



# Louisiana

## Positron Emission Tomography (PET) Oncology Applications

**Policy #** 00105

**Original Effective Date:** 01/28/2002

**Current Effective Date:** 01/02/2018

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

*Note: Cardiac applications of positron emission tomography (PET) scanning are considered in medical policy 00103.*

*Note: Miscellaneous applications of positron emission tomography (PET) scanning are considered in medical policy 00104.*

*Note: This policy only addresses the use of radiotracers detected with the use of dedicated PET scanners. Radiotracers such as fluorodeoxyglucose (FDG) may be detected using single photon emission computed tomography (SPECT) cameras, a hybrid PET/SPECT procedure that may be referred to as FDG-SPECT or molecular coincidence.*

*For this policy, PET scanning is discussed for the following four applications in oncology:*

*Diagnosis. Diagnosis refers to use of positron emission tomography (PET) as part of the testing used in establishing whether or not a patient has cancer.*

*Staging. This refers to use of positron emission tomography (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 or not the cancer is localized. This may also be referred to as initial staging.*

*Restaging. This refers to imaging following treatment in two situations. Restaging is part of the evaluation of a patient in whom a disease recurrence is suspected based on signs and/or symptoms. Restaging also includes determining the extent of malignancy following completion of a full course of treatment.*

*Surveillance. This 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 or more for lymphoma) following completion of treatment.*

### **Coverage Eligibility**

*The following apply to the listed oncologic applications of positron emission tomography (PET) scanning:*

#### ***Eligible for Coverage***

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- Benefits are available in the member's contract/certificate, and*

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- *Medical necessity criteria and guidelines are met.*

### ***Investigational***

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

All policy statements apply to both positron emission tomography (PET) scans and positron emission tomography (PET) plus computed tomography (CT) scans, i.e., positron emission tomography (PET) scans with or without positron emission tomography/computed tomography (PET/CT) fusion.

For the clinical situations indicated that may be considered medically necessary, this assumes that the results of the positron emission tomography (PET) scan will influence treatment decisions. If the results will not influence treatment decisions, these situations would be considered investigational.

Based on review of available data, the Company considers the use of positron emission tomography (PET) scans for oncology applications to be either **eligible for coverage** or **investigational\*** as indicated below:

### **Bone Cancer**

#### ***Eligible for Coverage***

*Staging* When used in the staging of Ewing sarcoma and osteosarcoma may be **eligible for coverage**.

*Restaging* When used in the restaging of Ewing sarcoma and osteosarcoma may be **eligible for coverage**.

#### ***Investigational***

*Staging* When used in the staging of chondrosarcoma is considered **investigational\***

### **Brain Cancer**

#### ***Eligible for Coverage***

*Diagnosis* When utilized to differentiate scar tissue or tumor necrosis from active disease following radiation or chemotherapy the use of positron emission tomography (PET) scanning may be **eligible for coverage**.

*Staging* When used for staging of brain cancer positron emission tomography (PET) scanning may be **eligible for coverage**.

*Restaging* When used for restaging of brain cancer positron emission tomography (PET) scanning may be **eligible for coverage**.

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### ***Investigational***

*Diagnosis* When used for diagnosis (other than described above) positron emission tomography (PET) scanning is considered **investigational**.\*

### **Breast Cancer**

#### ***Eligible for coverage***

*Staging* When used in the staging of breast cancer may be **eligible for coverage** for the following application:

- Detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes).

*Restaging* When used in restaging breast cancer may be **eligible for coverage** for the following application:

- Detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes).

### ***Investigational***

All other applications of positron emission tomography (PET) scans in the evaluation of breast cancer are considered **investigational**\* including, but not limited to, the following:

- Differential diagnosis in patients with suspicious lesions or an indeterminate/low suspicion finding on mammography;
- Staging axillary lymph nodes.
- Predicting pathologic response to neoadjuvant therapy for locally advanced disease.

### **Cervical Cancer**

#### ***Eligible for Coverage***

*Staging* When used in the staging of cervical cancer positron emission tomography (PET) scans may be **eligible for coverage**.

*Restaging* When used in the restaging of cervical cancer positron emission tomography (PET) scans may be **eligible for coverage**.

Positron emission tomography (PET) scanning in the evaluation of known or suspected recurrence of cervical cancer may be **eligible for coverage**.

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### **Colorectal Cancer**

#### ***Eligible for Coverage***

- Diagnosis** When PET results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o Avoiding an invasive diagnostic procedure, or
  - o Determining the optimal anatomical location to perform an invasive diagnostic procedure.
- Staging** When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o To detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer (CRC); or
  - o Cancer stage remains in doubt after completion of a standard diagnostic workup; or
  - o positron emission tomography (PET) could potentially replace one or more conventional imaging studies, when it is expected that conventional study information is insufficient for the clinical management of the patient, or
  - o Clinical management would differ depending on the cancer stage.
- Restaging** When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o To detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer (CRC); or
  - o Detecting residual disease (after completion of treatment), or
  - o Detecting suspected recurrence (example: rising carcinoembryonic antigen [CEA] levels; clinical signs/symptoms suspicious for recurrence); or
  - o Determination of the extent of known recurrence.

### ***Investigational***

#### ***Differentiation***

Positron emission tomography (PET) scanning is considered **investigational\*** as:

- A technique to assess the presence of scarring versus local bowel recurrence in patients with previously resected colorectal cancer (CRC).
- A technique contributing to radiotherapy treatment planning.

### **Endometrial Cancer**

#### ***Eligible for Coverage***

- Staging** Positron emission tomography (PET) scanning may be **eligible for coverage** in the:
- o Detection of lymph node metastases.

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- Restaging* When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o Assessment of endometrial cancer recurrence.

### **Esophageal Cancer**

#### ***Eligible for Coverage***

- Diagnosis* When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o To avoid an invasive diagnostic procedure; or
  - o To determine the optimal anatomical location to perform an invasive diagnostic procedure.

- Staging* When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o Staging of esophageal cancer; or
  - o Staging of esophageal cancer when the stage of the cancer remains in doubt after completion of a standard diagnostic workup.

- Restaging* When PET results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o Restaging after the completion of treatment; or
  - o Detection of residual disease, suspected recurrence, or to determine the extent of a known recurrence; or
  - o Determining response to preoperative induction therapy.

### ***Investigational***

- Diagnosis* When used in the evaluation and detection of primary esophageal cancer positron emission tomography (PET) scanning is considered **investigational**.\*

### **Gastric Cancer**

#### ***Eligible for Coverage***

- Diagnosis* When positron emission tomography (PET) results may assist in the following situation positron emission tomography (PET) scanning may be **eligible for coverage**:

- o Initial diagnosis of gastric cancer, and

- Staging* When positron emission tomography (PET) results may assist in the following situation positron emission tomography (PET) scanning may be **eligible for coverage**:

- o Initial staging of gastric cancer, and

- Restaging* Evaluation for recurrent gastric cancer after surgical resection, when other imaging modalities are inconclusive.

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### **Head and Neck Cancers (excluding CNS and Thyroid)**

#### ***Eligible for Coverage***

- Diagnosis** When positron emission tomography (PET) results may assist in the following situation positron emission tomography (PET) scanning may be **eligible for coverage**:
- o In the evaluation of head and neck cancer in the initial diagnosis of suspected cancer.
- Staging** When positron emission tomography (PET) results may assist in the following situation positron emission tomography (PET) scanning may be **eligible for coverage**:
- o In the evaluation of head and neck cancer in the initial staging of disease.
- Restaging** When positron emission tomography (PET) results may assist in the following situation positron emission tomography (PET) scanning may be **eligible for coverage**:
- o In the evaluation of head and neck cancer in the restaging of residual or recurrent disease during follow-up; and
  - o In the evaluation of response to treatment.

#### ***Investigational***

When used for applications not discussed above, positron emission tomography (PET) scanning for the evaluation of head and neck cancer is considered **investigational\***.

### **Lung Cancer/Solitary Pulmonary Nodule**

#### ***Eligible for Coverage***

- Diagnosis** When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o Solitary Pulmonary Nodule - In patients with a solitary pulmonary nodule to distinguish between benign and malignant disease when prior CT and chest x-ray findings are inconclusive or discordant; or
  - o Lung Cancer - To determine resectability for patients with a presumed solitary metastatic lesion from lung cancer; or
  - o Lung Cancer -To distinguish between benign and malignant disease when prior computed tomography (CT) scan and chest x-ray findings are inconclusive or discordant.
- Staging** When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:
- o In clinical situations in which the stage of cancer remains in doubt after completion of a standard diagnostic workup; or
  - o As staging technique in those with known non-small cell lung cancer (NSCLC).
- Restaging** When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:

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- o As a restaging technique in those with known non-small cell lung cancer (NSCLC); or
- o For restaging after the completion of treatment; or
- o For the purpose of detecting residual disease, detecting suspected recurrence, or to determine the extent of a known recurrence.

### ***Investigational***

***Staging*** When used as a technique in the staging of small cell lung cancer positron emission tomography (PET) scanning is **investigational**.\*

### **Lymphoma, including Hodgkin's Disease**

#### ***Eligible for Coverage***

***Diagnosis*** Only in clinical situations in which the positron emission tomography (PET) results may assist in avoiding an invasive diagnostic procedure, or in which the positron emission tomography (PET) results may assist in determining the optimal anatomical location to perform an invasive diagnostic procedure. In general, for most solid tumors, a tissue diagnosis is made prior to the performance of positron emission tomography (PET) scanning. Positron emission tomography (PET) scans following a tissue diagnosis are performed for the purpose of staging, not diagnosis. Therefore, the use of positron emission tomography (PET) in the diagnosis of lymphoma should be rare.

***Staging*** When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:

- o For staging lymphoma during initial staging; or
- o In clinical situations in which the stage of the cancer remains in doubt after completion of a standard diagnostic workup.

***Restaging*** When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:

- o For restaging at follow-up; or
- o For the purpose of detecting residual disease, detecting suspected recurrence, or to determine the extent of a known recurrence; or
- o For restaging after the completion of treatment.

### ***Investigational***

When used for applications not discussed above, positron emission tomography (PET) scanning for the evaluation of lymphoma is considered **investigational**\*.

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### **Melanoma**

#### ***Eligible for Coverage***

*Diagnosis* When positron emission tomography (PET) results may assist in the following situations PET scanning may be **eligible for coverage**:

- o Only in clinical situations in which the positron emission tomography (PET) results may assist in avoiding an invasive diagnostic procedure, or in which the positron emission tomography (PET) results may assist in determining the optimal anatomical location to perform an invasive diagnostic procedure. In general, for most solid tumors, a tissue diagnosis is made prior to the performance of positron emission tomography (PET) scanning. Positron emission tomography (PET) scans following a tissue diagnosis are performed for the purpose of staging, not diagnosis. Therefore, the use of positron emission tomography (PET) in the diagnosis of melanoma should be rare; or
- o As a technique for assessing extranodal spread of malignant melanoma at initial staging.

*Restaging* When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:

- o For assessing extranodal spread of malignant melanoma at initial staging or at restaging during follow-up treatment; or
- o For the purpose of detecting residual disease, detecting suspected recurrence, or to determine the extent of a known recurrence.

