Medical Policy

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Title: Positron Emission Tomography (PET) Scanning: Oncologic Applications

See also:
- *PET Scanning: Cardiac Applications*
- *PET Scanning: In Oncology to Detect Early Response during Treatment*
- *PET Scanning: Miscellaneous (Non-cardiac, Non-oncologic) Applications of Fluorine 18 Fluorodeoxyglucose*

Professional
Original Effective Date: October 1, 1997
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Current Effective Date: February 18, 2019

Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected or diagnosed muscle-invasive bladder cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity

Populations	Interventions	Comparators	Outcomes
Individuals: • Who are asymptomatic after completing muscle-invasive bladder cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • With suspected or diagnosed bone sarcoma and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing bone sarcoma treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed brain tumor and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET • ^{18}F-FET-PET • ^{11}C-methionine PET	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected brain tumor or who are asymptomatic after completing brain tumor treatment	Interventions of interest are: • ^{18}F-FDG-PET • ^{18}F-FET-PET • ^{11}C-methionine PET	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed breast cancer and inconclusive results from other imaging techniques	Interventions of interest are: • Adjunctive ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT for staging or restaging	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed breast cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing breast cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed cervical cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected cervical cancer or who are asymptomatic after completing cervical cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed colorectal cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity

Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected colorectal cancer or who are asymptomatic after completing colorectal cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed endometrial cancer in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing endometrial cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed esophageal cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected esophageal cancer or who are asymptomatic after completing esophageal cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed gastric cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing gastric cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed head and neck cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing head and neck cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected non-small-cell lung cancer and inconclusive results from other imaging techniques	Interventions of interest are: • Adjunct ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed non-small-cell lung cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity

Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected non-small-cell lung cancer or who are asymptomatic after completing non-small-cell lung treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed small-cell lung cancer diagnosis and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected small-cell lung cancer or who are asymptomatic after completing small-cell lung treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed Hodgkin lymphoma and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing Hodgkin lymphoma treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed non-Hodgkin lymphoma and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing non-Hodgkin lymphoma treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed stage I or II melanoma and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed advanced melanoma (stage III or IV) and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing melanoma treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity

Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected or diagnosed multiple myeloma in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing multiple myeloma treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed neuroendocrine tumors and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing neuroendocrine tumor treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed neuroendocrine tumors and in need of staging or restaging information	Interventions of interest are: • ^{68}Ga-PET or ^{68}Ga-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing neuroendocrine tumor treatment	Interventions of interest are: • ^{68}Ga-PET or ^{68}Ga-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed ovarian cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected ovarian cancer or who are asymptomatic after completing ovarian cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected pancreatic cancer and with inconclusive results from other imaging techniques	Interventions of interest are: • Adjunctive ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT for staging or restaging	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed pancreatic cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity

Populations	Interventions	Comparators	Outcomes
Individuals: • Who are asymptomatic after completing pancreatic cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed penile cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing penile cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed prostate cancer and in need of staging or restaging information	Interventions of interest are: • ^{11}C-choline-PET or ^{11}C-choline-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • Who are asymptomatic after completing prostate cancer treatment	Interventions of interest are: • ^{11}C-choline-PET or ^{11}C-choline-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected or diagnosed prostate cancer and in need of staging or restaging information	Interventions of interest are: • ^{68}Ga-PET or ^{68}Ga-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed renal cell carcinoma and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed soft tissue sarcoma and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed soft tissue sarcoma and in need of rapid reading of response to imatinib treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected soft tissue sarcoma or who are asymptomatic after completing soft tissue sarcoma treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed testicular cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity

Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected testicular cancer or who are asymptomatic after completing testicular cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With diagnosed thyroid cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With suspected thyroid cancer or who are asymptomatic after completing thyroid cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity
Individuals: • With cancer of unknown primary and single-site metastatic disease	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test accuracy • Test validity

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.

Objective

The objective of this evidence review is to examine whether the use of positron emission tomography for the diagnosis, staging and restaging, and/or surveillance of various carcinomas improves the net health outcome in individuals with cancer.

Background

A variety of tracers are used for positron emission tomography (PET) scanning, including oxygen 15, nitrogen 13, carbon 11, and fluorine 18. In 2016, 2 additional tracers, gallium 68, and fluciclovine 18, were approved by the Food and Drug Administration (FDA). 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. FDG 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 policy focuses on the use of radiotracers detected with dedicated PET scanners. Radiotracers such as FDG may be detected using single-photon emission computerized

tomography (SPECT) cameras, a technique that may be referred to as FDG-SPECT imaging. The use of SPECT cameras for PET radiotracers presents unique issues of diagnostic performance and is not considered in this policy.

Regulatory Status

The FDA website includes various PET-related documents.[1]

As of July 2018, the following radiopharmaceuticals have been granted approval by the FDA,[2] to be used with PET for carcinoma-related indications (see Table 1).

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 fluciclovine	Blue Earth Diagnostics	Axumin™	Suspected prostate cancer recurrence based on elevated blood PSA levels after treatment
Gallium-68 dotatate	Advanced Accelerator Applications	NETSPOT™	Localization of somatostatin receptor positive NETs in adult and pediatric patients

CT: computerized tomography; MRI: magnetic resonance imaging; NET: neuroendocrine tumors; PET: positron emission tomography; PSA: prostate-specific antigen.

POLICY

- All policy statements apply to both positron emission tomography (PET) scans and PET plus computed tomography (CT) scans, ie, 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.

A. **Bladder Cancer**

1. PET scanning may be considered **medically necessary** in the staging or restaging of muscle-invasive bladder cancer when CT or magnetic resonance imaging are not indicated or remained inconclusive on distant metastasis.

2. PET scanning is considered **experimental / investigational** for bladder tumors that have not invaded the muscle (stage <cT2).

B. **Bone Cancer**

1. PET scanning may be considered **medically necessary** in the staging or restaging of Ewing sarcoma and osteosarcoma.
2. PET scanning is considered **experimental / investigational** in the staging of chondrosarcoma.

C. **Brain Cancer**
1. PET scanning may be considered **medically necessary** in the staging or restaging of brain cancer.

D. **Breast Cancer**
1. PET scanning may be considered **medically necessary** in the staging and restaging of breast cancer for the following application:
    a. Detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes) when suspicion of disease is high and other imaging is inconclusive.
2. PET scanning is considered **experimental / investigational** in the evaluation of breast cancer for all other applications, including but not limited to the following:
    a. Differential diagnosis in patients 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.

E. **Cervical Cancer**
1. PET scanning may be considered **medically necessary** in the initial staging of patients with locally advanced cervical cancer.
2. PET scanning may be considered **medically necessary** in the evaluation of known or suspected recurrence.

F. **Colorectal Cancer**
1. PET scanning may be considered **medically necessary** as a technique for
    a. Staging or restaging to detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer, and
    b. To evaluate a rising and persistently elevated carcinoembryonic antigen level when standard imaging, including CT scan, is negative.
2. PET scanning is considered **experimental / investigational** as:
    a. A technique to assess the presence of scarring versus local bowel recurrence in patients with previously resected colorectal cancer.
    b. A technique contributing to radiotherapy treatment planning.

G. **Endometrial Cancer**

PET scanning is considered **medically necessary** in the:
1. Detection of lymph node metastases, and
2. Assessment of endometrial cancer recurrence.

H. **Esophageal Cancer**
1. PET scanning may be considered **medically necessary** in the
    a. Staging of esophageal cancer, and
    b. Determining response to preoperative induction therapy.
2. PET scanning is considered **experimental / investigational** in other aspects of the evaluation of esophageal cancer, including but not limited to the following applications:
    a. Detection of primary esophageal cancer.

I. **Gastric Cancer**
1. PET scanning may be considered **medically necessary** in the
   a. Initial diagnosis and staging of gastric cancer.
   b. Evaluation for recurrent gastric cancer after surgical resection, when other imaging modalities are inconclusive.

J. **Head and Neck Cancer**
1. PET scanning may be considered **medically necessary** in the evaluation of head and neck cancer in the
   a. Initial diagnosis of suspected cancer,
   b. Initial staging of disease, and restaging of residual or recurrent disease during follow-up; and
   c. Evaluation of response to treatment.

K. **Lung Cancer**
1. PET scanning may be considered **medically necessary** for any of the following applications:
   a. Patients 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. As staging or restaging technique in those with known non-small-cell lung cancer, and
   c. To determine resectability for patients with a presumed solitary metastatic lesion from lung cancer.
2. PET scanning may be considered **medically necessary** in staging of small-cell lung cancer if limited stage is suspected based on standard imaging.
3. PET scanning is considered **experimental / investigational** in staging of small-cell lung cancer if extensive stage is established and in all other aspects of managing small-cell lung cancer.

L. **Lymphoma, Including Hodgkin Disease**
1. PET scanning may be considered **medically necessary** as a technique for staging lymphoma either during initial staging or for restaging at follow-up.

M. **Melanoma**
1. PET scanning may be considered **medically necessary** as a technique for assessing extranodal spread of malignant melanoma at initial staging or at restaging during follow-up treatment for advanced disease (stage III or IV).
2. PET scanning is considered **experimental / investigational** in managing stage 0, I, or II melanoma.
3. PET scanning is considered **experimental / investigational** as a technique to detect regional lymph node metastases in patients with clinically localized melanoma who are candidates to undergo sentinel node biopsy.

N. **Multiple Myeloma**
1. PET scanning is considered **medically necessary** in the staging or restaging of multiple myeloma, particularly if the skeletal survey is negative.

O. **Neuroendocrine Tumors**

1. PET scanning with gallium 68 may be considered **medically necessary** as a technique for staging neuroendocrine tumors either during initial staging or for restaging at follow-up.
2. PET scanning with all other radiotracers is considered **experimental / investigational** in all aspects of managing neuroendocrine tumors.

