CIGNA MEDICAL COVERAGE POLICIES – RADIOLOGY

Oncology Imaging Guidelines

Effective Date: June 15, 2025

Instructions for use

The following coverage policy applies to health benefit plans administered by Cigna. Coverage policies are intended to provide guidance in interpreting certain standard Cigna benefit plans and are used by medical directors and other health care professionals in making medical necessity and other coverage determinations. Please note the terms of a customer's particular benefit plan document may differ significantly from the standard benefit plans upon which these coverage policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a coverage policy.

In the event of a conflict, a customer's benefit plan document always supersedes the information in the coverage policy. In the absence of federal or state coverage mandates, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of:

1. The terms of the applicable benefit plan document in effect on the date of service
2. Any applicable laws and regulations
3. Any relevant collateral source materials including coverage policies
4. The specific facts of the particular situation

Coverage policies relate exclusively to the administration of health benefit plans. Coverage policies are not recommendations for treatment and should never be used as treatment guidelines.

This evidence-based medical coverage policy has been developed by EviCore, Inc. Some information in this coverage policy may not apply to all benefit plans administered by Cigna.

These guidelines include procedures EviCore does not review for Cigna. Please refer to the **Cigna CPT code list** for the current list of high-tech imaging procedures that EviCore reviews for Cigna.

Table of Contents

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

General Guidelines (ONC-1)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Abbreviations for Oncology Imaging Guidelines

ON.GG.Abbreviations.A
v2.0.2025

Abbreviations for Oncology Imaging Guidelines	
ACTH	adrenocorticotropic hormone
AFP	alpha-fetoprotein
ALKP	alkaline phosphatase
AP	anteroposterior
betaHCG	beta human chorionic gonadotropin
CA 125	cancer antigen 125 test
CA 19-9	cancer antigen 19-9
CA 15-3	cancer antigen 15-3
CA 27-29	cancer antigen 27-29
CBC	complete blood count
CEA	carcinoembryonic antigen
CNS	central nervous system
CR	complete response
CTA	computed tomography angiography
DCIS	ductal carcinoma in situ
DLBCL	diffuse large B cell lymphomas
DRE	digital rectal exam
EGD	esophagogastroduodenoscopy
ENT	ear, nose, throat
EOT	end of therapy
ERCP	endoscopic retrograde cholangiopancreatography
ESR	erythrocyte sedimentation rate

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Abbreviations for Oncology Imaging Guidelines	
EUA	exam under anesthesia
EUS	endoscopic ultrasound
FDG	fluorodeoxyglucose
FNA	fine needle aspiration
FUO	fever of unknown origin
GE	gastroesophageal
GI	gastrointestinal
GU	genitourinary
GTR	gross total resection
HG	high-grade
HIV	human immunodeficiency disease
HRPC	hormone refractory prostate cancer
hypermet	hypermetabolic
IFRT	involved field radiation therapy
inv	invasive
LAR	low anterior resection
LCIS	lobular carcinoma in situ
LDH	lactate dehydrogenase
LFT	liver function tests
LND	lymph node dissection
MALT	mucosa associated lymphoid tissue
maint	maintenance
MEN	multiple endocrine neoplasia
MG	myasthenia gravis
MGUS	monoclonal gammopathy of unknown significance
MIBG	I-123 metaiodobenzylguanidine scintigraphy
MRA	magnetic resonance angiography

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Abbreviations for Oncology Imaging Guidelines	
MRI	magnetic resonance imaging
MUGA	'multiple gated acquisition' cardiac nuclear scan
MWA	microwave ablation
NaF	sodium fluoride
NET	neuroendocrine tumor
NCCN®	National Comprehensive Cancer Network
NHL	non-Hodgkin's lymphoma
NPC	nasopharyngeal carcinoma
NSABP	National Surgical Adjuvant Breast and Bowel Project
NSAIDS	nonsteroidal anti-inflammatory drugs
NSCLC	non-small cell lung cancer
NSGCT	non-seminomatous germ cell tumor
PA	posteroanterior
PCI	prophylactic cranial irradiation
PET	positron emission tomography
COG	Children's Oncology Group
PSA	prostate specific antigen
RFA	radiofrequency ablation
RPLND	retroperitoneal lymph node dissection
SqCCa	squamous cell carcinoma
SCLC	small cell lung cancer
SIADH	syndrome of inappropriate secretion of antidiuretic hormone
TCC	transitional cell carcinoma
TLH	total laparoscopic hysterectomy
TNM	tumor node metastasis staging system
TSH	thyroid-stimulating hormone
TURBT	trans-urethral resection of bladder tumor

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Abbreviations for Oncology Imaging Guidelines	
VIPoma	vasoactive intestinal polypeptide
WLE	wide local incision
WB-MRI	whole body MRI
WM	Waldenstrom's macroglobulinemia
WBXRT	whole brain radiation therapy

General Guidelines (ONC-1.0)

ON.GG.0001.0.C
v2.0.2025

- A relevant clinical evaluation or meaningful contact (telephone call, electronic mail or messaging) should be performed prior to considering advanced imaging, unless the individual is undergoing guideline-supported scheduled off therapy surveillance evaluation or cancer screening. The clinical evaluation may include a relevant history and physical examination, including biopsy, appropriate laboratory studies, and results of non-advanced or advanced imaging modalities.
- Unless otherwise stated in the disease-specific guideline, a histological confirmation of malignancy (or recurrence) and the stage of disease is required to perform a medical necessity review of the requested imaging.
- Generally, the studies listed in the disease-specific sections reflect the studies supported by current literature and research for that condition. If a study is not listed, then it is not supported.
- Routine imaging of brain, spine, neck, chest, abdomen, pelvis, bones, or other body areas is not indicated except where explicitly stated in a diagnosis-specific guideline section, or if one of the following applies:
  - Known prior disease involving the requested body area
  - New or worsening symptoms or physical exam findings involving the requested body area (including non-specific findings such as ascites or pleural effusion)
  - New finding on basic imaging study such as plain x-ray or ultrasound
  - New finding on adjacent body area CT/MRI study (i.e., pleural effusion observed on CT abdomen)
- Unless otherwise stated in the disease-specific guideline, advanced imaging of asymptomatic individuals is not routinely supported without signs or symptoms of systemic involvement of cancer.
- Repeat imaging studies are not generally necessary unless there is evidence of disease progression, recurrence of disease, and/or the repeat imaging will affect an individual's clinical management.
- Conventional imaging performed prior to diagnosis should not be repeated unless there is a delay of at least 6 weeks since previous imaging and treatment initiation or there are new or significantly worsening clinical signs or symptoms

Phase	Imaging Timeframe
After definitive local therapy of primary tumor (surgery or radiation therapy)	• Follow surveillance guidelines

Phase	Imaging Timeframe
During adjuvant chemotherapy	• Follow surveillance guidelines
After ablative therapy	• See disease-specific guidelines
During chemotherapy or immunotherapy for measurable disease	• Every 2 cycles (generally every 6 to 8 weeks)
During endocrine/hormonal therapy for measurable disease	• Every 3 months (12 weeks)
Measurable metastatic disease being monitored off therapy	• Every 3 months (12 weeks)
Minimal metastatic disease on maintenance therapy	• Every 3 months (12 weeks)
Surveillance for history of metastatic disease with complete response and being observed off-therapy	• Imaging typically not indicated beyond 5 years from completion of treatment for metastatic disease

- Advanced imaging is not indicated for evaluation of in situ or non-invasive cancers or cancer surveillance after complete surgical removal of primary disease unless otherwise stated in the cancer-specific guidelines.
- Advanced imaging is not indicated for monitoring disease in individuals who choose to not receive standard oncologic therapy but may be receiving alternative therapies or palliative care and/or hospice. All advanced imaging indicated for initial staging of the specific cancer type can be approved once when the individual is considering initiation of a standard therapeutic approach (surgery, chemotherapy, or radiation therapy).
- Brain imaging is performed for signs or symptoms of brain disease
  - MRI Brain without and with contrast (CPT® 70553) is the recommended study for evaluation of suspected or known brain metastases. If a non-contrast CT head shows suspicious lesion, MRI brain may be obtained to further characterize the lesion.
  - CT without and with contrast (CPT® 70470) can be approved when MRI is contraindicated or not available, or if there is skull bone involvement.
  - Certain malignancies including, but not limited to melanoma and lung cancer have indications for brain imaging for asymptomatic individuals.

  - If stage IV disease is demonstrated elsewhere or if systemic disease progression is noted, refer to disease specific guidelines.
  - Initiation of angiogenesis therapy is not an indication for advanced imaging of the brain in asymptomatic individuals (Avastin/Bevacizumab; < 3% risk of bleeding and < 1% risk of serious bleeding).
- Bone Scan:
  - Primarily used for evaluation of bone metastases in individuals with solid malignancies.
  - Indications for bone scan in individuals with history of malignancy include – bone pain, rising tumor markers, elevated alkaline phosphatase or in individuals with primary bone tumor.
  - For evaluation of suspected or known bony metastases, CPT® 78306 (Nuclear bone scan whole body), may be approved.
  - Radiopharmaceutical Localization scan SPECT (CPT® 78803 or CPT® 78831) or SPECT/CT (CPT® 78830 or CPT® 78832) may be approved as an add-on test for further evaluation of a specific area of interest.
  - CPT® codes 78300 (Nuclear bone scan limited), 78305 (Nuclear bone scan multiple areas) or 78315 do not have any indications in oncology nuclear medicine imaging.
- Bone scan supplemented by plain x-rays are the initial imaging modalities for suspected malignant bone pain. For specific imaging indications, see also:
  - **Bone (Non-Vertebral) Metastases (ONC-31.5)**
  - **Spinal/Vertebral Metastases (ONC-31.6)**
  - **Carcinoma of Unknown Primary Site (ONC-31.7)**
- Advanced imaging used for radiation therapy treatment planning should not be authorized using any of the diagnostic imaging codes for CT, MRI, or PET.
  - Advanced imaging performed in support of radiation therapy treatment planning should be reported with CPT® 76498 for Unlisted MRI or CPT® 76497 for Unlisted CT scan
- Delay PET/CT for at least 12 weeks after completion of radiation treatment, unless required sooner for imminent surgical resection.
- PET/CT may be considered prior to biopsy in order to determine a more favorable site for biopsy when a prior biopsy was nondiagnostic or a relatively inaccessible site is contemplated which would require invasive surgical intervention for biopsy attempt.
- PET/CT may be indicated if:
  - Conventional imaging (CT, MRI or bone scan) reveals findings that are inconclusive or negative, with continued suspicion for recurrence
- Unless specified in diagnosis-specific guideline section PET/CT Imaging is NOT indicated for:

- infection, inflammation, trauma, post-operative healing, granulomatous disease, rheumatological conditions
- concomitantly with separate diagnostic CT studies
- conclusive evidence of distant or diffuse metastatic disease on recent conventional imaging studies
- metastatic disease in the central nervous system (CNS)
- lesions less than 8 mm in size
- follow up after localized therapy (i.e. radiofrequency ablation, embolization, stereotactic radiation, etc.)
- rare malignancies, due to lack of available evidence regarding the diagnostic accuracy of PET in rare cancers
- surveillance
  - Serial monitoring of individuals who are not currently receiving anti-tumor treatment or are receiving maintenance treatment
  - Serial monitoring of FDG avidity until resolution.
  - PET/CT avidity in a residual mass at the end of planned therapy is not an indication for PET/CT imaging during surveillance.
  - Residual mass that has not changed in size since the last conventional imaging does not justify PET imaging

- Unless otherwise specified for a specific cancer type, once PET has been documented to be negative for a given individual's cancer or all PET-avid disease has been surgically resected, PET should not be used for continued disease monitoring or surveillance.
- PET/MRI is generally not supported by for a vast majority of oncologic conditions due to lack of standardization in imaging technique and interpretation. However, it may be approved select circumstances when the following criteria are met:
  - The individual meets condition-specific guidelines for PET/MRI OR
  - The individual meets ALL of the following:
    - The individual meets guideline criteria for PET/CT, AND
    - PET/CT is not available at the treating institution, AND
    - The provider requests PET/MRI in lieu of PET/CT
  - When the above criteria are met, PET/MRI may be reported using the code combination of PET Whole-Body (CPT® 78813) and MRI Unlisted (CPT® 76498). All other methods of reporting PET/MRI are inappropriate.
    - When clinically appropriate, diagnostic MRI codes may be indicated at the same time as the PET/MRI code combination.
- The specific radiotracer planned to be used with PET/CT imaging is required to perform a medical necessity review. Indications for PET/CT imaging using non-FDG radiotracers are listed in diagnosis-specific guidelines.
  - Supported radiotracers:

    - ^{18}F-FDG
    - ^{68}Ga-DOTATATE (NETSPOT®) for low-grade neuroendocrine tumors and medullary thyroid cancer
    - ^{64}Cu-DOTATATE (DETECTNET®) for low-grade neuroendocrine tumors
    - ^{68}Ga-DOTA-TOC for low-grade neuroendocrine tumors
    - ^{11}C Choline for prostate cancer
    - ^{18}F-Fluciclovine (AXUMIN®) for prostate cancer
    - ^{68}Ga PSMA-11 for prostate cancer
    - ^{18}F Piflufolastat (Pylarify®) for prostate cancer
    - ^{68}Ga Gozetotide (Illuccix® and Locametz®) for prostate cancer
    - ^{18}F Flotufolastat (Posluma®) for prostate cancer
    - ^{18}F Fluoroestradiol (Cerianna®) for breast cancer
    - ^{18}F Na Fluoride PET bone scan for breast cancer and prostate cancer
  - Unsupported radiotracers:
    - PET/CT imaging using isotopes other than those specified above
- Octreotide scan:
  - Specific for low and intermediate grade neuroendocrine tumors which express specific cell surface somatostatin receptors. See cancer specific guidelines for recommended use.
  - One of the following codes may be approved when Octreotide scan is requested:
  - CPT® 78802 (Radiopharmaceutical localization of tumor whole-body single day study)
  - CPT® 78804 (Radiopharmaceutical localization of tumor whole-body two or more days)
  - In addition to one of the above CPT codes, CPT® 78803 (Radiopharmaceutical localization of tumor SPECT), SPECT CPT® 78831, or hybrid SPECT/CT (CPT® 78830 or 78832) may be approved as an add-on test for further evaluation of a specific area of interest.

Clinical Trials

- Similar to investigational and experimental studies, clinical trial imaging requests will be considered to determine whether they meet these evidence-based guidelines.
- Imaging studies which are inconsistent with established clinical standards, or are requested for data collection and not used in direct clinical management are not supported.

Key Principles (ONC-1.1)

ON.GG.001.1.C
v2.0.2025

AGE APPROPRIATE GUIDELINES	
Age of Individual	**Appropriate Imaging Guidelines**
≥18 years old at initial diagnosis	• General Oncology Imaging Guidelines, except where directed otherwise by a specific guideline section
<18 years old at initial diagnosis	• Pediatric and Special Populations Oncology Imaging Guidelines, except where directed otherwise by a specific guideline section
15 to 39 years old at initial diagnosis (defined as Adolescent and Young Adult (AYA) oncology individuals)	• When unique guidelines for a specific cancer type exist only in either General Oncology or Pediatric and Special Populations Oncology, AYA individuals should be imaged according to the guideline section for their specific cancer type, regardless of the individual's age • When unique guidelines for a specific cancer type exist in both General Oncology and Pediatric and Special Populations Oncology, AYA individuals should be imaged according to the age rule in the previous bullet

- Conventional Imaging (mostly CT, sometimes MRI or bone scan) of the affected area(s) drives much of initial and re-staging and surveillance. PET is not indicated for surveillance imaging unless specifically stated in the diagnosis-specific guideline sections.
- Brain imaging is performed for signs or symptoms of brain disease.
  - MRI Brain without and with contrast (CPT® 70553) is the recommended study for evaluation of suspected or known brain metastases.
  - MRI Brain without and with contrast (CPT® 70553) may be obtained if a non-contrast CT Head shows suspicious lesion.
  - CT Head without and with contrast (CPT® 70470) can be approved when MRI is contraindicated or not available, or if there is skull bone involvement.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

  - Initiation of angiogenesis therapy is not an indication for advanced imaging of the brain in asymptomatic individuals (Avastin/bevacizumab; <3% risk of bleeding and <1% risk of serious bleeding).
- Individuals receiving cardiotoxic chemotherapy (such as doxorubicin, trastuzumab, pertuzumab, mitoxantrone, etc.) may undergo cardiac evaluation - at baseline and for monitoring while on active therapy.
  - Echocardiography (CPT® 93306, CPT® 93307, or CPT® 93308) rather than MUGA scan for determination of LVEF and/or wall motion
    - MUGA Scan may be performed instead of ECHO in individuals who have a low LV ejection fraction of <50% on a prior ECHO or MUGA, pre-existing left ventricular wall motion abnormalities from ischemic or non-ischemic cardiomyopathies, congestive heart failure or when ECHO is technically limited and prevents accurate assessment of LV function.
    - A prior MUGA is not a reason to approve another MUGA (it is not necessary to compare LVEF by the same modality).
  - The timeframe for monitoring the ejection fraction should be determined by the provider but no more often than baseline and at every 6 weeks.
  - May repeat every 4 weeks if cardiotoxic chemotherapeutic drug is withheld for significant left ventricular cardiac dysfunction.
  - See: **Oncologic Indications for Cancer Therapeutics-Related Cardiac Dysfunction (CTRCD) (CD-12.1)** in the Cardiology Imaging Guidelines
- CTA or MRA of a specific anatomic region is indicated when requested for surgical planning when there is suspected vascular proximity to proposed resection margin
- Adults (≥18 years) with a diagnosis of Li-Fraumeni Syndrome (LFS) may be screened for malignancy with a Whole-Body MRI (CPT® 76498) on an annual basis. Annual Brain MRI (CPT® 70553) may be performed as part of Whole-Body MRI or as a separate exam. Due to lack of standardization of technique, interpretation, and availability of Whole-Body MRI, individuals with LFS are encouraged to participate in clinical trials.

Use of Contrast

- CT imaging should be performed with contrast for known or suspected body regions, unless contraindicated.
  - Shellfish allergy is not a contraindication to contrast
  - For iodinated contrast dye allergy, either CT scans without contrast or MRI scan without and with contrast are indicated.
  - If CT scanning is considered strongly indicated in an individual with known contrast allergy, CT with contrast may be considered to be safely performed following prednisone premedication over a 24-hour period prior to the study.
- Severe renal insufficiency, i.e. an eGFR less than 30, is a contraindication for an MRI using a gadolinium-based contrast agent (GBCA). In individuals with eGFR

greater than 40, GBCA administration can be safely performed. GBCA administered to individuals with acute kidney injury or severe chronic kidney disease can result in a syndrome of nephrogenic systemic fibrosis (NSF), but GBCAs are not considered nephrotoxic at dosages approved for MRI.

- Gadolinium deposition has been found in individuals with normal renal function following the use of gadolinium based contrast agents (GBCAs).
  - The U.S. Food and Drug Administration (FDA) is investigating the risk of brain deposits following repeated use of GBCAs.
  - The FDA has noted that, “It is unknown whether these gadolinium deposits are harmful or can lead to adverse health effects.” and have recommended:
    - To reduce the potential for gadolinium accumulation, health care professionals should consider limiting GBCA use to clinical circumstances in which the additional information provided by the contrast is necessary.
    - Health care professionals are also urged to reassess the necessity of repetitive GBCA MRIs in established treatment protocols

Radiation Exposure

The use of MRI in place of CT scans to reduce risk of secondary malignancy from radiation exposure during CT is not supported by the peer-reviewed literature. Unless otherwise specified in the Guidelines, MRI in place of CT scans for this purpose alone is not indicated. In some instances (i.e., testicular cancer surveillance), MRI may be considered inferior to CT scans.

