# Medical Policy

BlueCross BlueShield Kansas
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# Title: PET Scanning- Oncologic Applications (Gastrointestinal and Pancreatic)

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| Related Policies: | ▪ *PET Scanning- Oncologic Applications (Breast and Gynecologic)*<br>▪ *PET Scanning- Oncologic Applications (Thyroid, Neuroendocrine, Head and Neck)*<br>▪ PET Scanning- Oncologic Applications *(Lung)*<br>▪ *PET Scanning- Oncologic Applications (Bone and Sarcoma)*<br>▪ *PET Scanning- Oncologic Applications (Hematologic)*<br>▪ *PET Scanning-* Oncologic *(Brain, Melanoma, Unknown Primary)*<br>▪ PET *Scanning- Oncologic Applications (Genitourinary)*<br>▪ *PET Scanning: Cardiac Applications*<br>▪ *PET Scanning: In Oncology to Detect Early Response during Treatment*<br>▪ *PET Scanning: Miscellaneous (Non-cardiac, Non-oncologic) Applications of Fluorine 18 Fluorodeoxyglucose* |

| **Professional / Institutional** |
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| Populations | Interventions | Comparators | Outcomes |
|---|---|---|---|
| Individuals:<br>• With diagnosed colorectal cancer and in need of staging or restaging information | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |
| Individuals:<br>• With suspected colorectal cancer or who are asymptomatic after completing colorectal cancer treatment | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |
| Individuals:<br>• With diagnosed esophageal cancer and in need of staging or restaging information | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |
| Individuals:<br>• With suspected esophageal cancer or who are asymptomatic after completing esophageal cancer treatment | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |
| Individuals:<br>• With suspected or diagnosed gastric cancer and in need of staging or restaging information | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |
| Individuals:<br>• Who are asymptomatic after completing gastric cancer treatment | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |
| Individuals:<br>• With suspected pancreatic cancer and with inconclusive results from other imaging techniques | Interventions of interest are:<br>• Adjunctive $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT for staging or restaging | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |
| Individuals:<br>• With suspected or diagnosed pancreatic cancer | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |

| Populations | Interventions | Comparators | Outcomes |
|---|---|---|---|
| and in need of staging or restaging information | | | |
| Individuals:<br>• Who are asymptomatic after completing pancreatic cancer treatment | Interventions of interest are:<br>• $^{18}$F-FDG-PET or $^{18}$F-FDG-PET/CT | Comparators of interest are:<br>• Conventional imaging techniques | Relevant outcomes include:<br>• Test validity |

## DESCRIPTION

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

The utility of PET scanning for the diagnosis, staging and restaging, and surveillance of malignancies varies by type of cancer. In general, PET scanning can distinguish benign from malignant masses in certain circumstances and improve the accuracy of staging by detecting additional disease not detected by other imaging modalities. Therefore, PET scanning for diagnosis and staging of malignancies can be considered medically necessary when specific criteria are met for specific cancers, as outlined in the policy statements. For follow-up, after initial diagnosis and staging have been performed, there are a few situations in which PET can improve detection of recurrence, and lead to changes in management that improve the net health outcome.

## OBJECTIVE

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

## BACKGROUND

A variety of tracers are used for positron emission tomography (PET) scanning, including oxygen 15, nitrogen 13, carbon 11 choline, fluorine 18, gallium 68, fluciclovine 18, and copper 64. Because of their short half-life, some tracers must be made locally using an onsite cyclotron. The radiotracer most commonly used in oncology imaging has been fluorine 18 coupled with fluorodeoxyglucose (FDG), which correlates with glucose metabolism. Fluorodeoxyglucose has been considered useful in cancer imaging because tumor cells show increased metabolism of glucose. The most common malignancies studied have been melanoma, lymphoma, lung, colorectal, and pancreatic cancer.

This evidence review focuses on the use of radiotracers detected with dedicated PET scanners. Radiotracers, such as FDG, may be detected using single-photon emission computerized tomography cameras, a technique that may be referred to as FDG-single-photon emission

computerized tomography imaging. The use of single-photon emission computerized tomography cameras for PET radiotracers presents unique issues of diagnostic performance and is not considered herein.

## REGULATORY STATUS

A number of radiopharmaceuticals have been granted approval by the U.S. Food and Drug Administration , to be used with PET for various cancer-related indications, however none are specific to gastrointestinal or pancreatic cancers. Fluorine-18 FDG is approved for use in suspected or existing diagnosis of cancer, all types.

## POLICY

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

- For the clinical situations indicated that may be considered medically necessary, this assumes that the results of the PET scan will influence treatment decisions. If the results will not influence treatment decisions, these situations would be considered not medically necessary.

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

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

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

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

## POLICY GUIDELINES

A. **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 PET scanning. Due to its expense, PET scanning is typically considered after other techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), or ultrasonography, provide inconclusive or discordant results. If so, the medical necessity of subsequent imaging

during the same diagnostic evaluation is unclear. Thus, PET should be considered for the medically necessary indications above only when standard imaging (eg, CT, MRI) is inconclusive or not indicated, including situations when an individual has a contraindication to intravenous contrast agents, making initial CT scans unattainable.