P. **Ovarian Cancer**

1. PET scanning may be considered **medically necessary** in the evaluation of patients with signs and/or symptoms of suspected ovarian cancer recurrence (restaging) when standard imaging, including CT scan, is inconclusive.
2. PET scanning is considered **experimental / investigational** in the initial evaluation of known or suspected ovarian cancer in all situations.

Q. **Pancreatic Cancer**

1. PET scanning may be considered **medically necessary** in the initial diagnosis and staging of pancreatic cancer when other imaging and biopsy are inconclusive.
2. PET scanning is considered **experimental / investigational** as a technique to evaluate other aspects of pancreatic cancer.

R. **Penile Cancer**

PET scanning is considered **experimental / investigational** in all aspects of managing penile cancer.

S. **Prostate Cancer**

1. PET scanning with 11 choline and fluorine 18 fluciclovine may be **medically necessary** for evaluating suspected or biochemically recurrent prostate cancer after primary treatment to detect small volume disease in soft tissues.
2. PET scanning with gallium 68 is considered **experimental / investigational** in all aspects of managing prostate cancer.
3. PET scanning for all other indications in known or suspected prostate cancer is considered **experimental / investigational**.

T. **Renal Cell Carcinoma**

PET scanning is considered **experimental / investigational** in all aspects of managing renal cancer.

U. **Soft Tissue Sarcoma**

1. PET scanning is considered **medically necessary** for evaluating response to imatinib and other treatments for gastrointestinal stromal tumors
2. PET scanning is considered **experimental / investigational** in evaluation of soft tissue sarcoma, including but not limited to the following applications:
    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

V. **Testicular Cancer**

1. PET scanning may be considered **medically necessary** in evaluation of residual mass following chemotherapy of stage IIB and III seminomas. (The scan should be completed no sooner than 6 weeks after chemotherapy.)
2. Except as noted above for seminoma, PET scanning is considered **experimental / investigational** in evaluation of testicular cancer, including but not limited to the following applications:
   a. Initial staging of testicular cancer
   b. Distinguishing between viable tumor and necrosis/fibrosis after treatment of testicular cancer, and
   c. Detection of recurrent disease after treatment of testicular cancer

W. **Thyroid Cancer**

1. PET scanning may be considered **medically necessary** in the restaging of patients with differentiated thyroid cancer when thyroglobulin levels are elevated and whole-body iodine-131 imaging is negative.
2. PET scanning is considered **experimental / investigational** in the evaluation of known or suspected differentiated or poorly differentiated thyroid cancer in all other situations.

X. **Cancer of Unknown Primary**

1. PET scanning may be considered **medically necessary** in patients with a cancer of unknown primary who meet **ALL** of the following criteria:
   a. In patients with a single site of disease outside the cervical lymph nodes; AND
   b. Patient is considering local or regional treatment for a single site of metastatic disease; AND
   c. After a negative workup for an occult primary tumor; AND
   d. PET scan will be used to rule out or detect additional sites of disease that would eliminate the rationale for local or regional treatment.
2. PET scanning is considered **experimental / investigational** for other indications in patients with a cancer of unknown primary, including, but not limited to the following:
   a. As part of the initial workup of an unknown primary, and
   b. As part of the workup of patients with multiple sites of disease

Y. **Cancer Surveillance**

1. PET scanning is considered **experimental / investigational** when used as a surveillance tool for patients 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).

Policy Guidelines

For this policy, PET scanning is discussed for the following 4 applications in oncology.

a. Diagnosis
   Diagnosis refers to use of PET as part of the testing used in establishing whether a patient has cancer.
b. Staging
   Staging refers to use of PET to determine the stage (extent) of the 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 may also be referred to as initial staging.
c. Restaging
   Restaging refers to imaging after treatment in 2 situations.
   1) Restaging is part of the evaluation of a patient in whom a disease recurrence is suspected based on signs and/or symptoms.
   2) Restaging also includes determining the extent of malignancy after completion of a full course of treatment.
d. Surveillance
   Surveillance refers to 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.

Patient Selection

1. 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. Due to its expense, 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, (eg, CT, MRI) is inconclusive or not indicated.
2. 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.

RATIONALE

This evidence review has been updated with searches of the MEDLINE database. The most recent literature update was performed through July 9, 2018.

The review has been informed by multiple evaluations of positron emission tomography (PET), including 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

There are 3 general oncologic purposes for PET and PET plus computed tomography (CT):

- To confirm a diagnosis in patients who are suspected of having cancer.
- To provide information on the extent of the condition (staging once the diagnosis has been confirmed or restaging following treatment) in patients with a cancer diagnosis.
- To detect the potential recurrence in patients who are asymptomatic following treatment completion is for surveillance purposes.

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 with cancer compared with conventional imaging techniques?

The following PICOTS were 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. PET 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 fluorodeoxyglucose (FDG). Radiation exposure from PET and PET/CT is considered moderate to high.

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, and positive and negative predictive values. 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.

Timing
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, depending on the type of cancer, from months or a few years for less aggressive cancers to many years for less aggressive cancers.

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

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, positive and negative predictive values. 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 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, or 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.[3] 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
The American College of Radiology (ACR; 2018) issued an Appropriateness Criteria for pretreatment staging of muscle-invasive bladder cancer.[4] 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.

National Comprehensive Cancer Network
Current National Comprehensive Cancer Network (NCCN) guidelines for bladder cancer (v.5.2018) state that PET/CT "may be beneficial in selected patients with T2 (muscle-invasive disease) and in patients with ≥cT3 disease"(category 2B)."[5] According to the guidelines, 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 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.[6] 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.[7] 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.2.2018) state that PET/CT may be considered for[8]:

- 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. 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.[9] Four studies (total N=109 patients) met inclusion criteria. All 4 studies included in the meta-analysis had scores greater than 10 in the 15-point QUADAS tool. ^{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.[10] 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 ^{18}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.[11] The literature search included studies published through February 2013; 24 studies provided data on the use of FDG-PET and 11 studies 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.[12] 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 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 slightly less specific.

Guidelines

Current NCCN guidelines for brain cancer (v.1.2018) state that 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.[13] The guidelines warn that limitations include accuracy of interpretations and availability of equipment and isotopes.

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) also conducted a meta-analysis on the use of PET/CT to assess axillary lymph node metastasis.[14] 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.[15] As previously noted, a false-negative rate of 15% (1 – 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.[16] 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.[17] A TEC Assessment (2003) reexamined all indications except for characterizing breast lesions.[18] 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).[19] 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%) 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.[20] 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.[21] 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.[18]

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.[22] 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.[23] The literature search, conducted through August 2015, identified 6 studies (total N=382 patients) for inclusion. Quality assessment of the studies was 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.[24] The inclusion criteria differed slightly from Liu (2016). Liu et al 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.[25] 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)[25]			
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)[22]			
FDG-PET or FDG-PET/CT	26 (1752)	90 (88 to 90)	81 (78 to 84)
Liu et al (2016)[23]			
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)
Sheikhbahaei et al (2016)[24]			
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.[26,27] 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.[28]

Guidelines

American College of Radiology

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.[29] 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.1.2018) include an optional category 2B recommendation for FDG-PET/CT in the workup of stage IIIA breast cancer.[30]

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. 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."

NCCN guidelines do not recommend routine use of PET in asymptomatic patients for surveillance and follow-up after breast cancer treatment. When monitoring 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. 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.[31] 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 a 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.[20] 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.[32] 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.[33] An NCCN report conducted by conducted by Podoloff et al (2009) also identified several studies supporting the use of PET for initial staging and identifying and staging recurrent disease.[34]

Guidelines

Current NCCN guidelines on cervical cancer (v2.2018) state that PET/CT may be considered under the following conditions[35]:

- Part of the initial nonfertility 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.

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

CRC 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.[36] 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-analyses. 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 of the assessors of 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.[37] Twelve studies met inclusion

criteria (total N=494 patients), Meta-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 vs recurrent disease as a technique to determine the necessity of tissue biopsy.[38]

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 scar, 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 postoperative scar. The key concern is whether the negative predictive value (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 then available 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.

CRC Staging

Systematic Reviews

Results from a meta-analysis by Albertsson et al (2018) found that PET/CT influenced treatment plans, though the impact on survival and quality of life could not be determined.[39]

A meta-analysis by Ye et al (2015) assessed the use of FDG-PET/CT in preoperative TNM staging of CRC.[40] 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.[41-43] 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.[44]

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).[40]
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.

CRC 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.[45] 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 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.[46] 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.[47] 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.[48] The literature search ran through April 2012. FDG-PET and PET/CT pooled sensitivity estimates 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.

CRC 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 (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.[49] A total of 239 patients in remission were enrolled, 120 in the intervention arm and 119 in the control arm. After 3 years 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

ACR (2017) issued an Appropriateness Criteria for the pretreatment staging of CRC.[50] 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.2.2018) "strongly discourage 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."[51] For initial workup of nonmetastatic patients, the guidelines state "PET/CT does not supplant a contrast-enhanced diagnostic CT scan. PET/CT should only be used to evaluate an equivocal finding on a contrast-enhanced CT 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. PET/CT is not recommended for surveillance. NCCN has noted that PET/CT should not be used to assess response to chemotherapy. NCCN was divided on the appropriateness of PET/CT when carcinoembryonic antigen level is rising; PET/CT might be considered when imaging study results (eg, a good quality CT scan) are normal.

Current NCCN guidelines for rectal cancer (v.2.2018) state that PET/CT is "not routinely indicated" and "should only be used to evaluate an equivocal finding on a contrast-enhanced CT scan or in patients with strong contraindications to IV contrast."[52] PET/CT is not recommended for restaging or for surveillance. 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 colorectal cancer 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 a 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.[53] 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.2.2018) state that whole body PET/CT can be considered in the initial workup, in both nonfertility and fertility-sparing management, if metastases are suspected in select patients (based on clinical symptoms, physical findings, or abnormal laboratory findings).[54] PET/CT may also be considered for patients with suspected recurrence or metastases who are candidates for surgery/locoregional therapy. Following treatment, PET/CT can be considered in select patients for surveillance, if clarification is needed.