Phases of Oncology Imaging and General Phase-Related Considerations (ONC-1.2)

ON.GG.0001.2.A
v2.0.2025

Phases of Oncology Imaging	Definition
Screening	Imaging requested for individuals at increased risk for a particular cancer in the absence of known clinical signs or symptoms
Suspected Diagnosis	Imaging requested to evaluate a suspicion of cancer, prior to histological confirmation
Initial work-up and Staging	Imaging requested after biopsy confirmation and prior to starting specific treatment
Treatment response or Interim Restaging	Imaging performed during active treatment with chemotherapy, targeted therapy, immunotherapy, or endocrine therapy
Restaging of locally treated lesions	Imaging performed to evaluate primary or metastatic lesions with ablation using cryoablation, radiofrequency, radioactive isotope, microwave or chemotherapy
Restaging / Suspected Recurrence	Imaging requested when there is suspicion for progression or recurrence of known cancer based on clinical signs/symptoms, laboratory tests or basic imaging studies
Surveillance	Imaging performed in individuals who: • Are asymptomatic or have chronic stable symptoms, and • Have no clinical suspicion of change in disease status, and • Are not receiving active anti-tumor treatment or are receiving maintenance treatment

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

General Phase-Related Considerations

- Conventional imaging performed prior to diagnosis should not be repeated unless there is a delay of at least 6 weeks since previous imaging and treatment initiation or there are new or significantly worsening clinical signs or symptoms.

Phase	Imaging Timeframe
After definitive local therapy of primary tumor (surgery or radiation therapy)	• Follow surveillance guidelines
During adjuvant chemotherapy or endocrine therapy	• Follow surveillance guidelines
After ablative therapy	• See disease-specific guidelines
During chemotherapy or immunotherapy for measurable disease	• Every 2 cycles (generally every 6 to 8 weeks)
During endocrine/hormonal therapy for measurable disease	• Every 3 months (12 weeks)
Metastatic disease on maintenance therapy	• Every 3 months (12 weeks)
Measurable metastatic disease being monitored off therapy	• Every 3 months (12 weeks) for up to 5 years after completion of treatment for metastatic disease

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

PET Imaging in Oncology (ONC-1.4)

ON.GG.0001.4.C
v2.0.2025

- CPT codes:
  - PET Imaging in oncology should use PET/CT fusion (CPT® 78815 or CPT® 78816). Unbundling PET/CT imaging into separate PET and diagnostic CT codes is otherwise not supported
  - "Limited area" protocol is done infrequently, but may be considered, and is reported with PET (CPT® 78811) or for PET/CT (CPT® 78814).
- Radiotracers:
  - Unless specified otherwise, the term "PET" refers to ^{18}F-FDG-PET and PET/CT fusion studies
  - Indications for PET/CT imaging using non-FDG radiotracers are listed in diagnosis-specific guidelines. The indications may be as follows:
- Supported radiotracers:
  - ^{18}F-FDG
  - ^{68}Ga-DOTATATE (NETSPOT®) for low-grade neuroendocrine tumors and medullary thyroid cancer
  - ^{64}Cu-DOTATATE (DETECTNET®) for low-grade neuroendocrine tumors
  - ^{68}Ga-DOTA-TOC for low-grade neuroendocrine tumors
  - ^{11}C Choline for prostate cancer
  - ^{18}F-Fluciclovine (AXUMIN®) for prostate cancer
  - ^{68}Ga PSMA-11 for prostate cancer
  - ^{18}F Piflufolastat (Pylarify®) for prostate cancer
  - ^{68}Ga Gozetotide (Illuccix® and Locametz®) for prostate cancer
  - ^{18}F Flotufolastat (Posluma®) for prostate cancer
  - ^{18}F Fluoroestradiol (Cerianna®) for breast cancer
  - ^{18}F Na Fluoride PET bone scan for breast cancer and prostate cancer
- Unsupported radiotracers:
  - PET/CT imaging using isotopes other than those specified above

CPT/ HCPCS Code	Code Description	Brand or common name	Guideline Section and Cancer Type
A9552	^{18}F Fluoro deoxyglucose	FDG	Various guideline sections where PET is indicated

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

CPT/ HCPCS Code	Code Description	Brand or common name	Guideline Section and Cancer Type
A9580	^{18}F Sodium fluoride	N/A	ONC-11: Breast Cancer, ONC-19: Prostate Cancer
A9587	^{68}Ga-68 Dotatate	NETSPOT®	ONC-15: Low-grade neuroendocrine tumors, ONC-6: Medullary thyroid cancer
A9515	^{11}C Choline	N/A	ONC-19, Prostate Cancer
A9588	^{18}F-Fluciclovine	AXUMIN®	ONC-19, Prostate Cancer
A9593 A9594	^{68}Ga PSMA-11	N/A	ONC-19, Prostate Cancer
A9595	^{18}F Piflufolastat	Pylarify®	ONC-19, Prostate Cancer
A9596	^{68}Ga Gozetotide	Illuccix®	ONC-19, Prostate Cancer
A9800	^{68}Ga Gozetotide	Locametz®	ONC-19, Prostate Cancer
A9608	^{18}F Flotufolastat	Posluma®	ONC-19, Prostate Cancer
A9591	^{18}F Fluoroestradiol	Cerianna®	ONC-11, Breast Cancer
A9592	^{64}Cu Copper dotatate	Detectnet®	ONC-15, Low-grade neuroendocrine tumors
C9067	^{68}Ga Gallium-DOTA-TOC	N/A	ONC-15, Low-grade neuroendocrine tumors

- Unless specified in diagnosis-specific guideline section PET/CT Imaging is not indicated for:
  - infection, inflammation, trauma, post-operative healing, granulomatous disease, rheumatologic conditions
  - concomitantly with separate diagnostic CT studies

- conclusive evidence of distant or diffuse metastatic disease on recent conventional imaging studies
- metastatic disease in the central nervous system (CNS)
- lesions less than 8 mm in size
- follow up after localized therapy (i.e. radiofrequency ablation, embolization, stereotactic radiation, etc.)
- rare malignancies, due to lack of available evidence regarding the diagnostic accuracy of PET in rare cancers
- surveillance:
  - Serial monitoring of individuals who are not currently receiving anti-tumor treatment or are receiving maintenance treatment
  - Serial monitoring of FDG avidity until resolution.
  - PET/CT avidity in a residual mass at the end of planned therapy is not an indication for PET/CT imaging during surveillance.
  - Residual mass that has not changed in size since the last conventional imaging does not justify PET imaging
- Unless otherwise specified for a specific cancer type, once PET has been documented to be negative for a given individual's cancer or all PET-avid disease has been surgically resected, PET should not be used for continued disease monitoring or surveillance.

- PET/CT may be indicated if:
  - Conventional imaging (CT, MRI or bone scan) reveals findings that are inconclusive or negative, with continued suspicion for recurrence
  - The individual is undergoing salvage treatment for a recurrent solid tumor with residual measurable disease on conventional imaging and confirmed repeat negative PET imaging will allow the individual to transition from active treatment to surveillance
  - PET/CT may be considered prior to biopsy in order to determine a more favorable site for biopsy when a prior biopsy was nondiagnostic or a relatively inaccessible site is contemplated which would require invasive surgical intervention for biopsy attempt
- PET/CT for rare malignancies is not covered by these guidelines due to lack of available evidence regarding diagnostic accuracy of PET/CT in the majority of rare cancers. Conventional imaging studies should be used for initial staging and treatment response for these diagnoses. PET/CT can be approved if all of the following apply:
  - Conventional imaging (CT, MRI or bone scan) reveals equivocal or suspicious findings.
  - No other specific metabolic imaging (MIBG, octreotide, technetium, etc.) is appropriate for the disease type.

  - The submitted clinical information describes a specific decision regarding the individual's care that will be made based on the PET/CT results.
- Delay PET/CT for at least 12 weeks after completion of radiation treatment, unless required sooner for imminent surgical resection.
- PET mammography (PEM, generally reported with CPT® 78811) is considered experimental and investigational at this time.
- PET/MRI is generally not supported for a vast majority of oncologic conditions due to lack of standardization in imaging technique and interpretation. However, it may be approved in select circumstances when the following criteria are met:
  - The individual meets condition-specific guidelines for PET/MRI OR
  - The individual meets ALL of the following:
    - The individual meets guideline criteria for PET/CT, AND
    - PET/CT is not available at the treating institution, AND
    - The provider requests PET/MRI in lieu of PET/CT
  - When the above criteria are met, PET/MRI may be reported using the code combination of PET Whole-Body (CPT® 78813) and MRI Unlisted (CPT® 76498). All other methods of reporting PET/MRI are inappropriate.
    - When clinically appropriate, diagnostic MRI codes may be indicated at the same time as the PET/MRI code combination.

Unlisted Procedure Codes in Oncology (ONC-1.5)

ON.GG.0001.5.C

v2.0.2025

- There is often no unique procedure code for a service performed solely for treatment planning purposes. AMA instructions in the CPT state that if no specific code exists for a particular service, the service is reported with an unlisted code.
- Advanced imaging being used for radiation therapy treatment planning should not be authorized using any of the diagnostic imaging codes for CT, MRI or PET. Advanced imaging performed in support of radiation therapy treatment planning should be reported with:
  - **CPT® 76498 for Unlisted MRI** – when MRI will be used for treatment planning of radiation therapy to be delivered ONLY to the brain, prostate and cervix. The use of this code for radiation treatment planning of any other cancers/body parts not listed above may be reviewed on a case-by-case basis.
  - **CPT® 76497 for Unlisted CT**– may NOT be used for radiation treatment planning. CT imaging performed in support of radiation therapy treatment planning is bundled in with the concurrent radiation treatment authorization codes and a separate authorization for treatment planning is not required.
  - Imaging associated with image-directed biopsy should be reported with the corresponding interventional codes.
  - For advanced imaging used solely for the purpose of Surgical planning, see: **Unlisted Procedures/Therapy treatment planning (Preface-4.3)** in the Preface Imaging Guidelines.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Predisposition Syndromes (ONC-1.6)

ON.GG.0001.6.A

v2.0.2025

- For predisposition syndrome screening in adult individuals, see: **Screening Imaging in Cancer Predisposition Syndromes (PEDONC-2)** in the Pediatric Oncology Imaging Guidelines

References (ONC-1)

v2.0.2025

1. ACR Committee on Drugs and Contrast Media. *ACR Manual on Contrast Media, version 10.3*. Reston, VA: American College of Radiology; 2018.
2. The American College of Radiology. *Practice parameter for the performance of skeletal scintigraphy (bone scan)*. Rev. 2017.
3. The American College of Radiology. *Practice parameter for performing FDG-PET/CT in oncology.* Rev. 2016.
4. The American College of Radiology. *Practice parameter for the performance of tumor scintigraphy with gamma cameras)*. Rev. 2015.
5. Erdi YE. Limits of tumor detectability in nuclear medicine and PET. *Mol Imaging Radionucl Ther.* 2012;21(1):23-28. doi:10.4274/Mirt.128.
6. Hapani S, Sher A, Chu D, Wu S. Increased risk of serious hemorrhage with bevacizumab in cancer patients: a meta-analysis. *Oncology*. 2010;79(1):27-38. doi:10.1159/000314980.
7. ACR Appropriateness Criteria. *Pretreatment planning of Invasive cancer of Cervix*. Rev. 2015.
8. ACR Appropriateness Criteria. *External Beam Radiation therapy treatment planning for clinically localized prostate cancer.* Rev. 2016.
9. Metcalfe P, Liney GP, Holloway L, et al. The potential for an enhanced role for MRI in radiation-therapy treatment planning. *Technol Cancer Res Treat*. 2013;12(5):429-46. doi:10.7785/tcrt.2012.500342.
10. Daly MB, Pal T, AlHilli Z, et. al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – November 7, 2024, Genetic/Familial High Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate available at: https://www.nccn.org/professionals/physician_gls/pdf/bopp.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Genetic/Familial High Risk Assessment: Breast and Ovarian V2.2025 – November 7, 2024 ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
11. Coverage of Clinical Trials under the Patient Protection and Affordable Care Act; 42 U.S.C.A. § 300gg-8.
12. Bergsland E, Goldner WS, Benson III AB, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – January 17, 2025. Neuroendocrine and Adrenal Tumors, available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Neuroendocrine and Adrenal Tumors V4.2024 – January 17, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
13. ASCO. (2021). Choosing Wisely. Retrieved from https://old-prod.asco.org/news-initiatives/current-initiatives/cancer-care-initiatives/value-cancer-care/choosing-wisely.

Primary Central Nervous System Tumors (ONC-2)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Primary Central Nervous System Tumors – General Considerations (ONC-2.1)

ON.CN.0002.1.C
v2.0.2025

- This guideline section applies to primary CNS tumors only. For imaging guidelines in metastatic brain cancer, see the appropriate diagnosis-specific section or **Brain Metastases (ONC-31.3)** for imaging guidelines.
- Primary brain tumors presenting only with uncomplicated headache are very uncommon. Most primary brain tumors present with specific CNS symptoms.
- Histologic confirmation is critical. Therapeutic decisions should not be made on radiographic findings alone, except for ANY of the following:
  - Medically fragile individuals for whom attempted biopsy carries excess medical risk, as stated in writing by both the attending physician and surgeon.
  - Brain stem tumors or other sites where the imaging findings are pathognomonic and the risk of permanent neurological damage is excessive with even a limited biopsy attempt
- For evaluation of known or suspected spinal cord compromise, see: **Spinal/Vertebral Metastases (ONC-31.6)**
- For suspected brain tumors in neurofibromatosis, see: **Screening Imaging in Cancer Predisposition Syndromes (PEDONC-2)** in the Pediatric Oncology Imaging Guidelines
- Rare tumors occurring more commonly in the pediatric population should be imaged according to the imaging guidelines in: **Pediatric Central Nervous System Tumors (PEDONC-4)** in the Pediatric Oncology Imaging Guidelines.

Indication	Imaging Study
Characterization and follow up of all brain tumors	• MRI Brain without and with contrast (CPT® 70553) • CT Head without and with contrast (CPT® 70470) can be approved when MRI is contraindicated or not available, or there is skull bone involvement • CT Head (contrast as requested) can be approved for preoperative planning when requested by the operating surgeon

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Preoperative planning or to clarify inconclusive findings on MRI or CT	• MRA Head (CPT® 70544) or CTA Head (CPT® 70496)
Within 24 to 72 hours following brain tumor surgery	• MRI Brain without and with contrast (CPT® 70553)
Clinical deterioration or development of new neurological features	• MRI Brain without and with contrast (CPT® 70553) • MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) for signs/symptoms of spinal involvement or if spinal involvement is suspected

MR Spectroscopy in Brain Tumors (MRS, CPT® 76390)

- MRS is only supported for use in brain tumors of specified histologies where diagnostic accuracy has been established in peer-reviewed literature.
  - See diagnosis-specific guidelines for MRS indications
- MRS is considered not medically necessary for all other histologies and indications not listed in a diagnosis-specific guideline section.

PET Brain Imaging (CPT® 78608 and CPT® 78609)

- PET Brain Metabolic Imaging (CPT® 78608) is considered not medically necessary for all other histologies and indications not listed in a diagnosis-specific guideline section.
- PET Brain Perfusion Imaging (CPT® 78609) is not indicated in the evaluation or management of primary CNS tumors.
- Body PET studies (CPT® 78811, CPT® 78812, and CPT® 78813) and fusion PET/CT studies (CPT® 78814, CPT® 78815, or CPT® 78816) are not indicated in the evaluation or management of primary CNS tumors.
- See: **Other Imaging Studies (HD-24)** in the Head Imaging Guidelines for details on other advanced neuro-imaging studies.

Evidence Discussion

Primary central nervous system tumors account for 1.4% of all new cancer diagnoses in the United States and 2.7% of deaths due to cancer. Primary central nervous system tumors develop within any region of the brain. Utilizing the WHO classification of tumors, Low grade tumors (WHO I, II) are the most common primary brain tumors. (71.7% of all

tumors). High grade tumors (WHO II/IV) account for 28.3% of all tumors. Meningioma is the most common low grade tumor accounting for 39.7% of all tumors. Glioblastoma is the most common malignant glioma accounting for 15.4% of all tumors. The most recent classification of these tumors is based on histology and on molecular diagnostics.

The primary imaging modality for the evaluation of primary brain tumors is an MRI Brain and Spine (with and without contrast). The standard MRI protocol minimally includes T1 and T2, fluid-attenuated inversion recovery (FLAIR), gradient-echo/ susceptibility, diffusion-weighted imaging, and post contrast T1-weighted images to characterize the tumor. MRI provides much better characterization of intracranial parenchymal tumors in comparison to CT. MRI is more sensitive in detecting lesions in the posterior fossa and in evaluation of leptomeningeal spread of tumor. CT imaging (with and/or without contrast) is valuable in the emergent scenario to assist in initial description of the disease. CT imaging of brain and spine should be used in patients with a contraindication for use of MRI (those with metallic implants or those who experience claustrophobia). If there is bone involvement, CT imaging may be included with MRI for disease assessment.

Advanced imaging modalities may be included to complement standard imaging to further characterize tumors and assist in treatment decisions. MRI perfusion measures blood flow in the tumor and can be useful in differentiating viable tumor versus radiation necrosis, in determining tumor grade and in determining optimal site for biopsy. MR Spectroscopy involves analysis of the levels of certain chemicals in pre-selected voxels (small regions) on an MRI scan done at the same time. MR spectroscopy may be useful in defining grade of tumor or differentiate viable tumor from radiation necrosis. The use of MR spectroscopy is limited to specific histologies based on peer-reviewed literature. A major limitation of both modalities is the added imaging time. Brain FDG-PET imaging may also be considered to differentiate viable tumor versus radiation necrosis, to determine optimal biopsy site and to determine tumor grade. The use of Brain FDG-PET imaging is limited to specific histologies based on peer-reviewed literature.