Selection criteria for PET scanning may also be complex. For example, it may be difficult to determine whether a PET scan in an individual with colorectal cancer is being performed to detect hepatic disease or evaluate local recurrence. Due to the complicated hierarchy of imaging options in individuals 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 PET scans.

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

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## RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through September 18, 2024.

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

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

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

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

## POSITRON EMISSION TOMOGRAPHY AND POSITRON EMISSION TOMOGRAPHY PLUS COMPUTED TOMOGRAPHY

### Clinical Context and Test Purpose

For this evidence review, PET and PET plus computed tomography (CT) scanning is discussed for the following 4 applications in oncology: diagnosis, staging, restaging, and surveillance. Diagnosis refers to the use of PET as part of the testing used in establishing whether an individual has cancer. Staging refers to the use of PET to determine the stage (extent) of cancer at the time of diagnosis before any treatment is given. Imaging during staging 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. First, restaging is part of the evaluation of an individual in whom disease recurrence is suspected based on signs and/or symptoms. Second, restaging also includes determining the extent of malignancy after completion of a full course of treatment. Surveillance refers to the use of imaging in asymptomatic individuals (individuals without objective signs or symptoms of recurrent disease). Surveillance is completed 6 months or more (≥12 months for lymphoma) after completion of treatment.

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

#### *Populations*

The relevant populations of interest are:

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

#### *Interventions*

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

#### *Comparators*

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

#### *Outcomes*

The general outcomes of interest are related to the clinical validity of PET and PET/CT in (1) diagnosing suspected cancers, (2) providing staging or restaging information, and (3) detecting recurrence following cancer treatment. Clinical validity is most often measured by sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV). For the clinical

utility of PET and PET/CT to be demonstrated, the tests would need to inform treatment decisions that would improve survival and quality of life.

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

**Study Selection Criteria**
Methodologically credible studies were selected using the following principles:

- To assess the clinical validity of PET and PET/CT, studies should report sensitivity, specificity, PPV, and NPV. Additionally, studies reporting false-positive rates and false-negative rates are informative.
- To assess the clinical utility of PET and PET/CT, studies should demonstrate how results of these imaging techniques impacted treatment decisions and overall management of the patient.

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

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

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

**Chain of Evidence**
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.
Most of the evidence on the use of PET scanning in oncology focuses on clinical validity (sensitivity, specificity), and consists mostly of systematic reviews and meta-analyses. There are few rigorous studies assessing the impact of PET on clinical utility. A few studies that have reported on changes in staging and/or treatment that result from the PET scan do not evaluate whether these changes resulted in improvements in the net health outcome. Due to the lack of direct evidence for clinical utility, evidence for clinical validity is presented first, followed by clinical guidelines, which help to outline the indications for which clinical utility is supported.

**REVIEW OF EVIDENCE**

**COLORECTAL CANCER**

**COLORECTAL CANCER DIAGNOSIS**

**Systematic Reviews**

Mahmud et al (2017) conducted a systematic review comparing the use of FDG-PET and FDG-PET/CT with conventional imaging techniques in the staging, treatment response, and follow-up of individuals with rectal cancer.[1,] The literature review, conducted through April 2016, identified 17 studies (N=791) for the qualitative review, with 8 of those studies (n=428) included in the meta-analysis. The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool was used to assess study quality. A limitation of many of the studies was that there was either no blinding or unclear blinding used for assessing the index test or the reference standard. For the detection of a primary tumor, pooled sensitivity and specificity were 99% (95% CI, 97% to 100%) and 67% (95% CI, 50% to 82%), respectively. For the detection of inguinal lymph nodes, the pooled sensitivity and specificity were 93% (95% CI, 76% to 99%) and 76% (95% CI, 61% to 87%), respectively.

A systematic review by Jones et al (2015) compared the role of FDG-PET and FDG-PET/CT with conventional imaging in the detection of primary nodal disease.[2,] Twelve studies met inclusion criteria (N=494). A meta-analysis for detecting primary disease in situ showed that PET and PET/CT had a higher sensitivity (99%; 95% CI, 96% to 100%) than CT alone (60%; 95% CI, 46% to 75%).

Two clinical applications of PET scanning were considered in a TEC Assessment (1999): (1) to detect hepatic or extrahepatic metastases and to assess their resectability in individuals with colorectal cancer (CRC), either as part of initial staging or after primary resection, and (2) to evaluate the presence of postoperative scar versus recurrent disease as a technique to determine the necessity of tissue biopsy.[3,]

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 individuals to avoid surgery. The strongest evidence came from a study that directly assessed the additional value of PET. In a group of 37 individuals thought to have a solitary liver metastasis by conventional imaging, PET correctly upstaged 4 individuals and falsely overstaged 1. This and another study found that when PET results were discordant with conventional imaging results, PET was correct in 88% and 97% of individuals, respectively. When PET affected management decisions, it was more often used to recommend against surgery.