### ***Investigational***

When used for applications not discussed above positron emission tomography (PET) scanning for the evaluation of melanoma is considered **investigational**.\*

Positron emission tomography (PET) scanning is considered **investigational**\* as a technique to detect regional lymph node metastases in patients with clinically localized melanoma who are candidates to undergo sentinel node biopsy.

When used as a technique for restaging in managing stage 0, I, or II melanoma, positron emission tomography (PET) scanning is considered **investigational**\*.

### **Multiple Myeloma**

#### ***Eligible for Coverage***

##### *Staging*

- o To assess extent of disease at time of diagnosis

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### *Restaging*

- o Restaging after completion of treatment
- o Detection of residual disease, suspected recurrence, or to determine the extent of a known recurrence.

### **Ovarian Cancer**

#### ***Eligible for Coverage***

*Diagnosis* When PET results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:

- o Avoiding an invasive diagnostic procedure, or
- o Determining the optimal anatomical location to perform an invasive diagnostic procedure.

*Staging* When positron emission tomography (PET) results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:

- o For staging ovarian cancer during initial staging; or
- o In clinical situations in which the stage of the cancer remains in doubt after completion of a standard diagnostic workup.

*Restaging* When PET results may assist in the following situations positron emission tomography (PET) scanning may be **eligible for coverage**:

- o For restaging at follow-up; or
- o For the purpose of detecting residual disease; or
- o For detecting suspected recurrence; or
- o To determine the extent of a known recurrence; or
- o For restaging after the completion of treatment.

### **Pancreatic Cancer**

#### ***Eligible for Coverage***

*Diagnosis* When used as a technique in the initial diagnosis of pancreatic cancer when other imaging and biopsy are inconclusive positron emission tomography (PET) scanning may be **eligible for coverage**.

*Staging* When used as a technique for staging of pancreatic cancer when other imaging and biopsy are inconclusive positron emission tomography (PET) scanning may be **eligible for coverage**.

#### ***Investigational***

When used as a technique to evaluate other aspects of pancreatic cancer positron emission tomography (PET) scanning is considered **investigational**.\*

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### **Prostate Cancer**

#### ***Eligible for Coverage***

*Restaging* When used with  $^{11}\text{C}$ -choline for evaluating response to primary treatment in prostate cancer positron emission tomography (PET) scanning may be **eligible for coverage**.

#### ***Investigational***

When used with  $^{68}\text{Ga}$  Gallium in all aspects of managing prostate cancer positron emission tomography (PET) scanning is considered **investigational\***.

When used for all other indications in known or suspected prostate cancer positron emission tomography (PET) scanning is considered **investigational\***.

### **Soft Tissue Sarcoma**

#### ***Investigational***

Positron emission tomography (PET) scanning is considered **investigational\*** in evaluation of soft tissue sarcoma, including but not limited to the following applications:

- Distinguishing between benign lesions and malignant soft tissue sarcoma; or
- Distinguishing between low grade and high grade soft tissue sarcoma; or
- Detecting locoregional recurrence; or
- Detecting distant metastasis.
- Evaluating response to imatinib and other treatments for gastrointestinal stromal tumors.

### **Testicular Cancer**

#### ***Eligible for Coverage***

*Restaging* When used as a technique in evaluation of residual mass following chemotherapy of stage IIB and III seminomas positron emission tomography (PET) scanning may be **eligible for coverage**.

*Note: The positron emission tomography (PET) scan should be completed not sooner than 6 weeks following chemotherapy.*

#### ***Investigational***

Except as noted above for seminoma, positron emission tomography (PET) scanning is **investigational\*** in evaluation of testicular cancer, including but not limited to the following applications:

- Initial staging of testicular cancer; or
- Distinguishing between viable tumor and necrosis/fibrosis after treatment of testicular cancer; or
- Detection of recurrent disease after treatment of testicular cancer.

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### **Thyroid Cancer, Differentiated**

#### ***Eligible for Coverage***

*Diagnosis* When used as a technique in the diagnosis of patients with differentiated thyroid cancer when thyroglobulin (Tg) levels are elevated and whole-body I-131 imaging is negative positron emission tomography (PET) scanning may be **eligible for coverage**

*Restaging* When used as a technique for restaging patients with differentiated thyroid cancer when thyroglobulin (Tg) levels are elevated and whole-body I-131 imaging is negative positron emission tomography (PET) scanning may be **eligible for coverage**

#### ***Investigational***

When used as a technique in the evaluation of known or suspected differentiated thyroid cancer in all other situations positron emission tomography (PET) scanning is considered **investigational**.\*

### **Unknown Primary**

#### ***Eligible for Coverage***

*Diagnosis* When used in patients with an unknown primary who meet all of the following criteria positron emission tomography (PET) scanning may be **eligible for coverage**:

- o Single site of disease outside the cervical lymph nodes; and
- o Patient is considering local or regional treatment for a single site of metastatic disease; and
- o Negative workup for an occult primary tumor; and
- o Positron emission tomography (PET) scan will be used to rule out or detect additional sites of disease that would eliminate the rationale for local or regional treatment.

#### ***Investigational***

*Diagnosis* Positron emission tomography (PET) scanning is considered **investigational**\* in evaluation of unknown primary, including but not limited to the following applications:

- o As part of the initial workup of an unknown primary; or
- o As part of the workup of patients with multiple sites of disease.

### **Cancer Surveillance**

Positron emission tomography (PET) scanning is considered **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.

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### **Other Oncologic Applications**

Positron emission tomography (PET) scanning for other oncologic applications is considered **investigational\*** for the following:

- In all aspects of managing neuroendocrine tumors; and
- In all aspects of managing penile cancer; and
- In all aspects of managing renal cancer.

### **POLICY GUIDELINES**

#### **PATIENT SELECTION**

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 positron emission tomography (PET) scanning. Due to its expense, positron emission tomography (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, positron emission tomography (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, positron emission tomography (PET) should be considered for the medically necessary indications above only when standard imaging (e.g., computed tomography [CT], magnetic resonance imaging [MRI]) is inconclusive or not indicated.

Patient selection criteria for positron emission tomography (PET) scanning also may be complex. For example, it may be difficult to determine from claims data whether a positron emission tomography (PET) scan in a patient with malignant melanoma is being done primarily to evaluate extranodal disease or regional lymph nodes. Similarly, it may be difficult to determine whether a positron emission tomography (PET) scan in a patient with colorectal cancer (CRC) is being performed to detect hepatic disease or evaluate local recurrence. Due to the complicated hierarchy of imaging options in patients with malignancy and complex patient selection criteria, a possible implementation strategy for this policy is its use for retrospective review, possibly focusing on cases with multiple imaging tests, including positron emission tomography (PET) scans.

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

### **Background/Overview**

A variety of tracers are used for PET scanning, including oxygen-15, nitrogen-13, carbon-11 choline, and fluorine-18. In 2016, 2 additional tracers, gallium-68, and fluciclovine-18, were approved by the Food and Drug

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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-<sup>18</sup> 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.

For this evidence review, PET scanning is discussed for the following 4 applications in oncology: diagnosis, staging, restaging, and surveillance. Diagnosis refers to use of PET as part of the testing used in establishing whether a patient has cancer. 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 also may be referred to as initial staging. Restaging refers to imaging after treatment in 2 situations. Restaging is part of the evaluation of a patient in whom disease recurrence is suspected based on signs and/or symptoms. Restaging also includes determining the extent of malignancy after completion of a full course of treatment. Surveillance refers to use of imaging in asymptomatic patients (patients without objective signs or symptoms of recurrent disease). This imaging is completed 6 months or more ( $\geq 12$  months for lymphoma) after completion of treatment.

This evidence review focuses on the use of radiotracers detected with dedicated PET scanners. Radiotracers such as FDG may be detected using single-photon emission computerized tomography (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 herein.

### **FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration

The FDA website includes various PET-related documents.

As of June 2016, the following radiopharmaceuticals have been granted FDA-approval, to be used with PET for carcinoma-related indications (see Table 1).

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**Table 1. Radiopharmaceuticals Approved for Use With PET**

Radiopharmaceutical	Manufacturer	Name	Carcinoma-Related Indication With PET
Carbon-11 choline	Various		Suspected prostate cancer recurrence based on elevated blood PSA after therapy and noninformative bone scintigraphy, CT, or MRI
Fluorine-18 fluorodeoxyglucose	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.

Centers for Medicare and Medicaid Services (CMS)

The Medicare coverage policy on PET scans was updated in 2009.

### **Rationale/Source**

This evidence review was based on multiple evaluations of PET, including TEC Assessments, other systematic reviews, meta-analyses, decision analyses, and cost-effectiveness analyses.

Assessment of a diagnostic technology typically focuses on 3 categories of evidence: (1) its technical performance (test-retest reliability or interrater reliability); (2) diagnostic accuracy (sensitivity, specificity, and positive and negative predictive value) in relevant populations of patients; and (3) demonstration that the diagnostic information has clinical utility (i.e., it can be used to improve patient outcomes).

The majority of evidence on the use of PET scanning in oncology focuses on diagnostic accuracy (sensitivity, specificity). There are few rigorous studies assessing the impact of PET on clinical outcomes. A few of the studies that have reported on changes in staging and/or treatment that result from the PET scan do not evaluate whether these changes result in an improvement in the net health outcome. Clinical guidelines help to outline the indications for which clinical utility is supported.

A 1997 TEC Assessment considered the use of PET scanning in the evaluation of solitary pulmonary nodules and staging of known lung cancer. A 2006 evidence report for the Agency for Healthcare Research and Quality (AHRQ) addressed use of PET for staging small-cell lung cancer (SCLC). Three 1999 TEC Assessments and one 2000 TEC Assessment considered the use of PET scanning in the evaluation of melanoma, lymphoma, colorectal, and head and neck cancer, respectively. TEC Assessments from 2000 and 2002 addressed unknown primaries. A 2001 TEC Assessment, a 2002 decision analysis, and a 2005 systematic review focused on esophageal cancer. Pancreatic cancer was evaluated in a 1999 TEC Assessment and a 2004 AHRQ systematic review. The 2004 AHRQ systematic review also assessed on

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ovarian cancer and testicular cancer. Soft tissue sarcoma was the subject of a 2002 AHRQ systematic review. Breast cancer was evaluated in 2 TEC Assessments (2001, 2003), a 2005 systematic review, a 2007 systematic review, and a 2005 cost-effectiveness analysis.

Several uses of PET were reviewed in National Comprehensive Cancer Network (NCCN) documents released in 2007 and 2009. Another AHRQ systematic review evaluating use of PET for 9 cancers was published in 2008. Systematic reviews and meta-analyses published in addressed 10 indications for 9 malignancies. In the Assessments, PET scanning was considered an adjunct to other imaging methods (i.e., CT, MRI, ultrasonography), often used when the results of previous imaging studies were inconclusive or discordant. In this setting, the clinical value of PET scans is the rate of discordance among imaging techniques and the percentage of time that PET scanning results in the correct diagnosis, as confirmed by tissue biopsy. These Assessments, systematic reviews, and randomized controlled trials (RCTs) offered the following observations and conclusions.

