

NCCN Practice Guidelines **Narrative Summary of Indications for FDG PET and PET/CT**

NCCN guidelines were reviewed on 2/14/2016 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 describes the specific indications for PET and PET/CT within these NCCN guidelines. Terminology used in this document is intended to correspond to 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 (v2.2015):** PET not recognized in guideline
2. **Acute Myeloid Leukemia (v1.2015):** PET not recognized in guideline
3. **Anal Carcinoma (v1.2016):**
 - Initial Treatment Strategy: consider PET/CT for initial staging of anal or anal marginal squamous cell carcinoma (but PET/CT alone does not replace diagnostic CT)
 - PET/CT suggested for radiation treatment planning
4. **Bladder cancer (v2.2015):** PET not recognized in guideline
Note: Bone scan recommended for staging if alkaline phosphatase elevated or if osseous symptoms, and in patients with metastatic disease
5. **Primary Bone cancer (v2.2016)**
 - a. Chondrosarcoma: PET not recognized in guideline
 - b. Chordoma: consider PET scan or bone scan (if PET negative) for staging
 - c. Ewing sarcoma: PET scan and/or bone scan for staging; consider PET scan or bone scan for restaging after chemotherapy; consider PET scan or bone scan for surveillance.
 - d. Osteosarcoma: PET scan and/or bone scan for staging; consider PET scan or bone scan for restaging after chemotherapy; consider PET and/or bone scan for surveillance.
6. **Breast cancer (v1.2016)**
 - Noninvasive Breast Cancer (DCIS/LCIS): PET not recommended
 - Invasive breast cancer:
 - Stage I, II or operable III: PET not recommended
 - Stage IIIA (T3, N1, M0) or IIIB: FDG PET/CT optional (Category 2B) for initial staging.
 - 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).
 - Recurrent or Stage IV: FDG PET/CT optional (Category 2B) for staging and restaging.
 - Inflammatory breast cancer
 - Stage T4d, No-N3, M0: FDG PET/CT recommended (Category 2B)

General Notes:

- 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.

- NCCN endorses use of NaF PET/CT as an alternative to conventional bone scan. 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 (v1.2015)

- Anaplastic gliomas/Glioblastoma: Consider MR spectroscopy, MR perfusion, or brain PET to differentiate viable tumor from radiation necrosis (recurrence).
- Metastatic lesions: Consider FDG PET or PET/CT if 2 or more brain lesions and no primary has been identified (diagnosis).
- Primary CNS lymphoma: Consider body FDG PET/CT scan for initial staging
- Metastatic Spine Tumors: if incidentally discovered in asymptomatic patient, systemic imaging (i.e., PET, CT, MRI, bone scan) recommended to identify primary (diagnosis/staging).

8. Cervical Cancer (v1.2016)

- Initial Treatment Strategy
 - Imaging (optional for \leq stage IB1) may include CXR, CT, PET/CT, or MRI as clinically indicated (staging).
 - If para-aortic lymph nodes positive by surgical staging: chest CT or PET/CT scan recommended (staging)
 - Incidental finding of invasive cancer at simple hysterectomy, Stage IA1 with LVSI or Stage \geq IA2: imaging (optional for \leq stage IB1) may include CXR, CT, PET/CT, or MRI as clinically indicated (staging).
- Subsequent Treatment Strategy: 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 not recommended for routine surveillance.
- PET/CT suggested for radiation treatment planning in patients who are not surgically staged (to help define nodal volume of coverage).

9. Chronic Myelogenous Leukemia (v1.2016): PET not recognized in guideline

10, 11. Colorectal Cancer

a. Colon cancer (v2.2016)

- Initial Treatment Strategy:
 - Resectable Disease: PET/CT not routinely indicated for staging and does not supplant contrast-enhanced CT. PET/CT should only be used to evaluate an equivocal finding on contrast-enhanced CT on in patients with strong contraindications to IV contrast.
 - Suspected or proven metastatic or synchronous adenocarcinoma from large bowel (any T, any N, M1): consider PET/CT scan if potentially curable M1 disease, to identify other potential sites of disease which might render patient unresectable for cure (staging).
- Subsequent Treatment Strategy:
 - Documented metachronous metastases by CT, MRI, and/or biopsy: consider PET/CT scan if potentially resectable, to identify other potential sites of disease which might render patient unresectable for cure (recurrence).
 - Serial CEA elevation: consider PET/CT scan if CT C/A/P and colonoscopy negative (recurrence)
- Surveillance: PET scan not routinely recommended.
- PET/CT should not be used to monitor progress of therapy.

b. Rectal cancer (v1.2016)