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.[55] 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.[56] The literature search, conducted through January 2016, identified 4 studies (n=192 patients) in which PET or PET/CT was performed during neoadjuvant chemoradiotherapy 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 chemoradiotherapy 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 -PET/CT for the detection of recurrent esophageal cancer after treatment with curative intent.[57] 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 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.[58]

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.[34] 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 described several studies in which response to chemotherapy, defined as a decline in standardized uptake values, correlated with long-term survival.[34] 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.2.2018) indicate that PET/CT can be considered under the following conditions[59]:

- 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.

There is no discussion on the use of PET/CT for surveillance. 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.[60] 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.[61] 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%), respectively.

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.[62] 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% (05% 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.2.2018) indicate that PET/CT (but not PET alone) can be used as part of an initial workup if there is no evidence of metastatic disease.[63] The guidelines note that the sensitivity of PET/CT is lower than for CT alone due to low tracer accumulation in diffuse and mucinous tumor types, but specificity is higher. PET/CT adds value to the diagnostic workup with higher accuracy in staging (identifying tumor and pertinent nodal groups). NCCN guidelines also indicate that PET/CT can be used to evaluate response to treatment, in cases of renal insufficiency or allergy to CT contrast. There is no discussion on the use of PET/CT for surveillance.

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, one 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.[64] 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			
Magnetic resonance imaging	8 (984)	95 (93 to 97)	76 (71 to 80)
CT alone	4 (404)	84 (79 to 88)	80 (71 to 88)
N staging			
Magnetic resonance imaging	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			
Magnetic resonance imaging	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).[64]
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.

A meta-analysis by Wei et al (2016) compared diagnostic capabilities of FDG-PET/CT, MRI, and single-photon emission computed tomography in patients with residual or recurrent nasopharyngeal carcinoma.[65] 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 computed tomography (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.[66,67] Results from these analyses are summarized in Table 5.

Table 5. Pooled Diagnostic Performance of FDG-PET or DG-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)[66]			
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)[67]			
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.[68] 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, 3.5; 95% CI, 2.3 to 5.4). The pooled hazard ratio 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)

Outcome	No. of Studies	2-Year RR (95% CI)	No. of Studies	3- to 5-Year RR (95% CI)
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).[68]
CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; PET: positron emission tomography; RR: relative risk.

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[69]) and for detecting head and neck cancer metastases (better than bone scintigraphy[70]) and recurrence.[71,72]

Additional meta-analyses by Li et al (2017)[73] and Lin et al (2017)[74] 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.

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.[75] When data from these 3 studies were pooled, 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.2.2018) indicate that PET/CT can be appropriate for stage III or IV 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).[76] 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

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 (ie, 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.[77]

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.[78] 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.[79] 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 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.[80] The literature search, conducted to May 2015, identified 12 studies (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.[81] 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.[82] 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).[83]

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)[80]	Solitary pulmonary nodules			
[1]FDG-PET/CT		82 (76 to 87)	81 (66 to 90)	18 (8 to 38)
Li et al (2017)[81]	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)[82]	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)[83]	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.6.2018) indicate that PET/CT can be used in the staging of the disease, detection of metastases, treatment planning, and detection of disease recurrence.[84] 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.

The American College of Chest Physicians (2013) issued guidelines for the diagnosis and management of NSCLC.[85] 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 extensive stage disease, which is characterized by distant metastases, malignant pericardial or pleural effusions, and/or contralateral hilar lymph node involvement. Limited stage SCLC is limited to 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.[86] 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 (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) of 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.[87]

In an AHRQ review conducted by Seidenfeld et al (2006) evidence review 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.[88] PET may correctly upstage and downstage disease, and studies have reported 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.2.2018) indicate PET/CT can be used in the staging of disease if limited stage is suspected. If extensive stage is established, brain imaging, MRI (preferred), or CT with contrast is recommended. PET/CT "is not recommended for routine follow-up."[89]

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 limited stage is suspected. 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.[90]

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 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. 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 treatment appropriate to 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)[91] and diffuse large B-cell lymphoma (2014).[92]

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.[93] 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 following 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.[94] 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.[95] 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 ^{1}-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 were 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.[96]

The literature search, conducted through July 2015, identified 11 studies (total N=745 patients) for inclusion. The overall quality of 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 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.[97] The literature search identified 11 studies (N=1081) for inclusion. The pooled hazard ratio 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.[98] 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.3.2018)[99] and non-Hodgkin lymphomas (v.4.2018)[100] indicate that PET/CT may be used in the diagnostic workup, staging, restaging, and evaluating treatment response. 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."

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 and meta-analyses. 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 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*. PET scanning has been investigated both as a technique to detect 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.[101]

> "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 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.[102]

Guidelines

Current NCCN guidelines for melanoma (v.3.2018) indicate that PET/CT can be used for staging and restaging more advanced disease (eg, stage III) in the presence of specific signs and symptoms.[103] PET/CT is not recommended for stage I or II disease. PET/CT also 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, systematic reviews, and meta-analyses. 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 FDGPET/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 FDGPET/CT for the diagnosis or staging and restaging of stage I or II melanoma.

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

MULTIPLE MYELOMA

Systematic Reviews
Two systematic reviews, one 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.[104]

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.[105] 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.1.2019) added PET/CT to the list of imaging techniques that may be useful under certain circumstances, to discern active from smoldering myeloma, particularly if the skeletal survey is negative.[106] 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 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.[107] 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.[108] 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.[109,110] One report included patients with thoracic and gastroenteropancreatic neuroendocrine tumors who had imaging with PET using ^{68}Ga-PET and ^{68}Ga-PET/CT.[109] 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.[110] 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.2.2018) have recommended somatostatin receptor-based imaging with PET/CT, using ^{68}Ga-dotatate as the radioactive tracer.[111] The guidelines note that ^{68}Ga-PET/CT is more sensitive than somatostatin receptor scintigraphy for determining somatostatin receptor status. ^{68}Ga-PET/CT is recommended for diagnosis, staging, and restaging. 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. ^{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: FDG-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 (ie, 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 scanning 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.[112] 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.[113] 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.[114] An AHRQ systematic review conducted by Ospina et al (2008) found that evidence supported the use of PET/CT for detecting recurrent ovarian cancer.[32] Evidence for initial diagnosis and staging of ovarian cancer was inconclusive.

Guidelines

American College of Radiology

ACR Appropriateness Criteria (2018) on staging and follow-up of ovarian cancer have stated that PET/CT and MRI may be appropriate when lesions are indeterminate with contrast-enhanced CT.[115]

National Comprehensive Cancer Network

Current NCCN guidelines for ovarian cancer (v.2.2018) indicate that PET/CT can be appropriate "for indeterminate lesions if results will alter management."[116] 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 CA-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 sensitivities 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 esophageal 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.[117] 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 positive predictive value 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.[118] 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. PET alone was not superior to CT alone (pooled 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.[119] 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.[32,34]

Both the AHRQ systematic review by Matchar et al (2004)[114] and the TEC Assessment (1999)[120] 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.

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 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 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.[114] 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.[121] 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.2.2018) state "the role of PET/CT remains unclear… [PET/CT] may be considered after formal pancreatic CT protocol in high-risk patients to detect extra pancreatic metastasis. It is not a substitute for high-quality contrast-enhanced CT."[122]

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.[123] 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.2.2018) states that PET/CT may be considered in patients with penile cancer for the evaluation of enlarged pelvic lymph nodes.[124]

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)[125] and Ouyang et al (2016)[126] 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) in detecting prostate cancer. 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 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)[125]				
^{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)[126]				
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
^{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; ^{11}C-acetate: carbon 11 acetate; ^{11}C-choline: carbon 11 choline; ^{18}F-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.[127] 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.[128] 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; odds ratio, 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 N=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%).[129] 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.[130] 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 Food and Drug Administration.

Other systematic reviews, including those by Sandgren et al (2017)[131] and Albisinni et al (2018),[132] have also reported that ^{11}C-choline PET/CT exhibits high sensitivity and specificity estimates in the staging and restaging of prostate cancer.

Both the NCCN report conducted by Podoloff et al (2009)[34] and the AHRQ review by Ospina et al (2008)[32] found the evidence insufficient to support the use of PET for any indication in patients with prostate cancer. Reports showed significant overlap between benign prostatic hyperplasia, malignant tumor, local recurrence, and postoperative scarring. 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.[133] 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.[134] 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.[135] 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 have indicated that ^{11}C-choline PET/CT has limited value unless PSA levels exceed 1.0 ng/mL.[136] 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.[137] 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.[128] Pooled positive predictive value and NPV were 70% and 85%, respectively.

Guidelines

American College of Radiology

ACR Appropriateness Criteria on posttreatment follow-up of patients with prostate cancer have stated 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.[138]

National Comprehensive Cancer Network

Current NCCN guidelines for prostate cancer (v.3.2018) indicate that ^{11}C-choline PET may be considered for evaluating biochemical failure after primary treatment (ie, radiotherapy or radical

prostatectomy).[139] To evaluate progression, ^{11}C-choline PET/CT or ^{18}F-fluciclovine PET/CT may be considered for soft tissue assessment and ^{18}F-sodium fluoride PET/CT may be considered for bone assessment. The guidelines note that ^{18}F-sodium fluoride PET/CT has greater sensitivity but lower specificity than standard bone scan imaging. 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)[132] review, discussed in the ^{11}C-choline PET/CT section, and a systematic review by Eissa et al (2018)[140] 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).

A systematic review by Perera et al (2016) calculated the sensitivity, specificity, and predictive value of ^{68}Ga-PSMA PET in advanced prostate cancer.[141] 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 PSMA 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.3.2018) note that ^{68}Ga-PSMA PET "may provide better detection of recurrences at lower PSA levels than reported for FDA-approved imaging agents."[139] 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).[142] 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 RCC (v.4.2018) state that "The value of PET in RCC [renal cell carcinoma] 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."[143]

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.[144] 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 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.[145] Reviewers found that PET had low diagnostic accuracy in distinguishing low-grade tumors from benign lesions. PET performed better at differentiating high- or intermediate-grade tumors from low-grade tumors; however, 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.2.2018) state that PET/CT may be useful in staging, prognostication, and grading.[146] PET/CT can be useful in determining response to

chemotherapy for lesions greater than 3 cm that are firm, deep, and not superficial. 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 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)[32] and studies evaluating residual masses in patients after chemotherapy for seminoma[147] have supported the use of PET.