Low Grade Gliomas (ONC-2.2)

ON.CN.0002.2.A
v2.0.2025

- These tumors are defined as having a WHO histologic grade of I or II (out of IV), can occur anywhere in the CNS, and includes the following tumors:
  - Pilocytic Astrocytoma
  - Fibrillary (or Diffuse) Astrocytoma
  - Optic Pathway Gliomas
  - Pilomyxoid Astrocytoma
  - Oligodendroglioma
  - Oligoastrocytoma
  - Oligodendrocytoma
  - Subependymal Giant Cell Astrocytoma (SEGA)
  - Ganglioglioma
  - Gangliocytoma
  - Dysembryoplastic infantile astrocytoma (DIA)
  - Dysembryoplastic infantile ganglioglioma (DIG)
  - Dysembryoplastic neuroepithelial tumor (DNT)
  - Tectal plate gliomas
  - Cervicomedullary gliomas
  - Pleomorphic xanthoastrocytoma (PXA)
  - Any other glial tumor with a WHO grade of I or II

Indication	Imaging Study
Initial Staging	• MRI Brain without and with contrast (CPT® 70553) if not already done • MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) ◦ MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) can be approved if being performed immediately following a contrast-enhanced MRI Brain

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
After initial resection or other treatment (radiation therapy, etc.)	• MRI Brain without and with contrast (CPT® 70553)
For individuals undergoing chemotherapy treatment	• MRI Brain without and with contrast (CPT® 70553) every 2 cycles • Individuals with spinal cord involvement at diagnosis can have MRI without and with contrast of the involved spinal region on the same schedule as MRI brain
ONE of the following: • Determine need for biopsy when transformation to high-grade glioma is suspected based on clinical symptoms or recent MRI findings • Evaluate a brain lesion of indeterminate nature when the study will be used to determine whether biopsy/resection can be safely postponed	ANY of the following: • PET Brain Metabolic Imaging (CPT® 78608) • MRI Perfusion imaging (CPT® 70553)
ONE of the following: • Distinguish low-grade from high-grade gliomas • Evaluate a brain lesion of indeterminate nature when the study will be used to determine whether biopsy/resection can be safely postponed • Distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy	ANY of the following: • MR Spectroscopy (CPT® 76390) • MRI Perfusion imaging (CPT® 70553)
Suspected intracranial or intraspinal recurrence	• All imaging supported for initial staging may be repeated

Indication	Imaging Study
Surveillance, grade I	• MRI Brain without and with contrast (CPT® 70553) every 3 months for up to 5 years • Individuals with spinal cord involvement at diagnosis can have MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) on the same schedule as MRI Brain
Surveillance, grade II (not poor performance status as defined below)	• MRI Brain without and with contrast (CPT® 70553) every 3 months for 5 years, then every 6 months thereafter • Individuals with spinal cord involvement at diagnosis can have MRI Spine without and with contrast (Cervical- CPT® 72156, Thoracic- CPT® 72157, Lumbar- CPT® 72158) on the same schedule as MRI Brain
Surveillance, grade II and poor performance status (Karnofsky Performance Score <60)	• MRI Brain without and with contrast (CPT® 70553) every 2 months for 3 years, then every 3 months thereafter • Individuals with spinal cord involvement at diagnosis can have MRI Spine without and with contrast (Cervical- CPT® 72156, Thoracic- CPT® 72157, Lumbar- CPT® 72158) on the same schedule as MRI Brain

Evidence Discussion

The primary brain tumors classified as low grade gliomas are listed in the guideline. Initial staging in low grade glioma includes both MRI Brain as well as MRI Whole Spine. Whole spine MRI imaging is indicated for initial staging as the finding of spinal metastases, leptomeningeal disease will impact prognosis, and treatment approaches. MRI studies should be completed both without and with gadolinium contrast. However, MRI Spine with contrast only can be approved if being performed immediately following a contrast-enhanced MRI Brain for patient-centricity to limit time in the MRI machine if requested since the non-contrast component is less essential for the evaluation of spine. MRI imaging is completed after initial resection or radiation to establish a new

baseline for disease monitoring. If intracranial or intraspinal recurrence is suspected or documented, MRI imaging that was completed for initial staging is repeated.

In patients undergoing active therapy, MRI imaging may be repeated after every 2 cycles of therapy for disease assessment. If there is spine involvement, MRI Spine of the involved spinal region can be included on this same schedule.

Advanced imaging modalities such as MRI perfusion imaging, MR Spectroscopy and/or PET Brain Metabolic Imaging used in conjunction with standard MRI imaging can be performed to characterize non-invasively changes in the tumor not noted on standard MRI or as problem solving tools with inconclusive findings on MRI imaging. Results of these advanced imaging modalities may be the basis to pursue additional treatment and/or surgical intervention; to define transition of the tumor to a higher grade or to distinguish between radiation-induced radiation necrosis and progressive disease within 18 months of completing radiation therapy.

Surveillance imaging is conducted at a frequency and interval based on published standards noted in the NCCN guidelines. Individuals with poor performance status require more frequent imaging than others because of their higher risk for complications or recurrence (NCCN, 2024). More frequent imaging may be done as clinically indicated by the treating physician, in the event of clinical changes such as development of seizures or neurologic deterioration that are suspicious for disease progression.

High Grade Gliomas (ONC-2.3)

ON.CN.0002.3.A
v2.0.2025

- These tumors are defined as having a WHO histologic grade of III or IV (out of IV can occur anywhere in the CNS (though the majority occur in the brain), and include the following tumors:
  - Anaplastic astrocytoma
  - Glioblastoma multiforme
  - Diffuse intrinsic pontine glioma (DIPG, or “brainstem glioma”)
  - Gliomatosis cerebri
  - Gliosarcoma
  - Anaplastic oligodendroglioma
  - Anaplastic ganglioglioma
  - Anaplastic mixed glioma
  - Anaplastic mixed ganglioneuronal tumors
  - Any other glial tumor with a WHO grade of III or IV

Indication	Imaging Study
Initial Staging	• MRI Brain without and with contrast (CPT® 70553) if not already done • MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) ◦ MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) can be approved if being performed immediately following a contrast-enhanced MRI Brain
Immediately following partial or complete resection	• MRI Brain without and with contrast (CPT® 70553)
Immediately following radiation therapy (XRT)	• MRI Brain without and with contrast (CPT® 70553) once within 2 to 8 weeks following completion of treatment, and then go to surveillance imaging

Indication	Imaging Study
For individuals undergoing chemotherapy treatment	• MRI Brain without and with contrast (CPT® 70553) every 2 cycles • Individuals with spinal cord involvement at diagnosis can have MRI without and with contrast of the involved spinal region on the same schedule as MRI Brain
ONE of the following: • Distinguish low-grade from high-grade gliomas • Evaluate a brain lesion of indeterminate nature when the study will be used to determine whether biopsy/resection can be safely postponed • Distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy	ANY of the following: • MR Spectroscopy (CPT® 76390) • MRI Perfusion imaging (CPT® 70553)
ONE of the following: • Distinguish radiation-induced tumor necrosis from progressive disease • Evaluate inconclusive MRI findings when the study will be used to determine need for biopsy or change in therapy, including a change from active therapy to surveillance • Evaluate a brain lesion of indeterminate nature when the study will be used to determine whether biopsy/resection can be safely postponed	ANY of the following: • MRI Perfusion imaging (CPT® 70553) • PET Brain metabolic imaging (CPT® 78608) ◦ PET Brain is not indicated in gliomas occurring in the brain stem due to poor uptake and lack of impact on individual outcomes
Suspected intracranial or intraspinal recurrence	• All imaging supported for initial staging may be repeated

Indication	Imaging Study
Surveillance	• MRI Brain without and with contrast (CPT® 70553) every 2 months for 3 years and every 3 months thereafter • Individuals with spinal cord involvement at diagnosis can have MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) on the same schedule as MRI Brain

Evidence Discussion

The primary brain tumors classified as high grade gliomas are listed in the guideline. Initial staging in high grade glioma includes both MRI Brain as well as MRI Whole spine. Whole spine MRI imaging is indicated for initial staging as the finding of spinal metastases and leptomeningeal disease will impact prognosis and treatment approaches. MRI studies should be completed both without and with gadolinium contrast. However, MRI Spine with contrast only can be approved if being performed immediately following a contrast-enhanced MRI Brain for patient-centricity to limit time in the MRI machine if requested, since the non-contrast component is less essential for the evaluation of spine. MRI imaging is indicated after initial resection or radiation to establish a new baseline for disease monitoring. If intracranial or intraspinal recurrence is suspected or documented, MRI imaging that was completed for initial staging is repeated.

In patients undergoing active therapy, MRI imaging may be repeated after every 2 cycles of therapy for disease assessment. If there is spine involvement, MRI spine of the involved spinal region can be included on this same schedule.

Advanced imaging modalities such as MRI perfusion imaging, MR Spectroscopy and/or PET Brain Metabolic Imaging used in conjunction with standard MRI imaging can be performed as problem solving tools to characterize non-invasively changes in the tumor noted on standard MRI. Results of these advanced imaging modalities may be the basis to pursue additional treatment and/or surgical intervention; to distinguish low-grade from high-grade gliomas; to distinguish between radiation-induced radiation necrosis and progressive disease within 18 months of completing radiation therapy.

Surveillance imaging is conducted at a frequency and interval based on published standards noted in the NCCN guidelines. More frequent imaging may be done as clinically indicated by the treating physician, in the event of a clinical change such as development of seizures or neurologic deterioration that is suspicious for disease progression.

Medulloblastoma and Supratentorial Primitive Neuroectodermal Tumors (sPNET) (ONC-2.4)

ON.CN.0002.4.A

v2.0.2025

- Medulloblastoma and sPNET imaging indications in adult individuals are identical to those for pediatric individuals. See: **Medulloblastoma (MDB), Supratentorial Primitive Neuroectodermal Tumors (sPNET), and Pineoblastoma (PEDONC-4.4)** in the Pediatric Oncology Imaging Guidelines.

Ependymoma (ONC-2.5)

ON.CN.0002.5.A

v2.0.2025

- Ependymoma imaging indications in adult individuals are identical to those for pediatric individuals. See: **Ependymoma (PEDONC-4.8)** in the Pediatric Oncology Imaging Guidelines.

Central Nervous System Germ Cell Tumors (ONC-2.6)

ON.CN.0002.6.A

v2.0.2025

- Central nervous system germ cell tumor imaging indications in adult individuals are identical to those for pediatric individuals. See: **CNS Germinomas and Non-Germinomatous Germ Cell Tumors (NGGCT) (PEDONC-4.7)** in the Pediatric Oncology Imaging Guidelines.

CNS Lymphoma (Also Known as Microglioma) (ONC-2.7)

ON.CN.0002.7.A
v2.0.2025

Indication	Imaging Study
Initial Staging	ALL of the following are indicated: • MRI Brain without and with contrast (CPT® 70553) • MRI Cervical Spine without and with contrast (CPT® 72156) • MRI Thoracic Spine without and with contrast (CPT® 72157) • MRI Lumbar Spine without and with contrast (CPT® 72158)
Extra-neural evaluation to confirm CNS primary *Individuals with CNS Lymphoma that is metastatic should be imaged according to: • **Non-Hodgkin Lymphomas (ONC-27)** for individuals age ≥18 years • **Pediatric Aggressive Mature B-Cell Non-Hodgkin Lymphomas (NHL) (PEDONC-5.3)** in the Pediatric Oncology Imaging Guidelines for individuals age ≤17 years	ANY or ALL of the following are indicated: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • PET/CT (CPT® 78815) can be approved for evaluation of inconclusive findings on CT imaging
Treatment Response	• MRI without and with contrast of all positive disease sites every 2 cycles
Suspected intracranial or intraspinal recurrence	• All imaging supported for initial staging may be repeated

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Surveillance	• MRI without and with contrast of all positive disease sites every 3 months for 2 years, then every 6 months for 3 years, then annually thereafter

Evidence Discussion

Primary central nervous system lymphoma is an aggressive non-Hodgkin lymphoma that can occur in any location within the intracranial neuraxis (brain, spine, cranial nerves, and leptomeninges). This malignancy can occur in immunocompromised patients or immunocompetent patients and represents approximately 4% of all intracranial malignancies. Individuals may present with focal neurological deficits or nonspecific neurological findings depending on the specific location of tumor involvement.

For initial staging, MRI Brain without and with contrast and whole spine imaging without and with gadolinium contrast are indicated. CNS lymphoma has potential to spread throughout the intracranial neuraxis. For confirmation as a primary central nervous system lymphoma, extra neural evaluation is indicated and follows the ONC-27 Non-Hodgkin Lymphoma Guideline. This evaluation includes CT Chest with contrast and CT Abdomen and Pelvis with contrast. FDG PET/CT can be approved if extra-neural CT imaging is inconclusive. Evaluation of treatment response can be assessed after every 2 cycles of treatment with MRI without and with contrast of all positive disease sites. All imaging obtained for initial staging is repeated for suspected disease recurrence to evaluate for metastatic disease. Surveillance imaging includes MRI Brain without and with of all positive disease sites on a schedule outlined in the guideline.

Meningiomas (Intracranial and Intraspinal) (ONC-2.8)

ON.CN.0002.8.A
v2.0.2025

Indication	Imaging Study
Initial Staging of Intracranial Meningioma	ANY or ALL of the following are indicated: • MRI Brain without and with contrast (CPT® 70553) • CT Head (contrast as requested)
Initial staging of Intraspinal Meningioma	ONE of the following: • MRI without and with contrast of appropriate spinal region (Cervical CPT® 72156, Thoracic CPT® 72157, and Lumbar CPT® 72158) OR • CT without and with contrast of the appropriate spinal region (Cervical CPT® 72127, Thoracic CPT® 72130, and Lumbar CPT® 72133)
Inconclusive MRI or CT and further imaging is needed to confirm diagnosis	• Dotatate PET/CT Brain (CPT® 78814)
Treatment Response	• MRI without and with contrast of all positive disease sites every 2 cycles
Suspected recurrence of intracranial or intraspinal disease	• All imaging supported for initial staging may be repeated
Suspected recurrence with inconclusive findings on MRI	Any ONE of the following studies: • Octreotide SPECT Brain (CPT® 78803) • Octreotide SPECT/CT Brain (CPT® 78830) • Dotatate PET/CT Brain (CPT® 78814)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Surveillance for Grade I (low-grade) and Grade II (atypical) intracranial meningioma (completely resected, partially resected, and unresected)	• MRI Brain without and with contrast (CPT® 70553) at 3, 6, and 12 months, then annually for 5 years ◦ Imaging beyond 5 years is only indicated for evaluation of new signs or symptoms
Surveillance for Grade I (low-grade) and Grade II (atypical) intraspinal meningioma (completely resected, partially resected, and unresected)	ONE of the following at 3, 6, and 12 months, and then every 6 months for 5 years: • MRI without and with contrast (CPT® 72156 [Cervical spine], CPT® 72157 [Thoracic spine], CPT® 72158 [Lumbar spine]) of the involved spinal level OR • CT without and with contrast (CPT® 72127 [Cervical spine], CPT® 72130 [Thoracic spine], CPT® 72133 [Lumbar spine]) of the involved spinal level • Imaging beyond 5 years is only indicated for evaluation of new signs or symptoms
Surveillance for Grade III (malignant or anaplastic) Meningioma	• Intracranial Meningioma: MRI Brain without and with contrast (CPT® 70553) every 2 months for 3 years, and then every 3 months thereafter • Intraspinal Meningioma: MRI or CT without and with contrast of the involved spinal region every 2 months for 3 years and then every 3 months thereafter

Evidence Discussion

Meningiomas are the most frequent primary central nervous system tumors, accounting for approximately 34% of all primary brain and spine tumors. Meningiomas are extra-axial, dural-based tumors that are derived from the dura and occur throughout the neuroaxis. Meningiomas are a heterogeneous group of tumors that have been classified in three histologic grades, WHO Grades I (benign), II and III (aggressive). Meningiomas can involve bone resulting in bone overgrowth or infiltration into bony structures. Meningiomas are associated with genetic syndromes and molecular alterations.

Approaches for classification are evolving to incorporate histopathologic, genetic and molecular characteristics.

The standard imaging modality is MRI without and with contrast. CT imaging is supported, as there is potential for bone involvement. Meningioma overexpresses somatostatin receptors. PET imaging using various radiolabeled somatostatin receptor ligands (SSAs) such as 68Ga-DOTA-Tyr3-octreotide (DOTATOC), 68Ga-DOTA-d-Phe1-Tyr3-octreotide (DOTATATE), or 68Ga-DOTA-l-Nal3-octreotide (DOTANOC) have been used for the diagnostic evaluation of meningioma. PET imaging with these ligands is supported for restaging to clarify inconclusive findings on MRI imaging. ^{111}In-octreotide scintigraphy (octreotide) imaging has a similar imaging indication as ^{68}Ga-DOTATATE PET/CT. In surveillance, the schedule for follow-up MRI/CT imaging is based on tumor grade and extent of residual disease.

Spinal Cord Tumors (Benign and Malignant) (ONC-2.9)

ON.CN.0002.9.A

v2.0.2025

- See: **Low Grade Gliomas (ONC-2.2)** and **High Grade Gliomas (ONC-2.3)** for imaging guidelines of low-grade and high-grade gliomas of the spinal cord
- See: **Malignant Tumors of the Spinal Cord (PEDONC-4.9)** in the Pediatric Oncology Imaging Guidelines for other malignant spinal cord tumors
- See: **Neurofibromatosis 1 and 2 (NF1 and NF2) (PEDONC-2.3)** in the Pediatric Oncology Imaging Guidelines for spinal tumors in individuals with Neurofibromatosis 1 or 2
- See: **Spinal/Vertebral Metastases (ONC-31.6)** for known secondary malignancy involving the spine/spinal canal/spinal cord

Choroid Plexus Tumors (ONC-2.10)

ON.CN.0002.10.A

v2.0.2025

- Choroid Plexus Tumor imaging indications in adult individuals are identical to those for pediatric individuals. See: **Choroid Plexus Tumors (PEDONC-4.13)** in the Pediatric Oncology Imaging Guidelines.

References (ONC-2)

v2.0.2025

1. Nabors LB, Portnow J, Baehring J, et. al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – January 21, 2025 Central Nervous System Cancers, available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Central Nervous System Tumors Cancer V4.2024. – January 21, 2025 ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Brandão LA, Castillo M. Adult brain tumors: clinical applications of magnetic resonance spectroscopy. *Magn Reson Imaging Clin N Am.* 2016;24(4):781-809. doi:10.1016/j.mric.2016.07.005.
3. Pasquier D, Bijmolt S, Veninga T, et al. Atypical and malignant meningioma: outcome and prognostic factors in 119 irradiated patients. A multicenter, retrospective study of the Rare Cancer Network. *Int J Radiat Oncol Biol Phys*. 2008;71(5):1388. doi:10.1016.j.ijrobp.2007.12.020.
4. Modha A, Gutin PH. Diagnosis and treatment of atypical and anaplastic meningiomas: a review. *Neurosurgery*. 2005;57(3):538-550.
5. Horská A, Barker PB. Imaging of brain tumors: MR spectroscopy and metabolic imaging. *Neuroimaging Clin N Am*. 2010;20(3):293-310. doi:10.1016/j.nic.2010.04.003.
6. Sundgren PC. MR Spectroscopy in radiation Injury. *Am J Neuroradiol*. 2009;30(8):1469-1476. doi:10.3174/ajnr.A1580.
7. American College of Radiology. ACR–ASNR-SPR practice parameter for the performance of intracranial magnetic resonance perfusion imaging. 2017; Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/MR-Perfusion.pdf?la=en.
8. Mabray MC, Barajas Jr. RF, Cha S. Modern brain tumor imaging. *Brain Tumor Res. Treat*. 2015;3:8–23.
9. Ostrom QT, Price M, Neff C, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2015-2019. *Neuro Oncol.* 2022;24(Suppl 5):v1.
10. American College of Radiology. ACR–ASNR-SPR practice parameter for the performance and interpretation of magnetic resonance spectroscopy of the central nervous system. www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en.
11. Brain tumours (primary) and brain metastases in adults. London: National Institute for Health and Care Excellence (NICE); 2021 Jan 29. (NICE Guideline, No. 99.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK544711/
12. WHO Classification of Tumors Editorial Board (2021) Central nervous system tumours, 5th edn. International Agency for Research on Cancer, Lyon.
13. Echevarría ME, Fangusaro J, Goldman S. Pediatric central nervous system germ cell tumors: a review. *Oncologist*. 2008;13(6):690.
14. Jung AY. Basics for Pediatric brain tumor imaging: techniques and protocol recommendations. *BrainTumor Res Treat*. 2004;12:1-13.
15. Jaju A, Li Y, Dahmoush et al. Imaging of pediatric brain tumors: A COG Diagnostic Imaging Committee/SPROncology Committee/ASPNR White Paper. *Pediatr Blood Cancer.* 2023;70(Suppl. 4):e30147. doi:10.1002/pbc.30147.
16. Grommes C, Rubenstein JL et al. Comprehensive approach to diagnosis and treatment of newly diagnosed primary CNS lymphoma. *Neuro-Oncol*. 2018;21(3):296-305. doi:10.1093/neuonc/noy192.
17. Galldiks N, Albert NL et al. PET imaging in patients with meningioma-report of the RANO/PET Group. *Neuro Oncol.* 2017;19(12):1576.
18. Huntoon K, Toland AMS, Dahiya S. Meningioma: a review of clinicopathological and molecular aspects. *Front Oncol*. 2020;10:579599. doi:10.3389/fonc.2020.579599.
19. Maas SLN, Stichel D et al. Integrated molecular-morphologic meningioma classification: a multicenter retrospective analysis, retrospectively and prospectively validated. *J Clin Oncol*. 2021;39(34):3839.