### **BONE CANCER AND <sup>18</sup>F-FDG-PET AND <sup>18</sup>F-FDG-PET/CT**

A systematic review and meta-analysis (35 studies, total N=2171 patients) by Liu et al (2015) evaluated fluorine <sup>18</sup>fludeoxyglucose PET (<sup>18</sup>F-FDG-PET) and <sup>18</sup>F-PET with/CT (<sup>18</sup>F-PET/CT) in the diagnosis, staging, and recurrence assessment of bone sarcoma. Most selected studies used PET/CT (n=29). Meta-analyses showed high sensitivity (96%; 95% confidence interval [CI], 93% to 98%) and specificity (79%; 95% CI, 63% to 90%) of <sup>18</sup>F-FDG-PET and -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 <sup>18</sup>F-FDG-PET and -PET/CT in Ewing sarcoma. The meta-analysis showed high estimates of sensitivity and specificity for <sup>18</sup>F-FDG-PET and -PET/CT (pooled sensitivity, 96%; pooled specificity, 92%).

In a prospective study by Völker et al (2007) of 46 pediatric patients with sarcoma (Ewing sarcoma, osteosarcoma, rhabdomyosarcoma), PET was compared with conventional imaging techniques (ultrasound, CT, MRI, bone scintigraphy). The study showed that PET was as effective as conventional imaging in detecting primary tumors, and PET was superior to conventional imaging in detecting lymph node and bone involvement. However, CT was more reliable in detecting lung metastases. The most thorough assessment of cancer involvement used both PET and conventional tests and resulted in important changes in therapy decisions.

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Current NCCN guidelines for bone cancer state that PET and CT may be considered for:

- 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 (category 2B).

### Section Summary: Bone Cancer

Evidence for the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and for the staging and restaging of bone cancer consists of systematic reviews and meta-analyses of many studies. Pooled analyses have shown that PET is effective in staging of bone cancer. 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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of bone cancer but does not support their use for surveillance.

### BRAIN TUMORS AND $^{18}\text{F}$ -FDG-PET, $^{18}\text{F}$ -FET-PET, AND $^{11}\text{C}$ METHIONINE PET

#### $^{18}\text{F}$ -FET PET

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  $^{18}\text{F}$ -fluoro-ethyl-tyrosine PET ( $^{18}\text{F}$ -FET-PET) and  $^{18}\text{F}$ -FDG-PET. 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 Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool.  $^{18}\text{F}$ -FET PET (pooled sensitivity, 94%; 95% CI, 79% to 98%; pooled specificity, 88%; 95% CI, 37% to 99%) performed better than  $^{18}\text{F}$ -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 including studies published through January 2011 addressed the use of FET in detecting primary brain tumors (Dunet et al, 2012). 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  $^{18}\text{F}$ -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 can be made about comparative effectiveness.

#### $^{11}\text{C}$ Methionine PET

A 2014 meta-analysis compared the diagnostic performance of  $^{18}\text{F}$ -FDG-PET with  $^{11}\text{C}$  methionine PET in the detection of suspected primary brain tumors and suspected recurrence of brain tumors following treatment. The literature search included studies published through February 2013; 24 studies provided

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data on the use of  $^{18}\text{F}$ -FDG-PET and 11 studies on the use of  $^{11}\text{C}$ -methionine PET. The pooled sensitivity and specificity of  $^{18}\text{F}$ -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  $^{11}\text{C}$ -methionine PET, with a pooled sensitivity and specificity of 91% (95% CI, 85% to 94%) and 86% (95% CI, 78% to 92%), respectively.

Another meta-analysis (Deng et al, 2013) assessed the ability of  $^{11}\text{C}$  methionine PET and MRI to detect glioma recurrence. The literature search included articles through March 2012. All selected studies were retrospective cohorts, 11 using  $^{11}\text{C}$ -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  $^{11}\text{C}$  methionine PET (pooled sensitivity, 87%; 95% CI, 81% to 92%; pooled specificity, 81%; 95% CI, 72% to 89%) in glioma recurrence detection, with  $^{11}\text{C}$  methionine slightly less specific.

Current NCCN guidelines for brain cancer state that PET can assess metabolism within 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 optimal area for biopsy. 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 depending on the radiotracer used. There was 1 direct comparison of radiotracers, with  $^{18}\text{F}$ -FET-PET showing better diagnostic accuracy than  $^{18}\text{F}$ -FDG-PET. An indirect comparison between  $^{18}\text{F}$ -FDG-PET and  $^{11}\text{C}$  methionine PET showed that  $^{11}\text{C}$  methionine PET performed better, and another indirect comparison of  $^{11}\text{C}$  methionine PET and MRI showed a comparable diagnostic capability between the 2 methods. The evidence supports the use of  $^{18}\text{F}$ -FDG-PET,  $^{18}\text{F}$ -FET-PET, and  $^{11}\text{C}$  methionine PET for the diagnosis and staging and restaging of brain tumors cancer but does not support their use for surveillance.

### BREAST CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT

The 2001 TEC Assessment 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. The 2003 TEC Assessment reexamined all indications except for characterizing breast lesions.

The bulk of the data on  $^{18}\text{F}$ -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

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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.

A 2005 meta-analysis focused on PET for detecting recurrence and metastases. 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 use of PET resulted in different management decisions and health outcomes.

A systematic review published in 2007 on PET for staging axillary lymph nodes identified 20 studies. Three of these 20 studies were rated highest 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.

### **Breast Cancer Diagnosis**

In a meta-analysis of 8 studies (total N=873 patients) of <sup>18</sup>F-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. As previously noted, a false-negative rate of 15% (1 – sensitivity) may be considered unacceptable given the relative ease of breast biopsy.

### **Breast Cancer Staging**

A 2013 meta-analysis by Hong et al reported a sensitivity and a specificity of <sup>18</sup>F-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). 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 <sup>18</sup>F-FDG-PET/CT were greater than bone scintigraphy for detecting bone metastasis in breast cancer patients. The sensitivity and specificity of <sup>18</sup>F-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.

### **Breast Cancer Restaging**

A 2016 systematic review by Xiao et al evaluated the diagnostic efficacy of <sup>18</sup>F-FDG-PET and <sup>18</sup>F-FDG-PET/CT in detecting breast cancer recurrence. The literature search, conducted through January 2016,

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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 for PET and PET/CT were 90% (95% CI, 88% to 90%) and 81% (95% CI, 78% to 84%), respectively. Subgroup analyses showed that PET/CT was more specific than PET alone in diagnosing recurrent breast cancer (p=0.035).

A 2016 systematic review by Liu et al compared <sup>18</sup>F-FDG-PET or PET/CT with MRI in assessing pathologic complete response to neoadjuvant chemotherapy (NAC) in patients with breast cancer. 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 showed that <sup>18</sup>F-FDG-PET or -PET/CT was more sensitive than MRI and MRI was more specific than <sup>18</sup>F-FDG- PET or -PET/CT in assessing complete response to NAC. The pooled sensitivities and specificities for <sup>18</sup>F-FDG-PET or -PET/CT were 86% (95% CI, 76% to 93%) and 72% (95% CI, 49% to 87%) and 65% (95% CI, 45% to 80%) and 88% (95% CI, 75% to 95%), for MRI, all respectively.

In another 2016 meta-analysis comparing <sup>18</sup>F-FDG-PET with MRI and evaluating pathologic complete response to NAC in patients with breast cancer, Sheikhabaei et al (2016) selected 10 studies for analysis. The inclusion criteria differed slightly from Liu (2016). Liu et al required that both <sup>18</sup>F-FDG-PET and MRI be performed before and during (or after) NAC, while Sheikhabaei did not require the scanning before NAC. Pooled sensitivities and specificities are listed in Table 2. Subgroup analysis was performed, by time of scanning (during NAC and after NAC was completed).

**Table 2. Pooled Diagnostic Performance of <sup>18</sup>F-FDG-PET and Magnetic Resonance Imaging in Detection of Residual Disease After NAC for Breast Cancer<sup>50</sup>**

Type of Imaging	No. of Studies (No. of Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %
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### All studies

Magnetic resonance imaging	10 (492)	88 (76 to 95)	55 (41 to 68)
<sup>18</sup> F-FDG-PET or -PET/CT	10 (535)	71 (52 to 85)	77 (58 to 89)
<sup>18</sup> F-FDG-PET/CT	7 (385)	82 (62 to 92)	79 (52 to 93)
<sup>18</sup> F-FDG-PET alone	3 (150)	43 (26 to 63)	73 (44 to 91)

### During NAC

Magnetic resonance imaging	3 (256)	89 (66 to 97)	42 (20 to 68)
<sup>18</sup> F-FDG-PET/CT	3 (256)	91 (86 to 95)	69 (25 to 93)

### After NAC completion

Magnetic resonance imaging	7 (236)	88 (71 to 96)	63 (51 to 74)
<sup>18</sup> F-FDG-PET or -PET/CT	7 (279)	57 (40 to 71)	80 (65 to 90)
<sup>18</sup> F-FDG-PET/CT	4 (129)	71 (42 to 89)	88 (73 to 95)

CI: confidence interval; CT: computed tomography; FDG: fluorodeoxyglucose; NAC: neoadjuvant chemotherapy; PET: positron emission tomography.

Two 2012 meta-analyses pooled studies on use of FDG-PET to predict pathologic response to neoadjuvant therapy before surgery for locally advanced breast cancer. These articles reported similar pooled point estimates for sensitivity and specificity. Both concluded that PET had reasonably high sensitivity and relatively low specificity. Neither analysis 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.

A 2007 NCCN review 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.

Current NCCN guidelines include an optional category 2B recommendation for FDG-PET/CT in the workup of stage IIIA breast cancer. NCCN recommends against FDG-PET/CT for lower stage breast cancer due to high false-negative rates in detecting low-grade lesions or lesions less than 1 cm; low sensitivity in detecting axillary node metastasis; 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%

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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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for staging and restaging only if standard staging methods are inconclusive, but does not support their use for diagnosis, staging/restaging when standard staging methods are conclusive, and or surveillance.

### **CERVICAL CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

An AHRQ review published in 2008 identified several studies using  $^{18}\text{F}$ -FDG-PET or -PET/CT to stage advanced cervical cancer and to detect and stage recurrent disease. 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 2004 study by Yen et al of 55 patients whose recurrences were initially considered curable with radical surgical treatment, 27 instead underwent palliative therapy based on PET results. An NCCN report on PET also identified several studies supporting the use of PET for initial staging and identifying and staging recurrent disease.

In a 2013 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. 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. In a systematic review of 20 studies, Chu et al (2014) reported 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. For local regional recurrence, pooled sensitivity and specificity were 82% (95% CI, 72% to 90%) and 98% (95% CI, 96% to 99%), respectively.

Current NCCN guidelines state that PET/CT may be considered part of the initial nonfertility sparing workup for patients with stage I cervical cancer. The guidelines also state that PET/CT may be considered as part of the initial workup for detection of stage II, III, or IV metastatic disease. A single PET/CT scan at 3 to 6 months after therapy for locally advanced cervical cancer is recommended to detect persistent or recurrent disease. PET/CT is not recommended for surveillance.

### **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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of cervical cancer but does not support their use for surveillance.

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### **COLORECTAL CANCER AND 18F-FDG-PET AND <sup>18</sup>F-FDG-PET/CT**

Two clinical applications of PET scanning were considered in the 1999 TEC Assessment: (1) To detect hepatic or extrahepatic metastases and to assess their resectability in patients with CRC, either as part of initial staging or after primary resection, and (2) to evaluate the presence of postoperative scar versus recurrent disease as a technique to determine the necessity of tissue biopsy.

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.

