Clinical Policy Bulletin:  
Positron Emission Tomography (PET)

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Policy

I. Cardiac Indications:

Aetna considers positron emission tomography (PET) medically necessary for the following cardiac indications:

A. Evaluation of Coronary Artery Disease:

PET scans using rubidium-82 (Rb-82) or N-13 ammonia done at rest or with pharmacological stress are considered medically necessary for non-invasive imaging of the perfusion of the heart for the diagnosis and management of members with known or suspected coronary artery disease, provided such scans meet either one of the two following criteria:

1. The PET scan is used in place of, but not in addition to, a single photon emission computed tomography (SPECT), in persons with conditions that may cause attenuation problems with SPECT (obesity (BMI greater than 40), large breasts, breast implants, mastectomy, chest wall deformity, pleural or pericardial effusion); or

2. The PET scan is used following an inconclusive SPECT scan (i.e., the results of the SPECT are equivocal, technically uninterpretable, or discordant with a member’s other clinical data).

In these cases, the PET scan must have been considered necessary in order to determine what medical or surgical intervention is required to treat the member.

B. Assessment of Myocardial Viability:

Fluorodeoxy-D-glucose (FDG)-PET scans are considered medically necessary for the determination of myocardial viability prior to re-
vascularization, either as a primary or initial diagnostic study or following an inconclusive SPECT. The greater specificity of PET makes a SPECT following an inconclusive PET not medically necessary.

The identification of members with partial loss of heart muscle movement or hibernating myocardium is important in selecting candidates with compromised ventricular function to determine appropriateness for re-vascularization. Diagnostic tests such as FDG-PET distinguish between dysfunctional but viable myocardial tissue and scar tissue in order to affect the management decisions in members with ischemic cardiomyopathy and left ventricular dysfunction.

II. Oncologic indications:

Aetna considers FDG-PET medically necessary for the following oncologic indications, when the following general and disease-specific criteria for diagnosis, staging, restaging and monitoring are met, and the FDG-PET scan is necessary to guide management:

- Anal cancer
- Appendiceal cancer
- Brain tumors
- Breast cancer
- Cervical cancer
- Chordoma
- Colorectal cancer
- Esophageal cancer
- Ewing sarcoma and osteosarcoma
- Fallopian tube cancer
- Gastric cancer
- Gastrointestinal stromal tumors
- Head and neck cancers (excluding cancers of the central nervous system)
- Lymphoma
- Melanoma
- Merkel cell carcinoma
- Mesothelioma
- Multiple myeloma and plasmacytomas
- Neuroendocrine tumors
- Non-small cell lung carcinoma
- Occult primary cancers
- Ovarian cancer
- Pancreatic cancer
- Paraneoplastic syndrome
- Penile cancer
- Primary peritoneal cancer
- Small cell lung carcinoma
- Small bowel adenocarcinoma
- Soft tissue sarcoma
- Solitary pulmonary nodules
- Testicular cancer
PET-CT Fusion: The fusion of PET and CT imaging into a single system (PET/CT fusion) is considered medically necessary for any oncologic indication where PET scanning is considered medically necessary. PET-CT fusion is considered experimental and investigational for cardiac and neurologic indications; a PET scan without CT is adequate to evaluate the brain and myocardium (NIA, 2005).

A. General Criteria

1. Diagnosis: The PET results may assist in avoiding an invasive diagnostic procedure, or the PET results may assist in determining the optimal anatomic location to perform an invasive diagnostic procedure. In general, for most solid tumors, a tissue diagnosis is made prior to the performance of PET scanning. PET scans following a tissue diagnosis are performed for the purpose of staging, not diagnosis. Therefore, the use of PET in the diagnosis of lymphoma, esophageal carcinoma, colorectal cancers, and melanoma is rarely considered medically necessary.

2. Staging: PET is considered medically necessary in situations in which clinical management of the member would differ depending on the stage of the cancer identified and either:

   - the stage of the cancer remains in doubt after completion of a standard diagnostic work-up, including conventional imaging (computed tomography, magnetic resonance imaging, or ultrasound); or

   - the use of PET would potentially replace one or more conventional imaging studies when it is expected that conventional study information is insufficient for the clinical management of the member.

3. Re-staging: PET is considered medically necessary for re-staging after completion of treatment for the purpose of detecting residual disease, for detecting suspected recurrence in persons with signs or symptoms of recurrence, or to determine the extent of recurrence. Use of PET is also considered medically necessary if it could potentially replace one or more conventional imaging studies when it is expected that conventional study information is insufficient for the clinical management of the member. PET for post-treatment surveillance is considered experimental and investigational, where surveillance is defined as use of PET beyond the completion of treatment, in the absence of signs or symptoms of cancer recurrence or progression, for the purpose of detecting recurrence or progression or predicting outcome.

4. Monitoring: PET for monitoring tumor response during the planned course of therapy is not considered medically necessary except...
for breast cancer. Re-staging occurs only after a course of treatment is completed.

B. Disease-Specific Criteria

1. Characterization of Solitary Pulmonary Nodules (SPNs):

FDG-PET is considered medically necessary for the characterization of newly discovered SPNs in persons without known malignancy when the general medical necessity criteria for oncologic indications (above) are met and the following conditions are met:

- A concurrent thoracic CT has been performed, which is necessary to ensure that the PET scan is properly coordinated with other diagnostic modalities; and
- A single indeterminate or possibly malignant lesion, more than 0.8 cm and not exceeding 4 cm in diameter, has been detected (usually by CT).

The primary purpose of the PET scan of SPN should be to determine the likelihood of malignancy in order to plan the management of the member.

Note: A biopsy is not considered medically necessary in the case of a negative PET scan for SPNs, because the member is presumed not to have a malignant lesion, based upon the PET scan results.

Note: In cases of serial evaluation of SPNs using both CT and regional PET chest scanning, such PET scans are not considered medically necessary if repeated within 90 days following a previous negative PET scan.

2. Non-Small Cell Lung Carcinoma (NSCLC):

FDG-PET scans are considered medically necessary for the diagnosis, staging and re-staging of non-small cell lung carcinoma (NSCLC) when the general medical necessity criteria for oncologic indications (II. A. listed above) are met.

3. Small Cell Lung Carcinoma (SCLC):

FDG-PET scans are considered medically necessary for staging of persons with SCLC that has been determined to be of limited-stage after standard staging evaluation (including CT of the chest and upper abdomen, bone scan, and brain imaging).

4. Mesothelioma

FDG-PET scans are considered medically necessary for diagnosis and staging of malignant pleural mesothelioma when the general medical necessity criteria for oncologic indications (II. A. listed
above) are met. According to National Comprehensive Cancer Network (NCCN) guidelines (2010), PET-CT scans may be useful in the pre-treatment evaluation of mesothelioma.

5. **Colorectal Cancer and Small Bowel Adenocarcinoma:**

FDG-PET scans are considered medically necessary for diagnosis*, staging, and re-staging of colorectal cancer and small bowel adenocarcinoma when the general medical necessity criteria for oncologic indications (II. A. listed above) are met. According to the Centers for Medicare & Medicaid Services (CMS), medical evidence supports the use of FDG-PET as a useful tool in determining the presence of hepatic/extra-hepatic metastases in the primary staging of colorectal carcinoma, prior to selecting the treatment regimen. Use of FDG-PET is also supported in evaluating recurrent colorectal cancer or small bowel adenocarcinoma where the member presents with clinical signs or symptoms of recurrence.

* **Note:** A diagnostic tissue sample is usually obtainable without PET localization. Therefore, PET for diagnosis of colorectal cancer is rarely considered medically necessary.

6. **Anal cancer**

FDG-PET scans are considered medically necessary for the diagnosis of anal canal carcinomas when medical necessity criteria for oncologic indications (II.A. listed above) are met. According to NCCN guidelines (2013), the routine use of a PET-CT scan for staging or treatment planning for anal cancer has not been validated.

7. **Lymphoma:**

FDG-PET scans are considered medically necessary for the diagnosis*, staging and re-staging of lymphoma when the general medical necessity criteria for oncologic indications (II. A. listed above) are met.

* **Note:** A diagnostic tissue sample is usually obtainable without PET localization. Therefore, PET for diagnosis of lymphoma is rarely considered medically necessary.

8. **Melanoma:**

FDG-PET scans are considered medically necessary for the diagnosis*, staging, and re-staging of melanoma when the general medical necessity criteria for oncologic indications (II. A. listed above) are met. FDG-PET is considered experimental and investigational and not medically necessary for use in evaluating regional nodes in persons with melanoma.
*Note: A diagnostic tissue sample is usually obtainable without PET localization. Therefore, PET for diagnosis of melanoma is rarely considered medically necessary.

9. **Esophageal Cancer**:

FDG-PET is considered medically necessary for the diagnosis*, staging and re-staging of esophageal carcinoma when general medical necessity criteria for oncologic indications (II. A. listed above) are met. Medical evidence is present to support the use of FDG-PET in pre-surgical staging of esophageal cancer.

*Note: A diagnostic tissue sample is usually obtainable without PET localization. Therefore, PET for diagnosis of esophageal cancer is rarely considered medically necessary.

10. **Gastric Cancer**:

FDG-PET is considered medically necessary for diagnosis*, staging and re-staging of gastric carcinoma when general medical necessity criteria for oncologic indications (II. A. listed above) are met. Consensus guidelines support the use of FDG-PET in the pre-surgical staging of gastric cancer.

*Note: A diagnostic tissue sample is usually obtainable without PET localization. Therefore, PET for diagnosis of gastric cancer is rarely considered medically necessary.

11. **Gastrointestinal Stromal Tumors**:

FDG-PET is considered medically necessary for diagnosis*, staging and re-staging of gastrointestinal stromal tumors (GIST) when general medical necessity criteria for oncologic indications (II. A. listed above) are met. Consensus guidelines support the use of FDG-PET in the pre-surgical staging of GIST.

*Note: A diagnostic tissue sample is usually obtainable without PET localization. Therefore, PET for diagnosis of GIST is rarely considered medically necessary.

12. **Head and Neck Cancers**:

FDG-PET scans are considered medically necessary for the diagnosis, staging, and re-staging of head and neck cancers when general medical necessity criteria for oncologic indications (II.A. listed above) are met. The head and neck cancers encompass a diverse set of malignancies of which the majority is squamous cell carcinomas. Persons with head and neck cancers may present with metastases to cervical lymph nodes but conventional forms of diagnostic imaging fail to identify the primary tumor. Persons with cancer of the head and neck are left with 2 options, either to have a neck dissection or to have radiation of both sides of the neck with random biopsies. PET scanning attempts to reveal the site of
primary tumor to prevent adverse effects of random biopsies or unneeded radiation.

13. **Thyroid Cancer:**

FDG-PET scans are considered medically necessary when general medical necessity criteria for oncologic indications (II. A. listed above) are met, for staging of thyroid cancer of follicular cell origin previously treated by thyroidectomy and radioiodine ablation with an elevated or rising serum thyroglobulin (Tg) greater than 10 ng/ml and negative I-131 whole body scintigraphy.

FDG-PET is considered not medically necessary for determining which members with metastatic thyroid cancer are at highest risk for death, because this information is for informational purposes only and has not been demonstrated to alter member management.

FDG-PET scans are considered experimental and investigational for other thyroid cancer indications, including:

- Use for the initial staging of post-surgical thyroid cancer of cell types that concentrate I-131 poorly; or

- Use of FDG-PET for re-staging of previously treated thyroid cancer of medullary cell origin in persons with an elevated serum calcitonin and negative standard imaging tests.

14. **Thymic malignancies**

FDG-PET scans are considered medically necessary for the diagnosis, staging, and re-staging of thymic malignancies (thymomas and thymic carcinomas) when the general medical necessity criteria for oncologic indications (II. A. listed above) are met.

15. **Breast Cancer:**

FDG-PET scans are considered medically necessary for members with breast cancer for the following indications, where general medical necessity criteria for oncologic indications (II. A. listed above) are met:

- Initial staging of members with stage III or higher when conventional imaging is equivocal; or

- Monitoring tumor response to treatment for persons with locally advanced and metastatic breast cancer when a change in therapy is contemplated; or

- Restaging of members with known metastases; or

- Evaluating suspected recurrence (new palpable lesions in axilla or adjacent area, rising tumor markers, changes in other imaging which are equivocal or suspicious).
FDG-PET is considered experimental and investigational for the initial diagnosis of breast cancer and for the staging of axillary lymph nodes.

Positron emission mammography is considered experimental and investigational.

16. **Cervical Cancer:**

FDG-PET scans are considered medically necessary for the diagnostic workup of cervical cancer, for detection of pre-treatment metastases (staging) in women who are newly diagnosed with cervical cancer and have negative conventional imaging (CT or MRI), and for restaging of cervical cancer when general medical necessity criteria for oncologic indications (II.A. listed above) are met.

17. **Ovarian Cancer, Fallopian Tube Cancer and Primary Peritoneal Cancer:**

FDG-PET scans are considered medically necessary for restaging (detecting recurrence) of previously treated women with a rising CA-125 level who have negative or equivocal conventional imaging (CT or MRI) when general medical necessity criteria for oncologic indications (II.A listed above) are met.

FDG-PET scans are considered experimental and investigational for diagnosis, staging, and monitoring of ovarian cancer, fallopian tube cancer and primary peritoneal cancer.

18. **Testicular Cancer:**

FDG-PET scans are considered medically necessary for restaging (detecting recurrence) of testicular cancer in men with previously treated disease who have a residual mass with normal or persistently elevated serum markers (e.g., alpha fetoprotein or serum chorionic gonadotropin) when general medical necessity criteria for oncologic indications (II.A. listed above) are met.

