRI) only to evaluate specific signs or symptoms (staging).
 - 3. Stage III: Consider baseline imaging (CT, PET/CT, MRI) for staging and to evaluate specific signs or symptoms (staging).
 - 4. Stage IV: Recommend chest and abdominal/pelvic CT, MRI brain, and/or PET/CT for baseline imaging and to evaluate specific signs and symptoms (staging).



b. Restaging:

- a. Stage IA IIA (NED): routine imaging to screen for asymptomatic recurrence / metastasis is not recommended.
- b. Stage IIB to IV (NED): consider chest X-ray, CT and/or PET/CT every 3-12 months to screen for recurrent/metastatic disease (Category 2B); routine imaging to screen for asymptomatic recurrence/metastasis is not recommended after 5 years (recurrence).
- c. Local, satellite in-transit or nodal recurrence: Recommend baseline imaging for staging and to evaluate specific signs or symptoms (Category 2B) (CT, PET/CT, MRI) (recurrence, restaging).
- d. Distant metastatic disease: Recommend chest/abdominal/pelvic CT, MRI brain and/or PET/CT for baseline imaging and to evaluate specific signs and symptoms (recurrence, restaging).

20, 21, 22. Multiple Myeloma/Other Plasma Cell Neoplasms (v.2.2013)

a. Multiple Myeloma

Initial staging: PET/CT scan (staging).

Follow-up/Surveillance:

- 1. Solitary osseous and solitary extraosseous: MRI and/or CT and/or PET/CT as clinically indicated (surveillance).
- 2. Smoldering (asymptomatic and active (symptomatic): PET/CT scan as clinically indicated (surveillance).
- 3. Active (symptomatic) myeloma: response after primary therapy: PET/CT scan as clinically indicated (restaging, surveillance).
- b. Systemic Light Chain Amyloidosis (v. 1.2013): No PET
- Waldenstrom Macroglobulinemia/Lymphoplasmatic Lymphoma (v.2.2013): No PET

23. Myelodysplastic Syndromes (v.2.2013): No PET.

24. Neuroendocrine Tumors (v.1.2012)

- a. Carcinoid Tumors: Octreoscan and PET not recommended for routine surveillance.
- b. Neuroendocrine, unknown primary: Consider FDG PET scan in poorly differentiated tumors only (diagnosis).

25. Non-Hodgkin's Lymphomas (v.1.2013)

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 (staging).

- 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 (restaging, treatment response). If PET/CT is used in follow-up, progressive disease should be histologically documented (e.g., biopsy) to rule out transformation (restaging).
- c. Non-gastric MALT lymphoma, marginal zone lymphoma (nodal, splenic),
 - a. Initial staging: PET/CT scan considered "useful in selected cases" (staging).
- d. Mantle cell lymphoma
 - a. Initial staging: PET/CT scan considered "useful under certain circumstances" (staging).
- e. Diffuse large B-cell lymphoma
 - a. Initial staging: PET/CT scan considered "essential" (staging)
 - b. Restaging after completion of treatment: repeat all positive studies. (restaging, treatment response).
 - 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 (restaging, treatment response).
- f. Burkitt lymphoma
 - a. Initial staging: PET/CT scan considered "useful in selected cases" because it is unlikely to alter therapy (staging)
 - 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" (staging)
 - 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" (staging)
- i. Primary Cutaneous B-Cell Lymphoma
 - a. Initial staging: PET/CT scan considered "useful in selected cases" (staging).
- j. Peripheral T-cell Lymphoma
 - a. Initial staging: Chest/Abdomen/Pelvis CT with contrast of diagnostic quality and/or PET/CT scan considered "essential" (staging).
 - b. Interim restaging for ALCL and ALK+: repeat all positive studies. If PET/CT is positive, re-biopsy before changing the course of treatment (restaging, treatment response).



- c. Restaging after completion of treatment: repeat all positive studies. If PET/CT is positive, re-biopsy before changing the course of treatment (restaging, treatment response).
- k. Mycosis Fungoides/Sezary Syndrome

Initial staging: PET/CT scan considered "useful in selected cases" (staging)

- l. Adult T-cell leukemia/lymphoma (ATLL)
 - a. Initial staging: PET/CT scan considered "useful in selected cases" (staging).
 - 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" (staging).

o. T-cell prolymphocytic leukemia

Initial staging: PET/CT scan considered "useful in selected cases" (staging)

- 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

26, 27, 28. Non-melanoma Skin Cancers (v.1-2.2012)

- a. Basal and squamous cell skin cancers: No PET.
- b. Dermatofibrosarcoma protuberans: No PET.
- c. Merkel cell carcinoma.
 - 1. Initial staging: Imaging (CT, MR, or PET) may be useful to identify and quantify regional and distant metastases. Imaging may also be useful to evaluate for the possibility of a skin metastasis from a noncutaneous primary neuroendocrine carcinoma (eg, small cell lung cancer), especially in cases where CK-20 is negative (diagnosis, staging).
 - 2. Clinical node positive: Imaging (CT, MR, or PET) may be indicated to evaluate extent of lymph node and/or visceral organ involvement (staging).

29. Non-Small Cell Lung Cancer (v.2.2013)

a. 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.