A 2012 systematic review of different imaging techniques for radiotherapy treatment planning of rectal cancer concluded that additional studies would be needed to validate use of PET in this setting. 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. 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 clarified.

### **CRC Diagnosis**

A 2015 systematic review by Jones et al evaluated the role of <sup>18</sup>F-FDG-PET and <sup>18</sup>F-FDG-PET/CT compared with conventional imaging in the detection of primary nodal disease. 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%).

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### CRC Staging

A 2015 meta-analysis by Ye et al assessed the use of <sup>18</sup>F-FDG-PET/CT in preoperative TNM staging of CRC. The literature search, conducted through July 2014, identified 28 studies for inclusion. Of the 28 studies, 12 assessed tumor detection rate; 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.

**Table 3. Pooled Diagnostic Performance of <sup>18</sup>F-FDG-PET, <sup>18</sup>F-FDG-PET/CT, and CT Alone in the Staging of Colorectal Cancer<sup>60</sup>**

Type of Imaging	No. of Studies	Diagnostic Threshold	Sensitivity (95% CI), %	Specificity (95% CI), %
<b>T staging</b>				
<sup>18</sup> F-FDG-PET or -PET/CT	4	Yes	73 (65 to 81)	99 (98 to 99)
<b>N staging</b>				
<sup>18</sup> F-FDG-PET or -PET/CT	20	Yes	62 (59 to 66)	70 (67 to 73)
<sup>18</sup> F-FDG-PET/CT alone	12	Yes	70 (66 to 74)	63 (59 to 67)
<sup>18</sup> F-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)
<b>M staging</b>				
<sup>18</sup> F-FDG-PET or -PET/CT	5	No	91 (80 to 96)	95 (91 to 98)
CT alone	5	No	91 (87 to 94)	16 (8 to 27)

CI: confidence interval; CT: computed tomography; M staging: distant metastases; N staging: regional lymph nodes; PET: positron emission tomography; T staging: primary tumor.

### CRC Restaging

A 2016 meta-analysis by Rymer et al evaluated use of <sup>18</sup>F-FDG-PET/CT in the assessment of the response of locally advanced rectal cancer to neoadjuvant chemoradiotherapy. The literature search, conducted through April 2014, identified 10 studies (total N=538 patients) for inclusion in the analysis. 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 2015 meta-analysis by Yu et al evaluated the diagnostic value of <sup>18</sup>F-FDG-PET/CT for detecting local recurrent CRC. 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.

In 2015, Maffione et al conducted a systematic review of <sup>18</sup>F-FDG-PET for predicting response to neoadjuvant therapy in patients with rectal cancer. The literature search was conducted through January

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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  $^{18}\text{F}$ -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 2013 systematic review, Lu et al evaluated 510 patients from 11 studies on  $^{18}\text{F}$ -FDG-PET for CRC tumor recurrence detection in patients with elevated carcinoembryonic antigen. 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.

Current NCCN guidelines for colon cancer “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.” 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 appropriateness of PET/CT when CEA level is rising; PET/CT might be considered when imaging study results (e.g., a good quality CT scan) are normal.

Current NCCN guidelines for rectal cancer state that PET/CT is “not routinely indicated” and “should only be used to evaluate an equivocal finding on a contrast-enhanced CT scan.” PET/CT is not recommended for surveillance. PET/CT can be considered if serial CEA elevation occurs or if there is documented metachronous metastases.

### **Section Summary: Colorectal Cancer**

Evidence for the detection of primary nodal disease, staging, restaging, and detecting recurrence of CRC consists of a TEC Assessment and several meta-analyses published after the assessment. A meta-analysis evaluating the diagnostic accuracy of PET or PET/CT found a high sensitivity but a low specificity. Several pooled analyses evaluating staging or restaging using PET or PET/CT resulted in sensitivities and specificities ranging low 60s to high 90s. 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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis, staging and restaging, or surveillance of CRC.

### **ENDOMETRIAL CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

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In 2016, Bollineni et al published a systematic review and meta-analysis on the diagnostic value of  $^{18}\text{F}$ -FDG-PET for endometrial cancer. 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  $^{18}\text{F}$ -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  $^{18}\text{F}$ -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.

Current NCCN guidelines for endometrial cancer state that whole body PET/CT can be considered if metastases are suspected in select patients (based on clinical symptoms, physical findings, or abnormal laboratory findings). Following treatment, PET/CT can be considered in select patients for surveillance.

### **Section Summary: Endometrial Cancer and $^{18}\text{F}$ -FDG-PET and $^{18}\text{F}$ -FDG-PET/CT**

The evidence supports the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis, staging and restaging, or surveillance of endometrial cancer.

### **ESOPHAGEAL CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

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

In 2016, Cong et al published a meta-analysis evaluating the predictive value of  $^{18}\text{F}$ -FDG-PET and -PET/CT for tumor response during or after neoadjuvant chemoradiotherapy in patients with esophageal cancer. 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 NRCT is 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.

In 2016, Goense et al published a systematic review evaluating  $^{18}\text{F}$ -FDG-PET and -PET/CT for the detection of recurrent esophageal cancer after treatment with curative intent. 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 a majority of the studies, and high risk of bias in a few studies for patient selection. Pooled estimates of sensitivity and specificity of  $^{18}\text{F}$ -FDG-PET and -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

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sensitivity due to heterogeneity. Specificity subgroup analysis showed no statistical difference between PET alone and PET/CT in detecting recurrent esophageal cancer.

A 2009 NCCN report found studies showing that PET is more sensitive than other diagnostic imaging in detecting stage IV disease with distant lymph node involvement. 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. In a 2013 meta-analysis of 245 patients with esophageal cancer from 6 studies, Shi et al 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.

Another use of PET in esophageal cancer is in determining whether to continue chemotherapy for potential curative resection. The 2009 NCCN report described several studies in which response to chemotherapy, defined as a decline in standardized uptake values, correlated with long-term survival. 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. Current NCCN guidelines for esophageal cancer recommend that PET/CT be considered to assess treatment response 5 to 6 weeks after preoperative therapy.

Current NCCN guidelines for esophageal cancer indicate that PET/CT be considered in the initial workup of esophageal cancer if there is no evidence of M1 disease and to assess response to preoperative or definitive chemoradiation. 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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of esophageal cancer, but does not support their use for surveillance.

### GASTRIC CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT

A 2016 systematic review by Li et al evaluated  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -FDG-PET/CT for detecting recurrent gastric cancer. The literature search, conducted through February 2015, identified 14 studies (total N=828 patients) to be included in the 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 2013 meta-analysis, Zou and Zhou evaluated studies published through May 2013 and calculated the sensitivity and specificity of  $^{18}\text{F}$ -FDG-PET/CT for detecting recurrence of gastric cancer after surgical

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resection. 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 (2012) pooled 9 studies (total N=562 patient) published through July 2011 that used <sup>18</sup>F-FDG-PET alone for evaluating recurrent gastric cancer. Each selected study fulfilled at least 9 of the 14 criteria in the QUADAS tool for methodologic quality. Pooled sensitivity and specificity were 78% (95% CI, 68% to 86%) and 82% (95% CI, 76% to 87%), respectively. Reviewers concluded that PET/CT might be more effective than either PET alone or CT alone, but it was unclear what sources reviewers used for their estimates for PET/CT and CT alone.

Current NCCN guidelines for gastric cancer 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. The guidelines note that the sensitivity of PET/CT is lower than that 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. 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.

### **Section Summary: Gastric Cancer**

Evidence for the use of PET to diagnose recurrent gastric cancer consists of meta-analyses. One meta-analysis evaluated <sup>18</sup>F-FDG-PET alone, one evaluated <sup>18</sup>F-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 <sup>18</sup>F-FDG-PET and <sup>18</sup>F-PET/CT for the diagnosis and staging and restaging of esophageal cancer, but does not support their use for surveillance.

### **HEAD AND NECK CANCER AND <sup>18</sup>F-FDG-PET AND <sup>18</sup>F-FDG-PET/CT**

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. When data from these 3 studies were pooled, PET was found to identify 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 head to head with other imaging modalities, pooled data from a variety of studies suggested that PET had 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.

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A 2016 meta-analysis by Chen et al compared MRI, CT, and <sup>18</sup>F-FDG-PET/CT in the detection of local and metastatic nasopharyngeal carcinomas. A literature search, conducted through April 2015, identified 23 studies (total N=2413 patients) for inclusion. Table 4 lists the results of the meta-analysis.

**Table 4. Pooled Diagnostic Performance of <sup>18</sup>F-FDG-PET/CT, Magnetic Resonance Imaging, and CT Alone in the Detection of Nasopharyngeal Carcinomas<sup>76</sup>**

Type of Imaging	No. of Studies (No. of Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %
<b>T staging</b>			
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)
<b>N staging</b>			
MRI	10 (750)	82 (79 to 84)	71 (65 to 78)
CT alone	4 (340)	92 (85 to 95)	93 (76 to 99)
<sup>18</sup> F-FDG-PET/CT	10 (629)	88 (85 to 90)	95 (93 to 97)
<b>M staging</b>			
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)
<sup>18</sup> F-FDG-PET/CT	7 (1009)	82 (74 to 88)	98 (96 to 99)

CI: confidence interval; CT: computed tomography; M staging: distant metastases; N staging: regional lymph nodes; PET: positron emission tomography; T staging: primary tumor.

A 2016 meta-analysis by Wei et al compared diagnostic capabilities of <sup>18</sup>F-FDG-PET/CT, MRI, and single-photon emission CT in patients with residual or recurrent nasopharyngeal carcinoma. 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 <sup>18</sup>F-FDG- PET/CT (n=12 studies) were 90% (95% CI, 85% to 94%) and 93% (95% CI, 90% to 95%), respectively. Pooled sensitivity and specificity for single-photon emission CT (n=8 studies) were 85% (95% CI, 77% to 92%) and 91% (95% CI, 85% to 95%), respectively. Pooled sensitivity and specificity for MRI (n=9 studies) were 77% (95% CI, 70% to 83%) and 76% (95% CI, 73% to 79%), respectively.

Two meta-analyses evaluated <sup>18</sup>F-FDG-PET or <sup>18</sup>F-FDG-PET/CT in the detection of residual or recurrent head and neck cancer at various times following treatment. Results from these analyses are summarized in Table 5.

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**Table 5. Pooled Diagnostic Performance of <sup>18</sup>F-FDG-PET or <sup>18</sup>F-FDG-PET/CT in the Detection of Head and Neck Cancer**

Indication	No. Studies (No. Patients)	Sensitivity (95%, CI), %	Specificity (95%, CI), %
<b>Cheung et al (2016)<sup>78</sup></b>			
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)
<b>Sheikhbahaei et al (2015)<sup>79</sup></b>			
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; NR: not reported; PET: positron emission tomography.

A 2015 systematic review by Sheikhbahaei et al calculated the predictive value of intrathoracic or posttherapy <sup>18</sup>F-FDG-PET or PET/CT for overall survival (OS) and event-free survival. 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 compared with 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). Two-year and 3- to 5-year relative risks for death or recurrence or progression were calculated, based on timing of <sup>18</sup>F-FDG-PET or -PET/CT. Results are summarized in Table 6.

