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:
Ampullary cancer
Anal cancer
Appendiceal cancer
Brain tumors
Breast cancer
Cervical cancer
Chordoma
Colorectal cancer
Eosophageal cancer
Ewing sarcoma and osteosarcoma
Fallopian tube cancer
Gastric cancer Gastrointestinal
stromal tumors
Head and neck cancers (excluding cancers of the central nervous system)
Hodgkin lymphoma
Melanoma
Merkel cell carcinoma
Mesothelioma
Multiple myeloma and plasmacytomas
Neuroendocrine tumors Non-
Hodgkin's lymphoma
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
Thymic malignancies
Thyroid cancer
Vaginal 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 (NSCL) 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, re-staging or surveillance, or treatment planning for anal cancer has not been validated.

7. Hodgkin's lymphoma:

FDG-PET scans are considered medically necessary for the diagnosis*, staging and re-staging of Hodgkin 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 Hodgkin lymphoma is rarely considered medically necessary.

8. **Non-Hodgkin's lymphoma (including post-transplant lymphoproliferative disorder and Castleman's disease):**

FDG-PET scans are considered medically necessary for the diagnosis*, staging and re-staging of non-Hodgkin's 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 non-Hodgkin's lymphoma is rarely considered medically necessary.

9. **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.

10. **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.

11. *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.

12. *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.

13. *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.

14. 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.

15. *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.

16. *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.
17. *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.

18. *Vaginal Cancer*

FDG-PET scans are considered medically necessary for the diagnostic workup of vaginal cancer for evaluating the primary vaginal tumor and abnormal lymph nodes. FDG-PET scans are considered medically necessary for evaluating tumor recurrence. FDG-PET scans are considered experimental and investigational for staging and restaging and for surveillance.

19. *Vulvar Cancer*

FDG-PET scans are considered medically necessary for the diagnostic workup of vulvar cancer for evaluating regional lymph node metastases in some patients and hematogenous spread in rare patients with distant dissemination at the time of diagnosis. FDG-PET scans are considered experimental and investigational for staging and restaging of vulvar cancer.

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

FDG-PET scans are considered medically necessary for re-staging (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.

21. *Testicular Cancer:*

FDG-PET scans are considered medically necessary for re-staging (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.

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

22. *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.

23. *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.

24. *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.

25. *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.

26. *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.

27. *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.

28. *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.

29. Paraneoplastic Syndromes:

FDG-PET is considered medically necessary for diagnosis and staging of persons suspected of having a paraneoplastic syndrome.

30. 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.

31. 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.

32. 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.

33. Cancer of Ampulla

PET scanning is considered medically necessary for
staging/re-staging of cancer of ampulla where conventional imaging is equivocal or where it appears that disease is localized and potentially curative resection is being considered.

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

There is no longer a temporary shortage of technetium 99-m ($^{99m}$Tc), which is used in nuclear medicine for skeletal scintigraphy (bone scans). Therefore, Aetna will no longer consider FDG-PET an acceptable alternative to bone scans for detecting skeletal abnormalities for medically necessary indications.

35. NaF-18 PET

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

36. 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.

37. Fluciclovine f-18 PET

Aetna considers fluciclovine f-18 PET experimental and investigational for prostate cancer and for all other indications because of insufficient evidence.

38. Choline c-11 PET

Aetna considers choline c-11 PET experimental and investigational for prostate cancer and for all other indications because of insufficient evidence.
39. **Gallium Ga 68 dotatate PET**

Aetna considers gallium Ga 68 dotatate PET experimental and investigational for neuroendocrine tumors and for all other indications.

40. **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, extragonadal seminoma including mediastinal seminoma, gallbladder cancer, gestational trophoblastic neoplasia, giant cell tumor of the bone, hemangioendothelioma, hepatic sarcoma, hepatobiliary cancer, hepatocellular carcinoma, 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, pilar tumor, placental cancer, plasmacytoid dendritic cell neoplasm, pleomorphic adenoma, prostate cancer, schwannoma, serous papillary endometrial carcinoma, skin cancer, spindle cell sarcoma, staging of biopsy-proven solitary fibrous tumor of pleura, uterine papillary mesothelioma, 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 presurgical evaluation for the purpose of localization of a focus of refractory seizure activity.

Aetna considers PET scans experimental and investigational for Alzheimer's 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:

Aetna considers FDG-PET medically necessary for diagnosis, staging and re-staging of Langerhans cell histiocytosis.

Aetna considers FDG-PET experimental and investigational for adrenoleukodystrophy, aortic/large-vessel vasculitis, chronic osteomyelitis, coccidiodomycosis (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, Moyamoya disease, opsoclonus (opsillopsia) myoclonus syndrome, pigmented villonodular synovitis, pleural effusion, pulmonary Langerhans histiocytosis, rheumatoid arthritis, Rosai-Dorfman disease, sarcoid/sarcoidosis, screening in Li-Fraumeni syndrome, splenomegaly, Takayasu's arteritis, xanthogranuloma, 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. Aetna considers PET scanning with a gamma camera experimental and investigational for all indications because of insufficient evidence of its effectiveness.
VI. Aetna considers PET/MRI experimental and investigational for all indications because of insufficient evidence of its effectiveness.

VII. Aetna considers positron emission mammography (PEM) experimental and investigational because of insufficient evidence of its effectiveness.

VIII. Aetna considers PET scans for screening of asymptomatic members for breast cancer, lung cancer and other indications experimental and investigational, 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.

PET assesses the function of tissues and organs by monitoring the metabolic or biochemical activity while tracking the movement and concentration of a radioactive contrast agent. The technique uses special computerized imaging equipment and rings of detectors surrounding the individual to record gamma radiation produced when positrons (positively charged particles) emitted by the radioactive agent collide with electrons. Integrated PET/CT imaging is a technique in which both PET and CT are performed sequentially during a single visit on a hybrid PET/CT scanner. The CT and PET images are then co-registered using fusion software, enabling the physiologic data obtained on PET to be localized according to the anatomic CT images. When PET/CT is performed, a low radiation dose CT
without contrast is typically used to keep the radiation dose as low as possible and to limit adverse events. A higher resolution CT requires a higher dose of radiation and intravenous (IV) contrast. The Biograph mCT-X and mCT-S (Biograph HD) are examples of PET/CT devices.

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. 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 ρ, 0.78 [95 % confidence interval, 0.58 to 0.89]; p < 0.001)) and silver stain neuritic plaque score (Bonferroni ρ, 0.71 [95 % CI: 0.47 to 0.86]);
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) \(^{(18)}F{\text{FDG-PET}}\) 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. PET/MRI systems use software to fuse image data from two separately performed imaging examinations. Performing the PET and MRI scans simultaneously in the same imaging session purportedly prevents issues associated with image data mismatching that may occur with image fusion software. A combined PET/MRI approach is suggested for imaging anatomical, biochemical and functional characteristics of
disease. The Biograph mMR is an example of a PET/MRI device. 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 PET-MRI systems. The report noted that initial, small scale studies indicate that PET-MRI hybrid scanning systems are as effective at imaging regions of interest in certain brain cancers and head and neck cancer as PET-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 PET-MRI may be a promising imaging modality, especially for pediatric patients, with the added benefit of reduced exposure to radiation compared to a PET-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 PET-MRI systems are not capable of producing as high-quality images as stand-alone imaging systems. The report concluded that "combined PET-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 PET-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 SLNB 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
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 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 extrathoracic 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
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 "endometr* 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 thorascoscopic 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 fluorodeoxyglucose. 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 Checklist-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”. Guidelines from the National Comprehensive Cancer Network (NCCN, 2015) recommend FDG-PET in the workup of patients with Castleman disease.

