6.01.26	Oncologic Applications of Positron Emission Tomography Scanning		
Original Policy Date:	January 26, 2009	**Effective Date:**	February 1, 2021
Section:	6.0 Radiology	**Page:**	Page 1 of 66

Policy Statement

Positron emission tomography (PET) scanning may be considered **medically necessary** in **any** of the following:

I. **Bladder Cancer** - PET scanning for staging or restaging of bladder cancer with documentation of **both** of the following:
   A. Presence of muscle-invasive bladder cancer
   B. When CT or magnetic resonance imaging are not indicated or remained inconclusive on distant metastasis

II. **Bone Sarcoma** - PET scanning for staging or restaging of Ewing sarcoma and osteosarcoma

III. **Brain Cancer** – PET scanning for staging or restaging of brain cancer

IV. **Breast Cancer** - PET scanning for staging or restaging of breast cancer for detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes) with documentation of **both** of the following:
   A. Suspicion of disease is high
   B. Other imaging is inconclusive

V. **Cervical Cancer** – PET scanning for **any** of the following:
   A. Initial staging of patient with locally advanced cervical cancer
   B. Evaluation of a known or suspected recurrence

VI. **Colorectal Cancer** – PET scanning for **any** of the following:
   A. Staging or restaging to detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer
   B. To evaluate a rising and persistently elevated carcinoembryonic antigen (CEA) levels when standard imaging, including CT scan, is negative

VII. **Endometrial Cancer** – PET scanning for **any** of the following:
   A. Detection of lymph node metastases
   B. Assessment of endometrial cancer recurrence

VIII. **Esophageal Cancer** - PET scanning for **any** of the following:
   A. Staging of esophageal cancer
   B. Determining response to preoperative induction therapy

IX. **Gastric Cancer** – PET scanning for **any** of the following:
   A. Initial diagnosis and staging of gastric cancer
   B. Evaluation for recurrent gastric cancer with documentation of **both** of the following:
   C. After surgical resection
   D. When other imaging modalities are inconclusive

X. **Head and Neck Cancer** – PET scanning for **any** of the following:
   A. Initial diagnosis of suspected cancer
   B. Initial staging of disease
   C. Restaging of residual or recurrent disease during follow-up
   D. Evaluation of response to treatment

XI. **Lung Cancer, Non-small cell (NSCLC)** – PET scanning for **any** of the following:
   A. Patient with a solitary pulmonary nodule as a single scan technique (not dual time) to distinguish between benign and malignant disease when prior CT scan and chest x-ray findings are inconclusive or discordant
   B. Staging or restaging technique in those with known non-small-cell lung cancer
   C. To determine resectability for patient with a presumed solitary metastatic lesion from lung cancer

XII. **Lung Cancer, small cell (SCLC)** - PET scanning for staging of small-cell lung cancer if limited stage is suspected based on standard imaging

XIII. **Lymphoma, Including Hodgkin Disease** – PET scanning as a technique for staging lymphoma either during initial staging or for restaging at follow-up

XIV. **Melanoma** – PET scanning as a technique for assessing extranodal spread of malignant melanoma at initial staging or at restaging during follow-up treatment every 4 to12 months to screen high-risk patient for advanced disease with documentation of **both** of the following:
   A. Stage IIB or higher
   B. Five years or less since date of diagnosis

XV. **Multiple Myeloma** – PET scanning for staging or restaging of multiple myeloma, particularly if the skeletal survey is negative

XVI. **Neuroendocrine tumors** – PET scanning for neuroendocrine tumors with documentation of **both** of the following:
   A. Gallium-68 PET
   B. For initial staging or for restaging

XVII. **Ovarian Cancer** – PET scanning in the evaluation of patient with a prior history of ovarian cancer with documentation of **both** of the following:
   A. Signs and/or symptoms of suspected ovarian cancer recurrence (restaging)
   B. Standard imaging, including CT scan, is inconclusive

XVIII. **Pancreatic Cancer** – PET scanning in the initial diagnosis and staging of pancreatic cancer with documentation of **both** of the following:
   A. Other imaging is inconclusive
   B. Biopsy is inconclusive

XIX. **Prostate Cancer** – PET scanning for evaluating suspected or biochemically recurrent small volume prostate cancer in soft tissues with documentation of **both** of the following:
   A. Tracer use as indicated by **any** of the following:
      1. Carbon 11 choline
      2. Fluorine 18 fluciclovine
   B. Primary treatment has been completed (e.g.: surgery, radiation therapy)

XX. **Soft Tissue Sarcoma** - PET scanning for gastrointestinal stromal tumors to evaluate response to imatinib and other treatments

XXI. **Testicular Cancer** – PET scanning in testicular cancer with **all** of the following:
   A. Stage IIB and III seminoma
   B. Initial chemotherapy has been completed
   C. Within 6 weeks of completion of chemotherapy

XXII. **Thyroid Cancer** – PET scanning in the restaging of patient with **all** of the following:
   A. Histology is differentiated (not anaplastic)
   B. Thyroglobulin levels (Tg) are elevated
   C. Whole-body iodine-131 imaging is negative

XXIII. **Cancer of Unknown Primary** – PET scanning in cancer of unknown primary with **all** of the following:
   A. Single site of disease outside the cervical lymph nodes and local or regional treatment is being considered for this single site of metastatic disease
   B. Negative workup for an occult primary tumor
   C. PET scan to be used to rule out or detect additional sites of disease that would eliminate the rationale for local or regional treatment

The following are considered **investigational**:

I. **Bladder Cancer** – PET scanning for bladder tumors that have not invaded the muscle (stage less than cT2)

II. **Bone Sarcoma** – PET scanning for staging of chondrosarcoma

III. **Breast Cancer** – PET scanning for evaluation of breast cancer due to **any** of the following:
   A. Differential diagnosis in patient with suspicious breast lesions or an indeterminate or low suspicion finding on mammography
   B. Staging axillary lymph nodes
   C. Predicting pathologic response to neoadjuvant therapy for locally advanced disease

IV. **Colorectal Cancer** - PET scanning for **any** of the following:

   A. A technique to assess the presence of scarring versus local bowel recurrence in patient with previously resected colorectal cancer
   B. A technique contributing to radiotherapy treatment planning

V. **Esophageal Cancer** – PET scanning for other aspects of the evaluation of esophageal cancer including detection of primary esophageal cancer
VI. **Lung Cancer** – PET scanning for staging of small-cell lung cancer if extensive stage is established
VII. **Melanoma** – PET scanning for **any** of the following:
   A. In managing stage 0, I, or II melanoma
   B. As a technique to detect regional lymph node metastases in patient with clinically localized melanoma who is a candidate to undergo sentinel node biopsy
VIII. **Neuroendocrine tumors** – PET scanning with radiotracers (other than Gallium-68) in all aspects for managing neuroendocrine tumors
IX. **Ovarian Cancer** – PET scanning in the initial evaluation of known or suspected ovarian cancer in all situations
X. **Pancreatic Cancer** – PET scanning as a technique to evaluate other aspects of pancreatic cancer
XI. **Penile Cancer** – PET scanning in all aspects of managing penile cancer
XII. **Prostate Cancer** – PET scanning in **any** of the following:
   A. With gallium 68 in all aspects of managing prostate cancer
   B. In all other indications in known or suspected prostate cancer
XIII. **Renal Cell Carcinoma** – PET scanning in all aspects of managing renal cancer
XIV. **Soft Tissue Sarcoma** - PET scanning for evaluation of soft tissue sarcoma in **any** of the following:
   A. Distinguishing between benign lesions and malignant soft tissue sarcoma
   B. Distinguishing between low-grade and high-grade soft tissue sarcoma
   C. Detecting locoregional recurrence
   D. Detecting distant metastasis
XV. **Testicular Cancer** – PET scanning in evaluation of testicular cancer in **any** of the following:
   A. Initial staging of testicular cancer
   B. Distinguishing between viable tumor and necrosis/fibrosis after treatment of testicular cancer
   C. Detection of recurrent disease after treatment of testicular cancer
XVI. **Thyroid Cancer** – PET scanning in the evaluation of known or suspected differentiated or poorly differentiated thyroid cancer in all other situations
XVII. **Cancer of Unknown Primary** – PET scanning for other indications in patient with a cancer of unknown primary, including but not limited to **any** of the following:
   A. As part of the initial workup of a cancer of unknown primary
   B. As part of the workup of patients with multiple sites of disease
XVIII. **Cancer Surveillance** – PET scanning when used as a surveillance tool for patient with cancer or with a history of cancer. A scan is considered surveillance if performed more than 6 months after completion of cancer therapy (12 months for lymphoma) in patients without objective signs or symptoms suggestive of cancer recurrence (see Policy Guidelines section).

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

As with any imaging technique, the medical necessity of positron emission tomography (PET) scanning depends in part on what imaging techniques are used before or after the PET scanning. PET scanning is typically considered after other techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), or ultrasonography, provide inconclusive or discordant results. In patients with melanoma or lymphoma, PET scanning may be considered an initial imaging technique. If so, the medical necessity of subsequent imaging during the same

diagnostic evaluation is unclear. Thus, PET should be considered for the medically necessary indications above only when standard imaging (e.g., CT, MRI) is inconclusive or not indicated.

Use of PET scanning for surveillance as described in the policy statement and policy rationale refers to the use of PET to detect disease in asymptomatic patients at various intervals. This is not the same as the use of PET for detecting recurrent disease in symptomatic patients; these applications of PET are considered within tumor-specific categories in the policy statements.

PET Scan
All policy statements apply to both positron emission tomography (PET) scans and PET plus computed tomography (CT) scans, (i.e., PET scans with or without PET/CT fusion). For the clinical situations indicated that may be considered medically necessary, this assumes that the results of the PET scan will influence treatment decisions. If the results will not influence treatment decisions, these situations would be considered not medically necessary.

If a PET scan is considered medically necessary per this policy, it is assumed the results will influence treatment decisions. If not, PET scanning would be considered not medically necessary.

Coding
A PET scan involves 3 separate activities:

- Manufacture of the radiopharmaceutical, which may be on site or at a regional center with delivery to the institution performing PET
- Actual performance of the pet scan
- Interpretation of the results

The following CPT and HCPCS codes are available to code for PET scans:
CPT Codes
The following CPT codes are available for reporting PET imaging:

- **78608**: Brain imaging, positron emission tomography (PET); metabolic evaluation
- **78609**: Brain imaging, positron emission tomography (PET); perfusion evaluation
- **78811**: Positron emission tomography (PET) imaging; limited area (e.g., chest, head/neck)
- **78812**: Positron emission tomography (PET) imaging; skull base to mid-thigh
- **78813**: Positron emission tomography (PET) imaging; whole body

The following are CPT codes for concurrently acquired PET and computed tomography (CT):

- **78814**: Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (e.g., chest, head/neck)
- **78815**: Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; skull base to mid-thigh
- **78816**: Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; whole body

When the radiopharmaceutical is provided by an outside distribution center, there may be an additional separate charge, or this charge may be passed through and included in the hospital bill. In addition, an extra transportation charge will be likely for radiopharmaceuticals that are not manufactured on site.

HCPCS Codes
The Centers for Medicare and Medicaid Services (CMS) has maintained a couple of HCPCS codes for Medicare noncovered indications:

- **G0219**: PET imaging whole body; melanoma for noncovered indications
- **G0235**: PET imaging, any site not otherwise specified

- **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)

The Centers for Medicare & Medicaid Services (CMS) added 2 new modifiers in 2009 to facilitate the changes in the Medicare national coverage policy for PET. The modifiers are:

- PI - Positron emission tomography (PET) or PET/computed tomography (CT) to inform the initial treatment strategy of tumors that are biopsy proven or strongly suspected of being cancerous based on other diagnostic testing, 1 per cancer diagnosis
- PS - Positron emission tomography (PET) or PET/computed tomography (CT) to inform the subsequent treatment strategy of cancerous tumors when the beneficiary's treating physician determines that the PET study is needed to inform subsequent anti-tumor strategy

The following are HCPCS codes specific to radiotracers used for PET:

- **A9515**: Choline C-11, diagnostic, per study dose up to 20 millicuries (mCi)
- **A9526**: Nitrogen N-13 ammonia, diagnostic, per study dose, up to 40 mCi
- **A9552**: Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 mCi
- **A9580**: Sodium fluoride F-18, diagnostic, per study dose, up to 30 mCi
- **A9587**: Gallium Ga-68, dotatate, diagnostic, 0.1 mCi
- **A9588**: Fluciclovine F-18, diagnostic, 1 mCi
- **A9598**: Positron emission tomography radiopharmaceutical, diagnostic, for nontumor identification, not otherwise classified

Effective January 1, 2021, the following HCPCS code will **replace HCPCS code C9060** as a radioactive diagnostic agent indicated for use with PET imaging for the detection of estrogen receptor-positive lesions as an adjunct to biopsy in patients with recurrent or metastatic breast cancer:

- **A9591**: Fluoroestradiol f 18, diagnostic, 1 mci

Effective January 1, 2021, there is a new HCPCS code which is a PET scan diagnostic agent intended for identification of somatostatin receptor expressing neuroendocrine tumors:

- **C9068**: Copper Cu-64, dotatate, diagnostic, 1 mci

Description

Positron emission tomography (PET) scans are based on the use of positron-emitting radionuclide tracers coupled to organic molecules, such as glucose, ammonia, or water. The radionuclide tracers simultaneously emit 2 high-energy photons in opposite directions that can be simultaneously detected (referred to as coincidence detection) by a PET scanner, comprising multiple stationary detectors that encircle the area of interest.

The utility of PET scanning for the diagnosis, staging and restaging, and surveillance of malignancies varies by type of cancer. In general, PET scanning can distinguish benign from malignant masses in certain circumstances and improve the accuracy of staging by detecting additional disease not detected by other imaging modalities. Therefore, PET scanning for diagnosis and staging of malignancies can be considered medically necessary when specific criteria are met for specific cancers, as outlined in the policy statements. For follow-up, after initial diagnosis and staging have been performed, there are a few situations in which PET can improve detection of recurrence, and lead to changes in management that improve the net health outcome. The use of PET for interim scanning to assess early response is addressed in Blue Shield of California Medical Policy: Interim Positron Emission Tomography Scanning in Oncology to Detect Early Response During Treatment.

Related Policies

- Cardiac Applications of Positron Emission Tomography Scanning
- Interim Positron Emission Tomography Scanning in Oncology to Detect Early Response During Treatment
- Miscellaneous (Noncardiac, Nononcologic) Applications of Fluorine 18 Fluorodeoxyglucose Positron Emission Tomography

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

The U.S. Food and Drug Administration (FDA) website includes various PET-related documents.[1,]

As of July 2020, the following radiopharmaceuticals have been granted approval by the FDA, to be used with PET for carcinoma-related indications (see Table 1).[2,]

Table 1. Radiopharmaceuticals Approved for Use With PET for Oncologic Applications

Radiopharmaceutical	Manufacturer	Name	Carcinoma-Related Indication With PET
Carbon-11 choline (C-11)	Various		Suspected prostate cancer recurrence based on elevated blood PSA after therapy and noninformative bone scintigraphy, CT, or MRI
Fluorine-18 fluorodeoxyglucose (FDG)	Various		Suspected or existing diagnosis of cancer, all types
Fluorine-18 fluoroestradiol[§]	Zionexa USA	Cerianna™	Detection of ER-positive lesions as an adjunct to biopsy in patients with recurrent or metastatic breast cancer
Fluorine-18 fluciclovine	Blue Earth Diagnostics	Axumin™	Suspected prostate cancer recurrence based on elevated blood PSA levels after treatment
Gallium-68 dotatoc	UIHC - PET Imaging Center		Localization of somatostatin receptor-positive NETs in adult and pediatric patients
Gallium-68 dotatate	Advanced Accelerator Applications	NETSPOT™	Localization of somatostatin receptor-positive NETs in adult and pediatric patients

[§]Approved on May 27, 2020. Projected release date in late 2020/early 2021.[3,]
CT: computerized tomography; ER: estrogen receptor; MRI: magnetic resonance imaging; NET: neuroendocrine tumors; PET: positron emission tomography; PSA: prostate-specific antigen.

Rationale

Background

A variety of tracers are used for positron emission tomography (PET) scanning, including oxygen 15, nitrogen 13, carbon 11 choline, fluorine 18, gallium 68, and fluciclovine 18. Because of their short half-life, some tracers must be made locally using an onsite cyclotron. The radiotracer most commonly used in oncology imaging has been fluorine 18 coupled with fluorodeoxyglucose (FDG), which correlates with glucose metabolism. Fluorodeoxyglucose has been considered useful in cancer imaging because tumor cells show increased metabolism of glucose. The most common malignancies studied have been melanoma, lymphoma, lung, colorectal, and pancreatic cancer.

This evidence review focuses on the use of radiotracers detected with dedicated PET scanners. Radiotracers, such as FDG, may be detected using single-photon emission computerized tomography cameras, a technique that may be referred to as FDG-single-photon emission computerized tomography imaging. The use of single-photon emission computerized tomography cameras for PET radiotracers presents unique issues of diagnostic performance and is not considered herein.

Literature Review

The review has been informed by multiple evaluations of positron emission tomography (PET), including Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessments, other systematic reviews, meta-analyses, and decision analyses.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Positron Emission Tomography and Positron Emission Tomography Plus Computed Tomography Clinical Context and Test Purpose

For this evidence review, PET and PET plus computed tomography (CT) scanning is discussed for the following 4 applications in oncology: diagnosis, staging, restaging, and surveillance. Diagnosis refers to the use of PET as part of the testing used in establishing whether a patient has cancer. Staging refers to the use of PET to determine the stage (extent) of cancer at the time of diagnosis before any treatment is given. Imaging at this time is generally to determine whether the cancer is localized. This also may be referred to as initial staging. Restaging refers to imaging after treatment in 2 situations. Restaging is part of the evaluation of a patient in whom disease recurrence is suspected based on signs and/or symptoms. Restaging also includes determining the extent of malignancy after completion of a full course of treatment. Surveillance refers to the use of imaging in asymptomatic patients (patients without objective signs or symptoms of recurrent disease). This imaging is completed 6 months or more (≥12 months for lymphoma) after completion of treatment. Interim scanning for early response is addressed in Blue Shield of California Medical Policy: Interim Positron Emission Tomography Scanning in Oncology to Detect Early Response During Treatment.

The question addressed in this evidence review is: Does the use of PET or PET/CT improve the net health outcome in patients with suspected, diagnosed, or treated cancer compared with conventional imaging techniques?

The following PICO was used to select literature to inform this review.

Patients
The relevant populations of interest are:
- Patients who are suspected of having cancer.
- Patients diagnosed with cancer and need information on the extent of cancer (initial staging upon diagnosis confirmation or restaging following treatment).
- Patients with cancer who have completed a round of treatment and may be at risk of recurrence.

Interventions
The test being considered is PET or PET/CT. A PET scan is a nuclear medicine 3-dimensional imaging technique. Radioactive tracers are ingested or injected, and radioactive emissions are detected by an imaging device, allowing observations on blood flow, oxygen use, and metabolic processes around the lesions. When CT is added to PET, the images are superimposed, providing additional anatomic information. The most common radioactive tracer used for oncologic applications is fluorine 18 (^{18}F) fluorodeoxyglucose (FDG). Radiation exposure from PET and PET/CT is considered moderate to high.

PET and PET/CT would be administered in a tertiary care center or a facility with the necessary equipment.

Comparators
The comparators of interest are conventional imaging techniques such as ultrasound, magnetic resonance imaging (MRI), and x-rays.

Outcomes
The general outcomes of interest are related to the clinical validity of PET and PET/CT in (1) diagnosing suspected cancers, (2) providing staging or restaging information, and (3) detecting recurrence following cancer treatment. Clinical validity is most often measured by sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV). For the clinical utility of PET and PET/CT to be demonstrated, the tests would need to inform treatment decisions that would improve survival and quality of life.

Clinical validity can be measured as soon as results from PET or PET/CT can be compared with results from conventional imaging techniques. Outcomes for clinical utility are long-term, which, depending on the type of cancer, can range from months or a few years for less aggressive cancers to many years for less aggressive cancers.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess the clinical validity of PET and PET/CT, studies should report sensitivity, specificity, PPV, and NPV. Additionally, studies reporting false-positive rates and false-negative rates are informative.
- To assess the clinical utility of PET and PET/CT, studies should demonstrate how results of these imaging techniques impacted treatment decisions and overall management of the patient.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires a review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy or more effective therapy, avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Most of the evidence on the use of PET scanning in oncology focuses on clinical validity (sensitivity, specificity), and consists mostly of systematic reviews and meta-analyses. There are few rigorous studies assessing the impact of PET on clinical utility. A few studies that have reported on changes in staging and/or treatment that result from the PET scan do not evaluate whether these changes resulted in improvements in the net health outcome. Due to the lack of direct evidence for clinical utility, evidence for clinical validity is presented first, followed by clinical guidelines, which help to outline the indications for which clinical utility is supported.

Bladder Cancer
Systematic Reviews
A systematic review and meta-analysis (10 studies, total N =433 patients) by Zhang et al (2015) evaluated the diagnostic accuracy of FDG-PET and FDG-PET with CT (FDG-PET/CT) in patients with urinary bladder cancer.[4] The 10 studies were assessed for quality using the 14-item Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool. Median QUADAS score was 9 (range, 7-10). Nine of the 10 studies used FDG-PET/CT and 1 used FDG-PET. Nine studies were retrospective and 1 prospective. Meta-analyses showed relatively high sensitivity (82%; 95% confidence interval [CI], 75% to 88%) and specificity (92%; 95% CI, 87% to 95%) in the diagnosis of bladder cancer, with the reference test of pathology results. The meta-analysis funnel plots showed some asymmetry, indicating a potential for publication bias.

Guidelines
American College of Radiology
In 2018, the American College of Radiology (ACR) issued an Appropriateness Criteria for pretreatment staging of muscle-invasive bladder cancer.[5] The ACR stated that FDG-PET/CT "may be appropriate" for the pretreatment staging of muscle-invasive bladder cancer. However, the ACR cited CT, MRI, and chest radiographs as the most appropriate imaging techniques for pretreatment staging.

In 2019, the ACR issued an Appropriateness Criteria for post-treatment surveillance of bladder cancer. For muscle-invasive bladder cancer, FDG-PET/CT may be appropriate for surveillance; however, the ACR states that chest radiograph, CT, and MRI are usually appropriate procedures.[6]

National Comprehensive Cancer Network
Current National Comprehensive Cancer Network (NCCN) guidelines for bladder cancer (v. 5.2020) state that FDG-PET/CT "may be beneficial in selected patients with T2 (muscle-invasive disease) and in patients with ≥cT3 disease (category 2B)."[7] According to the guidelines, FDG-

PET/CT may also be considered if metastasis is suspected in high-risk patients (category 2B). However, the guidelines note that "PET/CT should not be used to delineate the anatomy of the upper urinary tract" or in patients with nonmuscle invasive bladder cancer.

Section Summary: Bladder Cancer
Evidence for the use of FDG-PET and FDG-PET/CT for the diagnosis and for the staging and restaging of muscle-invasive bladder cancer consists of a systematic review and meta-analysis of several studies. Pooled analyses have shown that PET/CT is effective in the staging of muscle-invasive bladder cancer. The evidence supports the use of FDG-PET/CT for the diagnosis and staging and restaging of muscle-invasive bladder cancer.

The evidence does not support the use of FDG-PET/CT for nonmuscle invasive bladder cancer.

Bone Sarcoma
Systematic Reviews
A meta-analysis (12 studies, N=375) by Zhang et al (2020) evaluated FDG-PET and FDG-PET/CT in the diagnosis and staging of chondrosarcoma, a common type of bone sarcoma.[8] Six studies used PET/CT, 5 studies used PET, and 1 study utilized both. For differentiating between chondrosarcoma and benign lesions, the pooled sensitivity and specificity of FDG-PET were 84% (95% CI, 46% to 97%) and 82% (95% CI, 55% to 94%), respectively. The sensitivity and specificity for FDG-PET/CT were also found to be high at 94% (95% CI, 86% to 97%) and 89% (95% CI, 82% to 93%), respectively. There was substantial heterogeneity for sensitivity (I^2, 86.90%; 95% CI, 76.8% to 97.0%) and specificity (I^2, 70.32%; 95% CI, 42.57 to 98.07%) among studies. Most included studies were retrospective (75%) and included small sample sizes (n=7 to 95), potentially introducing bias and variability.