**Table 6. Pooled Diagnostic Performance of <sup>18</sup>F-FDG-PET or <sup>18</sup>F-FDG-PET/CT in the Detection of Head and Neck Cancer**

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Outcome	No. Studies	2-Year RR (95% CI)	No. Studies	3- to 5-Year RR (95% CI)
<b>Death</b>				
Final <sup>18</sup> F-FDG-PET or -PET/CT	6	8.3 (3.8 to 18.0)	6	2.2 (1.6 to 3.2)
<sup>18</sup> F-FDG-PET or -PET/CT, <12 wk posttreatment	8	3.0 (1.9 to 4.6)	4	2.0 (1.3 to 3.2)
<sup>18</sup> F-FDG-PET or -PET/CT, ≥12 wk posttreatment	3	8.5 (4.0 to 18.3)	6	2.8 (1.9 to 4.0)
<b>Recurrence or progression</b>				
Final <sup>18</sup> F-FDG-PET or -PET/CT	6	5.2 (3.3 to 8.3)	5	2.6 (1.7 to 4.1)
<sup>18</sup> F-FDG-PET or -PET/CT, <12 wk posttreatment	9	3.2 (2.0 to 5.2)	6	4.3 (2.1 to 8.7)
<sup>18</sup> F-FDG-PET or -PET/CT, ≥12 wk posttreatment	2	3.2 (2.0 to 5.2)	2	2.2 (1.5 to 3.1)

CI: confidence interval; CT: computed tomography; PET: positron emission tomography; RR: relative risk.

Meta-analyses in 2013 and 2014 reported good sensitivities and specificities with <sup>18</sup>F-FDG-PET/CT for diagnosing head and neck squamous cell cancers (better than CT and MRI) and for detecting head and neck cancer metastases (better than bone scintigraphy) and recurrence.

Current NCCN guidelines for head and neck cancer 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.

### Section Summary: Head and Neck Cancer

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Evidence for the use of <sup>18</sup>F-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 <sup>18</sup>F-FDG-PET/CT may be useful in predicting response to therapy. The evidence supports the use of <sup>18</sup>F-FDG-PET and <sup>18</sup>F-PET/CT for the diagnosis and staging and restaging of esophageal cancer, but does not support their use for surveillance.

### LUNG CANCER AND <sup>18</sup>F-FDG-PET AND <sup>18</sup>F-FDG-PET/CT

PET scanning may have a clinical role in patients with solitary pulmonary nodules for whom a diagnosis is uncertain after CT scan or chest radiograph. Younger patients who have no smoking history have a relatively low risk for lung cancer and, in this setting, the NPV of a PET scan is relatively high. If presented with a negative PET scan and information about the very low probability of undetected malignancy, it is quite likely that some patients would choose to avoid the harms of an invasive sampling procedure (i.e., biopsy). A 2012 meta-analysis on 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.

#### Non-Small-Cell Lung Cancer

In patients with known 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. The 1997 TEC Assessment discussed a decision analysis that suggested 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.<sup>3</sup> This suggests that the reduction in surgeries was not harmful to patients.

A 2017 systematic review by Ruilong et al evaluated the diagnostic value of <sup>18</sup>F-FDG PET/CT for detecting solitary pulmonary nodules. The literature search, conducted to May 2015, identified 12 studies (1297 patients) for inclusion in the analysis. The pooled sensitivity and specificity of <sup>18</sup>F-FDG-PET/CT to detect malignant pulmonary nodules were 82% (95% CI, 76% to 87%) and 81% (95% CI, 66% to 90%), respectively.

Other meta-analyses have reported good sensitivities and specificities in detection of lung cancer metastases and recurrence with PET/CT. A meta-analysis by Li et al (2013) calculated the following sensitivity and specificity for <sup>18</sup>F-FDG-PET/CT in detecting distant metastases in patients with lung cancer: 93% (95% CI, 88% to 96%) and 96% (95% CI, 95% to 96%), respectively. He et al (2014) compared PET, PET/CT, and conventional imaging techniques in detecting recurrent lung cancer. Table 7 summarizes the diagnostic performances of the different imaging techniques:

**Table 7. Pooled Diagnostic Performance of PET, PET/CT, and CIT in the Detection of Lung Cancer**

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Type of Imaging	Sensitivity (95% CI), %	Specificity (95% CI), %	DOR (95% CI)
<sup>18</sup> F-FDG PET	94 (91 to 97)	84 (73 to 89)	65.2 (19.5 to 218.5)
<sup>18</sup> F-FDG PET/CT	90 (84 to 95)	90 (87 to 93)	79.1 (18.7 to 334.8)
CIT	78 (71 to 84)	80 (75 to 84)	12.7 (4.0 to 40.4)

CI: confidence interval; CIT: conventional imaging technique; CT: computed tomography; DOR: diagnostic odds ratio; PET: positron emission tomography.

Current NCCN guidelines for NSCLC indicate that PET/CT can be used in the staging of disease, detection of metastases, treatment planning, and detection of disease recurrence. The guideline notes 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, and PET/CT is not routinely recommended for surveillance after completion of definitive therapy.

### Small-Cell Lung Cancer

Six studies of patients with SCLC have reported evidence suggesting that, for non- brain metastases, PET plus conventional staging is more sensitive in detecting disease than conventional staging alone. PET may correctly upstage and downstage disease, and studies 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.

A systematic review by Ruben and Ball (2012) of staging SCLC found PET to be more effective than conventional staging methods; however, this review was flawed because reviewers did not conduct a quality assessment of individual studies, so its conclusions may not be sound.

A 2014 systematic review included 12 studies (total N=369 patients) of <sup>18</sup>F-FDG-PET/CT for staging SCLC. 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 and poor quality evidence in this systematic review to determine whether use of PET adds value relative to conventional staging tests for SCLC.

The American College of Chest Physicians issued guidelines for the diagnosis and management of lung cancer in 2013. 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.

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Current NCCN guidelines for SCLC indicate PET can be used in the staging of disease and treatment planning but “is not recommended for routine follow-up.”

### **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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of NSCLC, but does not support their use for surveillance.

Evidence for PET or PET/CT for patients with SCLC consists of systematic reviews and meta-analyses. While these reviews have shown potential benefits in using PET for staging, the quality of the studies was low. The evidence does not support the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis, staging and restaging, or surveillance of SCLC.

### **LYMPHOMA, INCLUDING HODGKIN DISEASE, AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

Of the 14 studies reviewed in the 1999 TEC Assessment, 3 compared PET with anatomic imaging in initial staging and restaging of patients with Hodgkin disease and non-Hodgkin lymphoma. Two of these studies included data from both diseased and nondiseased sites for PET and CT. Both studies found PET to have 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 disease.

### **Lymphoma Diagnosis**

Meta-analyses have reported good sensitivities and specificities with PET/CT in the detection of newly diagnosed Hodgkin lymphoma (2014) and diffuse large B-cell lymphoma (2013).

### **Lymphoma Restaging**

A 2016 systematic review and meta-analysis by Adams and Kwee evaluated the proportion of false-positive lesions at interim and end-of-treatment as detected by  $^{18}\text{F}$ -FDG-PET in patients with lymphoma. 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  $^{18}\text{F}$ -FDG-PET false positive proportions for: interim non-Hodgkin lymphoma (83%; 95% CI, 72% to 90%); end-of-treatment non-Hodgkin

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lymphoma (31%; 95% CI, 4% to 84%), and end-of-treatment Hodgkin lymphoma (23%; 95% CI, 5% to 65%). We found no studies calculating the false-positive rate for interim Hodgkin lymphoma.

A 2015 systematic review by Adams et al focused for the outcomes of patients with Hodgkin lymphoma who had negative residual mass after treatment with  $^{18}\text{F}$ -FDG-PET. 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

A 2017 systematic review by Adams and Kwee evaluated the prognostic value of  $^{18}\text{F}$ -FDG-PET in patients with refractory or relapsed Hodgkin lymphoma considering autologous cell transplantation. The literature search, conducted through May 2016, identified 11 studies (total N=664 patients) for inclusion.

In general, the overall quality of selected studies was poor, based on Quality in Prognosis Studies (QUIPS). Pooled sensitivity and specificity of pretransplant  $^{18}\text{F}$ -FDG-PET in predicting treatment failure were 54% (95% CI, 44% to 63%) and 73% (95% CI, 67% to 79%), respectively. Pooled sensitivity and specificity of pretransplant  $^{18}\text{F}$ -FDG-PET in predicting death after treatment were 55% (95% CI, 39% to 70%) and 69% (95% CI, 61% to 76%), respectively.

A 2016 meta-analysis by Adams and Kwee evaluated the prognostic value of  $^{18}\text{F}$ -FDG-PET in patients with aggressive non-Hodgkin lymphoma considering autologous cell transplantation. 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  $^{18}\text{F}$ -FDG-PET results had progression-free survival (PFS) rates ranging from 0% to 52%. Patients with negative pretransplant  $^{18}\text{F}$ -FDG-PET results had PFS rates ranging from 55% to 85%. OS was 17% to 77% in patients with positive  $^{18}\text{F}$ -FDG-PET results and 78% to 100% in patients with negative  $^{18}\text{F}$ -FDG-PET results. Based on 5 studies, pooled sensitivity and specificity of pretransplant  $^{18}\text{F}$ -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 2015 systematic review by Zhu et al evaluated the prognostic value of  $^{18}\text{F}$ -FDG-PET in patients with diffuse B-cell lymphoma treated with rituximab-based immune chemotherapy. The literature search identified 11 studies (N=1081) for inclusion. The pooled hazard ratio comparing PFS of patients with positive interim  $^{18}\text{F}$ -FDG-PET results and negative interim  $^{18}\text{F}$ -FDG-PET results was 3.0 (95% CI, 2.3 to 3.9). Patients with a negative interim  $^{18}\text{F}$ -FDG-PET result had a higher complete remission rate than patients with a positive interim  $^{18}\text{F}$ -FDG-PET result (relative risk, 5.5; 95% CI, 2.6 to 11.8).

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Current NCCN guidelines for Hodgkin lymphoma and non-Hodgkin lymphomas 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 then be used to determine the course of treatment.

### **Section Summary: Lymphoma, Including Hodgkin Disease**

Evidence for the use of  $^{18}\text{F}$ -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  $^{18}\text{F}$ -FDG-PET/CT can be useful in predicting response to therapy in patients with lymphoma. The evidence supports the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of Hodgkin lymphoma and non-Hodgkin lymphoma, but does not support their use for surveillance.

### **MELANOMA AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

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 either 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 1999 TEC Assessment concluded that PET is not as beneficial as sentinel node biopsy for assessing regional lymph nodes.

“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.”

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.

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Current NCCN guidelines for melanoma indicate that PET/CT can be used for staging and restaging more advanced disease (e.g., stage III) in the presence of specific signs and symptoms. 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). Because most recurrences occur within the first 3 years, routine screening for asymptomatic recurrence is not recommended beyond 3 to 5 years.

### **Section Summary: Melanoma**

Evidence for the use of  $^{18}\text{F}$ -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 does not support the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis or staging and restaging of stage I or II melanoma. The evidence supports the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of stage III or IV melanoma. The evidence supports the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for surveillance of melanoma.

### **MULTIPLE MYELOMA AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

Two systematic reviews, one of which also conducted a meta-analysis, addressed PET for staging of multiple myeloma. Neither compared the diagnostic performance of PET with another imaging modality, so they do not support conclusions about comparative effectiveness.

### **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 does not support the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis, staging and restaging, or surveillance of multiple myeloma.