20. Han S, Suh CH, Woo S, Kim YJ, Lee JJ. Performance of 68Ga-DOTA-conjugated somatostatin receptor-targeting peptide PET in detection of pheochromocytoma and paraganglioma: a systematic review and metaanalysis. *J Nucl Med*. 2019; 60:369–376.
21. Duong LM, McCarthy BJ, McLendon RE, Dolecek TA, Kruchko C, Douglas LL, Ajani UA .. Descriptive epidemiology of malignant and nonmalignant primary spinal cord, spinal meninges, and cauda equina tumors, United States, 2004-2007. *Cancer*. 2012;118(17):4220. Epub 2012 Jan 3

Squamous Cell Carcinomas of the Head and Neck (ONC-3)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Squamous Cell Carcinomas of the Head and Neck – General Considerations (ONC-3.0)

ON.HN.0003.0.A

v2.0.2025

- Individuals with esthesioneuroblastoma should be imaged according to this guideline section.
- Stage III/IV disease encompasses any primary tumor larger than 4 cm or documented lymph node positive disease.

Squamous Cell Carcinomas of the Head and Neck – Suspected/Diagnosis (ONC-3.1)

ON.HN.0003.1.A

v2.0.2025

- See: **Neck Masses - Imaging (NECK-5.1)** in the Neck Imaging Guidelines for evaluation of suspected malignancy in the neck.
- PET may be considered prior to biopsy in order to determine a more favorable site for biopsy when:
  - a prior biopsy was nondiagnostic or
  - a relatively inaccessible site is contemplated which would require invasive surgical intervention for biopsy attempt

Squamous Cell Carcinomas of the Head and Neck – Initial Work-up/Staging (ONC-3.2)

ON.HN.0003.2.C
v2.0.2025

Indication	Imaging Study
All Stages of Disease	• CT Neck with contrast (CPT® 70491) **or** MRI Orbits/Face/Neck (OFN) without and with contrast (CPT® 70543) • CT Chest with contrast (CPT® 71260)
For sentinel lymph node evaluation when nodes are not clinically positive	• Lymph system imaging (lymphoscintigraphy, CPT® 78195) ◦ SPECT/CT (CPT® 78830) if requested
Nasal cavity and paranasal sinuses (bony erosion or skull base and intracranial involvement)	ONE of the following studies is indicated: • CT Maxillofacial with contrast (CPT® 70487) • CT Neck with contrast (CPT® 70491) • MRI Orbits/Face/Neck without and with contrast (CPT® 70543)
Nasopharyngeal Cancer (NPC)	• PET/CT (CPT® 78815) • MRI Orbits/Face/Neck without and with contrast (CPT® 70543) is the preferred study ◦ CT Neck (CPT® 70491) **and/or** CT Maxillofacial (CPT® 70487) with contrast can be approved if contraindication to MRI • CT Chest with contrast (CPT® 71260)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
For ANY of the following: • Known stage III or IV disease • To determine role for upfront surgery vs chemoradiation in T3-T4 size tumor • Prior to start of primary chemoradiotherapy and have not undergone definitive surgical resection • Inconclusive findings on conventional imaging (CT, MRI) • In order to direct laryngoscopy/exam under anesthesia for biopsy • Pulmonary nodule(s) ≥8 mm in size • Cervical lymph node biopsy positive for squamous cell carcinoma and no primary site identified on CT or MRI Neck and Chest	• PET/CT (CPT® 78815)
Signs or symptoms of abdominal metastatic disease, including elevated liver function tests	• CT Abdomen with contrast (CPT® 74160)
Any head and neck cancer with neurological findings or suspicion of skull base invasion	• MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

Accurate initial staging guides prognosis and management options. CT Neck with contrast or MRI Neck with and without contrast is required for correct tumor, nodal, and metastases (TNM) staging. A Contrasted CT of the chest is also supported if requested.

- Classification of tumor staging involves determination of mass size and extent of invasion, if present, of surrounding structures.
- Size and location (including laterality and nodal basin) of pathologic lymph nodes is also required for accurate nodal staging, which will further direct treatment planning to include the extent of potential neck dissection and/or field of radiation. Lymphoscintigraphy is supported, with SPECT if requested, for sentinel node evaluation when nodes are not clinically obviously positive.

- Assessment for potential distant metastases ("M") is based on clinical signs/ symptoms and the presence of advanced locoregional primary disease. Discovery of distant metastasis, or a second primary, shifts management to more systemic options. A heavy smoking history also may be a separate indication for advanced imaging of the chest. Up to 7-14% of patients may have a separate lung primary at the time of initial staging of head and neck SCCa. The use of IV contrast improves the detection of mediastinal and hilar adenopathy, and generally, CT Chest with contrast is preferred. Given the rarity of abdominal or pelvic metastatic disease, abdominopelvic imaging is only supported for signs and symptoms of metastatic disease.
    - Nasopharyngeal carcinoma (NPC) has a relatively high rate of distant metastases compared with other head and neck cancers, being found in 5-11% of patients at the time of initial diagnosis. The most common sites of metastasis are bone (20%), lung (13%), and liver (9%).
- FDG-PET/CT Skull Base to Mid-Thigh detects and localizes primary tumor site, and can be helpful in squamous cell carcinoma (SCCa) of the head and neck with unknown primary. It is also equivalent to and possibly superior to contrast-enhanced CT Neck for accurate diagnosis of regional nodal disease. It is helpful in confirming distant metastases as well. The National Comprehensive Cancer Network (NCCN) recommends FDG-PET/CT for initial staging of any NPC, as well as for patients with locoregionally advanced SCCa (ie, T3-T4 primary or >/= N1 nodal staging).
    - PET/CT alone, however, is not sufficient for initial staging. It does not provide the necessary anatomic detail of the primary tumor's extent for accurate "T" staging, which is required for best selection of local disease management options. Contrast-enhanced CT Neck or MRI Neck are necessary adjuncts.
    - If imaging fails to reveal an obvious primary, PET/CT should be completed before exam under anesthesia, biopsies, and tonsillectomy, to help identify potential primary sites before any intervention occurs.

Squamous Cell Carcinomas of the Head and Neck – Restaging/Recurrence (ONC-3.3)

ON.HN.0003.3.A
v2.0.2025

Indication	Imaging Study
Following complete resection and/or radical neck dissection	See: **Surveillance/Follow-up (ONC-3.4)**
Following primary chemoradiotherapy or radiation therapy in individuals who have not undergone surgical resection of primary tumor or neck dissection	ONE of the following: • CT Neck with contrast (CPT® 70491); **or** • MRI Orbits/Face/Neck without and with contrast (CPT® 70543); **or** • PET/CT (CPT® 78815) no sooner than 12 weeks (3 months) post completion of radiation therapy ◦ If post-treatment PET/CT scan is negative, further surveillance imaging is not routinely indicated.
Induction chemotherapy response	• CT Neck with contrast (CPT® 70491) or MRI Orbits/ Face/Neck without and with contrast (CPT® 70543) • PET not indicated to assess response to induction chemotherapy
Measurable or metastatic disease undergoing active treatment	Every 2 cycles (6-8 weeks): • CT Neck with contrast (CPT® 70491) OR • MRI Orbits/ Face/Neck without and with contrast (CPT® 70543) AND • CT with contrast of involved body sites
Suspected local recurrence	• CT Neck with contrast (CPT® 70491) or MRI Orbits/ Face/Neck without and with contrast (CPT® 70543) • CT Chest with contrast (CPT® 71260)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Biopsy proven local recurrence	ONE of the following: • PET/CT (CPT® 78815) **or** • CT Neck with contrast (CPT® 70491) or MRI Orbits/ Face/Neck without and with contrast (CPT® 70543) and CT Chest with contrast (CPT® 71260)
Inconclusive conventional imaging (CT or MRI)	• PET/CT (CPT® 78815)
Any of the following: • Known prior thoracic disease • New or worsening pulmonary symptoms • New or worsening chest x-ray findings	• CT Chest with contrast (CPT® 71260)

Evidence Discussion

Follow-up imaging is required for the evaluation of treatment response. In alignment with the NCCN, a PET/CT is supported following primary chemoradiotherapy in individuals who have not undergone surgical resection of the primary tumor or neck dissection. For patients receiving induction chemotherapy prior to definitive therapy, a CT or MRI of the primary tumor site to assess response is recommended by NCCN after 2-3 cycles of induction, but a repeat PET-CT is not routinely recommended by NCCN unless there are unclear findings on this CT or MRI. For patients with metastatic disease on active treatment, cross sectional imaging of involved body areas is supported every 2 cycles. PET-CT is supported for only as a problem-solving tool for inconclusive conventional imaging, as the incidence of false positive findings is high in the setting of ongoing inflammation with known disease.

For patients treated with primary chemoradiotherapy, a negative PET at the 3-6 month timeframe predicts improved survival at 2 years, with a negative predictive value of 95-97%. PET-CT performed earlier than this timeframe is associated with higher false-positive findings and should be avoided. CT or MRI neck may be performed **in lieu of** PET/CT, but PET/CT has excellent sensitivity and specificity in this setting, so these studies are generally not supported **in addition to** a PET/CT as they add additional radiation without a clear impact on management.

For suspected local recurrence, CT or MRI of the primary site (neck/face) is supported, as well as CT chest with contrast as lung and mediastinal nodes are the most common site of metastatic disease at recurrence, often without pulmonary symptoms. PET/CT has a relatively high false-positive rate due to ongoing inflammatory changes, and thus these guidelines do not support PET/CT for suspected recurrence until recurrence is proven by biopsy.

Squamous Cell Carcinomas of the Head and Neck – Surveillance/Follow-up (ONC-3.4)

ON.HN.0003.4.A
v2.0.2025

Indications	Imaging Study
Individuals treated with surgical resection of primary site and/or neck dissection (with or without postoperative radiation therapy)	Once within 6 months of completing all treatment: • CT Neck with contrast (CPT® 70491) **or** MRI Orbits/Face/Neck without and with contrast (CPT® 70543) • CT with contrast of any other involved body area
Individuals treated with definitive radiation therapy or combined chemoradiation, and post-treatment imaging is negative	Further surveillance imaging is not routinely indicated
If post-treatment imaging shows residual abnormalities	ONE of the following, once within 6 months of prior imaging: • CT Neck with contrast (CPT® 70491) OR • MRI Orbits/Face/Neck without and with contrast (CPT® 70543)
After initial post-treatment study, for ANY of the following: • Nasopharyngeal primary site • Physical exam unable to visualize deep-seated primary site	Annually for 3 years: • CT Neck with contrast (CPT® 70491) **or** MRI Orbits/Face/Neck without and with contrast (CPT® 70543)
• CT Chest is not indicated for surveillance. Individuals with smoking history may undergo annual low dose CT cancer screening if criteria are met (See: **Lung Cancer Screening (CH-33)** in the Chest Imaging Guidelines)	

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

Timely detection and accurate assessment of the extent of recurrent disease will direct salvage therapy and improve prognosis. A thorough head and neck clinical examination will typically guide any additional imaging that may be necessary, after post-treatment baseline imaging. There is no controlled prospective data showing a survival benefit for long term surveillance imaging. 3-year disease free survival in patients undergoing surveillance imaging vs those undergoing clinical surveillance only is not significantly different (41% vs 46%, P=0.91) . Given the excellent NPV of PET-CT 3-6 months post therapy, and the fact that median time to recurrence is 6 months, eviCore guidelines support cross sectional imaging once within 6 months of completion of therapy, following the initial post treatment PET-CT. For patients whose primary tumor site cannot be evaluated with physical exam and for patients with nasopharyngeal primary tumors, CT neck or MRI face/orbit neck are supported annually for 3 years, as 80-90% of recurrences occur within 3 years.

The role of annual CT Chest screening for surveillance of lung metastasis is controversial in head and neck cancer, following primary definitive treatment (surgery, XRT, or systemic therapy/XRT). Further study is needed to determine the extent of the positive effect and/or cost-effectiveness of this approach. Patients with a heavy smoking history may be at increased risk, and may meet criteria for low-dose CT lung cancer screening as defined in CH-33 in the Chest Imaging Guidelines.

References (ONC-3)

v2.0.2025

1. Pfister DG, Spencer S, Adkins D, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – May 1, 2024 Head and Neck Cancers, available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Head and Neck Cancer V4.2024 – May 1, 2024 ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Goel R, Moore W, Sumer B, Khan S, Sher D, Subramaniam RM. Clinical practice in PET/CT for the management of head and neck squamous cell cancer. *AJR Am J Roentgenol.* 2017;209(2):289-303. doi:10.2214/AJR.17.18301.
3. Moncrieff M, Pywell S, Snelling A, et. al. Effectiveness of SPECT/CT imaging for sentinel node biopsy staging of primary cutaneous melanoma and patient outcomes. *Ann Surg Oncol.* 2022;29(2):767-775. doi:10.1245/s10434-021-10911-4.
4. Quartuccio N, Garau LM, Arnone A, et. al. Comparsion of 99mTc-labeled colloid SPECT/CT and planar lymphoscintigraphy in sentinel lymph node detection in patients with melanoma: a meta-analysis. *J Clin Med*. 2020;9(6):1680. doi:10.3390/jcm9061680.
5. Bennie G, Vorster M, Buscombe J, Sathekge M. The added value of a single-photon emission computed tomography-computed in sentinel lymph node mapping in patients with breast cancer and malignant melanoma. *World J Nucl Med*. 2015;14(01):41-46. doi:10.4103/1450-1147.150543.
6. Gule-Monroe MK, Calle S, Policeni B, et al. ACR Appropriateness Criteria® Staging and Post-Therapy Assessment of Head and Neck Cancer. *J Am Coll Radiol*. 2023;20(11S):S521-S564. doi:10.1016/j.jacr.2023.08.008.
7. Yao M, Smith RB, Graham MM, et al. The role of FDG PET in management of neck metastasis from head-and-neck cancer after definitive radiation treatment. *Int J Radiat Oncol Biol Phys*. 2005;63(4):991-9. doi:10.1016/j.ijrobp.2005.03.066.
8. Moeller BJ, Rana V, Cannon BA, et al. Prospective risk-adjusted [18F] Fluorodeoxyglucose positron emission tomography and computed tomography assessment of radiation response in head and neck cancer. *J Clin Oncol.* 2009;27(15):2509-15. doi:10.1200/JCO.2008.19.3300.
9. Lowe VJ, Duan F, Subramaniam RM, et al. Multicenter Trial of [18F] fluorodeoxyglucose positron emission tomography/computed tomography staging of head and neck cancer and negative predictive value and surgical impact in the N0 neck: results from ACRIN 6685. *J Clin Oncol*. 2019;37(20):1704-1712. doi:10.1200/JCO.18.01182.
10. Awan MJ, Lavertu P, Zender C, et al. Post-treatment PET/CT and p16 status for predicting treatment outcomes in locally advanced head and neck cancer after definitive radiation. *Eur J Nucl Med Mol Imaging*. 2017;44(6):988-997. doi:10.1007/s00259-016-3612-1.
11. Ho AS, Tsao GJ, Chen FW, et al. Impact of positron emission tomography/computed tomography surveillance at 12 and 24 months for detecting head and neck cancer recurrence. *Cancer*. 2013;19:1349-1356.
12. Heineman TE, Kuan EC, St John MA. When should surveillance imaging be performed after treatment for head and neck cancer? *Laryngoscope*. 2017;127:533-534.

Salivary Gland Cancers (ONC-4)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Salivary Gland Cancers – General Considerations (ONC-4.0)

ON.SG.0004.0.A

v2.0.2025

- Salivary gland tumors may originate within the parotid, submandibular, sublingual or minor salivary glands in the mouth.
- Histological subtypes include:
  - mucoepidermoid
  - acinic
  - adenocarcinoma
  - adenoid cystic carcinoma
  - malignant myoepithelial tumors
  - squamous cell carcinoma
  - lymphoma and metastatic squamous carcinoma can occur in the parotid gland
- Over 80% of parotid gland tumors are benign. A bilateral parotid tumor is most likely Warthin's tumor.
- The use of PET in salivary gland tumors is considered not medically necessary.

Salivary Gland Cancers – Suspected/ Diagnosis (ONC-4.1)

ON.SG.0004.1.A
v2.0.2025

- See: **Salivary Gland Disorders (NECK-11)** and **Neck Masses – Imaging (NECK-5.1)** in the Neck Imaging Guidelines for evaluation of salivary gland masses, salivary gland stones and neck masses.

Salivary Gland Cancers – Initial Work-up/ Staging (ONC-4.2)

ON.SG.0004.2.A
v2.0.2025

Indication	Imaging Study
Biopsy-proven malignancy	ONE of the following can be approved: • MRI Orbits/Face/Neck without and with contrast (CPT® 70543) • CT Neck with contrast (CPT® 70491) • CT Neck without contrast (CPT® 70490)
Skull base invasion	• MRI Brain without and with contrast (CPT® 70553)
• Adenoid cystic carcinoma • Lymphadenopathy in the neck • Pulmonary signs or symptoms • Abnormal chest x-ray	• CT Chest with contrast (CPT® 71260)

Evidence Discussion

There are over 40 histologies of salivary gland malignancies, with different patterns of presentation and invasiveness. The choice of MRI vs CT depends on location of tumor, specific symptoms, and patient characteristics. CT may be useful to assess stones and sialadenitis, which may mimic tumor, and I superior for assessing cortical bone erosion. MRI is superior in the assessment of extent of soft tissue disease and perineural invasion. Contrast is recommended in all studies to better outline primary site and to better assess nodal involvement.

In patients who present with metastatic disease outside the neck, 90% are lung/ chest node metastases. Metastatic disease to lung is most common with adenoid cystic carcinoma and chest imaging is supported in all patients with this histology. Contrast should be used to allow for assessment of nodal disease in the chest. In other histologies, metastatic disease is less common, and thus chest imaging is only supported in patients with neck adenopathy, abnormal chest x-ray, or pulmonary signs and symptoms.

Perineural and skull base invasion may occur with salivary gland cancers, particularly with adenoid cystic carcinoma, where perineural spread is seen in 50-60% of patients.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

When skull base invasion is clinically suspected an MRI brain with and without contrast is supported by eviCore guidelines in the interest of patient safety. MRI with and without gadolinium and with fat-saturated, T1 weighted MRI sequences is the most sensitive technique to evaluate for invasion of skull base and perineural invasion.

The role of PET/CT remains controversial in salivary gland cancers. Several studies show no statistically significant different in outcomes with imaging with PET/CT vs conventional imaging. The rate of change in treatment plan based on imaging with PET/CT is widely variable across studies, ranging from 15-47%. PET/CT is not adequate to distinguish benign from malignant parotid tumors. Benign tumors such as Warthin tumor can have FDG uptake, and low-grade malignant tumors may not take up FDG. Healthy salivary glands may also exhibit FDG uptake and obscure tumors. While there is emerging evidence in the use of FDG-PET/CT and PET/MRI to assess for distant disease and perineural spread, it is not considered routine at this time and is not routinely recommended by the NCCN.