- b. Initial staging: PET/CT scan indicated for all stages (staging). Positive PET/CT scan findings need pathologic or other radiologic confirmation. If PET/CT scan is positive in the mediastinum, lymph node status needs pathologic confirmation.
- c. Restaging after induction therapy is difficult to interpret, but CT +/- PET should be performed to exclude disease progression or interval developing of metastatic disease (restaging).
- d. PET is not indicated for routine surveillance of NSCLC patients who are clinically felt to be NED (surveillance).
- e. Radiation therapy 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.

30. Occult Primary (v.1.2013)

a. Diagnosis: Routine use of PET/CT is not recommended. PET/CT may be warranted in some situations.

31. Ovarian Cancer (v.1.2013)

- a. Staging: PET/CT may be indicated for indeterminate lesions if results will alter management.
- b. Stage I-IV complete response: chest/abdominal/pelvic CT or PET/CT or PET (category 2B for PET) as clinically indicated (monitoring/follow-up).
- c. Recurrence: Rising CA-125 with or without previous chemotherapy, or clinical relapse with or without previous chemotherapy: Imaging studies: chest/abdominal/pelvic CT, MRI, PET or PET/CT (category 2B) as clinically indicated (recurrence).

32. Pancreatic Adenocarcinoma (v.2.2012)

The role of PET/CT scan remains unclear. PET/CT scan may be considered after formal pancreatic CT protocol in "high risk" patients to detect extra-pancreatic metastases. It is not a substitute for high quality enhanced CT scan.

Radiation therapy treatment planning: The GTV and pathologic nodes are contoured with assistance from structural (CT/MRI) and functional imaging (PET).

33. Penile cancer (v.1.2013): No PET

The role of FDG PET/CT in penile cancer needs larger validation studies



34. Prostate Cancer (v2.2013): No PET.

FDG or fluoride PET is considered investigational and should not be ordered outside of a registry.

35. Small Cell Lung Cancer (v.2.2013)

- a. Initial staging of small cell lung carcinoma and high grade / large cell neuroendocrine carcinoma: PET/CT is recommended if limited stage is suspected (staging). PET/CT has replaced bone scan in NCCN guidelines; bone scan is now only recommended if PET/CT is not available.
 If extensive stage is established, further staging evaluation is optional. However brain MRI should be obtained in all patients.
 Pathologic confirmation is recommended for lesions detected by PET/CT that alter stage.
- b. PET/CT not recommended for routine follow-up after initial therapy (restaging).
- c. PET/CT is suggested for radiation treatment planning purposes.
- d. 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.

36. Soft Tissue Sarcoma (v.3.2012)

- Extremity/Trunk: Under certain circumstances, PET may be useful in prognostication, grading, and determining response to therapy (diagnosis, staging, treatment response).
- b. Retroperitoneal/Abdominal: No PET.
- c. Gastrointestinal Stromal Tumor (GIST):
 - 1. Marginally resectable or resectable with risk of considerable morbidity: Consider PET (staging); and consider PET after 2-4 weeks of imatinib mesylate (treatment response).
 - 2. Definitely unresectable or metastatic disease: Consider baseline PET, if using PET during follow-up (staging); Assess therapeutic effect of imatinib mesylate within 3 months using CT. Progression may be determined by CT or MRI with clinical interpretation. May be useful to clarify if CT or MRI are ambiguous (treatment response).
 - 3. Progression: Increase imatinib dose or change to sunitinib; reassess therapeutic response with CT. Progression may be determined by CT or MRI with clinical interpretation. May be useful to clarify if CT or MRI are ambiguous (treatment response).
- d. Desmoid Tumors: No PET.
- e. Rhabdomyosarcoma:
 - PET scan may be useful for initial staging because of the possibility of nodal metastases and the appearance of unusual sites of initial metastases in adult patients.



37. Testicular Cancer (v.1.2012)

- a. Seminoma
 - 1. Stage IIB, IIC, III after orchiectomy and primary treatment with chemotherapy residual mass > 3 cm and normal tumor markers: PET scan approximately 6 weeks post-chemotherapy (restaging); if PET scan negative, follow-up PET scan as clinically indicated (recurrence).
 - 2. Stage IIB, IIC, III after orchiectomy and primary treatment with chemotherapy no residual mass or residual mass < 3 cm and normal tumor markers: follow-up PET scan as clinically indicated (recurrence).
- b. Non-seminoma: No PET (see note)
 Note: PET is not clinically indicated for non-seminoma. There is limited predictive value for PET scan for residual masses.

38. Thymic Malignancies (v.2.2013)

a. Initial evaluation of a mediastinal mass: FDG PET/CT scan optional (diagnosis, staging).

39. Thyroid Carcinoma (v.1.2013)

- a. 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) (recurrence).
- 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) (recurrence).
- c. 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) (recurrence).
- d. Anaplastic Carcinoma: Consider FDG PET +/- CT scan (staging).

40. Uterine Neoplasms (v.1.2013)

- a. Endometrial Carcinoma: No PET.
- b. Uterine Sarcoma:
 - a. Initial staging, known or suspected extrauterine disease: MRI or PET/CT or CT based on symptoms or clinical suspicion of metastases.
 - b. Surveillance: Other imaging (MRI/PET) as clinically indicated.