A systematic review and meta-analysis (35 studies, total N =2171 patients) by Liu et al (2015) evaluated FDG-PET and FDG-PET/CT in the diagnosis, staging, and recurrence assessment of bone sarcoma.[9] Most selected studies used PET/CT (n=29). Meta-analyses showed high sensitivity (96%; 95% CI, 93% to 98%) and specificity (79%; 95% CI, 63% to 90%) of FDG-PET and FDG-PET/CT to differentiate primary bone sarcomas from benign lesions. For pooled results for detecting recurrence, sensitivity was 92% (95% CI, 85% to 97%) and specificity was 93% (95% CI, 88% to 96%). For pooled results for detecting distant metastases, sensitivity was 90% (95% CI, 86% to 93%) and specificity was 85% (95% CI, 81% to 87%). Subgroup analysis by specific metastatic site revealed that PET alone was less effective in detecting lung metastases than other metastatic sites (sensitivity, 71%; 95% CI, 52% to 86%; specificity, 92%; 95% CI, 87% to 96%).

A systematic review (13 studies, total N =342 patients) and meta-analysis (5 studies, n=279 patients) by Treglia et al (2012) examined the diagnostic accuracy of FDG-PET and FDG-PET/CT in Ewing sarcoma.[10] The meta-analysis showed high estimates of sensitivity and specificity for FDG-PET and FDG-PET/CT (pooled sensitivity, 96%; pooled specificity, 92%).

Guidelines
Current NCCN guidelines for bone cancer (v.1.2020) state that PET/CT may be considered for[11]:

- Workup of patients with chordoma, Ewing sarcoma, or osteosarcoma,
- Restaging in patients with Ewing sarcoma or osteosarcoma, and
- Surveillance of patients with Ewing sarcoma or osteosarcoma, every 3 months for 2 years, every 4 months during year 3 , every 6 months during years 4 and 5 , then once annually (category 2B).

Section Summary: Bone Sarcoma
Evidence for the use of FDG-PET and FDG-PET/CT for the diagnosis and for the staging and restaging of bone sarcoma consists of systematic reviews and meta-analyses. Pooled analyses have shown that PET is effective in the staging of bone sarcoma, including chondrosarcoma. Use of PET has also shown high sensitivities and specificities in detecting metastases in bone and

lymph nodes but low sensitivity in detecting lung metastases. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of bone sarcoma.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of bone sarcoma.

Brain Tumors
FDG-PET and ^{18}F-FET PET

Systematic Reviews
A systematic review and meta-analysis by Dunet et al (2016) included studies published through January 2015 in which patients with suspected primary or recurrent brain tumors underwent both fluorine 18 fluoro-ethyl-tyrosine PET (^{18}F-FET-PET) and FDG-PET.[12] Four studies (total N =109 patients) met the inclusion criteria. All 4 studies included in the meta-analysis had scores greater than 10 in the 15-point QUADAS tool. The ^{18}F-FET PET (pooled sensitivity, 94%; 95% CI, 79% to 98%; pooled specificity, 88%; 95% CI, 37% to 99%) performed better than FDG-PET (pooled sensitivity, 38%; 95% CI, 27% to 50%; pooled specificity, 86%; 95% CI, 31% to 99%) in the diagnosis of brain tumors. Target to background ratios of both FDG and FET were similar in detecting low- and high-grade gliomas.
A systematic review and meta-analysis by Dunet et al (2012) included studies published through January 2011 and assessed the use of FET in detecting primary brain tumors.[13] Thirteen studies (total N =462 patients) were included in the systematic review and 5 (n=224 patients) were included in the meta-analysis. All 5 studies in the meta-analysis had scores above 10 on the 14-point QUADAS scale. The pooled sensitivity for F-FET PET in detecting primary brain tumors was 82% (95% CI, 74% to 88%) and pooled specificity was 76% (95% CI, 44% to 92%). Other imaging modalities for diagnosing brain tumors were not included in this analysis, so no conclusions could be made about comparative effectiveness.

FDG-PET and ^{11}C-Methionine PET
Systematic Reviews
A meta-analysis by Zhao et al (2014) compared the diagnostic performance of FDG-PET with carbon 11 (^{11}C) methionine PET in the detection of suspected primary brain tumors and suspected recurrence of brain tumors following treatment.[14] The literature search included studies published through February 2013. A total of 24 studies provided data on the use of FDG-PET and 11 studies reported on the use of ^{11}C-methionine PET. The pooled sensitivity and specificity of FDG-PET in detecting primary or recurrent brain tumors were 71% (95% CI, 63% to 78%) and 77% (95% CI, 67% to 85%), respectively. Diagnostic performance was better with ^{11}C-methionine PET, with a pooled sensitivity and specificity of 91% (95% CI, 85% to 94%) and 86% (95% CI, 78% to 92%), respectively.

In another meta-analysis, Deng et al (2013) assessed the ability of ^{11}C-methionine PET and MRI to detect glioma recurrence.[15] The literature search included articles through March 2012. All selected studies were retrospective cohorts, 11 using ^{11}C-methionine PET (n=244 patients) and 7 using MRI (n=214 patients). Meta-analyses found that the dynamic susceptibility contrast-enhanced MRI (pooled sensitivity, 88%; 95% CI, 82% to 93%; pooled specificity, 85%; 95% CI, 75% to 92%) performed similarly to ^{11}C-methionine PET (pooled sensitivity, 87%; 95% CI, 81% to 92%; pooled specificity, 81%; 95% CI, 72% to 89%) in glioma recurrence detection, with ^{11}C-methionine being slightly less specific.

Guidelines
Current NCCN guidelines for brain cancer (v. 2.2020) include these statements:[16]

- PET can assess metabolism within the tumor and normal tissue by using radio-labeled tracers, which may be useful in differentiating tumor from radiation necrosis, may correlate with tumor grade, or provide an optimal area for biopsy.
- Limitations include the accuracy of interpretations and availability of equipment and isotopes.

- Close follow-up imaging, MR perfusion, MR spectroscopy, PET/CT imaging, and repeat surgery may be necessary if clinically indicated. Educate patients on the uncertainty of imaging as a whole, and the potential need for corollary testing to interpret scans.

Section Summary: Brain Tumors
Evidence for the use of PET to diagnose and stage brain cancer consists of several systematic reviews and meta-analyses. The diagnostic capabilities of PET vary by radiotracer used. There was a direct comparison of radiotracers, with ^{18}F-FET-PET showing better diagnostic accuracy than FDG-PET. An indirect comparison between FDG-PET and ^{11}C-methionine PET showed that ^{11}C-methionine PET performed better, and another indirect comparison of ^{11}C-methionine PET and MRI showed a comparable diagnostic capability between methods. The evidence supports the use of FDG-PET, ^{18}F-FET-PET, and ^{11}C-methionine PET for the diagnosis and staging and restaging of brain tumors.

The evidence does not support the use of FDG-PET, ^{18}F-FET-PET, and ^{11}C-methionine PET for surveillance of brain tumors.

Breast Cancer
Breast Cancer Diagnosis

Systematic Reviews
Liang et al (2017) conducted a meta-analysis on the use of PET/CT to assess axillary lymph node metastasis.[17.] Results from the meta-analyses of 14 studies using MRI and 10 studies using PET/CT showed that MRI had a higher sensitivity in diagnosing axillary lymph node status.

In a meta-analysis of 8 studies (total N =873 patients) on FDG-PET performed in women with newly discovered suspicious breast lesions, Caldarella et al (2014) reported pooled sensitivity and specificity of 85% (95% CI, 83% to 88%) and 79% (95% CI, 74% to 83%), respectively, on a per lesion basis.[18.] As previously noted, a false-negative rate of 15% (100% - sensitivity) may be considered unacceptable given the relative ease of breast biopsy.

A systematic review by Sloka et al (2007) on PET for staging axillary lymph nodes identified 20 studies.[19.] Three of these 20 studies were rated high quality, indicating broad generalizability to a variety of patients and no significant flaws in research methods. The remaining studies were less generalizable due to flaws in the methodology. Reviewers observed that there was great variability in estimates of sensitivity and specificity from the selected studies and that it was difficult to draw conclusions from the evidence.

A TEC Assessment (2001) focused on multiple applications of PET scanning in breast cancer, including characterizing breast lesions, staging axillary lymph nodes, detecting recurrence, and evaluating response to treatment.[20.] A TEC Assessment (2003) reexamined all indications except for characterizing breast lesions.[21.] The bulk of the data on FDG-PET for breast cancer focuses on its ability to characterize breast lesions further such that patients could avoid biopsy of a mammographically indeterminate or suspicious lesion. The key statistic in this analysis is the false-negative rate, because patients with a false-negative result on a PET scan may inappropriately forgo a biopsy and subsequent treatment. The false-negative rate will vary with the underlying prevalence of the disease but may range from 5.5% to 8.5%. Given the relative ease of breast biopsy, this false-negative rate may be considered unacceptable, and thus patients may undergo biopsy regardless of the results of a PET scan.

Breast Cancer Staging
A meta-analysis by Hong et al (2013) reported a sensitivity and a specificity of FDG-PET/CT in diagnosing distant metastases in breast cancer patients of 96% (95% CI, 90% to 98%) and 95% (95% CI, 92% to 97%), respectively, based on 8 studies (N =748).[22.] In a meta-analysis of 6 comparative studies (n=664 patients), the sensitivity and specificity were 97% (95% CI, 84% to

99%) and 95% (95% CI, 93% to 97%) with FDG-PET/CT compared with 56% (95% CI, 38% to 74%) and 91% (95% CI, 78% to 97%) with conventional imaging, all respectively.

Rong et al (2013) conducted a meta-analysis of 7 studies (total N =668 patients) and reported that the sensitivity and specificity of FDG-PET/CT were greater than bone scintigraphy for detecting bone metastasis in breast cancer patients.[23] The sensitivity and specificity of FDG-PET/CT were 93% (95% CI, 82% to 98%) and 99% (95% CI, 95% to 100%) compared with 81% (95% CI, 58% to 93%) and 96% (95% CI, 76% to 100%) for bone scintigraphy, all respectively.

A meta-analysis by Isasi et al (2005) focused on PET for detecting recurrence and metastases.[24] The analysis concluded that PET is a valuable tool; however, they did not compare PET performance with that of other diagnostic modalities, so it is unclear whether the use of PET resulted in different management decisions and health outcomes.

The TEC Assessment (2003) described above in the Breast Cancer Diagnosis section concluded that the use of FDG-PET for staging axillary lymph nodes did not meet TEC criteria.[21]

Breast Cancer Restaging
A systematic review by Xiao et al (2016) evaluated the diagnostic efficacy of FDG-PET and FDG-PET/CT in detecting breast cancer recurrence.[25] The literature search, conducted through January 2016, identified 26 studies (total N =1752 patients) for inclusion in the analysis; 12 studies used PET and 14 studies used PET/CT. Fourteen studies had QUADAS scores greater than 10. Reasons for suspected recurrence in the 1752 patients were: elevated tumor markers (57%), suspicion from conventional imaging modalities (34%), and suggestive clinical symptoms or physical examination results (9%). Pooled sensitivity and specificity are presented in Table 2. Subgroup analyses showed that PET/CT was more specific than PET alone in diagnosing recurrent breast cancer (p=0.035).

A systematic review by Liu et al (2016) compared FDG-PET or FDG-PET/CT with MRI in assessing pathologic complete response to neoadjuvant chemotherapy in patients with breast cancer.[26] The literature search, conducted through August 2015, identified 6 studies (total N =382 patients) for inclusion. Quality assessment of the studies was deemed satisfactory using the QUADAS-2 scale. Meta-analysis results are presented in Table 2.

In another meta-analysis comparing FDG-PET with MRI and evaluating pathologic complete response to neoadjuvant chemotherapy (NAC) in patients with breast cancer, Sheikhbahaei et al (2016) selected 10 studies for analysis.[27] The inclusion criteria differed slightly from Liu et al (2016). Liu et al (2016) required that both FDG-PET and MRI be performed before and during (or after) NAC, while Sheikhbahaei et al (2016) did not require the scanning before NAC. Pooled sensitivities and specificities are listed in Table 2. Subgroup analysis was performed, by the time of scanning (during NAC and after NAC was completed).

Other reviews, including Li et al (2018), have also compared MRI with PET or PET/CT in evaluating response to NAC.[28] Meta-analytic results are similar to previous studies and are presented in Table 2.

Table 2. Pooled Diagnostic Performance of FDG-PET and MRI in Detection of Residual Disease After NAC for Breast Cancer

Type of Imaging	No. of Studies (Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %
Li et al (2018)[28]			
MRI	13 (575)	88 (78 to 94)	69 (51 to 83)
FDG-PET or FDG-PET/CT	13 (618)	77 (58 to 90)	78 (63 to 88)
Xiao et al (2016)[25]			
FDG-PET or FDG-PET/CT	26 (1752)	90 (88 to 90)	81 (78 to 84)
Liu et al (2016)[26]			
MRI	6 (382)	65 (45 to 80)	88 (75 to 95)
FDG-PET or FDG-PET/CT	6 (382)	86 (76 to 93)	72 (49 to 87)

Type of Imaging	No. of Studies (Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %
Sheikhbahaei et al (2016)[27]			
All studies			
MRI	10 (492)	88 (76 to 95)	55 (41 to 68)
FDG-PET or FDG-PET/CT	10 (535)	71 (52 to 85)	77 (58 to 89)
FDG-PET/CT	7 (385)	82 (62 to 92)	79 (52 to 93)
FDG-PET	3 (150)	43 (26 to 63)	73 (44 to 91)
During NAC			
MRI	3 (256)	89 (66 to 97)	42 (20 to 68)
FDG-PET/CT	3 (256)	91 (86 to 95)	69 (25 to 93)
After NAC completion			
MRI	7 (236)	88 (71 to 96)	63 (51 to 74)
FDG-PET or FDG-PET/CT	7 (279)	57 (40 to 71)	80 (65 to 90)
FDG-PET/CT	4 (129)	71 (42 to 89)	88 (73 to 95)

CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; MRI: magnetic resonance imaging; NAC: neoadjuvant chemotherapy; PET: positron emission tomography.

Two 2012 meta-analyses pooled studies on the use of FDG-PET to predict pathologic response to neoadjuvant therapy before surgery for locally advanced breast cancer.[29,30] Both reviews reported similar pooled point estimates for sensitivity and specificity. Both concluded that PET had reasonably high sensitivity and relatively low specificity. Neither described how PET should be used to influence patient management decisions and therefore whether health outcomes would be changed relative to decisions not based on PET results. Thus, it is unclear whether PET improves outcomes for predicting pathologic response to neoadjuvant therapy for locally advanced breast cancer.

An NCCN review conducted by Podoloff et al (2007) concluded that PET was optional and might be useful for staging and restaging regional or distant metastasis when suspicion is high and other imaging is inconclusive.[31]

Guidelines

American College of Radiology

In 2017, the ACR issued an Appropriateness Criteria for the initial workup and surveillance for local recurrence and distant metastases in asymptomatic women with stage I breast cancer.[32] The ACR noted that FDG-PET/CT is usually not appropriate during initial workup or surveillance of these patients to rule out metastases.

National Comprehensive Cancer Network

Current NCCN guidelines on breast cancer (v. 5.2020) include a category 2B recommendation for FDG-PET/CT as an optional test in the workup of stage IIIA breast cancer.[33]

The NCCN recommends against FDG-PET/CT for lower stage breast cancer (I, II, or operable III) due to high false-negative rates in detecting low-grade lesions or lesions less than 1 cm , low sensitivity in detecting axillary node metastasis , the low prior probability of detectable metastases in these patients , and high false-positive rates. The NCCN considers PET or PET/CT most helpful when "standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease."

The NCCN guidelines do not recommend routine use of PET in asymptomatic patients for surveillance and follow-up after breast cancer treatment. When monitoring the metastatic disease, the guidelines note that PET is "challenging because of the absence of a reproducible, validated, and widely accepted set of standards for disease activity assessment."

Section Summary: Breast Cancer

Evidence for the use of PET or PET/CT in patients with breast cancer consists of TEC Assessments, systematic reviews, and meta-analyses. There is no evidence that PET is useful in diagnosing breast cancer. The false-negative rates of PET in patients with breast cancer are estimated to be

between 5.5% and 8.5%, which can be considered unacceptable, given that breast biopsy can provide more definitive results. Use of PET/CT might be useful in detecting metastases when results from other imaging techniques are inconclusive. The evidence supports the use of FDG-PET and FDG-PET/CT for staging and restaging only if standard staging methods are inconclusive.

The evidence does not support the use of FDG-PET and FDG-PET/CT for diagnosis, staging, and restaging when standard staging methods are conclusive.

The evidence does not support the use of FDG-PET or FDG-PET/CT for surveillance of breast cancer.

Cervical Cancer

Systematic Reviews

In a systematic review of 20 studies, Chu et al (2014) reported a pooled sensitivity and specificity for FDG-PET or FDG-PET/CT of 87% (95% CI, 80% to 92%) and 97% (95% CI, 96% to 98%), respectively, for distant metastasis in recurrent cervical cancer.[34.] For local-regional recurrence, pooled sensitivity and specificity were 82% (95% CI, 72% to 90%) and 98% (95% CI, 96% to 99%), respectively.

In a meta-analysis of 9 cervical cancer recurrence studies, Rong et al (2013) reported sensitivity and a specificity for PET/CT of 94.8% (95% CI, 91.2% to 96.9%) and 86.9% (95% CI, 82.2% to 90.5%), respectively.[23.] Reviewers found the quality of studies on recurrence was average with some limitations. For example, studies included mostly symptomatic women and did not differentiate between PET for diagnosis or surveillance.

An Agency for Healthcare Research and Quality (AHRQ) review (2008) identified several studies using FDG-PET or FDG-PET/CT to stage advanced cervical cancer and to detect and stage recurrent disease.[35.] The report concluded that most studies supported enhanced diagnostic accuracy, which would improve the selection of appropriate treatment for patients. For recurrent disease, PET identified additional sites of metastasis, which would alter treatment decisions in some cases. For example, in a study by Yen et al (2004) of 55 patients whose recurrences were initially considered curable with radical surgical treatment, 27 instead underwent palliative therapy based on PET results.[36.] An NCCN report conducted by Podoloff et al (2009) also identified several studies supporting the use of PET for initial staging and identifying and staging recurrent disease.[37.]

Guidelines

Current NCCN guidelines on cervical cancer (v. 1.2020) state that PET/CT may be considered under the following conditions.[38.]

- Part of the initial non-fertility and fertility-sparing workup for patients with stage I cervical cancer.
- Part of the initial staging workup for detection of stage II, III, or IV metastatic disease.
- Follow-up/surveillance for stage I (only nonfertility sparing) through stage IV at 3 to 6 months after completion of therapy or if there is suspected recurrence or metastases. For stage II-IV, whole-body PET/CT is preferred.

Section Summary: Cervical Cancer

Evidence for the use of PET in patients with cervical cancer consists of systematic reviews and meta-analyses. Pooled results have shown that PET can be used for staging or restaging and detecting recurrent disease. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of cervical cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of cervical cancer.

Colorectal Cancer
Colorectal Cancer Diagnosis

Systematic Reviews
Mahmud et al (2017) conducted a systematic review comparing the use of FDG-PET and FDG-PET/CT with conventional imaging techniques in the staging, treatment response, and follow-up of patients with rectal cancer.[39] The literature review, conducted through April 2016, identified 17 studies (total N =791 patients) for the qualitative review, with 8 of those studies (n=428 patients) included in the meta- analysis. The QUADAS-2 tool was used to assess study quality. A limitation of many of the studies was that there was either no blinding or unclear blinding used for assessing the index test or the reference standard. For the detection of a primary tumor, pooled sensitivity and specificity were 99% (95% CI, 97% to 100%) and 67% (95% CI, 50% to 82%), respectively. For the detection of inguinal lymph nodes, the pooled sensitivity and specificity were 93% (95% CI, 76% to 99%) and 76% (95% CI, 61% to 87%), respectively.

A systematic review by Jones et al (2015) compared the role of FDG-PET and FDG-PET/CT with conventional imaging in the detection of primary nodal disease.[40] Twelve studies met inclusion criteria (total N =494 patients). A m eta-analysis for detecting primary disease in situ showed that PET and PET/CT had a higher sensitivity (99%; 95% CI, 96% to 100%) than CT alone (60%; 95% CI, 46% to 75%).
Two clinical applications of PET scanning were considered in a TEC Assessment (1999): (1) to detect hepatic or extrahepatic metastases and to assess their resectability in patients with colorectal cancer (CRC), either as part of initial staging or after primary resection, and (2) to evaluate the presence of postoperative scar versus recurrent disease as a technique to determine the necessity of tissue biopsy.[41]

The body of evidence indicated that PET scanning added useful information to conventional imaging in detecting hepatic and extrahepatic metastases. In particular, PET detected additional metastases leading to more identification of nonresectable disease, allowing patients to avoid surgery. The strongest evidence came from a study that directly assessed the additional value of PET. In a group of 37 patients thought to have a solitary liver metastasis by conventional imaging, PET correctly upstaged 4 patients and falsely overstaged 1 patient. This and another study found that when PET results were discordant with conventional imaging results, PET was correct in 88% and 97% of patients, respectively. When PET affected management decisions, it was more often used to recommend against surgery.

When used to distinguish between local recurrence and scarring, the comparison is between performing histologic sampling in all patients with a suspected local recurrence and avoiding sampling in patients whose PET scans suggest the presence of a postoperative scar. The key concern is whether the NPV for PET is sufficiently high to influence decision making, specifically to avoid tissue biopsy when the PET scan is negative. The TEC Assessment found that studies available at that time suggested an 8% probability of false-negative results, making it unlikely that patients and physicians would forgo histologic sampling and delay potentially curative repeat resection.

Colorectal Cancer Staging
Systematic Reviews
Results from a meta-analysis of 10 studies by Albertsson et al (2018) found that PET/CT influenced treatment plans for anal cancer, though the impact on survival and quality of life could not be determined.[42]

A meta-analysis by Ye et al (2015) assessed the use of FDG-PET/CT in preoperative TNM staging of CRC.[43] The literature search, conducted through July 2014, identified 28 studies for inclusion. Of the 28 studies, 12 assessed tumor detection rates; 4 evaluated T staging, 20 N staging, and 5 M staging; while 8 examined stage change. Using the QUADAS tool, all studies met 9 or more of the 14 criteria. Pooled diagnostic estimates are listed in Table 3.

Three systematic reviews published in 2014 included overlapping studies that assessed the predictive value of FDG-PET/CT in patients with locally advanced rectal cancer who received neoadjuvant chemoradiotherapy.[44,45,46,] Various PET parameters were investigated (standardized uptake value, response index [percentage of the standardized uptake value decrease from baseline to post neoadjuvant treatment]), and cutoff values varied. Pooled sensitivities ranged from 74% to 82%, and pooled specificities ranged from 64% to 85%. The value of FDG-PET/CT in this setting has yet to be established.

Two systematic reviews were conducted to evaluate the use of PET/CT for radiotherapy planning in patients with rectal cancer. Gwynne et al (2012) compared different imaging techniques for radiotherapy treatment planning and concluded that additional studies would be needed to validate the use of PET in this setting.[47,]

Table 3. Pooled Diagnostic Performance of FDG-PET, FDG-PET/CT, and CT Alone in the Staging of Colorectal Cancer

Type of Imaging	No. of Studies	Diagnostic Threshold	Sensitivity (95% CI), %	Specificity (95% CI), %
T staging				
FDG-PET or FDG-PET/CT	4	Yes	73 (65 to 81)	99 (98 to 99)
N staging				
FDG-PET or FDG-PET/CT	20	Yes	62 (59 to 66)	70 (67 to 73)
FDG-PET/CT alone	12	Yes	70 (66 to 74)	63 (59 to 67)
FDG-PET alone	8	No	36 (29 to 44)	93 (89 to 96)
CT alone	7	No	79 (75 to 80)	46 (41 to 51)
M staging				
FDG-PET or FDG--PET/CT	5	No	91 (80 to 96)	95 (91 to 98)
CT alone	5	No	91 (87 to 94)	16 (8 to 27)

Adapted from Ye et al (2015).[43,]
CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; M staging: distant metastases; N staging: regional lymph nodes; PET: positron emission tomography; T staging: primary tumor.

Colorectal Cancer Restaging

Systematic Reviews

A systematic review by Rymer et al (2016) evaluated the use of FDG-PET/CT in the assessment of the response of locally advanced rectal cancer to neoadjuvant chemoradiotherapy.[48,] The literature search, conducted through April 2014, identified 10 studies (total N =538 patients) for inclusion. Selected studies were high quality, complying with an average 12.7 items on the 14-item QUADAS checklist. Tumors confirmed to have regressed following chemoradiotherapy (responders) had a higher response index with a mean difference of 12% (95% CI, 7% to 18%) and a lower standardized uptake value of -2.5 (95% CI, -3.0 to -1.9%) compared with nonresponders.