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

**COLORECTAL CANCER STAGING**

**Systematic Reviews**

Results from a meta-analysis of 10 studies by Albertsson et al (2018) found that PET/CT influenced treatment plans for anal cancer, though the impact on survival and quality of life could not be determined.[4,]

A meta-analysis by Ye et al (2015) assessed the use of FDG-PET/CT in preoperative TNM staging of CRC.[5,] The literature search, conducted through July 2014, identified 28 studies for inclusion. Of the 28 studies, 12 assessed tumor detection rates; 4 evaluated T staging, 20 N staging, and 5 M staging; while 8 examined stage change. Using the QUADAS tool, all studies met 9 or more of the 14 criteria. Pooled diagnostic estimates are listed in Table 1.

Three systematic reviews published in 2014 included overlapping studies that assessed the predictive value of FDG-PET/CT in individuals with locally advanced rectal cancer who received neoadjuvant chemoradiotherapy.[6,7,8,] Various PET parameters were investigated (standardized uptake value, response index [percentage of the standardized uptake value decrease from baseline to post neoadjuvant treatment]), and cutoff values varied. Pooled sensitivities ranged from 74% to 82%, and pooled specificities ranged from 64% to 85%. The value of FDG-PET/CT in this setting has yet to be established.

Two systematic reviews were conducted to evaluate the use of PET/CT for radiotherapy planning in individuals with rectal cancer. Gwynne et al (2012) compared different imaging techniques for radiotherapy treatment planning and concluded that additional studies would be needed to validate the use of PET in this setting.[9,]

**Table 1. Pooled Diagnostic Performance of FDG-PET, FDG-PET/CT, and CT Alone in the Staging of Colorectal Cancer**

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

Adapted from Ye et al (2015).[5,]
CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; M staging: distant metastases; N staging: regional lymph nodes; PET: positron emission tomography; T staging: primary tumor.

**COLORECTAL CANCER RESTAGING**

### Systematic Reviews

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

A meta-analysis by Yu et al (2015) evaluated the diagnostic value of FDG-PET/CT for detecting local recurrent CRC.[11,] The literature search, conducted through October 2014, identified 26 studies (N=1794) for inclusion. Study quality was assessed using QUADAS. Pooled sensitivity and specificity were 95% (95% CI, 93% to 97%) and 93% (95% CI, 92% to 95%), respectively.

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

In a systematic review, Lu et al (2013), evaluated 510 individuals from 11 studies on FDG-PET for CRC tumor recurrence detection in individuals with elevated carcinoembryonic antigen.[13,] The literature search ran through April 2012. Estimates for FDG-PET and PET/CT pooled sensitivity were 90.3% (95% CI, 85.5% to 94.0%) and 94.1% (95% CI, 89.4% to 97.1%), respectively, and specificities were 80.0% (95% CI, 67.0% to 89.6%) and 77.2% (95% CI, 66.4% to 85.9%), respectively.

## COLORECTAL CANCER SURVEILLANCE

### Randomized Controlled Trials

Sobhani et al (2018) conducted an open-label RCT to determine whether adding 6 monthly FDG-PET/CT scans to usual surveillance (ie, 3 monthly physicals and tumor marker assays; 6 monthly liver ultrasounds and chest radiographs; 6 monthly CT scans) of individuals with CRC following surgery and/or chemotherapy improves health outcomes.[14,] A total of 239 individuals in remission were enrolled, with 120 in the intervention arm and 119 in the control arm. After 3 years of follow-up, the failure rate in the intervention group was 29% (31 unresectable recurrences, 4 deaths) and 24% in the control group (27 unresectable recurrences, 1 death), which was not a statistically significant difference.

## GUIDELINES

### American College of Radiology

In 2017, the American College of Radiology (ACR) issued Appropriateness Criteria for the pretreatment staging of CRC,[15,]which were updated in 2021.[16,]The criteria for locoregional staging for initial imaging and postneoadjuvant therapy states that FDG-PET/CT "may be appropriate", and that "FDG-PET/CT is...sometimes helpful to more definitively suggest residual local or nodual

disease in patient's post CRT [chemoradiotherapy]...but does not significantly add benefit or suggest complete response in patients who have been identified as complete or near-complete responders by the more conventional combination of post-CRT MRI and endoscopy." The guidelines state "it [FDG-PET/CT] is widely considered a specific but not sensitive examination for evaluating distant rather than local disease." In the evaluation of distant metastases, the criteria stated FDG-PET/CT "may be appropriate" and "may help to exclude other sites of disease beyond the liver or, in complex cases, to improve staging accuracy in which it has been shown to result in a change in management in up to 8% to 11% of patients."