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.[114] 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.2.2018) support the use of PET to evaluate residual masses that are greater than 3 cm following primary treatment with chemotherapy (at ≥6 weeks posttreatment).[148] If a PET scan is negative, surveillance is recommended. If a PET scan is positive, resection or biopsy of residual mass is recommended. The guidelines warn that there is "limited predictive value for PET/CT scan for residual masses." 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.[149] 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.[150] 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.[34] Additionally, PET was found to be prognostic in this setting: More metabolically active lesions on PET were strongly correlated with reduced survival.[151]

Guidelines

Current NCCN guidelines for thyroid carcinoma 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.[152]

Medullary

A meta-analysis of studies on detecting recurrent or metastatic medullary thyroid carcinoma was conducted by Cheng et al (2012).[153] 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.1.2018) recommend contrast-enhanced CT with or without PET at 2 to 3 months postoperative surveillance.[152] Additionally, PET/CT may be considered if recurrent disease is suspected.

Section Summary: Thyroid Cancer
Evidence for the use of PET and PET/CT to diagnose recurrent 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.[154] 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.[155] 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 a 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 (ie, 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."[34] 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.[148]

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 FDG-PET or FDG-PET/CT, the evidence includes a systematic review and meta-analysis. The 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. The 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. The relevant outcome is test validity. Pooled analyses have shown that PET or PET/CT can effectively diagnose and stage bone sarcoma. 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. The 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-FET-PET, or carbon 11 (^{11}C) methionine PET, the evidence includes several systematic reviews and meta-analyses. The 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, fluorine 18 fluoro-ethyl-tyrosine-PET, or ^{11}C-methionine PET, the evidence includes systematic reviews and meta-analyses. The 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. The relevant outcome is test validity 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. The relevant outcome is test validity. There is no evidence supporting the use of PET in diagnosing breast cancer. The false-negative rates (5.5%-8.5%) using PET in patients with breast cancer can be considered unacceptable, given that breast biopsy can provide more definitive results. PET/CT may be considered for 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. The 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 AHRQ report and a meta-analysis. The 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 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. The 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 colorectal cancer or who are asymptomatic after completing colorectal cancer treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment and meta-analysis. The relevant outcome is test validity. A meta-analysis evaluating the diagnostic accuracy of PET or PET/CT showed a 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 colorectal cancer. 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. The 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. The 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. The 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 with gastric cancer and in need of staging or restaging information, who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. The 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. The 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 who need staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment and several meta-analyses. The 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 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. The 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 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. The 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 NSCLC treatment who receive FDG-PET or -FDG-PET/CT, there is no evidence. The 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 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. The 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 small-cell lung cancer if 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 small-cell lung cancer or who are asymptomatic after completing small-cell lung cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. The 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 and several meta-analyses. The relevant outcome is test validity. 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. The 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. The 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. The 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. The 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. The 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, one of which conducted a meta-analysis. The 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 in certain circumstances, to discern active from smoldering myeloma, particularly if the skeletal survey is negative. 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. The 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. The 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 ^{68}Ga-PET or ^{68}Ga-PET/CT, the evidence includes several systematic reviews with meta-analyses. The 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. The 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. The 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. The 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. The 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 F-FDG-PET or F-FDG-PET/CT, there is no evidence. The 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. The 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. The 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, ^{18}F-fluciclovine PET/CT, evidence includes several meta-analyses. The 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, ^{18}F-fluciclovine PET/CT, there is no evidence. The 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. The 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 RCC 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. The relevant outcome is test validity. The review concluded that PET has the potential to detect metastatic or recurrent lesions in patients with RCC, 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. The 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. The 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. The relevant outcome is test validity. The review concluded that there was insufficient evidence on the use of PET for 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. The 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. The 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. The 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. The 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. The relevant outcome is test validity. Studies reviewed in the Assessment showed that PET identified previously undetected metastases confirmed by biopsy. 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.

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.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

A search of ClinicalTrials.gov in July 2018 identified a considerably large number of ongoing and unpublished trials that would likely influence this review.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

CPT/HCPCS

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	Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; limited area (e.g. chest, head/neck)
78815	Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; skull base to mid-thigh
78816	Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; whole body
A4641	Radiopharmaceutical, diagnostic, not otherwise classified
A9515	Choline C-11, diagnostic, per study dose up to 20 millicuries
A9526	Nitrogen N-13 ammonia, diagnostic, per study dose, up to 40 millicuries
A9552	Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries
A9580	Sodium fluoride F-18, diagnostic, per study dose, up to 30 millicuries
A9587	Gallium ga-68, dotatate, diagnostic, 0.1 millicurie
A9588	Fluciclovine f-18, diagnostic, 1 millicurie
A9598	Positron emission tomography radiopharmaceutical, diagnostic, for non-tumor identification, not otherwise classified
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)

- A PET scan involves 3 separate activities:
  (1) manufacture of the radiopharmaceutical, which may be on site or at a regional center with delivery to the institution performing PET;
  (2) actual performance of the PET scanner; and
  (3) interpretation of the results.
- Two 2 new modifiers were added in July 2009. 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

ICD-10 Diagnosis Codes

C00.0	Malignant neoplasm of external upper lip
C00.1	Malignant neoplasm of external lower lip
C00.3	Malignant neoplasm of upper lip, inner aspect
C00.4	Malignant neoplasm of lower lip, inner aspect
C00.6	Malignant neoplasm of commissure of lip, unspecified
C00.8	Malignant neoplasm of overlapping sites of lip
C00.9	Malignant neoplasm of lip, unspecified
C01	Malignant neoplasm of base of tongue
C02.0	Malignant neoplasm of dorsal surface of tongue
C02.1	Malignant neoplasm of border of tongue
C02.2	Malignant neoplasm of ventral surface of tongue
C02.3	Malignant neoplasm of anterior two-thirds of tongue, part unspecified

ICD-10 Diagnosis Codes

C02.4	Malignant neoplasm of lingual tonsil
C02.8	Malignant neoplasm of overlapping sites of tongue
C03.0	Malignant neoplasm of upper gum
C03.1	Malignant neoplasm of lower gum
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C05.2	Malignant neoplasm of uvula
C05.8	Malignant neoplasm of overlapping sites of palate
C06.0	Malignant neoplasm of cheek mucosa
C06.1	Malignant neoplasm of vestibule of mouth
C06.2	Malignant neoplasm of retromolar area
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C09.0	Malignant neoplasm of tonsillar fossa
C09.1	Malignant neoplasm of tonsillar pillar (anterior) (posterior)
C09.8	Malignant neoplasm of overlapping sites of tonsil
C10.0	Malignant neoplasm of vallecula
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C12	Malignant neoplasm of pyriform sinus
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
C13.2	Malignant neoplasm of posterior wall of hypopharynx
C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure

ICD-10 Diagnosis Codes

C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.4	Malignant neoplasm of endocrine pancreas
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C26.1	Malignant neoplasm of spleen
C26.9	Malignant neoplasm of ill-defined sites within the digestive system
C30.0	Malignant neoplasm of nasal cavity
C30.1	Malignant neoplasm of middle ear
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C31.2	Malignant neoplasm of frontal sinus
C31.3	Malignant neoplasm of sphenoid sinus
C31.8	Malignant neoplasm of overlapping sites of accessory sinuses
C32.0	Malignant neoplasm of glottis
C32.1	Malignant neoplasm of supraglottis
C32.2	Malignant neoplasm of subglottis
C32.3	Malignant neoplasm of laryngeal cartilage
C32.8	Malignant neoplasm of overlapping sites of larynx
C33	Malignant neoplasm of trachea
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb

ICD-10 Diagnosis Codes

C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C47.22	Malignant neoplasm of peripheral nerves of left lower limb, including hip
C47.3	Malignant neoplasm of peripheral nerves of thorax
C47.4	Malignant neoplasm of peripheral nerves of abdomen
C47.5	Malignant neoplasm of peripheral nerves of pelvis
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system
C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49A1	Gastrointestinal stromal tumor of esophagus
C49A2	Gastrointestinal stromal tumor of stomach
C49A3	Gastrointestinal stromal tumor of small intestine
C49A4	Gastrointestinal stromal tumor of large intestine
C49A5	Gastrointestinal stromal tumor of rectum
C49A9	Gastrointestinal stromal tumor of other sites
C4A.0	Merkel cell carcinoma of lip
C4A.111	Merkel cell carcinoma of right upper eyelid, inc canthus

ICD-10 Diagnosis Codes

C4A.112 Merkel cell carcinoma of right lower eyelid, inc canthus
C4A.121 Merkel cell carcinoma of left upper eyelid, inc canthus
C4A.122 Merkel cell carcinoma of left lower eyelid, inc canthus
C4A.21 Merkel cell carcinoma of right ear and external auricular canal
C4A.22 Merkel cell carcinoma of left ear and external auricular canal
C4A.31 Merkel cell carcinoma of nose
C4A.39 Merkel cell carcinoma of other parts of face
C4A.4 Merkel cell carcinoma of scalp and neck
C4A.51 Merkel cell carcinoma of anal skin
C4A.52 Merkel cell carcinoma of skin of breast
C4A.59 Merkel cell carcinoma of other part of trunk
C4A.61 Merkel cell carcinoma of right upper limb, including shoulder
C4A.62 Merkel cell carcinoma of left upper limb, including shoulder
C4A.71 Merkel cell carcinoma of right lower limb, including hip
C4A.72 Merkel cell carcinoma of left lower limb, including hip
C4A.8 Merkel cell carcinoma of overlapping sites
C50.011 Malignant neoplasm of nipple and areola, right female breast
C50.012 Malignant neoplasm of nipple and areola, left female breast
C50.021 Malignant neoplasm of nipple and areola, right male breast
C50.022 Malignant neoplasm of nipple and areola, left male breast
C50.111 Malignant neoplasm of central portion of right female breast
C50.112 Malignant neoplasm of central portion of left female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast
C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C51.8 Malignant neoplasm of overlapping sites of vulva
C53.0 Malignant neoplasm of endocervix
C53.1 Malignant neoplasm of exocervix
C53.8 Malignant neoplasm of overlapping sites of cervix uteri