19. FDG-PET scans are considered experimental and investigational for diagnosis, staging and monitoring of testicular cancer.

20. **Multiple Myeloma and Plasmacytomas:**

FDG-PET scans are considered medically necessary for evaluating suspected plasmacytomas (staging) in persons with multiple myeloma and for re-staging of persons with solitary plasmacytomas.

21. **Ewing Sarcoma, Chordoma and Osteosarcoma:**
FDG-PET scans are considered medically necessary for the diagnosis, staging and re-staging of osteosarcoma, chordoma, and Ewing sarcoma family of tumors.

22. Soft Tissue Sarcoma:

FDG-PET scans are rarely medically necessary for soft tissue sarcomas. FDG-PET scans are considered medically necessary for staging prior to resection of an apparently solitary metastasis, or for grading unresectable lesions when the grade of the histopathological specimen is in doubt.

FDG-PET scans are considered experimental and investigational for re-staging of soft tissue sarcomas.

23. Neuroendocrine Tumors:

FDG-PET scans are considered medically necessary for the diagnosis, staging and re-staging of persons with pheochromocytoma/paragangliomas and other neuroendocrine tumors when general medical necessity criteria for oncologic indications (II.A. listed above) are met.

24. Pancreatic Tumors:

FDG-PET scans are considered medically necessary for diagnosis and staging of pancreatic tumors where imaging tests (CT or MRI) are equivocal. FDG-PET scans are considered experimental and investigational for restaging of pancreatic cancer.

25. Brain Cancer:

FDG-PET scans are considered medically necessary for diagnosis and staging, where lesions metastatic from the brain are identified but no primary is found, and for restaging, to distinguish recurrent tumor from radiation necrosis.

26. Occult Primary:

FDG-PET is considered medically necessary for staging in carcinomas of unknown primary site in tumors of indeterminate histology where the primary site can not be identified by endoscopy or other imaging studies (CT, MRI) and where loco-regional therapy for a single site of disease is being considered. FDG-PET scans are considered experimental and investigational for diagnosis or re-staging of carcinomas of unknown primary.

27. Paraneoplastic Syndromes:

FDG-PET is considered medically necessary for diagnosis and staging of persons suspected of having a paraneoplastic syndrome.
28. **Merkel Cell Carcinoma:**

FDG-PET is considered medically necessary for evaluating (i) the possibility of a skin metastasis from a non-cutaneous carcinoma (e.g., small cell carcinoma of the lung), especially in cases where CK20 is negative, (ii) to evaluate regional and distant metastases, and (iii) the extent of lymph node and/or visceral organ involvement.

29. **Penile Cancer:**

FDG-PET is considered medically necessary for evaluation of persons with penile cancer who have positive lymph nodes (PLNs) and an abnormal CT or MRI.

30. **Uterine Sarcoma**

FDG-PET is considered medically necessary for diagnosis, staging and restaging of persons with uterine sarcoma in persons with known or suspected extrauterine disease.

31. **FDG-PET in Place of $^{99m}$Tc Skeletal Scintigraphy:**

Due to an interruption in production, there is a temporary shortage of technetium 99-m ($^{99m}$Tc), which is used in nuclear medicine for skeletal scintigraphy (bone scans). During this shortage, Aetna will consider FDG-PET an acceptable alternative to bone scans for detecting skeletal abnormalities for medically necessary indications.

32. **NaF-18 PET**

Aetna considers NaF-18 PET experimental and investigational for identifying bone metastasis of cancer because of insufficient evidence.

33. **Carbon-11 labeled 5-HTP PET**

Aetna considers carbon-11 labeled 5-HTP PET experimental and investigational for carcinoid and all other indications because of insufficient evidence.

34. **Additional Experimental and Investigational Oncological Indications:**

Aetna considers PET scans experimental and investigational for the evaluation of adrenal carcinoma, bladder cancer, chondrosarcoma, clear cell carcinoma of the uterus, desmoid tumors/fibromatosis, endometrial cancer, extra-gonadal seminoma including mediastinal seminoma, gestational trophoblastic neoplasia, hemangioendothelioma, hepatobiliary cancer, hepatocellular carcinoma/hepatic sarcoma, hypercalcemia of
malignancy, kidney cancer, leukemia, lymphangiomatosis, malignant degeneration of neurofibromas, myeloid sarcoma, neuroblastoma, neurofibromatosis, Paget's disease (including extra-mammary Paget's disease), peri-ampullary cancer, pilarch tumor, placental cancer, pleomorphic adenoma, prostate cancer, schwannoma, serous papillary endometrial carcinoma, skin cancer, spindle cell sarcoma, uterine papillary mesothelioma; vulvar cancer, xanthogranuloma, Wilms tumor, or for other oncologic indications (e.g., treatment planning for atypical teratoid/rhabdoid tumor) not listed as medically necessary in this policy because of insufficient evidence of effectiveness. Aetna considers PET-probe guided surgical resection experimental and investigational for recurrent ovarian cancer and other indications because its effectiveness has not been established.

III. Neurologic Indications:

Aetna considers FDG-PET medically necessary only for pre-surgical evaluation for the purpose of localization of a focus of refractory seizure activity.

Aetna considers PET scans experimental and investigational for Alzheimer disease (including the use of florbetapir-PET and flutemetamol F18-PET for imaging beta-amyloid), dementia, Huntington disease, Parkinson's disease, or for other neurologic indications not listed as medically necessary in this policy because of insufficient evidence of its effectiveness.

IV. Other Indications:

FDG-PET is considered medically necessary for diagnosis, staging and restaging of Langerhans cell histiocytosis.

Aetna considers FDG-PET experimental and investigational for adrenoleukodystrophy, aortic/large-vessel vasculitis, chronic osteomyelitis, coccidioidomycosis (also known as valley fever, San Joaquin Valley fever, California valley fever, and desert fever), eosinophilia, Erdheim-Chester disease, fever of unknown origin, hepatic encephalopathy, infection of knee replacement prostheses, infection of hip arthroplasty, opsoclonus (opsillopsia) myoclonus syndrome, pigmented villonodular synovitis, pleural effusion, pulmonary Langerhans histiocytosis, multi-centric Castleman's disease, rheumatoid arthritis, Rosai-Dorfman disease, sarcoid/sarcoidosis, screening in Li-Fraumeni syndrome, splenomegaly, Takayasu's arteritis, and other indications not listed as medically necessary in this policy because of a lack of sufficient evidence of the effectiveness of FDG-PET for these indications.

V. PET scanning with a gamma camera is considered experimental and investigational for all indications because of insufficient evidence of its effectiveness.

VI. PET/MRI is considered experimental and investigational for all indications because of insufficient evidence of its effectiveness.
Note: PET scans for routine screening of asymptomatic members are not considered medically necessary, regardless of the number and severity of risk factors applicable to the member.

**Background**

Positron emission tomography (PET) also known as positron emission transverse tomography (PETT), or positron emission coincident imaging (PECI), is a non-invasive diagnostic imaging procedure that assesses the level of metabolic activity and perfusion in various organ systems of the human body. A positron camera (tomograph) is used to produce cross-sectional tomographic images, which are obtained from positron emitting radioactive tracer substances (radiopharmaceuticals) such as 2-[F-18] fluoro-d-glucose (FDG) that are administered intravenously to the member.

Although PET scans using the radioactive glucose analog FDG have proven to be a highly accurate imaging test for diagnosing and staging a variety of non-urologic cancer types, its role in the management of prostate malignancies is still being defined. The use of PET scanning in the diagnosis and staging of prostate cancer is hampered by the generally low metabolic activity of most prostate tumors and their metastases. It has shown promise for staging and re-staging persons with advanced-stage disease and aggressive tumors suspected by a high tumor grade and high prostate-specific antigen velocity. Further investigations are needed to ascertain the eventual place of PET scans in prostate cancer.

Vees et al (2007) evaluated the value of PET/computed tomography (CT) with either (18)F-choline and/or (11)C-acetate, of residual or recurrent tumor after radical prostatectomy (RP) in patients with a prostate-specific antigen (PSA) level of less than 1 ng/ml and referred for adjuvant or salvage radiotherapy. In all, 22 PET/CT studies were performed, 11 with (18)F-choline (group A) and 11 with (11)C-acetate (group B), in 20 consecutive patients (2 undergoing PET/CT scans with both tracers). The median (range) PSA level before PET/CT was 0.33 (0.08 to 0.76) ng/ml. Endorectal-coil magnetic resonance imaging (MRI) was used in 18 patients. A total of 19 patients were eligible for evaluation of biochemical response after salvage radiotherapy. There was abnormal local tracer uptake in 5 and 6 patients in group A and B, respectively. Except for a single positive obturator lymph node, there was no other site of metastasis. In the 2 patients evaluated with both tracers there was no pathological uptake. Endorectal MRI was locally positive in 15 of 18 patients; 12 of 19 responded with a marked decrease in PSA level (half or more from baseline) 6 months after salvage radiotherapy. The authors concluded that although (18)F-choline and (11)C-acetate PET/CT studies succeeded in detecting local residual or recurrent disease in about 50 % of the patients with PSA levels of less than 1 ng/ml after RP, these studies can not yet be recommended as a standard diagnostic tool for early relapse or suspicion of subclinical minimally persistent disease after surgery. Endorectal MRI might be more helpful, especially in patients with a low likelihood of distant metastases. Nevertheless, further research with (18)F-choline and/or (11)C-acetate PET with optimal spatial resolution might be needed for patients with a high risk of distant relapse after RP even at low PSA values.
Takahashi et al (2007) noted that 2-(18)F-fluoro-2-deoxy-D-glucose (FDG)-PET imaging in prostate cancer is challenging because glucose utilization in well-differentiated prostate cancer is often lower than in other tumor types. Nonetheless, FDG-PET has a high positive predictive value for untreated metastases in viscera, but not lymph nodes. A positive FDG-PET can provide useful information to aid the clinician's decision on future management in selected patients who have low PSA levels and visceral changes as a result of metastases. On the other hand, FDG-PET is limited in the identification of prostate tumors, as normal urinary excretion of radioisotope can mask pathological uptake. Moreover, there is an overlap in the degree of uptake between prostate cancer, benign prostatic hyperplasia and inflammation. The tracer choice is also important. (11)C-choline has the advantage of reduced urinary excretion, and thus (11)C-choline PET may provide more accurate information on the localization of main primary prostate cancer lesions than MRI or MR spectroscopy. (11)C-choline PET is sensitive and accurate in the pre-operative staging of pelvic lymph nodes in prostate cancer. A few studies are available but there were no PET or PET/CT studies with a large number of patients for tissue confirmation of prostate cancer; further investigations are required.

Greco et al (2008) stated that the patient population with a rising PSA post-therapy with no evidence of disease on standard imaging studies currently represents the second largest group of prostate cancer patients. Little information is still available regarding the specificity and sensitivity of PET tracers in the assessment of early biochemical recurrence. Ideally, PET imaging would allow one to accurately discriminate between local versus nodal versus distant relapse, thus enabling appropriate selection of patients for salvage local therapy. The vast majority of studies show a relatively poor yield of positive scans with PSA values less than 4 ng/ml. So far, no tracer has been shown to be able to detect local recurrence within the clinically useful 1 ng/ml PSA threshold, clearly limiting the use of PET imaging in the post-surgical setting. Preliminary evidence, however, suggested that 11C-choline PET may be useful in selecting out patients with early biochemical relapse (PSA less than 2 ng/ml) who have pelvic nodal oligometastasis potentially amenable to local treatment. The authors concluded that the role of PET imaging in prostate cancer is gradually evolving but still remains within the experimental realm. Well-conducted studies comparing the merits of different tracers are needed.

An assessment by the Blue Cross and Blue Shield Association Technology Evaluation Center on PET for breast cancer (2003) stated that FDG-PET for evaluating breast cancer does not meet its criteria for initial staging of axillary lymph nodes, for detection of loco-regional recurrence or distant metastasis/recurrence, or for evaluating response to treatment.

The Centers for Medicare & Medicaid Services (CMS) has released a decision memorandum on PET for suspected dementia. Although CMS has announced limited coverage of PET to distinguish Alzheimer's disease from fronto-temporal dementia when the distinction is uncertain and other criteria are met, the decision memorandum recognized that there is no available literature that directly evaluated the impact on patient outcomes of adding PET in patients with early dementia who have undergone standard evaluation who do not meet the criteria for Alzheimer disease due to variations in the onset, presentation, or clinical course (suggesting other neurodegenerative causes for the disorder such as fronto-temporal dementia). In
addition, CMS found no trials that examined the impact of PET in changing the management as a surrogate for evaluating PET impact on health outcomes in patients with this sort of difficult differential diagnosis. The assessment also recognized that there are no established cures for either Alzheimer disease or fronto-temporal dementia. A paucity of medications are available for Alzheimer's disease, which have a limited ability to decrease the rate of cognitive decline when administered early in the course of the disease. CMS coverage determination was primarily based on the value of PET in providing information useful in “non-medical decision-making.” Aetna, however, does not consider non-medical decision-making a medically necessary indication for testing. Because of a lack of adequate evidence that PET scanning alters clinical management of such persons such that clinical outcomes are improved, Aetna considers PET scanning for differentiating Alzheimer disease from fronto-temporal dementia experimental and investigational.

An assessment prepared for the California Technology Assessment Forum (CTAF) concluded that PET for Alzheimer's disease does not meet CTAF's criteria (Feldman, 2004). The assessment stated: “The critical question that remains unanswered by this and the other studies of PET in the evaluation of AD/dementia is: To what extent does PET improve diagnostic accuracy beyond what can be obtained with a thorough clinical evaluation? Given that the sensitivity of clinical criteria are reported to be about 80% to 90%, it is difficult for any diagnostic test to significantly improve diagnostic accuracy. And given the fact that treatment of the most common non-AD dementias (e.g., Dementia of Lewy Bodies or vascular dementias) with cholinesterase inhibitor drugs is not likely to be harmful and in fact may be beneficial to these patients, it may be that an empirical approach of ruling out reversible causes of dementia and treating all others with cholinesterase inhibitor drugs is appropriate and cost effective.”