11C-Acetate PET for Prostate Cancer:

In a systematic review and meta-analysis, Moshen and colleagues (2013) evaluated 23 studies of 11C-acetate PET in prostate cancer. For evaluation of primary tumor, pooled sensitivity was 75.1 (69.8 to 79.8) % and specificity was 75.8 (72.4 to 78.9) %. For detection of recurrence, sensitivity was 64 (59 to 69) % and specificity was 93 (83 to 98) %. Sensitivity for recurrence detection was higher in post-surgical versus post-radiotherapy patients and in patients with PSA at relapse of greater than 1 ng/ml. Studies using PET/computed tomography versus PET also showed higher sensitivity for detection of recurrence. Imaging with 11C-acetate PET can be useful in patients with prostate cancer. This is especially true for evaluation of patients at PSA relapse, although the sensitivity is overall low. For primary tumor evaluation (localization of tumor in the prostate and differentiation of malignant from benign lesions), 11C-acetate is of limited value due to low sensitivity and specificity. The authors concluded
that due to the poor quality of the included studies, the results should be interpreted with caution and further high-quality studies are needed. They stated that the quality of the conducted studies on the application of 11C-acetate in prostate cancer was usually poor. This is especially true for studies on re-staging at PSA relapse. The major drawback in the quality of the included studies in the present meta-analysis was poor and/or inconsistent gold standard. The researchers rarely provided histology results as the main gold standard method and usually relied on follow-up and conventional imaging (i.e., CT, bone scan, etc.). This is a major issue of the present study and these findings should be interpreted with the knowledge of this limitation. They noted that high quality prospective studies with consecutive patient recruitment and applying the best gold standard (histology confirmation preferably) are definitely needed.

Ceci et al (2014) investigated the clinical impact of (11)C-choline PET/CT on treatment management decisions in patients with recurrent prostate cancer (rPCa) after radical therapy. Enrolled in this retrospective study were 150 patients (95 from Bologna, 55 from Wurzburg) with rPCa and biochemical relapse (PSA mean ± SD 4.3 ± 5.5 ng/ml, range of 0.2 to 39.4 ng/ml) after radical therapy. The intended treatment before PET/CT was salvage radiotherapy of the prostatic bed in 95 patients and palliative androgen deprivation therapy (ADT) in 55 patients. The effective clinical impact of (11)C-choline PET/CT was rated as major (change in therapeutic approach), minor (same treatment, but modified therapeutic strategy) or none. Multivariate binary logistic regression analysis included PSA level, PSA kinetics, ongoing ADT, Gleason score, TNM, age and time to relapse. Changes in therapy after (11)C-choline PET/CT were implemented in 70 of the 150 patients (46.7 %). A major clinical impact was observed in 27 patients (18 %) and a minor clinical impact in 43 (28.7 %). (11)C-choline PET/CT was positive in 109 patients (72.7 %) detecting local relapse (prostate bed and/or iliac lymph nodes and/or para-rectal lymph nodes) in 64 patients (42.7 %). Distant relapse (para-aortic and/or retroperitoneal lymph nodes and/or bone lesions) was seen in
31 patients (20.7 %), and both local and distant relapse in 14 (9.3 %). A significant difference was observed in PSA level and PSA kinetics between PET-positive and PET-negative patients (p < 0.05). In multi-variate analysis, PSA level, PSA doubling time and ongoing ADT were significant predictors of a positive scan (p < 0.05). In statistical analysis no significant differences were observed between the Bologna and Wurzburg patients (p > 0.05). In both centers the same criteria to validate PET-positive findings were used: in 17.3 % of patients by histology and in 82.7 % of patients by correlative imaging and/or clinical follow-up (mean follow-up of 20.5 months, median of 18.3 months, range of 6.2 to 60 months). The authors concluded that (11)C-Choline PET/CT had a significant impact on therapeutic management in rPCa patients. It led to an overall change in 46.7 % of patients, with a major clinical change implemented in 18 % of patients. Moreover, they stated that further prospective studies are needed to evaluate the effect of such treatment changes on patient survival.

Giovacchini et al (2015) examined if [11C]choline PET/CT can predict survival in hormone-naive PCa patients with biochemical failure. This retrospective study included 302 hormone-naive PCa patients treated with radical prostatectomy who underwent [11C]choline PET/CT from December 1, 2004 to July 31, 2007 because of biochemical failure (prostate-specific antigen, PSA, greater than 0.2 ng/ml). Median PSA was 1.02 ng/ml. PCa-specific survival was estimated using Kaplan-Meier curves. Cox regression analysis was used to evaluate the association between clinicopathological variables and PCa-specific survival. The coefficients of the covariates included in the Cox regression analysis were used to develop a novel nomogram. Median follow-up was 7.2 years (1.4 to 18.9 years). [11C]Choline PET/CT was positive in 101 of 302 patients (33 %). Median PCa-specific survival after prostatectomy was 14.9 years (95 % CI: 9.7 to 20.1 years) in patients with positive [11C]choline PET/CT. Median survival was not achieved in patients with negative [11C]choline PET/CT. The 15-year PCa-specific survival probability was 42.4 % (95 % CI: 31.7 to 53.1 %) in patients with positive [11C]choline PET/CT and 95.5
% (95 % CI: 93.5 to 97.5 %) in patients with negative
PET/CT (hazard ratio [HR] 6.36, 95 % CI: 2.14 to 18.94, p <
0.001) and Gleason score greater than 7 (HR 3.11, 95 % CI: 1.11
to 8.66, p = 0.030) predicted PCa-specific survival. An internally
validated nomogram predicted 15-year PCa-specific survival
probability with an accuracy of 80 %. The authors concluded
that positive [11C]choline PET/CT after biochemical failure
predicts PCa-specific survival in hormone-naive PCa patients.
Moreover, they stated that prospective studies are needed to
confirm our results before more extensive use of [11C]choline
PET/CT for prognostic stratification of PCa patients.

An UpToDate review on “Rising serum PSA following local
therapy for prostate cancer: Diagnostic evaluation” (Moul and
Lee, 2015) states that “Newer imaging techniques using 18F-
NaF positron emission tomography (PET)/computed
tomography (CT) and 11-choline PET/CT are under development
and appear to offer improved sensitivity and specificity
compared with technetium 99 radionuclide bone scans.
However, false-positive scans remain a significant concern and
there is a steep learning curve associated with interpretation of
this approach. The Prostate Cancer Radiographic Assessments
for Detection of Advanced Recurrence (RADAR) Working Group
recommends using 18F-NaF PET/CT for skeletal assessment in
biochemical recurrence as an initial scan with PSA >5 ng/mL or
for doubling of PSA after a prior negative scan .... Early studies
suggest that 18-fluorine-labeled choline, 18-F sodium fluoride,
and 11-carbon-labeled acetate may be better tracers for use in
recurrent prostate cancer. PET and PET/CT with these tracers is
still considered investigational in men with a PSA-only
recurrence”.