**National Comprehensive Cancer Network**

Current National Comprehensive Cancer Network (NCCN) guidelines for colon cancer (v.5.2024 ) "strongly discourages the routine use of PET/CT scanning for staging, baseline imaging, or routine follow-up" for metastatic disease and "recommend consideration of a preoperative PET/CT scan at baseline in selected cases if prior anatomic imaging indicates the presence of potentially surgically curable M1 disease."[17,] For initial workup of nonmetastatic individuals, the guidelines state that PET/CT is not routinely indicated, and "PET/CT does not supplant a contrast-enhanced diagnostic CT or MR scan and should only be used to evaluate an equivocal finding on a contrast-enhanced CT scan or MRI scan or in individuals with strong contraindications to IV [intravenous] contrast." PET/CT can be considered in select individuals "considered for image-guided liver-directed therapies," "for assessment of response and liver recurrence after image-guided liver-directed therapies, or serial carcinoembryonic antigen elevation during follow-up." Otherwise, use of PET/CT is not recommended for surveillance. The NCCN has noted that PET/CT should not be used to assess response to chemotherapy. The NCCN was divided on the appropriateness of PET/CT when carcinoembryonic antigen level is rising; PET/CT might be considered when imaging study results (eg, a good quality CT scan) are normal.

Current NCCN guidelines for rectal cancer (v.4.2024 ) state that PET/CT is "not routinely indicated" and "should only be used to evaluate an equivocal finding on a contrast-enhanced CT or MR scan or in patients with strong contraindications to IV contrast."[18,] For certain individuals with potential surgically-curable M1 disease or who are being considered for image-guided liver-directed therapies, a PET/CT may be considered. Use of PET/CT is not recommended for restaging or for surveillance with the exception of surveillance in individuals who are considered for image-guided liver-directed therapies for hepatic metastases. Use of PET/CT can be considered if serial carcinoembryonic antigen elevation occurs during follow-up.

**Section Summary: Colorectal Cancer**

Evidence for the detection of primary nodal disease, staging, restaging, and detecting recurrence of CRC consists of several meta-analyses and a RCT. A meta-analysis evaluating the diagnostic accuracy of PET or PET/CT found a high sensitivity but low specificity. Several pooled analyses evaluating staging or restaging using PET or PET/CT resulted in sensitivities and specificities ranging from 16% to 99%. The evidence for the use of PET or PET/CT did not show a benefit over the use of contrast CT in individuals with CRC. The RCT found no differences in outcomes when FDG-PET/CT was added to usual surveillance compared to usual surveillance only. The evidence does not support the use of FDG-PET and PET/CT for the diagnosis, staging and restaging, or surveillance of CRC.

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

**Systematic Reviews**
Kroese et al (2018) conducted a systematic review of the use of FDG-PET and FDG-PET/CT for detecting interval metastases following neoadjuvant therapy in individuals with esophageal cancer.[19,] The literature search identified 14 studies for inclusion. The QUADAS tool was used to assess quality, with most studies rated moderate. The pooled proportion of individuals with true distant metastases as detected by FDG-PET and FDG-PET/CT was 8% (95% CI, 5% to 13%). The pooled proportion of individuals with false-positive distant findings was 5% (95% CI, 3% to 9%).

Cong et al (2016) published a meta-analysis evaluating the predictive value of FDG-PET and FDG-PET/CT for tumor response during or after neoadjuvant chemoradiotherapy in individuals with esophageal cancer.[20,] The literature search, conducted through January 2016, identified 4 studies (n=192 ) in which PET or PET/CT was performed during neoadjuvant chemoradiotherapy and 11 studies (n=490) in which PET or PET/CT was performed after neoadjuvant chemoradiotherapy. All studies scored between 9 and 12 using the QUADAS tool. Pooled sensitivity and specificity for PET and PET/CT performed during neoadjuvant chemoradiotherapy were 85% (95% CI, 76% to 91%) and 59% (95% CI, 48% to 69%), respectively. Pooled sensitivity and specificity for PET and PET/CT performed after neoadjuvant chemoradiotherapy were 67% (95% CI, 60% to 73%) and 69% (95% CI, 63% to 74%), respectively.

Goense et al (2015) published a systematic review evaluating FDG-PET and FDG-PET/CT for the detection of recurrent esophageal cancer after treatment with curative intent.[21,] The literature search, conducted through December 2014, identified 8 studies (N=486) for inclusion. The quality of the studies was considered reasonable using the QUADAS tool, with a low-risk of bias for most studies, and high-risk of bias in a few studies for patient selection. Pooled estimates of sensitivity and specificity of FDG-PET and FDG-PET/CT combined were 96% (95% CI, 93% to 97%) and 78% (95% CI, 66% to 86%), respectively. Subgroup analysis by technique (PET alone and PET/CT) was not possible for sensitivity due to heterogeneity. Specificity subgroup analysis showed no statistical difference between PET alone and PET/CT in detecting recurrent esophageal cancer.

In a meta-analysis of 245 individuals with esophageal cancer from 6 studies, Shi et al (2013) reported that, for detection of regional nodal metastases, FDG-PET/CT had a sensitivity of 55% (95% CI, 34% to 74%) and specificity of 76% (95% CI, 66% to 83%), respectively.[22,]

An NCCN report conducted by Podoloff et al (2009) found studies showing that PET is more sensitive than other diagnostic imaging in detecting stage IV disease with distant lymph node involvement.[23,] A meta-analysis described in the report found a 67% pooled sensitivity, 97% specificity, and small added value after conventional staging in detecting distant metastasis.