The assessment noted that the greatest promise of PET in Alzheimer disease is likely to be in improving a clinician's ability to identify at-risk patients and to offer them treatment before they are significantly affected by Alzheimer disease. Few studies, however, have enrolled patients with mild symptoms or mild cognitive impairment so it is unclear what role PET is destined to play in identifying this subgroup of patients most likely to benefit from current and emerging therapies for Alzheimer's disease.

Clark et al (2011) examined if florbetapir F 18 PET imaging performed during life accurately predicts the presence of β-amyloid in the brain at autopsy. Prospective clinical evaluation conducted February 2009 through March 2010 of florbetapir-PET imaging performed on 35 patients from hospice, long-term care, and community health care facilities near the end of their lives (6 patients to establish the protocol and 29 to validate) compared with immunohistochemistry and silver stain measures of brain β-amyloid after their death used as the reference standard. PET images were also obtained in 74 young individuals (18 to 50 years) presumed free of brain amyloid to better understand the frequency of a false-positive interpretation of a florbetapir-PET image. Major outcome measures were correlation of florbetapir-PET image interpretation (based on the median of 3 nuclear medicine physicians’ ratings) and semi-automated quantification of cortical retention with post-mortem β-amyloid burden, neuritic amyloid plaque density, and neuropathological diagnosis of Alzheimer disease in the first 35 participants autopsied (out of 152 individuals enrolled in the PET pathological correlation study). Florbetapir-PET imaging was performed a mean of 99 days (range of 1 to 377 days) before death for the 29 individuals in the primary analysis cohort. Fifteen of the 29 individuals (51.7%) met pathological criteria for Alzheimer disease.
disease. Both visual interpretation of the florbetapir-PET images and mean quantitative estimates of cortical uptake were correlated with presence and quantity of β-amyloid pathology at autopsy as measured by immunohistochemistry (Bonferroni p, 0.78 [95 % confidence interval, 0.58 to 0.89]; p < 0.001) and silver stain neuritic plaque score (Bonferroni p, 0.71 [95 % CI: 0.47 to 0.86]; p < 0.001). Florbetapir-PET images and postmortem results rated as positive or negative for β-amyloid agreed in 96 % of the 29 individuals in the primary analysis cohort. The florbetapir-PET image was rated as amyloid negative in the 74 younger individuals in the non-autopsy cohort. The authors concluded that florbetapir-PET imaging was correlated with the presence and density of β-amyloid. These data provided evidence that a molecular imaging procedure can identify β-amyloid pathology in the brains of individuals during life. Moreover, they stated that additional studies are needed to understand the appropriate use of florbetapir-PET imaging in the clinical diagnosis of Alzheimer disease and for the prediction of progression to dementia.

In an editorial that accompanied the afore-mentioned study, Breteler (2011) stated that "[o]nly through future studies using rigorous study design can the role of either florbetapir-PET imaging or plasma β-amyloid 42/40 in diagnosis or prediction of AD be determined".

A proposed decision memo for FDG-PET for infection and inflammation from the CMS (Phurrough et al, 2007) stated that there is insufficient evidence to conclude that FDG-PET for chronic osteomyelitis, infection of hip arthroplasty and fever of unknown origin are reasonable and necessary. Thus, CMS proposed to continue national non-coverage for these indications.

Positron emission tomography has limited sensitivity for mesothelioma. Furthermore, current guidelines have not incorporated PET scanning into the management of persons with mesothelioma. The available literature on the effect of PET on clinical outcomes of malignant mesothelioma are limited. In a small feasibility study, Francis and colleagues (2007) evaluated the role of serial (18)F-FDG PET in the assessment of response to chemotherapy in patients with mesothelioma. Patients were prospectively recruited and underwent both (18)F-FDG PET and conventional radiological response assessment before and after 1 cycle of chemotherapy. Quantitative volume-based (18)F-FDG PET analysis was performed to obtain the total glycolytic volume (TGV) of the tumor. Survival outcomes were measured. A total of 23 patients were suitable for both radiological and (18)F-FDG PET analysis, of whom 20 had CT measurable disease. After 1 cycle of chemotherapy, 7 patients attained a partial response and 13 had stable disease on CT assessment by modified RECIST (Response Evaluation Criteria in Solid Tumors) criteria. In the 7 patients with radiological partial response, the median TGV on quantitative PET analysis fell to 30 % of baseline (range of 11 % to 71 %). After 1 cycle of chemotherapy, Cox regression analysis demonstrated a statistically significant relationship between a fall in TGV and improved patient survival (p = 0.015). Neither a reduction in the maximum standardized uptake value (p = 0.097) nor CT (p = 0.131) demonstrated a statistically significant association with patient survival. The authors concluded that semi-quantitative (18)F-FDG PET using the volume-based parameter of TGV is feasible in mesothelioma and may predict response to chemotherapy and patient survival after 1 cycle of treatment. Therefore, metabolic imaging has the potential to improve the care of patients receiving chemotherapy for mesothelioma by the early identification of responding patients. This technology may also be useful in the assessment of new systemic treatments for mesothelioma.
Ceresoli et al (2007) noted that most patients with malignant pleural mesothelioma (MPM) are candidates for chemotherapy during the course of their disease. Assessment of the response with conventional criteria based on computed tomography (CT) measurements is challenging, due to the circumferential and axial pattern of growth of MPM. Such difficulties hinder an accurate evaluation of clinical study results and make the clinical management of patients critical. Several radiological response systems have been proposed, but neither WHO criteria nor the more recent RECIST uni-dimensional criteria nor hybrid uni- and bi-dimensional criteria seem to apply to tumor measurement in this disease. Recently, modified RECIST criteria for MPM have been published. Although they are already being used in current clinical trials, they have been criticized based on the high grade of inter-observer variability and on theoretical studies of mesothelioma growth according to non-spherical models. Computer-assisted techniques for CT measurement are being developed. The use of FDG-PET for prediction of response and, more importantly, of survival outcomes of MPM patients is promising and warrants validation in large prospective series. New serum markers such as osteopontin and mesothelin-related proteins are under evaluation and in the future might play a role in assessing the response of MPM to treatment.

Spiro et al (2008) stated that guidelines issued by the National Institute for Clinical Excellence (NICE) in the England and Wales recommend that rapid access to (18)F-deoxyglucose positron emission tomography (FDG-PET) is made available to all appropriate patients with non-small-cell lung cancer (NSCLC). The clinical evidence for the benefits of PET scanning in NSCLC is substantial, showing that PET has high accuracy, sensitivity and specificity for disease staging, as well as pre-therapeutic assessment in candidates for surgery and radical radiotherapy. Moreover, PET scanning can provide important information to assist in radiotherapy treatment planning, and has also been shown to correlate with responses to treatment and overall outcomes. If the government cancer waiting time targets are to be met, rapid referral from primary to secondary healthcare is essential, as is early diagnostic referral within secondary and tertiary care for techniques such as PET. Studies are also required to explore new areas in which PET may be of benefit, such as surveillance studies in high-risk patients to allow early diagnosis and optimal treatment, while PET scanning to identify treatment non-responders may help optimize therapy, with benefits both for patients and healthcare resource use. Further studies are needed into other forms of lung cancer, including small-cell lung cancer and mesothelioma. The authors concluded that PET scanning has the potential to improve the diagnosis and management of lung cancer for many patients. Further studies and refinement of guidelines and procedures will maximize the benefit of this important technique.

Sorensen et al (2008) stated that extra-pleural pneumonectomy (EPP) in MPM may be confined with both morbidity and mortality, and careful pre-operative staging identifying resectable patients is important. Staging is difficult and the accuracy of pre-operative CT scan, 18F-FDG PET/CT scan (PET/CT), and mediastinoscopy is unclear. These investigators compared these staging techniques to each other and to surgical-pathological findings. Subjects were patients with epithelial subtype MPM, aged less than or equal to 70 years, and had lung function test allowing pneumonectomy. Pre-operative staging after 3 to 6 courses of induction chemotherapy included conventional CT scan, PET/CT, and mediastinoscopy. Surgical-pathological findings were compared to pre-operative findings. A total of 42 consecutive patients were without T4
or M on CT scan. PET/CT showed inoperability in 12 patients (29%) due to T4 (7 patients) and M1 (7 patients). Among 30 patients with subsequent mediastinoscopy, including 10 with N2/N3 on PET/CT, N2 were histologically verified in 6 (20%). Among 24 resected patients, T4 occurred in 2 patients (8%), and N2 in 4 (17%), all being PET/CT negative. The PET/CT accuracy of T4 and N2/N3 compared to combined histological results of mediastinoscopy and EPP showed sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios of 78% and 50%, 100% and 75%, 100% and 50%, 94% and 75%, not applicable and 5.0, and 0.22 and 0.67, respectively. The authors concluded that non-curative surgery is avoided in 29% out of 42 MPM patients by pre-operative PET/CT and in further 14% by mediastinoscopy. Even though both procedures are valuable, there are false negative findings with both, urging for even more accurate staging procedures.

Manthey and co-workers (2002) described 18F-FDG-PET findings in patients referred for evaluation of painful hip or knee prostheses. These investigators studied 23 patients with 28 prostheses, 14 hip and 14 knee prostheses, who had a complete operative or clinical follow-up. 18F-FDG-PET scans were obtained with an ECAT EXACT HR+ PET scanner. High glucose uptake in the bone prostheses interface was considered as positive for infection, an intermediate uptake as suspect for loosening, and uptake only in the synovia was considered as synovitis. The imaging results were compared with operative findings or clinical outcome. FDG-PET correctly identified 3 hip and 1 knee prostheses as infected, 2 hip and 2 knee prostheses as loosening, 4 hip and 9 knee prostheses as synovitis, and 2 hip and 1 knee prostheses as unsuspected for loosening or infection. In 3 patients covered with an expander after explantation of an infected prosthesis, FDG-PET revealed no further evidence of infection in concordance with the clinical follow-up. FDG-PET was false-negative for loosening in 1 case. The authors concluded that these preliminary findings suggested that FDG-PET could be a useful tool for differentiating between infected and loose orthopedic prostheses as well as for detecting only inflammatory tissue such as synovitis.

Beckers et al (2006) evaluated rheumatoid arthritis (RA) synovitis with FDG-PET in comparison with dynamic MRI and ultrasonography (US). A total of 16 knees in 16 patients with active RA were assessed with FDG-PET, MRI and US at baseline and 4 weeks after initiation of anti-TNF-alpha treatment. All studies were performed within 4 days. Visual and semi-quantitative (standardized uptake value, SUV) analyses of the synovial uptake of FDG were performed. The dynamic enhancement rate and the static enhancement were measured after intravenous gadolinium injection and the synovial thickness was measured in the medial, lateral patellar and suprapatellar recesses by US. Serum levels of C-reactive protein (CRP) and metalloproteinase-3 (MMP-3) were also measured. FDG-PET was positive in 69% of knees, while MRI and US were positive in 69% and 75%, respectively. Positivity on one imaging technique was strongly associated with positivity on the other two. FDG-PET-positive knees exhibited significantly higher SUVs, higher MRI parameters and greater synovial thickness compared with PET-negative knees, whereas serum CRP and MMP-3 levels were not significantly different. SUVs were significantly correlated with all MRI parameters, with synovial thickness and with serum CRP and MMP-3 levels at baseline. Changes in SUVs after 4 weeks were also correlated with changes in MRI parameters and in serum CRP and MMP-3 levels, but not with changes in synovial thickness. The authors concluded that FDG-PET is a unique imaging technique for assessing the metabolic activity of synovitis. The FDG-PET findings are correlated with MRI and US assessments of the pannus in RA, as well as with the classical serum
parameter of inflammation, CRP, and the synovium-derived parameter, serum MMP-3. They stated that further studies are needed to establish the place of metabolic imaging of synovitis in RA.

Karapetis and colleagues (2003) stated that FDG-PET may detect residual or recurrent malignancy in patients with germ cell tumors (GCT) following chemotherapy. The objective of the present study was to evaluate the use of FDG-PET in the setting of advanced GCT, and to determine the influence of FDG-PET on subsequent patient management. A computerized search of the patient database of the Department of Medical Oncology, Guy's Hospital, London, United Kingdom, and a manual search of medical records, were conducted. All male patients with metastatic or extra-gonadal GCT treated with chemotherapy between July 1996 and June 1999 inclusive were identified. Data from patients that had a PET scan following chemotherapy were analyzed. Reported PET scan findings were compared with subsequent clinical management and patient outcome. A total of 30 patients with metastatic testicular GCT and 3 patients with extra-gonadal GCT were treated with chemotherapy. Of these, 15 patients (12 testicular; 3 extra-gonadal; 10 non-seminoma; and 5 seminoma) were investigated following chemo-therapy with at least 1 FDG-PET scan. Seven patients had 2 or more PET scans, and a total of 26 FDG-PET scans was performed. The most frequent indication for PET scan was evaluation of a residual mass (11 patients). Three patients had an FDG-PET to evaluate thymic prominence. Minimum follow-up from first PET scan was 18 months. Three of 26 PET scans had false-positive findings. Four PET scans yielded findings of equivocal significance with repeat PET scan recommended. Relapse of disease occurred in 3 patients; 2 of whom had normal previous PET scans and 1 had a previous equivocal result. Moreover, PET had an impact on patient management in only 1 case where it "prompted" surgical excision of a residual mass. Normal PET scans provided reassurance in patients with residual small masses but did not alter their subsequent management. The authors concluded that a residual mass was the most common indication for PET. For the majority of patients PET did not have a discernible influence on clinical management. They stated that (i) oncologists should exercise caution in their interpretation of PET scan findings and guidelines for the appropriate use of PET in testicular cancer management need to be developed, and (ii) prospective trials are required to define the clinical role of PET in this setting.