A meta-analysis by Yu et al (2015) evaluated the diagnostic value of FDG-PET/CT for detecting local recurrent CRC.[49,] The literature search, conducted through October 2014, identified 26 studies (total N =1794 patients) for inclusion. Study quality was assessed using QUADAS. Pooled sensitivity and specificity were 95% (95% CI, 93% to 97%) and 93% (95% CI, 92% to 95%), respectively.

Maffione et al (2015) conducted a systematic review of FDG-PET for predicting response to neoadjuvant therapy in patients with rectal cancer.[50,] The literature search was conducted through January 2014, with 29 studies meeting inclusion criteria for the meta-analysis. The studies had QUADAS scores ranging from 8 to 14 (median, 12). The pooled sensitivity and specificity for FDG-PET assessment of response to chemoradiotherapy in locally advanced rectal cancer were 73% (95% CI, 71% to 76%) and 77% (95% CI, 75% to 79%), respectively.

In a systematic review, Lu et al (2013), evaluated 510 patients from 11 studies on FDG-PET for CRC tumor recurrence detection in patients with elevated carcinoembryonic antigen.[51] The literature search ran through April 2012. Estimates for FDG-PET and PET/CT pooled sensitivity were 90.3% (95% CI, 85.5% to 94.0%) and 94.1% (95% CI, 89.4% to 97.1%), respectively, and specificities were 80.0% (95% CI, 67.0% to 89.6%) and 77.2% (95% CI, 66.4% to 85.9%), respectively.

Colorectal Cancer Surveillance

Randomized Controlled Trials

Sobhani et al (2018) conducted an open-label RCT to determine whether adding 6 monthly FDG-PET/CT scans to usual surveillance (i.e., 3 monthly physicals and tumor marker assays; 6 monthly liver ultrasounds and chest radiographs; 6 monthly CT scans) of patients with CRC following surgery and/or chemotherapy improves health outcomes.[52] A total of 239 patients in remission were enrolled, with 120 in the intervention arm and 119 in the control arm. After 3 years of follow-up, the failure rate in the intervention group was 29% (31 unresectable recurrences, 4 deaths) and 24% in the control group (27 unresectable recurrences, 1 death), which was not a statistically significant difference.

Guidelines

American College of Radiology

In 2017, the ACR issued Appropriateness Criteria for the pretreatment staging of CRC.[53] In the evaluation of distant metastases, the criteria stated that "routine use of PET/CT is likely not indicated; however, it may provide guidance in cases of advanced, bilobar liver disease to exclude extrahepatic metastases prior to surgical intent to cure."

National Comprehensive Cancer Network

Current NCCN guidelines for colon cancer (v.4.2020) "strongly discourages the routine use of PET/CT scanning for staging, baseline imaging, or routine follow-up" and "recommend consideration of a preoperative PET/CT scan at baseline only if prior anatomic imaging indicates the presence of potentially surgically curable M1 disease."[54] For initial workup of nonmetastatic patients, the guidelines state "PET/CT does not supplant a contrast-enhanced diagnostic CT or MR scan and should only be used to evaluate an equivocal finding on a contrast-enhanced CT scan or MR scan or in patients with strong contraindications to IV [intravenous] contrast." For workup of proven metastatic synchronous adenocarcinoma, the guidelines state that PET/CT may be considered; however, it is generally discouraged in most cases. Use of PET/CT is not recommended for surveillance. The NCCN has noted that PET/CT should not be used to assess response to chemotherapy. The NCCN was divided on the appropriateness of PET/CT when carcinoembryonic antigen level is rising; PET/CT might be considered when imaging study results (e.g., a good quality CT scan) are normal.

Current NCCN guidelines for rectal cancer (v.6.2020) state that PET/CT is "not routinely indicated" and "should only be used to evaluate an equivocal finding on a contrast-enhanced CT or MR scan or in patients with strong contraindications to IV contrast." For certain patients with potential surgically-curable M1 disease, a PET/CT may be considered. Use of PET/CT is not recommended for restaging or for surveillance. Use of PET/CT can be considered if serial carcinoembryonic antigen elevation occurs or if there is documented metachronous metastases.

Section Summary: Colorectal Cancer

Evidence for the detection of primary nodal disease, staging, restaging, and detecting recurrence of CRC consists of a TEC Assessment and several meta-analyses published after the assessment. A meta-analysis evaluating the diagnostic accuracy of PET or PET/CT found a high sensitivity but low specificity. Several pooled analyses evaluating staging or restaging using PET or PET/CT resulted in sensitivities and specificities ranging from 16% to 99%. The evidence for the use of PET or PET/CT did not show a benefit over the use of contrast CT in patients with CRC. The evidence does not support the use of FDG-PET and PET/CT for the diagnosis, staging and restaging, or surveillance of CRC.

Endometrial Cancer

Systematic Review

Bollineni et al (2016) published a systematic review and meta-analysis on the diagnostic value of FDG-PET for endometrial cancer.[55.] The literature search, conducted through August 2015, identified 21 studies for inclusion in the meta-analysis: 13 on detection of lymph node metastases (n=861) and 8 on detection of endometrial cancer recurrence (n=378). Pooled sensitivity and specificity for FDG-PET for detecting lymph node metastases were 72% (95% CI, 63% to 80%) and 94% (95% CI, 93% to 96%), respectively. Pooled sensitivity and specificity for FDG-PET for detecting endometrial cancer recurrence following primary surgical treatment were 95% (95% CI, 91% to 98%) and 91% (95% CI, 86% to 94%), respectively.

Guidelines

Current NCCN guidelines for endometrial cancer (v.1.2020) state that whole-body PET/CT can be considered in the initial workup, in both non-fertility and fertility-sparing management, if metastases are suspected in select patients (based on clinical symptoms, physical findings, or abnormal laboratory findings). PET/CT may also be considered for patients with suspected recurrence or metastases as clinically indicated. Following treatment, PET/CT can be considered in select patients for surveillance, if clarification is needed and metastasis is suspected.

Section Summary: Endometrial Cancer

The evidence supports the use of FDG-PET and PET/CT for the diagnosis, staging and restaging, or surveillance of endometrial cancer.

Esophageal Cancer

For initial diagnosis, PET is generally not considered for detecting primary esophageal tumors, and evidence is lacking in its ability to differentiate between esophageal cancer and benign conditions.

Systematic Reviews

Kroese et al (2018) conducted a systematic review of the use of FDG-PET and FDG-PET/CT for detecting interval metastases following neoadjuvant therapy in patients with esophageal cancer.[56.] The literature search identified 14 studies for inclusion. The QUADAS tool was used to assess quality, with most studies rated moderate. The pooled proportion of patients with true distant metastases as detected by FDG-PET and FDG-PET/CT was 8% (95% CI, 5% to 13%). The pooled proportion of patients with false-positive distant findings was 5% (95% CI, 3% to 9%).

Cong et al (2016) published a meta-analysis evaluating the predictive value of FDG-PET and FDG-PET/CT for tumor response during or after neoadjuvant chemoradiotherapy in patients with esophageal cancer.[57.] The literature search, conducted through January 2016, identified 4 studies (n=192 patients) in which PET or PET/CT was performed during neoadjuvant chemo radiotherapy and 11 studies (n=490 patients) in which PET or PET/CT was performed after neoadjuvant chemoradiotherapy. All studies scored between 9 and 12 using the QUADAS tool. Pooled sensitivity and specificity for PET and PET/CT performed during neoadjuvant chemo radiotherapy were 85% (95% CI, 76% to 91%) and 59% (95% CI, 48% to 69%), respectively. Pooled sensitivity and specificity for PET and PET/CT performed after neoadjuvant chemoradiotherapy were 67% (95% CI, 60% to 73%) and 69% (95% CI, 63% to 74%), respectively.

Goense et al (2015) published a systematic review evaluating FDG-PET and FDG-PET/CT for the detection of recurrent esophageal cancer after treatment with curative intent.[58.] The literature search, conducted through December 2014, identified 8 studies (total N =486 patients) for inclusion. The quality of the studies was considered reasonable using the QUADAS tool, with a low-risk of bias for most studies, and high-risk of bias in a few studies for patient selection. Pooled estimates of sensitivity and specificity of FDG-PET and FDG-PET/CT combined were 96% (95% CI, 93% to 97%) and 78% (95% CI, 66% to 86%), respectively. Subgroup analysis by technique (PET alone and PET/CT) was not possible for sensitivity due to heterogeneity. Specificity subgroup

analysis showed no statistical difference between PET alone and PET/CT in detecting recurrent esophageal cancer.

In a meta-analysis of 245 patients with esophageal cancer from 6 studies, Shi et al (2013) reported that, for detection of regional nodal metastases, FDG-PET/CT had a sensitivity of 55% (95% CI, 34% to 74%) and specificity of 76% (95% CI, 66% to 83%), respectively.[59]

An NCCN report conducted by Podoloff et al (2009) found studies showing that PET is more sensitive than other diagnostic imaging in detecting stage IV disease with distant lymph node involvement.[37] A meta-analysis described in the report found a 67% pooled sensitivity, 97% specificity, and small added value after conventional staging in detecting distant metastasis.

Another use of PET in esophageal cancer is in determining whether to continue chemotherapy for potentially curative resection. The NCCN report by Podoloff et al (2009) described several studies in which response to chemotherapy, defined as a decline in standardized uptake values, correlated with long-term survival.[37] Patients who do not respond to chemotherapy might benefit from this test by being spared futile and toxic chemotherapy. However, the treatment strategy of PET-directed chemotherapy does not appear to have been validated with RCTs showing improved net health outcome.

Guidelines
Current NCCN guidelines for esophageal cancer (v.3.2020) indicate that PET/CT can be considered under the following conditions[60]

- Part of the initial workup if there is no evidence of M1 disease.
- To assess response to preoperative or definitive chemoradiation.
- For staging purposes, prior to surgery to obtain nodal distribution information

The guidelines note that PET/CT for these indications is preferable to PET alone.

Section Summary: Esophageal Cancer
Evidence for PET or PET/CT to detect metastases, predict tumor response to treatment, or to detect recurrence in patients with esophageal cancer consists of meta-analyses. The meta-analyses have shown high sensitivity and specificity estimates for these indications. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of esophageal cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of esophageal cancer.

Gastric Cancer
Systematic Reviews
A systematic review by Li et al (2016) evaluated FDG-PET and FDG-PET/CT for detecting recurrent gastric cancer.[61] The literature search, conducted through February 2015, identified 14 studies (total N =828 patients) for analysis. The analysis combined both imaging techniques; 3 studies used PET alone and 11 studies used PET/CT. Pooled sensitivity and specificity were 85% (95% CI, 75% to 92%) and 78% (95% CI, 72% to 84%), respectively.

In a meta-analysis, Zou and Zhou (2013) evaluated studies published through May 2013 and calculated the sensitivity and specificity of FDG-PET/CT for detecting recurrence of gastric cancer after surgical resection.[62] Eight studies (total N =500 patients) were eligible for the meta-analysis. The studies fulfilled 12 of the 14 QUADAS criteria for methodologic quality. Pooled sensitivity was 86% (95% CI, 71% to 94%) and pooled specificity was 88% (95% CI, 75% to 94%).

A systematic review by Wu et al (2012) pooled 9 studies (total N =562 patient) published through July 2011 that used FDG-PET alone for evaluating recurrent gastric cancer.[63] Each selected study fulfilled at least 9 of the 14 criteria in the QUADAS tool for methodologic quality. Pooled sensitivity

and specificity were 78% (95% CI, 68% to 86%) and 82% (95% CI, 76% to 87%), respectively. Reviewers concluded that PET/CT might be more effective than either PET alone or CT alone, but it was unclear what sources reviewers used for their estimates for PET/CT and CT alone.

Guidelines

Current NCCN guidelines for gastric cancer (v.2.2020) indicate that FDG-PET/CT (but not PET alone) can be used as part of an initial workup if there is no evidence of metastatic disease.[64,]The guidelines note that the sensitivity of FDG-PET/CT is lower than for CT alone due to low tracer accumulation in diffuse and mucinous tumor types but specificity is higher. Use of FDG-PET/CT adds value to the diagnostic workup with higher accuracy in staging (identifying tumor and pertinent nodal groups). The NCCN guidelines also indicate that FDG-PET/CT can be used to evaluate response to treatment, in cases of renal insufficiency or allergy to CT contrast. For surveillance in patients with stage II or III disease, FDG-PET/CT can be considered as clinically indicated but CT scan with oral and IV contrast is preferred.

Section Summary: Gastric Cancer

Evidence for the use of PET to diagnose recurrent gastric cancer consists of meta-analyses. One meta-analysis evaluated FDG-PET alone, 1 evaluated FDG-PET/CT, and another combined the 2 techniques into a single estimate. Sensitivity estimates ranged from 78% to 85% and specificity estimates ranged from 78% to 88%. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of gastric cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of gastric cancer.

Head and Neck Cancer

Systematic Reviews

A meta-analysis by Chen et al (2016) compared MRI, CT, and FDG-PET/CT in the detection of local and metastatic nasopharyngeal carcinomas.[65,] A literature search, conducted through April 2015, identified 23 studies (total N =2413 patients) for inclusion. Table 4 summarizes the results of the meta-analysis.

Table 4. Pooled Diagnostic Performance of FDG-PET/CT, Magnetic Resonance Imaging, and CT Alone in the Detection of Nasopharyngeal Carcinomas

Type of Imaging	No. of Studies (Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %
T staging			
MRI	8 (984)	95 (93 to 97)	76 (71 to 80)
CT alone	4 (404)	84 (79 to 88)	80 (71 to 88)
N staging			
MRI	10 (750)	82 (79 to 84)	71 (65 to 78)
CT alone	4 (340)	92 (85 to 95)	93 (76 to 99)
FDG-PET/CT	10 (629)	88 (85 to 90)	95 (93 to 97)
M staging			
MRI	2 (261)	53 (35 to 70)	99 (96 to 100)
CT alone	2 (98)	80 (44 to 97)	93 (86 to 97)
FDG-PET/CT	7 (1009)	82 (74 to 88)	98 (96 to 99)

Adapted from Chen et al (2016).[65,]
CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; MRI: magnetic resonance imaging; M staging: distant metastases; N staging: regional lymph nodes; PET: positron emission tomography; T staging: primary tumor.

A meta-analysis by Wei et al (2016) compared diagnostic capabilities of FDG-PET/CT, MRI, and single-photon emission CT in patients with residual or recurrent nasopharyngeal carcinoma.[66,] The literature search, conducted through December 2014, identified 17 studies for inclusion. All studies scored at least 9 of 14 in the QUADAS tool. Pooled sensitivity and specificity for F-FDG-PET/CT (n=12 studies) were 90% (95% CI, 85% to 94%) and 93% (95% CI, 90% to 95%), respectively. Pooled sensitivity and specificity for single-photon emission CT (n=8 studies) were 85% (95% CI,

77% to 92%) and 91% (95% CI, 85% to 95%), respectively. Pooled sensitivity and specificity for MRI (n=9 studies) were 77% (95% CI, 70% to 83%) and 76% (95% CI, 73% to 79%), respectively.

Two meta-analyses evaluated FDG-PET or FDG-PET/CT in the detection of residual or recurrent head and neck cancer at various times following treatment.[67,68] Results from these analyses are summarized in Table 5.

Table 5. Pooled Diagnostic Performance of FDG-PET or FDG-PET/CT in the Detection of Head and Neck Cancer

Indication	No. of Studies(Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %
Cheung et al (2016)[67]			
Residual/recurrent at primary site	18 (805)	86 (80 to 91)	82 (79 to 85)
Residual/recurrent at neck nodes	15 (726)	72 (63 to 80)	88 (85 to 91)
Recurrent at distant metastases	3 (184)	85 (65 to 96)	95 (90 to 98)
Local residual/recurrent, <12 wk since therapy	NR	85 (75 to 92)	80 (76 to 83)
Local residual/recurrent, ≥12 wk since therapy	NR	87 (78 to 94)	88 (83 to 93)
Nodal residual/recurrent, <12 wk since therapy	NR	67 (56 to 78)	86 (83 to 89)
Nodal residual/recurrent, ≥12 wk since therapy	NR	83 (61 to 95)	96 (90 to 99)
Sheikhbahaei et al (2015)[68]			
Local recurrence, ≥4 mo since therapy	10 (992)	91 (86 to 95)	89 (83 to 94)
Regional recurrence, ≥4 mo since therapy	8 (885)	88 (80 to 93)	95 (92 to 97)
Distant metastases/second primary, ≥4 mo since therapy	9 (958)	93 (86 to 96)	97 (95 to 98)
Overall diagnostic performance, 4-12 mo since therapy	11 (1003)	95 (91 to 97)	78 (70 to 84)
Overall diagnostic performance, ≥12 mo since therapy	7 (923)	92 (85 to 96)	91 (78 to 96)

CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; NR: not reported; PET: positron emission tomography.

A systematic review by Sheikhbahaei et al (2015) calculated the predictive value of intratherapy or posttherapy FDG-PET or FDG-PET/CT for overall survival (OS) and event-free survival.[69] The literature search, conducted through November 2014, identified 9 studies (n=600 patients) for inclusion in OS calculations and 8 studies (n=479 patients) for inclusion in event-free survival calculations. Patients with a positive scan had significantly worse OS than patients with negative scans (hazard ratio [HR], 3.5; 95% CI, 2.3 to 5.4). The pooled HR for event-free survival was 4.7 (95% CI, 2.6 to 8.6). Relative risks at 2 years and at 3 to 5 years for death and recurrence or progression were calculated, based on the timing of FDG-PET or FDG-PET/CT (see Table 6).

Table 6. Pooled Diagnostic Performance of FDG-PET or FDG-PET/CT in the Detection of Head and Neck Cancer

Outcome	No. of Studies	2 Year RR (95% CI)	No. of Studies	3 to 5 Year RR (95% CI)
Death				
Final FDG-PET or FDG-PET/CT	6	8.3 (3.8 to 18.0)	6	2.2 (1.6 to 3.2)
FDG-PET or FDG-PET/CT, <12 wk posttreatment	8	3.0 (1.9 to 4.6)	4	2.0 (1.3 to 3.2)
FDG-PET or FDG-PET/CT, ≥12 wk posttreatment	3	8.5 (4.0 to 18.3)	6	2.8 (1.9 to 4.0)
Recurrence or progression				
Final FDG-PET or FDG-PET/CT	6	5.2 (3.3 to 8.3)	5	2.6 (1.7 to 4.1)
FDG-PET or FDG-PET/CT, <12 wk posttreatment	9	3.2 (2.0 to 5.2)	6	4.3 (2.1 to 8.7)
FDG-PET or FDG-PET/CT, ≥12 wk posttreatment	2	3.2 (2.0 to 5.2)	2	2.2 (1.5 to 3.1)

Adapted from Sheikhbahaei et al (2015).[69]
CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; PET: positron emission tomography; RR: relative risk.

Four meta-analyses in 2013, 2014, and 2018 reported good sensitivities and specificities with FDG-PET/CT for diagnosing head and neck squamous cell cancers (better than CT and MRI) , detecting head and neck cancer metastases (better than bone scintigraphy), and detecting recurrence.[70,-73]

Additional meta-analyses by Li et al (2017) and Lin et al (2017) have reported that higher values of standard uptake value, metabolic tumor volume, and total lesion glycolysis from FDG-PET/CT might predict a poorer prognosis for patients with nasopharyngeal cancer.[74,75]

Among the 3 studies identified in the TEC Assessment (2000) that used other diagnostic modalities to identify a primary tumor in patients with positive cervical lymph nodes, PET found more primary tumors than the other modalities in 2 studies and identified similar proportions in the third.[76] When data from these 3 studies were pooled, the PET was found to identify a tumor in 38% of cases and other modalities in 21% of cases.

When PET was used to stage cervical lymph nodes initially, the addition of PET to other imaging modalities increased the proportion of patients correctly staged, as confirmed histologically. When compared directly with other imaging modalities, pooled data from several studies has suggested that PET has a better diagnostic performance than CT and MRI. Of 8 studies focusing on the use of PET to detect residual or recurrent disease, 5 found PET to be more specific and sensitive, 2 reported mixed or equivalent results, and 1 reported worse results compared with CT.

Guidelines
Current NCCN guidelines on head and neck cancer (v. 2.2020) indicate that PET/CT can be appropriate for disease evaluation, for detection of metastases or recurrence, and for evaluation of response to treatment (at a minimum of 12 weeks posttreatment to reduce false-positive rate).[77] There is no discussion on the use of PET/CT for surveillance.

Section Summary: Head and Neck Cancer
Evidence for the use of FDG-PET/CT in the management of patients with head and neck cancer consists of systematic reviews and meta-analyses. In patients with head and neck cancers, PET or PET/CT is better able to detect local and metastatic disease than other imaging techniques. Evidence has also shown that FDG-PET/CT may be useful in predicting response to therapy. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of head and neck cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of head and neck cancer.

Lung Cancer
Use of PET scanning may have a clinical role in patients with solitary pulmonary nodules for whom a diagnosis is uncertain after CT scan or chest radiograph. Younger patients who have no smoking history have a relatively low-risk for lung cancer and, in this setting, the NPV of a PET scan is relatively high. If presented with a negative PET scan and information about the very low probability of undetected malignancy, it is quite likely that some patients would choose to avoid the harms of an invasive sampling procedure (i.e., biopsy). A meta-analysis by Barger et al (2012) evaluating pulmonary nodules using dual-time PET (a second scan added after a delay) found that its additive value relative to a single PET scan is questionable.[78]

Non-Small-Cell Lung Cancer
In patients with known non-small-cell lung cancer (NSCLC), the clinical value of PET scanning relates to improved staging information regarding the involvement of mediastinal lymph nodes, which generally excludes patients from surgical excision. A TEC Assessment (1997) discussed a

decision analysis that suggested the use of CT plus PET scanning in staging mediastinal lymph nodes resulted in fewer surgeries and an average gain in life expectancy of 2.96 days.[79] This suggests that the reduction in surgeries was not harmful to patients.

Systematic Reviews

Brea et al (2018) conducted a systematic review comparing MRI, CT, FDG-PET, and FDG-PET/CT in differentiating metastatic and nonmetastatic lymph nodes.[80] A meta-analysis was not conducted. Reviewers reported that most studies showed MRI had higher sensitivities, specificities, and diagnostic accuracy than CT and PET in determining the malignancy of lymph nodes in patients with NSCLC.

A systematic review by Ruilong et al (2017) evaluated the diagnostic value of FDG-PET/CT for detecting solitary pulmonary nodules.[81] The literature search, conducted to May 2015, identified 12 studies (N=1297 patients) for inclusion in the analysis. The pooled sensitivity and specificity of FDG-PET/CT to detect malignant pulmonary nodules are presented in Table 7.

Li et al (2017) conducted a meta-analysis of studies that compared FDG-PET/CT with gadolinium-enhanced MRI in the detection of brain metastases in patients with NSCLC.[82] The literature search identified 5 studies (total N =941 patients) for inclusion. Study quality was assessed using criteria recommended by the Cochrane Methods Working Group, with scores ranging from 9 to 11 on the 12-point scale. Meta-analyses results are presented in Table 7.

He et al (2014) compared PET, PET/CT, and conventional imaging techniques for detecting recurrent lung cancer.[83] Table 7 summarizes the diagnostic performances of the different imaging techniques.

Other meta-analyses have reported good sensitivities and specificities in the detection of lung cancer metastases and recurrence with PET/CT. A meta-analysis by Li et al (2013) calculated the sensitivity and specificity of PET/CT in the detection of distant metastases in patients with lung cancer and with NSCLC (see Table 7).[84]

Table 7. Pooled Diagnostic Performance of Various Imaging Techniques in Patients With Lung Cancer

Type of Imaging	Detection Measured	Sensitivity (95% CI), %	Specificity (95% CI), %	DOR (95% CI)
Ruilong et al (2017)[81]	Solitary pulmonary nodules			
[1]FDG-PET/CT		82 (76 to 87)	81 (66 to 90)	18 (8 to 38)
Li et al (2017)[82]	Brain metastases			
FDG-PET/CT		21 (13 to 32)	100 (99 to 100)	235 (31 to 1799)
Gadolinium MRI		77 (60 to 89)	99 (97 to 100)	657 (112 to 3841)
He et al (2014)[83]	Recurrent NSCLC			
FDG-PET		94 (91 to 97)	84 (73 to 89)	65 (19 to 219)
FDG-PET/CT		90 (84 to 95)	90 (87 to 93)	79 (19 to 335)
CIT		78 (71 to 84)	80 (75 to 84)	13 (4 to 40)
Li et al (2013)[84]	Distant metastases			
FDG-PET/CT		87 (55 to 98)	96 (93 to 98)	196 (22 to 1741)

CI: confidence interval; CIT: conventional imaging technique; CT: computed tomography; DOR: diagnostic odds ratio; FDG: fluorine 18 fluorodeoxyglucose; MRI: magnetic resonance imaging; NSCLC: non-small-cell lung cancer; PET: positron emission tomography.