Another use of PET in esophageal cancer is in determining whether to continue chemotherapy for potentially curative resection. The NCCN report by Podoloff et al (2009) described several studies in which response to chemotherapy, defined as a decline in standardized uptake values,

correlated with long-term survival.[23,] Individuals who do not respond to chemotherapy might benefit from this test by being spared futile and toxic chemotherapy. However, the treatment strategy of PET-directed chemotherapy does not appear to have been validated with RCTs showing improved net health outcome.

## GUIDELINES

### American College of Radiology

In 2022, the ACR issued Appropriateness Criteria for staging and follow-up of esophageal cancer.[24,] Skull base to mid-thigh PET/CT is considered usually appropriate for pretreatment clinical staging, imaging during treatment, and for post-treatment imaging in individuals with or without suspected or known recurrence.

### National Comprehensive Cancer Network

Current NCCN guidelines for esophageal cancer (v.4.2024 )[25,] indicate that PET/CT (but not PET alone) can be considered under the following conditions:

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

### Section Summary: Esophageal Cancer

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

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

## GASTRIC CANCER

### Systematic Reviews

A systematic review by Choi et al (2023) evaluated FDG-PET and FDG-PET/CT for detecting recurrent gastric cancer after curative resection.[26,] The literature search, conducted through November 2019, identified 17 studies (N=1732) for analysis. Only 1 included study was conducted in the United States. Table 2 compares studies included in analysis to studies included in other systematic reviews. The analysis combined both imaging techniques; 3 studies used PET alone and 14 studies used PET/CT. Pooled sensitivity and specificity were 82% (95% CI, 74% to 88%) and 86% (95% CI, 78% to 91%), respectively, with high heterogeneity for both measures across studies.

A systematic review by Li et al (2016) evaluated FDG-PET and FDG-PET/CT for detecting recurrent gastric cancer.[27,] The literature search, conducted through February 2015, identified 14 studies (N=828) for analysis. The analysis combined both imaging techniques; 3 studies used PET alone and 11 studies used PET/CT. Pooled sensitivity and specificity were 85% (95% CI, 75% to 92%) and 78% (95% CI, 72% to 84%), respectively.

In a meta-analysis, Zou and Zhao (2013) evaluated studies published through May 2013 and calculated the sensitivity and specificity of FDG-PET/CT for detecting recurrence of gastric cancer after surgical resection.[28,] Eight studies (N=500) 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%).

**Table 2. Comparison of Studies Included in Systematic Review & Meta-Analysis**

| Study | Choi et al (2023)[26,] | Li et al (2016)[27,] | Zou and Zhao (2013)[28,] |
|---|---|---|---|
| Bilici et al (2011) | ● | ● | ● |
| De Potter et al (2002) | ● | ● | |
| Graziosi et al (2011) | ● | ● | ● |
| Jadvar et al (2003) | ● | ● | |
| Kim et al (2011) | ● | ● | ● |
| Kim et al (2016) | ● | | |
| Kim et al (2017) | ● | | |
| Lee et al (2011) | ● | ● | |
| Lee et al (2012) | ● | | ● |
| Lee et al (2014) | ● | ● | |
| Lee et al (2016) | ● | | |
| Ma et al (2009) | | ● | ● |
| Nakamoto et al (2009) | ● | ● | |
| Park et al (2009) | ● | ● | ● |
| Sharma et al (2012) | ● | ● | |
| Sim et al (2009) | ● | ● | ● |
| Sun et al (2008) | ● | ● | ● |
| Yun et al (2005) | ● | ● | |

## GUIDELINES

### National Comprehensive Cancer Network

Current NCCN guidelines for gastric cancer (v.4.2024 ) indicate that FDG-PET/CT (but not PET alone) can be used as part of an initial workup for locally advanced or metastatic disease or if its use is clinically indicated.[17,] The guidelines note that the accuracy of FDG-PET/CT is lower than for CT alone due to low tracer accumulation in diffuse and mucinous tumor types but specificity for detecting local lymph note involvement is higher. Use of FDG-PET/CT adds value to the

diagnostic workup with higher accuracy in staging (identifying tumor and pertinent nodal groups). The NCCN guidelines also indicate that FDG-PET/CT can be used to evaluate response to treatment, in cases of renal insufficiency or allergy to CT contrast. For surveillance in individuals with stage II or III disease, FDG-PET/CT can be considered as clinically indicated, but CT scan with oral and intravenous contrast is preferred.

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

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

## PANCREATIC CANCER

### Systematic Reviews

A Cochrane review by Best et al (2017) compared the diagnostic accuracy of several imaging techniques (CT, MRI, PET, and endoscopic ultrasound) in detecting cancerous and precancerous lesions in the pancreas.[29,] The literature review, conducted through July 2016, identified 54 studies total, 10 using PET. Assessment of the selected studies found none to have high methodologic quality. A meta-analysis of 3 studies reported a sensitivity and specificity in diagnosing pancreatic cancer of 92% (95% CI, 80% to 97%) and 65% (95% CI, 39% to 84%), respectively. The PPV and NPV (calculated by BCBSA) were 89% and 71%, respectively. Reviewers could not adequately compare the various techniques due to the imprecision of estimates, poor quality of studies, and heterogeneity in categorizing lesions.