Mody and colleagues (2006) described the use of FDG-PET in a series of 7 children (11 scans) with primary hepatic malignancies (5 patients with hepatoblastoma, 2 patients with hepatic embryonal rhabdomyosarcoma), together with other imaging (CT and MRI), serum tumor markers, and tumor pathology. These patients with pathologically proven hepatic malignancies underwent 11 FDG-PET scans for staging (1 patient) or restaging (6 patients). Tumor uptake of FDG was assessed qualitatively and compared with biochemical and radiological findings. Abnormal uptake was demonstrated in 6 of 7 patients (10 of 11 scans). Three patients subsequently underwent partial hepatic resection, and 1 underwent brain biopsy, confirming in each that the abnormal uptake of FDG indicated viable tumor. In 1 patient, intense uptake was due to necrotizing granulomas. In 1 patient, images were suboptimal due to non-compliance with fasting. The authors concluded that primary hepatic tumors of childhood usually demonstrate increased glycolytic activity, which allows them to be imaged using PET and the tracer 18F-FDG. The technique is probably most useful for assessing response to therapy, in following alfa-fetoprotein (AFP)-negative cases and for detecting metastatic disease although a large series of patients will need to be
studied to confirm these initial findings. Non-neoplastic inflammation may also accumulate FDG and could be confused with malignancy. As these tumors are rare, prospective multi-center studies are needed to determine the true clinical utility of FDG-PET imaging in the management of children with primary hepatic malignancies.

Wolfert et al (2010) the effectiveness of FDG-PET for the detection and staging of hepatocellular carcinoma (HCC). In addition, these researchers also assessed the correlation between FDG-PET positivity, tumor size, AFP, and histological grade. All patients on the hepatobiliary and liver transplant service with biopsy proven HCC that underwent FDG-PET between January 2000 and December 2004 were selected for a retrospective review. Results of the FDG-PET scans were compared with other imaging studies (CT, MRI, ultrasonography), intra-operative findings, tumor size, AFP levels, and histological grade. Of the 20 patients who underwent 18F-FDG PET, increased FDG uptake was noted in 14 scans (70%). These 20 patients fell into 2 groups: (i) for detecting HCC (group A) and (ii) for staging HCC (group B). There were 7 patients in group A; only 2 scans (28.6 %) showed increased uptake. There were 13 patients in group B; 12 scans (92.3 %) showed increased uptake. In group B, 11 of the 13 scans (84.6 %) provided an accurate representation of the disease process. Two scans failed to accurately portray the disease; 1 scan failed to show any increase in uptake, and the other scan failed to detect positive nodes that were found during surgery. FDG-PET detected only 2 of 8 tumors (25 %) less than or equal to 5 cm in size. All 12 PET scans (100 %) in tumors greater than or equal to 5 cm and/or multiple in number were detected by FDG-PET. FDG-PET scans with AFP levels less than 100 ng/ml were positive in 5 of 9 patients (55.6 %). In patients with levels greater than 100 ng/ml, 6 of 7 patients (85.7 %) had positive scans. Histologically, there were 6 well-differentiated, 6 moderately differentiated, and 2 poorly differentiated HCCs. FDG-PET detected 4 of 6 for both well- and moderately-differentiated HCCs. Both poorly-differentiated HCCs were detected. The intensity was evenly distributed between the different histological grades. There was a strong correlation of FDG uptake with tumor size. There were 5 HCCs with primary tumors greater than 10 cm in size; 4 showed intense uptake on the scan. In contrast, of the 8 tumors less than or equal to 5 cm in size, 6 were negative for uptake. The sensitivity of FDG-PET in detecting HCC less than or equal to 5 cm in size is low and therefore may not be helpful in detecting all of these tumors. For larger tumors, there is a strong correlation of sensitivity and uptake intensity with tumor size and elevated AFP levels. FDG-PET sensitivity and uptake intensity did not correlate with histological grade. In the setting of extra-hepatic disease, FDG-PET seems to be an effective accurate method for HCC staging; however, whether PET offers any benefit over traditional imaging has yet to be determined.

An UpToDate review on “Staging and prognostic factors in hepatocellular carcinoma” (Curley et al, 2013) states that “Positron emission tomography with fluorodeoxyglucose (FDG-PET) is being investigated as a complementary staging tool that may help to define prognosis in some patients .... Positron-emitting radionuclides other than FDG (such as 11C-acetate) are under investigation as potentially more useful agents for imaging and staging HCC”. Furthermore, National Comprehensive Cancer Network (NCCN)’s clinical guideline on “Hepatobiliary cancers” (Version 2.2013) notes that PET/CT is not adequate for screening and diagnosis of hepatocellular carcinoma. There is no mentioning of its use for staging either.
Murphy et al (2008) stated that PET/CT scan provides both functional and anatomical information in a single diagnostic test. It has the potential to be a valuable tool in the evaluation of pediatric abdominal tumors. The goal of this study was to report the authors’ early experience with this technology. Children who underwent PET/CT scan in the work-up for abdominal neoplasms between July 2005 and January 2008 were identified. Retrospective reviews of all radiological studies, operative notes, and pathological reports were undertaken. A total of 36 patients were collected. These included Burkitt’s lymphoma (n = 8), neuroblastoma (n = 7), rhabdomyosarcoma (n = 6), ovarian tumor (n = 3), Wilms tumor (n = 2), HCC (n = 2), paraganglioma (n = 1), germ cell tumor (n = 1), undifferentiated sarcoma (n = 1), renal primitive neuroectodermal tumor (n = 1), gastro-intestinal stromal tumor (n = 1), adrenocortical carcinoma (n = 1), inflammatory pseudotumor (n = 1), and adrenal adenoma (n = 1). All neoplasms were FDG were avid. These investigators identified several potential uses for PET/CT scan in this group of patients. These included (i) pre-operative staging, (ii) selection of appropriate site for biopsy, (iii) identification of occult metastatic disease, (iv) follow-up for residual or recurrent disease, and (v) assessment of response to chemotherapy. It can also be valuable when the standard diagnostic studies are equivocal or conflicting. The authors concluded that these preliminary data indicated that PET/CT is a promising tool in the evaluation of pediatric abdominal malignancies. The delineation of the exact role of this diagnostic modality will require additional experience. It should also be noted that the National Comprehensive Cancer Network’s clinical practice guideline on kidney cancer (2010) states that a PET scan is not a routine part of the initial work-up.

Phillips and colleagues (2009) assessed the effectiveness of FDG-PET scans in identifying sites of active disease and assessing response to therapy in patients with Langerhans cell histiocytosis (LCH). Changes in standardized uptake value (SUV) indicated increased or decreased disease activity before changes are evident by plain films or bone scans. A total fo 102 PET scans for 44 patients (3 adults and 41 children) with biopsy-proven LCH were compared with 83 corollary imaging modalities and were rated for overall clinical utility: false positive or negative ("inferior"), confirming lesions identified by another imaging modality ("confirmatory"), or showing additional lesions, response to therapy or recurrence of disease activity ("superior"), in comparison to bone scans, MRI, CT or plain films. FDG-PET was rated superior in that 90/256 (35 %) new, recurrent, or lesions responding to therapy were identified via change in SUV before other radiographical changes. Positron emission tomography scans confirmed active LCH in 146/256 (57 %). FDG-PET was superior to bone scans in that 8/23 (34 %) lesions, 11/53 (21 %) comparisons to lesions found by MRI, 13/64 (20 %) CT, and 58/116 (50 %) plain films. Positron emission tomography scans confirmed lesions found by: 14/23 (61 %) bone scans, 33/53 (62 %) MRI, 45/64 (65 %) CT, and 54/116 (46 %) of plain films. The authors concluded that whole body FDG-PET scans can detect LCH activity and early response to therapy with greater accuracy than other imaging modalities in patients with LCH lesions in the bones and soft tissues. Whole-body FDG-PET scanning is an important and informative study at diagnosis and for following disease course in patients with LCH.

Blockmans et al (2009) stated that ultrasonography, MRI, and PET are increasingly studied in large-vessel vasculitis. These imaging modalities have broadened the knowledge on these disorders and have a place in the diagnostic approach of these patients. Temporal artery ultrasonography can be used to guide the surgeon to that
artery segment with the clearest "halo" sign to perform a biopsy, or in experienced hands can even replace biopsy. The distal subclavian, axillary, and brachial arteries can also be examined. High-resolution MRI depicts superficial cranial and extra-cranial involvement patterns in giant cell arteritis (GCA). Contrast enhancement is prominent in active inflammation and decreases under successful steroid therapy. Presence of aortic complications such as aneurysm or dissection can be ruled out within the same investigation. Large thoracic vessel FDG-uptake is seen in the majority of patients with GCA, especially at the subclavian arteries and the aorta. However, FDG-PET can not predict which patients are bound to relapse, and once steroids are started, interpretation is hazardous, which makes its role in follow-up uncertain. Increased thoracic aortic FDG-uptake at diagnosis of GCA may be a bad prognostic factor for later aortic dilatation. In patients with isolated polymyalgia rheumatica -- who have less intense vascular FDG uptake -- symptoms are caused by inflammation around the shoulders, hips, and spine. The authors concluded that ultrasonography, MRI, and PET remain promising techniques in the scientific and clinical approach of large-vessel vasculitis.

In a phase I trial, Taggart et al (2009) compared 2 functional imaging modalities for neuroblastoma: (i) metaiodobenzylguanidine (MIBG) scan for uptake by the norepinephrine transporter and (ii) (18)F(FDG-PET) uptake for glucose metabolic activity. Patients were eligible for inclusion if they had concomitant FDG-PET and MIBG scans. (131)I-MIBG therapy was administered on days 0 and 14. For each patient, these researchers compared all lesions identified on concomitant FDG-PET and MIBG scans and gave scans a semi-quantitative score. The overall concordance of positive lesions on concomitant MIBG and FDG-PET scans was 39.6% when examining the 139 unique anatomical lesions. MIBG imaging was significantly more sensitive than FDG-PET overall and for the detection of bone lesions (p < 0.001). There was a trend for increased sensitivity of FDG-PET for detection of soft tissue lesions. Both modalities showed similar improvement in number of lesions identified from day 0 to day 56 scan and in semi-quantitative scores that correlated with overall response. FDG-PET scans became completely negative more often than MIBG scans after treatment. The authors concluded that MIBG scan is significantly more sensitive for individual lesion detection in relapsed neuroblastoma than FDG-PET, though FDG-PET can sometimes play a complementary role, particularly in soft tissue lesions. Complete response by FDG-PET metabolic evaluation did not always correlate with complete response by MIBG uptake.

A BlueCross BlueSheild Association's special report on PET for post-treatment surveillance of cancer (2009) found that there is simply inadequate direct and indirect evidence supporting the effectiveness of PET scanning for the purpose of surveillance. Reflecting this lack of evidence, current practice guidelines appear unanimously to recommend against the use of PET for surveillance. No strong support of the use of PET for surveillance was found in editorials, case reports, or other studies. The report concluded that given such problems such as lead time bias, length bias, and the uncertain diagnostic characteristics of PET in the surveillance setting, it would be difficult to determine if the effectiveness of PET for surveillance could be determined with observational data. Clinical trials may be necessary to determine whether PET surveillance is effective in improving health outcomes. (Note: surveillance is defined as use of PET beyond the completion of treatment, in the absence of signs or symptoms of cancer recurrence or progression, for the purpose of detecting recurrence or progression or predicting outcome).
Sharma (2009) reviewed the role of various imaging modalities in the evaluation of cardiac sarcoidosis and other cardiomyopathies. No study prospectively established the accuracy of each of the various techniques for diagnosing myocardial involvement in patients with suspected cardiac sarcoidosis. Cardiac magnetic resonance imaging (CMR) is demonstrated to have a sensitivity of 100% and specificity of approximately 80%, and positive predictive value of approximately 55% in diagnosing cardiac sarcoidosis. Recent studies have shown that FDG-PET has 100% sensitivity of detecting earlier stages of sarcoidosis. Both FDG-PET and CMR may provide complementary information for the diagnosis and assessment of efficacy of therapy in patients with cardiac involvement from sarcoidosis. The author concluded that clinical and sub-clinical cardiac involvement is common among patients with sarcoidosis. A structured clinical assessment incorporating advanced cardiac imaging with CMR and FDG-PET scanning is more sensitive than the established clinical criteria. Cardiac MRI is an established imaging modality in the diagnosis of various other cardiomyopathies. The author stated that well designed prospective clinical trials are awaited to define the exact role of these imaging studies in the diagnosis and guidance of therapy.

According to CMS (2010), there is insufficient evidence to determine that the results of NaF-18 PET imaging to identify bone metastases improve health outcomes of beneficiaries with cancer. Thus, the CMS decided that this use is not reasonable and necessary under §1862(a)(1)(A) of the Social Security Act.