ICD-10 Diagnosis Codes

C54.1	Malignant neoplasm of endometrium
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.2	Malignant neoplasm of body of penis
C60.8	Malignant neoplasm of overlapping sites of penis
C61	Malignant neoplasm of prostate
C62.01	Malignant neoplasm of undescended right testis
C62.02	Malignant neoplasm of undescended left testis
C62.11	Malignant neoplasm of descended right testis
C62.12	Malignant neoplasm of descended left testis
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C70.0	Malignant neoplasm of cerebral meninges
C70.1	Malignant neoplasm of spinal meninges
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C72.21	Malignant neoplasm of right olfactory nerve
C72.22	Malignant neoplasm of left olfactory nerve
C72.31	Malignant neoplasm of right optic nerve
C72.32	Malignant neoplasm of left optic nerve
C72.41	Malignant neoplasm of right acoustic nerve
C72.42	Malignant neoplasm of left acoustic nerve
C72.59	Malignant neoplasm of other cranial nerves
C72.9	Malignant neoplasm of central nervous system, unspecified
C73	Malignant neoplasm of thyroid gland
C74.01	Malignant neoplasm of cortex of right adrenal gland

ICD-10 Diagnosis Codes

C74.02	Malignant neoplasm of cortex of left adrenal gland
C74.11	Malignant neoplasm of medulla of right adrenal gland
C74.12	Malignant neoplasm of medulla of left adrenal gland
C75.1	Malignant neoplasm of pituitary gland
C75.2	Malignant neoplasm of craniopharyngeal duct
C75.3	Malignant neoplasm of pineal gland
C75.4	Malignant neoplasm of carotid body
C75.5	Malignant neoplasm of aortic body and other paraganglia
C76.0	Malignant neoplasm of head, face and neck
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.2	Secondary malignant neoplasm of pleura
C78.5	Secondary malignant neoplasm of large intestine and rectum
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C78.89	Secondary malignant neoplasm of other digestive organs
C79.31	Secondary malignant neoplasm of brain
C79.49	Secondary malignant neoplasm of other parts of nervous system
C79.61	Secondary malignant neoplasm of right ovary
C79.62	Secondary malignant neoplasm of left ovary
C79.81	Secondary malignant neoplasm of breast
C79.82	Secondary malignant neoplasm of genital organs
C7A.010	Malignant carcinoid tumor of the duodenum
C7A.011	Malignant carcinoid tumor of the jejunum
C7A.012	Malignant carcinoid tumor of the ileum
C7A.019	Malignant carcinoid tumor of the small intestine, unspecified portion
C7A.020	Malignant carcinoid tumor of the appendix
C7A.021	Malignant carcinoid tumor of the cecum
C7A.022	Malignant carcinoid tumor of the ascending colon
C7A.023	Malignant carcinoid tumor of the transverse colon
C7A.024	Malignant carcinoid tumor of the descending colon
C7A.025	Malignant carcinoid tumor of the sigmoid colon
C7A.026	Malignant carcinoid tumor of the rectum
C7A.029	Malignant carcinoid tumor of the large intestine, unspecified portion
C7A.090	Malignant carcinoid tumor of the bronchus and lung
C7A.091	Malignant carcinoid tumor of the thymus
C7A.092	Malignant carcinoid tumor of the stomach
C7A.093	Malignant carcinoid tumor of the kidney
C7A.094	Malignant carcinoid tumor of the foregut, unspecified
C7A.095	Malignant carcinoid tumor of the midgut unspecified
C7A.096	Malignant carcinoid tumor of the hindgut unspecified
C7A.098	Malignant carcinoid tumors of other sites
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7A.8	Other malignant neuroendocrine tumors
C80.0	Disseminated malignant neoplasm, unspecified
C81.01	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.02	Nodular lymphocyte predominant Hodgkin lymphoma, intrathoracic lymph nodes
C81.03	Nodular lymphocyte predominant Hodgkin lymphoma, intra-abdominal lymph nodes
C81.04	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.05	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.06	Nodular lymphocyte predominant Hodgkin lymphoma, intrapelvic lymph nodes

ICD-10 Diagnosis Codes

C81.07 Nodular lymphocyte predominant Hodgkin lymphoma, spleen
C81.08 Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of multiple sites
C81.09 Nodular lymphocyte predominant Hodgkin lymphoma, extranodal and solid organ sites
C81.11 Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12 Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13 Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14 Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15 Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16 Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17 Nodular sclerosis Hodgkin lymphoma, spleen
C81.18 Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19 Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.21 Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22 Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.23 Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24 Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25 Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26 Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes
C81.27 Mixed cellularity Hodgkin lymphoma, spleen
C81.28 Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29 Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.31 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32 Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33 Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36 Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37 Lymphocyte depleted Hodgkin lymphoma, spleen
C81.38 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39 Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.41 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42 Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.43 Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46 Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47 Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites
C81.49 Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.71 Other Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.72 Other Hodgkin lymphoma, intrathoracic lymph nodes
C81.73 Other Hodgkin lymphoma, intra-abdominal lymph nodes
C81.74 Other Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.75 Other Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.76 Other Hodgkin lymphoma, intrapelvic lymph nodes
C81.77 Other Hodgkin lymphoma, spleen
C81.78 Other Hodgkin lymphoma, lymph nodes of multiple sites
C81.79 Other Hodgkin lymphoma, extranodal and solid organ sites
C82.01 Follicular lymphoma grade I, lymph nodes of head, face, and neck
C82.02 Follicular lymphoma grade I, intrathoracic lymph nodes
C82.03 Follicular lymphoma grade I, intra-abdominal lymph nodes
C82.04 Follicular lymphoma grade I, lymph nodes of axilla and upper limb

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C82.05 Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb
C82.06 Follicular lymphoma grade I, intrapelvic lymph nodes
C82.07 Follicular lymphoma grade I, spleen
C82.08 Follicular lymphoma grade I, lymph nodes of multiple sites
C82.09 Follicular lymphoma grade I, extranodal and solid organ sites
C82.11 Follicular lymphoma grade II, lymph nodes of head, face, and neck
C82.12 Follicular lymphoma grade II, intrathoracic lymph nodes
C82.13 Follicular lymphoma grade II, intra-abdominal lymph nodes
C82.14 Follicular lymphoma grade II, lymph nodes of axilla and upper limb
C82.15 Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb
C82.16 Follicular lymphoma grade II, intrapelvic lymph nodes
C82.17 Follicular lymphoma grade II, spleen
C82.18 Follicular lymphoma grade II, lymph nodes of multiple sites
C82.19 Follicular lymphoma grade II, extranodal and solid organ sites
C82.21 Follicular lymphoma grade III, unspecified, lymph nodes of head, face, and neck
C82.22 Follicular lymphoma grade III, unspecified, intrathoracic lymph nodes
C82.23 Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes
C82.24 Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb
C82.25 Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb
C82.26 Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes
C82.28 Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites
C82.29 Follicular lymphoma grade III, unspecified, extranodal and solid organ sites
C82.31 Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck
C82.32 Follicular lymphoma grade IIIa, intrathoracic lymph nodes
C82.33 Follicular lymphoma grade IIIa, intra-abdominal lymph nodes
C82.34 Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb
C82.35 Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb
C82.36 Follicular lymphoma grade IIIa, intrapelvic lymph nodes
C82.37 Follicular lymphoma grade IIIa, spleen
C82.38 Follicular lymphoma grade IIIa, lymph nodes of multiple sites
C82.39 Follicular lymphoma grade IIIa, extranodal and solid organ sites
C82.41 Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck
C82.42 Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.43 Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44 Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45 Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46 Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47 Follicular lymphoma grade IIIb, spleen
C82.48 Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49 Follicular lymphoma grade IIIb, extranodal and solid organ sites
C82.51 Diffuse follicle center lymphoma, lymph nodes of head, face, and neck
C82.52 Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.53 Diffuse follicle center lymphoma, intra-abdominal lymph nodes
C82.54 Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb
C82.55 Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.56 Diffuse follicle center lymphoma, intrapelvic lymph nodes
C82.57 Diffuse follicle center lymphoma, spleen
C82.58 Diffuse follicle center lymphoma, lymph nodes of multiple sites
C82.59 Diffuse follicle center lymphoma, extranodal and solid organ sites
C82.61 Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck
C82.62 Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.63 Cutaneous follicle center lymphoma, intra-abdominal lymph nodes

ICD-10 Diagnosis Codes

C82.64 Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb
C82.65 Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.66 Cutaneous follicle center lymphoma, intrapelvic lymph nodes
C82.67 Cutaneous follicle center lymphoma, spleen
C82.68 Cutaneous follicle center lymphoma, lymph nodes of multiple sites
C82.69 Cutaneous follicle center lymphoma, extranodal and solid organ sites
C82.81 Other types of follicular lymphoma, lymph nodes of head, face, and neck
C82.82 Other types of follicular lymphoma, intrathoracic lymph nodes
C82.83 Other types of follicular lymphoma, intra-abdominal lymph nodes
C82.84 Other types of follicular lymphoma, lymph nodes of axilla and upper limb
C82.85 Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb
C82.86 Other types of follicular lymphoma, intrapelvic lymph nodes
C82.87 Other types of follicular lymphoma, spleen
C82.88 Other types of follicular lymphoma, lymph nodes of multiple sites
C82.89 Other types of follicular lymphoma, extranodal and solid organ sites
C83.01 Small cell B-cell lymphoma, lymph nodes of head, face, and neck
C83.02 Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03 Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04 Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05 Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06 Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07 Small cell B-cell lymphoma, spleen
C83.08 Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09 Small cell B-cell lymphoma, extranodal and solid organ sites
C83.11 Mantle cell lymphoma, lymph nodes of head, face, and neck
C83.12 Mantle cell lymphoma, intrathoracic lymph nodes
C83.13 Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14 Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15 Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16 Mantle cell lymphoma, intrapelvic lymph nodes
C83.17 Mantle cell lymphoma, spleen
C83.18 Mantle cell lymphoma, lymph nodes of multiple sites
C83.19 Mantle cell lymphoma, extranodal and solid organ sites
C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32 Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36 Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37 Diffuse large B-cell lymphoma, spleen
C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83.39 Diffuse large B-cell lymphoma, extranodal and solid organ sites
C83.51 Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52 Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53 Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54 Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55 Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56 Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57 Lymphoblastic (diffuse) lymphoma, spleen
C83.58 Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59 Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C83.71 Burkitt lymphoma, lymph nodes of head, face, and neck