Guidelines

Current NCCN guidelines for NSCLC (v.6. 2020) indicate that PET/CT can be used in the staging of the disease, detection of metastases, treatment planning, and detection of disease recurrence.[85.] The guidelines note that PET is "best performed before a diagnostic biopsy site is chosen in cases of high clinical suspicion for aggressive, advanced-stage tumors." However, PET is not recommended for detection of brain metastasis from lung cancers. While PET/CT is not routinely recommended for surveillance after completion of definitive therapy, it may be considered to differentiate between true malignancies and benign conditions (eg, atelectasis, consolidation, and radiation fibrosis), which may have been detected by CT imaging. If PET/CT detects recurrent disease, biopsy confirmation is necessary prior to initiating additional treatment because FDG remains avid up to 2 years.

In 2013 the American College of Chest Physicians issued guidelines for the diagnosis and management of NSCLC.[86.] The guidelines stated that RCTs support the use of PET or PET/CT scanning as a component of lung cancer treatment and recommended PET or PET/CT for staging, detection of metastases, and avoidance of noncurative surgical resections.

Small-Cell Lung Cancer

Approximately 15% of all lung cancers are small-cell lung cancer (SCLC). Patients with SCLC are typically defined as having either limited stage or extensive-stage disease. Most patients diagnosed with SCLC have an extensive-stage disease, which is characterized by distant metastases, malignant pericardial or pleural effusions, and/or contralateral hilar lymph node involvement. Limited stage SCLC includes the ipsilateral hemithorax and regional or mediastinal lymph nodes and can be encompassed in a safe radiotherapy field.

Systematic Reviews

A systematic review by Lu et al (2014) included 12 studies (total N =369 patients) of F-FDG-PET/CT for staging SCLC.[87.] Although estimated pooled sensitivity and pooled specificity were 98% (95% CI, 94% to 99%) and 98% (95% CI, 95% to 100%), respectively, included studies were small (median sample size, 22 patients); of primarily fair to moderate quality; and heterogeneous in design (e.g., retrospective, prospective), PET parameter assessed, indication for PET, and reference standard used. It is not possible from the limited, poor-quality evidence in this systematic review to determine whether the use of PET adds value relative to conventional staging tests for SCLC.

A systematic review by Ruben and Ball (2012) on staging SCLC found PET to be more effective than conventional staging methods; however, a limitation of this review is that the reviewers did not conduct a quality assessment of individual studies.[88.]

In an AHRQ review conducted by Seidenfeld et al (2006) that included 6 studies of patients with SCLC and non-brain metastases, PET plus conventional staging was more sensitive in detecting disease than conventional staging alone.[89.]Use of PET may correctly upstage and downstage disease, and studies have reported a very high occurrence of patient management changes attributed to PET. However, the quality of these studies was consistently poor, and insufficient detail in reporting was the norm, especially with respect to the reference standard.

Guidelines

Current NCCN guidelines for SCLC (v.4.2020) indicate PET/CT can be used in the staging of the disease if limited stage is suspected or if needed to clarify stage. If extensive-stage is established, brain imaging, MRI (preferred), or CT with contrast is recommended. Use of PET/CT "is not recommended for routine follow-up.[90.]

Section Summary: Lung Cancer
Evidence for PET or PET/CT in patients with NSCLC consists of meta-analyses. The meta-analyses have shown that use of PET or PET/CT in patients with lung cancer can aid in the diagnosis, staging, as well as detecting metastases and recurrence. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of NSCLC.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of NSCLC. Evidence for PET or PET/CT for patients with SCLC consists of systematic reviews and meta-analyses. These reviews have shown potential benefits in using PET for staging, though the quality of the studies was low. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis, staging, and restaging of SCLC. Guidelines support the use of PET/CT if a limited stage is suspected or to clarify staging. If extensive-stage is established, other imaging techniques (MRI or CT with contrast) are preferred.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of SCLC.

Lymphoma, Including Hodgkin Disease
Systematic Reviews
Of the 14 studies reviewed in a TEC Assessment (1999), 3 compared PET with anatomic imaging in initial staging and restaging of patients with Hodgkin disease and non-Hodgkin lymphoma.[91.] Two of these studies included data from both diseased and nondiseased sites for PET and CT. Both studies found PET had better overall diagnostic accuracy than CT. The third study addressed the detection of diseased sites only and found PET to have a sensitivity similar to that of CT or MRI. Among the 6 studies that reported on concordance between PET and other imaging modalities, PET was discordant with other modalities in 11% to 50% of cases; PET was correct among discordances in 40% to 75% of cases. Use of PET has been reported to affect patient management decisions in 8% to 20% of patients in 5 studies, mainly by correctly upstaging disease, but also by correctly downstaging disease. Thus, when PET is added to conventional imaging, it can provide useful information for selecting effective and appropriate treatment for the correct stage of the disease.

Lymphoma Diagnosis
Meta-analyses have reported good sensitivities and specificities with PET/CT in the detection of newly diagnosed Hodgkin lymphoma (2014) and diffuse large B-cell lymphoma (2014).[92,93.]

Lymphoma Restaging
A systematic review and meta-analysis by Adams and Kwee (2016) evaluated the proportion of false-positive lesions at interim and end-of-treatment as detected by FDG-PET in patients with lymphoma.[94.] The literature search, conducted through January 2016, identified 11 studies (total N =139 patients) for inclusion. Study quality was moderate, as assessed by the QUADAS-2 tool. The weighted summary proportion of false-positive results among all biopsied lesions both during and after completion of treatment was 56% (95% CI, 33% to 77%). Subgroup analyses found the FDG-PET false-positive proportions for: interim non-Hodgkin lymphoma (83%; 95% CI, 72% to 90%) , end-of-treatment non-Hodgkin lymphoma (31%; 95% CI, 4% to 84%), and end-of-treatment Hodgkin lymphoma (23%; 95% CI, 5% to 65%). No studies calculating the false-positive rate for interim Hodgkin lymphoma were identified.

A systematic review by Adams et al (2015) focused on the outcomes of patients with Hodgkin lymphoma who had negative residual mass after FDG-PET scanning.[95.] When a persistent mass is non-FDG-avid, the patient is considered to be in complete remission, though the significance of having a residual mass is unclear. The literature search, conducted through December 2014, identified 5 studies (total N =727 patients) for inclusion. Follow-up of patients in the studies ranged from 1 to 13 years. The pooled relapse proportion was 6.8% (95% CI, 2.6% to 12.5%).

Lymphoma Management

Systematic Reviews

Another systematic review by Adams and Kwee (2017) evaluated the prognostic value of FDG-PET in patients with refractory or relapsed Hodgkin lymphoma considering autologous cell transplantation.[96] The literature search, conducted through May 2016, identified 11 studies (total N =664 patients) for inclusion. In general, the overall quality of selected studies was poor, based on Quality in Prognosis Studies (QUIPS). Pooled sensitivity and specificity of pretransplant ^{18}F-FDG-PET in predicting treatment failure were 54% (95% CI, 44% to 63%) and 73% (95% CI, 67% to 79%), respectively. Pooled sensitivity and specificity of pretransplant FDG-PET in predicting death after treatment was 55% (95% CI, 39% to 70%) and 69% (95% CI, 61% to 76%), respectively.

A meta-analysis by Adams and Kwee (2016) evaluated the prognostic value of FDG-PET in patients with aggressive non-Hodgkin lymphoma considering autologous cell transplantation.[97] The literature search, conducted through July 2015, identified 11 studies (total N=745 patients) for inclusion. The overall quality of the selected studies was moderate, based on QUIPS criteria. Patients with positive pretransplant FDG-PET results had progression-free survival (PFS) rates ranging from 0% to 52%. Patients with negative pretransplant FDG-PET results had PFS rates ranging from 55% to 85%. OS was 17% to 77% in patients with positive FDG-PET results and 78% to 100% in patients with negative FDG-PET results. Based on 5 studies, pooled sensitivity and specificity of pretransplant FDG-PET for predicting treatment failure (defined as progressive, residual, or relapsed disease) were 67% (95% CI, 58% to 75%) and 71% (95% CI, 64% to 77%), respectively.

A systematic review by Zhu et al (2015) evaluated the prognostic value of FDG-PET in patients with diffuse B-cell lymphoma treated with rituximab-based immune chemotherapy.[98] The literature search identified 11 studies (N =1081) for inclusion. The pooled HR comparing PFS of patients with positive interim FDG-PET results and negative interim FDG-PET results was 3.0 (95% CI, 2.3 to 3.9). Patients with a negative interim FDG-PET result had a higher complete remission rate than patients with a positive interim FDG-PET result (relative risk, 5.5; 95% CI, 2.6 to 11.8).

Randomized Controlled Trials

Borchmann et al (2017) reported on an open-label phase 3 RCT by the German Hodgkin Study Group, which randomized patients newly diagnosed with advanced Hodgkin lymphoma to different levels of eBEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone), based on PET results.[99] After 2 cycles of eBEACOPP, PET-positive patients were randomized to 6 more cycles of eBEACOPP (n=217) or eBEACOPP plus rituximab (n=217). PET-negative patients were randomized to 6 more cycles of eBEACOPP (n=504) or 4 more cycles of eBEACOPP (n=501). Five-year PFS rates for the PET-positive 6-cycle eBEACOPP and 6-cycle eBEACOPP plus rituximab arms were 90% (95% CI, 85% to 94%) and 88% (95% CI, 83% to 93%), respectively. Five-year PFS rates for the PET-negative 6-cycle and 4-cycle arms were 91% (95% CI, 88% to 94%) and 92% (95% CI, 89% to 95%), respectively. Results showed that PET-negative patients can receive fewer cycles of treatment without a negative impact on PFS and that PET-positive patients do not need an intensified treatment (addition of rituximab) to improve PFS.

Guidelines

Current NCCN guidelines for Hodgkin lymphoma (v.2.2020)[100] and non-Hodgkin lymphoma (chronic lymphocytic leukemia/small lymphocytic lymphoma [v.4.2020], b-cell lymphomas [v.2.2020],[101] hairy cell leukemia [v.1.2020],[102] primary cutaneous lymphomas [v.2.2020], and t-cell lymphomas [v.1.2020]) indicate that PET/CT may be used in the diagnostic workup, staging, restaging, and evaluating treatment response.[103] The guidelines recommend using the internationally recognized Deauville 5-point PET scale for initial staging and assessment of treatment response. The following PET/CT results are assigned the corresponding scores: 1=no uptake; 2=uptake ≤ mediastinum; 3=uptake > mediastinum but ≤ liver; 4=uptake moderately higher than liver; and 5=uptake markedly higher than liver and/or new lesions. The Deauville PET scores can be used to determine the course of treatment. The guidelines note that if PET/CT

detects 3 or more skeletal lesions, the marrow may be assumed to be involved and marrow biopsies are no longer indicated. The guidelines also note "Surveillance PET should not be done routinely due to risks for false-positives. Management decisions should not be based on PET scan alone; clinical or pathologic correlation is needed."[104.]

Section Summary: Lymphoma, Including Hodgkin Disease
Evidence for the use of FDG-PET/CT in the management of patients with lymphoma consists of systematic reviews, meta-analyses, and an RCT. In patients with lymphoma, PET can provide information for staging or restaging. Evidence has also shown that FDG-PET/CT can be useful in predicting response to therapy in patients with lymphoma. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of Hodgkin lymphoma and non-Hodgkin lymphoma.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of Hodgkin lymphoma and non-Hodgkin lymphoma.

Melanoma
Surgical resection for melanoma is limited to those with local disease. Patients with widespread disease are not candidates for resection. Frequently, there is a microscopic spread of cancer cells to the proximal lymph nodes. Therefore, patients with a high-risk of nodal spread, as assessed by the thickness of the primary melanoma, may be candidates for lymph node sampling, termed *sentinel node biopsy*. Use of PET scanning has been investigated both as a technique to detect the widespread disease as part of an initial staging procedure and to evaluate the status of local lymph nodes to determine the necessity of sentinel node biopsy.

To consider PET as a useful alternative to sentinel node biopsy, it must have high sensitivity and specificity when sentinel node biopsy or lymph node dissection serves as the reference standard. In the only study of this kind, PET had a sensitivity of only 17%, suggesting that PET rarely detects small metastases that can be discovered by sentinel node biopsy. Thus, a TEC Assessment (1999) concluded that PET is not as beneficial as sentinel node biopsy for assessing regional lymph nodes.[105.]

"The intent of using PET to detect extranodal metastases is to aid in selecting treatment appropriate to the patient's extent of disease.... It may be inferred from [the evidence] that PET was usually correct when discordant with other modalities. PET affects management in approximately 18% of patients."

Systematic Reviews
In a meta-analysis of 9 studies (total N =623 patients), Rodriquez Rivera et al (2014) reported pooled sensitivity and specificity of FDG-PET for detecting systemic metastases in patients with stage III cutaneous melanoma of 89% (95% CI, 65% to 98%) and 89% (95% CI, 77% to 95%), respectively.[106.]

Guidelines
Current NCCN guidelines for cutaneous melanoma (v.3.2020) indicate that PET/CT can be used for staging and restaging more advanced disease (i.e., stage III and IV) in the presence of specific signs and symptoms. Use of PET/CT is not recommended for stage I or II diseases. Also, PET/CT is listed as an option for surveillance screening for recurrence every 3 to 12 months (category 2B) at the physician's discretion. Because most recurrences occur within the first 3 years, routine screening for asymptomatic recurrence is not recommended beyond 3 to 5 years. The guidelines note that the safety of PET/CT is of concern due to cumulative radiation exposure.

Section Summary: Melanoma
Evidence for the use of FDG-PET/CT in the management of patients with melanoma consists of a TEC Assessment, a systematic review , and a meta-analysis. In patients with melanoma, PET can provide information for staging or restaging in patients with more advanced disease (stage III or

higher). The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of stage III or IV melanoma.

The evidence does not support the use of FDG-PET and FDG-PET/CT for the diagnosis or staging and restaging of stage I or II melanoma.

The evidence supports the use of FDG-PET and FDG-PET/CT for surveillance of melanoma.

Multiple Myeloma
Systematic Reviews
Two systematic reviews, 1 of which also conducted a meta-analysis, addressed PET for the staging of multiple myeloma.

Lu et al (2012) included 14 studies (N =395 patients) and reported pooled estimates of sensitivity and specificity of 96% (95% CI, 80% to 100%) and 78% (95% CI, 40% to 95%), respectively, in the detection of extramedullary lesions in patients with multiple myeloma.[107.]

Van Lammeren-Venema et al (2012) included 18 studies (N =798 patients) in a systematic review that compared FDG-PET with whole-body x-ray in staging and response assessment of patients with multiple myeloma.[108.] Using the QUADAS tool to assess quality, the studies received a mean percentage of the maximum score of 61%. Reviewers reported that, in general, FDG-PET is more sensitive than whole body x-ray in detecting myeloma bone lesions.

Guidelines
Current NCCN guidelines for multiple myeloma (v. 4.2020) recommend PET/CT as an imaging technique option for initial workup. The NCCN recommends using PET/CT for follow-up and surveillance as indicated, if utilized for initial workup. Use of PET/CT is considered first choice during initial work up of solitary extraosseous plasmacytoma. PET/CT may also be considered to detect disease progression.

Section Summary: Multiple Myeloma
Evidence for the use of PET or PET/CT in the management of patients with multiple myeloma consists of systematic reviews and a meta-analysis. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis, staging, and restaging.

The evidence does not support the use of FDG-PET and FDG-PET/CT for routine surveillance of multiple myeloma.

Neuroendocrine Tumors
Systematic Reviews

^{68}Ga-PET and ^{68}Ga-PET/CT
Barrio et al (2017) conducted a systematic review and meta-analysis on the impact of gallium 68 (^{68}Ga) PET/CT on management decisions in patients with neuroendocrine tumors.[109.] Reviewers selected 14 studies (N =1561 patients). Change in management occurred in 44% of the patients following ^{68}Ga-PET/CT. Clinical outcomes were not reported.

Deppen et al (2016) conducted a systematic review assessing the use of ^{68}Ga-PET/CT for the diagnosis and staging of gastroenteropancreatic neuroendocrine tumors.[110.] Seventeen studies (total N =971 patients) were included in the analysis. Comparators differed among the studies: octreotide and conventional imaging (3 studies), other radiopharmaceuticals without direct imaging comparators (5 studies), and conventional imaging (9 studies). Meta-analysis of the 9 studies that compared ^{68}Ga-PET/CT scanning with conventional imaging resulted in a sensitivity of 91% (95% CI, 81% to 96%) and a specificity of 91% (95% CI, 78% to 96%).

Two meta-analyses from Treglia et al (2012) addressed the use of PET in patients with neuroendocrine tumors.[111,112] One report included patients with thoracic and gastroentero-pancreatic neuroendocrine tumors who had imaging with PET using ^{68}Ga-PET and ^{68}Ga-PET/CT.[111] Sixteen studies (total N =567 patients) were included in the analysis. The studies were considered medium to high quality, based on an assessment using the QUADAS tool. Meta-analysis showed a sensitivity and specificity of 93% (95% CI, 91% to 95%) and 91% (95% CI, 82% to 97%), respectively, with histology and/or clinical or imaging follow-up as the reference standard in diagnostic accuracy.

^{18}F-DOPA PET and ^{18}F-DOPA PET/CT

The other meta-analysis included studies of patients with paragangliomas scanned by PET with fluorine 18-dihydroxyphenylalanine (^{18}F-DOPA) PET and ^{18}F-DOPA PET/CT.[112] Eleven studies (total N =275 patients) were analyzed. The QUADAS tool was used to assess quality: 2 studies had a B rating, 4 a C rating, and 5 a D rating. Reference standards varied across studies, with 2 using MRI, 3 using histology on all patients, and the remaining using histology only when feasible. Meta-analysis showed a sensitivity and specificity of 91% (95% CI, 87% to 94%) and 79% (95% CI, 76% to 81%), respectively.

Guidelines

Current NCCN guidelines for neuroendocrine tumors (v. 1.2020) have recommended somatostatin receptor-based imaging with PET/CT or PET/MRI, using ^{68}Ga-dotatate as the radioactive tracer.[113] The NCCN recommends ^{68}Ga-PET/CT or PET/MRI for diagnosis, staging, and restaging. Use of FDG-PET may be considered in poorly differentiated carcinomas only in biopsy-proven neuroendocrine tumors of unknown primary. Neither ^{68}Ga-PET/CT nor FDG-PET are recommended for surveillance. Use of ^{18}F-DOPA PET/CT is not discussed in the guidelines.

Section Summary: Neuroendocrine Tumors

Evidence for the use of PET or PET/CT in the management of patients with neuroendocrine tumors consists of meta-analyses. Two different radiopharmaceuticals were used: ^{18}F-DOPA PET/CT and ^{68}Ga-PET/CT. Meta-analyses of studies using ^{68}Ga-PET/CT as the radiotracer for diagnosis and staging of neuroendocrine tumors report relatively high sensitivities and specificities compared with conventional imaging techniques.

The evidence does not support the use of FDG-PET/CT for the diagnosis, staging, and restaging, or surveillance of neuroendocrine tumors.

The evidence does not support the use of FDG-PET/CT for surveillance of neuroendocrine tumors.

The evidence supports the use of ^{68}Ga-PET/CT for the diagnosis, staging, and restaging of neuroendocrine tumors.

The evidence does not support the use of ^{68}Ga-PET/CT for surveillance of neuroendocrine tumors.

Ovarian Cancer

For primary evaluation (i.e., suspected ovarian cancer), the ability to rule out malignancy with a high NPV would change management by avoiding unnecessary exploratory surgery. However, available studies have suggested that PET scanning has a poorer NPV than other options, including transvaginal ultrasound, Doppler studies, or MRI. Adding PET scan to ultrasound or MRI did not improve results.

Positive predictive value is of greatest importance in evaluating patients with known ovarian cancer, either to detect disease recurrence or progression or to monitor response to treatment.

Systematic Reviews
A meta-analysis by Xu et al (2017) evaluated the diagnostic value of PET and PET/CT for recurrent or metastatic ovarian cancer.[114.] The literature search, conducted through August 2014, identified 64 studies for inclusion: 15 studies (n=657 patients) using PET and 49 studies (n=3065 patients) using PET/CT. The pooled sensitivity and specificity for PET were 89% (95% CI, 86% to 92%) and 90% (95% CI, 84% to 93%), respectively. The pooled sensitivity and specificity for PET/CT were 92% (95% CI, 90% to 93%) and 91% (95% CI, 89% to 93%), respectively. Subgroup analyses were conducted by study region (Asia, Europe, and America). For PET/CT, sensitivities in the Asia and Europe studies were significantly higher compared with the sensitivity in the America studies.

A meta-analysis by Limei et al (2013), included 28 studies (total N =1651 patients) published through December 2012; it evaluated the diagnostic value of PET/CT in suspected recurrent ovarian cancer.[115.] Using the Oxford Evidence rating system for quality, 7 studies were considered high quality and 21 were low-quality. Reviewers found PET/CT was useful for detecting ovarian cancer recurrence, with pooled sensitivity and specificity of 89% and 75% for the high-quality studies and 89% and 93% for the low-quality studies, respectively.

An AHRQ systematic review conducted by Matchar et al (2004) suggested that PET might have value for detecting recurrence when cancer antigen 125 is elevated and conventional imaging does not clearly show recurrence, this had not been demonstrated in an adequately powered prospective study.[116.] An AHRQ systematic review conducted by Ospina et al (2008) found that evidence supported the use of PET/CT for detecting recurrent ovarian cancer.[35.] Evidence for initial diagnosis and staging of ovarian cancer was inconclusive.

Guidelines
American College of Radiology
In 2018, the ACR published Appropriateness Criteria (2018) on staging and follow-up of ovarian cancer have stating that PET/CT and MRI may be appropriate when lesions are indeterminate with contrast-enhanced CT.[117.]

National Comprehensive Cancer Network
Current NCCN guidelines for ovarian cancer (v.1.2020) indicate that PET/CT can be appropriate "for indeterminate lesions if results will alter management."[118.] Use of PET/CT may be considered for monitoring patients with stage II through IV ovarian cancer receiving primary chemotherapy if clinically indicated. PET/CT also can be considered if clinically indicated after complete remission, for follow-up and for monitoring for recurrence if cancer antigen 125 is rising or clinical relapse is suspected.

Section Summary: Ovarian Cancer
Evidence for PET and PET/CT for the initial diagnosis of ovarian cancer consists of an AHRQ systematic review (2014), which reported that the evidence is inconclusive. Evidence on the use of PET and PET/CT for the detection of ovarian cancer recurrence includes 2 meta-analyses and an AHRQ systematic review (2008). Pooled sensitivities and specificities support the use of PET and PET/CT for the detection of recurrent ovarian cancer. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of ovarian cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of ovarian cancer.

Pancreatic Cancer
Systematic Reviews
A Cochrane review by Best et al (2017) compared the diagnostic accuracy of several imaging techniques (CT, MRI, PET, and endoscopic ultrasound) in detecting cancerous and precancerous lesions in the pancreas.[119.] The literature review, conducted through July 2016, identified 54 studies total, 10 using PET. Assessment of the selected studies found none to have

high methodologic quality. A meta-analysis of 3 studies reported a sensitivity and specificity in diagnosing pancreatic cancer of 92% (95% CI, 80% to 97%) and 65% (95% CI, 39% to 84%), respectively. The PPV and NPV (calculated by BCBSA) were 89% and 71%, respectively. Reviewers could not adequately compare the various techniques due to the imprecision of estimates, poor quality of studies, and heterogeneity in categorizing lesions.

Wang et al (2017) conducted a meta-analysis comparing CT alone, PET alone, and PET/CT in the preoperative assessment of patients with pancreatic cancer.[120.] The literature review identified 13 studies (total n=1343 patients). The Newcastle-Ottawa Scale was used to assess study quality, with scores ranging from 6 to 8 on the 9-point scale. Use of PET alone was not superior to CT alone (pooled odds ratio [OR], 1.0; 95% CI, 0.6 to 1.6) in detecting distant metastases. However, PET/CT was superior to CT alone (pooled OR=1.7; 95% CI, 1.3 to 2.1) in detecting distant metastases. Neither PET nor PET/CT was superior to CT alone in detecting lymph node invasion (pooled OR , 1.0; 95% CI, 0.6 to 1.5).

In a meta-analysis of 9 studies (total N =526 patients), Rijkers et al (2014) reported pooled sensitivity and specificity of FDG-PET/CT for confirming suspected pancreatic cancer of 90% (95% CI, 87% to 93%) and 76% (95% CI, 66% to 84%), respectively.[121.] Two reviews on pancreatic carcinoma, conducted by Ospina et al (2008) and Podoloff et al (2009) have suggested that PET/CT can be useful for staging certain patients when the standard staging protocol is inconclusive.[35,37.]