In a meta-analysis, Chen et al (2011) evaluated the ability of FDG PET or PET/CT scan to ascertain the presence of bone marrow (BM) involvement in aggressive and indolent non-Hodgkin's lymphoma (NHL). These researchers conducted a systematic Medline search of articles published (last update, May 2010). Two reviewers independently assessed the methodological quality of each study. A meta-analysis of the reported sensitivity and specificity of each study was performed. A total of 8 studies met the inclusion criteria. The studies had several design deficiencies. Pooled sensitivity and specificity for the detection of non-Hodgkin aggressive lymphoma were 0.74 (95% CI: 0.65 to 0.83) and 0.84 (95% CI: 0.80 to 0.89), respectively. Pooled sensitivity and specificity for the detection of non-Hodgkin indolent lymphoma were 0.46 (95% CI: 0.33 to 0.59) and 0.93 (95% CI: 0.88 to 0.98), respectively. The authors concluded that diagnostic accuracy of FDG PET or PET/CT scans was slightly higher but without significant statistical difference (p = 0.1507) in patients with non-Hodgkin aggressive lymphoma as compared with those with non-Hodgkin indolent lymphoma. The sensitivity to detect indolent lymphoma BM infiltration was low for FDG PET or PET/CT.

Dengel et al (2011) stated that the false-negative rate for sentinel lymph node biopsy (SLNB) for melanoma is approximately 17%, for which failure to identify the sentinel lymph node (SLN) is a major cause. Intra-operative imaging may aid in detection of SLN near the primary site, in ambiguous locations, and after excision of each SLN. In a pilot study, these researchers (2011) evaluated the sensitivity and clinical utility of intra-operative mobile gamma camera (MGC) imaging in SLNB in melanoma. From April to September 2008, 20 patients underwent Tc99 sulfur colloid lymphoscintigraphy, and SLNB was performed with use of a conventional fixed gamma camera (FGC), and gamma probe followed by intra-operative MGC imaging. Sensitivity was calculated for each detection method. Intra-operative logistical challenges were scored. Cases in which MGC provided clinical benefit were recorded. Sensitivity for detecting SLN basins was 97% for the FGC and 90% for the MGC. A total of 46 SLN were identified.
32 (70 %) were identified as distinct hot spots by pre-operative FGC imaging, 31 (67 %) by pre-operative MGC imaging, and 43 (93 %) by MGC imaging pre- or intra-operatively. The gamma probe identified 44 (96 %) independent of MGC imaging. The MGC provided defined clinical benefit as an addition to standard practice in 5 (25 %) of 20 patients. Mean score for MGC logistic feasibility was 2 on a scale of 1 to 9 (1 = best). The authors concluded that intra-operative MGC imaging provides additional information when standard techniques fail or are ambiguous. Sensitivity is 90 % and can be increased. This pilot study has identified ways to improve the usefulness of an MGC for intra-operative imaging, which holds promise for reducing false negatives of SLNB for melanoma.

Schwannoma (also known as an acoustic neuromas) are benign nerve sheath tumors composed of Schwann cells, which normally produce the insulating myelin sheath covering peripheral nerves. They are mostly benign and less than 1 % become malignant, degenerating into a form of cancer known as neurofibrosarcoma. Schwannomas can arise from a genetic disorder called neurofibromatosis. Schwannomas can be removed surgically, but can then recur. The imaging procedure of choice for schwannomas is magnetic resonance imaging, with or without gadolinium contrast, which can detect tumors as small as 1 to 2 mm in diameter. There are studies reporting FDG uptake in schwannomas, but no studies demonstrating better accuracy or improvements in clinical outcomes with PET over MRI.

Dickinson et al (2010) noted that the utility of (18)F-FDG-PET for predicting outcome after autologous stem cell transplantation (ASCT) for diffuse large B cell lymphoma (DLBCL) is uncertain -- existing studies include a range of histological subtypes or have a limited duration of follow-up. A total of 39 patients with primary-refractory or relapsed DLBCL with pre-ASCT PET scans were analyzed. The median follow-up was 3 years. The 3-year progression-free survival (PFS) for patients with positive PET scans pre-ASCT was 35 % versus 81 % for those who had negative PET scans (p = 0.003). The overall survival (OS) in these groups was 39 % and 81 % (p = 0.01), respectively. In a multi-variate analysis, PET result, number of salvage cycles and the presence of relapsed or refractory disease were shown to predict a longer PFS; PET negativity (p = 0.04) was predictive of a longer OS. PET is useful for defining those with an excellent prognosis post-ASCT. Although those with positive scans can still be salvaged with current treatments, PET may be useful for selecting patients eligible for novel consolidation strategies after salvage therapies. The findings of this small study need to be validated by well-designed studies.

Guidelines on screening for tumors in paraneoplastic syndromes from the European Federation of Neurological Societies (Titulaer, et al., 2011) state that, for screening of the thoracic region, a CT-thorax is recommended, which if negative is followed by fluorodeoxyglucose-positron emission tomography (FDG-PET). The guidelines recommend mammography for breast cancer screening, followed by MRI. Ultrasound is the investigation of first choice for the pelvic region, followed by CT. The guidelines state that dermatomyositis patients should have CT of the thorax and abdomen, ultrasound of the pelvic region and mammography in women, ultrasound of testes in men under 50 years and colonoscopy in men and women over 50 years. The guidelines recommend, if primary screening is negative, repeat screening after 3 to 6 months and screening every 6 months up until four years. In Lambert-Eaton myasthenic syndrome, screening for 2 years is sufficient.
PET/MRI is a hybrid imaging technology that incorporates MRI soft tissue morphological imaging and PET functional imaging. There are few studies that have focused on PET/MRI technology and its advantages over PET/CT fusion, which is the current standard of care. An assessment by the Australian Health Policy Advisory Committee on Technology (Mundy, 2012) concluded that there are few clinical studies in the literature reporting on the use of hybrid PETâ€€MRI systems. The report noted that initial, small scale studies indicate that PETâ€€MRI hybrid scanning systems are as effective at imaging regions of interest in certain brain cancers and head and neck cancer as PETâ€€CT hybrid scanners; however these imaging studies do not indicate the effect on clinical outcomes for these patients or a change in patient management. The review stated that, based on the small number of published studies it appears that hybrid PETâ€€MRI may be a promising imaging modality, especially for pediatric patients, with the added benefit of reduced exposure to radiation compared to a PETâ€€CT scan. The report noted, however, that recent developments in CT design have resulted in scanners that deliver a reduced radiation dose. In addition, combined PETâ€€MRI systems are not capable of producing as highâ€€quality images as stand-alone imaging systems. The report concluded that "combined PETâ€€MRI systems are currently of benefit in the research, rather than clinical setting." The report stated that larger studies with clinical outcomes are required to demonstrate the effectiveness of the modality. The report noted concerns regarding the paucity of evidence in respect to the clinical effectiveness of hybrid PETâ€€MRI scanners and the potential for increased costs due to workforce issues including training requirements, time taken for interpretation of images, increasing capacity for image storage and the impact on patient flow.

Pritchard et al (2012) studied the use of 2-[(18)F] FDG PET in assessing lymph nodes and detecting distant metastases in women with primary breast cancer. Women diagnosed with operable breast cancer within 3 months underwent FDG-PET at 1 of 5 Ontario study centers followed by axillary lymph node assessment (ALNA) consisting of sentinel lymph node biopsy (SLNB) alone if sentinel lymph nodes (SLNs) were negative, SLNB with axillary lymph node dissection (ALND) if SLN or PET was positive, or ALND alone if SLNs were not identified. Between January 2005 and March 2007, a total of 325 analyzable women entered this study. Sentinel nodes were found for 312 (96 %) of 325 women and were positive for tumor in 90 (29 %) of 312. ALND was positive in 7 additional women. Using ALNA as the gold standard, sensitivity for PET was 23.7 % (95 % CI: 15.9 % to 33.6 %), specificity was 99.6 % (95 % CI: 97.2 % to 99.9 %), positive-predictive value was 95.8 % (95 % CI: 76.9 % to 99.8 %), negative-predictive value was 75.4 % (95 % CI: 70.1 % to 80.1 %), and prevalence was 29.8 % (95 % CI: 25.0 % to 35.2 %). Using logistic regression, tumor size was predictive for prevalence of tumor in the axilla and for PET sensitivity. PET scan was suspicious for distant metastases in 13 patients; 3 (0.9 %) were confirmed as metastatic disease and 10 (3.0 %) were false-positive. The authors concluded that FDG-PET is not sufficiently sensitive to detect positive axillary lymph nodes, nor is it sufficiently specific to appropriately identify distant metastases. However, the very high positive-predictive value (96 %) suggests that PET when positive is indicative of disease in axillary nodes, which may influence surgical care.

Yang and colleagues (2012) noted that important florbetapir scan limitations are (i) positive scan does not establish a diagnosis of AD or other cognitive disorder, and (ii) the scan has not been shown to be useful in predicting the development of dementia or
any other neurologic condition, nor has usefulness been shown for monitoring responses to therapies. The authors stated that “the ultimate clinical value of florbetapir imaging awaits further studies to assess the role, if any, that it plays in providing prognostic and predictive information. For example, the prognostic usefulness of florbetapir imaging in identifying persons with mild cognitive impairment or cognitive symptoms who may be at risk for progression to dementia has not been determined. Nor are data available to determine whether florbetapir imaging could prove useful for predicting responses to medication. These concerns prompted the FDA to require a specific “Limitations of Use” section in the florbetapir label”.

Kim et al (2010) reviewed the FDG PET findings of focal eosinophilic liver disease (FELD) and correlated them with radiologic and pathologic findings. A total of 14 patients, who were clinically or pathologically diagnosed as FELD and underwent CT and/or MR and PET, were enrolled. Two radiologists analyzed CT and MRI regarding size, shape, margin, attenuation, signal intensity (SI), and enhancement patterns of the lesion, both qualitatively and quantitatively. One pathologist determined whether the lesion is eosinophilic abscess (EA) or infiltration. One nuclear medicine physician reviewed the PET images and calculated the peak SUV of the lesion. PET findings were then correlated with CT or MRI, and pathologic findings. Eighty-five lesions were detected on CT (n = 85) and MRI (n = 10). Only 4 of the lesions showed FDG uptake and their mean SUV was 4.0. The size of the lesions with FDG uptake (26.5 mm) was significantly larger than those without uptake (11.8 mm). Mean attenuation and SI differences between the lesion and adjacent liver on CT and T2-weighted MRI tended to be larger in the uptake group (64.3 and 124.5) than the group without uptake (28.5 and 43.5). Among the 4 histologically confirmed lesions, 2 EAs and 1 of the 2 EIs showed FDG uptake. The authors concluded that most FELD do not show FDG uptake on PET. However, larger nodules with greater attenuation or SI differences from the background liver on CT or T2-weighted MRI or those with EA on pathology tend to show FDG uptake on PET.

Also, an UpToDate review on “Clinical manifestations, pathophysiology, and diagnosis of the hypereosinophilic syndromes” (Roufosse et al, 2012) does not mention the use of PET/positron emission tomography.

An UpToDate review on “Erdheim-Chester disease” (Jacobsen, 2012) states that “imaging studies include magnetic resonance imaging (MRI) of the brain, a computed tomography (CT) scan or an MRI of the entire aorta, a cardiac MRI, a CT scan of the chest, abdomen, and pelvis (which can also be used to image the entire aorta), and a transthoracic echocardiography. An MRI of the spinal cord is only necessary if the patient has signs or symptoms of spinal cord involvement. The utility of positron emission tomography (FDG-PET) scanning is unclear and not routinely recommended at present”.

UpToDate reviews on “Opsoclonus myoclonus ataxia” (Dalmau and Rosenfeld, 2012) and “Symptomatic (secondary) myoclonus” (Caviness, 2012) do not mention the use of PET and/or CT.

Available evidence on the use of PET for penile cancer is limited to use of PET in evaluation of inguinal lymph nodes, with most of the evidence limited to case reports. A recent review article in UpToDate (Lynch, 2012) on “Carcinoma of the penis: Diagnosis, treatment, and prognosis” states describes PET scans as a “evolving imaging technique” that is “promising”. Furthermore, the NCCN’s clinical practice
Positron Emission Tomography (PET)

guideline on penile cancer (NCCCN, version 1.2013) states that (for evaluation and risk stratification) "while studies have looked at the use of nanoparticle-enhanced MRI, positron emission tomography-CT (PET/CT), and 18F-fluorodeoxyglucose (FDG) PET/CT, their small sample requires validation in larger prospective studies".

Krajicek et al (2009) stated that pulmonary Langerhans cell histiocytosis (PLCH) is an inflammatory lung disease strongly associated with cigarette smoking and an increased risk of malignant neoplasms. Although the chest CT scan characteristics of PLCH are well-recognized, the PET scan characteristics of adults with PLCH are unknown. These researchers identified 11 patients with PLCH who underwent PET scanning over a 6-year period from July 2001 to June 2007. The presenting clinic-radiologic features including PET scan and chest CT scan findings were analyzed. Five of 11 patients had positive PET scan findings. Of the 5 PET scan-positive patients, 4 (80%) were women, 4 (80%) were current smokers, and the median age was 45 years (age range of 31 to 52 years). PET scan-positive findings were more likely to be present if the scan was performed early in the clinical course. Three PET scan-positive patients (60%) had multi-organ involvement. PET scan-positive patients had predominantly nodular inflammatory lung disease (greater than 100 nodules) with most nodules measuring less than 8 mm, whereas all PET scan-negative patients had predominantly cystic lung disease with fewer nodules (less than 25 nodules). Notable abnormal PET scan findings included foci of increased uptake in nodular lung lesions, thick-walled cysts, bone, and liver lesions. The mean maximum standardized uptake value of the PET scan-positive lesions ranged from 2.0 to 18.2. The authors concluded that PLCH may be associated with abnormal thoracic and extra-thoracic PET scan results. Patients with nodular disease seen on chest CT scans appear more likely to have abnormal PET scan findings. They stated that these findings suggested that PET scan imaging cannot reliably distinguish between the benign inflammatory nodular lesions of PLCH and malignant lesions.