Salivary Gland Cancers – Restaging/ Recurrence (ONC-4.3)

ON.SG.0004.3.A
v2.0.2025

Indication	Imaging Study
After complete surgical resection	See: **Salivary Gland Cancers - Surveillance (ONC-4.4)**
Individuals with unresected disease receiving systemic therapy (chemotherapy)	The following may be approved every 2 cycles: • CT Neck with contrast (CPT® 70491) OR MRI Orbits/Face/Neck without and with contrast (CPT® 70543) • CT with contrast or MRI without and with for any other sites of disease
Recurrence or progression suspected based on new or worsening signs or symptoms	ONE of the following may be approved: • CT Neck with contrast (CPT® 70491) • MRI Orbits/Face/Neck without and with contrast (CPT® 70543) In addition, for all individuals: • CT Chest with contrast (CPT® 71260)
All other individuals	• No routine advanced imaging indicated

Evidence Discussion

CT or MRI based on initial tumor and patient characteristics is supported every 2 cycles of systemic chemotherapy. If recurrence of progression is clinically suspected at any time, CT neck with contrast or MRI without and with contrast is supported based on prior tumor characteristics and symptoms, per NCCN recommendations and ACR appropriateness criteria. The incidence of metastatic disease to the chest is higher at recurrence than at initial presentation, with 63% of patients with metastatic recurrence presenting with metastatic disease to the chest, so CT chest is supported for suspected recurrence. Contrast should be used to allow better assessment of nodal disease, in addition to parenchymal lesions. Any CNS symptoms warrant MRI with further guidance in guideline ONC-31.3.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Salivary Gland Cancers – Surveillance/ Follow-up (ONC-4.4)

ON.SG.0004.4.A
v2.0.2025

Indication	Imaging Study
Total surgical resection	• No routine advanced imaging indicated
Unresectable or partially resected disease, including those treated with radiation therapy	• Either CT Neck with contrast (CPT® 70491) or MRI Orbits/Face/Neck without and with contrast (CPT® 70543) once within 6 months of completion of treatment
Adenoid cystic carcinoma	ANY of the following, annually for up to 10 years: • CT Neck with contrast (CPT® 70491) or MRI Orbits/Face/Neck without and with contrast (CPT® 70543) • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250)

Evidence Discussion

The mainstay of surveillance for head and neck cancers including salivary gland carcinoma are frequent history and physical examination. For most histologies, no survival benefit has been documented with imaging surveillance over clinical surveillance. The NCCN notes most recurrences are picked up by patient report of symptoms. For all histologies other than adenoid cystic carcinoma, guidelines support imaging of the primary tumor site once within 6 months from completion of therapy to establish post-treatment baseline, with further imaging guided by signs and symptoms of recurrence. Adenoid cystic carcinoma has the highest incidence of metastatic disease, with over 60 percent of patients presenting with metastatic disease at recurrence having a history of this histology. They also have the longest risk of recurrence, with a median time to recurrence of 3 years with some recurrences occurring as late as 10 years from diagnosis. For patients with a history of adenoid cystic carcinoma, CT Neck with contrast or MRI orbit/face/neck as well as CT Chest with or without contrast are supported annually for up to 10 years.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-4)

v2.0.2025

1. Pfister DG, Spencer S, Adkins D et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – May 1, 2024 Head and Neck Cancers, available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Head and Neck Cancer V4.2024 – May 1, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Palacios E, Ellis M, Lam EC, Neitzschman H, Haile M. Pitfalls in imaging the submandibular glands with PET/CT. *Ear Nose Throat* J. 2015;94(10-11):E37-E39.
3. Seo YL, Yoon DY, Baek S, et al. Incidental focal FDG uptake in the parotid glands on PET/CT in patients with head and neck malignancy. *Eur Radiol*. 2015;25(1):171-177. doi:10.1007/s00330-0140339701.
4. Park HL, Yoo le R, Lee N, et al. The value of F-18 FDG PET for planning treatment and detecting recurrence in malignant salivary gland tumors: comparison with conventional imaging studies. *Nucl Med Mol Imaging*. 2013;47(4):242-248. doi:10.1007/s13139-013-0222-8.
5. Bertagna F, Nicolai P, Maroldi R. Diagnostic role of 18F-FDG-PET or PET/CT in salivary gland tumors: a systematic review. *Rev Esp Med Nucl Imagen Mol*.2015;34(5):295-302.
6. Garg M, Tudor-Green B, Bisase B. Current thinking in the management of adenoid cystic carcinoma of the head and neck. *British Journal of Oral and Maxillofacial Surgery*. 2019;57(8):716-721. doi:10.1016/j.bjoms.2019.07.021.
7. Geiger JL, Ismaila N, Beadle B, et al. Management of salivary gland malignancy: ASCO guideline. *Journal of Clinical Oncology*. 2021;39(17):1909-1941. doi:10.1200/JCO.21.00449.
8. Gule-Monroe MK, Calle S, Policeni B, et al. ACR Appropriateness Criteria® Staging and Post-Therapy Assessment of Head and Neck Cancer. *J Am Coll Radiol*. 2023;20(11S):S521-S564. doi:10.1016/j.jacr.2023.08.008.
9. National Cancer Institute PDQ for Salivary Gland Cancer Treatment-Health Professional Version. Salivary Gland Cancer Treatment (PDQ®) - NCI.
10. Kim MJ, Kim JS, Roh JL, et al. Utility of 18F-FDG PET/CT for detecting neck metastasis in patients with salivary gland carcinomas: preoperative planning for necessity and extent of neck dissection. *Ann Surg Oncol.* 2013;20(3):899-905. doi:10.1245/s10434-012-2716-5.
11. Larson CR, Wiggins RH. FDG-PET imaging of salivary gland tumors. *Semin Ultrasound CT MR*. 2019;40(5):391-399. doi:10.1053/j.sult.2019.07.003.
12. Yousem DM, Kraut MA, Chalian AA. Major salivary gland imaging. *Radiology*. 2000;216(1):19-29. doi:10.1148/radiology.216.1.r00jl4519.
13. Mimica X, McGill M, Hay A, et al. Distant metastasis of salivary gland cancer: Incidence, management, and outcomes. *Cancer*. 2020;126(10):2153-2162. doi:10.1002/cncr.32792.

Melanomas and Other Skin Cancers (ONC-5)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Melanoma – General Considerations (ONC-5.0)

ON.SC.0005.0.A
v2.0.2025

- Melanomas can metastasize in an unpredictable fashion.

Melanoma – Suspected/Diagnosis (ONC-5.1)

ON.SC.0005.1.A
v2.0.2025

Indication	Imaging Study
All	• Imaging is not indicated until histologic diagnosis is confirmed

Melanoma – Initial Work-up/Staging (ONC-5.2)

ON.SC.0005.2.A
v2.0.2025

Indication	Imaging Study
Stage 0 or IA (in situ or disease <1 mm)	• Routine advanced imaging is not indicated
• Stage IB (<0.8 mm with ulceration or 0.8-1 mm without or with ulceration) • Stage II (lesions >1 mm thick, but node negative)	• CT with contrast or MRI without and with contrast of specific areas, only if signs or symptoms indicate need for further evaluation
For sentinel lymph node evaluation in stages IB and II	• Lymph system imaging (lymphoscintigraphy, CPT® 78195) ◦ SPECT/CT (CPT® 78830) if requested
Any of the following: • Stage III (sentinel node positive, palpable regional nodes) • Stage IV (metastatic)	• MRI Brain without and with contrast (CPT® 70553) AND one of the following: • PET/CT (CPT® 78815 or CPT® 78816) OR • CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)
• Head or neck primary site • Palpable lymphadenopathy in the neck • Mucosal melanoma of the head or neck region	In addition to above initial staging imaging, if PET/CT not performed: • CT Neck with contrast (CPT® 70491)
• Primary site of melanoma is unknown **and** CT Chest, Abdomen, and Pelvis are negative	• PET/CT (CPT® 78815 or CPT® 78816)

Evidence Discussion

Formal diagnosis and clinical staging of melanoma needs to take place before any imaging is completed as 84% of patients present with localized disease, 9% with regional disease and 4% with distant metastatic disease. Stage 0 (in situ) or 1A does not require routine advanced imaging as the 5 year survival rate is >98% with very little risk for recurrence or metastases. For Stage IB or II disease, sentinel lymph node mapping is indicated and depending on results, survival rates range from 50-90% that also incorporates tumor thickness, ulceration and mitotic rate. The yield of imaging in screening patients with clinical Stage 0-II disease for asymptomatic distant metastatic disease is very low due to low sensitivity and false positive findings. Therefore, the NCCN does not recommend imaging unless needed for surgical planning or to evaluate specific signs or symptoms of disease. Stage III or IV disease can be staged using PET/CT or CT Chest/Abdomen/Pelvis, with PET/CT often preferred due to its superiority over CT in detecting distant metastases. Baseline MRI brain is indicated with or without symptoms due to high risk of CNS involvement estimated to be 15.8% at 5 years for Stage III and up to 60% overall in individuals with advanced stage disease. If primary site of melanoma is unknown and CT Chest/Abdomen/Pelvis negative, PET/CT can be performed due to its higher sensitivity and ability to image the extremities.

Melanoma – Restaging/Recurrence (ONC-5.3)

ON.SC.0005.3.C
v2.0.2025

- All recurrences should be confirmed histologically, except when excessive morbidity from a biopsy may occur, such as a biopsy requiring craniotomy

Indication	Imaging Study
Individuals receiving chemotherapy, with measurable disease, after every 2 cycles	• CT Chest with contrast (CPT® 71260); **and** CT Abdomen and Pelvis with contrast (CPT® 74177) In addition, for individuals receiving systemic treatment for brain metastases: • MRI Brain without and with contrast (CPT® 70553)
All in situ recurrences	• Restaging imaging is not needed after adequate aggressive local therapy (See Surveillance)
Documented or clinically suspected (see top of page regarding biopsy morbidity) recurrence at: • True scar recurrence (if re-excision suggests more than in situ disease) • In-transit disease • Regional lymph nodes • Metastatic site	• CT Chest with contrast (CPT® 71260); **and** CT Abdomen and Pelvis with contrast (CPT® 74177) In addition, for all individuals: • MRI Brain without and with contrast (CPT® 70553) In addition, for head or neck primary: • CT Neck with contrast (CPT® 71491)
ANY of the following: • Inconclusive findings on conventional imaging • Isolated metastatic site found on conventional imaging	• PET/CT (CPT® 78815 or CPT® 78816)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Brain imaging is indicated for: • New discovery of metastatic disease or progression of metastatic disease • Signs or symptoms of CNS disease • If considering Interleukin (IL-2) therapy	• MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

Individuals receiving chemotherapy with measurable disease can undergo CT Chest/Abdomen/Pelvis every 2 cycles. In situ recurrences do not require restaging imaging due to its high cure rate while recurrence at the primary site, in-transit disease, regional nodes and metastatic site can undergo CT Chest/Abdomen/Pelvis and MRI Brain due to the higher risk of CNS involvement. PET/CT is reserved for inconclusive findings or isolated metastatic site found on CT imaging to guide decisions on local versus systemic therapy. MRI Brain is also indicated for newly diagnosed or progressive metastatic disease, signs or symptoms of CNS involvement or if IL-2 therapy is being considered.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Melanoma – Surveillance/Follow-up (ONC-5.4)

ON.SC.0005.4.A
v2.0.2025

Indication	Imaging Study
Stage 0, IA, IB and IIA Melanomas	• No routine advanced imaging indicated
Stage IIB, IIC, IIIA and IIIB Melanomas	• CT Chest (CPT® 71260) **and** CT Abdomen and Pelvis (CPT® 74177) with contrast every 6 months for 2 years, then annually for 3 years • For melanoma arising from extremities, advanced imaging of the primary site is not routinely indicated for surveillance in asymptomatic individuals.
Stage IIIC and IV Melanomas	• CT Chest (CPT® 71260) **and** CT Abdomen and Pelvis (CPT® 74177) with contrast every 3 months for 2 years, then every 6 months for 3 years • MRI Brain without and with contrast (CPT® 70553) annually for 3 years • For melanoma arising from extremities, advanced imaging of the primary site is not routinely indicated for surveillance in asymptomatic individuals.
Mucosal Melanoma of the head or neck region	In addition to above stage-based surveillance imaging, the following may be obtained ONCE within 6 months of completing all treatment: • CT Neck with contrast (CPT® 70491) or MRI Orbits/Face/Neck without and with contrast (CPT® 70543) • CT with contrast of any other involved body area
Liver metastases treated with focal therapy	• See: **Liver Metastases (ONC-31.2)**

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

The majority of recurrences, especially in those with early stage disease, are detected clinically by either the patient or during physical exam thus supporting no surveillance imaging in Stage 0, 1A, 1B and IIA disease. Furthermore, additional studies have reported low yield, significant false positivity (often associated with increased patient anxiety and medical costs) and risks of cumulative radiation exposure. 7 Patient with more advanced disease are more likely to recur, and recur more quickly, with the risk of recurrence reaching low levels after only 2.7 years, thereby supporting Stage IIB/IIC as well as Stage IIIA/IIIB undergoing CT Chest/Abdomen/Pelvis every 6 months for 2 years then annually for 3 years. Due to the even high risk of early distant recurrence, Stage IIIC/IV should undergo CT Chest/Abdomen/Pelvis every 3 months for 2 years then every 6 months for 3 years as well as MRI brain annually for 3 years. The utility of PET/CT scan in sentinel lymph positive Stage III melanoma was minimal with only 2 out of 38 patients (108 total scans) being true positive with 9 scans showing false positive results thus supporting CT rather than PET/CT imaging in this setting. For melanoma arising from extremities, advanced imaging of the primary site is not indicated in asymptomatic individuals. Mucosal melanoma of the head or neck region can also undergo on a one-time basis CT Neck or MRI Orbits/Face/Neck or CT of any other involved body area within 6 months of completing treatment.

The NCCN (Principles of Imaging) does not specify the type of imaging required during the workup, response assessment or surveillance other than listing "cross-sectional with or without brain imaging" thus allowing the provider to determine if CT or PET/CT may be most appropriate. Amongst the many factors playing a role in this decision include cost, convenience, false positives/false negatives, dye and radiation exposure.

Non-Melanoma Skin Cancers – General Considerations (ONC-5.5)

ON.SC.0005.5.A

v2.0.2025

- Advanced imaging is generally not indicated for basal cell and squamous cell skin cancers.
- PET/CT scan is not indicated for evaluation of non-melanoma skin cancers unless specified within the guidelines below (e.g. Merkel cell carcinoma).
- Merkel cell carcinoma is an unusual skin cancer with neuroendocrine-like histologic features, which has a high propensity (25% to 33%) for regional lymph node spread and occasionally, metastatic spread to lungs.
- Merkel cell carcinoma may present as a primary cancer or as a skin metastasis from a non-cutaneous primary neuroendocrine carcinoma (i.e., small cell lung cancer), therefore conventional imaging is indicated initially to confirm the absence of metastasis prior to considering PET scan.

Evidence Discussion

Advanced imaging to include PET/CT is generally not indicated for basal cell (BCC) or squamous cell (SCC) skin cancers. The incidence of metastatic BCC was found to be <1% at 14 years of follow-up while metastatic SCC is noted to be rare. Merkel cell carcinoma, due to its high propensity (25-33%) for regional lymph node spread as well as distant metastases (12-20%), conventional imaging is indicated initially prior to considering PET scan.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Non-Melanoma Skin Cancers – Initial Work-up/Staging (ONC-5.6)

ON.SC.0005.6.A
v2.0.2025

Indication	Imaging Study
Body area with unexplained signs or symptoms	• CT with contrast of that body area
Perineural invasion or local regional extension (i.e. bone; deep soft tissue) involvement	ONE of the following may be approved of the primary site: • MRI without contrast **or** without and with contrast • CT (contrast as requested)
Skin lesion may be a dermal metastasis from distant primary	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • PET/CT (CPT® 78815 or CPT® 78816) is indicated if conventional imaging (CT or MRI) is unable to identify a primary site
Squamous cell carcinoma head or neck skin with regional lymphadenopathy	• CT Neck (CPT® 70491) and CT Chest (CPT® 71260) with contrast
Merkel Cell carcinoma	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of other involved body area(s) • PET/CT (CPT® 78815 or CPT® 78816) if inconclusive conventional imaging • Lymph system imaging (lymphoscintigraphy, CPT® 78195) for sentinel lymph node evaluation ◦ SPECT/CT (CPT® 78830) if requested
Signs or symptoms of CNS involvement	• MRI Brain with and without contrast (CPT® 70553)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

A body area with unexplained signs or symptoms can undergo imaging with CT with contrast. For SCC, MRI or CT of the primary site with MRI favored if there is perineural or deep soft tissue involvement while CT is preferred for bone disease. If the skin lesion is felt to be a dermal metastasis from a distant primary, CT Chest/Abdomen/Pelvis with contrast is the initial recommended imaging with PET/CT indicated if conventional imaging is unable to identify a primary site and especially if the primary tumor may involve an extremity.

Non-Melanoma Skin Cancers – Restaging/Recurrence (ONC-5.7)

ON.SC.0005.7.A
v2.0.2025

- All recurrences should be confirmed histologically, except when excessive morbidity from a biopsy may occur, such as a biopsy requiring craniotomy.

Indication	Imaging Study
Recurrence where planned therapy is more extensive than simple wide local excision	• CT with contrast of the primary and recurrent site(s)
Suspected or biopsy-proven recurrence of Merkel cell carcinoma	• CT Chest (CPT® 71260) **and** CT Abdomen and Pelvis (CPT® 74177) with contrast • CT with contrast of other symptomatic body area(s)
Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815 or 78816)
Signs or symptoms of CNS involvement	• MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

For recurrences where planned therapy is more extensive than simple wide local excision, CT with contrast of primary site and recurrent site(s) is indicated. Merkel cell carcinoma recurrence can be evaluated with CT Chest/Abdomen/Pelvis plus any other symptomatic areas. PET/CT can be done for inconclusive findings on conventional imaging. MRI Brain indicated for signs or symptoms of CNS involvement.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Non-Melanoma Skin Cancers – Surveillance/Follow-up (ONC-5.8)

ON.SC.0005.8.A
v2.0.2025

Indication	Imaging Study
Merkel cell cancer with any of the following high-risk factors: • Stage II-IV • Individuals assigned male at birth • Immunosuppression • Merkel Cell polyomavirus negative status • Age ≥70 • Non-sentinel lymph node metastases	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast every 6 months for 5 years • Add CT Neck with contrast (CPT® 70491) if known prior neck disease or scalp/facial/neck disease
All others	• Routine advanced imaging for surveillance is not indicated • Imaging indicated only for signs and symptoms of recurrent disease

Evidence Discussion

In node positive Merkel cell carcinoma, recurrence rates have been found to be up to 33% at 5 years. In addition, individuals assigned male at birth are twice as likely to develop Merkel Cell carcinoma. Also, the likelihood of developing Merkel Cell increases with age. One study showed that 73.6% of Merkel Cell cases are diagnosed at age greater than 70 (Grabowski, 2008). Additional risk factors for recurrence of Merkel Cell are polyomavirus negative status, non-sentinel lymph node metastases, and immunosuppression (Bordeaux, 2025). Routine imaging is not indicated for SCC or BCC in the absence of signs and symptoms of recurrence.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Ocular Melanoma (ONC-5.9)

ON.SC.0005.9.A
v2.0.2025

General Considerations

- Approximately 95% of ocular melanomas arise from the uvea (iris, ciliary body and choroid) and 5% arise from the conjunctiva or orbit.
- Biopsy is usually not necessary for initial diagnosis of uveal melanoma but may be useful in cases when diagnosis is uncertain (e.g. amelanotic tumors, retinal detachment) or for prognostic analysis and risk stratification.
- Treatment is directed to the affected eye with systemic therapy reserved only for known metastatic disease.
- The most common site of metastatic disease is the liver.
- Surveillance of the affected eye is with clinical examination only; advanced imaging is supported for surveillance of systemic metastatic disease based on individual risk factors. See risk categories below for surveillance recommendations.