Both the AHRQ systematic review by Matchar et al (2004) and the TEC Assessment (1999) focused on 2 clinical applications of PET scanning in patients with known or suspected pancreatic cancer: the use of PET to distinguish between benign or malignant pancreatic masses, and the use of PET as a staging technique in patients with known pancreatic cancer.[116,122.]

In terms of distinguishing between benign and malignant disease, the criterion standard is a percutaneous or open biopsy. If PET were to be used to allow patients with scans suggesting benign masses to avoid a biopsy, a very high NPV would be required. The key statistic underlying the NPV is the false-negative rate. Patients with false-negative results are incorrectly considered to have a benign disease and thus are not promptly treated for pancreatic cancer. Based on the TEC literature review, the NPV ranged between 75% and 92%, depending on an underlying prevalence of disease ranging from 50% to 75%. The TEC Assessment concluded that this level of diagnostic performance would not be adequate to recommend against biopsy. The Matchar AHRQ report found that sometimes PET was more accurate than other modalities, but a meta-analysis showed that it is unclear whether PET's diagnostic performance would surpass decision thresholds for biopsy or laparotomy.[116.] In both the TEC and AHRQ reviews, data were inadequate to permit conclusions on the role of PET scanning as a technique to stage known pancreatic cancer.

Observational Studies
Ghaneh et al (2018) conducted the largest study to date, measuring the incremental diagnostic value of PET/CT when added to a standard diagnostic workup with multidetector CT.[123.] The study was a prospective nonrandomized study of 550 patients. Sensitivity and specificity were 88.5% and 70.6%, respectively, which was a significant improvement from CT alone. PET/CT also correctly changed staging in 56 patients, influenced management in 250 patients, and stopped resection in 58 patients scheduled for surgery.

Guidelines
Current NCCN guidelines for pancreatic cancer (v. 1.2020) state "the role of PET/CT (without iodinated intravenous contrast)remains unclear…[PET/CT] may be considered after formal pancreatic CT protocol in high-risk patients to detect extrapancreatic metastasis. It is not a substitute for high-quality, contrast-enhanced CT."

Section Summary: Pancreatic Cancer
Evidence for PET and PET/CT for the initial diagnosis of pancreatic cancer consists of a TEC Assessment, a Cochrane review, a meta-analysis, and a large observational study published subsequent to the reviews. The TEC Assessment reported that the NPVs in several studies were inadequate to influence the decision for a biopsy. Other reviews also noted limitations such as imprecise estimates and poor quality of studies. Studies published subsequent to the reviews also reported low NPVs. The large observational study, which assessed the incremental diagnostic value of PET/CT when added to standard workup with CT, showed significant improvements in sensitivity and specificity compared with CT alone.

The evidence supports the use of FDG-PET and FDG-PET/CT for suspected pancreatic cancer when results from other imaging techniques are inconclusive.

The evidence does not support the use of FDG-PET and FDG-PET/CT for the diagnosis, staging and restaging, or surveillance of pancreatic cancer.

Penile Cancer
Systematic Reviews
A systematic review with meta-analysis of PET by Sadeghi et al (2012) focused on staging inguinal lymph nodes among patients with penile squamous cell carcinoma.[124.] No comparisons were made with other imaging modalities. The report found that PET had low sensitivity, and reviewers concluded that PET is not suited for routine clinical use in this setting.

Guidelines
Current NCCN guidelines for penile cancer (v. 1.2020) state that PET/CT may be considered in patients with penile cancer for the evaluation of enlarged pelvic lymph nodes.[125.]

Section Summary: Penile Cancer
Evidence for the use of PET or PET/CT in the management of patients with penile cancer consists of a systematic review. The evidence does not support the use of FDG-PET and FDG-PET/CT for the diagnosis, staging, and restaging, or surveillance of penile cancer.

Prostate Cancer
^{11}C-Choline PET, ^{11}C-Choline PET/CT, ^{18}F-Fluciclovine PET

Prostate Cancer Diagnosis
Liu et al (2016) and Ouyang et al (2016) conducted meta-analyses comparing the diagnostic accuracy of 4 radiotracers (FDG, carbon 11 choline [^{11}C-choline], fluorine 18 fluorocholine [^{18}F-FCH], and carbon 11 acetate [^{11}C-acetate]) in detecting prostate cancer.[126,127.] The literature search for the Liu review, conducted through July 2015, identified 56 studies (total N =3586 patients) for inclusion. Using the QUADAS-2 system to evaluate study quality, reviewers determined that the studies were reliable, with scores of 6 to 9 out of 10. Pooled estimates for the 4 types of radiotracers are summarized below (see Table 8). The literature search for the Ouyang et al (2016) review included studies using elastography and was conducted through April 2015. Study quality was not addressed.

Table 8. Pooled Diagnostic Performance of Different Radiotracers in Detecting Prostate Cancer

Imaging Technique	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	AUC (95% CI)
Liu et al (2016)[126.]				
^{11}C-choline PET/CT	31	81 (77 to 88)	82 (73 to 88)	0.89 (0.86 to 0.91)
^{18}F-FCH-PET/CT	15	76 (49 to 91)	93 (84 to 97)	0.94 (0.92 to 0.96)
^{11}C-acetate PET/CT	5	79 (70 to 86)	59 (43 to 73)	0.78 (0.74 to 0.81)
FDG-PET/CT	5	67 (55 to 77)	72 (50 to 87)	0.73 (0.69 to 0.77)
Ouyang et al (2016)[127.]				
Elastography[a]	26	76 (68 to 83)	78 (72 to 83)	0.84
^{11}C-choline PET/CT	31	78 (72 to 84)	79 (71 to 82)	0.85

Imaging Technique	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	AUC (95% CI)
^{18}F-FCH-PET/CT	15	73 (54 to 87)	59 (41 to 75)	0.91
^{11}C-acetate PET/CT	5	79 (68 to 86)	59 (41 to 75)	0.77
FDG-PET/CT	5	76 (68 to 83)	78 (72 to 83)	0.84

AUC: area under the curve; CI: confidence interval; CT: computed tomography;FDG: fluorine 18 fluorodeoxyglucose; PET: positron emission tomography; 11C-acetate: carbon 11 acetate; 11C-choline: carbon 11 choline; 18F-FCH: fluorine 18 fluorocholine.
a Includes transrectal real-time elastosonography and shear-wave elastography.

Prostate Cancer Staging and Restaging
Systematic Reviews
A meta-analysis by Fanti et al (2016) assessed the accuracy of ^{11}C-choline PET/CT in the restaging of prostate cancer patients with biochemical recurrence after initial treatment with curative intent.[128] The literature search, conducted through December 2014, identified 12 studies (total N =1270 patients) for inclusion in the analysis. Pooled sensitivity and specificity were 89% (95% CI, 83% to 93%) and 89% (95% CI, 73% to 96%), respectively.

In a meta-analysis by von Eyben and Kairemo (2014), the pooled sensitivity and specificity of ^{11}C-choline PET/CT for detecting prostate cancer recurrence in 609 patients were 62% (95% CI, 51% to 66%) and 92% (95% CI, 89% to 94%), respectively.[129] In an evaluation of 280 patients from head-to-head studies comparing choline PET/CT with bone scans, PET/CT identified metastases significantly more often than did bone scanning (127 [45%] vs 46 [16%], respectively; OR , 2.8; 95% CI, 1.9 to 4.1; p<0.001). Reviewers also reported that ^{11}C-choline PET/CT changed treatment in 381 (41%) of 938 patients. Complete prostate-specific antigen (PSA) response occurred in 101 (25%) of 404 patients.

A systematic review by Umbehr et al (2013) investigated the use of ^{11}C-choline and ^{18}F-FCH-PET and ^{18}F-FCH-PET/CT in staging and restaging of prostate cancer. The literature search, conducted through July 2012, identified 10 studies (total =637 patients) to be included in the initial prostate cancer staging analysis; pooled sensitivity was 84% (95% CI, 68% to 93%) and specificity was 79% (95% CI, 53% to 93%).[130] Twelve studies (total n=1055 patients) were included in the restaging analysis; pooled sensitivity and specificity were 85% (95% CI, 79% to 89%) and 88% (95% CI, 73% to 95%), respectively.

Mohsen et al (2013) conducted a systematic review of 23 studies on ^{11}C-acetate PET imaging for the detection of primary or recurrent prostate cancer.[131] For detection of recurrence, 14 studies were included in a meta-analysis. The pooled sensitivity was 68% (95% CI, 63% to 73%) and pooled specificity was 93% (95% CI, 83% to 98%). Study quality was considered poor, and low sensitivities and specificities appear to limit the validity of ^{11}C-acetate imaging in prostate cancer. Currently, ^{11}C-acetate is not approved by the U.S. Food and Drug Administration.

Other systematic reviews, including those by Sandgren et al (2017) and Albisinni et al (2018), have also reported that ^{11}C-choline PET/CT exhibits high sensitivity and specificity estimates in the staging and restaging of prostate cancer.[132,133]

Both the NCCN report conducted by Podoloff et al (2009) and the AHRQ review by Ospina et al (2008) found the evidence insufficient to support the use of PET for any indication in patients with prostate cancer.[37,35] Reports showed significant overlap between benign prostatic hyperplasia, malignant tumor, local recurrence, and postoperative scarring. Use of PET may have limited sensitivity in detecting distant metastatic disease. The AHRQ report identified only 4 studies of PET for the indications of restaging and recurrence, none of which addressed the effect of PET on management decisions.

Observational Studies
Bach-Gansmo et al (2017) conducted a retrospective study assessing the use of anti-1-amino-3-[18F] fluorocyclobutane-1-carboxylic acid (^{18}F-fluciclovine) in the staging of biochemically recurrent prostate cancer.[134] The reference standard was histologic confirmation, which was

blinded to PET findings. Detection rates were calculated for the prostate, extra-prostate, and whole-body at quartiles of PSA levels. At the highest quartile (>6.0 ng/mL), detection rates were 69%, 69%, and 86% for the prostate, extra-prostate, and whole-body scans, respectively. For PSA levels from 2.0 to 6.0 ng/mL, detection rates were 50% 46%, and 75%, respectively. For PSA levels from 0.8 to 2.0 ng/mL, detection rates were 22%, 45%, and 59%, respectively. For the lowest quartile (≤0.8 ng/mL), detection rates were 14%, 31%, and 41%, respectively. (Note that BCBSA extrapolated detection rates from a graphic.)

Prostate Cancer Management

Andriole et al (2018) presented results from the LOCATE trial.[135.] The study population consisted of 213 men who had undergone curative-intent treatment of histologically confirmed prostate cancer and were suspected to have recurrence based on rising PSA levels. Fluciclovine-avid lesions were detected in 122 (57%) patients. Compared with management plans specified by the treating physicians prior to the PET scans, 126 (59%) patients had a change in management. The most frequent change in management was from salvage or noncurative systemic therapy to watchful waiting (n=32) and from noncurative systemic therapy to salvage therapy (n=30).

Akin-Akintayo et al (2017) evaluated the role of fluciclovine PET/CT in the management of post-prostatectomy patients with PSA failure being considered for salvage radiotherapy.[136.] Forty-two patients who were initially planning radiotherapy due to post-prostatectomy PSA failure underwent fluciclovine PET/CT. Based on the PET/CT results, 17 (40.5%) patients changed a decision relating to the radiotherapy: 2 patients received hormonal therapy rather than radiotherapy when fluciclovine showed extrapelvic disease; 11 patients increased the radiotherapy field from prostate bed only to prostate plus pelvis, and 4 patients reduced the radiotherapy fields from prostate plus pelvis to prostate bed only.

The European Association of Urology's guidelines (2014) for prostate cancer has indicated that ^{11}C-choline PET/CT has limited value unless PSA levels exceed 1.0 ng/mL.[137.] In meta-analysis of 14 studies (total N =1667 patients) of radiolabeled choline PET/CT for restaging prostate cancer, Treglia et al (2014) reported a maximum pooled sensitivity of 77% (95% CI, 71% to 82%) in patients with a PSA velocity of greater than 2 ng/mL per year.[138.] Pooled sensitivity was lower for patients with a PSA velocity of less than 2 ng/mL per year or with a PSA level doubling time of 6 months or less. In meta-analysis of 11 studies (total N =609 patients) of radiolabeled choline PET/CT for staging or restaging prostate cancer, von Eyben et al (2014) reported a pooled sensitivity and specificity of 59% (95% CI, 51% to 66%) and 92% (95% CI, 89% to 94%), respectively.[129.] Pooled PPV and NPV were 70% and 85%, respectively.

Guidelines

American College of Radiology

In 2018, the ACR published an Appropriateness Criteria on the posttreatment follow-up of patients with prostate cancer stating that PET and PET/CT using ^{11}C-choline or ^{18}F-fluciclovine radiotracers is usually appropriate for patients with a clinical concern for residual or recurrent disease following radical prostatectomy, nonsurgical treatments, or systemic therapy.[139.]

National Comprehensive Cancer Network

Current NCCN guidelines for prostate cancer (v. 2.2020) indicate that ^{11}C-choline PET or PET/MRI may be considered for evaluating biochemical failure after primary treatment (i.e., radiotherapy or radical prostatectomy).[140.] To evaluate progression, ^{11}C-choline PET/CT or PET/MRI, or ^{18}F-fluciclovine PET/CT or PET/MRI may be considered for soft tissue and bone assessment and ^{18}F-sodium fluoride PET/CT or PET/MRI may be considered for further bone assessment. The guidelines note that ^{18}F-sodium fluoride PET/CT or PET/MRI has greater sensitivity but lower specificity than standard bone scan imaging. Use of FDG-PET should not be used routinely for initial assessment or in other settings, due to limited evidence of clinical utility.

Subsection Summary: ^{11}C-Choline PET, ^{11}C-Choline PET/CT, ^{18}F-Fluciclovine PET, and ^{18}F-Fluciclovine PET/CT for Prostate Cancer

The choice of radiotracer affects the sensitivity and specificity of the scans. Evidence for the use of ^{11}C-choline PET and ^{11}C-choline PET/CT for diagnosis, staging, and restaging of prostate cancer, consists of meta-analyses, which have shown that the use of ^{11}C-choline results in the highest sensitivities and specificities compared with other radiotracers. Evidence for the use of fluciclovine PET/CT for staging, restaging, and management of prostate cancer consists of observational studies. The studies reported increased detection with fluciclovine PET/CT; however, detection rates decreased as PSA levels decreased. Two prospective studies reported that a majority of management decisions were changed based on fluciclovine PET results among men with suspected recurrence. Further study is needed to compare PET and PET/CT with other imaging techniques, such as MRI and radionuclide bone scan. The evidence supports the use of ^{11}C-choline PET and PET/CT and ^{18}F-fluciclovine PET and PET/CT for the diagnosis, staging, and restaging of prostate cancer.

The evidence does not support the use of ^{11}C-choline PET and PET/CT and ^{18}F-fluciclovine PET and PET/CT for surveillance of prostate cancer.

^{68}Ga-PET and ^{68}Ga-PET/CT

Systematic Reviews

The Albisinni et al (2018) review, discussed in the ^{11}C-choline PET/CT section, and a systematic review by Eissa et al (2018) noted that an advantage of using ^{68}Ga prostate-specific membrane antigen (PSMA) PET compared with other radiotracers is the potential to detect local and distant recurrences in patients with lower PSA levels (<0.5 ng/ml).[133,141.]

A systematic review by Perera et al (2016) calculated the sensitivity, specificity, and predictive value of ^{68}Ga-PSMA PET in advanced prostate cancer.[142.] The literature search, conducted through April 2016, identified 16 studies (total N =1309 patients) for inclusion, though only 11 studies reported histopathologic correlations. Four studies provided data for calculating the predictive ability of ^{68}Ga-PSMA PET: a pooled sensitivity of 86% (95% CI, 37% to 98%) and a pooled specificity of 86% (95% CI, 3% to 100%). The other studies assessed ^{68}Ga-PSMA PET positivity by the amount of radiopharmaceutical injected and for detection of primary and metastatic lesions. Reviewers noted that these analyses were exploratory, because most studies were small, retrospective, from single-institutions, and had heterogeneous patient cohorts.

Guidelines

The current NCCN guidelines for prostate cancer (v.2.2020) note that ^{68}Ga-PSMA PET "may provide better detection of recurrences at lower PSA levels than reported for the U.S. Food and Drug Administration approved imaging agents."[125.] However, NCCN guidelines consider ^{68}Ga-PSMA investigational at this time.

Subsection Summary: ^{68}Ga-PET and ^{68}Ga-PET/CT for Prostate Cancer

Evidence for the use of ^{68}Ga-PET and ^{68}Ga-PET/CT consists of a systematic review of small single-institution studies. The confidence intervals of the sensitivity and specificity are wide, indicating uncertainty in the results. The evidence does not support the use of ^{68}Ga-PET and ^{68}Ga-PET/CT for the diagnosis, staging and restaging, and surveillance of prostate cancer.

Renal Cell Carcinoma

Systematic Reviews

A systematic review by Ma et al (2017) evaluated the use of FDG-PET or FDG--PET/CT for restaging renal cell carcinoma (RCC).[143.] The literature search, conducted through July 2016, identified 15 studies, mostly retrospective, for inclusion into a meta-analysis. Pooled estimates for sensitivity and specificity were 86% (95% CI, 88% to 93%) and 88% (95% CI, 84% to 91%), respectively. Reviewers concluded that PET showed potential for identifying metastatic or recurrent lesions in patients with RCC but that more prospective studies would be needed.

Guidelines
Current NCCN guidelines for kidney cancer (v. 1.2021) state that "The value of PET in RCC remains to be determined. Currently, PET alone is not a tool that is standardly used to diagnose kidney cancer or follow for evidence of relapse after nephrectomy."[144.]

Section Summary: Renal Cell Carcinoma
The evidence does not support the use of FDG-PET and FDG-PET/CT for the diagnosis, staging and restaging, or surveillance of RCC.

Soft Tissue Sarcoma
Systematic Reviews
A systematic review by Treglia et al (2012) evaluated PET for assessing response to imatinib and other treatments for gastrointestinal stromal tumors.[145.] Reviewers included 19 studies. They concluded there was sufficient evidence that PET/CT can be used to monitor response to imatinib treatment, and that the information can be used to adapt treatment strategies. However, the review had the following limitations: it lacked appraisal of the methodologic quality of individual studies and lacked comparison of decision making and outcomes between PET-guided and non-PET-guided management.

An AHRQ systematic review by Ioannidis et al (2002) on the use of PET for soft tissue sarcoma evaluated 5 indications: distinguishing between benign lesions and malignant soft tissue sarcoma, distinguishing between low-grade and high-grade soft tissue sarcoma, detecting locoregional recurrence, detecting distant metastases, and evaluating response to therapy.[146.] Reviewers found that PET had low diagnostic accuracy in distinguishing low-grade tumors from benign lesions ; however, PET performed better at differentiating high- or intermediate-grade tumors from low-grade tumors. It is unclear whether this would impact management decisions and health outcomes. Evidence was insufficient on the comparative diagnostic performance of PET and alternative diagnostic modalities in the diagnosis of soft tissue sarcoma, detection of locoregional recurrence, detection of distant metastasis, and evaluation of treatment response.

Guidelines
Current NCCN guidelines for soft tissue sarcoma (v. 2.2020) state that PET/CT may be useful in staging, prognostication, grading, and determining response to chemotherapy.[147.] The guidelines also state that PET can provide information on imatinib activity after 2 to 4 weeks of therapy when rapid reading of activity is considered necessary; however, long-term PET follow-up is rarely indicated. The guidelines also indicate that PET can be used to assess the progression of the disease if results from other imaging techniques (CT or MRI) are inconclusive.

Section Summary: Soft Tissue Sarcoma
Evidence for the use of PET or PET/CT in patients with soft tissue sarcoma consists of 2 systematic reviews. Results of the ARHQ review showed that PET or PET/CT had low diagnostic accuracy. Another systematic review reported evidence supporting the use of PET/CT in monitoring response to imatinib treatment.

The evidence does not support the use of FDG-PET and FDG--PET/CT for the diagnosis and staging and restaging of soft tissue sarcoma.

The evidence supports the use of FDG-PET and FDG-PET/CT for rapid reading of response to imatinib therapy.

The evidence does not support the use of FDG-PET and FDG--PET/CT for surveillance of soft tissue sarcoma.

Testicular Cancer

Systematic Reviews

An AHRQ technology assessment conducted by Ospina et al (2008) and studies evaluating residual masses in patients after chemotherapy for seminoma has supported the use of PET. [35,148]

The AHRQ systematic review conducted by Matchar et al (2004) found 1 prospective study and 4 retrospective studies that generally showed higher sensitivity and specificity for PET compared with CT.[116] However, these studies were small in size and failed to report separate results for patients with and without seminoma. Studies also failed to report separate results by clinical stage of the disease.

In addition, studies on PET's ability to discriminate viable tumor and necrosis or fibrosis after treatment of testicular cancer were flawed in 2 main ways. First, most studies did not compare the diagnostic accuracy of PET with other imaging modalities. Second, studies that did compare PET and CT did not state a clear threshold for a positive CT test, making study results difficult to interpret. Therefore, it is uncertain whether the use of PET leads to different patient management decisions and health outcomes compared with other imaging modalities.

Guidelines

Current NCCN guidelines for testicular cancer (v.3.2020) support the use of PET to evaluate residual masses that are greater than 3 cm following primary treatment with chemotherapy (at ≥6 weeks posttreatment).[149] If a PET scan is negative, surveillance is recommended. If a PET scan is positive, resection or biopsy of the residual mass is recommended. The guidelines warn that there is "limited predictive value for PET/CT scan for residual masses." Use of PET is not recommended for nonseminoma patients.

Section Summary: Testicular Cancer

Evidence for the use of PET or PET/CT in patients with testicular cancer consists of an AHRQ systematic review of small studies. Results showed that PET or PET/CT can be useful in evaluating residual masses following chemotherapy for seminoma. There is no evidence supporting the use of PET or PET/CT in nonseminoma patients. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of testicular cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of testicular cancer.

Thyroid Cancer

Systematic Reviews

Differentiated

Schutz et al (2018) conducted a systematic review and meta-analysis of 29 prospective studies (22 differentiated, 7 medullary) investigating the staging, restaging, and recurrence of thyroid cancer.[150] Meta-analyses showed higher sensitivity and specificity with PET compared with conventional imaging.

Haslerud et al (2016) conducted a systematic review of studies using FDG-PET to detect recurrent differentiated thyroid cancer in patients who had undergone ablative therapy.[151] The literature search, conducted through December 2014, identified 34 studies (total N =2639 patients) for inclusion: 17 using FDG-PET/CT, 11 using FDG-PET, and 6 using both methods. Study quality was assessed using the QUADAS tool. Pooled sensitivity and specificity for FDG-PET/CT were 80% (95% CI, 74% to 86%) and 76% (95% CI, 63% to 85%), respectively. Pooled sensitivity and specificity for FDG-PET alone were 77% (95% CI, 63% to 86%) and 76% (95% CI, 60% to 87%), respectively. Combining all 34 studies in the meta-analysis resulted in a pooled sensitivity and specificity of 79% (95% CI, 74% to 84%) and 79% (95% CI, 71% to 85%), respectively.

The NCCN report conducted by Podoloff et al (2009) showed that PET can localize recurrent disease when other imaging tests are negative.[37,] Additionally, PET was found to be prognostic in this setting, showing that more metabolically active lesions on PET were strongly correlated with reduced survival.[152,]

Guidelines
Current NCCN guidelines for thyroid carcinoma (v.2.2020) continue to support the use of FDG-PET/CT in thyroid cancer evaluations, such as when iodine-131 imaging is negative and stimulated thyroglobulin is greater than 2 to 5 ng/mL.[153,]

Medullary
A meta-analysis of studies on detecting recurrent or metastatic medullary thyroid carcinoma was conducted by Cheng et al (2012).[154,] The literature search, conducted through December 2010, identified 15 studies to be included in the meta-analysis: 8 used FDG-PET and 7 used FDG-PET/CT. The pooled sensitivity for FDG-PET alone in detecting recurrent or metastatic medullary thyroid cancer was 68% (95% CI, 64% to 72%). The pooled sensitivity for FDG-PET/CT was 69% (95% CI, 64% to 74%).

Guidelines
Current NCCN guidelines for medullary thyroid cancer (v. 2.2020) state that Ga-68 DOTATATE PET/CT may be considered as part of the diagnostic workup, and recommend contrast-enhanced CT with or without PET at 2 to 3 months postoperative surveillance.[153,] Additionally, PET/CT may be considered if the recurrent disease is suspected.