Adam et al (2010) noted that PLCH manifests with dyspnea and a cough with no significant expectoration, with spontaneous pneumothorax being the first symptom in some patients. The disease is caused by multiple granulomas in terminal bronchioles, visible on high resolution CT (HRCT) as nodules. During the further course of the disease, these nodules progress through cavitating nodules into thick-walled and, subsequently, thin-walled cysts. LCH may affect the lungs only or multiple organs simultaneously. Pulmonary LCH may continually progress or remit spontaneously. Treatment is indicated in patients in whom pulmonary involvement is associated with multi-system involvement or when a progression of the pulmonary lesions has been confirmed. To document the disease progression, examination of the lungs using HRCT is routinely applied. Increasing number of nodules suggests disease progression. However, determining the number of nodules is extremely difficult. Measuring radioactivity of the individual small pulmonary loci (nodules) using PET is not possible due to the high number and small size of the nodules. The authors' center has a register of 23 patients with LCH; the pulmonary form had been diagnosed in 7 patients. A total of 19 PET and PET-CT examinations were performed in 6 of these patients. PET-CT was performed using the technique of maximum fluorodeoxyglucose accumulation in a defined volume of the right lung - SUV(max) Pulmo. In order to compare the results of examinations performed using the same and different machines over time as well as in order to evaluate pulmonary activity, the maximum fluorodeoxyglucose accumulation in a defined volume of the right lung (SUV(max) Pulmo) to maximum fluorodeoxyglucose accumulation in a defined volume of the liver
tissue (SUV(max) Hepar) ratio (index) was used. The disease progression was evaluated using the SUV(max) Pulmo/SUV(max) Hepar index in the six patients with pulmonary LCH. The index value was compared to other parameters characterizing the disease activity (HRCT of the lungs, examination of pulmonary function and clinical picture). The SUV(max) Pulmo/SUV(max) Hepar index correlated closely with other disease activity parameters. The traditional PET-CT examination is useful in detecting the LCH loci in the bone, nodes and other tissue but not in the presence of diffuse involvement of pulmonary parenchyma. Measuring the maximum fluorodeoxyglucose accumulation in a defined volume of the right lung and expressing this activity as the SUV(max) Pulmo/SUV(max) Hepar index appears to be a promising approach. The authors concluded that their initial experience suggested that the results obtained using this method correlate well with other parameters that characterize activity of P LCH. However, they noted that this was a pilot study and further verification is required.

An UpToDate review on “Pulmonary Langerhans cell histiocytosis” (King, 2012) states that “Fluorodeoxyglucose-PET (FDG-PET) scans may show increased uptake in patients with PLCH, particularly when obtained early in the course of disease. This was evaluated in a series of 11 patients with PLCH, five of whom had abnormal FDG uptake in the lungs [41]. The patients with FDG-PET positivity were more likely to have nodular radiographic pattern, suggesting earlier disease; those with negative FDG-PET scans were more likely to have a cystic pattern and fewer nodules, suggesting later disease”. The study cited was that by Krajicek et al (2009).

The Society for Gynecologic Oncology guidelines on serous papillary endometrial cancer made no recommendation for PET (Boruta et al, 2009). Also, NCCN guidelines on uterine neoplasms (2012) include uterine papillary serous carcinomas and make no recommendation for PET.

Kakhki et al (2013) systematically searched the available literature on the accuracy of 18F-FDG PET imaging for staging of endometrial cancer. PubMed, SCOPUS, ISI Web of Knowledge, Science Direct, and Springer were searched using "endomet* and PET" as the search terms. All studies evaluating the accuracy of 18F-FDG PET in the staging of endometrial carcinoma were included. Statistical pooling of diagnostic accuracy indices was done using random-effects model. Cochrane Q test and I index were used for heterogeneity evaluation. A total of 16 studies (807 patients in total) were included in the meta-analysis. Sensitivity and specificity for detection of the primary lesions were 81.8 % (77.9 % to 85.3 %) and 89.8 % (79.2 % to 96.2 %); for lymph node staging were 72.3 % (63.8 % to 79.8 %) and 92.9 % (90.6 % to 94.8 %); and for distant metastasis detection were 95.7 % (85.5 % to 99.5 %) and 95.4 % (92.7 % to 97.3 %). The authors concluded that because of low sensitivity, diagnostic utility of 18F-FDG PET imaging is limited in primary tumor detection and lymph node staging of endometrial cancer patients. However, high specificities ensure high positive-predictive values in these 2 indications. Diagnostic performance of 18F-FDG PET imaging is much better in detection of distant metastases. Moreover, they stated that larger studies with better design are needed to draw any more definite conclusion.

Sadeghi et al (2013) reviewed the medical literature on the application of 18F-FDG PET imaging in the management of uterine sarcomas and presented the results in systematic review and meta-analysis format. Medline, SCOPUS, and ISI Web of Knowledge were searched electronically with "PET and (uterine or uterus)" as key words. All studies evaluating the accuracy of 18F-FDG imaging in the staging or
restaging of uterine sarcomas were included if enough data could be extracted for
calculation of sensitivity and/or specificity. A total of 8 studies were included in the
systematic review. Only 2 studies reported the accuracy of 18F-FDG PET imaging in
the primary staging of uterine sarcoma with low sensitivity for lymph node staging. For
re-staging (detection of recurrence), all 8 included studies had quantitative data, and
the patient-based pooled sensitivity and specificity were 92.1 % (95 % CI: 82.4 to 97.4)
and 96.2 % (95 % CI: 87 to 99.5), respectively. On a lesion-based analysis, sensitivity
was 86.3 % (95 % CI: 76.7 to 92.9), and specificity was 94.4 % (95 % CI: 72.7 to 99.9).
Device used (PET versus PET/CT), spectrum of studied patients, and histology of the
sarcoma seem to be factors influencing the overall accuracy of 18F-FDG PET imaging.

The authors concluded that 18F-FDG PET and PET/CT seem to be accurate methods
for detection and localization of recurrence in patients with uterine sarcoma. Moreover,
they stated that further large multi-center studies are needed to validate these findings
and to correlate both sarcoma type and spectrum of patients to the diagnostic
performance of 18F-FDG PET imaging in recurrence detection. The studies evaluating
the accuracy of 18F-FDG PET imaging for the primary staging of uterine sarcoma are
very limited, and no definite conclusion can be made in this regard.

Spindle cell sarcoma is a type of connective tissue cancer in which the cells are spindle
-shaped when examined under a microscope. It is considered a type of soft tissue
sarcoma. An UpToDate review on "Clinical presentation, histopathology, diagnostic
evaluation, and staging of soft tissue sarcoma" (Ryan and Meyer, 2012) states that "A
number of studies report that PET and integrated PET/CT using fluorodeoxyglucose
(FDG) can distinguish benign soft tissue tumors from sarcomas, with the greatest
sensitivity for high grade sarcomas. However, the ability to differentiate benign soft
tissue tumors from low or intermediate grade sarcomas is limited, and PET and
PET/CT are not routinely recommended for the initial work-up of a soft tissue mass.

One exception may be in the characterization of a suspected peripheral nerve sheath
tumor in a patient with neurofibromatosis; in this scenario, PET imaging can be helpful
in distinguishing an MPNST from a neurofibroma. Consensus guidelines for workup of
a soft tissue sarcoma of the extremity and trunk issued by the National Comprehensive
Care Network (NCCN) suggest that PET scan may be useful in the prognostication,
grading, and determining response to neoadjuvant chemotherapy in patients with soft
tissue sarcoma. However, this recommendation is based upon a single study from the
University of Washington that found that FDG-PET was useful to predict the outcomes
of patients with high-grade extremity soft tissue sarcomas who were treated initially
with chemotherapy. Patients with a baseline tumor SUV max ≥ 6 who had a < 40
percent decrease in FDG uptake after neoadjuvant chemotherapy were found to be at
high risk of systemic disease recurrence. The clinical utility of having this information
prior to surgical treatment is unclear. At present, the use of PET for prognostication or
assessment of treatment response is not considered routine at most institutions .... PET
scanning can achieve whole body imaging, and it is widely considered to be more
sensitive than CT for the detection of occult distant metastases in a variety of solid
tumors. However, the utility of PET alone or with integrated CT for staging of distant
disease extent in STS (soft tissue sarcomas) is unclear as evidenced by the following
reports".

An UpToDate review on "Clinical features and diagnosis of cutaneous squamous cell
carcinoma (SCC)" (Lim and Asgari, 2012) does not mention the use of PET. Current
guidelines on squamous cell carcinoma of the skin from NCCN and NCI (PDQ) have no
recommendation for PET in skin cancer.
A recent review on malignant peritoneal mesothelioma (Turner et al, 2012) stated the role of PET in the diagnosis of malignant peritoneal mesothelioma is "unclear". The British Thoracic Society pleural disease guideline on “Investigation of a unilateral pleural effusion in adults” (Hooper et al, 2010) mentioned the use of CT, but not the use of PET.

Zahid et al (2011) addressed the question -- which diagnostic modality [computed tomography (CT), positron emission tomography (PET), combination PET/CT and magnetic resonance imaging (MRI)] provides the best diagnostic and staging information in patients with malignant pleural mesothelioma (MPM). Overall, 61 papers were found using the reported search, of which 14 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results are tabulated. These investigators concluded that fluorodeoxyglucose (FDG)-PET is superior to MRI and CT but inferior to PET-CT, in terms of diagnostic specificity, sensitivity and staging of MPM. Four studies reported outcomes using FDG-PET to diagnose MPM. PET diagnosed MPM with high sensitivity (92 %) and specificity (87.9 %). Mean standardized uptake value (SUV) was higher in malignant than benign disease (4.91 versus 1.41, p < 0.0001). Lymph node metastases were detected with higher accuracy (80 % versus 66.7 %) compared to extra-thoracic disease. Three studies assessed the utility of PET-CT to diagnose MPM. Mean SUV was higher in malignant than benign disease (6.5 versus 0.8, p < 0.001). MPM was diagnosed with high sensitivity (88.2 %), specificity (92.9 %) and accuracy (88.9 %). PET-CT had low sensitivity for stage N2 (38 %) and T4 (67 %) disease. CT-guided needle biopsy definitively diagnosed MPM after just 1 biopsy (100 % versus 9 %) much more often than a 'blind' approach. CT had a lower success rate (92 % versus 100 %) than thoracoscopic pleural biopsy but was equivalent to MRI in terms of detection of lymph node metastases (p = 0.85) and visceral pleural tumor (p = 0.64). CT had a lower specificity for stage II (77 % versus 100 %, p < 0.01) and stage III (75 % versus 100 %, p < 0.01) disease compared to PET-CT. Overall, the high specificity and sensitivity rates seen with open pleural biopsy make it a superior diagnostic modality to CT, MRI or PET for diagnosing patients with MPM.

An UpToDate review on “Diagnostic evaluation of pleural effusion in adults: Additional tests for undetermined etiology” (Lee, 2012) states that “Positron emission tomography (PET)/CT has an emerging role: 18-fluorodeoxyglucose (FDG)-avidity confirms, but cannot differentiate between inflammatory and malignant disease. Focal increased uptake of FDG in the pleura and the presence of solid pleural abnormalities on CT are suggestive of malignant pleural disease. A PET-CT pattern composed of pleural uptake and increased effusion activity had an accuracy of 90 percent in predicting malignant pleural effusions in 31 patients with known extrapulmonary malignancy and a pleural effusion [24]. A negative PET/CT would favor a benign etiology [25]. PET/CT may also highlight extrapleural abnormalities that may be the cause of the effusion …. CT scan of the thorax with contrast should be performed in virtually all patients with an undiagnosed pleural effusion. Additional imaging modalities that may be helpful are CT pulmonary angiogram and positron emission tomography (PET)/CT scans”.

Furthermore, the NCCN clinical practice guideline on “Malignant Pleural Mesothelioma” (Version 1.2013) mentions the use of CT, but not PET. Also, the NCCN
clinical practice guideline on “Non-Small Cell Lung Cancer” (Version 1.2013) does not mention the use of PET in the management of patients with pleural effusion.

The National Wilms Tumor Study Group and the International Society for Paediatric Oncology protocols recommend chest x-ray and CT imaging for lung metastases (Bhatnager, et al., 2009). There is no recommendation for use of PET in these protocols.

A review on renal neoplasms in childhood in Radiology Clinics of North America (Geller & Kochan, 2011) states that current Central Oncology Group (COG) protocols call for the use of chest CT for documentation and follow-up of pulmonary metastases. The review makes no recommendation for use of PET in Wilm's tumor.

A GeneReviews review of Wilms tumor (Dome & Huff, 2011) states that: “Positron emission tomography (PET) is not a routine component of the initial evaluation of Wilms tumor, though most Wilms tumors take up the radiotracer fluoro-deoxyglucose. PET may play a role in the detection of occult metastatic sites at recurrence.” This GeneReviews article provides one reference in support of the use of PET for detection of occult metastases (Moinul Hossain, et al., 2010) of 27 patients with Wilm's tumor, reporting that there were 34 positive scans, of which 8 were in lungs. The Moinus Hossain article noted, however, that lung lesions less than 10 mm were not consistently visualized on PET scans. The study was done in persons with known Wilms tumor, and did not report whether the PET scans were more accurate than other imaging modalities.

Current NCCN guidelines on kidney cancer (2013) make no recommendation for use of PET. The guidelines state that the value of PET in kidney cancer “remains to be determined” and that “PET alone is not a tool that is standardly used to diagnose kidney cancer or follow for evidence of relapse after nephrectomy.” Although NCCN guidelines address kidney cancer, they do not have specific recommendations on Wilms tumors.