Ocular Melanoma Risk Categories

Low Risk	Medium Risk	High-Risk
T1	T2 and T3	T4
Class IA	Class IB	Class 2
Spindle cell histology	Mixed Spindle and Epitheloid cells	Epitheloid cell histology
No extraoccular extension	No extraoccular extension	Extraoccular extension present
No ciliary body involvement	No ciliary body involvement	Ciliary body involvement present
Chromosome mutations: • Disomy 3 • EIF1AX mutation • Gain of chromosome 6p	Chromosome mutations: • SF3B1 mutation	Chromosome mutations: • BAP1 mutation • PRAME mutation • Monosomy 3 • Gain of chromosome 8q

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Initial staging of suspected or biopsy-proven uveal melanoma	ANY or ALL of the following: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177), OR MRI Abdomen without and with contrast (CPT® 74183) with CT Pelvis with contrast (CPT® 72913), OR MRI Abdomen without and with contrast (CPT® 74183) with MRI Pelvis without and with contrast (CPT® 72197) • MRI Orbits/Face/Neck without and with contrast (CPT® 70543)
Neurological signs/ symptoms	• MRI Brain without and with contrast (CPT® 70553)
Restaging/Suspected Recurrence	ANY or ALL of the following: • MRI Brain without and with contrast (CPT® 70553) • MRI Orbits/Face/Neck without and with contrast (CPT® 70543) • CT Chest with contrast (CPT® 71260) AND one of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) OR • MRI Abdomen without and with contrast (CPT® 74183) with CT Pelvis with contrast (CPT® 72913) OR ◦ Ultrasound Abdomen may be substituted for MRI Abdomen if requested • MRI Abdomen without and with contrast (CPT® 74183) with MRI Pelvis without and with contrast (CPT® 72197)
Surveillance for Low Risk disease	Annually for 10 years: • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) or MRI Abdomen without and with contrast (CPT® 74183)
Surveillance for Medium Risk disease	Every 6 months up to year 10: • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) or MRI Abdomen without and with contrast (CPT® 74183)

Indication	Imaging Study
Surveillance for High-risk disease	Every 3 months for 5 years, then every 6 months up to year 10: • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) or MRI Abdomen without and with contrast (CPT® 74183)

Evidence Discussion

Approximately 95% of ocular melanoma occur in the uvea and 5% from the conjunctiva or orbit. Biopsy may not be mandatory for diagnosis but should be performed if diagnosis is uncertain or for prognostic analysis and risk stratification. Less than 3% of cases present with metastatic disease with 5 year risk of metastasis ranging from 3-5% in Stage I to 44% or higher in Stage III. The most common site of metastatic disease is the liver (80%) but may also spread to the lungs, bone, skin/soft tissue and lymph nodes. Surveillance of the affected eye is with clinical examination only with advanced imaging supported based on individual risk factors. Initial staging includes MRI orbits/face/neck to determine extraocular extension that impacts treatment planning (radiation therapy versus enucleation). While the risk of baseline metastases may be low, the NCCN favors baseline staging before treatment to include CT Chest/Abdomen/Pelvis in addition to aforementioned MRI. MRI brain indicated with any neurologic signs or symptoms. Restaging/recurrence with same imaging as initial staging as well as including MRI brain. Surveillance: Local recurrence is rare (<10%) and the development of metastatic disease is much more common (up to 70% up to 20 years after initial diagnosis) hence the following recommendations for surveillance that does not include local imaging unless clinically indicated. For low risk disease, CT Chest with CT or MRI of the abdomen annually for 10 years. For medium risk disease, same as low risk but every 6 months for a total of 10 years. For high risk disease, every 3 months for 5 years, then annually for a total of 10 years. The NCCN recognizes the optimal surveillance strategy is an issue of debate due to overall low yield of testing and the risk of cumulative radiation exposure.

References (ONC-5)

v2.0.2025

1. Swetter SM, Johnson, D, Albertini MR, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – January 28, 2025 Melanoma: Cutaneous, available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Melanoma: Cutaneous V2.2025 – January 28, 2025 ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Swetter S, Johnson D, Albertini MR, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – February 11, 2025 Melanoma: Uveal, available at: https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Melanoma: Uveal V1.2025 – February 11, 2025 ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Bordeaux J, Blitzblau R, Aasi SZ, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – January 13, 2025 Merkel Cell Carcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Merkel Cell Carcinoma V1.2025 – January 13, 2025 ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
4. Bordeaux J, Aasi SZ, Alam M, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – February 7, 2025 Basal Cell Skin Cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Basal Cell Skin Cancer V2.2025 – February 7, 2025 ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org
5. Bordeaux J, Aasi SZ, Alam M, et al, National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – February 7, 2025 Squamous Cell Skin Cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Squamous Cell Skin Cancer V2.2025 – February 7, 2025 ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
6. Schröer-Günther MA, Wolff RF, Westwood ME, et al. F-18-fluoro-2-deoxyglucose positron emission tomography (PET) and PET/computed tomography imaging in primary staging of patients with malignant melanoma: a systematic review. *Syst Rev*. 2012;1:62. doi:10.1186/2046-4053-1-62.
7. Xing Y, Bronstein Y, Ross MI, et al. Contemporary diagnostic imaging modalities for the staging and surveillance of melanoma patients: a meta-analysis. *J Natl Cancer Inst*. 2011;103(2):129-142. doi:10.1093/jnci/djq455.
8. Rodriguez Rivera AM, Alabbas H, Ramjuan A, Meguerditchian AN. Value of positron emission tomography scan in stage III cutaneous melanoma: a systematic review and meta-analysis. *Surg Oncol*. 2014;23(1):11-16. doi:10.1016/j.suronc.2014.01.002.
9. Nathan P, Cohen V, Coupland S, et al. Uveal melanoma UK national guidelines. *European Journal of Cancer.* 2015;51(16):2404-2412. doi:10.1016/j.ejca/2015.07.013.
10. Moncrieff M, Pywell S, Snelling A, et. al. Effectiveness of SPECT/CT imaging for sentinel node biopsy staging of primary cutaneous melanoma and patient outcomes. *Ann Surg Oncol*. 2022;29(2):767-775. doi:10.1245/s10434-021-10911-4.

11. Bennie G, Vorster M, Buscombe J, Sathekge M. The added value of a single-photon emission computed tomography-computed in sentinel lymph node mapping in patients with breast cancer and malignant melanoma. *World J Nucl Med.* 2015;14(01):41-46. doi:10.4103/1450-1147.150543
12. Quartuccio N, Garau LM, Arnone A, et. al. Comparsion of 99mTc-labeled colloid SPECT/CT and planar lymphoscintigraphy in sentinel lymph node detection in patients with melanoma: a meta-analysis. *J Clin Med*. 2020;9(6):1680. doi:10.3390/jcm9061680.
13. Echanique KA, Ghazizadeh S, Moon A, et al. Head and neck melanomas: a 22-year experience of recurrence following sentinel lymph node biopsy. *Laryngoscope Investigative Otolaryngology*. 2021;6:738-746. doi:10.1002/lio2.605.
14. Licata G, Scharf, Ronchi A, et al. Diagnosis and management of melanoma of the scalp: a review of the literature. *Clinical, Cosmetic and Investigative Dermatology*. 2021;14:1435-1447. doi:10.2147/CCID.S293115.
15. Shreve C, Shropshire C, Cotter D. Metastatic Squamous cell carcinoma: a cautionary tale. *Cureus*, 2020;12(10): e10879.
16. Nguyen-Nielsen M, Wang L, Pedersen L, et al. The incidence of metastatic basal cell carcinoma (mBCC) in Denmark, 1997-2010. *Eur J Dermatol*. 2015;25:463-468.
17. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin*. 2015;65:5-29.
18. Melanoma Survival Rates - Melanoma Research Alliance (curemelanoma.org)
19. Haydu L, Lo S, et al. Cumulative Incidence and predictors of CNS metastasis for patient with AJCC 8th edition stage III melanoma. *Journal of Clinical Oncology*. 2020;38.
20. Ajithkumar T, Parkinson C, Fife K, Corrie P, Jefferies S. Evolving treatment options for melanoma brain metastases. *Lancet Oncol*. 2015;16:e486–e497. doi:10.1016/S1470-2045(15)00141-2.
21. Garbe C, Paul A, Kohler-Spath H, et al. Prospective evaluation of a follow-up schedule in cutaneous melanoma patients: recommendations for an effective follow-up strategy. *J Clin Oncol*. 2003;21:520-529.
22. Baker JJ, Meyers MO, Frank J, et al. Routine restaging PET/CT and detection of initial recurrence in sentinel lymph node positive stage III melanoma. *Am J Surg*. 2014;207:549-554.
23. Rajagopal S, Yao X, Abadir W, et al. Surveillance evaluations in patients with stage I, II, III, or resectable IV melanoma who were treated with curative intent: a systematic review. *Surgical Oncology*. 2024;54:102077. doi:10.1016/j.suronc.2024.102077.
24. Grabowski J, Saltzstein SL, Sadler GR, Tahir Z, Blair S. A comparison of Merkel cell carcinoma and melanoma: results from the California cancer registry. *Clin Med Oncol*. 2008;2:327-333. doi:10.4137/cmo.s423.

Thyroid Cancer (ONC-6)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Thyroid Cancer – General Considerations (ONC-6.0)

ON.TC.0006.0.A

v2.0.2025

- Individuals of all ages with thyroid cancer are imaged according to this guideline.
- Whole-Body Thyroid Nuclear scan (also known as whole-body radioiodine scan) is coded with CPT® 78018. If CPT® 78018 is obtained and found to be positive, CPT® 78020 may be approved as an add-on test to evaluate the degree of iodine uptake.
- Single photon emission computed tomography (SPECT) imaging – Radiopharmaceutical Localization of Tumor SPECT (CPT® 78803 or CPT® 78831) or SPECT/CT Hybrid study (CPT® 78830 or CPT® 78832) may complement planar and pinhole imaging and can be approved as an add-on wherever radioiodine (RAI) scans are indicated.
- Whole-Body Thyroid Nuclear scan (also known as whole-body RAI scan) is the imaging modality of choice for differentiated thyroid cancers, as these are usually not well visualized on FDG-PET/CT scans. Individuals who have RAI-diagnostic scan negative and PET-positive disease will generally not respond to RAI treatment, whereas individuals who have PET-negative and RAI-diagnostic scan negative disease may still be candidates for empiric RAI treatment.
- Radioiodine (RAI) refractory disease is defined as: (i) the malignant/metastatic tissue does not ever concentrate RAI (no uptake outside the thyroid bed at the first therapeutic WBS), (ii)the tumor tissue loses the ability to concentrate RAI after previous evidence of RAI-avid disease (in the absence of stable iodine contamination), (iii) RAI is concentrated in some lesions but not in others, and (iv) metastatic disease progresses despite significant concentration of RAI[6].

Thyroid Cancer – Suspected/Diagnosis (ONC-6.1)

ON.TC.0006.1.A
v2.0.2025

- See: **Thyroid Nodule (NECK-8.1)** in the Neck Imaging Guidelines for suspected thyroid malignancies.

Thyroid Cancer – Initial Work-Up/Staging (ONC-6.2)

ON.TC.006.2.C
v2.0.2025

Follicular, Papillary and Hürthle Cell Carcinomas	Imaging Study
ONE of the following: • Locally advanced disease or fixation suggested by clinical exam and/or ultrasound • Substernal or bulky disease • Disease precluding full ultrasound examination • Vocal cord paresis	ONE of the following: • MRI Neck without contrast (CPT® 70540) • MRI Neck without and with contrast (CPT® 70543) • CT Neck without contrast (CPT® 70490) • CT Neck with contrast (CPT® 70491) can be approved if contrast study is necessary for complete pre-operative assessment and use of IV contrast will not delay post-operative use of RAI therapy.
Post-thyroidectomy to assess thyroid remnant and/or to look for iodine-avid metastases for ONE of the following: • Extent of thyroid remnant cannot be accurately ascertained from the surgical report or neck ultrasound • When the results may alter the decision to treat • Prior to administration of RAI therapy	• Whole-Body Thyroid Nuclear scan (CPT® 78018) • CPT® 78020 is indicated as an add-on test to evaluate the degree of iodine uptake AND/OR • SPECT (CPT® 78803, or CPT® 78831), OR SPECT/CT Hybrid study (CPT® 78830, or CPT® 78832)
Skeletal pain	• Bone scan (CPT® 78306) • Whole-Body Thyroid Nuclear scan (CPT® 78018) • CPT® 78020 is indicated as an add-on test to evaluate the degree of iodine uptake AND/OR • SPECT (CPT® 78803, or CPT® 78831), OR SPECT/CT Hybrid study (CPT® 78830, or CPT® 78832)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Follicular, Papillary and Hürthle Cell Carcinomas	Imaging Study
Suspicious findings on Chest X-ray, US, or substernal extension of mass	• CT Chest without contrast (CPT® 71250)
All other individuals	• Routine preoperative advanced imaging is not indicated

Medullary Thyroid Carcinomas	Imaging Study
ANY of the following: • Elevated CEA levels • Calcitonin level >400pg/mL • Positive lymph nodes	ANY or ALL of the following: • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) **or** CT Abdomen without and with contrast (CPT® 74170) • Bone scan (CPT® 78306)
Skeletal pain	• Bone scan (CPT® 78306)
Inconclusive findings on conventional imaging	• ^{68}Gallium-labeled PET/CT (CPT® 78815)

Anaplastic Thyroid Carcinomas	Imaging Study
All	ONE of the following combinations, not both: • CT Neck with contrast (CPT® 70491), CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177) **OR** • FDG PET/CT (CPT® 78815) In addition to one of the above studies: • MRI Brain without and with contrast (CPT® 70553)
Skeletal pain	• Bone scan

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

For Follicular, Papillary and Hurthle Cell carcinomas, focused imaging of the neck using contrast enhanced CT or MRI is recommended to assess extent of local disease and guide pre-surgical planning. CT Chest with contrast may be indicated based on these results to include substernal extension of the thyroid mass. There are no established guidelines regarding the minimum gap between contrast enhanced CT with iodinated contrast agents and iodine-131/123 for whole body scintigraphy (WBS) in the treatment of residual disease and distant metastases, with majority recommendation of a gap of 4 weeks and 2 months. In the post-thyroidectomy setting, WBS is recommended to assess for either extent of thyroid remnant, when results may alter the decision to treat and prior to administration of radioactive iodine (RAI) therapy. In the presence of skeletal pain, whole body bone scan or WBS to assess for osseous metastases. Medullary thyroid carcinoma is frequently aggressive with 48% of patients having localized disease, 35% with tumors extending beyond the thyroid into surrounding tissues or regional nodes and 13% with distant metastases typically to the lung, liver or bones. Due to these concerns, more extensive staging is indicated that includes contrast enhanced CT of neck, chest and abdomen as well as bone scan if there are elevated CEA levels, calcitonin level >400 pg/nL or positive lymph nodes. Skeletal pain can be imaged with bone scan. Gallium-68 labelled Dotatate PET/CT or if not available Indium-111-pentetreotide (Octreoscan) is useful due to high expression of somatostatin receptors in MTC and is indicated if conventional imaging is inconclusive due to its high sensitivity compared to other imaging modalities especially if calcitonin levels are >500. Anaplastic thyroid carcinoma is the most aggressive variant of thyroid cancer with distant metastases in over 50% of cases at presentation most commonly involving the lung, bone and brain with 5 year survival < 10%. Complete staging with CT Neck, Chest, Abdomen and Pelvis or FDG PET/CT is indicated at diagnosis as well as MRI of the brain.

Thyroid Cancer – Restaging/Recurrence (ONC-6.3)

ON.TC.0006.3.C
v2.0.2025

Follicular, Papillary and Hürthle Cell Carcinomas	Imaging Study
Gross residual disease found in the neck post-thyroidectomy	ANY one of the following: • CT Neck with contrast (CPT® 70491) • MRI Neck without and with contrast (CPT® 70543)
Within 2 weeks (ideally 7 to 10 days) following the administration of Radioactive Iodine therapy	• Whole-body Thyroid Nuclear Scan (CPT® 78018) • The following may be approved as an add-on test: ◦ CPT® 78020 to evaluate the degree of iodine uptake ◦ SPECT (CPT® 78803, or CPT® 78831) or SPECT/CT Hybrid study (CPT® 78830, or CPT® 78832)

Follicular, Papillary and Hürthle Cell Carcinomas	Imaging Study
ANY of the following: • Recurrence documented by biopsy • Increasing thyroglobulin level without Thyrogen® stimulation • Thyroglobulin level >2 ng/mL or higher than previous after Thyrogen® stimulation • Anti-thyroglobulin antibody present • Evidence of residual thyroid tissue on ultrasound or physical exam after thyroidectomy or ablation	ALL of the following: • CT Neck with contrast (CPT® 70491) or MRI Neck without and with contrast (CPT® 70543) • CT Chest with contrast (CPT® 71260) • CT with contrast of any symptomatic body area • Whole-body Thyroid Nuclear Scan (CPT® 78018) ◦ The following may be approved as an add-on test: ▪ CPT® 78020 to evaluate the degree of iodine uptake ▪ SPECT (CPT® 78803 or CPT® 78831), or SPECT/CT Hybrid study (CPT® 78830, or CPT® 78832)
ANY of the following: • Rising thyroglobulin level with negative CT scans AND radioiodine scan • Inconclusive findings on conventional imaging (CT scans and radioiodine scan) • Known radioiodine-refractory disease and CT scans are negative or inconclusive	• FDG PET/CT (CPT® 78815)
Measurable metastatic disease on systemic therapy (no more often than every 2 cycles)	• CT Chest with contrast (CPT® 71260) • CT with contrast of affected or symptomatic body area

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Medullary Thyroid Carcinoma	Imaging Study
ANY of the following: • Elevated CEA levels • Calcitonin level ≥150 pg/mL • Signs or symptoms of recurrence	ANY or ALL of the following: • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) **or** CT Abdomen without and with contrast (CPT® 74170) • Bone scan (CPT® 78306)
Inconclusive conventional imaging with calcitonin ≥150 pg per mL	• ^{68}Gallium-labeled DOTATATE PET/CT (CPT® 78815)

Anaplastic Thyroid Carcinoma	Imaging Study
Measurable metastatic disease on systemic treatment	Any of the following every 2 cycles (usually every 6-8 weeks): • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT of any other involved/symptomatic sites
Signs or symptoms of recurrence	ONE of the following combinations, not both: • CT Neck with contrast (CPT® 70491), CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177) **OR** • FDG PET/CT (CPT® 78815) In addition to one of the above studies: • MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

For Follicular, Papillary and Hurthle Cell carcinomas, CT or MRI neck can be performed if gross residual disease is found in the neck post-thyroidectomy. RAI therapy is administered after thyroidectomy for several reasons to include remnant ablation, treat presumed foci of neoplastic cells and/or treat persistent or recurrent disease.

Within 2 weeks of treatment, WBS is indicated to stage the disease and document the I-131 avidity of any structural lesion. Follow-up is usually a combination of exam, laboratories (thyroglobulin and anti-thyroglobulin antibody levels) and ultrasound. If there is concern for recurrence, CT of the neck/chest as well as any symptomatic body area along with WBS should be performed to complete restaging. In the setting of rising thyroglobulin level with negative conventional imaging, inconclusive conventional imaging or known RAI-refractory disease with negative/inconclusive CT scans, FDG PET/CT can be performed due to its high sensitivity (94%) and specificity (80-84%) compared to conventional imaging. FDG uptake is associated with a worse prognosis and refractoriness to RAI therapy. Initial imaging for MTC recurrence based on elevated CEA levels, calcitonin level >150 pg/mL or signs/symptoms of recurrence should undergo CT neck/chest/abdomen and bone scan. If this imaging is inconclusive and calcitonin is >150, Gallium-68 labeled Dotatate PET/CT or if not available Indium-111-pentetreotide (Octreoscan) is indicated as outlined in the initial work-up/staging section. Initial imaging for ATC recurrence includes either CT Neck, Chest, Abdomen and Pelvis or FDG PET/CT as well as MRI Brain due to its aggressive and widespread behavior. For individuals on systemic therapy, CT of neck/chest/abdomen/pelvis with any additional involved/symptomatic sites can be done every 2 cycles.