Wang et al (2017) conducted a meta-analysis comparing CT alone, PET alone, and PET/CT in the preoperative assessment of individuals with pancreatic cancer.[30,] The literature review identified 13 studies (N=1343). The Newcastle-Ottawa Scale was used to assess study quality, with scores ranging from 6 to 8 on the 9-point scale. Use of PET alone was not superior to CT alone (pooled odds ratio [OR], 1.0; 95% CI, 0.6 to 1.6) in detecting distant metastases. However, PET/CT was superior to CT alone (pooled OR=1.7; 95% CI, 1.3 to 2.1) in detecting distant metastases. Neither PET nor PET/CT was superior to CT alone in detecting lymph node invasion (pooled OR, 1.0; 95% CI, 0.6 to 1.5).

In a meta-analysis of 9 studies (N=526), 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.[31,] Two reviews on pancreatic carcinoma, conducted by Ospina et al (2008) and Podoloff et al (2009) have suggested that PET/CT can be useful for staging certain individuals when the standard staging protocol is inconclusive.[32,23,]

An Agency for Healthcare Research and Quality (AHRQ) systematic review by Matchar et al (2004) focused on 2 clinical applications of PET scanning in individuals 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 individuals with known pancreatic cancer.[33,]

In terms of distinguishing between benign and malignant disease, the criterion standard is a percutaneous or open biopsy. If PET were to be used to allow individuals with scans suggesting benign masses to avoid a biopsy, a very high NPV would be required. The key statistic underlying the NPV is the false-negative rate. Individuals with false-negative results are incorrectly considered to have a benign disease and thus are not promptly treated for pancreatic cancer. Based on the TEC literature review, the NPV ranged between 75% and 92%, depending on an underlying prevalence of disease ranging from 50% to 75%. The TEC Assessment concluded that this level of diagnostic performance would not be adequate to recommend against biopsy. The Matchar et al 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.[33,] In both the TEC and AHRQ reviews, data were inadequate to permit conclusions on the role of PET scanning as a technique to stage known pancreatic cancer.

**Observational Studies**
Ghaneh et al (2018) conducted the largest study to date, measuring the incremental diagnostic value of PET/CT when added to a standard diagnostic workup with multidetector CT.[34,] The study was a prospective nonrandomized study of 550 individuals. Sensitivity and specificity were 88.5% and 70.6%, respectively, which was a significant improvement from CT alone. Use of PET/CT also correctly changed staging in 56 individuals, influenced management in 250 individuals, and stopped resection in 58 individuals scheduled for surgery.

## GUIDELINES

**American College of Radiology**
In 2017, the ACR published Appropriateness Criteria on staging of pancreatic ductal adenocarcinoma, which note that PET/CT may be appropriate as a supplemental imaging evaluation to detect additional distant metastases.[35,]

**National Comprehensive Cancer Network**
Current NCCN guidelines for pancreatic cancer (v.3.2024) state " [PET/CT] may be considered after formal pancreatic CT protocol in high-risk patients to detect extrapancreatic metastasis.[36,] It is not a substitute for high-quality, contrast-enhanced CT."

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

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

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

## SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

### Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Current National Comprehensive Cancer Network, American College of Radiology, and other relevant U.S.-based guidelines are summarized in each section of the Rationale.

### U.S. Preventive Services Task Force Recommendations

Not applicable.

### Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 4.

**Table 4. Summary of Key Trials**

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| ***Ongoing*** | | | |
| NCT05687552 | Role of 18F-FDG PET/CT in Gastric Cancer | 50 | Jan 2024 (not yet recruiting) |

NCT: national clinical trial.

## CODING

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.**

**Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.**

| **CPT/HCPCS** | |
|---|---|
| 78608 | Brain imaging, positron emission tomography (PET); metabolic evaluation |
| 78609 | Brain imaging, positron emission tomography (PET); perfusion evaluation |
| 78811 | Positron emission tomography (PET) imaging; limited area (e.g. Chest, head/neck) |
| 78812 | Positron emission tomography (PET) imaging; skull base to mid-thigh |
| 78813 | Positron emission tomography (PET) imaging; whole body |
| 78814 | Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; limited area (e.g. chest, head/neck) |
| 78815 | Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; skull base to mid-thigh |
| 78816 | Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; whole body |
| A9552 | Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries |
| A9597 | Positron emission tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified |
| A9598 | Positron emission tomography radiopharmaceutical, diagnostic, for non-tumor identification, not otherwise classified |
| G0235 | PET imaging, any site not otherwise specified |

| **REVISIONS** | |
|---|---|
| Posted 01-28-2025 Effective 02-27-25 | Oncologic Applications Gastrointestinal and Pancreatic was originally part of the Positron Emission Tomography (PET) Scanning: Oncologic Applications medical policy. Oncologic Applications for Gastrointestinal and Pancreatic has been pulled out and placed into a separate medical policy, Positron Emission Tomography (PET) Scanning: Oncologic Applications (Gastrointestinal and Pancreatic). The medical policy language was unchanged. |