- Initial Treatment Strategy:
 - Resectable Disease: PET/CT not routinely indicated for staging and does not supplant contrasted-enhanced CT. PET/CT should only be used to evaluate an equivocal finding on contrast-enhanced CT on in patients with strong contraindications to IV contrast.
 - Suspected or proven metastatic or synchronous adenocarcinoma from large bowel (any T, any N, M1): consider PET/CT scan if potentially curable M1 disease, to identify other potential sites of disease which might render patient unresectable for cure (staging).
- Subsequent Treatment Strategy:
 - Documented metachronous metastases by CT, MRI, and/or biopsy: consider PET/CT scan if potentially resectable, to identify other potential sites of disease which might render patient unresectable for cure (recurrence).
 - Serial CEA elevation: consider PET/CT scan if CT C/A/P and colonoscopy negative (recurrence)
- Surveillance: PET scan not routinely recommended.
- PET/CT should not be used to monitor progress of therapy.

12. Esophageal Cancer (v3.2015)

- Initial Treatment Strategy: PET/CT recommended for staging if no evidence of M1 disease (staging).
- Subsequent Treatment Strategy: PET or PET/CT recommended to assess treatment response following both neoadjuvant and definitive chemoradiation (Category 2B), >5-6 weeks after completion of therapy (restaging).
- Surveillance: PET/CT or CT chest+abdomen to be considered for T1b or greater, with interval depending on stage (see chart in guideline)
- Radiation therapy planning: 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 (v3.2015)

- Initial Treatment Strategy: PET/CT recommended for staging if no evidence of M1 disease (staging).
- Subsequent Treatment Strategy: PET/CT as clinically indicated for restaging of unresectable or medically unfit patients following primary treatment.
- Radiation therapy planning: 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.

14. Head and Neck Cancers (v1.2015)

- Initial Treatment Strategy:
 - Occult primary: PET/CT scan as indicated (before exam under anesthesia) (diagnosis).
 - Cancers of oral cavity, oropharynx, hypopharynx, glottic larynx, supraglottic larynx, ethmoid and maxillary sinuses: consider PET/CT for initial staging of clinically suspected stage III-IV disease.
 - Mucosal melanoma: consider PET/CT scan for initial staging.
 - Cancer of nasopharynx: imaging for distant metastases (chest, liver, bone) for WHO class 2-3/N2-3 disease (may include PET scan and/or CT).
- Subsequent Treatment Strategy: post-treatment evaluation of cancers of the head and neck (minimum 12 weeks after completion of therapy) - PET/CT (suggest full dose CT with IV contrast) recommended; if PET/CT is negative for suspicion of persistent cancer, further cross sectional imaging is optional (restaging).

15. Hepatobiliary (Hepatocellular, Gallbladder, Cholangiocarcinoma) Cancers (v1.2016):

- HCC: PET/CT is not adequate for diagnosis of HCC, but could be considered for evaluation of metastatic disease.
- Gallbladder CA and Cholangiocarcinoma: PET/CT not routinely recommended, but emerging evidence suggests that it may be useful for detection of regional nodal metastases and distant metastatic disease in patients with otherwise potentially resectable disease (i.e., detection of disease which would render patient unresectable).

16. Hodgkin Disease/Lymphoma (v2.2015)

- Initial Treatment Strategy: PET/CT scan is considered "essential" during initial workup. A separate diagnostic (contrast-enhanced) CT scan need not be performed if it was done as part of the integrated PET/CT scan (staging).
- Subsequent Treatment Strategy:
 - Early / Interim Restaging: recent studies have confirmed 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).
 - Restaging after radiation therapy: PET/CT is recommended, typically 3 months following completion of radiation (treatment response, restaging).
 - 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.
 - Radiation therapy planning is enhanced by PET and MRI.

17. Kidney Cancer (v2.2016): PET not recognized in guideline

18. Malignant Pleural Mesothelioma (v1.2016)

- Initial Treatment Strategy: PET/CT may be considered for staging in clinical stage I-III disease and epithelial or mixed histology to evaluate for distant metastasis prior to surgery; PET/CT should be performed before pleurodesis.
- PET/CT may be considered for radiation treatment planning.

19. Melanoma (v2.2016)

- Initial Treatment Strategy:
 - Stage 0 to II: Imaging only to evaluate specific signs or symptoms (CT, PET/CT, MRI) (staging)
 - Stage III: Consider baseline imaging (CT, PET/CT, MRI) for staging and to evaluate specific signs or symptoms (staging).
 - 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).
- Subsequent Treatment Strategy:
 - Stage IA - IIA (NED): routine imaging to screen for asymptomatic recurrent / metastatic disease is not recommended.
 - 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).
 - 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).