Furthermore, NCCN’s clinical practice guideline on “Prostate
cancer” (Version 1.2015) notes that “further study is needed to
determine the best use of choline PET/CT imaging in men with
prostate cancer”.

**Giant Cell Tumor of the Bone:**
Muheremu and Niu (2015) examined PET/CT and its applications for the diagnosis and treatment of bone tumors. The advantages and disadvantages of PET/CT were also evaluated and compared with other imaging methods and the prospects of PET/CT were discussed. The PubMed, Medline, Elsevier, Wanfang and China International Knowledge Infrastructure databases were searched for studies published between 1995 and 2013, using the terms “PET/CT”, “positron emission tomography”, “bone tumor”, “osteosarcoma”, “giant cell bone tumor” and “Ewing sarcoma”. All the relevant information was extracted and analyzed. A total of 73 studies were selected for the final analysis. The extracted information indicated that at present, PET/CT is the imaging method that exhibits the highest sensitivity, specificity and accuracy. The authors concluded that although difficulties and problems remain to be solved, PET/CT is a promising non-invasive method for the diagnostic evaluation of and clinical guidance for bone tumors.

An UpToDate review on “Giant cell tumor of bone” (Thomas and Desai, 2015) states that “There are limited data regarding the utility of fluorine-18 fluorodeoxyglucose (18F-FDG)-PET for newly diagnosed GCTB. Unlike many benign bone tumors, GCTB accumulate the FDG tracer, presumably because the osteoclast-like giant cells are intensely metabolically active. However, whether there are any advantages to evaluation with FDG PET as compared to conventional imaging with CT, MRI, and bone scan is unclear”.

Furthermore, NCCN’s clinical practice guideline on “Bone cancer” (Version 1.2016) does not mention PET imaging as a management tool.

**Plasmacytoid Dendritic Cell Neoplasm:**

Kharfan-Dabaja et al. (2013) stated that blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an exceedingly rare disorder categorized under acute myeloid leukemia by the World Health Organization (WHO). Phenotypically, malignant cells co-express
CD4(+) and CD56(+) without co-expressing common lymphoid or myeloid lineage markers. BPDCN frequently expresses CD123, TCL1, BDC2-1, and CD2AP. Restriction of CD2AP expression to plasmacytoid dendritic cells makes it a useful tool to help confirm diagnosis. Clonal complex chromosome aberrations are described in 2/3 of cases; 80 % of BPDCN cases present with non-specific dermatological manifestations, prompting inclusion in the differential diagnosis of atypical skin rashes refractory to standard treatment. Prognosis is poor, with a median survival of less than 18 months. No prospective randomized data exist to define the most optimal frontline chemotherapy. Current practice considers acute myeloid leukemia-like or acute lymphoblastic leukemia-like regimens acceptable for induction treatment. Unfortunately, responses are short-lived, with second remissions difficult to achieve, underscoring the need to consider hematopoietic cell transplantation early in the disease course. Allografting, especially if offered in first remission, can result in long-term remissions. The authors concluded that pre-clinical data suggested a potential role for immunomodulatory agents in BPDCN. However, further research efforts are needed to better understand BPDCN biology and to establish evidence-based treatment algorithms that might ultimately improve overall prognosis of this disease.

Also, an UpToDate review on “Blastic plasmacytoid dendritic cell neoplasm” (Gurbuxani, 2015) does not mention PET scan as a management tool.

**Vaginal Squamous Cell Carcinoma:**

Bentivegna et al (2011) stated that [(18)F]fluoro-deoxy-glucose positron-emission tomography combined with integrated computed tomography (FDG-PET/CT) is commonly used for advanced stage cervical cancer but its efficiency is discussed in early stage. These researchers evaluated false negative rate of FDG-PET/CT in early-stage cervical and vaginal cancer. Patients treated between 2005 and 2008 for stage IB1 cervical cancer and stage I vaginal cancer and who underwent a FDG-PET/CT
followed by a pelvic lymphadenectomy were studied. A total of 18 patients were included with bilateral pelvic lymphadenectomy (16 cervical cancers, 2 vaginal cancers). The median age of patients was 41 years. Radical hysterectomy was performed for 16 patients, by a laparoscopic approach in 15 cases and by a laparotomic approach in 1 case. One patient had a simple hysterectomy and 1 had exclusive radiotherapy. No patient had pelvic or para-aortic fixation on FDG-PET/CT; 3 patients have proven pelvic involvement and 1 had para-aortic metastases. The false-negative rate and negative predictive value of FDG-PET/CT were 17% and 83%, respectively. The authors concluded that the accuracy of FDG-PET/CT imaging in predicting the pelvic nodal status is very low in patients with early-stage cervical and vaginal cancer and is not able to replace surgical exploration.

An UpToDate review on “Vaginal cancer” (Karam et al, 2015) states that “Imaging studies -- The only imaging studies that are part of the International Federation of Gynecology and Obstetrics (FIGO) staging for vaginal cancer are chest and skeletal radiography . However, advanced imaging, such as computed tomography (CT), magnetic resonance imaging (MRI) and 18-fluoro-2-deoxyglucose-positron emission tomography and CT (FDG-PET/CT) can be helpful for treatment planning. MRI can assist in determining the primary vaginal tumor size and local extent. Vaginal tumors generally are best seen on T2 imaging, and instilling gel into the vaginal canal, which distends the vaginal walls, often aids in visualizing and assessing the thickness of the vaginal tumor. FDG-PET can also be helpful for evaluating the primary vaginal tumor and abnormal lymph nodes .... Routine use of imaging studies was not recommended. Computed tomography (CT) and/or positron emission tomography (PET) should be performed ONLY if recurrence is suspected”.

Alzheimer’s Disease:

Yeo et al (2015) noted that amyloid imaging using fluorine 18-labeled tracers florbetapir, florbetaben, and flutemetamol
has recently been reported in Alzheimer's disease (AD). These researchers systematically searched Medline and Embase for relevant studies published from January 1980 to March 2014. Studies comparing imaging findings in AD and normal controls (NCs) were pooled in a meta-analysis, calculating pooled weighted sensitivity, specificity, and diagnostic odds ratio (OR) using the DerSimonian-Laird random-effects model. A total of 19 studies, investigating 682 patients with AD, met inclusion criteria. Meta-analysis demonstrated a sensitivity of 89.6 %, a specificity of 87.2 %, and an OR of 91.7 for florbetapir in differentiating AD patients from NCs, and a sensitivity of 89.3 %, a specificity of 87.6 %, and a diagnostic OR of 69.9 for florbetaben. There were insufficient data to complete analyses for flutemetamol. The authors concluded that these findings suggested favorable sensitivity and specificity of amyloid imaging with fluorine 18-labeled tracers in AD. They stated that prospective studies are needed to determine optimal imaging analysis methods and resolve outstanding clinical uncertainties.