**NEUROENDOCRINE TUMORS AND  $^{18}\text{F}$ -FDG-PET,  $^{18}\text{F}$ -FDG-PET/CT,  $^{68}\text{Ga}$ -PET, AND  $^{68}\text{Ga}$ -PET/CT** Two meta-analyses from the same investigators addressed use of PET in patients with neuroendocrine tumors. One report included patients with thoracic and gastroenteropancreatic neuroendocrine tumors who had imaging with PET using gallium  $^{68}$ -somatostatin receptor radiotracers. The other included studies of paragangliomas scanned by PET with fluorine- $^{18}$ -dihydroxyphenylalanine. Neither compared PET with another imaging modalities, precluding conclusions about comparative diagnostic performance.

### **Section Summary: Neuroendocrine Tumors**

Evidence for the use of PET or PET/CT in the management of patients with neuroendocrine tumors consists of meta-analyses. Two different radiopharmaceuticals were used:  $^{18}\text{F}$ -FDG-PET/CT and  $^{68}\text{Ga}$ -PET/CT. The evidence does not support the use of either radiopharmaceutical for the diagnosis, staging and restaging, or surveillance of neuroendocrine tumors.

### **OVARIAN CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

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

Positive predictive value (PPV) is of greatest importance in evaluating patients with known ovarian cancer, either to detect disease recurrence or progression or to monitor response to treatment. Although the 2004 AHRQ systematic review suggested that PET might have value for detecting recurrence when CA125 is elevated and conventional imaging does not clearly show recurrence, this had not been demonstrated in an adequately powered prospective study. A 2008 AHRQ systematic review found that evidence supported the use of PET/CT for detecting recurrent ovarian cancer. Evidence for initial diagnosis and staging of ovarian cancer was inconclusive.

A 2017 meta-analysis by Xu et al evaluated the diagnostic value of PET and PET/CT for recurrent or metastatic ovarian cancer. 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 2013 meta-analysis by Limei et al, included 28 studies (total N=1651 patients) published through December 2012; it evaluated the diagnostic value of PET/CT in suspected recurrent ovarian cancer. 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.

American College of Radiology Appropriateness Criteria, also issued in 2013, have indicated that PET/CT is appropriate for detecting and restaging ovarian cancer recurrence.

Current NCCN guidelines for ovarian cancer indicate that PET/CT can be appropriate “for indeterminate lesions if results will alter management.” PET/CT may be considered for monitoring patients 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.

### Section Summary: Ovarian Cancer

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Evidence for PET and PET/CT for the initial diagnosis of ovarian cancer consists of a 2014 AHRQ systematic review, which reported that the evidence is inconclusive. Evidence for the use of PET and PET/CT for the detection of ovarian cancer recurrence included 2 meta-analyses and a 2008 AHRQ systematic review. Pooled sensitivities and specificities support the use of PET and PET/CT for the detection of recurrent ovarian cancer. The evidence supports the use of <sup>18</sup>F-FDG-PET and <sup>18</sup>F-PET/CT for the diagnosis and staging and restaging of esophageal cancer, but does not support their use for surveillance.

### **PANCREATIC CANCER AND <sup>18</sup>F-FDG-PET AND <sup>18</sup>F-FDG-PET/CT**

Both the 2004 AHRQ systematic review and the 1999 TEC Assessment<sup>13</sup> 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 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 assumed to have benign disease and thus are not promptly treated for pancreatic cancer. Based on the TEC literature review, 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 2004 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.<sup>14</sup> 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.

In 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. A 2008 AHRQ review for pancreatic carcinoma has suggested that PET/CT can be useful for staging in certain patients when the standard staging protocol is inconclusive.

Current NCCN guidelines state that "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."

### **Section Summary: Pancreatic Cancer**

Evidence for PET and PET/CT for the initial diagnosis of pancreatic cancer consists of a TEC Assessment, which reported that the NPVs in several studies were inadequate to influence the decision for a biopsy. The use of PET or PET/CT for the staging or restaging of pancreatic cancer was evaluated in an AHRQ

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systematic review and a TEC Assessment. Both reported a lack of evidence to determine whether PET could provide useful information in staging or restaging pancreatic cancer. The evidence does not support the use of <sup>18</sup>F-FDG-PET and <sup>18</sup>F-PET/CT for the diagnosis, staging and restaging, or surveillance of pancreatic cancer.

### **PENILE CANCER AND <sup>18</sup>F-FDG-PET AND <sup>18</sup>F-FDG-PET/CT**

A systematic review with meta-analysis of PET has focused on staging inguinal lymph nodes among patients with penile squamous cell carcinoma. No comparisons were made with other imaging modalities. The 2012 report found that PET had low sensitivity, and reviewers concluded that PET is not suited for routine clinical use in this setting.

#### **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 supports the use of <sup>18</sup>F-FDG-PET and <sup>18</sup>F-PET/CT for the diagnosis, staging and restaging, or surveillance of penile cancer.

### **PROSTATE CANCER AND <sup>11</sup>C-CHOLINE PET AND <sup>11</sup>C-CHOLINE PET/CT**

#### **Prostate Cancer Diagnosis**

In 2016, Liu et al and Ouyang et al conducted meta-analyses comparing the diagnostic accuracy of 4 radiotracers (fluorine-<sup>18</sup> FDG, carbon-<sup>11</sup>choline [<sup>11</sup>C-choline], fluorine <sup>18</sup>fluorocholeline [<sup>18</sup>F-FCH], and carbon-<sup>11</sup>acetate) in detecting prostate cancer. The literature search by Liu et al, conducted through July 2015, identified 56 studies (total N=3586 patients) for inclusion. Using the QUADAS-2 system to evaluate study quality, the authors determined that the studies were reliable, with scores of 6 to 9 out of 10. Pooled estimates for the 4 types of PET are summarized below (see Table 8). The search by Ouyang et al 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**

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

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<sup>18</sup> F-FCH PET/CT	15	73 (54 to 87)	59 (41 to 75)	0.91
<sup>11</sup> C-acetate PET/CT	5	79 (68 to 86)	59 (41 to 75)	0.77
<sup>18</sup> F-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; PET: positron emission tomography; <sup>11</sup>C-acetate: carbon-<sup>11</sup> acetate; <sup>11</sup>C-choline: carbon-<sup>11</sup> choline; <sup>18</sup>F-FCH: fluorine <sup>18</sup> fluorocholine; <sup>18</sup>F-FDG: fluorine-<sup>18</sup> fluorodeoxyglucose.

<sup>a</sup> includes transrectal real-time elastosonography and shear-wave elastography.

### Prostate Cancer Staging

A 2013 systematic review by Umbehr et al investigated the use of <sup>11</sup>C-choline and <sup>18</sup>F-FCH-PET and -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%).

### Prostate Cancer Restaging

A 2016 meta-analysis by Fanti et al assessed <sup>11</sup>C-choline PET/CT accuracy in restaging of prostate cancer patients with biochemical recurrence after initial treatment with curative intent. The literature search, conducted through December 2014, identified 12 studies (total N=1270 patients) for inclusion in the analysis. Pooled sensitivity and specificity was 89% (95% CI, 83% to 93%) and 89% (95% CI, 73% to 96%).

In a 2014 meta-analysis by von Eyben and Kairemo, pooled sensitivity and specificity of <sup>11</sup>C-choline PET/CT for detecting prostate cancer recurrence in 609 patients was 62% (95% CI, 51% to 66%) and 92% (95% CI, 89% to 94%), respectively. 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 <sup>11</sup>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 2013 systematic review by Umbehr et al investigated the use of <sup>11</sup>C-choline and <sup>18</sup>F-FCH-PET and -PET/CT in staging and restaging of prostate cancer. The literature search, conducted through July 2012, identified 12 studies (total N=1055 patients) to be 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 <sup>11</sup>C-acetate PET imaging for the detection of primary or recurrent prostate cancer. For detection of recurrence, 14 studies were included in a meta-analysis. 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 utility of <sup>11</sup>C-acetate imaging in prostate cancer. Currently, <sup>11</sup>C-acetate is not FDA-approved.

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Both a 2009 NCCN report and a 2008 AHRQ systematic review 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.

### Prostate Cancer Management

In 2017, Akin-Akintayo et al evaluated the role of FACBC (anti-1-amino-3-[<sup>18</sup>F] fluorocyclobutane-1-carboxylic acid or fluciclovine) PET/CT in the management of post-prostatectomy patients with PSA failure being considered for salvage radiotherapy. 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 2014 guidelines for prostate cancer have indicated that <sup>11</sup>C- choline PET/CT has limited value unless PSA levels exceed 1.0 ng/mL. 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 rate of increase greater than 2 ng/mL per year. Pooled sensitivity was lower for patients with a PSA rate of increase 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 pooled sensitivity and specificity of 59% (95% CI, 51% to 66%) and 92% (95% CI, 89% to 94%), respectively. Pooled PPV and NPV were 70% and 85%, respectively.

Current NCCN guidelines for prostate cancer indicate that <sup>11</sup>C-choline PET may be considered for biochemical failure after primary treatment (i.e., radiotherapy or radical prostatectomy), although further study is needed to determine the best use of this imaging modality in patients with prostate cancer. FDG or fluoride PET should not be used routinely for initial assessment or in other settings, due to limited evidence of clinical utility.

### Section Summary: Prostate Cancer and <sup>11</sup>C-CHOLINE

Evidence for the use of <sup>11</sup>C-choline PET and -PET/CT for diagnosis, staging, and restaging of prostate cancer, consists of meta-analyses. The choice of radiotracer affects the sensitivity and specificity of the scans, with most evidence showing that the use of <sup>11</sup>C-choline results in the highest sensitivities and

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# Louisiana

## Positron Emission Tomography (PET) Oncology Applications

Policy # 00105

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specificities. Further study is needed to compare PET and PET/CT with other imaging techniques, such as MRI and radionuclide bone scan. One prospective study has looked at the use of FACBC PET/CT in the management of post-prostatectomy patients with PSA failure considering salvage radiotherapy. PET/CT results altered the radiotherapy treatment plans in 40% of the patients. The evidence supports the use of  $^{11}\text{C}$ -choline PET and PET/CT for the diagnosis, staging and restaging, and surveillance of prostate cancer.

### **PROSTATE CANCER AND $^{68}\text{Ga}$ -PET, AND $^{68}\text{Ga}$ -PET/CT**

A 2016 systematic review by Perera calculated the sensitivity, specificity, and predictive value of  $^{68}\text{Ga}$ -prostate-specific membrane antigen (PSMA) PET in advanced prostate cancer. 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 allowed for calculating the predictive ability of  $^{68}\text{Ga}$ -PSMA PET; they showed a pooled sensitivity of 86% (95% CI, 37% to 98%) and a pooled specificity of 86% (95% CI, 3% to 100%). The other studies were used to assess  $^{68}\text{Ga}$ -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.

#### **Section Summary: Prostate Cancer and $^{68}\text{Ga}$**

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

### **RENAL CELL CARCINOMA AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

A 2017 systematic review by Ma et al evaluated the use of  $^{18}\text{F}$ -FDG-PET or -PET/CT for restaging renal cell carcinoma.<sup>120</sup> 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 renal cell carcinoma, but that more prospective studies would be needed.

Current NCCN guidelines for renal cell carcinoma 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.”