ICD-10 Diagnosis Codes

C83.72 Burkitt lymphoma, intrathoracic lymph nodes
C83.73 Burkitt lymphoma, intra-abdominal lymph nodes
C83.74 Burkitt lymphoma, lymph nodes of axilla and upper limb
C83.75 Burkitt lymphoma, lymph nodes of inguinal region and lower limb
C83.76 Burkitt lymphoma, intrapelvic lymph nodes
C83.77 Burkitt lymphoma, spleen
C83.78 Burkitt lymphoma, lymph nodes of multiple sites
C83.79 Burkitt lymphoma, extranodal and solid organ sites
C83.81 Other non-follicular lymphoma, lymph nodes of head, face, and neck
C83.82 Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83 Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84 Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85 Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86 Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87 Other non-follicular lymphoma, spleen
C83.88 Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89 Other non-follicular lymphoma, extranodal and solid organ sites
C83.91 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck
C83.92 Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C83.93 Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes
C83.94 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb
C83.95 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C83.96 Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes
C83.97 Non-follicular (diffuse) lymphoma, unspecified, spleen
C83.98 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites
C83.99 Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites
C84.01 Mycosis fungoides, lymph nodes of head, face, and neck
C84.02 Mycosis fungoides, intrathoracic lymph nodes
C84.03 Mycosis fungoides, intra-abdominal lymph nodes
C84.04 Mycosis fungoides, lymph nodes of axilla and upper limb
C84.05 Mycosis fungoides, lymph nodes of inguinal region and lower limb
C84.06 Mycosis fungoides, intrapelvic lymph nodes
C84.07 Mycosis fungoides, spleen
C84.08 Mycosis fungoides, lymph nodes of multiple sites
C84.09 Mycosis fungoides, extranodal and solid organ sites
C84.11 Sezary disease, lymph nodes of head, face, and neck
C84.12 Sezary disease, intrathoracic lymph nodes
C84.13 Sezary disease, intra-abdominal lymph nodes
C84.14 Sezary disease, lymph nodes of axilla and upper limb
C84.15 Sezary disease, lymph nodes of inguinal region and lower limb
C84.16 Sezary disease, intrapelvic lymph nodes
C84.17 Sezary disease, spleen
C84.18 Sezary disease, lymph nodes of multiple sites
C84.19 Sezary disease, extranodal and solid organ sites
C84.41 Peripheral T-cell lymphoma, not classified, lymph nodes of head, face, and neck
C84.42 Peripheral T-cell lymphoma, not classified, intrathoracic lymph nodes
C84.43 Peripheral T-cell lymphoma, not classified, intra-abdominal lymph nodes
C84.44 Peripheral T-cell lymphoma, not classified, lymph nodes of axilla and upper limb
C84.45 Peripheral T-cell lymphoma, not classified, lymph nodes of inguinal region and lower limb
C84.46 Peripheral T-cell lymphoma, not classified, intrapelvic lymph nodes
C84.47 Peripheral T-cell lymphoma, not classified, spleen
C84.48 Peripheral T-cell lymphoma, not classified, lymph nodes of multiple sites

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C84.49 Peripheral T-cell lymphoma, not classified, extranodal and solid organ sites
C84.61 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of head, face, and neck
C84.62 Anaplastic large cell lymphoma, ALK-positive, intrathoracic lymph nodes
C84.63 Anaplastic large cell lymphoma, ALK-positive, intra-abdominal lymph nodes
C84.64 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of axilla and upper limb
C84.65 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of inguinal region and lower limb
C84.66 Anaplastic large cell lymphoma, ALK-positive, intrapelvic lymph nodes
C84.67 Anaplastic large cell lymphoma, ALK-positive, spleen
C84.68 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of multiple sites
C84.69 Anaplastic large cell lymphoma, ALK-positive, extranodal and solid organ sites
C84.71 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of head, face, and neck
C84.72 Anaplastic large cell lymphoma, ALK-negative, intrathoracic lymph nodes
C84.73 Anaplastic large cell lymphoma, ALK-negative, intra-abdominal lymph nodes
C84.74 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of axilla and upper limb
C84.75 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of inguinal region and lower limb
C84.76 Anaplastic large cell lymphoma, ALK-negative, intrapelvic lymph nodes
C84.77 Anaplastic large cell lymphoma, ALK-negative, spleen
C84.78 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of multiple sites
C84.79 Anaplastic large cell lymphoma, ALK-negative, extranodal and solid organ sites
C84.91 Mature T/NK-cell lymphomas, unspecified, lymph nodes of head, face, and neck
C84.92 Mature T/NK-cell lymphomas, unspecified, intrathoracic lymph nodes
C84.93 Mature T/NK-cell lymphomas, unspecified, intra-abdominal lymph nodes
C84.94 Mature T/NK-cell lymphomas, unspecified, lymph nodes of axilla and upper limb
C84.95 Mature T/NK-cell lymphomas, unspecified, lymph nodes of inguinal region and lower limb
C84.96 Mature T/NK-cell lymphomas, unspecified, intrapelvic lymph nodes
C84.97 Mature T/NK-cell lymphomas, unspecified, spleen
C84.98 Mature T/NK-cell lymphomas, unspecified, lymph nodes of multiple sites
C84.99 Mature T/NK-cell lymphomas, unspecified, extranodal and solid organ sites
C84.A1 Cutaneous T-cell lymphoma, unspecified lymph nodes of head, face, and neck
C84.A2 Cutaneous T-cell lymphoma, unspecified, intrathoracic lymph nodes
C84.A3 Cutaneous T-cell lymphoma, unspecified, intra-abdominal lymph nodes
C84.A4 Cutaneous T-cell lymphoma, unspecified, lymph nodes of axilla and upper limb
C84.A5 Cutaneous T-cell lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C84.A6 Cutaneous T-cell lymphoma, unspecified, intrapelvic lymph nodes
C84.A7 Cutaneous T-cell lymphoma, unspecified, spleen
C84.A8 Cutaneous T-cell lymphoma, unspecified, lymph nodes of multiple sites
C84.A9 Cutaneous T-cell lymphoma, unspecified, extranodal and solid organ sites
C84.Z1 Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck
C84.Z2 Other mature T/NK-cell lymphomas, intrathoracic lymph nodes
C84.Z3 Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes
C84.Z4 Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb
C84.Z5 Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb
C84.Z6 Other mature T/NK-cell lymphomas, intrapelvic lymph nodes
C84.Z7 Other mature T/NK-cell lymphomas, spleen
C84.Z8 Other mature T/NK-cell lymphomas, lymph nodes of multiple sites
C84.Z9 Other mature T/NK-cell lymphomas, extranodal and solid organ sites
C85.11 Unspecified B-cell lymphoma, lymph nodes of head, face, and neck
C85.13 Unspecified B-cell lymphoma, intra-abdominal lymph nodes
C85.14 Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb
C85.16 Unspecified B-cell lymphoma, intrapelvic lymph nodes
C85.17 Unspecified B-cell lymphoma, spleen
C85.18 Unspecified B-cell lymphoma, lymph nodes of multiple sites

ICD-10 Diagnosis Codes

C85.19 Unspecified B-cell lymphoma, extranodal and solid organ sites
C85.21 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85.22 Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23 Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26 Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27 Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29 Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C85.81 Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck
C85.82 Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83 Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84 Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85 Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C85.86 Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87 Other specified types of non-Hodgkin lymphoma, spleen
C85.88 Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89 Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C85.91 Non-Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
C85.92 Non-Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C85.93 Non-Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C85.94 Non-Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C85.95 Non-Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C85.96 Non-Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C85.97 Non-Hodgkin lymphoma, unspecified, spleen
C85.98 Non-Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C85.99 Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites
C86.0 Extranodal NK/T-cell lymphoma, nasal type
C86.1 Hepatosplenic T-cell lymphoma
C86.2 Enteropathy-type (intestinal) T-cell lymphoma
C86.3 Subcutaneous panniculitis-like T-cell lymphoma
C86.4 Blastic NK-cell lymphoma
C86.5 Angioimmunoblastic T-cell lymphoma
C86.6 Primary cutaneous CD30-positive T-cell proliferations
C88.0 Waldenstrom macroglobulinemia
C88.2 Heavy chain disease
C88.3 Immunoproliferative small intestinal disease
C88.4 Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
C88.8 Other malignant immunoproliferative diseases
C88.9 Malignant immunoproliferative disease, unspecified
C90.00 Multiple myeloma not having achieved remission
C90.01 Multiple myeloma in remission
C90.02 Multiple myeloma in relapse
C90.20 Extramedullary plasmacytoma not having achieved remission
C90.21 Extramedullary plasmacytoma in remission
C90.22 Extramedullary plasmacytoma in relapse
C90.30 Solitary plasmacytoma not having achieved remission
C90.31 Solitary plasmacytoma in remission
C90.32 Solitary plasmacytoma in relapse