In a Cochrane review, Smailagic and colleagues (2015) determined the diagnostic accuracy of the $^{18}$F-FDG PET index test for detecting people with mild cognitive impairment (MCI) at baseline who would clinically convert to AD dementia or other forms of dementia at follow-up. These investigators searched the Cochrane Register of Diagnostic Test Accuracy Studies, Medline, Embase, Science Citation Index, PsycINFO, BIOSIS previews, LILACS, MEDION, (Meta-analyses van Diagnostisch Onderzoek), DARE (Database of Abstracts of Reviews of Effects), HTA (Health Technology Assessment Database), ARIF (Aggressive Research Intelligence Facility) and C-EBLM (International Federation of Clinical Chemistry and Laboratory Medicine Committee for Evidence-based Laboratory Medicine) databases to January 2013. They checked the reference lists of any relevant studies and systematic reviews for additional studies. The authors included studies that evaluated the diagnostic accuracy of $^{18}$F-FDG PET to determine the conversion from MCI to AD dementia or to other forms of dementia, i.e., any or all of vascular dementia, dementia with Lewy bodies, and fronto-temporal dementia. These studies
necessarily employ delayed verification of conversion to dementia and are sometimes labelled as 'delayed verification cross-sectional studies'. Two blinded review authors independently extracted data, resolving disagreement by discussion, with the option to involve a third review author as arbiter if necessary. They extracted and summarized graphically the data for 2-by-2 tables. They conducted exploratory analyses by plotting estimates of sensitivity and specificity from each study on forest plots and in receiver operating characteristic (ROC) space. When studies had mixed thresholds, they derived estimates of sensitivity and likelihood ratios at fixed values (lower quartile, median and upper quartile) of specificity from the hierarchical summary ROC (HSROC) models. These researches included 14 studies (421 participants) in the analysis. The sensitivities for conversion from MCI to AD dementia were between 25% and 100% while the specificities were between 15% and 100%. From the summary ROC curve we fitted we estimated that the sensitivity was 76% (95% confidence interval (CI): 53.8 to 89.7) at the included study median specificity of 82%. This equated to a positive likelihood ratio of 4.03 (95% CI: 2.97 to 5.47), and a negative likelihood ratio of 0.34 (95% CI: 0.15 to 0.75). Three studies recruited participants from the same Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort but only the largest ADNI study (Herholz 2011) was included in the meta-analysis. In order to demonstrate whether the choice of ADNI study or discriminating brain region (Chetelat 2003) or reader assessment (Pardo 2010) made a difference to the pooled estimate, the authors performed 5 additional analyses. At the median specificity of 82%, the estimated sensitivity was between 74% and 76%. There was no impact on their findings. In addition to evaluating AD dementia, 5 studies evaluated the accuracy of 18F-FDG PET for all types of dementia. The sensitivities were between 46% and 95% while the specificities were between 29% and 100%; however, they did not conduct a meta-analysis because of too few studies, and those studies which we had found recruited small numbers of subjects. These findings were based on studies with poor reporting, and the majority of included studies had an unclear
risk of bias, mainly for the reference standard and participant selection domains. According to the assessment of Index test domain, more than 50% of studies were of poor methodological quality. The authors concluded that it was difficult to determine to what extent the findings from the meta-analysis can be applied to clinical practice. Given the considerable variability of specificity values and lack of defined thresholds for determination of test positivity in the included studies, the current evidence does not support the routine use of \({^{18}}\text{F-FDG}\) PET scans in clinical practice in people with MCI. The \({^{18}}\text{F-FDG}\) PET scan is a high-cost investigation, and it is therefore important to clearly demonstrate its accuracy and to standardize the process of \({^{18}}\text{F-FDG}\) PET diagnostic modality prior to its being widely used. They stated that future studies with more uniform approaches to thresholds, analysis and study conduct may provide a more homogeneous estimate than the one available from the included studies we have identified.

Morris et al (2016) stated that imaging or tissue biomarker evidence has been introduced into the core diagnostic pathway for AD; and PET using \((18)\text{F}\)-labelled beta-amyloid PET tracers has shown promise for the early diagnosis of AD. However, most studies included only small numbers of participants and no consensus has been reached as to which radiotracer has the highest diagnostic accuracy. First, these researchers performed a systematic review of the literature published between 1990 and 2014 for studies exploring the diagnostic accuracy of florbetaben, florbetapir and flutemetamol in AD. The included studies were analyzed using the QUADAS assessment of methodological quality. A meta-analysis of the sensitivity and specificity reported within each study was performed. Pooled values were calculated for each radiotracer and for visual or quantitative analysis by population included. The systematic review identified 9 studies eligible for inclusion. There were limited variations in the methods between studies reporting the same radiotracer. The meta-analysis results showed that pooled sensitivity and specificity values were in general high for all tracers. This was confirmed by calculating likelihood ratios. A patient with a positive ratio is much more likely to have AD
than a patient with a negative ratio, and vice versa. However, specificity was higher when only patients with AD were compared with healthy controls. This systematic review and meta-analysis found no marked differences in the diagnostic accuracy of the 3 beta-amyloid radiotracers. All tracers performed better when used to discriminate between patients with AD and healthy controls. The sensitivity and specificity for quantitative and visual analysis were comparable to those of other imaging or biomarker techniques used to diagnose AD. The authors concluded that further research is needed to identify the combination of tests that provides the highest sensitivity and specificity, and to identify the most suitable position for the tracer in the clinical pathway.

Tiepolt et al (2016) investigated the value of early PET images using the novel Aβ tracer [(18)F]FBB in the diagnosis of AD. This retrospective analysis included 22 patients with MCI or dementia who underwent dual time-point PET imaging with either [(11)C]PiB (11 patients) or [(18)F]FBB (11 patients) in routine clinical practice. Images were acquired 1 to 9 mins after administration of both tracers and 40 to 70 mins and 90 to 110 mins after administration of [(11)C]PiB and [(18)F]FBB, respectively. The patients also underwent [(18)F]FDG brain PET imaging; PET data were analyzed visually and semi-quantitatively. Associations between early Aβ tracer uptake and dementia as well as brain atrophy were investigated. Regional visual scores of early Aβ tracer and [(18)F]FDG PET images were significantly correlated (Spearman’s $p = 0.780$, $p < 0.001$). Global brain visual analysis revealed identical results between early Aβ tracer and [(18)F]FDG PET images. In a VOI-based analysis, the early Aβ tracer data correlated significantly with the [(18)F]FDG data ($r = 0.779$, $p < 0.001$), but there were no differences between [(18)F]FBB and [(11)C]PiB. Cortical SUVRs in regions typically affected in AD on early Aβ tracer and [(18)F]FDG PET images were correlated with MMSE scores ($p = 0.458$, $p = 0.032$, and $p = 0.456$, $p = 0.033$, respectively). A voxel-wise group-based search for areas with relatively higher tracer uptake on early Aβ tracer PET images compared with [(18)F]FDG PET images
revealed a small cluster in the midbrain/pons; no significant clusters were found for the opposite comparison. The authors concluded that early [(18)F]FBB and [(11)C]PiB PET brain images were similar to [(18)F]FDG PET images in AD patients, and these tracers could potentially be used as biomarkers in place of [(18)F]FDG. Thus, Aβ tracer PET imaging has the potential to provide biomarker information on AD pathology and neuronal injury. They stated that the potential of this approach for supporting the diagnosis of AD needs to be confirmed in prospective studies in larger cohorts.