#### **Section Summary: Renal Cell Carcinoma**

The evidence does not support the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis, staging and restaging, or surveillance of renal cell carcinoma.

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### **SOFT TISSUE SARCOMA**

A 2002 AHRQ systematic review 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 loco-regional recurrence, detecting distant metastases, and evaluating response to therapy.

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 loco-regional recurrence, detection of distant metastasis, and evaluation of treatment response.

A 2012 systematic review by Treglia et al evaluated PET for assessing response to imatinib and other treatments for gastrointestinal stromal tumors. Reviewers selected 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.

Current NCCN guidelines for soft tissue sarcoma state that 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 progression of disease if results from other imaging techniques 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 AHRQ 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 supports the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of soft tissue sarcoma, but does not support their use for surveillance.

### **TESTICULAR CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT**

The 2004 AHRQ systematic review found 1 prospective study and 4 retrospective studies that generally showed higher sensitivity and specificity for PET compared with CT. However these studies were small in

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size and failed to report separate results for patients with and without seminoma. Studies also failed to report separate results by clinical stage of 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 use of PET leads to different patient management decisions and health outcomes compared with other imaging modalities.

A 2008 AHRQ technology assessment and studies evaluating residual masses in patients after chemotherapy for seminoma support the use of PET.

Current NCCN guidelines also support the use of PET to evaluate residual masses that are greater than 3 cm following primary treatment with chemotherapy. 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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of testicular cancer, but does not support their use for surveillance.

### THYROID CANCER AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT

#### Differentiated

In 2016, Haslerud et al conducted a systematic review of studies using  $^{18}\text{F}$ -FDG-PET to detect recurrent differentiated thyroid cancer in patients who had undergone ablative therapy. The literature search, conducted through December 2014, identified 34 studies (total N=2639 patients) for inclusion: 17 using  $^{18}\text{F}$ -FDG-PET/CT, 11 using  $^{18}\text{F}$ -FDG-PET, and 6 using both methods. Study quality was assessed using the QUADAS tool. Pooled sensitivity and specificity for  $^{18}\text{F}$ -FDG-PET/CT were 80% (95% CI, 74% to 86%) and 76% (95% CI, 63% to 85%), respectively. Pooled sensitivity and specificity for  $^{18}\text{F}$ -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 2009 NCCN report on PET showed that PET can localize recurrent disease when other imaging tests are negative. Additionally, PET was found to be prognostic in this setting: More metabolically active lesions on PET were strongly correlated with reduced survival. Current NCCN guidelines for thyroid carcinoma

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continue to support the use of  $^{18}\text{F}$ -FDG-PET/CT in thyroid cancer evaluations, such as when iodine-131 imaging is negative and stimulated Tg is greater than 2 to 5 ng/mL.

### Medullary

A meta-analysis of studies on detecting recurrent or metastatic medullary thyroid carcinoma was conducted by Cheng et al (2012). The literature search, conducted through December 2010, identified 15 studies to be included in the meta-analysis: 8 used  $^{18}\text{F}$ -FDG-PET and 7 used  $^{18}\text{F}$ -FDG-PET/CT. The pooled sensitivity for  $^{18}\text{F}$ -FDG-PET alone in detecting recurrent or metastatic medullary thyroid cancer was 68% (95% CI, 64% to 72%). The pooled sensitivity for  $^{18}\text{F}$ -FDG-PET/CT was 69% (95% CI, 64% to 74%).

Current NCCN guidelines for medullary thyroid cancer recommend contrast-enhanced CT with or without PET at 2 to 3 months postoperative surveillance.

### 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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -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  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis and staging and restaging of thyroid cancer, but does not support their use for surveillance.

### CANCER OF UNKNOWN PRIMARY AND $^{18}\text{F}$ -FDG-PET AND $^{18}\text{F}$ -FDG-PET/CT

The 2002 TEC Assessment concluded that FDG-PET met TEC criteria for the workup and management of patients with unknown primaries and a single site of metastatic disease. 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 an 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.

### Section Summary: Cancer of Unknown Primary

The evidence supports the use of  $^{18}\text{F}$ -FDG-PET and  $^{18}\text{F}$ -PET/CT for the diagnosis, staging and restaging, and surveillance of cancer of unknown primary.

### CANCER SURVEILLANCE

Clinical utility of PET scanning in surveillance (i.e., in performing follow-up PET scans in asymptomatic patients to detect early disease recurrence) is not well-studied. (For this evidence review, a scan is

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considered a surveillance scan if performed more than 6 months after therapy [but 12 months for lymphoma].) The 2009 NCCN report stated that "PET as a surveillance tool should only be used in clinical trials." 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.

### **OTHER ONCOLOGIC APPLICATIONS**

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

### **SUMMARY OF EVIDENCE**

#### **Bone Sarcoma**

For individuals who have suspected or diagnosed bone sarcoma and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT, the evidence includes systematic reviews and meta-analyses of many studies. Relevant outcomes are test accuracy and test validity. Pooled analyses have shown that PET or PET/CT can effectively diagnose and stage bone cancer. 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

#### **Brain Tumors**

For individuals who have diagnosed brain tumors and in need of staging or restaging information or who have suspected brain cancer or are asymptomatic after completing brain cancer treatment who receive  $^{18}\text{F}$ -FDG-PET,  $^{18}\text{F}$ -FET-PET, or  $^{11}\text{C}$ -methionine PET, the evidence includes several systematic reviews and meta-analyses. Relevant outcomes are test accuracy and 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  $^{11}\text{C}$ -methionine and  $^{18}\text{F}$ -FDG have shown that  $^{11}\text{C}$ -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.

#### **Breast Cancer**

For individuals who have diagnosed breast cancer and inconclusive results from other imaging techniques who receive adjunctive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT for staging or restaging, the evidence includes

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meta-analyses. Relevant outcomes are test accuracy and test validity. While studies included in the meta-analyses report variability in estimates of sensitivity and specificity,  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT, the evidence includes a TEC Assessment, several systematic reviews, and meta-analyses. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### **Cervical Cancer**

For individuals who have diagnosed cervical cancer and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes an AHRQ report and a meta-analysis. Relevant outcomes are test accuracy and test validity. Pooled results show that PET can be used for staging or restaging and for detection of 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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 CRC and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a TEC Assessment and several meta-analyses. Relevant outcomes are test accuracy and test validity. Several pooled analyses evaluating staging or restaging using PET or PET/CT resulted in wide ranges of sensitivities and specificities, from the low 60s to the high 90s. The evidence is insufficient to determine the effects of the technology on health outcomes.

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For individuals who have suspected CRC or who are asymptomatic after completing CRC treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a TEC Assessment and meta-analysis. Relevant outcomes are test accuracy and 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 CRC. The evidence is insufficient to determine the effects of the technology on health outcomes.

### **Endometrial Cancer**

For individuals who have diagnosed endometrial cancer in need of staging or restaging information or who are asymptomatic after completing endometrial cancer treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a systematic review and meta-analysis. Relevant outcomes are test accuracy and test validity. Pooled estimates from the meta-analysis showed high sensitivities and specificities for  $^{18}\text{F}$ -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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes several meta-analyses. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT, the evidence includes meta-analyses. Relevant outcomes are test accuracy and test validity. Pooled analyses showed adequate sensitivities but low specificities. The evidence is insufficient to determine the effects of the technology on health outcomes.

### **Gastric Cancer**

For individuals who have suspected or diagnosed gastric cancer and in need of staging or restaging information, who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes several meta-analyses. Relevant outcomes are test accuracy and test validity. Pooled analyses, with sensitivities and specificities ranging from the high 70s to the high 80s, 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.

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For individuals who are asymptomatic after completing gastric cancer treatment who receive  $^{18}\text{F}$ -FDG- PET or  $^{18}\text{F}$ -FDG-PET/CT, the evidence includes meta-analyses. Relevant outcomes are test accuracy and test validity. Pooled analyses showed 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a TEC Assessment and several meta-analyses. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET/CT may be useful in predicting response to therapy. Two meta-analyses calculated the ability of  $^{18}\text{F}$ -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 OS 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes several meta-analyses. Relevant outcomes are test accuracy and test validity. Pooled analyses have shown that PET and PET/CT have better diagnostic performance compared with 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### Small-Cell Lung Cancer

For individuals with diagnosed SCLC and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a systematic review and a meta-analysis. Relevant outcomes are test accuracy and test validity. While the quality of the studies was considered low, PET and PET/CT can be considered for staging or restaging in patients with SCLC. Clinical guidelines include PET/CT to

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inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected SCLC or who are asymptomatic after completing SCLC treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT, there is no evidence. Relevant outcomes are test accuracy and test validity. The evidence is insufficient to determine the effects of the technology on health outcomes.

### **Hodgkin and Non-Hodgkin Lymphoma**

For individuals who have suspected or diagnosed Hodgkin and non-Hodgkin lymphoma in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or PET/CT, the evidence includes a TEC Assessment and several meta-analyses. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

For individuals who are asymptomatic after completing non-Hodgkin lymphoma treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### **Melanoma**

For individuals who have suspected or diagnosed stage I or II melanoma and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a TEC Assessment. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a TEC Assessment and a meta-analysis. Relevant outcomes are test accuracy and 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.

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For individuals who are asymptomatic after completing melanoma treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT, the evidence includes retrospective and observational studies. Relevant outcomes are test accuracy and test validity. At the discretion of the physician, imaging surveillance can be considered every 3 to 12 months. Since 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes 2 systematic reviews. Relevant outcomes are test accuracy and 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 are asymptomatic after completing multiple myeloma treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### 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  $^{18}\text{F}$ -FDG-PET,  $^{18}\text{F}$ -PET/CT,  $^{68}\text{Ga}$ -PET, or  $^{68}\text{Ga}$ -PET/CT, the evidence includes 2 meta-analyses. Relevant outcomes are test accuracy and test validity. The evidence did not compare PET, PET/CT, Ga-PET, or Ga-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.

### Ovarian Cancer

For individuals who have diagnosed ovarian cancer and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes an AHRQ systematic review and several meta-analyses. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

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# Louisiana

## Positron Emission Tomography (PET) Oncology Applications

Policy # 00105

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### **Pancreatic Cancer**

For individuals who have suspected or diagnosed pancreatic cancer and with inconclusive results from other imaging techniques who receive adjunctive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT for staging or restaging, the evidence includes a TEC Assessment and a systematic review. Relevant outcomes are test accuracy and test validity. The evidence has shown that PET and PET/CT do not have a high enough NPV to surpass current standard decision thresholds. Therefore PET or PET/CT should only be considered if 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes an AHRQ systematic review, a TEC Assessment, and a meta-analysis published after the review and assessment. Relevant outcomes are test accuracy and test validity. The evidence has shown that PET and PET/CT do not have a high enough NPV to surpass current standard decision thresholds. Therefore PET or PET/CT should only be considered if 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### **Penile Cancer**

For individuals who have suspected or diagnosed penile cancer and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a systematic review and a meta-analysis. Relevant outcomes are test accuracy and test validity. The evidence have 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### **Prostate Cancer**

For individuals who have suspected or diagnosed prostate cancer and in need of staging or restaging information who receive  $^{11}\text{C}$ -choline PET or  $^{11}\text{C}$ -choline PET/CT, evidence includes several meta- analyses. Relevant outcomes are test accuracy and 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

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$^{11}\text{C}$ -choline results in the highest sensitivities and specificities compared with  $^{18}\text{F}$ -FDG-PET and  $^{11}\text{C}$ -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  $^{11}\text{C}$ -choline PET or  $^{11}\text{C}$ -choline 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.