- 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 (v3.2016)

a. Multiple Myeloma

- Initial Treatment Strategy: Whole body MRI or PET/CT recommended during initial diagnostic workup to discern active from smoldering myeloma if skeletal survey is negative.
- Subsequent Treatment Strategy
 - Solitary osseous and extraosseous plasmacytoma: MRI or CT or PET/CT as clinically indicated following radiation and/or surgical treatment (restaging).
 - Smoldering and active / symptomatic myeloma: PET/CT scan as clinically indicated to assess treatment response (restaging).

b. Systemic Light Chain Amyloidosis (v1.2016): PET not recognized in guideline

c. Waldenstrom Macroglobulinemia / Lymphoplasmatic Lymphoma (v.2.2016): PET not recognized in guideline

23. Myelodysplastic Syndromes (v1.2016): PET not recognized in guideline

24. Neuroendocrine Tumors (v1.2015)

a. Carcinoid Tumors and Neuroendocrine Tumors of Known Primary Site: PET not recommended for staging, restaging or routine surveillance.

b. Neuroendocrine Tumor of Unknown Primary: consider FDG PET scan in poorly differentiated tumors only (diagnosis).

c. Pheochromocytoma / Paraganglioma: chest/abdominal multiphasic CT, MRI or PET/CT in initial staging; consider CT, MRI or PET/CT in follow-up (restaging / surveillance).

25. Non-Hodgkin's Lymphomas (v1.2016)

- CLL/SLL: PET/CT generally not useful but can assist in directing nodal biopsy if Richer's transformation is suspected.
- Follicular Lymphoma, grades 1-2
 - CE CT C/A/P and/or PET/CT considered "essential" in initial workup (PET/CT essential if RT for stage I,II disease planned)
 - If indication for treatment, PET/CT can be used to guide treatment and/or detect transformation to high-grade disease
- Gastric and Non-Gastric MALT Lymphoma
 - CE CT C/A/P and/or PET/CT considered "essential" in initial workup (PET/CT essential if ISRT planned)
- Nodal Marginal Zone Lymphoma
Splenic Marginal Zone Lymphoma
Mantle Cell Lymphoma
AIDS-related B-Cell Lymphoma
Primary cutaneous B-cell and T-cell Lymphomas
Peripheral T-cell Lymphoma
Extranodal NK/T cell Lymphoma, Nasal Type
PTLD
Castleman Disease
 - CE CT C/A/P and/or PET/CT considered "essential" in initial workup
- Diffuse Large B-Cell Lymphoma
 - PET/CT +/- CT CAP considered "essential" in initial workup
 - Early / Interim Restaging: recommended for select stages / clinical scenarios
 - 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).
 - CE CT C/A/P and/or PET/CT considered "essential" in initial workup

- Burkitt Lymphoma
Lymphoblastic Lymphoma
Adult T-cell Leukemia/Lymphoma
- PET/CT scan considered "useful in selected cases"
- Mycosis Fungoides
- CE CT C/A/P or PET/CT considered "essential" in initial workup if \geq T2 or large cell transformed or folliculotropic MF or with palpable adenopathy or abnormal lab studies

26, 27, 28. Non-melanoma Skin Cancers (v.1-2.2016)

- Basal and squamous cell skin cancers: PET not recognized in guideline
- Dermatofibrosarcoma protuberans: PET not recognized in guideline
- Merkel cell carcinoma.
 - Initial Treatment Strategy:
 - General: Imaging (CT, MR, or PET) may be useful to identify and quantify regional and distant metastases during initial staging. 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.
 - Clinical node positive: Imaging (CT, MR, or PET) recommended to evaluate extent of lymph node and/or visceral organ involvement (staging).
 - Subsequent Treatment Strategy: Imaging (CT, MR, or PET) as clinically indicated for high risk patients to identify and quantify regional and distant metastases (restaging / surveillance).

29. Non-Small Cell Lung Cancer (v4.2016)

- Diagnosis: PET/CT for metabolic characterization of solid, non-calcified pulmonary nodule >8 mm in size
- Initial Treatment Strategy: PET/CT scan is indicated for initial staging in essentially all cases. 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.
- Subsequent Treatment Strategy:
 - Restaging after induction therapy is difficult to interpret, but CT +/- PET should be performed to exclude disease progression or interval developing of metastatic disease.
 - PET not indicated for routine surveillance of NSCLC patients clinically felt to be NED.
 - 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 (v2.2016)

- Routine use of PET/CT is not recommended, but PET/CT may be warranted in some situations, especially when considering local or regional therapy.