Stefaniak and O'Brien (2016) stated that management strategies for dementia are still very limited, and establishing effective disease modifying therapies based on amyloid or tau remains elusive. Neuroinflammation has been increasingly implicated as a pathological mechanism in dementia and demonstration that it is a key event accelerating cognitive or functional decline would inform novel therapeutic approaches, and may aid diagnosis. Much research has therefore been done to develop technology capable of imaging neuroinflammation in-vivo. The authors performed a systematic search of the literature and found 28 studies that used in-vivo neuroimaging of 1 or more markers of neuroinflammation on human patients with dementia. The majority of the studies used PET imaging of the 18kDa translocator protein (TSPO) microglial marker and found increased neuroinflammation in at least 1 neuroanatomical region in dementia patients, most usually AD, relative to controls, but the published evidence to date does not indicate whether the regional distribution of neuroinflammation differs between dementia types or even whether it is reproducible within a single dementia type between individuals. It is less clear that neuroinflammation is increased relative to controls in MCI than it is for dementia, and therefore it is unclear whether neuroinflammation is part of the pathogenesis in early stages of dementia. The authors concluded that despite its great potential, this review demonstrated that imaging of neuroinflammation has not thus far clearly established brain inflammation as an early pathological event. They stated that further studies are
needed, including those of different dementia subtypes at early stages, and newer, more sensitive, PET imaging probes need to be developed.

Rodriguez-Vieitez et al (2016) stated that for amyloid PET tracers, the simplified reference tissue model derived ratio of influx rate in target relative to reference region (R1) has been shown to serve as a marker of brain perfusion, and, due to the strong coupling between perfusion and metabolism, as a proxy for glucose metabolism. In the present study, 11 prodromal AD and 9 AD dementia patients underwent [18F]THK5317, carbon-11 Pittsburgh Compound-B ([11C]PIB), and 2-deoxy-2-[18F]fluoro-D-glucose ([18F]FDG) PET to assess the possible use of early-phase [18F]THK5317 and R1 as proxies for brain perfusion, and thus, for glucose metabolism. Discriminative performance (prodromal versus AD dementia) of [18F]THK5317 (early-phase SUVr and R1) was compared with that of [11C]PIB (early-phase SUVr and R1) and [18F]FDG. Strong positive correlations were found between [18F]THK5317 (early-phase, R1) and [18F]FDG, particularly in frontal and temporo-parietal regions. Differences in correlations between early-phase and R1 ([18F]THK5317 and [11C]PIB) and [18F]FDG, were not statistically significant, nor were differences in area under the curve values in the discriminative analysis. The authors concluded that these findings suggested that early-phase [18F]THK5317 and R1 provide information on brain perfusion, closely related to glucose metabolism. As such, a single PET study with [18F]THK5317 may provide information about both tau pathology and brain perfusion in AD, with potential clinical applications.

Pancreatic Cancer:

The American Society of Clinical Oncology (ASCO)’s clinical practice guideline on “Locally advanced, unresectable pancreatic cancer” (Balaban et al, 2016) stated that “The routine use of positron emission tomography imaging for the management of locally advanced, unresectable pancreatic cancer is not recommended”.

Pancreatic Cancer:
**Infectious Endocarditis:**

Yan and colleagues (2016) systematically conducted a meta-analysis of the available evidence for PET/CT using 18F-fluorodeoxyglucose as tracers in the imaging of infectious endocarditis (IE). Databases, including PubMed, Embase, and Web of Science, were searched for studies that examined the diagnostic value of 18F-FDG PET/CT for patients with IE. The reference lists following review articles and those of the included articles were checked to complement the electronic searches. The data extraction and methodological quality assessment were completed by 2 independent reviewers, and the meta-analysis was then conducted using Meta-Disc software, version 1.4. A total of 6 studies involving 246 patients was included. The results of the meta-analysis indicated that the pooled sensitivity was 61% (95% CI: 52 to 88%), and the pooled specificity was 88% (95% CI: 80 to 93%). The positive likelihood ratio was 3.24 (95% CI: 1.67 to 6.28, p = 0.224), and the negative likelihood ratio was 0.50 (95% CI: 0.32 to 0.77, p = 0.015). The diagnostic odds ratio (OR) was 6.98 (95% CI: 2.55 to 19.10, p = 0.145), the overall area under the curve (AUC) was 0.8230 (SE = 0.1085), and the Q* value was 0.7563 (SE = 0.0979). The authors concluded that 18F-FDG PET/CT is currently not sufficient for the diagnosis of IE because of its low sensitivity.

**Diagnosis of Gallbladder Cancer:**

National Comprehensive Cancer Network’s clinical practice guideline on “Hepatobiliary cancers” (Version 2.2016) states that “Although the role of PET scan has not been established in the evaluation of patients with gallbladder, emerging evidence from retrospective studies indicates that it may be useful for the detection of regional lymph node and distant metastatic disease in patients with otherwise potentially resectable disease”.

**Interim FDG-PET for Prognosis in Follicular Lymphoma:**
Adams and colleagues (2016) systematically reviewed the prognostic value of interim and end-of-treatment FDG-PET in follicular lymphoma during and after first-line therapy. The PubMed/Medline database was searched for relevant original studies. Included studies were methodologically assessed, and their results were extracted and descriptively analyzed. A total of 3 studies on the prognostic value of interim FDG-PET and 8 studies on the prognostic value of end-of-treatment FDG-PET were included. Overall, studies were of poor methodological quality. In addition, there was incomplete reporting of PFS and OS data by several studies, and none of the studies incorporated the Follicular Lymphoma International Prognostic Index (FLIPI) in the OS analyses. Two studies reported no significant difference in PFS between interim FDG-PET positive and negative patients, whereas 1 study reported a significant difference in PFS between the 2 groups. Two studies reported no significant difference in OS between interim FDG-PET positive and negative patients; 5 studies reported end-of-treatment FDG-PET positive patients to have a significantly worse PFS than end-of-treatment FDG-PET negative patients, and 1 study reported a non-significant trend towards a worse PFS for end-of-treatment FDG-PET positive patients. Three studies reported end-of-treatment FDG-PET positive patients to have a significantly worse OS than end-of-treatment FDG-PET negative patients. The authors concluded that the available evidence does not support the use of interim FDG-PET in follicular lymphoma. Although published studies suggested end-of-treatment FDG-PET to be predictive of PFS and OS, they suffered from numerous biases and failure to correct OS prediction for the FLIPI.

**Moyamoya Disease:**

An UpToDate review on “Moyamoya disease: Etiology, clinical features, and diagnosis” (Suwanwela, 2016) states that “Although supporting evidence is limited, additional methods that may be useful to determine the extent of inadequate resting brain perfusion and blood flow reserve in patients with Moyamoya disease prior to and after treatment include
perfusion CT, Xenon-enhanced CT, perfusion-weighted MRI, PET, and SPECT with acetazolamide challenge”.