Thyroid Cancer – Surveillance/Follow-up (ONC-6.4)

ON.TC.0006.4.A
v2.0.2025

Follicular, Papillary and Hürthle Cell Carcinomas	Imaging Study
Individuals being monitored on active surveillance	• Neck ultrasound (CPT® 76536) every 6 months for 2 years, and then annually thereafter
All other individuals post-treatment	• Neck ultrasound (CPT® 76536) once at 6-12 months post-treatment, and then annually thereafter
For individuals with ANY of the following: • Node positive disease • RAI-avid metastases	• Whole-body Thyroid Nuclear Scan annually (CPT® 78018) ◦ CPT® 78020 is indicated as an add-on test to evaluate the degree of iodine uptake AND/OR • SPECT (CPT® 78803, or CPT® 78831), OR SPECT/CT Hybrid study (CPT® 78830, or CPT® 78832)

Medullary Carcinomas	Imaging Study
All individuals	• CEA and calcitonin are required for monitoring medullary carcinomas • Routine surveillance imaging is not indicated

Anaplastic Thyroid Carcinomas	Imaging Study
All individuals	Every 3 months for 2 years: • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Brain without and with contrast (CPT® 70553)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

For Follicular, Papillary and Hurthle Cell carcinomas, all individuals are monitored with ultrasound either every 6 months for 2 years then annually (active surveillance) or once at 6-12 months then annually (post-treatment). For node positive disease or RAI-avid metastases, WBS annually. MTC is monitored with CEA and calcitonin levels with no routine imaging indicated. ATC requires close monitoring with CT neck/chest/abdomen/pelvis and MRI Brain every 3 months for 2 years as the vast majority of relapses occur within this timeframe.

References (ONC-6)

v2.0.2025

1. Haddad RH, Bischoff L, Ball D, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2023 – July 27, 2023 Thyroid carcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Thyroid carcinoma V3.2023 – Juy 27, 2023 ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Slough CM, Randolph GW. Workup of well-differentiated thyroid carcinoma. *Cancer Control*. 2006;13(2):99-105. doi:10.1177/107327480601300203.
3. Smallridge RC, Ain KB, Asa SL, et al. American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. *Thyroid*. 2012;22(11):1104-1139. doi:10.1089/thy.2012.0302.
4. Wells SA Jr, Asa SL, Dralle H, et al. American Thyroid Association guidelines for the management of medullary thyroid carcinoma. *Thyroid.* 2015;25(6):567-610. doi:10.1089/thy.2014.0335.
5. Yeh MW, Bauer AJ, Bernet VA, et al. American Thyroid Association statement on preoperative imaging for thyroid cancer surgery. *Thyroid.* 2015;25:3-14. doi:10.1089/thy.2014.0096.
6. Haugen BR, Alexander EK, Bible KB, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26(1):1-133. doi:10.1089/thy.2015.0020.
7. Silberstein EB, Alavi A, Balon HR, et al. The SNMMI Practice Guideline for therapy of thyroid disease with ^{131}I3.0.*J Nucl Med*. 2012;53(10):1633-1651. doi:10.2967/jnumed.112.105148.
8. Avram AM, Fig LM, Frey KA, Gross MD, Wong KK. Preablation 131-I scans with SPECT/CT in postoperative thyroid cancer patients: what is the impact on staging? *J Clin Endocrinol Metab*. February 21, 2013 [Epub ahead of print].

Small Cell Lung Cancer (ONC-7)

Guideline Page

Small Cell Lung Cancer – General Considerations (ONC-7.0)

ON.SL.0007.0.A

v2.0.2025

- Combined histologies of small and non-small cell are considered small cell lung cancer. Use this guideline for imaging recommendations for small and large cell high-grade (poorly differentiated) neuroendocrine tumors of the lung.
- Imaging is presently guided by traditional staging of limited or extensive disease.
  - Extensive stage is either metastatic disease or an extent which cannot be encompassed by a single radiotherapy portal.
  - Limited staging is confined to one side of the chest.
- Individuals treated curatively for SCLC are at increased risk for developing a second lung cancer. If new lung nodule is seen on imaging without any evidence of other systemic disease, follow **Lung Metastases (ONC-31.1)** for work-up of nodule.
- For carcinoid (low-grade neuroendocrine tumors) of the lung, see: **Neuroendocrine Cancers and Adrenal Tumors (ONC-15)**.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Small Cell Lung Cancer – Suspected/ Diagnosis (ONC-7.1)

ON.SL.0007.1.A
v2.0.2025

Indication	Imaging Study
• Abnormal chest x-ray or clinical suspicion remains high despite a normal chest x-ray in symptomatic individual	• CT Chest without contrast (CPT® 71250) **or** • CT Chest with contrast (CPT® 71260)
• Pulmonary nodule <8 mm in size noted on CT Chest	• See: **Incidental Pulmonary Nodules Detected on CT Images (CH-16.2)** in the Chest Imaging Guidelines
• Pulmonary nodule 8 mm (0.8 cm) to 30 mm (3 cm) seen on CT Chest or MRI Chest	• PET/CT (CPT® 78815) • PET is Positive: Qualifies as initial staging PET/CT
• Pulmonary mass 31 mm (3.1 cm) or greater seen on CT or MRI	• PET/CT (CPT® 78815) can be approved prior to biopsy if ONE or MORE of the following applies: ◦ Definitive treatment with resection or radiation will be utilized instead of biopsy if PET confirms limited disease ◦ Multiple possible biopsy options are present within the chest and PET findings will be used to determine the most favorable biopsy site • Biopsy is indicated prior to PET imaging for all other indications in pulmonary masses ≥31 mm (3.1 cm) in size
• Mediastinal/Hilar Mass	See: **Lymphadenopathy (CH-2)** in the Chest Imaging Guidelines
• Paraneoplastic syndrome suspected	See: **Paraneoplastic Syndromes (ONC-30.3)**

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

For patients with suspected lung cancer and an abnormal chest x-ray or a high suspicion for lung cancer with symptoms of lung cancer, a CT Chest is indicated, with or without contrast. If a PET/CT is performed in the workup of a pulmonary nodule and is positive, it qualifies as the initial staging PET. The radiotracer supported for PET/CT for lung cancer is 18-FDG (NCI 2024, Megyesfalvi 2023). While some small cell lung cancer (SCLC) has a neuroendocrine component, the sensitivity, specificity and predictive value of dotatate PET/CT are uncertain at this time and dotatate PET is not supported (NCI 2024, Megyesfalvi 2023). Lesions 31mm or greater are considered masses rather than nodules, and should be biopsied rather than re-imaged with PET/CT (MacMahon 2017).

Small Cell Lung Cancer – Initial Workup/ Staging (ONC-7.2)

ON.SL.0007.2.C
v2.0.2025

Indication	Imaging Study
Initial staging	ANY or ALL of the following: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Brain without and with contrast (CPT® 70553) • Bone scan (CPT® 78306), if PET/CT not being done
To confirm the extent of disease when initial CT Chest/Abdomen/ Pelvis and MRI Brain indicate limited stage disease (confined to one side of the chest)	• PET/CT (CPT® 78815)

Evidence Discussion

SCLC has widespread distant metastatic potential, with 2/3 of patients having metastatic disease at diagnosis and 10-15% including central nervous system disease (NCI 2024, Megyesfalvi 2023). Diagnostic, contrasted CTs of chest, abdomen and pelvis as well as MRI brain with and without contrast are supported (Ganti 2024). If PET has been completed in the pulmonary nodule workup, a repeat PET/CT is generally not supported. If a PET/CT was done prior to diagnosis and conventional imaging clearly shows extensive stage disease, a PET/CT does not change management. However, if a PET/ CT was not done prior to diagnosis, a PET/CT is supported to confirm limited stage disease prior to treatment, as FDG PET/CT changes stage versus conventional imaging in up to 25% of patients(NCI 2024, Megyesfalvi 2023). Bony metastatic disease is not unusual in SCLC; thus, evaluation for bony metastatic disease is supported (NCI 2024, Ganti 2024).

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Small Cell Lung Cancer – Restaging/ Recurrence (ONC-7.3)

ON.SL.0007.3.C
v2.0.2025

Indication	Imaging Study
Treatment Response: • After every 2 cycles of chemotherapy • Following completion of chemoradiation	ANY or ALL of the following: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Brain without and with contrast (CPT® 70553) for measurable brain metastases being treated with systemic therapy • Bone scan (CPT® 78306) • PET is not indicated for evaluation of treatment response in SCLC, but can be considered on a case-by-case basis.
Restaging (suspected recurrence)	ANY or ALL of the following: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Brain without and with contrast (CPT® 70553) • Bone scan (CPT® 78306) • PET is not indicated for evaluation of recurrent SCLC but can be considered on a case-by-case basis.
For response assessment following primary treatment	• MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

Conventional imaging with contrasted CT Chest, Abdomen and Pelvis is supported every 2 cycles of chemotherapy and at the end of chemoradiation. MRI Brain with and without contrast is supported when there is measurable CNS disease being treated with systemic therapy. If prophylactic cranial irradiation (PCI) is planned, an MRI brain is

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

supported at end of initial treatment as some patients will harbor asymptomatic brain metastases and will require different management (Ganti 2024, Gaebe 2024), and PCI would expose the patient to radiation doses and neurotoxicity without benefit. CT Chest, Abdomen and Pelvis as well as MRI Brain and bone scan are supported if recurrence is suspected. Further literature is emerging to determine the role of FDG PET-CT for treatment response and suspected recurrence; these guidelines do not routinely support PET/CT for treatment response or suspected recurrence of SCLC, but provide flexibility on a case by case basis, particularly for patients with bony metastatic disease (Quartuccio 2019 and 2021, NCI 2024, Ganti 2024).

Small Cell Lung Cancer – Surveillance/ Follow-up ONC-7.4

ON.PC.0007.4.A
v2.0.2025

Indication	Imaging Study
Limited stage SCLC	Every 3 months for one year, every 6 months for two years, and then annually: • CT Chest without (CPT® 71250) or CT Chest with (CPT® 71260) contrast • CT Abdomen and Pelvis with contrast (CPT® 74177)
Extensive stage SCLC	Every 2 months for one year, every 4 months for two years, every 6 months for two years, and then annually: • CT Chest without (CPT® 71250) or CT Chest with (CPT® 71260) contrast • CT Abdomen and Pelvis with contrast (CPT® 74177)
Screening for brain metastases, regardless of PCI status	• MRI Brain without and with contrast (CPT® 70553) every 4 months for 1 year and then every 6 months thereafter
Surveillance of known and/or treated brain metastases	• See: **Brain Metastases (ONC-31.3)**
New lung nodule(s)	• See: **Lung Metastases (ONC-31.1)**

Evidence Discussion

Surveillance with CT contrasted chest, abdomen and pelvis is supported. MRI chest is less sensitive than CT chest and usually not supported as a substitution for lung cancer, and CT abdomen/pelvis are favored by ACR over MRI for this indication as well (ACR 2024). Follow up is supported more frequently in the first two years post treatment, as that is when recurrence is most common (NCI 2024, Ganti 2024, Megyesfalvi 2023). The surveillance timeframe is determined by the initial extent of disease. For those with limited stage disease, these guidelines support the above CT imaging every 3 months for 1 year, every 6 months for 2 years, and then annually. For those with extensive stage disease, imaging with above CTs is supported every 2 months for 1 year, every 4 months for two years, and then every 6 months for 1 year. This is within

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

the wide timeframe recommended by the NCCN, determined with support from other data (Ganti 2024, Carter 2014, Kalemkenian 2011). Up to 30% of patients develop metastatic disease to the brain. Screening for brain metastases is supported to allow early treatment of brain metastases prior to potentially impairing neurologic symptoms. MRI is preferred over CT for its increased sensitivity and specificity, at an interval of every 4 months for 1 year then every 6 months indefinitely (Ganti 2024, NCI 2024, Gaebe 2024). PET/CT is not supported for surveillance due to excessive radiation exposure, false positive incidental findings, and financial toxicity.

References (ONC-7)

v2.0.2025

1. Ganti AKP, Loo Jr. BW, Badiyan S, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – June 11, 2024 Small Cell Lung Cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Small Cell Lung Cancer V3.2024 – June 11, 2024 ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Lu YY, Chen JH, Liang JA, Chu S, Lin WY, Kao CH. 18F-FDG PET or PET/CT for detecting extensive disease in small-cell lung cancer: a systematic review and meta-analysis. *Nucl Med Commun*. 2014;35(7):697-703. doi:10.1097/MNM.0000000000000122.
3. Carter BW, Glisson BS, Truong MT, Erasmus JJ. Small cell lung carcinoma: staging, imaging, and treatment considerations. *Radiographics*. 2014;34(6):1707-1721. doi:10.1148/rg.346140178.
4. Kalemkerian G. Staging and imaging of small cell lung cancer. *Cancer Imag*. 2011;11(1):253-258.doi:10.1102/1470-7330.2011.0036.
5. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: From the Fleischner Society 2017. *Radiology*. 2017;284(1):228-243. doi:10.1148/radiol.2017161659.
6. Megyesfalvi Z, Gay CM, Popper H, et al. Clinical insights into small cell lung cancer: Tumor heterogeneity, diagnosis, therapy, and future directions. *CA Cancer J Clin*. 2023;73(6):620-652. doi:10.3322/caac.21785.
7. Gaebe K, Erickson AW, Li AY, et al. Re-examining prophylactic cranial irradiation in small cell lung cancer: a systematic review and meta-analysis. *EClinicalMedicine*. 2024;67:102396. doi:10.1016/j.eclinm.2023.102396.
8. Quartuccio N, Evangelista L, Alongi P, et al. Prognostic and diagnostic value of [18F]FDG-PET/CT in restaging patients with small cell lung carcinoma: an Italian multicenter study. *Nucl Med Commun*. 2019;40(8):808-814. doi:10.1097/MNM.0000000000001038.
9. PDQ® Adult Treatment Editorial Board. PDQ Small Cell Lung Cancer Treatment. Bethesda, MD: National Cancer Institute. Available at: https://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq.

Non-Small Cell Lung Cancer (ONC-8)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Non-Small Cell Lung Cancer – General Considerations (ONC-8.0)

ON.NL.0008.0.C
v2.0.2025

- Non-small cell lung cancer includes adenocarcinoma, squamous cell carcinoma, adenosquamous, and large cell tumors.
- See: **Bronchopulmonary or Thymic Carcinoid – Initial Staging (ONC-15.6)** for evaluation of low-grade neuroendocrine tumors (carcinoid) of the lung.
- See: **Small Cell Lung Cancer (ONC-7)** for evaluation of high-grade small cell and large cell neuroendocrine tumors of the lung.
- PET/CT may be considered to confirm solitary focus of extra-pulmonary metastatic disease (i.e., brain or adrenal) if the individual is being considered for an aggressive treatment for oligometastatic disease.

Non-Small Cell Lung Cancer – Asymptomatic Screening (ONC-8.1)

ON.NL.0008.1.A

v2.0.2025

- See: **Lung Cancer Screening (CH-33)** in the Chest Imaging Guidelines for criteria for Low-dose CT Chest for lung cancer screening.

Non-Small Cell Lung Cancer – Suspected/Diagnosis (ONC-8.2)

ON.NL.0008.2.A
v2.0.2025

Indication	Imaging Study
Abnormal chest x-ray or clinical suspicion remains high despite a normal chest x-ray in symptomatic individual	• CT Chest without contrast (CPT® 71250) **or** • CT Chest with contrast (CPT® 71260)
Pulmonary nodule <8 mm in size noted on CT Chest	• See: **Incidental Pulmonary Nodules Detected on CT Images (CH-16.2)** in the Chest Imaging Guidelines
Pulmonary nodule 8 mm (0.8 cm) to 30 mm (3 cm) seen on CT Chest or MRI Chest	• PET/CT (CPT® 78815) • If PET is Positive: Qualifies as initial staging PET/CT
Pulmonary mass 31 mm (3.1 cm) or greater seen on CT or MRI	• PET/CT (CPT® 78815) can be approved prior to biopsy if ONE or MORE of the following applies: ◦ Definitive treatment with resection or radiation will be utilized instead of biopsy if PET confirms limited disease ◦ Multiple possible biopsy options are present within the chest and PET findings will be used to determine the most favorable biopsy site • Biopsy is indicated prior to PET imaging for all other indications in pulmonary masses ≥31 mm (3.1 cm) in size
Mediastinal/Hilar Lymphadenopathy	See: **Mediastinal Lymphadenopathy (CH-2.3)** in the Chest Imaging Guidelines
Mediastinal/Hilar Mass	See: **Mediastinal Mass (CH-20)** in the Chest Imaging Guidelines
Paraneoplastic syndrome suspected	See: **Paraneoplastic Syndromes (ONC-30.3)**

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

For patients with suspected lung cancer and an abnormal chest x-ray or a high suspicion for lung cancer with symptoms of lung cancer, a CT Chest is indicated, with or without contrast. If a PET/CT is performed in the workup of a pulmonary nodule and is positive, it qualifies as the initial staging PET. The radiotracer supported for PET/CT for lung cancer is 18-FDG (NCI 2024, MacMahon 2017). Lesions 31mm or greater are considered masses rather than nodules (MacMahon 2017). There is no clear evidence for PET/CT over biopsy in this case. Generally, masses should be biopsied rather than re-imaged. PET/CT is supported if definitive treatment with resection or radiation will be utilized instead of biopsy (if PET confirms limited disease), or if multiple biopsy sites are present within the chest and PET findings will be used to determine the most favorable biopsy site. This maximizes patient safety when making decisions regarding invasive procedures.

Non-Small Cell Lung Cancer – Initial Work-Up/Staging (ONC-8.3)

ON.NL.0008.3.C
v2.0.2025

Indication	Imaging Study
All individuals	ANY or ALL of the following: • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) ◦ CT Abdomen may be omitted if CT Chest report clearly documents upper abdomen through level of adrenals • PET/CT (CPT® 78815) (if not already completed prior to histological diagnosis) • Bone scan (CPT® 78306, if PET/CT not being done)
ANY of the following: • All Stage IB-IV disease	• MRI Brain without and with contrast (CPT® 70553)
Superior sulcus (Pancoast) tumor suspected	ANY or ALL of the following: • MRI Chest without and with contrast (CPT® 71552) • MRI Cervical Spine without and with contrast (CPT® 72156) • MRI Thoracic Spine without and with contrast (CPT® 72157)

Evidence Discussion

CT Chest and upper abdomen to the level of the adrenals is supported for initial staging, as liver and adrenal metastatic disease are common in NSCLC. Pelvic disease is rare and imaging of the pelvis without pelvic symptoms is not recommended by NCCN (Riely, 2025). FDG PET-CT is supported by NCCN in all patients (Riely, 2025).

Over 10% of patients with stage III or IV disease present with metastatic disease to the brain, and 4-5% of patients with stage II disease. MRI Brain with and without contrast has a higher detection rate for metastatic disease to the brain than CT, and is indicated

in all patients with stage II-IV disease (Riely, 2025). For patients with stage IB disease, MRI Brain with and without contrast is optional in this setting but can be considered to prevent under-staging and under-treatment, since a small number of patients with apparent stage I disease and no CNS symptoms will have occult brain lesions (Riely 2025, NCI 2024) and will require additional therapies.

For patients with superior sulcus (Pancoast) tumor, MRI Chest and MRI Cervical and Thoracic Spine with and without contrast have higher specificity for chest wall invasion, neurologic involvement, and fibrosis than CT alone, and are supported in addition to the imaging stated above (Unal 2024, Riely 2025).