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

### **Renal Cell Carcinoma**

For individuals who are diagnosed renal cell carcinoma and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a systematic review and meta-analysis. Relevant outcomes are test accuracy and test validity. The review concluded that PET has potential to detect metastatic or recurrent lesions in patients with renal cell cancer, but that additional prospective studies are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

### **Soft Tissue Sarcoma**

For individuals who have diagnosed soft tissue sarcoma and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes an AHRQ systematic review. Another systematic review evaluated PET for assessing response to imatinib. Relevant outcomes are test accuracy and 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 activity following imatinib treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a systematic review. Relevant outcomes are test accuracy and 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.

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For individuals who have soft tissue sarcoma or who are asymptomatic after completing soft tissue sarcoma treatment who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -FDG-PET/CT, the evidence includes a systematic review. Relevant outcomes are test accuracy and test validity. The review concluded that there was insufficient evidence on the use of PET for detection of loco-regional 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes an AHRQ systematic review and assessment. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### **Thyroid Cancer**

For individuals with diagnosed thyroid cancer and in need of staging or restaging information who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes systematic reviews and meta-analyses. Relevant outcomes are test accuracy and 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  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -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.

### **Unknown Primary and Single-Site Metastatic Disease**

For individuals with unknown primary and single-site metastatic disease who receive  $^{18}\text{F}$ -FDG-PET or  $^{18}\text{F}$ -PET/CT, the evidence includes a TEC Assessment. Relevant outcomes are test accuracy and test validity. Studies reviewed in the Assessment showed that PET identified previously undetected metastases

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confirmed by biopsy. PET can contribute to the management of patients with 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.

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# Louisiana

## Positron Emission Tomography (PET) Oncology Applications

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Original Effective Date: 01/28/2002

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## Positron Emission Tomography (PET) Oncology Applications

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Original Effective Date: 01/28/2002

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# Louisiana

## Positron Emission Tomography (PET) Oncology Applications

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### **Policy History**

- Original Effective Date: 01/28/2002  
 Current Effective Date: 01/02/2018
- 10/18/2001 Medical Policy Committee review
- 11/12/2001 Managed Care Advisory Council approval
- 06/24/2002 Format revision. No substance change to policy
- 10/05/2004 Medical Director review
- 12/14/2004 Medical Policy Committee review. Format revision. Coverage eligibility criteria for Unknown Primary and Thyroid Cancer added.
- 01/31/2005 Managed Care Advisory Council approval
- 07/19/2005 Omission corrected: Melanoma, Staging and Restaging for the purpose of detecting disease was corrected to reflect policy intent: "for the purpose of detecting residual disease".
- 10/10/2005 Medical Director review
- 10/18/2005 Medical Policy Committee review. Format revision. Coverage eligibility criteria for Thyroid Cancer updated and Cervical Cancer added.
- 10/27/2005 Quality Care Advisory Council approval
- 12/20/2005 Medical Policy Committee review. Coverage eligibility coverage changes: The terms Staging and Restaging have been substituted for "differentiation" for Colorectal Cancer indications. Use of PET in the restaging of colorectal cancer was added; "To detect recurrence of colorectal cancer in patients with rising CEA levels and/or in patients who present with signs and symptoms of recurrence".
- Appendix 1 Table 1 removed from the policy.
- 02/23/2006 Quality Care Advisory Council approval
- 08/09/2006 Medical Policy Committee approval. PET for follicular and papillary thyroid cancer is now eligible for coverage to detect recurrent thyroid cancer or metastasis when Tg and 131 scans are non-diagnostic.
- 12/06/2006 Medical Director review
- 12/20/2006 Medical Policy Committee approval. Coverage eligibility updated:  
 Breast Cancer changed from:
- Diagnosis*
    - o in clinical situations in which the PET results may assist in avoiding an invasive diagnostic procedure, or in which the PET results may assist in determining the optimal anatomical location to perform an invasive diagnostic procedure. In general, for most solid tumors, a tissue diagnosis is made prior to the performance of PET scanning. PET scans following a tissue diagnosis are performed for the purpose of staging, not diagnosis.
  - Staging and/or Restaging*
    - o in clinical situations in which the stage of the cancer remains in doubt after completion of standard diagnostic workup or for restaging after the completion of treatment; or
    - o for the purpose of detecting residual disease; or

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- o for detecting suspected recurrence; or
- o to determine the extent of a known recurrence.

Changed To:

*Staging (before any treatment)*

- o As an adjunct to standard imaging modalities in the staging of breast cancer with distant metastases, excluding staging of axillary lymph nodes.
- o Restaging (after treatment has been completed)
- o As an adjunct to standard imaging in the restaging of loco-regional recurrence or metastases

- o For women with locally advanced and metastatic breast cancer, when a change in therapy is anticipated.

Colorectal Cancer changed from:

*Diagnosis*

- o as a technique to detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer.
- o to assess the presence of scarring versus local bowel recurrence in patients with previously resected colorectal cancer.
- o to detect recurrence of colorectal cancer in patients with rising CEA levels and/or in patients who present with signs and symptoms of recurrence.

Changed To:

- o Avoiding an invasive diagnostic procedure, or
- o Determining the optimal anatomical location to perform an invasive diagnostic procedure
- o The diagnosis has not been confirmed by tissue biopsy
- o The cancer stage remains in doubt after completion of a standard diagnostic workup.
- o PET could potentially replace one or more conventional imaging studies, when it is expected that conventional study information is insufficient for the clinical management of the patient, or
- o Clinical management would differ depending on the cancer stage
- Detecting residual disease (after completion of treatment),or
- Detecting suspected recurrence (ex: rising CEA levels; clinical signs/symptoms suspicious for recurrence)
- Determination of the extent of known recurrence  
Potentially replacing one or more conventional imaging studies, when it is expected that information from these studies will be insufficient for clinical management of the patient.

06/13/2007

Medical Director review

06/20/2007

Medical Policy Committee approval. No change to coverage eligibility. Decided not to differentiate between small cell and non small cell lung cancer.

08/06/2008

Medical Director review

08/20/2008

Medical Policy Committee approval. No change to coverage eligibility.

08/06/2009

Medical Policy Committee approval

08/26/2009

Medical Policy Implementation Committee approval. No change to coverage eligibility.

01/01/2010

Coding revision

08/05/2010

Medical Policy Committee review

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08/18/2010	Medical Policy Implementation Committee approval. Coverage eligibility extensively updated.
12/08/2011	Medical Policy Committee review
12/21/2011	Medical Policy Implementation Committee approval. Revised the ovarian cancer coverage so that diagnosis, staging and restaging is covered for certain situations.
12/06/2012	Medical Policy Committee review
12/19/2012	Medical Policy Implementation Committee approval. Added that bone cancer in the staging of Ewing Sarcoma and osteosarcoma may be eligible for coverage, but is investigational in the staging of chondrosarcoma. Reworded the eligible for coverage statements for breast cancer. Added that PET scanning may be eligible for coverage in the evaluation of known or suspected recurrence of cervical cancer. Reworded coverage for head and neck cancer to be more liberal. Prostate cancer given a separate section as investigational. All other oncologic applications are remain investigational, but examples of some investigational applications were removed.
06/06/2013	Medical Policy Committee review
06/25/2013	Medical Policy Implementation Committee approval. Added coverage for staging and restaging of multiple myeloma.
05/01/2014	Medical Policy Committee review
05/21/2014	Medical Policy Implementation Committee approval. Deleted "when suspicion of disease is high and other imaging is inconclusive" from the Eligible for Coverage statements for breast cancer staging and restaging.
06/25/2015	Medical Policy Committee approval
07/15/2015	Medical Policy Implementation Committee approval. Added Evaluation of neuroendocrine tumors and Staging inguinal lymph nodes in patients with squamous cell carcinoma of the penis to Investigational statement under Other Oncologic Applications. Added Predicting pathologic response to neoadjuvant therapy for locally advanced disease to the INV statement under Breast Cancer. Added Evaluating response to imatinib and other treatments for gastrointestinal stromal tumors to INV statement under Soft Tissue Sarcoma section.
06/30/2016	Medical Policy Committee approval
07/20/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
09/07/2017	Medical Policy Committee approval
09/20/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/05/2017	Medical Policy Committee approval
10/18/2017	Medical Policy Implementation Committee approval. Additional details added to policy statements. The following statements were changed to eligible for coverage: restaging of Ewing sarcoma and osteosarcoma for bone cancer, staging or restaging of brain cancer; restaging in the evaluation of response to treatment in head and neck cancer; restaging of esophageal cancer for determining response to preoperative induction therapy, and restaging when used with testing with <sup>11</sup> C-choline for evaluating response to primary treatment in prostate cancer. Three additional indications were added to be eligible for coverage (endometrial cancer, gastric cancer and renal cell carcinoma). Added that colorectal cancer is investigational as a technique contributing to radiotherapy treatment planning. Added that PET scanning of melanomas is investigational as a technique to detect regional lymph node metastases in patients with clinically localized melanoma who are candidates to undergo sentinel node biopsy and when used as a technique for restaging in managing stage 0, I, or II melanoma. Added that prostate cancer is investigational when managed using <sup>68</sup> Gallium in

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all aspects and for all other indications, known or suspected. Added that managing all aspects of neuroendocrine tumors, penile cancer and renal cancer are investigational.

Next Scheduled Review Date: 10/2018

### **Coding**

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	78811, 78812, 78813, 78814, 78815, 78816
HCPCS	A9515, A9526, A9552, A9580, A9587, A9588, A9598, C9461, G0219, G0235, G0252
ICD-10 Diagnosis	C00.0-C00.9      C15.3-C15.9      C30.0-C30.01      C30.10-C30.19
	C30.20-C30.29      C33      C34.00-C34.02      C34.10-C34.12
	C34.2      C34.30-C34.32      C34.80-C34.82      C34.90-C34.92
	C40.00-C40.02      C40.10-C40.12      C40.20-C40.22      C40.30-C40.32
	C40.80-C40.82      C40.90-C40.92      C41.0-C41.9      C43.0
	C43.10-C43.12      C43.20-C43.22      C43.30-C43.39      C43.4
	C43.51-C43.59      C43.60-C43.62      C43.70-C43.72      C43.8-C43.9
	C47.0      C47.10-C47.22      C47.3-C47.9      C49.0
	C49.10-C49.22      C49.3-C49.9      C50.011-C50.029      C50.211-C50.229
	C50.311-C50.329      C50.311-C50.329      C50.411-C50.429      C50.511-C50.529
	C50.611-C50.629      C50.811-C50.829      C50.911-C50.929      C53.0-C53.9
	C56.1-C56.9      C62.00-C62.292      C73      C76.0

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# Louisiana

## Positron Emission Tomography (PET) Oncology Applications

Policy # 00105

Original Effective Date: 01/28/2002

Current Effective Date: 01/02/2018

	C78.00-C78.02	C81.00-C81.99	C82.00-C82.99	D03.0
	D03.10-D03.339	D03.4	D03.51-D03.72	D03.8-D03.9

**\*Investigational** – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  - 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
  - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  - 3. Reference to federal regulations.

**\*\*Medically Necessary (or "Medical Necessity")** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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