Pre-Transplant PET Scans for Prognosis in Refractory/Relapsed Hodgkin Lymphoma Treated with Autologous Stem Cell Transplantation:

Adams and Kwee (2016) systematically reviewed the prognostic value of pre-transplant FDG-PET in refractory/relapsed Hodgkin lymphoma treated with ASCT. Medline was searched for appropriate studies; included studies were methodologically appraised. Results of individual studies were meta-analyzed, if possible. A total of 11 studies, comprising 745 refractory/relapsed Hodgkin lymphoma patients who underwent FDG-PET before autologous SCT, were included. The overall methodological quality of these studies was moderate. The proportion of pre-transplant FDG-PET positive patients ranged between 25 and 65.2 %; PFS ranged between 0 and 52 % in pre-transplant FDG-PET positive patients, and between 55 and 85 % in pre-transplant FDG-PET negative patients; OS ranged between 17 and 77 % in pre-transplant FDG-PET positive patients, and between 78 and 100 % in FDG-PET negative patients. Based on 5 studies that provided sufficient data for meta-analysis, pooled sensitivity and specificity of pre-transplant FDG-PET in predicting treatment failure (i.e., either progressive, residual, or relapsed disease) were 67.2 % (95 % CI: 58.2 to 75.3 %) and 70.7 % (95 % CI: 64.2 to 76.5 %), respectively. Based on 2 studies that provided sufficient data for meta-analysis, pooled sensitivity and specificity of pre-transplant FDG-PET in predicting death during follow-up were 74.4 % (95 % CI: 58.8 to 86.5 %) and 58.0 % (95 % CI: 49.3 to 66.3 %), respectively. The authors concluded that the moderate quality evidence suggested pre-transplant FDG-PET to have value in predicting outcome in refractory/relapsed Hodgkin lymphoma patients treated with ASCT.

Solitary Fibrous Tumor:

A Medscape review on “Solitary fibrous tumor workup” (Ng,
2015), an UpToDate review on “Solitary fibrous tumor” (Demicco and Meyer, 2016), and NCCN’s clinical practice guideline on “Soft tissue sarcoma” (Version 1.2016) had no recommendation for PET scanning.

| CPT Codes / HCPCS Codes / ICD-10 Codes
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<tr>
<td>I50.1 - I50.9</td>
<td>Heart failure</td>
</tr>
</tbody>
</table>

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

# CPT codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>78608</td>
<td>Brain imaging, positron emission tomography (PET); metabolic evaluation</td>
</tr>
<tr>
<td>78609</td>
<td>perfusion evaluation</td>
</tr>
<tr>
<td>78811</td>
<td>Positron emission tomography (PET) imaging; limited area (e.g., chest, head/neck)</td>
</tr>
<tr>
<td>78812</td>
<td>skull base to mid-thigh</td>
</tr>
<tr>
<td>78813</td>
<td>whole body</td>
</tr>
<tr>
<td>78814</td>
<td>Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (e.g., chest, head/neck)</td>
</tr>
<tr>
<td>78815</td>
<td>skull base to mid-thigh</td>
</tr>
<tr>
<td>78816</td>
<td>whole body</td>
</tr>
</tbody>
</table>

# Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>32095</td>
<td>Thoracotomy, limited, for biopsy of lung or pleura</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>32097</td>
<td>Thoracotomy, with diagnostic biopsy(ies) of lung nodule(s) or mass(es) (eg, wedge, incisional), unilateral</td>
</tr>
<tr>
<td>32100</td>
<td>Thoracotomy; with exploration</td>
</tr>
<tr>
<td>32405</td>
<td>Biopsy, lung or mediastinum, percutaneous needle</td>
</tr>
<tr>
<td>38500 - 38530</td>
<td>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)</td>
</tr>
<tr>
<td>61534</td>
<td>Craniotomy with elevation of bone flap; for excision of epileptogenic focus without electrocorticography during surgery</td>
</tr>
<tr>
<td>61536</td>
<td>for excision of cerebral epileptogenic focus, with electrocorticography during surgery (includes removal of electrode array)</td>
</tr>
<tr>
<td>82378</td>
<td>Carcinoembryonic antigen (CEA)</td>
</tr>
</tbody>
</table>

**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:**

- C9461  Choline C 11, diagnostic, per study dose
- 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:**
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A4641</td>
<td>Radiopharmaceutical, diagnostic, not otherwise classified</td>
</tr>
<tr>
<td>A9580</td>
<td>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]</td>
</tr>
<tr>
<td>Q9951</td>
<td>Low osmolar contrast material, 400 or greater mg/ml iodine concentration, per ml</td>
</tr>
<tr>
<td>Q9958 - Q9967</td>
<td>High osmolar contrast material</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met:**

- C00.0 - C21.8, C25.0 - C25.9, C30.0 - C34.92, C38.0 - C43.9, C48.0 - C52, C53.0 - C53.9, C56.1 - C57.9, C62.0 - C62.92, C69.00 - C69.92, C71.0 - C71.9, C73, C76.0 - C81.00 - C96.9

  - Malignant neoplasm of lip, oral cavity, and pharynx, esophagus, stomach, small intestine, colon, rectum, rectosigmoid junction, and anus [PET not covered for re-staging and surveillance], pancreas, peritoneum, nasal cavities, middle ear, and accessory sinuses, mediastinum, mesothelioma, respiratory system [PET not covered for screening of asymptomatic members for lung cancer] and other intrathoracic organs, bones of skull and face, mandible, connective tissue and other soft tissue, [PET not covered for schwannoma], melanoma of skin, skin, breast, vulva, vagina [PET not covered for staging and restaging of vulvar or vaginal cancer], cervix uteri, ovary, fallopian tube, testis, eye, brain, [PET not covered for atypical teratoid/rhabdoid tumor], thyroid gland, thymus, head, face, and neck, other endocrine glands and related structures [including paragangliomas], Other malignant neoplasm without specification of site [occult primary cancers] Malignant neoplasm of lymphatic and hematopoietic tissue [except xanthogranuloma]
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D00.00 - D01.3, D02.0 - D02.4, D05.0 - D05.92, D09.0 - D09.92</td>
<td>Carcinoma in situ, oral cavity, and pharynx, esophagus, stomach, colon, rectum, respiratory system, breast, and eye [major salivary glands not covered]</td>
</tr>
<tr>
<td>D37.01 - D37.09, D38.0 - D38.6</td>
<td>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</td>
</tr>
<tr>
<td>D3a.00 - D3a.8</td>
<td>Neuroendocrine tumors</td>
</tr>
<tr>
<td>D43.0 - D43.9</td>
<td>Neoplasm of uncertain behavior of brain and central nervous system</td>
</tr>
<tr>
<td>D47.Z1</td>
<td>Post-transplant lymphoproliferative disorder (PTLD)</td>
</tr>
<tr>
<td>D47.Z2</td>
<td>Castleman disease [not covered for re-staging of multi-centric Castleman's disease]</td>
</tr>
<tr>
<td>G40.00 - G40.919</td>
<td>Epilepsy and recurrent seizures [pre-surgical evaluation for localization of seizure focus]</td>
</tr>
<tr>
<td>R22.0 - R22.1, R90.0</td>
<td>Swelling, mass, or lump in head and neck</td>
</tr>
<tr>
<td>R56.1</td>
<td>Post traumatic seizures</td>
</tr>
<tr>
<td>R56.9</td>
<td>Unspecified convulsions [pre-surgical evaluation for localization of seizure focus only]</td>
</tr>
<tr>
<td>R91.1</td>
<td>Solitary pulmonary nodule</td>
</tr>
<tr>
<td>T66.xxx+</td>
<td>Radiation sickness, unspecified [radiation necrosis]</td>
</tr>
<tr>
<td>ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>B38.0 - B38.9</td>
<td>Coccidioidomycosis</td>
</tr>
<tr>
<td>C22.0 - C48.0</td>
<td>Malignant neoplasm of liver and intrahepatic bile ducts, gallbladder and extrahepatic bile ducts and retroperitoneum</td>
</tr>
<tr>
<td>C38.0</td>
<td>Malignant neoplasm of heart</td>
</tr>
<tr>
<td>C44.00 - C44.99</td>
<td>Other and unspecified malignant neoplasm of skin</td>
</tr>
<tr>
<td>C46.0 - C55</td>
<td>Malignant neoplasm of Kaposi's sarcoma and uterus, part unspecified</td>
</tr>
</tbody>
</table>