ICD-10 Diagnosis Codes

C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
C96.4	Sarcoma of dendritic cells (accessory cells)
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.A	Histiocytic sarcoma
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D00.1	Carcinoma in situ of esophagus
D01.0	Carcinoma in situ of colon
D01.1	Carcinoma in situ of rectosigmoid junction
D01.2	Carcinoma in situ of rectum
D01.3	Carcinoma in situ of anus and anal canal
D01.7	Carcinoma in situ of other specified digestive organs
D02.21	Carcinoma in situ of right bronchus and lung
D02.22	Carcinoma in situ of left bronchus and lung
D03.0	Melanoma in situ of lip
D03.111	Melanoma in situ of right upper eyelid, including canthus
D03.112	Melanoma in situ of right lower eyelid, including canthus
D03.121	Melanoma in situ of left upper eyelid, including canthus
D03.122	Melanoma in situ of left lower eyelid, including canthus
D03.21	Melanoma in situ of right ear and external auricular canal
D03.22	Melanoma in situ of left ear and external auricular canal
D03.39	Melanoma in situ of other parts of face
D03.4	Melanoma in situ of scalp and neck
D03.51	Melanoma in situ of anal skin
D03.52	Melanoma in situ of breast (skin) (soft tissue)
D03.59	Melanoma in situ of other part of trunk
D03.61	Melanoma in situ of right upper limb, including shoulder
D03.62	Melanoma in situ of left upper limb, including shoulder
D03.71	Melanoma in situ of right lower limb, including hip
D03.72	Melanoma in situ of left lower limb, including hip
D03.8	Melanoma in situ of other sites
D06.0	Carcinoma in situ of endocervix
D06.1	Carcinoma in situ of exocervix
D06.7	Carcinoma in situ of other parts of cervix
D07.39	Carcinoma in situ of other female genital organs
D09.3	Carcinoma in situ of thyroid and other endocrine glands
D09.8	Carcinoma in situ of other specified sites
D12.0	Benign neoplasm of cecum
D12.1	Benign neoplasm of appendix
D12.2	Benign neoplasm of ascending colon
D12.3	Benign neoplasm of transverse colon
D12.4	Benign neoplasm of descending colon
D12.5	Benign neoplasm of sigmoid colon
D12.7	Benign neoplasm of rectosigmoid junction
D12.8	Benign neoplasm of rectum
D12.9	Benign neoplasm of anus and anal canal
D13.0	Benign neoplasm of esophagus
D14.31	Benign neoplasm of right bronchus and lung
D14.32	Benign neoplasm of left bronchus and lung

ICD-10 Diagnosis Codes

D35.01	Benign neoplasm of right adrenal gland
D35.02	Benign neoplasm of left adrenal gland
D37.1	Neoplasm of uncertain behavior of stomach
D37.2	Neoplasm of uncertain behavior of small intestine
D37.3	Neoplasm of uncertain behavior of appendix
D37.4	Neoplasm of uncertain behavior of colon
D37.5	Neoplasm of uncertain behavior of rectum
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
D38.1	Neoplasm of uncertain behavior of trachea, bronchus and lung
D3A.010	Benign carcinoid tumor of the duodenum
D3A.011	Benign carcinoid tumor of the jejunum
D3A.012	Benign carcinoid tumor of the ileum
D3A.019	Benign carcinoid tumor of the small intestine, unspecified portion
D3A.020	Benign carcinoid tumor of the appendix
D3A.021	Benign carcinoid tumor of the cecum
D3A.022	Benign carcinoid tumor of the ascending colon
D3A.023	Benign carcinoid tumor of the transverse colon
D3A.024	Benign carcinoid tumor of the descending colon
D3A.025	Benign carcinoid tumor of the sigmoid colon
D3A.026	Benign carcinoid tumor of the rectum
D3A.029	Benign carcinoid tumor of the large intestine, unspecified portion
D3A.090	Benign carcinoid tumor of the bronchus and lung
D3A.091	Benign carcinoid tumor of the thymus
D3A.092	Benign carcinoid tumor of the stomach
D3A.093	Benign carcinoid tumor of the kidney
D3A.094	Benign carcinoid tumor of the foregut , unspecified
D3A.095	Benign carcinoid tumor of the midgut , unspecified
D3A.096	Benign carcinoid tumor of the hindgut , unspecified
D3A.098	Benign carcinoid tumors of other sites
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.4	Neoplasm of uncertain behavior of spinal cord
D44.6	Neoplasm of uncertain behavior of carotid body
D44.7	Neoplasm of uncertain behavior of aortic body and other paraganglia
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
D48.1	Neoplasm of uncertain behavior of connective and other soft tissue
D48.2	Neoplasm of uncertain behavior of peripheral nerves and autonomic nervous system
D49.0	Neoplasm of unspecified behavior of digestive system
D49.1	Neoplasm of unspecified behavior of respiratory system
D49.6	Neoplasm of unspecified behavior of brain
R76.0	Raised antibody titer
R76.8	Other specified abnormal immunological findings in serum
R76.9	Abnormal immunological finding in serum, unspecified
R90.0	Intracranial space-occupying lesion found on diagnostic imaging of central nervous system
R91.1	Solitary pulmonary nodule

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10-30-2013	Oncologic Applications was originally part of the Positron Emission Tomography (PET) medical policy. Oncologic Applications has been pulled out and placed into a separate medical policy, Positron Emission Tomography (PET): Oncologic Applications. The medical policy language was unchanged.
	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Added ICD-10 Diagnosis codes *(Effective October 1,2014)*
	Updated Reference section.
10-28-2014	In Coding section: ▪ Removed ICD-9 Diagnosis code 793.1 (expired 09/30/2011) ▪ Added ICD-9 Diagnosis code 793.19
10-22-2015	Description section updated
	In Policy section: ▪ Revised to current policy language by location of cancer from the following policy language by diagnosing, staging, re-staging: "I. PET scan with or without PET/CT fusion is considered medically necessary for the following tumors when results are expected to influence treatment decisions and standard imaging (e.g., CT, MRI or ultrasound) is inconclusive or not indicated: A. Diagnosing or Staging 1. Bone—Ewing sarcoma and osteosarcoma; 2. Brain; 3. Breast (except initial staging of axillary lymph nodes); 4. Cervix; 5. Colorectal; 6. Esophageal; 7. Gastric Cancer; 8.Gastrointestinal Stromal Tumors; 9. Kidney Cancer; 10. Head and Neck; 11. Lung: •Non-Small Cell (NSCLC), •Small Cell (SCLC), •Evaluation of Solitary Pulmonary Nodule; 12. Lymphoma: •Hodgkin's, •Non-Hodgkin's; 13. Melanoma (except initial evaluation of regional lymph nodes); 14. Musculoskeletal (including soft tissue sarcoma); 15. Myeloma; 16. Neuroblastoma; 17. Neuroendocrine Tumor, poorly differentiated; 18. Pancreas; 19. Thyroid; 20. Cancer of Unknown Primary; 21. Paraneoplastic Syndromes; B. Re-Staging 1. Brain; 2. Breast; 3. Cervix; 4. Colorectal; 5. Esophageal; 6. Gastric Cancer; 7. Gastrointestinal Stromal Tumors; 8. Head and Neck; 9. Kidney Cancer; 10 Lung – Non-Small Cell (NSCLC); 11. Lymphoma: •Hodgkin's, •Non-Hodgkin's; 12. Melanoma; 13. Myeloma; 14.Musculoskeletal (including Soft Tissue Sarcoma); 15. Neuroblastoma; 16. Neuroendocrine Tumor, poorly differentiated; 17. Ovarian 18. Testicular; 19. Thyroid C. Other oncologic indications may be considered medically necessary on a case by case basis when results are expected to influence treatment decisions. D. Experimental / experimental / investigational oncologic application include, but not limited to: 1. Initial therapy for ovarian cancer or testicular cancer; or 2. Subsequent therapy for small cell lung cancer (SCLC) or pancreatic cancer; or 3. Diagnosis and management of prostate cancer; or 4. To determine early response to treatments (PET scans done during a course of chemotherapy of reduction therapy). E. Surveillance Intermittent surveillance scanning for Ewing Sarcoma is considered medically necessary." ▪ Policy Guidelines Updated
	Rationale section updated
	In Coding section: ▪ Added CPT and HCPCS Codes: 78608, 78609, G0252