## REFERENCES

1. Mahmud A, Poon R, Jonker D. PET imaging in anal canal cancer: a systematic review and meta-analysis. Br J Radiol. Dec 2017; 90(1080): 20170370. PMID 28972796

2. Jones M, Hruby G, Solomon M, et al. The Role of FDG-PET in the Initial Staging and Response Assessment of Anal Cancer: A Systematic Review and Meta-analysis. Ann Surg Oncol. Oct 2015; 22(11): 3574-81. PMID 25652048
3. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography in Colorectal Cancer. Technol Eval Cent Assess. 1999;14(25)
4. Albertsson P, Alverbratt C, Liljegren A, et al. Positron emission tomography and computed tomographic (PET/CT) imaging for radiation therapy planning in anal cancer: A systematic review and meta-analysis. Crit Rev Oncol Hematol. Jun 2018; 126: 6-12. PMID 29759568
5. Ye Y, Liu T, Lu L, et al. Pre-operative TNM staging of primary colorectal cancer by (18)F-FDG PET-CT or PET: a meta-analysis including 2283 patients. Int J Clin Exp Med. 2015; 8(11): 21773-85. PMID 26885142
6. Li C, Lan X, Yuan H, et al. 18F-FDG PET predicts pathological response to preoperative chemoradiotherapy in patients with primary rectal cancer: a meta-analysis. Ann Nucl Med. Jun 2014; 28(5): 436-46. PMID 24623152
7. Maffione AM, Chondrogiannis S, Capirci C, et al. Early prediction of response by $^{18}$F-FDG PET/CT during preoperative therapy in locally advanced rectal cancer: a systematic review. Eur J Surg Oncol. Oct 2014; 40(10): 1186-94. PMID 25060221
8. Memon S, Lynch AC, Akhurst T, et al. Systematic review of FDG-PET prediction of complete pathological response and survival in rectal cancer. Ann Surg Oncol. Oct 2014; 21(11): 3598-607. PMID 24802909
9. Gwynne S, Mukherjee S, Webster R, et al. Imaging for target volume delineation in rectal cancer radiotherapy--a systematic review. Clin Oncol (R Coll Radiol). Feb 2012; 24(1): 52-63. PMID 22035634
10. Rymer B, Curtis NJ, Siddiqui MR, et al. FDG PET/CT Can Assess the Response of Locally Advanced Rectal Cancer to Neoadjuvant Chemoradiotherapy: Evidence From Meta-analysis and Systematic Review. Clin Nucl Med. May 2016; 41(5): 371-5. PMID 26914561
11. Yu T, Meng N, Chi D, et al. Diagnostic Value of (18)F-FDG PET/CT in Detecting Local Recurrent Colorectal Cancer: A Pooled Analysis of 26 Individual Studies. Cell Biochem Biophys. Jun 2015; 72(2): 443-51. PMID 25737131
12. Maffione AM, Marzola MC, Capirci C, et al. Value of (18)F-FDG PET for Predicting Response to Neoadjuvant Therapy in Rectal Cancer: Systematic Review and Meta-Analysis. AJR Am J Roentgenol. Jun 2015; 204(6): 1261-8. PMID 26001237
13. Lu YY, Chen JH, Chien CR, et al. Use of FDG-PET or PET/CT to detect recurrent colorectal cancer in patients with elevated CEA: a systematic review and meta-analysis. Int J Colorectal Dis. Aug 2013; 28(8): 1039-47. PMID 23407908
14. Sobhani I, Itti E, Luciani A, et al. Colorectal cancer (CRC) monitoring by 6-monthly 18FDG-PET/CT: an open-label multicentre randomised trial. Ann Oncol. Apr 01 2018; 29(4): 931-937. PMID 29365058
15. Fowler KJ, Kaur H, Cash BD, et al. ACR Appropriateness Criteria ® Pretreatment Staging of Colorectal Cancer. J Am Coll Radiol. May 2017; 14(5S): S234-S244. PMID 28473079
16. Korngold EK, Moreno C, Kim DH, et al. ACR Appropriateness Criteria® Staging of Colorectal Cancer: 2021 Update. J Am Coll Radiol. May 2022; 19(5S): S208-S222. PMID 35550803
17. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Gastric Cancer. Version 4.2024. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed September 16, 2024.

18. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Rectal Cancer. Version 4.2024. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed September 14, 2024.
19. Kroese TE, Goense L, van Hillegersberg R, et al. Detection of distant interval metastases after neoadjuvant therapy for esophageal cancer with 18F-FDG PET(/CT): a systematic review and meta-analysis. Dis Esophagus. Dec 01 2018; 31(12). PMID 29917073
20. Cong L, Wang S, Gao T, et al. The predictive value of 18F-FDG PET for pathological response of primary tumor in patients with esophageal cancer during or after neoadjuvant chemoradiotherapy: a meta-analysis. Jpn J Clin Oncol. Dec 2016; 46(12): 1118-1126. PMID 27702836
21. Goense L, van Rossum PS, Reitsma JB, et al. Diagnostic Performance of $^{18}$F-FDG PET and PET/CT for the Detection of Recurrent Esophageal Cancer After Treatment with Curative Intent: A Systematic Review and Meta-Analysis. J Nucl Med. Jul 2015; 56(7): 995-1002. PMID 25952733
22. Shi W, Wang W, Wang J, et al. Meta-analysis of 18FDG PET-CT for nodal staging in patients with esophageal cancer. Surg Oncol. Jun 2013; 22(2): 112-6. PMID 23478047
23. Podoloff DA, Ball DW, Ben-Josef E, et al. NCCN task force: clinical utility of PET in a variety of tumor types. J Natl Compr Canc Netw. Jun 2009; 7 Suppl 2: S1-26. PMID 19555588
24. Raptis CA, Goldstein A, Henry TS, et al. ACR Appropriateness Criteria® Staging and Follow-Up of Esophageal Cancer. J Am Coll Radiol. Nov 2022; 19(11S): S462-S472. PMID 36436970
25. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Junction Cancers. Version 4.2024. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed September 17, 2024.
26. Choi CI, Park JK, Jeon TY, et al. Diagnostic performance of F-18 FDG PET or PET/CT for detection of recurrent gastric cancer: a systematic review and meta-analysis. J Yeungnam Med Sci. Nov 2023; 40(Suppl): S37-S46. PMID 37587035
27. Li P, Liu Q, Wang C, et al. Fluorine-18-fluorodeoxyglucose positron emission tomography to evaluate recurrent gastric cancer after surgical resection: a systematic review and meta-analysis. Ann Nucl Med. Apr 2016; 30(3): 179-87. PMID 26830546
28. Zou H, Zhao Y. 18FDG PET-CT for detecting gastric cancer recurrence after surgical resection: a meta-analysis. Surg Oncol. Sep 2013; 22(3): 162-6. PMID 23747134
29. Best LM, Rawji V, Pereira SP, et al. Imaging modalities for characterising focal pancreatic lesions. Cochrane Database Syst Rev. Apr 17 2017; 4(4): CD010213. PMID 28415140
30. Wang L, Dong P, Wang WG, et al. Positron emission tomography modalities prevent futile radical resection of pancreatic cancer: A meta-analysis. Int J Surg. Oct 2017; 46: 119-125. PMID 28890410
31. Rijkers AP, Valkema R, Duivenvoorden HJ, et al. Usefulness of F-18-fluorodeoxyglucose positron emission tomography to confirm suspected pancreatic cancer: a meta-analysis. Eur J Surg Oncol. Jul 2014; 40(7): 794-804. PMID 24755095
32. Ospina MB, Horton J, Seida J, et al. Technology Assessment Report : Positron emission tomography for nine cancers (bladder, brain, cervical, kidney, ovarian, pancreatic, prostate, small cell lung, testicular). Rockville, MD: Agency for Healthcare Research and Quality; 2008

33. Matchar DB, Kulasingam SL, Havrilesky L, et al. Positron Emission Testing for Six Cancers (Brain, Cervical, Small Cell Lung, Ovarian, Pancreatic and Testicular). Rockville, MD: Agency for Healthcare Research and Quality; 2004.
34. Ghaneh P, Hanson R, Titman A, et al. PET-PANC: multicentre prospective diagnostic accuracy and health economic analysis study of the impact of combined modality 18fluorine-2-fluoro-2-deoxy-d-glucose positron emission tomography with computed tomography scanning in the diagnosis and management of pancreatic cancer. Health Technol Assess. Feb 2018; 22(7): 1-114. PMID 29402376
35. Qayyum A, Tamm EP, Kamel IR, et al. ACR Appropriateness Criteria ® Staging of Pancreatic Ductal Adenocarcinoma. J Am Coll Radiol. Nov 2017; 14(11S): S560-S569. PMID 29101993
36. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. Version 3.2024. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed September 15, 2024.
37. Centers for Medicare & Medicaid Services (CMS). 2013. Pub 100-03 National Coverage Determination (NCD) for Positron Emission Tomography (FDG) for Oncologic Conditions (220.6.17). https://tinyurl.com/7hc7hvpr. Accessed September 18, 2024.

**OTHER REFERENCES**

1. MCMC, Medical Care Ombudsman Program (MCOP), August 11, 2006, MCOP ID 1071-0720.
2. Considine oncology consultant (#372), January 23, 2007, Reference: Semin Nucl Med. 2006 Jan;36(1):93-104. Links Positron emission tomography in gynecologic cancer. Yen TC, Lai CH.
3. Blue Cross and Blue Shield of Kansas, Oncology Liaison Committee meeting, February 2003, February 2004, June 2022, July 2023.
4. Blue Cross and Blue Shield of Kansas, Radiology Liaison Committee meeting, February 2002, February 2003. February 2009, January 2018, May 2019.
5. Blue Cross and Blue Shield of Kansas Urology Liaison Committee August 2018, June 2020.