Section Summary: Thyroid Cancer
Evidence for the use of PET and PET/CT to diagnose recurrently differentiated and medullary thyroid cancer consists of systematic reviews and meta-analyses. Pooled sensitivity and specificity for FDG-PET and FDG-PET/CT in detecting recurrent differentiated thyroid cancer were comparable, ranging from 76% to 80%. Pooled sensitivity for both PET and PET/CT in detecting recurrent medullary thyroid cancer were also comparable (68% to 69%). The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of thyroid cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of thyroid cancer.

Cancer of Unknown Primary
Burglin et al (2017) conducted a systematic review and meta-analysis on the use of PET/CT for the detection of the primary tumor in patients with extra cervical metastases.[155,] The literature search identified 20 studies (total N =1942 patients) published between 2005 and 2016 for inclusion. The QUADAS tool was used to assess the risk of bias. In regard to patient selection and reference standard, the risk of bias was low; however, the risk of bias was high or unclear for most studies in regard to flow and timing of the index test. The pooled detection rate was 41% (95% CI, 39% to 43%), with large heterogeneity among the studies.

A TEC Assessment (2002) concluded that FDG-PET met TEC criteria for the workup and management of patients with cancers of unknown primary and a single site of metastatic disease.[156,] Specifically, local or regional therapy might be offered to these patients. In this setting, PET scanning might be used to verify the absence of disseminated disease.

Regarding this application, the TEC Assessment identified 4 reports of 47 total patients referred for imaging of a single known metastatic site from cancer of unknown primary. In 13 (28%) of these patients, PET scanning identified previously undetected metastases that were confirmed by biopsy. Therefore, the use of PET was found to contribute to optimal decision making regarding the appropriateness of local or regional therapy.

No evidence was identified that evaluated the use of FDG-PET for surveillance of patients with cancer of unknown primary.

Section Summary: Cancer of Unknown Primary
The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis, staging, and restaging of cancer of unknown primary.

Cancer Surveillance
Clinical utility of PET scanning in surveillance (i.e., in performing follow-up PET scans in asymptomatic patients to detect early disease recurrence) is not well-studied. (For this evidence review, a scan is considered a surveillance scan if performed more than 6 months after therapy [but 12 months for lymphoma].) The NCCN report by Podoloff et al (2009) stated that "PET as a surveillance tool should only be used in clinical trials."[37.] Additionally, NCCN guidelines for various malignancies often note that PET scans are not recommended in asymptomatic patients. For example, current NCCN guidelines for breast cancer comment that PET scans (as well as many other imaging modalities) provide no advantage in survival or ability to palliate recurrent disease and are not recommended.[33.]

Other Oncologic Applications
There are inadequate scientific data to permit conclusions on the role of PET scanning in other malignancies.

Summary of Evidence
Bladder Cancer
For individuals who have suspected or diagnosed bladder cancer in need of staging or restaging information who receive fluorine 18 (^{18}F) coupled with fluorodeoxyglucose (FDG) PET or FDG-PET/computed tomography (CT), the evidence includes a systematic review and meta-analysis. Relevant outcome is test validity. Pooled analyses showed relatively high sensitivity and specificity. Clinical guidelines include PET and PET/CT as considerations in staging bladder cancer, though CT, magnetic resonance imaging, and chest radiographs are also appropriate techniques for staging purposes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing bladder cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Bone Sarcoma
For individuals who have suspected or diagnosed bone sarcoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes systematic reviews and meta-analyses. Relevant outcome is test validity. Pooled analyses have shown that PET or PET/CT can effectively diagnose and stage bone sarcoma, including chondrosarcoma. Use of PET or PET/CT has high sensitivities and specificities in detecting metastases in bone and lymph nodes; however, the tests have low sensitivity in detecting lung metastases. Clinical guidelines include PET and CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing bone sarcoma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Brain Tumors
For individuals who have diagnosed brain tumors and in need of staging or restaging information or who have suspected brain tumor who receive FDG-PET, ^{18}F fluoro-ethyl-tyrosine PET, or carbon 11 (^{11}C) methionine PET, the evidence includes several systematic reviews and meta-analyses.

Relevant outcome is test validity. Pooled analyses have shown that PET or PET/CT can be effective in distinguishing brain tumors from normal tissue. Indirect comparisons between the radiotracers ^{11}C-methionine and FDG have shown that ^{11}C-methionine may have better diagnostic performance. Clinical guidelines include PET to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing brain cancer treatment who receive FDG-PET, ^{18}F fluoro-ethyl-tyrosine-PET, or ^{11}C-methionine PET, the evidence includes systematic reviews and meta-analyses. Relevant outcome is test validity. Pooled analyses did not support the use of PET for surveillance of brain cancer following treatment. The evidence is insufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Breast Cancer
For individuals who have diagnosed breast cancer and inconclusive results from other imaging techniques who receive adjunctive FDG-PET or FDG-PET/CT for staging or restaging, the evidence includes meta-analyses. Relevant outcome is test validity. While studies included in the meta-analyses reported variability in estimates of sensitivity and specificity, FDG-PET or FDG-PET/CT may be helpful in situations in which standard staging results are equivocal or suspicious, particularly in patients with locally advanced or metastatic disease. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected or diagnosed breast cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment, several systematic reviews, and meta-analyses. Relevant outcome is test validity. There is no evidence supporting the use of PET in diagnosing breast cancer. The false-negative rates (5.5% to 8.5%) using PET in patients with breast cancer can be considered unacceptable, given that breast biopsy can provide more definitive results. Use of PET/CT may be considered for the detection of metastases only when results from other imaging techniques are inconclusive. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic after completing breast cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Cervical Cancer
For individuals who have diagnosed cervical cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an Agency for Healthcare Research and Quality (AHRQ) report and a meta-analysis. Relevant outcome is test validity. Pooled results have shown that PET can be used for staging or restaging and for detecting recurrent disease. Clinical guidelines include PET and CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected cervical cancer or who are asymptomatic after completing cervical cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcomes are test accuracy and test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Colorectal Cancer
For individuals who have diagnosed colorectal cancer (CRC) and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment and several meta-analyses. Relevant outcome is test validity. Several pooled analyses evaluating staging or restaging using PET or PET/CT resulted in wide ranges of

sensitivities and specificities, from 16% to 99%. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspected CRC or who are asymptomatic after completing CRC treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment and meta-analysis. Relevant outcome is test validity. A meta-analysis evaluating the diagnostic accuracy of PET or PET/CT showed high sensitivity but low specificity. The evidence for the use of PET or PET/CT does not show a benefit over the use of contrast CT in patients with CRC. The evidence is insufficient to determine the effects of the technology on health outcomes.

Endometrial Cancer
For individuals who have diagnosed endometrial cancer in need of staging or restaging information or who are asymptomatic after completing endometrial cancer treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review and meta-analysis. Relevant outcome is test validity. Pooled estimates from the meta-analysis showed high sensitivities and specificities for FDG-PET/CT in detecting lymph node metastases and endometrial cancer recurrence following treatment. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Esophageal Cancer
For individuals who have diagnosed esophageal cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. Pooled estimates have shown high sensitivities and specificities compared to other diagnostic imaging techniques. Clinical guidelines include PET and CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected esophageal cancer or who are asymptomatic after completing esophageal cancer treatment who receive FDG-PET or FDG-PET/CT, the evidence includes meta-analyses. Relevant outcome is test validity. Pooled analyses have shown adequate sensitivities but low specificities. The evidence is insufficient to determine the effects of the technology on health outcomes.

Gastric Cancer
For individuals who have suspected or diagnosed gastric cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. Pooled analyses, with sensitivities and specificities ranging from 78% to 88%, have shown that PET or PET/CT can inform staging or restaging of patients with gastric cancer. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing gastric cancer treatment who receive FDG-PET or FDG-PET/CT, the evidence includes meta-analyses. Relevant outcome is test validity. Pooled analyses have shown low sensitivities and specificities. The evidence is insufficient to determine the effects of the technology on health outcomes.

Head and Neck Cancer
For individuals who have suspected or diagnosed head and neck cancer in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment and several meta-analyses. Relevant outcome is test validity. In patients with head and neck cancers, PET and PET/CT are better able to detect local and metastatic disease compared with other imaging techniques. Evidence has also shown that FDG-PET/CT may be useful in predicting response to therapy. Two meta-analyses calculated the ability of FDG-PET or PET/CT to detect the residual or recurrent disease during various stages of treatment and another meta-analysis calculated the ability of positive PET or PET/CT results to predict overall

survival and event-free survival. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing head and neck cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Non-Small-Cell Lung Cancer
For individuals who have suspected non-small-cell lung cancer (NSCLC) and inconclusive results from other imaging techniques or who have diagnosed NSCLC and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. Pooled analyses have shown that PET and PET/CT have better diagnostic performance than conventional imaging techniques. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected NSCLC or who are asymptomatic after completing non-small-cell lung cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Small-Cell Lung Cancer
For individuals with diagnosed small-cell lung cancer (SCLC) and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review and a meta-analysis. Relevant outcome is test validity. While the quality of the studies was considered low, PET and PET/CT can be considered for staging or restaging in patients with SCLC if a limited stage is suspected. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected SCLC or who are asymptomatic after completing SCLC treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcomes are test accuracy and test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Hodgkin and Non-Hodgkin Lymphoma
For individuals who have suspected or diagnosed Hodgkin and non-Hodgkin lymphoma in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment, several meta-analyses, and an RCT. Relevant outcome is test validity. Both PET and PET/CT have been found to provide useful information in the management of Hodgkin and non-Hodgkin lymphoma. The Deauville 5-point scale was developed based on PET results and can be used for staging and treatment response for patients with lymphoma. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing Hodgkin lymphoma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic after completing non-Hodgkin lymphoma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Melanoma
For individuals who have suspected or diagnosed stage I or II melanoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment. Relevant outcome is test validity. Evidence has shown PET and PET/CT are not as beneficial as the reference standard (sentinel node biopsy) for assessing regional lymph nodes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have diagnosed advanced melanoma (stage III or IV) and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment and a meta-analysis. Relevant outcome is test validity. Evidence has shown PET and PET/CT can detect systemic metastases in patients with advanced melanoma. Clinical guidelines include PET/CT for staging or restaging stage III or IV disease and for surveillance. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing melanoma treatment who receive FDG-PET or FDG-PET/CT, the evidence includes retrospective and observational studies. Relevant outcome is test validity. At the discretion of the physician, imaging surveillance can be considered every 3 to 12 months. Because recurrences usually occur within 3 years, screening asymptomatic patients beyond 3 to 5 years is not recommended. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Multiple Myeloma
For individuals who have suspected or diagnosed multiple myeloma in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes 2 systematic reviews, 1 of which conducted a meta-analysis. Relevant outcome is test validity. The meta-analysis reported high sensitivity in detecting extramedullary lesions in patients with multiple myeloma. The other systematic review compared FDG-PET with whole-body x-ray and reported that FDG-PET was more sensitive in detecting myeloma bone lesions. Clinical guidelines include PET/CT on the list of imaging techniques that may be useful for initial workup, as well as follow-up and surveillance as indicated. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing multiple myeloma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Neuroendocrine Tumors
For individuals who have suspected or diagnosed neuroendocrine tumors and in need of staging or restaging information or who are asymptomatic after completing neuroendocrine tumor treatment who receive FDG-PET or FDG-PET/CT, the evidence includes 2 meta-analyses. Relevant outcome is test validity. The evidence did not compare PET or PET/CT with other modalities and, therefore, did not provide comparative effectiveness information. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspected or diagnosed neuroendocrine tumors and in need of staging or restaging information who receive gallium 68 (^{68}Ga) PET or ^{68}Ga-PET/CT, the evidence includes several systematic reviews with meta-analyses. Relevant outcome is test validity. The meta-analyses showed relatively high sensitivities and specificities compared with other imaging techniques in the diagnosis and staging of neuroendocrine tumors. Clinical guidelines support the use of the ^{68}Ga radiotracer in the diagnosis and staging of neuroendocrine tumors. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing neuroendocrine tumor treatment who receive ^{68}Ga-PET or ^{68}Ga-PET/CT, there is no evidence. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ovarian Cancer
For individuals who have diagnosed ovarian cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ systematic review and several meta-analyses. Relevant outcome is test validity. Pooled sensitivities and specificities have supported the use of PET and PET/CT for the detection of recurrent ovarian cancer. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected ovarian cancer or who are asymptomatic after completing ovarian cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Pancreatic Cancer
For individuals who have suspected or diagnosed pancreatic cancer and with inconclusive results from other imaging techniques who receive adjunctive FDG-PET or FDG-PET/CT for staging or restaging, the evidence includes a TEC Assessment and a systematic review. Relevant outcome is test validity. The evidence has shown that PET and PET/CT do not have a high enough negative predictive value to surpass current standard decision thresholds. Therefore, PET or PET/CT should only be considered if the results from standard staging methods are inconclusive. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected or diagnosed pancreatic cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ systematic review, a TEC Assessment, and a meta-analysis published after the review and assessment. Relevant outcome is test validity. The evidence has shown that PET and PET/CT do not have a high enough negative predictive value to surpass current standard decision thresholds. Therefore, PET or PET/CT should only be considered if the results from standard staging methods are inconclusive. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic after completing pancreatic cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Penile Cancer
For individuals who have suspected or diagnosed penile cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review and a meta-analysis. Relevant outcome is test validity. The evidence has shown that PET had a low sensitivity, and no comparisons were made with other modalities. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic after completing penile cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Prostate Cancer
For individuals who have suspected or diagnosed prostate cancer and in need of staging or restaging information who receive ^{11}C-choline PET, ^{11}C-choline PET/CT, ^{18}F-fluciclovine PET, or ^{18}F-fluciclovine PET/CT, the evidence includes several meta-analyses. Relevant outcome is test

validity. Meta-analyses have reported that the choice of radiotracer affects the sensitivity and specificity of the scans, with most evidence showing that the use of ^{11}C-choline or ^{18}F-fluciclovine results in the highest sensitivities and specificities compared with FDG-PET and ^{11}C-acetate. Of interest is a single-study that investigated the use of PET/CT results to inform patient decisions on radiotherapy treatment plans. The study reported that 40% of the patients altered the extent of the treatment planned based on the PET/CT results. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic after completing prostate cancer treatment who receive ^{11}C-choline PET, ^{11}C-choline PET/CT, ^{18}F-fluciclovine PET, or^{18}F-fluciclovine PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspected or diagnosed prostate cancer and in need of staging or restaging information who receive ^{68}Ga-PET or ^{68}Ga-PET/CT, the evidence includes a meta-analysis of small single-institution studies. Relevant outcome is test validity. The evidence is limited, resulting in estimates with large confidence intervals. The evidence is insufficient to determine the effects of the technology on health outcomes.

Renal Cell Carcinoma
For individuals who are diagnosed with renal cell carcinoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review and meta-analysis. Relevant outcome is test validity. The review concluded that PET has the potential to detect metastatic or recurrent lesions in patients with renal cell cancer but that additional prospective studies are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Soft Tissue Sarcoma
For individuals who have diagnosed soft tissue sarcoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ review and a systematic review using PET for assessing response to imatinib. Relevant outcome is test validity. The review reported that PET had low diagnostic accuracy and there was a lack of studies comparing PET with alternative diagnostic modalities. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with diagnosed soft tissue sarcoma and in need of rapid reading of response to imatinib treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review. Relevant outcome is test validity. The review concluded that PET/CT can be used to monitor treatment response to imatinib, which can lead to individually adapted treatment strategies. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected soft tissue sarcoma or who are asymptomatic after completing soft tissue sarcoma treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review. Relevant outcome is test validity. The review concluded that there was insufficient evidence on the use of PET for the detection of locoregional recurrence. The evidence is insufficient to determine the effects of the technology on health outcomes.

Testicular Cancer
For individuals with diagnosed testicular cancer in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ systematic review and assessment. Relevant outcome is test validity. Results have shown that PET or PET/CT can evaluate residual masses following chemotherapy for seminoma. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. There is no evidence supporting the use of PET or PET/CT in nonseminoma patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected testicular cancer or who are asymptomatic after completing testicular cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Thyroid Cancer
For individuals with diagnosed thyroid cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes systematic reviews and meta-analyses. Relevant outcome is test validity. Pooled analyses have shown that PET or PET/CT can effectively detect recurrent differentiated thyroid cancer. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected thyroid cancer or who are asymptomatic after completing thyroid cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Cancer of Unknown Primary and Single-Site Metastatic Disease
For individuals with cancer of unknown primary and single-site metastatic disease who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment. Relevant outcome is test validity. Studies reviewed in the assessment showed that PET identified previously undetected metastases confirmed by biopsy. Additionally, PET can contribute to the management of patients with cancer of unknown primary. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Supplemental Information
Practice Guidelines and Position Statements
Current National Comprehensive Cancer Network and American College of Radiology guidelines are summarized in each section of the Rationale.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
The Medicare coverage policy on positron emission tomography scans, which was updated in 2013, is summarized in Appendix Table 1.[157,]

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in July 2020 identified a considerably large number of ongoing and unpublished trials that would likely influence this review.

Appendix 1

Appendix Table 1. Medicare Coverage of FDG PET for Oncologic Conditions
Effective for claims with dates of service on and after June 11, 2013, the chart below summarizes national FDG PET coverage for oncologic conditions:

FDG PET for Cancers by Tumor Type	Initial Treatment Strategy (formerly "diagnosis" & "staging")	Subsequent Treatment Strategy (formerly "restaging" & "monitoring response to treatment")
Colorectal	Cover	Cover
Esophagus	Cover	Cover
Head and Neck (not thyroid, CNS)	Cover	Cover
Lymphoma	Cover	Cover

FDG PET for Cancers by Tumor Type	Initial Treatment Strategy (formerly "diagnosis" & "staging")	Subsequent Treatment Strategy (formerly "restaging" & "monitoring response to treatment")
Non-small cell lung	Cover	Cover
Ovary	Cover	Cover
Brain	Cover	Cover
Cervix	Cover with exceptions *	Cover
Small cell lung	Cover	Cover
Soft tissue sarcoma	Cover	Cover
Pancreas	Cover	Cover
Testes	Cover	Cover
Prostate	**Non-cover**	Cover
Thyroid	Cover	Cover
Breast (male and female)	Cover with exceptions *	Cover
Melanoma	Cover with exceptions *	Cover
All other solid tumors	Cover	Cover
Myeloma	Cover	Cover
All other cancers not listed	Cover	Cover

*Cervix: Nationally non-covered for the initial diagnosis of cervical cancer related to initial anti-tumor treatment strategy. All other indications for initial anti-tumor treatment strategy for cervical cancer are nationally covered.
*Breast: Nationally non-covered for initial diagnosis and/or staging of axillary lymph nodes. Nationally covered for initial staging of metastatic disease. All other indications for initial anti-tumor treatment strategy for breast cancer are nationally covered.
*Melanoma: Nationally non-covered for initial staging of regional lymph nodes. All other indications for initial anti-tumor treatment strategy for melanoma are nationally covered.

References

1. Food and Drug Administration. Positron Emission Tomography (PET). 2016; http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm085783.htm. Accessed July 20, 2020.
2. Riberich R. FDA-Approved PET Radiopharmaceuticals. http://www.radiopharmaceuticals.info/pet-radiopharmaceuticals.html. Accessed July 15, 2020.
3. Zionexa. Zionexa USA and PETNET Solutions announce FDA approval of Cerianna (Fluoroestradiol F18). Accessed July 15, 2020. https://www.zionexa.com/2020/05/27/zionexa-usa-and-petnet-solutions-announce-fda-approval-of-cerianna-fluoroestradiol-f18/
4. Zhang H, Xing W, Kang Q, et al. Diagnostic value of [18F] FDG-PET and PET/CT in urinary bladder cancer: a meta-analysis. Tumour Biol. May 2015; 36(5): 3209-14. PMID 25809703
5. van der Pol CB, Sahni VA, Eberhardt SC, et al. ACR Appropriateness Criteria (R) Pretreatment Staging of Muscle-Invasive Bladder Cancer. J Am Coll Radiol. May 2018; 15(5S): S150-S159. PMID 29724418
6. Allen BC, Oto A, Akin O, et al. ACR Appropriateness Criteria(R) Post-Treatment Surveillance of Bladder Cancer. J Am Coll Radiol. Nov 2019; 16(11S): S417-S427. PMID 31685109
7. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Bladder Cancer. Version 5.2020. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed July 16, 2020.
8. Zhang Q, Xi Y, Li D, et al. The utility of 18 F-FDG PET and PET/CT in the diagnosis and staging of chondrosarcoma: a meta-analysis. J Orthop Surg Res. Jun 22 2020; 15(1): 229. PMID 32571371
9. Liu F, Zhang Q, Zhu D, et al. Performance of Positron Emission Tomography and Positron Emission Tomography/Computed Tomography Using Fluorine-18-Fluorodeoxyglucose for the Diagnosis, Staging, and Recurrence Assessment of Bone Sarcoma: A Systematic Review and Meta-Analysis. Medicine (Baltimore). Sep 2015; 94(36): e1462. PMID 26356700

10. Treglia G, Salsano M, Stefanelli A, et al. Diagnostic accuracy of F-FDG-PET and PET/CT in patients with Ewing sarcoma family tumours: a systematic review and a meta-analysis. Skeletal Radiol. Mar 2012; 41(3): 249-56. PMID 22072239
11. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed July 24, 2020.
12. Dunet V, Pomoni A, Hottinger A, et al. Performance of 18F-FET versus 18F-FDG-PET for the diagnosis and grading of brain tumors: systematic review and meta-analysis. Neuro-oncology. Mar 2016; 18(3): 426-34. PMID 26243791
13. Dunet V, Rossier C, Buck A, et al. Performance of 18F-fluoro-ethyl-tyrosine (18F-FET) PET for the differential diagnosis of primary brain tumor: a systematic review and Metaanalysis. J Nucl Med. Feb 2012; 53(2): 207-14. PMID 22302961
14. Zhao C, Zhang Y, Wang J. A meta-analysis on the diagnostic performance of (18)F-FDG and (11)C-methionine PET for differentiating brain tumors. AJNR Am J Neuroradiol. Jun 2014; 35(6): 1058-65. PMID 24029389
15. Deng SM, Zhang B, Wu YW, et al. Detection of glioma recurrence by C-methionine positron emission tomography and dynamic susceptibility contrast-enhanced magnetic resonance imaging: a meta-analysis. Nucl Med Commun. Aug 2013; 34(8): 758-66. PMID 23670103
16. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Central Nervous System Cancers. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed July 16, 2020.
17. Liang X, Yu J, Wen B, et al. MRI and FDG-PET/CT based assessment of axillary lymph node metastasis in early breast cancer: a meta-analysis. Clin Radiol. Apr 2017; 72(4): 295-301. PMID 28139203
18. Caldarella C, Treglia G, Giordano A. Diagnostic performance of dedicated positron emission mammography using fluorine-18-fluorodeoxyglucose in women with suspicious breast lesions: a meta-analysis. Clin Breast Cancer. Aug 2014; 14(4): 241-8. PMID 24472718
19. Sloka JS, Hollett PD, Mathews M. A quantitative review of the use of FDG-PET in the axillary staging of breast cancer. Med Sci Monit. Mar 2007; 13(3): RA37-46. PMID 17325645
20. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Positron Emission Tomography in Breast Cancer. Technol Eval Cent Assess. 2001;16(5).
21. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography for Evaluating Breast Cancer. Technol Eval Cent Assess. 2003;18(14).
22. Hong S, Li J, Wang S. 18FDG PET-CT for diagnosis of distant metastases in breast cancer patients. A meta-analysis. Surg Oncol. Jun 2013; 22(2): 139-43. PMID 23566435
23. Rong J, Wang S, Ding Q, et al. Comparison of 18 FDG PET-CT and bone scintigraphy for detection of bone metastases in breast cancer patients. A meta-analysis. Surg Oncol. Jun 2013; 22(2): 86-91. PMID 23726506
24. Isasi CR, Moadel RM, Blaufox MD. A meta-analysis of FDG-PET for the evaluation of breast cancer recurrence and metastases. Breast Cancer Res Treat. Mar 2005; 90(2): 105-12. PMID 15803356
25. Xiao Y, Wang L, Jiang X, et al. Diagnostic efficacy of 18F-FDG-PET or PET/CT in breast cancer with suspected recurrence: a systematic review and meta-analysis. Nucl Med Commun. Nov 2016; 37(11): 1180-8. PMID 27428888
26. Liu Q, Wang C, Li P, et al. The Role of (18)F-FDG PET/CT and MRI in Assessing Pathological Complete Response to Neoadjuvant Chemotherapy in Patients with Breast Cancer: A Systematic Review and Meta-Analysis. Biomed Res Int. 2016; 2016: 3746232. PMID 26981529
27. Sheikhbahaei S, Trahan TJ, Xiao J, et al. FDG-PET/CT and MRI for Evaluation of Pathologic Response to Neoadjuvant Chemotherapy in Patients With Breast Cancer: A Meta-Analysis of Diagnostic Accuracy Studies. Oncologist. Aug 2016; 21(8): 931-9. PMID 27401897