PET-probe guided (assisted) surgery is used for intraoperative localization of PET-positive recurrent/metastatic lesions. The surgery utilizes a hand-held PET probe, essentially is a high energy gamma probe designed to process the 511 keV photons of PET tracers, to localize areas of uptake and guide excision. There is no clinical evidence to support the use of PET-probe guided surgical resection for recurrent ovarian cancer.

Siddha et al (2007) stated that pilar tumor is a rare neoplasm arising from the external root sheath of the hair follicle and is most commonly observed on the scalp. These tumors are largely benign, often cystic, and are characterized by trichilemmal keratinization. Wide local excision has been the standard treatment. Recent reports have described a rare malignant variant with an aggressive clinical course and a propensity for nodal and distant metastases which, therefore, merits aggressive treatment.

Khachemoune et al (2011) stated that a proliferating pilar tumor is a rare neoplasm arising from the isthmus region of the outer root sheath of the hair follicle. It is also commonly called a proliferating trichilemmal cyst. It was first described by Wilson-Jones as a proliferating epidermoid cyst in 1966. Proliferating pilar tumor was then distinguished from proliferating epidermoid cysts in 1995. It occurs most commonly on
the scalp in women older than 50 years. Most tumors arise within a pre-existing pilar cyst. Even though they usually are benign in nature, malignant transformation with local invasion and metastasis has been described. A tentative stratification of proliferating pilar tumors into groups as benign, low-grade malignancy, and high-grade malignancy has been introduced. They may be inherited in an autosomal-dominant mode, linked to chromosome 3. Imaging studies are not usually indicated, but they may show a lobulated cystic mass, coarse calcification, or ring-like mineralization. Because some subcutaneous tumors located in the midline of the body may have connections to the central nervous system (e.g., scalp cavernous angioma, which may be part of the symptom complex known as sinus pericranii), imaging tumors in this location with CT or MRI prior to removal should be considered. The best modality to determine bony invasion or erosion is CT scanning, and proliferating pilar tumors are frequently found as incidental subcutaneous nodules on brain CT scans. They most frequently display iso-intensity on T1-weighted images and heterogeneous signal on T2-weighted images. However, for deeper tissue invasion, MRI is best.

Currently, there is insufficient evidence to support PET scan for restaging of pancreatic cancer.

Topkan et al (2013) examined the impact of [(18)F]fluorodeoxyglucose-positron emission tomography (PET)/computed tomography (CT) restaging on management decisions and outcomes in patients with locally advanced pancreatic carcinoma (LAPC) scheduled for concurrent chemoradiotherapy (CRT). A total of 71 consecutive patients with conventionally staged LAPC were restaged with PET/CT before CRT, and were categorized into non-metastatic (M0) and metastatic (M1) groups. M0 patients received 50.4 Gy CRT with 5-fluorouracil followed by maintenance gemcitabine, whereas M1 patients received chemotherapy immediately or after palliative radiotherapy. In 19 patients (26.8 %), PET/CT restaging showed distant metastases not detected by conventional staging. PET/CT restaging of M0 patients showed additional regional lymph nodes in 3 patients and tumors larger than CT-defined borders in 4. PET/CT therefore altered or revised initial management decisions in 26 (36.6 %) patients. At median follow-up times of 11.3, 14.5, and 6.2 months for the entire cohort and the M0 and M1 cohorts, respectively, median overall survival was 16.1, 11.4, and 6.2 months, respectively; median loco-regional progression-free survival was 9.9, 7.8, and 3.4 months, respectively; and median progression-free survival was 7.4, 5.1, and 2.5 months, respectively (p < 0.05 each). The authors concluded that these findings suggested that PET/CT-based restaging may help select patients suitable for CRT, sparing those with metastases from futile radical protocols, and increasing the accuracy of estimated survival. (This was a small study examining the use of PET/CT for restaging in loco-regional pancreatic cancer; and the findings were preliminary)

Javery et al (2013) evaluated the impact of FDG-PET or PET/CT (PI) on pancreatic cancer management when added to CT or MRI (CDI). A total of 49 patients underwent 79 PI examinations. Discordant findings on PI and CDI were assessed for clinical impact. Overall, 15 of 79 PI-CDI pairs were discordant; 10 of 79 PI favorably; and 5 of 79 unfavorably altered management. PI favorably altered management more often when ordered for therapy monitoring compared to staging [risk ratio 13.00 (95 % confidence interval [CI]: 1.77 to 95.30)] or restaging [risk ratio 18.5 (95 % CI: 2.50 to 137.22)]. The authors concluded that PI favorably alters management more often when used for therapy monitoring compared to staging or restaging.
Furthermore, a UpToDate review on “Clinical manifestations, diagnosis, and staging of exocrine pancreatic cancer” (Fernandez-del Castillo, 2013) states that “The utility of PET scans in the diagnostic and staging evaluation of suspected pancreatic cancer, particularly whether PET provides information beyond that obtained by contrast-enhanced MDCT, remains uncertain …. Taken together, the data are insufficient to conclude that PET or integrated PET/CT provides useful information above that provided by contrast-enhanced CT. Consensus-based guidelines for staging of pancreatic cancer from the NCCN state that the role of PET/CT remains unclear. Definitive assessment of the role of PET as a component of the diagnostic and/or staging evaluation awaits a large prospective study designed to assess the benefit of PET (preferably integrated PET with a contrast-enhanced CT) in patients with a negative or indeterminate CT scan, with a prospectively designed cost effectiveness analysis”.

Funauchi et al (2008) reported the case of a 35-year old woman was admitted to the authors’ hospital because of high fever and skin rash, and subsequently diagnosed as having adult onset Still’s disease (AOSD). Because of resistance to the steroid hormones, high levels of the serum-soluble form of the interleukin-2 receptor and splenomegaly, these researchers suspected a possible diagnosis of malignant lymphoma and performed PET, which disclosed an intense accumulation of 2-deoxy-2 [F18] fluoro-D-glucose (FDG) in the liver and spleen. However, bone marrow aspiration and liver biopsy did not reveal any malignant cells. After the treatment of high-dose adrenocorticosteroids and plasma exchange, her symptoms and laboratory data, including PET findings, gradually improved. The authors concluded that this was a rare case of severe AOSD in which an intense accumulation of FDG was detected by PET, and a differential diagnosis from malignant lymphoma may be difficult by FDG-PET alone, so that careful evaluation by techniques including histopathological examination may be necessary.

Kawano et al (2012) stated that sarcoidosis is a multi-systemic granulomatous disease of unknown etiology. These researchers reported an unusual case of sarcoidosis in a woman presenting with cardiac sarcoidosis and massive splenomegaly with a familial history of cardiac sarcoidosis. Cardiac sarcoidosis was diagnosed based on electrocardiogram, echocardiogram, 18F-fluoro-2-deoxyglucose positron emission tomography (18F-FDG-PET) and skin histological findings. They performed splenectomy to rule out malignant lymphoma, and histological findings confirmed sarcoidosis. After splenectomy, these investigators initiated prednisolone therapy. At 20 months following diagnosis, she was symptom free. The authors concluded that echocardiography and 18F-FDG-PET may be a key diagnostic tool and prednisolone therapy may be safe, effective, and feasible for cardiac sarcoidosis.

An UpToDate review on “Approach to the adult patient with splenomegaly and other splenic disorders” (Landaw and Schrier, 2014) states that “A variety of imaging techniques are available for assessment of splenic lesions (e.g., splenic cysts, other space-occupying lesions), including CT scanning, magnetic resonance imaging, ultrasound, Tc-99m sulfur colloid scintigraphy, and 18F-FDG PET. Although the age of the patient, clinical symptomatology, and imaging characteristics might help the radiologist arrive at the correct diagnosis, one study has concluded that PET scanning offered no additional information over that obtained using CT scanning alone, and that
a history of prior malignancy was the only independent predictor for a splenic lesion being malignant (odds ratio 6.3; 95% CI 2.3-17)."

Salsano et al (2014) investigated the cerebral glucose metabolism in subjects with X-linked adrenoleukodystrophy (X-ALD) by using brain [(18)F]-fluorodeoxyglucose PET (FDG-PET). This was a cross-sectional study in which 12 adults with various forms of X-ALD underwent clinical evaluation and brain MRI, followed by brain FDG-PET, neuropsychological assessment, and personality and psychopathology evaluation using the Symptom Checkist-90-Revised (SCL-90-R) and the Millon Clinical Multiaxial Inventory-III (MCMI-III). When compared to healthy control subjects (n = 27) by using Statistical Parametric Mapping 8 software, the patients with X-ALD-with or without brain MRI changes showed a pattern of increased glucose metabolism in frontal lobes and reduced glucose metabolism in cerebellum and temporal lobe areas. On single case analysis by Scenium software, these researchers found a similar pattern, with significant (p < 0.02) correlation between the degree of hyper-metabolism in the frontal lobes of each patient and the corresponding X-ALD clinical scores. With respect to personality, these investigators found that patients with X-ALD usually present with an obsessive-compulsive personality disorder on the MCMI-III, with significant (p < 0.05) correlation between glucose uptake in ventral striatum and severity of score on the obsessive-compulsive subscale. The authors concluded that they examined cerebral glucose metabolism using FDG-PET in a cohort of patients with X-ALD and provided definite evidence that in X-ALD the analysis of brain glucose metabolism reveals abnormalities independent from morphologic and signal changes detected by MRI and related to clinical severity. They stated that brain FDG-PET may be a useful neuroimaging technique for the characterization of X-ALD and possibly other leukodystrophies.

The drawbacks of this study were: (i) the number of patients was limited because of the rarity of X-ALD, (ii) patients were not randomized, and (iii) the use of some drugs (e.g., corticosteroids, baclofen and valproic acid) by some symptomatic patients; these drugs might influence FDG-PET data. Furthermore, these investigators stated that the findings of this study lay the foundations of larger studies that might assess whether the abnormal brain glucose metabolism detected in X-ALD can be used as a surrogate marker.

National Comprehensive Cancer Network’s clinical practice guideline on “Melanoma” (Version 1.2015) states that “Routine blood tests are not recommended for patients with melanoma in situ or stage I and II disease. Routine cross-sectional imaging (CT, PET/CT, or MRI) is also not recommended for these patients”.

A review of PET in HIV-associated multi-centric Castleman disease (Rossotti et al, 2012) concluded “So far, FDG-PET/CT use for diagnosing Castleman disease has been reported in only a small number of patients. Data defining sensitivity and specificity of FDG-PET/CT for Castleman disease diagnosis are lacking”. Guidelines from the European Association of Nuclear Medicine and the Society for Nuclear Medicine and Molecular Imaging on PET in inflammation and infection (Jamar et al, 2013) stated that Castleman disease is one of several “well-described applications, but without sufficient evidence-based indication” for PET. Furthermore, current British guidelines for HIV-associated malignancies (Bower et al, 2014) states that regarding Castleman disease, “The role of functional imaging such as fluorodeoxyglucose positron emission tomography (FDG-PET) scans is uncertain; although a small study
indicated that in individuals with active MCD, FDG-PET scans more frequently detected abnormal uptake than CT”.

CPT Codes / HCPCS Codes / ICD-9 Codes

Cardiac indications:

CPT codes covered if selection criteria are met:

78459  Myocardial imaging, positron emission tomography (PET), metabolic evaluation
78491  Myocardial imaging, positron emission tomography (PET), perfusion; single study at rest or stress
78492  multiple studies at rest and/or stress

Other CPT codes related to the CPB:

78464  Myocardial perfusion imaging; tomographic (SPECT), single study (including attenuation correction when performed), at rest or stress (exercise and/or pharmacologic), with or without quantification
78465  tomographic (SPECT), multiple studies, (including attenuation correction when performed), at rest and/or stress (exercise and/or pharmacologic) and redistribution and/or rest injection, with or without quantification

HCPCS codes covered if selection criteria are met:

A9526  Nitrogen N-13 ammonia, diagnostic, per study dose, up to 40 millicuries
A9552  Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries
A9555  Rubidium Rb-82, diagnostic, per study dose, up to 60 millicuries

ICD-9 codes covered if selection criteria are met (not all-inclusive):

410.00 - 410.92  Acute myocardial infarction
411.0 - 411.89  Other acute and subacute forms of ischemic heart disease
412  Old myocardial infarction
413.0 - 413.9  Angina pectoris
426.2 - 426.6  Atrioventricular, bundle branch, and other heart block
427.31  Atrial fibrillation
428.0 - 428.9  Heart failure
Other ICD-9 codes related to the CPB:

414.00 - 414.07 Coronary atherosclerosis

420 - 420.99 Pericarditis

423.8 - 423.9 Other and unspecified diseases of pericardium

511.1 Pleurisy with effusion, with mention of a bacterial cause other than tuberculosis

511.81 Malignant pleural effusion

511.89 Other specified forms of effusion, except tuberculous

511.9 Unspecified pleural effusion

611.1 Hypertrophy of breast [large breasts]

754.89 Other specified nonteratogenic anomalies [chest wall deformity]

V43.82 Organ or tissue replaced by other means, breast [breast implants]

V45.71 Acquired absence of breast [status post mastectomy]

V45.81 Aortocoronary bypass status

V45.82 Percutaneous transluminal coronary angioplasty status

V85.4 Body Mass Index 40 and over, adult

Oncologic indications and conditions other than cardiac and neurologic for PET and PET-CT Fusion:

CPT codes covered if selection criteria are met:

78608 Brain imaging, positron emission tomography (PET); metabolic evaluation

78609 perfusion evaluation

78811 Positron emission tomography (PET) imaging; limited area (e.g., chest, head/neck)

78812 skull base to mid-thigh

78813 whole body

78814 Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (e.g., chest, head/neck)