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	▪ Updated Coding notations
	References updated
10-22-2015	Published 10-22-2015. Effective 10-22-2015.
	▪ Correction to 10-22-2015 Revision section above. ▪ In Coding section changed "G0525" to "G0252" to read, "Added CPT and HCPCS Codes: 78608, 78609, G0252"
10-01-2015	Published 11-10-2015. Effective 10-01-2015 with ICD-10 coding implementation.
	In Coding Section: ▪ Removed ICD-10 Codes: C34.10, C47.10, C47.20, C49.10, C49.20, C50.911, C50.912, C50.921, C50.922, C74.91, C74.92, C84.70 ▪ Added ICD-10 Codes: C16.5, C16.6, C47.9, C4A.0, C4A.11, C4A.12, C4A.21, C4A.22, C4A.31, C4A.39, C4A.4, C4A.51, C4A.52, C4A.59, C4A.61, C4A.62, C4A.71, C4A.72, C4A.8, C7A.010, C7A.011, C7A.012, C7A.019, C7A.020, C7A.021, C7A.022, C7A.023, C7A.024, C7A.025, C7A.026, C7A.029, C7A.090, C7A.091, C7A.092, C7A.093, C7A.094, C7A.095, C7A.096, C7A.098, C7A.1, C7A.8, C80.0, C80.1, C81.01, C81.02, C81.03, C81.04, C81.05, C81.06, C81.07, C81.08, C81.09, C81.11, C81.12, C81.13, C81.14, C81.15, C81.16, C81.17, C81.18, C81.19, C81.21, C81.22, C81.23, C81.24, C81.25, C81.26, C81.27, C81.28, C81.29, C81.31, C81.32, C81.33, C81.34, C81.35, C81.36, C81.37, C81.38, C81.39, C81.41, C81.42, C81.43, C81.44, C81.45, C81.46, C81.47, C81.48, C81.49, C81.71, C81.72, C81.73, C81.74, C81.75, C81.76, C81.77, C81.78, C81.79, C81.91, C81.92, C81.93, C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, C82.01, C82.02, C82.03, C82.04, C82.05, C82.06, C82.07, C82.08, C82.09, C82.11, C82.12, C82.13, C82.14, C82.15, C82.16, C82.17, C82.18, C82.19, C82.22, C82.23, C82.24, C82.25, C82.26, C82.28, C82.29, C82.31, C82.32, C82.33, C82.34, C82.35, C82.36, C82.37, C82.38, C82.39, C82.41, C82.42, C82.43, C82.44, C82.45, C82.46, C82.47, C82.48, C82.49, C82.51, C82.52, C82.53, C82.54, C82.55, C82.56, C82.57, C82.58, C82.59, C82.61, C82.62, C82.63, C82.64, C82.65, C82.66, C82.67, C82.68, C82.69, C82.81, C82.85, C82.89, C82.90, C82.91, C82.95, C82.99, C84.01, C84.02, C84.03, C84.04, C84.05, C84.06, C84.07, C84.08, C84.09, C84.11, C84.12, C84.13, C84.14, C84.15, C84.16, C84.17, C84.18, C84.19, C84.41, C84.42, C84.43, C84.44, C84.45, C84.46, C84.47, C84.48, C84.49, C84.90, C84.91, C84.93, C84.95, C84.96, C84.97, C84.98, C84.99, C84.A1, C84.A3, C84.A5, C84.A6, C84.A7, C84.A8, C84.A9, C84.Z1, C84.Z2, C84.Z3, C84.Z4, C84.Z5, C84.Z6, C84.Z7, C84.Z8, C84.Z9, C85.11, C85.13, C85.14, C85.16, C85.17, C85.18, C85.19, C85.81, C85.82, C85.83, C85.84, C85.85, C85.86, C85.87, C85.88, C85.89, C85.91, C85.92, C85.93, C85.94, C85.95, C85.96, C85.97, C85.98, C85.99, C86.0, C86.1, C86.2, C86.3, C86.4, C88.2, C88.3, C88.4, C88.8, C88.9, C90.00, C90.01, C90.02, C90.20, C90.21, C90.22, C90.30, C90.31, C90.32, C91.40, C91.41, C91.42, C96.0, C96.2, C96.4, C96.9, C96.A, C96.Z, D00.1, D01.0, D01.1, D01.2, D01.3, D01.7, D02.21, D02.22, D06.0, D06.1, D06.7, D07.39, D09.3, D09.8, D12.0, D12.1, D12.2, D12.3, D12.4, D12.5, D12.7, D12.8, D12.9, D13.0, D14.31, D14.32, D35.01, D35.02, D37.1, D37.2, D37.3, D37.4, D37.5, D37.8, D37.9, D38.1, D3A.010, D3A.011, D3A.012, D3A.019, D3A.020, D3A.021, D3A.022, D3A.023, D3A.024, D3A.025, D3A.026, D3A.029, D3A.090, D3A.091, D3A.092, D3A.093, D3A.094, D3A.095, D3A.096, D3A.098, D3A.8, D43.0, D43.1, D43.4, D44.6, D44.7, D47.Z9, D48.1, D48.2, D49.0, D49.1, D49.6, J98.4, K63.5, R22.0, R22.1, R59.0, R59.1, R59.9, R76.0, R76.8, R76.9, R90.0, Z85.01, Z85.038, Z85.048, Z85.118, Z85.12, Z85.20, Z85.21, Z85.22, Z85.238, Z85.29, Z85.43, Z85.71, Z85.72, Z85.79, Z85.810, Z85.818, Z85.819, Z85.820, Z85.850
10-01-2016	In Coding section: ▪ ICD-10 Codes Added Effective 10-01-2016: C49.A1, C49.A2, C49.A3, C49.A4, C49.A5, C49.A9 ▪ ICD-10 Codes Revised Effective 10-01-2016: C7A.094, C7A.095, C7A.096, C81.11, C81.12, C81.13, C81.14, C81.15, C81.16, C81.17, C81.18, C81.19, C81.21, C81.22,

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	C81.23, C81.24, C81.25, C81.26, C81.27, C81.28, C81.29, C81.31, C81.32, C81.33, C81.34, C81.35, C81.36, C81.37, C81.38, C81.39, C81.41, C81.42, C81.43, C81.44, C81.45, C81.46, C81.47, C81.48, C81.49, C81.71, C81.72, C81.73, C81.74, C81.75, C81.76, C81.77, C81.78, C81.79, D3A.094, D3A.095, D3A.096
10-01-2017	In Coding section: ▪ Added HCPCS Codes: A9515, A9587, A9588, A9598 ▪ Added ICD Codes: C96.20, C96.21, C96.22, C96.29 ▪ Removed ICD Code: C96.2 ▪ Updated Coding notations.
10-01-2018	In Coding section: ▪ Added ICD-10 Codes: C43.111, C43.112, C43.121, C43.122, C4A.111, C4A.112, C4A.121, C4A.122, D03.111, D03.112, D03.121, D03.122 ▪ Removed ICD-10 Codes: C43.11, C43.12, C4A.11, C4A.12, D03.11, D03.12
02-18-2019	Policy published 01-18-2019. Policy effective 02-18-2019.
	Description section updated
	In Policy section: ▪ Added Bladder Cancer indication to read "A. Bladder Cancer 1. PET scanning may be considered medically necessary in the staging or restaging of muscle-invasive bladder cancer when CT or magnetic resonance imaging are not indicated or remained inconclusive on distant metastasis. 2. PET scanning is considered experimental / investigational for bladder tumors that have not invaded the muscle (stage <cT2). ▪ In Item B added "or restaging" to read "PET scanning may be considered medically necessary in the staging or restaging of Ewing sarcoma and osteosarcoma." ▪ Added Brain Cancer indication to read "C. Brain Cancer 1. PET scanning may be considered medically necessary in the staging or restaging of brain cancer." ▪ In Item G added "Endometrial Cancer PET scanning is considered medically necessary in the: 1. Detection of lymph node metastases, and 2. Assessment of endometrial cancer recurrence." ▪ In Item J 1 a added "Initial" to read "Initial diagnosis of suspected cancer" ▪ In Item J added 1 c "Evaluation of response to treatment" ▪ In Item K added "2. PET scanning may be considered medically necessary in staging of small-cell lung cancer if limited stage is suspected based on standard imaging." ▪ In Item K 3 added "if extensive stage is established and in all other aspects of managing small cell lung cancer" to read "PET scanning is considered experimental / investigational in staging of small-cell lung cancer if extensive stage is established and in all other aspects of managing small-cell lung cancer." ▪ In Item M 1 added "for advanced disease (stage III or IV)" to read "PET scanning may be considered medically necessary as a technique for assessing extranodal spread of malignant melanoma at initial staging or at restaging during follow-up treatment for advanced disease (stage III or IV)." ▪ In Item M added "2. PET scanning is considered experimental / investigational in managing stage 0, I, or II melanoma" ▪ In Item N (Multiple Myeloma) removed "PET scanning is considered experimental / investigational in all aspects of managing multiple myeloma" and added "1. PET scanning is considered medically necessary in the staging or restaging of multiple myeloma, particularly if the skeletal survey is negative." This item was previously listed in an E/I section, so is not new to the policy, but the policy position is changed. ▪ In Item O (Neuroendocrine Tumors) added "1. PET scanning is considered experimental / investigational in all aspects of managing neuroendocrine tumors." This item was

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	previously listed in an E/I section, so is not new to the policy but the policy position is changed. ▪ In Item O 2 (Neuroendocrine Tumors) added "with all other radiotracers" to read "PET scanning with all other radiotracers is considered experimental / investigational in all aspects of managing neuroendocrine tumors." ▪ In Item R added "Penile Cancer PET scanning is considered experimental / investigational in all aspects of managing penile cancer." This item was previously listed in an E/I section, so is not new to the policy. ▪ Added Item S "Prostate Cancer "1. PET scanning with 11 choline and fluorine 18 fluciclovine may be medically necessary for evaluating suspected or biochemically recurrent prostate cancer after primary treatment to detect small volume disease in soft tissues. 2. PET scanning with gallium 68 is considered experimental / investigational in all aspects of managing prostate cancer. 3. PET scanning for all other indications in known or suspected prostate cancer is considered experimental / investigational. This item was previously listed in an E/I section, so is not new to the policy but the policy position is changed. Added Item T "Renal Cell Carcinoma PET scanning is considered experimental / investigational in all aspects of managing renal cancer." ▪ In Item U (Soft Tissue Sarcoma) removed "Evaluating response to imatinib and other treatments for gastrointestinal stromal tumors" and added "1. PET scanning is considered medically necessary for evaluating response to imatinib and other treatments for gastrointestinal stromal tumors" ▪ In Item X added "Cancer of" to "Unknown Primary" to read "Cancer of Unknown Primary" ▪ Removed "Other Oncologic Applications 1. Other oncologic applications of PET scanning, including but not limited to the following, are considered experimental / investigational: a. Diagnosis and management of known or suspected prostate cancer b. Diagnosis of brain tumors c. Staging of multiple myeloma d. Evaluation of neuroendocrine tumors e. Staging inguinal lymph nodes in patients with squamous cell carcinoma of the penis. Policy Guidelines updated
	Rationale section updated
	In Coding section: ▪ Added CPT Code: A4641 ▪ Added ICD Codes: C00.0, C00.1, C00.3, C00.4, C00.6, C00.8, C00.9, C01, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C03.0, C03.1, C43.111, C43.112, C43.121, C43.122, C48.0, C4A.111, C4A.112, C4A.121, C4A.122, C54.1, C60.1, C60.2, C60.8, C61, C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.7, C67.8, C67.9, C70.0, C70.1,C78.2, C78.6, C82.21, C82.82, C82.83, C82.84, C82.86, C82.87, C82.88, C84.92, C84.94, C84.A2, C84.A4, C88.0, D03.111, D03.112, D03.121, D03.122, R91.1, ▪ Removed ICD Codes: C34.91, C34.92, C62.91, C62.92, C80.1, C81.91, C81.92, C81.93, C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, C82.90, C82.91, C82.92, C82.93, C82.94, C82.95, C82.96, C82.97, C82.98, C82.99, C84.90, C91.40, C91.41, C91.42, D3A.8, J98.4, K63.5, R22.0, R22.1, R59.0, R59.1, R59.9, Z85.01, Z85.038, Z85.048, Z85.118, Z85.12, Z85.20, Z85.21, Z85.22, Z85.238, Z85.29, Z85.43, Z85.71, Z85.72, Z85.79, Z85.810, Z85.818, Z85.819, Z85.820, Z85.850 ▪ Updated Coding notations

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	References updated

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