Z85.01, Z85.028, Z85.030 - Z85.038, Z85.040 - Z85.048, Z85.110 - Z85.12, Z85.21 - Z85.22, Z85.3, Z85.41, Z85.43, Z85.47, Z85.71 - Z85.79, Z85.820, Z85.830, Z85.840 - Z85.841, Z85.850 - Z85.858

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
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C49.8</td>
<td>Malignant neoplasm of overlapping sites of connective and soft tissue [not covered for spindle cell sarcoma]</td>
</tr>
<tr>
<td>C54.0 - C54.9</td>
<td>Malignant neoplasm of corpus uteri</td>
</tr>
<tr>
<td>C58</td>
<td>Malignant neoplasm of placenta</td>
</tr>
<tr>
<td>C60.0 - C67.9</td>
<td>Malignant neoplasm of penis and other male genital organs, bladder, and kidney and other and unspecified urinary organs [including Wilms’ tumor]</td>
</tr>
<tr>
<td>C61</td>
<td>Malignant neoplasm of prostate</td>
</tr>
<tr>
<td>C70.0 - C70.9, C72.0 - C72.1, C72.50 - C72.9</td>
<td>Malignant neoplasm of other and unspecified parts of nervous system</td>
</tr>
<tr>
<td>C77.9</td>
<td>Secondary and unspecified malignant neoplasm of lymph nodes, site unspecified</td>
</tr>
<tr>
<td>C78.2 - C78.39</td>
<td>Secondary malignant neoplasm of pleura and other respiratory organs</td>
</tr>
<tr>
<td>C78.6 - C78.7</td>
<td>Secondary malignant neoplasm of retroperitoneum and peritoneum, and liver, specified as secondary</td>
</tr>
<tr>
<td>C79.00 - C79.52</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>
</tr>
<tr>
<td>C79.70 - C79.72</td>
<td>Secondary malignant neoplasm of adrenal gland</td>
</tr>
<tr>
<td>C79.82</td>
<td>Secondary malignant neoplasm of genital organs</td>
</tr>
<tr>
<td>C79.89</td>
<td>Secondary malignant neoplasm of other specified sites</td>
</tr>
<tr>
<td>C86.3</td>
<td>Blastic NK-cell lymphoma [plasmacytoid dendritic cell neoplasm]</td>
</tr>
<tr>
<td>C88.8, C90.10 - C95.92</td>
<td>Plasma cell leukemia and immunoproliferative neoplasms, lymphoid leukemia, myeloid leukemia, monocytic leukemia, and other specified leukemia</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>C94.40 -</td>
<td>Neoplasm of uncertain behavior of breast and other lymphatic and hematopoietic tissues</td>
</tr>
<tr>
<td>C94.46</td>
<td></td>
</tr>
<tr>
<td>D45 - D71, D47.3, D47.21 - D47.9</td>
<td></td>
</tr>
<tr>
<td>D01.3 - D01.9</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>D04.0 - D04.9</td>
<td>Carcinoma in situ of skin</td>
</tr>
<tr>
<td>D07.1</td>
<td>Carcinoma in situ of vulva</td>
</tr>
<tr>
<td>D09.3 - D09.9</td>
<td>Carcinoma in situ of other and unspecified sites</td>
</tr>
<tr>
<td>D10.0 - D36.9</td>
<td>Benign neoplasms [including paraganglioma]</td>
</tr>
<tr>
<td>D37.6, D48.3 - D8.4</td>
<td>Neoplasm of uncertain behavior of liver and biliary passages, and retroperitoneum and peritoneum</td>
</tr>
<tr>
<td>D38.5 - D41.9, D44.0 - D44.9</td>
<td>Neoplasm of uncertain behavior of other and unspecified respiratory organs, genitourinary organs, and endocrine glands</td>
</tr>
<tr>
<td>D45, D46.0 - D46.9, D47.0 - D47.4, D47.29, D48.60 - D48.62</td>
<td>Neoplasm of uncertain behavior of breast and other lymphatic and hematopoietic tissues</td>
</tr>
<tr>
<td>D48.1</td>
<td>Neoplasm of uncertain behavior of connective and other soft tissue [includes giant cell tumor of the bone]</td>
</tr>
<tr>
<td>D49.3 - D49.7</td>
<td>Neoplasm of unspecified behavior of breast, bladder, other genitourinary organs, brain, and endocrine glands and other parts of nervous system</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>D49.9</td>
<td>Neoplasm of unspecified behavior, of unspecified site</td>
</tr>
<tr>
<td>D73.2</td>
<td>Chronic congestive splenomegaly</td>
</tr>
<tr>
<td>E71.520 - E71.529</td>
<td>X-linked adrenoleukodystrophy</td>
</tr>
<tr>
<td>D72.1</td>
<td>Eosinophilia</td>
</tr>
<tr>
<td>D76.3</td>
<td>Other histiocytosis with massive lymphadenopathy [Roasi-Dorfman disease]</td>
</tr>
<tr>
<td>D86.0 - D86.9</td>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>E83.52</td>
<td>Hypercalcemia</td>
</tr>
<tr>
<td>F01 - F99</td>
<td>Mental disorders</td>
</tr>
<tr>
<td>G00.0 - G37.9, G43.001 - G99.8</td>
<td>Diseases of the nervous system and sense organs [except pre-surgical evaluation for localization of seizure focus]</td>
</tr>
<tr>
<td>H00,011 - H59.89, H60.00 - H95.89</td>
<td>Heart disease</td>
</tr>
<tr>
<td>I00 - I52</td>
<td>Heart disease</td>
</tr>
<tr>
<td>J84.82</td>
<td>Adult pulmonary Langerhans cell histiocytosis</td>
</tr>
<tr>
<td>J90 - J91.8</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>K72.01, K72.11, K72.91</td>
<td>Hepatic encephalopathy</td>
</tr>
<tr>
<td>L72.11</td>
<td>Pilar cysts [Pilar tumor]</td>
</tr>
<tr>
<td>M01.x51 - M01.x59</td>
<td>Direct infection of hip in infectious and parasitic diseases classified elsewhere</td>
</tr>
<tr>
<td>M05.00 - M14.89</td>
<td>Inflammatory polyarthropathies</td>
</tr>
<tr>
<td>M12.20 - M12.29</td>
<td>Villonodular synovitis (pigmented)</td>
</tr>
<tr>
<td>M31.4</td>
<td>Aortic arch syndrome [Takayasu]</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>M86.30 -</td>
<td>Chronic multifocal osteomyelitis</td>
</tr>
<tr>
<td>M86.9</td>
<td></td>
</tr>
<tr>
<td>M88.0 -</td>
<td>Osteitis deformans [Paget's disease of bone]</td>
</tr>
<tr>
<td>M88.9</td>
<td></td>
</tr>
<tr>
<td>O01.0 -</td>
<td>Hydatidiform mole [gestational trophoblastic neoplasia]</td>
</tr>
<tr>
<td>O01.9</td>
<td></td>
</tr>
<tr>
<td>Q89.09</td>
<td>Congenital malformations of spleen [congenital splenomegaly]</td>
</tr>
<tr>
<td>R16.1</td>
<td>Splenomegaly, not elsewhere classified</td>
</tr>
<tr>
<td>R25.0 -</td>
<td>Symptoms and signs involving nervous and musculoskeletal systems</td>
</tr>
<tr>
<td>R29.91</td>
<td></td>
</tr>
<tr>
<td>R40.0 -</td>
<td>Somnolence, stupor and coma</td>
</tr>
<tr>
<td>R40.4</td>
<td></td>
</tr>
<tr>
<td>R41.1 -</td>
<td>Amnesia</td>
</tr>
<tr>
<td>R41.3</td>
<td></td>
</tr>
<tr>
<td>R41.9,</td>
<td>Other general symptoms</td>
</tr>
<tr>
<td>R68.89</td>
<td></td>
</tr>
<tr>
<td>R42.0</td>
<td>Dizziness and giddiness</td>
</tr>
<tr>
<td>R44.0,</td>
<td>Hallucinations and syncope and collapse</td>
</tr>
<tr>
<td>R44.2 -</td>
<td></td>
</tr>
<tr>
<td>R44.3</td>
<td></td>
</tr>
<tr>
<td>R55</td>
<td></td>
</tr>
<tr>
<td>R50.9</td>
<td>Fever, unspecified [fever of unknown origin (FUO)]</td>
</tr>
<tr>
<td>R93.0</td>
<td>Abnormal findings on diagnostic imaging of skull and head, not elsewhere</td>
</tr>
<tr>
<td>R93.1 -</td>
<td>classified</td>
</tr>
<tr>
<td>R93.5</td>
<td></td>
</tr>
<tr>
<td>R94.01 -</td>
<td>Abnormal results of function studies of brain and central nervous system</td>
</tr>
<tr>
<td>R94.138</td>
<td>and peripheral nervous system and special senses</td>
</tr>
<tr>
<td>R94.30 -</td>
<td>Abnormal results of cardiovascular function studies,</td>
</tr>
<tr>
<td>R94.39</td>
<td></td>
</tr>
<tr>
<td>T81.4xx+</td>
<td>Infection following a procedure [infection of hip arthroplasty]</td>
</tr>
<tr>
<td>ICD-10-CM Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>T84.51x+</td>
<td>Infection and inflammatory reaction due to internal joint prosthesis [infection of hip arthroplasty or knee replacement protheses]</td>
</tr>
<tr>
<td>Z00.00 - Z13.9</td>
<td>Persons encountering health services for examination</td>
</tr>
<tr>
<td>Z15.01</td>
<td>Genetic susceptibility to malignant neoplasm of breast [Li-Fraumeni syndrome]</td>
</tr>
<tr>
<td>Z85.00, Z85.810 - Z85.819</td>
<td>Personal history of malignant neoplasm of gastrointestinal tract, unspecified</td>
</tr>
<tr>
<td>Z85.05 - Z85.09</td>
<td>Personal history of malignant neoplasm of liver and of other gastrointestinal tract</td>
</tr>
<tr>
<td>Z85.20 - Z85.29</td>
<td>Personal history of malignant neoplasm of other respiratory and intrathoracic organs</td>
</tr>
<tr>
<td>Z85.42</td>
<td>Personal history of malignant neoplasm of other parts of uterus</td>
</tr>
<tr>
<td>Z85.46</td>
<td>Personal history of malignant neoplasm of prostate</td>
</tr>
<tr>
<td>Z85.48 - Z85.59</td>
<td>Personal history of malignant neoplasm of epididymis, other male genital organs, urinary organs, unspecified</td>
</tr>
<tr>
<td>Z85.6</td>
<td>Personal history of leukemia</td>
</tr>
<tr>
<td>Z85.71 - Z85.79</td>
<td>Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues</td>
</tr>
<tr>
<td>Z85.820 - Z85.828</td>
<td>Personal history of other malignant neoplasm of skin</td>
</tr>
<tr>
<td>Z85.848</td>
<td>Personal history of malignant neoplasm of other parts of nervous system</td>
</tr>
<tr>
<td>Z85.858 - Z85.859</td>
<td>Personal history of malignant neoplasm of other endocrine glands and related structures, other, and unspecified sites</td>
</tr>
<tr>
<td>Z96.641 - Z96.649</td>
<td>Presence of artificial hip</td>
</tr>
</tbody>
</table>