78815 skull base to mid-thigh
78816  whole body

**Other CPT codes related to the CPB:**

32096  Thoracotomy, with diagnostic biopsy(ies) of lung infiltrate(s) (eg, wedge, incisional), unilateral

32097  Thoracotomy, with diagnostic biopsy(ies) of lung nodule(s) or mass (es) (eg, wedge, incisional), unilateral

32098  Thoracotomy, with biopsy(ies) of pleura

32100  Thoracotomy; with exploration

32405  Biopsy, lung or mediastinum, percutaneous needle

38500 - 38530  Biopsy or excision of lymph node(s); open, superficial, by needle, superficial (e.g., cervical, inguinal, axillary), open, deep cervical node(s), with or without excision scalene fat pad, open deep axillary node(s) or open, internal mammary node(s)

61534  Craniotomy with elevation of bone flap; for excision of epileptogenic focus without electrocorticography during surgery

61536  for excision of cerebral epileptogenic focus, with electrocorticography during surgery (includes removal of electrode array)

82378  Carcinoembryonic antigen (CEA)

**HCPCS codes covered if selection criteria are met:**

A9552  Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries

G0235  PET imaging, any site, not otherwise specified

**HCPCS codes not covered for indications listed in the CPB:**

G0219  PET imaging whole body; melanoma for non-covered indications

G0252  PET imaging, full and partial-ring PET scanners only, for initial diagnosis of breast cancer and/or surgical planning for breast cancer (e.g., initial staging of axillary lymph nodes)

S8085  Fluorine-18 fluorodeoxyglucose (F-18 FDG) imaging using dual-head coincidence detection system (non-dedicated PET scan) [when described as an FDG-SPECT scan]

**Other HCPCS codes related to the CPB:**

A4641  Radiopharmaceutical, diagnostic, not otherwise classified
A9580  Sodium fluoride F-18, diagnostic, per study dose, up to 30 millicuries[ not covered when with NaF-18 PET for identifying bone metastasis of cancer]

ICD-9 codes covered if selection criteria are met:

140.0 - 154.8, Malignant neoplasm of lip, oral cavity, and pharynx, esophagus, 157.0 - 157.9, stomach, small intestine, colon, rectum, rectosigmoid junction, and 158.8 - 158.9, anus, pancreas, peritoneum, nasal cavities, middle ear, and 160.0 - 163.9, accessory sinuses, mediastinum, mesothelioma, respiratory 164.0, 164.2 - system and other intrathoracic organs, bones of skull and face, 165.8, 170.0 - mandible, connective tissue and other soft tissue, [PET not covered for schwannoma] melanoma of skin, skin, breast, cervix 175.9, 180.0 - uteri, ovary, fallopian tube, testis, eye, brain, [PET not covered for atypical teratoid/rhabdoid tumor], thyroid gland, thymus, head, 180.9 - 186.0 - face, and neck 186.9, 190.0 - 191.9, 193, 195.0 194.0 - 194.9 Malignant neoplasm of other endocrine glands and related structures [including paragangliomas] 199.1 Other malignant neoplasm without specification of site [occult primary cancers] 200.00 - Malignant neoplasm of lymphatic and hematopoietic tissue [except xanthogranuloma] 202.58, 202.60 - 202.98 Multiple myeloma 203.00 - 203.02 Neuroendocrine tumors 209.00 - 209.69, 209.75 Carcinoma in situ lip, oral cavity, and pharynx, esophagus, 230.0 - 230.4, stomach, colon, rectum, respiratory system, breast, and eye [major salivary glands not covered] 231.0 - 231.9, 233.0, 234.0 Carcinoma in situ lip, oral cavity, and pharynx, larynx, trachea, bronchus, and lung, pleura, thymus, and mediastinum, and other and unspecified respiratory organs 235.0 - 235.1, 235.6 - 235.9 Neoplasm of uncertain behavior of major salivary glands, lip, oral cavity, and pharynx, larynx, trachea, bronchus, and lung, pleura, thymus, and mediastinum, and other and unspecified respiratory organs 237.5 - 237.9 Neoplasm of uncertain behavior of brain and nervous system 345.00 - Epilepsy and recurrent seizures [pre-surgical evaluation for localization of seizure focus] 345.91 Other emphysema 492.8 Other emphysema 518.89 Other diseases of lung, not elsewhere classified
530.89 Other specified disorders of esophagus
560.9 Unspecified intestinal obstruction
569.89 Other specified disorders of intestine
709.9 Unspecified disorder of skin and subcutaneous tissue
780.33 Post traumatic seizures
780.39 Other convulsions [pre-surgical evaluation for localization of seizure focus only]
784.2 Swelling, mass, or lump in head and neck
785.6 Enlargement of lymph nodes
793.11 Solitary pulmonary nodule
990 Effects of radiation, unspecified [radiation necrosis]

V10.03 - Personal history of malignant neoplasm of esophagus, large intestine, rectum, rectosigmoid junction, and anus, trachea, bronchus and lung, larynx, nasal cavities, middle ear, and accessory sinuses, breast, stomach, cervix uteri, ovary, testis, lymphosarcoma and reticulosarcoma, Hodgkin's disease, bone, melanoma of skin, eye, brain, thyroid and neuroendocrine tumor
V10.41, V10.43, V10.47, V10.71 -
V10.72, V10.81 -
V10.82, V10.84 -
V10.85, V10.87, V10.91

ICD-9 codes not covered for indications listed in the CPB (not all-inclusive):

114.0 - 114.9 Coccidioidomycosis
135 Sarcoidosis
142.0 - 142.9 Malignant neoplasm of major salivary glands
155.0 - 156.9, 158.0 Malignant neoplasm of liver and intrahepatic bile ducts, gallbladder and extrahepatic bile ducts and retroperitoneum
164.1 Malignant neoplasm of heart
171.8 Other specified sites of connective and other soft tissue [not covered for spindle cell sarcoma]
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>173.0 - 173.9</td>
<td>Malignant neoplasm of skin</td>
</tr>
<tr>
<td>176.0 - 179</td>
<td>Malignant neoplasm of Kaposi's sarcoma and uterus, part unspecified</td>
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<tr>
<td>181</td>
<td>Malignant neoplasm of placenta</td>
</tr>
<tr>
<td>182.0 - 182.8</td>
<td>Malignant neoplasm of body of uterus</td>
</tr>
<tr>
<td>184.0 - 184.9</td>
<td>Malignant neoplasm of other and unspecified female genital organs</td>
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<td>185</td>
<td>Malignant neoplasm of prostate</td>
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<tr>
<td>187.1 - 189.9</td>
<td>Malignant neoplasm of penis and other male genital organs, bladder, and kidney and other unspecified urinary organs [including Wilms' tumor]</td>
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<tr>
<td>192.0 - 192.9</td>
<td>Malignant neoplasm of other and unspecified parts of nervous system</td>
</tr>
<tr>
<td>196.9</td>
<td>Secondary and unspecified malignant neoplasm of lymph nodes, site unspecified</td>
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<tr>
<td>197.2 - 197.3</td>
<td>Secondary malignant neoplasm of pleura and other respiratory organs</td>
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<tr>
<td>197.6 - 197.7</td>
<td>Secondary malignant neoplasm of retroperitoneum and peritoneum, and liver, specified as secondary</td>
</tr>
<tr>
<td>198.0 - 198.5</td>
<td>Secondary malignant neoplasm of kidney, other urinary organs, skin, brain and spinal cord, other parts of nervous system, and bone and bone marrow</td>
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<tr>
<td>198.7</td>
<td>Secondary malignant neoplasm of adrenal gland</td>
</tr>
<tr>
<td>198.82</td>
<td>Secondary malignant neoplasm of genital organs</td>
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<tr>
<td>198.89</td>
<td>Secondary malignant neoplasm of other specified sites</td>
</tr>
<tr>
<td>203.10 - 208.92</td>
<td>Plasma cell leukemia and immunoproliferative neoplasms, lymphoid leukemia, myeloid leukemia, monocytic leukemia, and other specified leukemia</td>
</tr>
<tr>
<td>210.0 - 229.9</td>
<td>Benign neoplasms [including paraganglioma]</td>
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<tr>
<td>230.5 - 230.9</td>
<td>Carcinoma in situ of anal canal, anus, unspecified, other and unspecified parts of intestine, liver and biliary system, and other and unspecified digestive organs</td>
</tr>
<tr>
<td>232.0 - 232.9</td>
<td>Carcinoma in situ of skin</td>
</tr>
<tr>
<td>233.32</td>
<td>Carcinoma in situ of vulva</td>
</tr>
<tr>
<td>234.8 - 234.9</td>
<td>Carcinoma in situ of other and unspecified sites</td>
</tr>
</tbody>
</table>
235.3 - 235.4 Neoplasm of uncertain behavior of liver and biliary passages, and retroperitoneum and peritoneum

235.9 - 237.4 Neoplasm of uncertain behavior of other and unspecified respiratory organs, genitourinary organs, and endocrine glands

238.1 Neoplasm of uncertain behavior of connective and other soft tissue

238.3 - 238.79 Neoplasm of uncertain behavior of breast and other lymphatic and hematopoietic tissues

239.3 - 239.7 Neoplasm of uncertain behavior of breast, bladder, other genitourinary organs, brain, and endocrine glands and other parts of nervous system

239.9 Neoplasm of uncertain behavior, site unspecified

275.42 Hypercalcemia [of malignancy]

277.89 Other specified disorders of metabolism [Roasi-Dorfman disease]

288.3 Eosinophilia

290.0 - 319 Mental disorders

320 - 344.9, 346.00 - 389.9 Diseases of the nervous system and sense organs [except presurgical evaluation for localization of seizure focus]

390 - 429.9 Heart disease

447.6 Arteritis [Takayasu’s disease]

511.1 Pleurisy with effusion, with mention of a bacterial cause other than tuberculosis

511.81 Malignant pleural effusion

511.89 Other specified forms of effusion, except tuberculous

511.9 Unspecified pleural effusion

516.5 Adult pulmonary Langerhans cell histiocytosis

572.2 Hepatic encephalopathy

630 Hydatidiform mole [gestational trophoblastic neoplasia]

704.3 Pilar and trichilemmal cysts [Pilar tumor]

711.95 Unspecified infective arthritis [infection of hip arthroplasty]

714.0 Rheumatoid arthritis

727.02 Giant cell tumor of the tendon sheath [pigmented villonodular synovitis]
730.10 - 730.19  Chronic osteomyelitis

731.0  Osteitis deformans without mention of bone tumor [Paget's disease of bone]

780.01 - 780.09  Alteration of consciousness

780.1 - 780.2  Hallucinations and syncope and collapse

780.4  Dizziness and giddiness

780.60  Fever, unspecified [fever of unknown origin (FUO)]

780.93  Memory loss

780.99  Other general symptoms

781.0 - 781.99  Symptoms involving nervous and musculoskeletal systems

793.0  Nonspecific abnormal findings on radiological and other examination of skull and head

793.2  Nonspecific abnormal findings on radiological and other examination of other intrathoracic organ

794.00 - 794.19  Nonspecific abnormal results of function studies of brain and central nervous system and peripheral nervous system and special senses

794.30 - 794.39  Nonspecific abnormal results of function studies, cardiovascular

996.66  Infection and inflammatory reaction due to internal joint prosthesis [infection of hip arthroplasty or knee replacement prostheses]

998.59  Other postoperative infection [infection of hip arthroplasty]

V10.00 - V10.02  Personal history of malignant neoplasm of gastrointestinal tract, unspecified

V10.07 - V10.09  Personal history of malignant neoplasm of liver and of gastrointestinal tract, other

V10.29  Personal history of malignant neoplasm of other respiratory and intrathoracic organs

V10.42  Personal history of malignant neoplasm of other parts of uterus

V10.46  Personal history of malignant neoplasm of prostate

V10.48 - V10.60  Personal history of malignant neoplasm of epididymis, other male genital organs, urinary organs, and leukemia, unspecified
Personal history of malignant neoplasm, myeloid, monocyti c, and other leukemia

Personal history of other lymphatic and hematopoietic neoplasms

Personal history of other malignant neoplasm of skin

Personal history of malignant neoplasm of other parts of nervous system

Personal history of malignant neoplasm of other endocrine glands and related structures, other, and unspecified sites

Hip joint replaced by other means [infection of hip arthroplasty]

Persons without reported diagnosis encountered during examination and investigation of individuals and populations

Genetic susceptibility to malignant neoplasm of breast [Li-Fraumeni syndrome]

**Neurologic indications for PET:**

**CPT codes covered for indications listed in the CPB:**

- 78608 Brain imaging, positron emission tomography (PET); metabolic evaluation
- 78609 perfusion evaluation

**HCPCS codes not covered for indications listed in the CPB:**

- A9586 Florbetapir F18, diagnostic, per study dose, up to 10 millicuries
- A9599 Radiopharmaceutical, diagnostic, for beta-amyloid positron emission tomography (pet) imaging, per study dose

**ICD-9 codes not covered for indications listed in the CPB (not all-inclusive):**

- 290.0 - 290.9 Dementias
- 294.10 - Dementia in conditions classified elsewhere
  - 294.11
- 294.20 - Dementia, unspecified, without or with behavioral disturbance
  - 294.21
- 310.1 Personality change due to conditions classified elsewhere
- 331.0 Alzheimer's disease
- 332.0 - 332.1 Parkinson's disease
- 333.4 Huntington's chorea
- 780.93 Memory loss

http://qawww.aetna.com/cpb/medical/data/1_99/0071_draft.html 03/04/2015
781.1 Disturbances of sensation of smell and taste
V17.2 Family history of other neurological diseases
V80.0 Special screening for neurological conditions

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