28. Li H, Yao L, Jin P, et al. MRI and PET/CT for evaluation of the pathological response to neoadjuvant chemotherapy in breast cancer: A systematic review and meta-analysis. Breast. Aug 2018; 40: 106-115. PMID 29758503
29. Cheng X, Li Y, Liu B, et al. 18F-FDG PET/CT and PET for evaluation of pathological response to neoadjuvant chemotherapy in breast cancer: a meta-analysis. Acta Radiol. Jul 2012; 53(6): 615-27. PMID 22734080
30. Wang Y, Zhang C, Liu J, et al. Is 18F-FDG PET accurate to predict neoadjuvant therapy response in breast cancer? A meta-analysis. Breast Cancer Res Treat. Jan 2012; 131(2): 357-69. PMID 21960111
31. Podoloff DA, Advani RH, Allred C, et al. NCCN task force report: positron emission tomography (PET)/computed tomography (CT) scanning in cancer. J Natl Compr Canc Netw. May 2007; 5 Suppl 1: S1-22; quiz S23-2. PMID 17509259
32. Moy L, Bailey L, D'Orsi C, et al. ACR Appropriateness Criteria (R) Stage I Breast Cancer: Initial Workup and Surveillance for Local Recurrence and Distant Metastases in Asymptomatic Women. J Am Coll Radiol. May 2017; 14(5S): S282-S292. PMID 28473085
33. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 5.2020. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 16, 2020.
34. Chu Y, Zheng A, Wang F, et al. Diagnostic value of 18F-FDG-PET or PET-CT in recurrent cervical cancer: a systematic review and meta-analysis. Nucl Med Commun. Feb 2014; 35(2): 144-50. PMID 24177043
35. Ospina MB, Horton J, Seida J, et al. Technology Assessment Report : Positron emission tomography for nine cancers (bladder, brain, cervical, kidney, ovarian, pancreatic, prostate, small cell lung, testicular). Rockville, MD: Agency for Healthcare Research and Quality; 2008.
36. Yen TC, See LC, Chang TC, et al. Defining the priority of using 18F-FDG PET for recurrent cervical cancer. J Nucl Med. Oct 2004; 45(10): 1632-9. PMID 15471826
37. Podoloff DA, Ball DW, Ben-Josef E, et al. NCCN task force: clinical utility of PET in a variety of tumor types. J Natl Compr Canc Netw. Jun 2009; 7 Suppl 2: S1-26. PMID 19555588
38. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Rectal Cancer. Version 6.2020. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed July 24, 2020.
39. Mahmud A, Poon R, Jonker D. PET imaging in anal canal cancer: a systematic review and meta-analysis. Br J Radiol. Dec 2017; 90(1080): 20170370. PMID 28972796
40. Jones M, Hruby G, Solomon M, et al. The Role of FDG-PET in the Initial Staging and Response Assessment of Anal Cancer: A Systematic Review and Meta-analysis. Ann Surg Oncol. Oct 2015; 22(11): 3574-81. PMID 25652048
41. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography in Colorectal Cancer. Technol Eval Cent Assess. 1999;14(25).
42. Albertsson P, Alverbratt C, Liljegren A, et al. Positron emission tomography and computed tomographic (PET/CT) imaging for radiation therapy planning in anal cancer: A systematic review and meta-analysis. Crit Rev Oncol Hematol. Jun 2018; 126: 6-12. PMID 29759568
43. Ye Y, Liu T, Lu L, et al. Pre-operative TNM staging of primary colorectal cancer by (18)F-FDG PET-CT or PET: a meta-analysis including 2283 patients. Int J Clin Exp Med. 2015; 8(11): 21773-85. PMID 26885142
44. Li C, Lan X, Yuan H, et al. 18F-FDG PET predicts pathological response to preoperative chemoradiotherapy in patients with primary rectal cancer: a meta-analysis. Ann Nucl Med. Jun 2014; 28(5): 436-46. PMID 24623152
45. Maffione AM, Chondrogiannis S, Capirci C, et al. Early prediction of response by F-FDG PET/CT during preoperative therapy in locally advanced rectal cancer: a systematic review. Eur J Surg Oncol. Oct 2014; 40(10): 1186-94. PMID 25060221

46. Memon S, Lynch AC, Akhurst T, et al. Systematic review of FDG-PET prediction of complete pathological response and survival in rectal cancer. Ann Surg Oncol. Oct 2014; 21(11): 3598-607. PMID 24802909
47. Gwynne S, Mukherjee S, Webster R, et al. Imaging for target volume delineation in rectal cancer radiotherapy--a systematic review. Clin Oncol (R Coll Radiol). Feb 2012; 24(1): 52-63. PMID 22035634
48. Rymer B, Curtis NJ, Siddiqui MR, et al. FDG PET/CT Can Assess the Response of Locally Advanced Rectal Cancer to Neoadjuvant Chemoradiotherapy: Evidence From Meta-analysis and Systematic Review. Clin Nucl Med. May 2016; 41(5): 371-5. PMID 26914561
49. Yu T, Meng N, Chi D, et al. Diagnostic Value of (18)F-FDG PET/CT in Detecting Local Recurrent Colorectal Cancer: A Pooled Analysis of 26 Individual Studies. Cell Biochem Biophys. Jun 2015; 72(2): 443-51. PMID 25737131
50. Maffione AM, Marzola MC, Capirci C, et al. Value of (18)F-FDG PET for Predicting Response to Neoadjuvant Therapy in Rectal Cancer: Systematic Review and Meta-Analysis. AJR Am J Roentgenol. Jun 2015; 204(6): 1261-8. PMID 26001237
51. Lu YY, Chen JH, Chien CR, et al. Use of FDG-PET or PET/CT to detect recurrent colorectal cancer in patients with elevated CEA: a systematic review and meta-analysis. Int J Colorectal Dis. Aug 2013; 28(8): 1039-47. PMID 23407908
52. Sobhani I, Itti E, Luciani A, et al. Colorectal cancer (CRC) monitoring by 6-monthly 18FDG-PET/CT: an open-label multicentre randomised trial. Ann Oncol. Apr 01 2018; 29(4): 931-937. PMID 29365058
53. Fowler KJ, Kaur H, Cash BD, et al. ACR Appropriateness Criteria (R) Pretreatment Staging of Colorectal Cancer. J Am Coll Radiol. May 2017; 14(5S): S234-S244. PMID 28473079
54. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Colon Cancer. Version 4.2020. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed July 16, 2020.
55. Bollineni VR, Ytre-Hauge S, Bollineni-Balabay O, et al. High Diagnostic Value of 18F-FDG PET/CT in Endometrial Cancer: Systematic Review and Meta-Analysis of the Literature. J Nucl Med. Jun 2016; 57(6): 879-85. PMID 26823564
56. Kroese TE, Goense L, van Hillegersberg R, et al. Detection of distant interval metastases after neoadjuvant therapy for esophageal cancer with 18F-FDG PET(/CT): a systematic review and meta-analysis. Dis Esophagus. Dec 01 2018; 31(12). PMID 29917073
57. Cong L, Wang S, Gao T, et al. The predictive value of 18F-FDG PET for pathological response of primary tumor in patients with esophageal cancer during or after neoadjuvant chemoradiotherapy: a meta-analysis. Jpn J Clin Oncol. Dec 2016; 46(12): 1118-1126. PMID 27702836
58. Goense L, van Rossum PS, Reitsma JB, et al. Diagnostic Performance of F-FDG PET and PET/CT for the Detection of Recurrent Esophageal Cancer After Treatment with Curative Intent: A Systematic Review and Meta-Analysis. J Nucl Med. Jul 2015; 56(7): 995-1002. PMID 25952733
59. Shi W, Wang W, Wang J, et al. Meta-analysis of 18FDG PET-CT for nodal staging in patients with esophageal cancer. Surg Oncol. Jun 2013; 22(2): 112-6. PMID 23478047
60. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Cancer. Version 3.2020. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed August 5, 2020.
61. Li P, Liu Q, Wang C, et al. Fluorine-18-fluorodeoxyglucose positron emission tomography to evaluate recurrent gastric cancer after surgical resection: a systematic review and meta-analysis. Ann Nucl Med. Apr 2016; 30(3): 179-87. PMID 26830546
62. Zou H, Zhao Y. 18FDG PET-CT for detecting gastric cancer recurrence after surgical resection: a meta-analysis. Surg Oncol. Sep 2013; 22(3): 162-6. PMID 23747134
63. Wu LM, Hu JN, Hua J, et al. 18 F-fluorodeoxyglucose positron emission tomography to evaluate recurrent gastric cancer: a systematic review and meta-analysis. J Gastroenterol Hepatol. Mar 2012; 27(3): 472-80. PMID 21916986

64. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Gastric Cancer. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed July 4, 2020.
65. Chen WS, Li JJ, Hong L, et al. Comparison of MRI, CT and 18F-FDG PET/CT in the diagnosis of local and metastatic of nasopharyngeal carcinomas: an updated meta analysis of clinical studies. Am J Transl Res. 2016; 8(11): 4532-4547. PMID 27904660
66. Wei J, Pei S, Zhu X. Comparison of 18F-FDG PET/CT, MRI and SPECT in the diagnosis of local residual/recurrent nasopharyngeal carcinoma: A meta-analysis. Oral Oncol. Jan 2016; 52: 11-7. PMID 26547126
67. Cheung PK, Chin RY, Eslick GD. Detecting Residual/Recurrent Head Neck Squamous Cell Carcinomas Using PET or PET/CT: Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg. Mar 2016; 154(3): 421-32. PMID 26715675
68. Sheikhbahaei S, Taghipour M, Ahmad R, et al. Diagnostic Accuracy of Follow-Up FDG PET or PET/CT in Patients With Head and Neck Cancer After Definitive Treatment: A Systematic Review and Meta-Analysis. AJR Am J Roentgenol. Sep 2015; 205(3): 629-39. PMID 26295652
69. Sheikhbahaei S, Ahn SJ, Moriarty E, et al. Intratherapy or Posttherapy FDG PET or FDG PET/CT for Patients With Head and Neck Cancer: A Systematic Review and Meta-analysis of Prognostic Studies. AJR Am J Roentgenol. Nov 2015; 205(5): 1102-13. PMID 26496559
70. Rohde M, Dyrvig AK, Johansen J, et al. 18F-fluoro-deoxy-glucose-positron emission tomography/computed tomography in diagnosis of head and neck squamous cell carcinoma: a systematic review and meta-analysis. Eur J Cancer. Sep 2014; 50(13): 2271-9. PMID 25011659
71. Yi X, Fan M, Liu Y, et al. 18 FDG PET and PET-CT for the detection of bone metastases in patients with head and neck cancer. A meta-analysis. J Med Imaging Radiat Oncol. Dec 2013; 57(6): 674-9. PMID 24283555
72. Gao S, Li S, Yang X, et al. 18FDG PET-CT for distant metastases in patients with recurrent head and neck cancer after definitive treatment. A meta-analysis. Oral Oncol. Mar 2014; 50(3): 163-7. PMID 24368204
73. Helsen N, Van den Wyngaert T, Carp L, et al. FDG-PET/CT for treatment response assessment in head and neck squamous cell carcinoma: a systematic review and meta-analysis of diagnostic performance. Eur J Nucl Med Mol Imaging. Jun 2018; 45(6): 1063-1071. PMID 29478080
74. Li Q, Zhang J, Cheng W, et al. Prognostic value of maximum standard uptake value, metabolic tumor volume, and total lesion glycolysis of positron emission tomography/computed tomography in patients with nasopharyngeal carcinoma: A systematic review and meta-analysis. Medicine (Baltimore). Sep 2017; 96(37): e8084. PMID 28906411
75. Lin J, Xie G, Liao G, et al. Prognostic value of 18F-FDG-PET/CT in patients with nasopharyngeal carcinoma: a systematic review and meta-analysis. Oncotarget. May 16 2017; 8(20): 33884-33896. PMID 27980228
76. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography in Head and Neck Cancer. Technol Eval Cent Assess. 2000;15(4).
77. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed July 17, 2020.
78. Barger RL, Nandalur KR. Diagnostic performance of dual-time 18F-FDG PET in the diagnosis of pulmonary nodules: a meta-analysis. Acad Radiol. Feb 2012; 19(2): 153-8. PMID 22104289
79. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography for Non-CNS Cancers. Technol Eval Cent Assess. 1997;12(3).
80. Brea TP, Ravina AR, Villamor JMC, et al. Use of Magnetic Resonance Imaging for N-Staging in Patients with Non-Small Cell Lung Cancer. A Systematic Review. Arch Bronconeumol. Jan 2019; 55(1): 9-16. PMID 29803524

81. Ruilong Z, Daohai X, Li G, et al. Diagnostic value of 18F-FDG-PET/CT for the evaluation of solitary pulmonary nodules: a systematic review and meta-analysis. Nucl Med Commun. Jan 2017; 38(1): 67-75. PMID 27741214
82. Li Y, Jin G, Su D. Comparison of Gadolinium-enhanced MRI and 18FDG PET/PET-CT for the diagnosis of brain metastases in lung cancer patients: A meta-analysis of 5 prospective studies. Oncotarget. May 30 2017; 8(22): 35743-35749. PMID 28415747
83. He YQ, Gong HL, Deng YF, et al. Diagnostic efficacy of PET and PET/CT for recurrent lung cancer: a meta-analysis. Acta Radiol. Apr 2014; 55(3): 309-17. PMID 24081215
84. Li J, Xu W, Kong F, et al. Meta-analysis: accuracy of 18FDG PET-CT for distant metastasis staging in lung cancer patients. Surg Oncol. Sep 2013; 22(3): 151-5. PMID 23664848
85. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 6.2020. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed July 7, 2020.
86. Silvestri GA, Gonzalez AV, Jantz MA, et al. Methods for staging non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. May 2013; 143(5 Suppl): e211S-e250S. PMID 23649440
87. Lu YY, Chen JH, Liang JA, et al. 18F-FDG PET or PET/CT for detecting extensive disease in small-cell lung cancer: a systematic review and meta-analysis. Nucl Med Commun. Jul 2014; 35(7): 697-703. PMID 24694775
88. Ruben JD, Ball DL. The efficacy of PET staging for small-cell lung cancer: a systematic review and cost analysis in the Australian setting. J Thorac Oncol. Jun 2012; 7(6): 1015-20. PMID 22534816
89. Seidenfeld J, Samson DJ, Bonnell CJ, et al. Management of small cell lung cancer. Evid Rep Technol Assess (Full Rep). Jul 2006(143):1-154.
90. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Small Cell Lung Cancer. Version 4.2020. https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed July 6, 2020.
91. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography in Lymphoma. Technol Eval Cent Assess. 1999;14(26).
92. Adams HJ, Kwee TC, de Keizer B, et al. Systematic review and meta-analysis on the diagnostic performance of FDG-PET/CT in detecting bone marrow involvement in newly diagnosed Hodgkin lymphoma: is bone marrow biopsy still necessary?. Ann Oncol. May 2014; 25(5): 921-7. PMID 24351400
93. Adams HJ, Kwee TC, de Keizer B, et al. FDG PET/CT for the detection of bone marrow involvement in diffuse large B-cell lymphoma: systematic review and meta-analysis. Eur J Nucl Med Mol Imaging. Mar 2014; 41(3): 565-74. PMID 24281821
94. Adams HJA, Kwee TC. Proportion of false-positive lesions at interim and end-of-treatment FDG-PET in lymphoma as determined by histology: Systematic review and meta-analysis. Eur J Radiol. Nov 2016; 85(11): 1963-1970. PMID 27776647
95. Adams HJ, Nievelstein RA, Kwee TC. Outcome of Hodgkin Lymphoma Patients With a Posttreatment 18F-Fluoro-2-Deoxy-d-Glucose Positron Emission Tomography (FDG-PET)-Negative Residual Mass: Systematic Review and Meta-analysis. Pediatr Hematol Oncol. 2015; 32(8): 515-24. PMID 26561044
96. Adams HJ, Kwee TC. Pretransplant FDG-PET in aggressive non-Hodgkin lymphoma: systematic review and meta-analysis. Eur J Haematol. Apr 2017; 98(4): 337-347. PMID 27943422
97. Adams HJ, Kwee TC. Prognostic value of pretransplant FDG-PET in refractory/relapsed Hodgkin lymphoma treated with autologous stem cell transplantation: systematic review and meta-analysis. Ann Hematol. Apr 2016; 95(5): 695-706. PMID 26931115
98. Zhu D, Xu XL, Fang C, et al. Prognostic value of interim (18)F-FDG-PET in diffuse large B cell lymphoma treated with rituximab-based immune-chemotherapy: a systematic review and meta-analysis. Int J Clin Exp Med. 2015; 8(9): 15340-50. PMID 26629023
99. Borchmann P, Goergen H, Kobe C, et al. PET-guided treatment in patients with advanced-stage Hodgkin's lymphoma (HD18): final results of an open-label,

international, randomised phase 3 trial by the German Hodgkin Study Group. Lancet. Dec 23 2018; 390(10114): 2790-2802. PMID 29061295
100. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Hodgkin Lymphoma. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed July 8, 2020.
101. National Comprehensive Cancer Network (NCCN). NCCN Clincal Practice Guidelines in Oncology: B-Cell Lymphomas. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 1, 2020.
102. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Hairy Cell Leukemia. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed July 2, 2020.
103. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: T-Cell Lymphomas. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed August 2, 2020.
104. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 4.2020. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August July 31, 2020.
105. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography in Melanoma. Technol Eval Cent Assess. 1999;14(27).
106. Rodriguez Rivera AM, Alabbas H, Ramjaun A, et al. Value of positron emission tomography scan in stage III cutaneous melanoma: a systematic review and meta-analysis. Surg Oncol. Mar 2014; 23(1): 11-6. PMID 24556310
107. Lu YY, Chen JH, Lin WY, et al. FDG PET or PET/CT for detecting intramedullary and extramedullary lesions in multiple Myeloma: a systematic review and meta-analysis. Clin Nucl Med. Sep 2012; 37(9): 833-7. PMID 22889770
108. van Lammeren-Venema D, Regelink JC, Riphagen II, et al. F-fluoro-deoxyglucose positron emission tomography in assessment of myeloma-related bone disease: a systematic review. Cancer. Apr 15 2012; 118(8): 1971-81. PMID 21887677
109. Barrio M, Czernin J, Fanti S, et al. The Impact of Somatostatin Receptor-Directed PET/CT on the Management of Patients with Neuroendocrine Tumor: A Systematic Review and Meta-Analysis. J Nucl Med. May 2017; 58(5): 756-761. PMID 28082438
110. Deppen SA, Blume J, Bobbey AJ, et al. 68Ga-DOTATATE Compared with 111In-DTPA-Octreotide and Conventional Imaging for Pulmonary and Gastroenteropancreatic Neuroendocrine Tumors: A Systematic Review and Meta-Analysis. J Nucl Med. Jun 2016; 57(6): 872-8. PMID 26769864
111. Treglia G, Castaldi P, Rindi G, et al. Diagnostic performance of Gallium-68 somatostatin receptor PET and PET/CT in patients with thoracic and gastroenteropancreatic neuroendocrine tumours: a meta-analysis. Endocrine. Aug 2012; 42(1): 80-7. PMID 22350660
112. Treglia G, Cocciolillo F, de Waure C, et al. Diagnostic performance of 18F-dihydroxyphenylalanine positron emission tomography in patients with paraganglioma: a meta-analysis. Eur J Nucl Med Mol Imaging. Jul 2012; 39(7): 1144-53. PMID 22358431
113. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed July 17, 2020.
114. Xu B, Ma J, Jiang G, et al. Diagnostic value of positron emission tomography (PET) and PET/computed tomography in recurrent/metastatic ovarian cancer: A meta-analysis. J Obstet Gynaecol Res. Feb 2017; 43(2): 378-386. PMID 28150407
115. Limei Z, Yong C, Yan X, et al. Accuracy of positron emission tomography/computed tomography in the diagnosis and restaging for recurrent ovarian cancer: a meta-analysis. Int J Gynecol Cancer. May 2013; 23(4): 598-607. PMID 23502451

116. Matchar DB, Kulasingam SL, Havrilesky L, et al. Positron Emission Testing for Six Cancers (Brain, Cervical, Small Cell Lung, Ovarian, Pancreatic and Testicular). Rockville, MD: Agency for Healthcare Research and Quality; 2004.
117. Kang SK, Reinhold C, Atri M, et al. ACR Appropriateness Criteria (R) Staging and Follow-Up of Ovarian Cancer. J Am Coll Radiol. May 2018; 15(5S): S198-S207. PMID 29724422
118. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed July 17, 2020.
119. Best LM, Rawji V, Pereira SP, et al. Imaging modalities for characterising focal pancreatic lesions. Cochrane Database Syst Rev. Apr 17 2017; 4: CD010213. PMID 28415140
120. Wang L, Dong P, Wang WG, et al. Positron emission tomography modalities prevent futile radical resection of pancreatic cancer: A meta-analysis. Int J Surg. Oct 2017; 46: 119-125. PMID 28890410
121. Rijkers AP, Valkema R, Duivenvoorden HJ, et al. Usefulness of F-18-fluorodeoxyglucose positron emission tomography to confirm suspected pancreatic cancer: a meta-analysis. Eur J Surg Oncol. Jul 2014; 40(7): 794-804. PMID 24755095
122. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography in Pancreatic Cancer. Technol Eval Cent Assess. 1999;14(28).
123. Ghaneh P, Hanson R, Titman A, et al. PET-PANC: multicentre prospective diagnostic accuracy and health economic analysis study of the impact of combined modality 18fluorine-2-fluoro-2-deoxy-d-glucose positron emission tomography with computed tomography scanning in the diagnosis and management of pancreatic cancer. Health Technol Assess. Feb 2018; 22(7): 1-114. PMID 29402376
124. Sadeghi R, Gholami H, Zakavi SR, et al. Accuracy of 18F-FDG PET/CT for diagnosing inguinal lymph node involvement in penile squamous cell carcinoma: systematic review and meta-analysis of the literature. Clin Nucl Med. May 2012; 37(5): 436-41. PMID 22475891
125. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Penile Cancer. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/penile.pdf. Accessed July 30, 2020.
126. Liu J, Chen Z, Wang T, et al. Influence of Four Radiotracers in PET/CT on Diagnostic Accuracy for Prostate Cancer: A Bivariate Random-Effects Meta-Analysis. Cell Physiol Biochem. 2016; 39(2): 467-80. PMID 27383216
127. Ouyang Q, Duan Z, Lei J, et al. Comparison of meta-analyses among elastosonography (ES) and positron emission tomography/computed tomography (PET/CT) imaging techniques in the application of prostate cancer diagnosis. Tumour Biol. Mar 2016; 37(3): 2999-3007. PMID 26415734
128. Fanti S, Minozzi S, Castellucci P, et al. PET/CT with (11)C-choline for evaluation of prostate cancer patients with biochemical recurrence: meta-analysis and critical review of available data. Eur J Nucl Med Mol Imaging. Jan 2016; 43(1): 55-69. PMID 26450693
129. von Eyben FE, Kairemo K. Meta-analysis of (11)C-choline and (18)F-choline PET/CT for management of patients with prostate cancer. Nucl Med Commun. Mar 2014; 35(3): 221-30. PMID 24240194
130. Umbehr MH, Muntener M, Hany T, et al. The role of 11C-choline and 18F-fluorocholine positron emission tomography (PET) and PET/CT in prostate cancer: a systematic review and meta-analysis. Eur Urol. Jul 2013; 64(1): 106-17. PMID 23628493
131. Mohsen B, Giorgio T, Rasoul ZS, et al. Application of C-11-acetate positron-emission tomography (PET) imaging in prostate cancer: systematic review and meta-analysis of the literature. BJU Int. Dec 2013; 112(8): 1062-72. PMID 23937453
132. Sandgren K, Westerlinck P, Jonsson JH, et al. Imaging for the Detection of Locoregional Recurrences in Biochemical Progression After Radical Prostatectomy-A Systematic Review. Eur Urol Focus. Jul 2019; 5(4): 550-560. PMID 29133278