**Neurologic indications for PET:**

**CPT codes covered for indications listed in the CPB:**
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>78608</td>
<td>Brain imaging, positron emission tomography (PET); metabolic evaluation</td>
</tr>
<tr>
<td>78609</td>
<td>perfusion evaluation</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A9586</td>
<td>Florbetapir F18, diagnostic, per study dose, up to 10 millicuries</td>
</tr>
<tr>
<td>A9599</td>
<td>Radiopharmaceutical, diagnostic, for beta-amyloid positron emission tomography (pet) imaging, per study dose</td>
</tr>
<tr>
<td>C9458</td>
<td>Florbetaben f18, diagnostic, per study dose, up to 8.1 millicuries</td>
</tr>
<tr>
<td>C9459</td>
<td>Flutemetamol f18, diagnostic, per study dose, up to 5 millicuries</td>
</tr>
<tr>
<td>Q9982</td>
<td>Flutemetamol F18, diagnostic, per study dose, up to 5 millicuries</td>
</tr>
<tr>
<td>Q9983</td>
<td>Florbetaben f18, diagnostic, per study dose, up to 8.1 millicuries</td>
</tr>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F01.50 -</td>
<td>Dementias</td>
</tr>
<tr>
<td>F01.51</td>
<td></td>
</tr>
<tr>
<td>F03.90 -</td>
<td></td>
</tr>
<tr>
<td>F03.91</td>
<td></td>
</tr>
<tr>
<td>F02.80 -</td>
<td>Dementia in other diseases classified elsewhere with or without behavioral disturbance</td>
</tr>
<tr>
<td>F02.81</td>
<td></td>
</tr>
<tr>
<td>F07.0</td>
<td>Personality change due to known physiological condition</td>
</tr>
<tr>
<td>F03.90 -</td>
<td>Unspecified dementia, without and with behavioral disturbance</td>
</tr>
<tr>
<td>F03.91</td>
<td></td>
</tr>
<tr>
<td>G10</td>
<td>Huntington's disease</td>
</tr>
<tr>
<td>G20 - G21.9</td>
<td>Parkinson's disease</td>
</tr>
<tr>
<td>G30.0 -</td>
<td>Alzheimer's disease</td>
</tr>
<tr>
<td>G30.9</td>
<td></td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>R41.1 - R41.3</td>
<td>Amnesia</td>
</tr>
<tr>
<td>R43.0 - R43.9</td>
<td>Disturbances of smell and taste</td>
</tr>
<tr>
<td>Z13.858`</td>
<td>Encounter for screening for other nervous system disorders</td>
</tr>
<tr>
<td>Z82.0</td>
<td>Family history of epilepsy and other diseases of the nervous system</td>
</tr>
</tbody>
</table>

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Amendment to
Aetna Clinical Policy Bulletin Number:0071
Positron Emission Tomography (PET)

There are no amendments for Medicaid.