31. Ovarian Cancer (v2.2015)

- Initial Treatment Strategy: PET/CT may be indicated for indeterminate pelvic lesions if results will alter management.
- Subsequent Treatment Strategy
 - Stage I-IV complete response: CT C/A/P, PET/CT or PET (category 2B for PET) as clinically indicated (monitoring/follow-up).
 - Serially rising CA-125 with or without previous chemotherapy, or clinical relapse with or without previous chemotherapy: CT C/A/P, MRI, PET or PET/CT (category 2B) as clinically indicated (recurrence).

32. Pancreatic Adenocarcinoma (v2.2015)

The role of PET/CT (without iodinated IV contrast) scan remains unclear. Diagnostic CT or MRI with IV contrast in conjunction with functional PET imaging can be used per institutional preference. 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, contrast 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 (v1.2016):Initial Treatment Strategy: If palpable inguinal lymph nodes, imaging is recommended (abdominopelvic CT or MRI and chest imaging, or consider PET/CT)

34. Prostate Cancer (v2.2016): No PET.

- ^{11}C choline PET can be considered in setting of biochemical failure following prostatectomy or radiation therapy.
- NaF PET can be used as alternative to $^{99\text{m}}\text{Tc}$ MDP/HDP for bone scan.
- In certain clinical settings the use of FDG PET/CT may provide useful information, but FDG PET/CT should not be used routinely since data on its utility in prostate cancer is limited.

35. Small Cell Lung Cancer (v1.2016)

- Initial Treatment Strategy: PET/CT is recommended for initial staging of small cell or combined small cell / non small cell lung carcinoma if limited stage is suspected. PET/CT is optional for staging of low and intermediate grade neuroendocrine carcinomas (e.g., carcinoid tumor); PET is undergoing evaluation in clinical trials and should only be considered as a supplement and not a replacement to other studies.
 - PET/CT has replaced bone scan in NCCN guidelines; bone scan is now only recommended if PET/CT is not available. If extensive stage disease 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.
- Subsequent Treatment Strategy:
 - PET/CT not recommended for routine follow-up after initial therapy (restaging).
 - PET/CT is suggested for radiation treatment planning.

36. Soft Tissue Sarcoma (v1.2016)

- Extremity/Trunk: Under certain circumstances, PET may be useful in staging, prognostication, grading, and determining response to therapy (diagnosis, staging, treatment response).
- 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.
- Retroperitoneal/Abdominal Sarcomas; Desmoid Tumors: No PET.
- 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).

37. Testicular Cancer (v1.2016)

- Seminoma
 - Subsequent Treatment Strategy:
 - Stage IIA, IIB, IIC, III after orchiectomy and primary treatment with chemotherapy: if CT shows residual mass > 3 cm and normal tumor markers, PET scan recommended

approximately 6 weeks post-chemotherapy (restaging); if PET scan negative, follow-up PET scan as clinically indicated (recurrence).

- Stage IIB, IIC, III after orchiectomy and primary treatment with chemotherapy: if CT shows no residual mass or residual mass < 3 cm and normal tumor markers, follow-up PET scan as clinically indicated (recurrence).

- Non-seminoma: PET is not clinically indicated for non-seminoma as there is limited predictive value for PET scan for residual masses.

38. Thymic Neoplasia (v1.2016)

- Initial Treatment Strategy: PET/CT optional for metabolic characterization / staging of a mediastinal mass.

39. Thyroid Carcinoma (v2.2015)

- Papillary, Follicular and Hurthle Cell Carcinoma: consider non-radioiodine imaging (e.g. neck ultrasound, neck CT, chest CT, FDG PET/CT) if stimulated Tg > 2-5 ng/mL and I-131 imaging negative.
- Anaplastic Carcinoma: FDG PET/CT scan recommended for initial staging and assessment of treatment response 3-6 months after initial therapy.

40. Uterine Neoplasms (v2.2016)

- Endometrial Carcinoma: PET for initial staging as clinically indicated if extrauterine disease is suspected.
- Uterine Sarcoma:
 - Initial Treatment Strategy: CT C/A/P or MRI or PET/CT recommended for initial staging.
 - Subsequent Treatment Strategy: consider MRI or PET in surveillance as clinically indicated

41. Vulvar Squamous Cell Carcinoma (v1.2016)

- Initial Treatment Strategy: Imaging (CT/PET/MRI) as needed for delineating extent of tumor or for treatment planning.
- Subsequent Treatment Strategy: Imaging (CXR, CT, PET, PET/CT, MRI) as indicated based on symptoms or examination findings suspicious for recurrence.