133. Albisinni S, Aoun F, Marcelis Q, et al. Innovations in imaging modalities for recurrent and metastatic prostate cancer: a systematic review. Minerva Urol Nefrol. Aug 2018; 70(4): 347-360. PMID 29388415
134. Bach-Gansmo T, Nanni C, Nieh PT, et al. Multisite Experience of the Safety, Detection Rate and Diagnostic Performance of Fluciclovine (18 F) Positron Emission Tomography/Computerized Tomography Imaging in the Staging of Biochemically Recurrent Prostate Cancer. J Urol. Mar 2017; 197(3 Pt 1): 676-683. PMID 27746282
135. Andriole GL, Kostakoglu L, Chau A, et al. The Impact of Positron Emission Tomography with 18F-Fluciclovine on the Treatment of Biochemical Recurrence of Prostate Cancer: Results from the LOCATE Trial. J Urol. Feb 2019; 201(2): 322-331. PMID 30179618
136. Akin-Akintayo OO, Jani AB, Odewole O, et al. Change in Salvage Radiotherapy Management Based on Guidance With FACBC (Fluciclovine) PET/CT in Postprostatectomy Recurrent Prostate Cancer. Clin Nucl Med. Jan 2017; 42(1): e22-e28. PMID 27749412
137. Heidenreich A, Bastian PJ, Bellmunt J, et al. EAU guidelines on prostate cancer. Part II: Treatment of advanced, relapsing, and castration-resistant prostate cancer. Eur Urol. Feb 2014; 65(2): 467-79. PMID 24321502
138. Treglia G, Ceriani L, Sadeghi R, et al. Relationship between prostate-specific antigen kinetics and detection rate of radiolabelled choline PET/CT in restaging prostate cancer patients: a meta-analysis. Clin Chem Lab Med. May 2014; 52(5): 725-33. PMID 24310773
139. Froemming AT, Verma S, Eberhardt SC, et al. ACR Appropriateness Criteria (R) Post-treatment Follow-up Prostate Cancer. J Am Coll Radiol. May 2018; 15(5S): S132-S149. PMID 29724417
140. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed August 1, 2020.
141. Eissa A, Elsherbiny A, Coelho RF, et al. The role of 68Ga-PSMA PET/CT scan in biochemical recurrence after primary treatment for prostate cancer: a systematic review of the literature. Minerva Urol Nefrol. Oct 2018; 70(5): 462-478. PMID 29664244
142. Perera M, Papa N, Christidis D, et al. Sensitivity, Specificity, and Predictors of Positive 68 Ga-Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol. Dec 2016; 70(6): 926-937. PMID 27363387
143. Ma H, Shen G, Liu B, et al. Diagnostic performance of 18F-FDG PET or PET/CT in restaging renal cell carcinoma: a systematic review and meta-analysis. Nucl Med Commun. Feb 2017; 38(2): 156-163. PMID 27824726
144. National Comprehensive Cancer Network (NCCN). NCCN Clincal Practice Guidelines in Oncology: Kidney Cancer. Version 1.2021. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed July 20, 2020.
145. Treglia G, Mirk P, Stefanelli A, et al. 18F-Fluorodeoxyglucose positron emission tomography in evaluating treatment response to imatinib or other drugs in gastrointestinal stromal tumors: a systematic review. Clin Imaging. May-Jun 2012; 36(3): 167-75. PMID 22542374
146. Ioannidis JPA, Lau J. FDG-PET for the Diagnosis and Management of Soft Tissue Sarcoma (Contract No. 290- 97-0019). Rockville, MD: Agency for Healthcare Research and Quality; 2002.
147. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma, Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed July 20, 2020.
148. Becherer A, De Santis M, Karanikas G, et al. FDG PET is superior to CT in the prediction of viable tumour in post-chemotherapy seminoma residuals. Eur J Radiol. May 2005; 54(2): 284-8. PMID 15837411

149. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Testicular Cancer. Version 3.2020. https://www.nccn.org/professionals/physician_gls/pdf/testicular.pdf. Accessed July 20, 2020.
150. Schutz F, Lautenschlager C, Lorenz K, et al. Positron Emission Tomography (PET) and PET/CT in Thyroid Cancer: A Systematic Review and Meta-Analysis. Eur Thyroid J. Jan 2018; 7(1): 13-20. PMID 29594049
151. Haslerud T, Brauckhoff K, Reisaeter L, et al. F18-FDG-PET for recurrent differentiated thyroid cancer: a systematic meta-analysis. Acta Radiol. Oct 2016; 57(10): 1193-200. PMID 26163534
152. Pace L, Klain M, Salvatore B, et al. Prognostic role of 18F-FDG PET/CT in the postoperative evaluation of differentiated thyroid cancer patients. Clin Nucl Med. Feb 2015; 40(2): 111-5. PMID 25546215
153. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed July 20, 2020.
154. Cheng X, Bao L, Xu Z, et al. F-FDG-PET and F-FDG-PET/CT in the detection of recurrent or metastatic medullary thyroid carcinoma: a systematic review and meta-analysis. J Med Imaging Radiat Oncol. Apr 2012; 56(2): 136-42. PMID 22498184
155. Burglin SA, Hess S, Hoilund-Carlsen PF, et al. 18F-FDG PET/CT for detection of the primary tumor in adults with extracervical metastases from cancer of unknown primary: A systematic review and meta-analysis. Medicine (Baltimore). Apr 2017; 96(16): e6713. PMID 28422888
156. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography to Manage Patients with an Occult Primary Carcinoma and Metastasis outside the Cervical Lymph Nodes. Technol Eval Cent Assess. 2002;17(14).
157. Centers for Medicare & Medicaid Services (CMS). Pub 100-03 National Coverage Determination (NCD) for Positron Emission TOMOGRAPHY (FDG) for Oncologic Conditions (220.6.17); https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=331&ncdver=4&NCAId=232&TAId=22&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=tomography&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAACAAAAAA&. Accessed July 15, 2020.
158. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 6.01.26 (September 2020).

Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - Indication for PET scan
  - Previous treatment and response
- Previous Imaging reports (e.g., CT, MRI, SPECT)
- Pathology reports (if applicable)

Post Service (in addition to the above, please include the following):

- PET report

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

Type	Code	Description
CPT®	78608	Brain imaging, positron emission tomography (PET); metabolic evaluation
	78609	Brain imaging, positron emission tomography (PET); perfusion evaluation
	78811	Positron emission tomography (PET) imaging; limited area (e.g., chest, head/neck)
	78812	Positron emission tomography (PET) imaging; skull base to mid-thigh
	78813	Positron emission tomography (PET) imaging; whole body
	78814	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (e.g., chest, head/neck)
	78815	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; skull base to mid-thigh
	78816	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; whole body
HCPCS	A9515	Choline C11 injection, diagnostic, per study dose up to 20 mCi
	A9526	Nitrogen N-13 ammonia, diagnostic, per study dose, up to 40 mCi
	A9552	Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 mCi
	A9580	Sodium fluoride F-18, diagnostic, per study dose, up to 30 mCi
	A9587	Gallium Ga-68, dotatate, diagnostic, 0.1 mCi
	A9588	Fluciclovine F-18, diagnostic, 1 mCi
	A9591	Fluoroestradiol f 18, diagnostic, 1 mci ***(Code effective 1/1/2021)***
	A9597	Positron emission tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified
	A9598	Positron emission tomography radiopharmaceutical, diagnostic, for nontumor identification, not otherwise classified
	C9060	Fluoroestradiol F18, diagnostic, 1 mCi ***(Deleted code effective 1/1/2021)***
	C9068	Copper Cu-64, dotatate, diagnostic, 1 mci ***(Code effective 1/1/2021)***
	G0219	Pet imaging whole body; melanoma for non-covered indications
	G0235	Pet imaging, any site, not otherwise specified
	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)

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
01/26/2009	Policy revision with position change Policy Title Revision, criteria revised. Combined Polices: • Positron Emission Tomography(PET) Indications for Diagnosis Evaluation and Staging for Breast Cancer; • Positron Emission Tomography(PET) Indications - Excluding PET for Breast

Effective Date	Action
	• Positron Emission Tomography(PET) in the Evaluation of (suspected) Alzheimers/Dementia Positron Emission Tomography(PET) Coronary Artery Disease Indication
04/03/2009	Policy revision with position change
06/24/2009	Policy revision with position change
04/02/2010	Policy revision with position change. Coding update.
01/07/2011	Policy revision with position change
10/07/2011	Policy revision with position change
12/15/2014	Policy title change from Positron Emission Tomography (PET). Policy revision with position change effective 2/15/2015.
02/15/2015	Policy revision with position change
03/30/2015	Policy revision without position change
04/01/2016	Coding update
02/01/2017	Coding update
09/01/2017	Policy revision with position change
05/01/2018	Policy revision without position change
11/01/2018	Policy revision with position change
11/01/2019	Policy revision with position change
05/01/2020	Administrative update. Policy statement and guidelines updated.
10/01/2020	Administrative update. Policy statement updated.
11/01/2020	Annual review. No change to policy statement. Policy guidelines and literature updated.
02/01/2021	Coding update.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
Oncologic Applications of Positron Emission Tomography Scanning 6.01.26 **Policy Statement:** Positron emission tomography (PET) scanning may be considered **medically necessary** in **any** of the following: I. **Bladder Cancer** - PET scanning for staging or restaging of bladder cancer with documentation of **both** of the following: A. Presence of muscle-invasive bladder cancer B. When CT or magnetic resonance imaging are not indicated or remained inconclusive on distant metastasis II. **Bone Sarcoma** - PET scanning for staging or restaging of Ewing sarcoma and osteosarcoma III. **Brain Cancer** – PET scanning for staging or restaging of brain cancer IV. **Breast Cancer** - PET scanning for staging or restaging of breast cancer for detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes) with documentation of **both** of the following: A. Suspicion of disease is high B. Other imaging is inconclusive V. **Cervical Cancer** – PET scanning for **any** of the following: A. Initial staging of patient with locally advanced cervical cancer B. Evaluation of a known or suspected recurrence VI. **Colorectal Cancer** – PET scanning for **any** of the following: A. Staging or restaging to detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer B. To evaluate a rising and persistently elevated carcinoembryonic antigen (CEA) levels when standard imaging, including CT scan, is negative VII. **Endometrial Cancer** – PET scanning for **any** of the following: A. Detection of lymph node metastases B. Assessment of endometrial cancer recurrence VIII. **Esophageal Cancer** - PET scanning for **any** of the following:	**Oncologic Applications of Positron Emission Tomography Scanning 6.01.26** **Policy Statement:** Positron emission tomography (PET) scanning may be considered **medically necessary** in **any** of the following: I. **Bladder Cancer** - PET scanning for staging or restaging of bladder cancer with documentation of **both** of the following: A. Presence of muscle-invasive bladder cancer B. When CT or magnetic resonance imaging are not indicated or remained inconclusive on distant metastasis II. **Bone Sarcoma** - PET scanning for staging or restaging of Ewing sarcoma and osteosarcoma III. **Brain Cancer** – PET scanning for staging or restaging of brain cancer IV. **Breast Cancer** - PET scanning for staging or restaging of breast cancer for detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes) with documentation of **both** of the following: A. Suspicion of disease is high B. Other imaging is inconclusive V. **Cervical Cancer** – PET scanning for **any** of the following: A. Initial staging of patient with locally advanced cervical cancer B. Evaluation of a known or suspected recurrence VI. **Colorectal Cancer** – PET scanning for **any** of the following: A. Staging or restaging to detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer B. To evaluate a rising and persistently elevated carcinoembryonic antigen (CEA) levels when standard imaging, including CT scan, is negative VII. **Endometrial Cancer** – PET scanning for **any** of the following: A. Detection of lymph node metastases B. Assessment of endometrial cancer recurrence VIII. **Esophageal Cancer** - PET scanning for **any** of the following:

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
A. Staging of esophageal cancer B. Determining response to preoperative induction therapy	A. Staging of esophageal cancer B. Determining response to preoperative induction therapy
IX. **Gastric Cancer** – PET scanning for **any** of the following: A. Initial diagnosis and staging of gastric cancer B. Evaluation for recurrent gastric cancer with documentation of **both** of the following: C. After surgical resection D. When other imaging modalities are inconclusive	IX. **Gastric Cancer** – PET scanning for **any** of the following: A. Initial diagnosis and staging of gastric cancer B. Evaluation for recurrent gastric cancer with documentation of **both** of the following: C. After surgical resection D. When other imaging modalities are inconclusive
X. **Head and Neck Cancer** – PET scanning for **any** of the following: A. Initial diagnosis of suspected cancer B. Initial staging of disease C. Restaging of residual or recurrent disease during follow-up D. Evaluation of response to treatment	X. **Head and Neck Cancer** – PET scanning for **any** of the following: A. Initial diagnosis of suspected cancer B. Initial staging of disease C. Restaging of residual or recurrent disease during follow-up D. Evaluation of response to treatment
XI. **Lung Cancer, Non-small cell (NSCLC)** – PET scanning for **any** of the following: A. Patient with a solitary pulmonary nodule as a single scan technique (not dual time) to distinguish between benign and malignant disease when prior CT scan and chest x-ray findings are inconclusive or discordant B. Staging or restaging technique in those with known non-small-cell lung cancer C. To determine resectability for patient with a presumed solitary metastatic lesion from lung cancer	XI. **Lung Cancer, Non-small cell (NSCLC)** – PET scanning for **any** of the following: A. Patient with a solitary pulmonary nodule as a single scan technique (not dual time) to distinguish between benign and malignant disease when prior CT scan and chest x-ray findings are inconclusive or discordant B. Staging or restaging technique in those with known non-small-cell lung cancer C. To determine resectability for patient with a presumed solitary metastatic lesion from lung cancer
XII. **Lung Cancer, small cell (SCLC)** - PET scanning for staging of small-cell lung cancer if limited stage is suspected based on standard imaging	XII. **Lung Cancer, small cell (SCLC)** - PET scanning for staging of small-cell lung cancer if limited stage is suspected based on standard imaging
XIII. **Lymphoma, Including Hodgkin Disease** – PET scanning as a technique for staging lymphoma either during initial staging or for restaging at follow-up	XIII. **Lymphoma, Including Hodgkin Disease** – PET scanning as a technique for staging lymphoma either during initial staging or for restaging at follow-up
XIV. **Melanoma** – PET scanning as a technique for assessing extranodal spread of malignant melanoma at initial staging or at restaging during follow-up treatment every 4 to12 months to screen high-risk patient for advanced disease with documentation of **both** of the following: A. Stage IIB or higher B. Five years or less since date of diagnosis	XIV. **Melanoma** – PET scanning as a technique for assessing extranodal spread of malignant melanoma at initial staging or at restaging during follow-up treatment every 4 to12 months to screen high-risk patient for advanced disease with documentation of **both** of the following: A. Stage IIB or higher B. Five years or less since date of diagnosis
XV. **Multiple Myeloma** – PET scanning for staging or restaging of multiple myeloma, particularly if the skeletal survey is negative	XV. **Multiple Myeloma** – PET scanning for staging or restaging of multiple myeloma, particularly if the skeletal survey is negative

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
XVI. **Neuroendocrine tumors** – PET scanning for neuroendocrine tumors with documentation of **both** of the following: A. Gallium-68 PET B. For initial staging or for restaging	XVI. **Neuroendocrine tumors** – PET scanning for neuroendocrine tumors with documentation of **both** of the following: A. Gallium-68 PET B. For initial staging or for restaging
XVII. **Ovarian Cancer** – PET scanning in the evaluation of patient with a prior history of ovarian cancer with documentation of **both** of the following: A. Signs and/or symptoms of suspected ovarian cancer recurrence (restaging) B. Standard imaging, including CT scan, is inconclusive	XVII. **Ovarian Cancer** – PET scanning in the evaluation of patient with a prior history of ovarian cancer with documentation of **both** of the following: A. Signs and/or symptoms of suspected ovarian cancer recurrence (restaging) B. Standard imaging, including CT scan, is inconclusive
XVIII. **Pancreatic Cancer** – PET scanning in the initial diagnosis and staging of pancreatic cancer with documentation of **both** of the following: A. Other imaging is inconclusive B. Biopsy is inconclusive	XVIII. **Pancreatic Cancer** – PET scanning in the initial diagnosis and staging of pancreatic cancer with documentation of **both** of the following: A. Other imaging is inconclusive B. Biopsy is inconclusive
XIX. **Prostate Cancer** – PET scanning for evaluating suspected or biochemically recurrent small volume prostate cancer in soft tissues with documentation of **both** of the following: A. Tracer use as indicated by **any** of the following: 1. Carbon 11 choline 2. Fluorine 18 fluciclovine B. Primary treatment has been completed (e.g.: surgery, radiation therapy)	XIX. **Prostate Cancer** – PET scanning for evaluating suspected or biochemically recurrent small volume prostate cancer in soft tissues with documentation of **both** of the following: A. Tracer use as indicated by **any** of the following: 1. Carbon 11 choline 2. Fluorine 18 fluciclovine B. Primary treatment has been completed (e.g.: surgery, radiation therapy)
XX. **Soft Tissue Sarcoma** - PET scanning for gastrointestinal stromal tumors to evaluate response to imatinib and other treatments	XX. **Soft Tissue Sarcoma** - PET scanning for gastrointestinal stromal tumors to evaluate response to imatinib and other treatments
XXI. **Testicular Cancer** – PET scanning in testicular cancer with **all** of the following: A. Stage IIB and III seminoma B. Initial chemotherapy has been completed C. Within 6 weeks of completion of chemotherapy	XXI. **Testicular Cancer** – PET scanning in testicular cancer with **all** of the following: A. Stage IIB and III seminoma B. Initial chemotherapy has been completed C. Within 6 weeks of completion of chemotherapy
XXII. **Thyroid Cancer** – PET scanning in the restaging of patient with **all** of the following: A. Histology is differentiated (not anaplastic) B. Thyroglobulin levels (Tg) are elevated C. Whole-body iodine-131 imaging is negative	XXII. **Thyroid Cancer** – PET scanning in the restaging of patient with **all** of the following: A. Histology is differentiated (not anaplastic) B. Thyroglobulin levels (Tg) are elevated C. Whole-body iodine-131 imaging is negative
XXIII. **Cancer of Unknown Primary** – PET scanning in cancer of unknown primary with **all** of the following:	XXIII. **Cancer of Unknown Primary** – PET scanning in cancer of unknown primary with **all** of the following:

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
A. Single site of disease outside the cervical lymph nodes and local or regional treatment is being considered for this single site of metastatic disease B. Negative workup for an occult primary tumor C. PET scan to be used to rule out or detect additional sites of disease that would eliminate the rationale for local or regional treatment The following are considered **investigational**: I. **Bladder Cancer** – PET scanning for bladder tumors that have not invaded the muscle (stage less than cT2) II. **Bone Sarcoma** – PET scanning for staging of chondrosarcoma III. **Breast Cancer** – PET scanning for evaluation of breast cancer due to **any** of the following: A. Differential diagnosis in patient with suspicious breast lesions or an indeterminate or low suspicion finding on mammography B. Staging axillary lymph nodes C. Predicting pathologic response to neoadjuvant therapy for locally advanced disease IV. **Colorectal Cancer** - PET scanning for **any** of the following: A. A technique to assess the presence of scarring versus local bowel recurrence in patient with previously resected colorectal cancer B. A technique contributing to radiotherapy treatment planning V. **Esophageal Cancer** – PET scanning for other aspects of the evaluation of esophageal cancer including detection of primary esophageal cancer VI. **Lung Cancer** – PET scanning for staging of small-cell lung cancer if extensive stage is established VII. **Melanoma** – PET scanning for **any** of the following: A. In managing stage 0, I, or II melanoma B. As a technique to detect regional lymph node metastases in patient with clinically localized melanoma who is a candidate to undergo sentinel node biopsy	A. Single site of disease outside the cervical lymph nodes and local or regional treatment is being considered for this single site of metastatic disease B. Negative workup for an occult primary tumor C. PET scan to be used to rule out or detect additional sites of disease that would eliminate the rationale for local or regional treatment The following are considered **investigational**: I. **Bladder Cancer** – PET scanning for bladder tumors that have not invaded the muscle (stage less than cT2) II. **Bone Sarcoma** – PET scanning for staging of chondrosarcoma III. **Breast Cancer** – PET scanning for evaluation of breast cancer due to **any** of the following: A. Differential diagnosis in patient with suspicious breast lesions or an indeterminate or low suspicion finding on mammography B. Staging axillary lymph nodes C. Predicting pathologic response to neoadjuvant therapy for locally advanced disease IV. **Colorectal Cancer** - PET scanning for **any** of the following: A. A technique to assess the presence of scarring versus local bowel recurrence in patient with previously resected colorectal cancer B. A technique contributing to radiotherapy treatment planning V. **Esophageal Cancer** – PET scanning for other aspects of the evaluation of esophageal cancer including detection of primary esophageal cancer VI. **Lung Cancer** – PET scanning for staging of small-cell lung cancer if extensive stage is established VII. **Melanoma** – PET scanning for **any** of the following: A. In managing stage 0, I, or II melanoma B. As a technique to detect regional lymph node metastases in patient with clinically localized melanoma who is a candidate to undergo sentinel node biopsy

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
VIII. **Neuroendocrine tumors** – PET scanning with radiotracers (other than Gallium-68) in all aspects for managing neuroendocrine tumors	VIII. **Neuroendocrine tumors** – PET scanning with radiotracers (other than Gallium-68) in all aspects for managing neuroendocrine tumors
IX. **Ovarian Cancer** – PET scanning in the initial evaluation of known or suspected ovarian cancer in all situations	IX. **Ovarian Cancer** – PET scanning in the initial evaluation of known or suspected ovarian cancer in all situations
X. **Pancreatic Cancer** – PET scanning as a technique to evaluate other aspects of pancreatic cancer	X. **Pancreatic Cancer** – PET scanning as a technique to evaluate other aspects of pancreatic cancer
XI. **Penile Cancer** – PET scanning in all aspects of managing penile cancer	XI. **Penile Cancer** – PET scanning in all aspects of managing penile cancer
XII. **Prostate Cancer** – PET scanning in **any** of the following: A. With gallium 68 in all aspects of managing prostate cancer B. In all other indications in known or suspected prostate cancer	XII. **Prostate Cancer** – PET scanning in **any** of the following: A. With gallium 68 in all aspects of managing prostate cancer B. In all other indications in known or suspected prostate cancer
XIII. **Renal Cell Carcinoma** – PET scanning in all aspects of managing renal cancer	XIII. **Renal Cell Carcinoma** – PET scanning in all aspects of managing renal cancer
XIV. **Soft Tissue Sarcoma** - PET scanning for evaluation of soft tissue sarcoma in **any** of the following: A. Distinguishing between benign lesions and malignant soft tissue sarcoma B. Distinguishing between low-grade and high-grade soft tissue sarcoma C. Detecting locoregional recurrence D. Detecting distant metastasis	XIV. **Soft Tissue Sarcoma** - PET scanning for evaluation of soft tissue sarcoma in **any** of the following: A. Distinguishing between benign lesions and malignant soft tissue sarcoma B. Distinguishing between low-grade and high-grade soft tissue sarcoma C. Detecting locoregional recurrence D. Detecting distant metastasis
XV. **Testicular Cancer** – PET scanning in evaluation of testicular cancer in **any** of the following: A. Initial staging of testicular cancer B. Distinguishing between viable tumor and necrosis/fibrosis after treatment of testicular cancer C. Detection of recurrent disease after treatment of testicular cancer	XV. **Testicular Cancer** – PET scanning in evaluation of testicular cancer in **any** of the following: A. Initial staging of testicular cancer B. Distinguishing between viable tumor and necrosis/fibrosis after treatment of testicular cancer C. Detection of recurrent disease after treatment of testicular cancer
XVI. **Thyroid Cancer** – PET scanning in the evaluation of known or suspected differentiated or poorly differentiated thyroid cancer in all other situations	XVI. **Thyroid Cancer** – PET scanning in the evaluation of known or suspected differentiated or poorly differentiated thyroid cancer in all other situations
XVII. **Cancer of Unknown Primary** – PET scanning for other indications in patient with a cancer of unknown primary, including but not limited to **any** of the following: A. As part of the initial workup of a cancer of unknown primary	XVII. **Cancer of Unknown Primary** – PET scanning for other indications in patient with a cancer of unknown primary, including but not limited to **any** of the following: A. As part of the initial workup of a cancer of unknown primary

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
B. As part of the workup of patients with multiple sites of disease	B. As part of the workup of patients with multiple sites of disease
XVIII. **Cancer Surveillance** – PET scanning when used as a surveillance tool for patient with cancer or with a history of cancer. A scan is considered surveillance if performed more than 6 months after completion of cancer therapy (12 months) in patients without objective signs or symptoms suggestive of cancer recurrence (see Policy Guidelines section).	XVIII. **Cancer Surveillance** – PET scanning when used as a surveillance tool for patient with cancer or with a history of cancer. A scan is considered surveillance if performed more than 6 months after completion of cancer therapy (12 months for lymphoma) in patients without objective signs or symptoms suggestive of cancer recurrence (see Policy Guidelines section).