Non-Small Cell Lung Cancer – Restaging/Recurrence (ONC-8.4)

ON.NL.0008.4.C
v2.0.2025

Indication	Imaging Study
Stage I or II individuals who undergo definitive local treatment with surgery, radiation, or radiosurgery	• Restaging imaging is not indicated. See: **Surveillance/Follow-Up (ONC-8.5)**
ANY of the following: • After neoadjuvant treatment for evaluation of surgical resectability • Prior to starting adjuvant therapy • Inadequately resected disease	• CT Chest with contrast (CPT® 71260) **or** CT Chest without contrast (CPT® 71250)

Indication	Imaging Study
Measurable metastatic disease, undergoing active treatment, after every 2 cycles of chemotherapy	ANY or ALL of the following studies: • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be substituted for known pelvic disease or pelvic symptoms • CT with contrast of other involved body areas In addition to the above studies, for individuals receiving systemic treatment for brain metastases: • MRI Brain without and with contrast (CPT® 70553) In addition to the above studies, for individuals receiving systemic treatment for bone metastases: • Bone scan • PET/CT is not indicated for routine evaluation of NSCLC that is metastatic outside the chest cavity
Suspected recurrence	• CT Chest with contrast (CPT® 71260); **and** CT Abdomen with contrast (CPT® 74160) ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be substituted for known pelvic disease or pelvic symptoms For individuals with prior history of brain metastases or current signs or symptoms of brain metastasis: • MRI Brain without and with contrast (CPT® 70553)

Indication	Imaging Study
ANY of the following: • Biopsy proven recurrence localized to the chest cavity • Inconclusive findings conventional imaging • To differentiate tumor from radiation scar/fibrosis • Stage IV with oligometastatic disease on conventional imaging and individual is a candidate for aggressive surgical resection or other localized treatment of metastases with a curative intent	• PET/CT (CPT® 78815)
ANY of the following: • Following a demonstrated adequate response to neoadjuvant therapy if intracranial disease will preclude surgery • Documented recurrence/progression • New or worsening neurological signs or symptoms	• MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

In alignment with the NCCN, CT Chest and Abdomen with contrast are supported every two cycles, with pelvic imaging only for a history of pelvic disease or new pelvic symptoms. These are also supported at any time for clinically suspected recurrence.

MRI brain with and without contrast is supported every 2 cycles for patients with known brain metastases being treated with systemic therapy, or at any time for patients with new neurologic symptoms or documented systemic progression (Riely, 2025). An additional CT chest is supported if requested after neoadjuvant therapy to evaluate for resectability, in the interest of safe resection. CT is also supported post-operatively to assess baseline prior to starting adjuvant therapy, in alignment with NCCN (Riely, 2025).

Non-Small Cell Lung Cancer – Surveillance/Follow-up (ONC-8.5)

ON.NL.0008.5.A
v2.0.2025

Indication	Study
Stage I-II (treatment including surgery and/ or chemotherapy, but no radiation)	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 6 months for 3 years and then annually
Stage I-II treated with radiation therapy Stage III-IV (metastatic sites treated with definitive intent)	• CT Chest with contrast (CPT® 71260) **or** CT Chest without contrast (CPT® 71250) every 3-6 months for 3 years, every 6 months for 2 years and then annually
New lung nodule	• See: **Lung Metastases (ONC-31.1)**

Evidence Discussion

CT Chest with or without contrast is recommended by national guidelines every 6 months for 3 years and then annually for patients with stage I or II disease. To prevent under-treatment, patients treated with radiation who have residual abnormalities on imaging may undergo more frequent imaging every 3-6 months for the first year then every 6 months for 2 years, then annually thereafter (Riely 2025, Schneider 2020). Patients with stage II disease or definitively treated metastatic disease are at higher risk for relapse particularly in the first 2 years, and NCCN recommends CT Chest every 3-6 months for 3 years, every 6 months for 2 years, then annually. (Riely, 2025, Schneider 2020). Asymptomatic abdominal and pelvic imaging exposes to radiation with low-yield for metastatic disease detection and is not supported (Riely 2025, Schneider 2020). FDG-PET is not supported for surveillance due to excessive false positive rates, radiation exposure, and increased risk of unnecessary procedures for incidental false positive findings (Schneider 2020, Riely 2025). MRI brain for asymptomatic surveillance is low yield in asymptomatic NSCLC surveillance and is not routinely recommended (Schneider 2020, Riely 2025).

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-8)

v2.0.2025

1. Riely GJ, Wood DE, Aisner DL, et al, National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2025 – January 14, 2025. Non-small cell lung cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Non-small cell lung cancer V3.2025 – January 14, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Scheider BJ, Ismaila N, Aerts J, et al. Lung cancer surveillance after definitive curative-intent therapy: ASCO guideline. *J Clin Oncol*. 2020;38(7):753-766. doi:10.1200/JCO.19.02748.
3. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. *Radiology*. 2017;284(1):228-243. doi:10.1148/radiol.2017161659.
4. Calman L, Beaver K, Hind D, Lorigan P, Roberts C, Lloyd-Jones M. Survival benefits from follow-up of patients with lung cancer: a systematic review and meta-analysis. *J Thorac Oncol*. 2011;6(12):1993-2004. doi:10.1097/JTO.0b013e31822b01a1.
5. Lou F, Huang J, Sima CS et al. Patterns of recurrence and second primary lung cancer in early-stage lung cancer survivors followed with routine computed tomography surveillance. *J Thorac Cardiovasc Surg*. 2013;145:75-81. https://www.ncbi.nlm.nih.gov/pubmed/23127371 .
6. Colt HG, Murgu SD, Korst RJ, et al. Follow-up and surveillance of the patient with lung cancer after curative-intent therapy: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143:e437S-454S. https://www.ncbi.nlm.nih.gov/pubmed/23649451 .
7. Dane B, Grechushkin V, Plank A, et al. PET/CT vs. non-contrast CT alone for surveillance 1-year post lobectomy for stage I non-small cell lung cancer. *Am J Nucl Med Mol Imaging*. 2013; 3:408-416. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3784804/ .
8. Zhao L, He ZY, Zhong XN, et al. (18)FDG-PET/CT for detection of mediastinal nodal metastasis in non-small cell lung cancer: a meta-analysis. *Surg Oncol*. 2012;21(3):230-236. https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0049561/ .
9. Li J, Xu W, Kong F, et al. Meta-analysis: accuracy of 18FDG PET-CT for distant metastasis in lung cancer patients. *Surg Oncol*. 2013;22(3):151-155. https://www.ncbi.nlm.nih.gov/pubmed/23664848 .
10. Ravenel JG. Evidence-based imaging in lung cancer: a systematic review. *J Thorac Imaging*. 2012; 27(5):315-324. http://journals.lww.com/thoracicimaging/Abstract/2012/09000/Evidence_based_Imaging_in_Lung_Cancer__A.8.aspx .
11. Bille A, Pelosi E, Skanjeti A, et al. Preoperative intrathoracic lymph node staging in patients with non-small-cell lung cancer: accuracy of integrated positron emission tomography and computed tomography. *Eur J Cardiothorac Surg*. 2009;36(3):440-445. https://academic.oup.com/ejcts/article-lookup/doi/10.1016/j.ejcts.2009.04.003.
12. Ravenel JG, Rosenzweig KE, Kirsch J, et al. ACR Appropriateness Criteria non-invasive clinical staging of bronchogenic carcinoma. *J Am Coll Radiol*. 2014;11(9):849-56. doi:10.1016/j.jacr.2014.05.020.
13. Ünal S, Heineman DJ, van Dorp M, et al. Chest wall resections for sulcus superior tumors. *J Thorac Dis*. 2024;16(2):1715-1723. doi: 10.21037/jtd-23-828.
14. PDQ® Adult Treatment Editorial Board. PDQ Non-Small Cell Lung Cancer Treatment. Bethesda, MD: National Cancer Institute. Available at Non-Small Cell Lung Cancer Treatment (PDQ®) - NCI.

Esophageal and GE Junction Cancer (ONC-9)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Esophageal and GE Junction Cancer – General Considerations (ONC-9.0)

ON.EJ.0009.0.C

v2.0.2025

- Imaging for esophageal cancer is determined by the cell type and in which third of the esophagus it occurs.
- These guidelines may be used for imaging of esophageal and gastroesophageal (GE) junction cancers.

Esophageal and GE Junction Cancer – Suspected/Diagnosis (ONC-9.1)

ON.EJ.0009.1.A

v2.0.2025

- See: **Dysphagia and Upper Digestive Tract Disorders (NECK-3.1)** in the Neck Imaging Guidelines for evaluation of suspected esophageal malignancy.

Esophageal and GE Junction Cancer – Initial Work-up/Staging (ONC-9.2)

ON.EJ.0009.2.A
v2.0.2025

Indication	Imaging Study
Biopsy proven	• CT Chest (CPT® 71260) and CT Abdomen (CPT® 74160) with contrast ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be approved instead of CT Abdomen if there are pelvic signs or symptoms
In addition to the above, for any of the following: • Upper 1/3 of esophagus • Neck mass	• CT Neck with contrast (CPT® 70491)
If no evidence of metastatic disease on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

- Upon initial diagnosis of cancer, CT Chest/Abdomen is recommended with the addition of pelvis if there are signs/symptoms of disease. NCCN states that "CT can be used to determine the location of the primary tumor and its proximity to other structures" (Ajani, 2024).
- Cancers diagnosed in the upper 1/3 of the esophagus should also obtain CT of the neck due to concern for nodal spread.
- If CT imaging does not show evidence of metastatic disease, PET/CT is indicated to assess for occult metastases to help finalize treatment options (curative versus palliative). PET/CT is not sensitive for locoregional nodal assessment as often these nodes are obscured by metabolic activity in the primary tumor but is more sensitive than CT for detecting distant metastases.
- NCCN also states that PET/CT has "limited ability to ability to differentiate between cT1, cT2, and cT3 tumors. Therefore, CT should be performed as part of initial workup (as well as pelvic CT scan with contrast if clinically indicated) while FDG-PET/CT should be reserved for patients with no evidence of M1 disease" (Ajani, 2024).

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Esophageal and GE Junction Cancer – Restaging/Recurrence (ONC-9.3)

ON.EJ.0009.3.A
v2.0.2025

Indication	Imaging Study
After primary chemoradiation therapy prior to surgery	Any ONE of the following, not both: • PET/CT (CPT® 78815) no sooner than 5 weeks post completion of radiation therapy OR • CT Chest (CPT® 71260) and CT Abdomen (CPT® 74160) with contrast ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be approved instead of CT Abdomen if there are pelvic signs or symptoms or known pelvic disease
Post-surgical resection	• See: **Surveillance/Follow-up (ONC-9.4)**
Monitoring response to chemotherapy for stage IV/ metastatic disease	Every 2 cycles of treatment (~every 6-8 weeks): • CT Abdomen with contrast (CPT® 74160) • CT Chest with contrast (CPT® 71260)
• If conventional imaging is inconclusive **or** • Salvage surgical candidate with recurrence and no metastatic disease documented by conventional imaging	• PET/CT (CPT® 78815)
For ANY of the following: • Signs or symptoms of recurrence • Biopsy proven on follow-up endoscopy • Recurrence suggested by other imaging (i.e. chest x-ray or barium swallow)	• CT Chest (CPT® 71260) and CT Abdomen (CPT® 74160) with contrast

Indication	Imaging Study
If previously involved or new signs or symptoms	• CT Pelvis with contrast (CPT® 72193) and/or CT Neck with contrast (CPT® 70491)

Evidence Discussion

- Primary treatment typically involves chemoradiotherapy alone, surgery alone or both.
- After primary chemoradiation has been completed and prior to surgery, one of the following is recommended: CT Chest/Abdomen or PET/CT, with the latter ideally no sooner than 5 weeks after completion of radiation to minimize risk of false positives.
- Post-surgical resection is handled as disease surveillance.
- For Stage IV disease on chemotherapy, CT Chest/Abdomen indicated every 2 cycles.
- If conventional imaging is inconclusive or the member is a candidate for salvage surgery upon recurrence with no evidence of metastatic disease, PET/CT is indicated.
- CT Chest/Abdomen for signs/symptoms of recurrence, biopsy proven recurrence on follow-up endoscopy and recurrence suggested by other imaging.
- CT imaging of any appropriate area (e.g. neck, pelvis) if new signs/symptoms or known previous involvement.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Esophageal and GE Junction Cancer – Surveillance/Follow-up (ONC-9.4)

ON.EJ.0009.4.A
v2.0.2025

Indication	Imaging Study
Stage 0-IA (Tis, T1a) disease	• No routine advanced imaging indicated
Stage IB (T1b)-III disease	• CT Chest (CPT® 71260) and CT Abdomen (CPT® 74160) with contrast every 6 months for 2 years and then annually for 3 more years
Stage IV disease	• See: **Phases of Oncology Imaging and General Phase-Related Considerations (ONC-1.2)**

Evidence Discussion

- Stage 0-IA (Tis, T1a): No routine advanced imaging indicated. Fully treated Tis and T1aN0 disease have prognoses that approximate a non-cancer cohort.
- Stage IB (T1b): CT Chest/Abdomen with contrast annually for 3 years. T1b does not perform as well as fully treated Tis and T1aN0 disease, thus supporting current recommendations.
- Stage II-III: CT Chest/Abdomen every 6 months for 2 years then annually for 3 years.
- Stage IV: CT Chest/Abdomen (additional sites as clinically indicated) every 3 months while on maintenance therapy or every 3 months up to 5 years if being monitored off therapy.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-9)

v2.0.2025

1. Ajani JA, D'Amico TA, Barzi A, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 5.2024 – December 20, 2024. Esophageal and esophagogastric junction cancers, available at: https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Esophageal and esophagogastric junction cancers V5.2024 – December 20, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Klaeser B, Nitzsche E, Schuller JC, et al. Limited predictive value of FDG-PET for response assessment in the preoperative treatment of esophageal cancer: results of a prospective multi-center trial (SAKK 75/02). *Onkologie*. 2009;32(12):724-730. doi:10.1159/000251842.
3. Malik V, Lucey JA, Duffy GJ, et al. Early repeated 18F-FDG PET scans during neoadjuvant chemoradiation fail to predict histopathologic response or survival benefit in adenocarcinoma of the esophagus. *J Nucl Med*. 2010;51(12):1863-1869. doi:10.2967/jnumed.110.079566.
4. Stiekema J, Vermeulen D, Vegt E, et al. Detecting interval metastases and response assessment using 18F-FDG PET/CT after neoadjuvant chemoradiotherapy for esophageal cancer. *Clin Nucl Med.* 2014;39(10):862-867. doi:10.1097/RLU.0000000000000517.
5. Sudo K, Xiao L, Wadhwa R, et al. Importance of surveillance and success of salvage strategies after definitive chemoradiation in patients with esophageal cancer. *J Clin Oncol*. 2014;32(30):3400-3405. doi:10.1200/JCO.2014.56.7156.
6. Lou F, Sima CS, Adusumilli PS, et al. Esophageal cancer recurrence patterns and implications for surveillance. *J Thorac Oncol.* 2013;8(12):1558–1562. doi:10.1097/01.JTO.0000437420.38972.fb.
7. Goense L, van Rossum PS, Reitsma JB, et al. Diagnostic performance of 18F-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*. 2015;56(7):995-1002. doi:10.2967/jnumed.115.155580.
8. van Westreenen HL, Westerterp M, Bossuyt PMM, et al. Systematic review of the staging performance of 18F-fluorodeoxyglucose positron emission tomography in esophageal cancer. *J Clin Oncol*. 2004;22:3805- 3812.
9. van Westreenen HL, Heeren PA, van Dullemen HM, et al. Positron emission tomography with F-18-fluorodeoxyglucose in a combined staging strategy of esophageal cancer prevents unnecessary surgical explorations. *J Gastrointest Surg*. 2005;9:54-61.
10. Nilsson K, Klevebro F, Sunde B, et al. Oncologic outcomes of standard versus prolonged time to surgery after neoadjuvant chemoradiotherapy for oesophageal cancer in the multicenter, randomized, controlled NeoRes II trial. *Annals of Oncology*. 2023;34:1015-1024.

Other Thoracic Tumors (ONC-10)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Malignant Pleural Mesothelioma – Suspected/Diagnosis (ONC-10.1)

ON.OT.0010.1.A

v2.0.2025

- See: **Asbestos Exposure (CH-9.1)** in the Chest Imaging Guidelines for evaluation of suspected mesothelioma.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Malignant Pleural Mesothelioma – Initial Work-up/Staging (ONC-10.2)

ON.OT.0010.2.A
v2.0.2025

Indication	Imaging Study
Cytologically or pathologically proven	• CT Chest (CPT® 71260) **and** CT Abdomen (CPT® 74160) with contrast ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be approved instead of CT Abdomen if there are pelvic signs or symptoms • PET/CT (CPT® 78815) if no evidence of metastatic disease or inconclusive conventional imaging
Preoperative planning	• MRI Chest without and with contrast (CPT® 71552)

Evidence Discussion

Initial staging guidelines are based on National Comprehensive Cancer Network (NCCN) recommendations. Contrasted CT chest and CT abdomen are supported for initial staging once mesothelioma is proven with lung fluid cytology or tissue biopsy. Contrast allows better evaluation of nodal disease in addition to parenchymal disease and offers improved characterization of direct extrapulmonary tumor invasion. MRI is inferior for parenchymal lung imaging thus CT is essential. Anatomic soft tissue detail, differentiation from progressive benign fibrosis, and brachiocephalic vascular involvement may be better demonstrated on MRI without and with contrast, so this study is supported for preoperative planning. The most common site of metastatic disease outside the chest is the liver, so CT abdomen is an important part of the initial workup. However, pelvic disease is rare and pelvic CT exposes to additional radiation and is low yield in patients without pelvic signs and symptoms. Pelvis may be added to contrasted CT in patients with signs and symptoms of pelvic involvement, including direct abdominoperitoneal invasion. National Cancer Database review of over 40,000 patients treated between 2004 and 2020 reveals that 50% of patients are metastatic upon presentation. Signs and symptoms of metastatic disease in body areas not addressed in ONC 10 may be imaged according to their respective sections in ONC 31, for which separate evidence summaries are provided.

PET/CT is not first line imaging for mesothelioma as it is inadequate for differentiating benign vs malignant changes in exposure-related progressive massive pulmonary

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

fibrosis, but of which take up FDG in unpredictable fashions. Understaging of the primary site is common with PET/CT alone. Conventional imaging is essential. However, PET/CT is supported to confirm the absence of metastatic disease on conventional imaging (negative or inconclusive) prior to resection, as up to 29% of patients initially identified as operable may be reclassified as inoperable due to identification of distant metastatic disease on PET/CT during pre-operative evaluation.

Malignant Pleural Mesothelioma – Restaging (ONC-10.3)

ON.OT.0010.3.A
v2.0.2025

Indication	Imaging Study
Signs or symptoms of recurrence	• CT Chest (CPT® 71260) **and** CT Abdomen (CPT® 74160) with contrast ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be approved instead of CT Abdomen if there are pelvic signs or symptoms
Treatment with chemotherapy	Every 2 cycles: • CT Chest (CPT® 71260) **and** CT Abdomen (CPT® 74160) with contrast ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be approved instead of CT Abdomen if there are pelvic signs or symptoms
Following induction chemotherapy prior to surgical resection	• CT Chest (CPT® 71260) **and** CT Abdomen (CPT® 74160) with contrast ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) may be approved instead of CT Abdomen if there are pelvic signs or symptoms • PET/CT (CPT® 78815) if no evidence of metastatic disease
Inconclusive CT Chest	• MRI Chest without and with contrast (CPT® 71552)

Evidence Discussion

For patients on chemotherapy, contrasted CT of chest and abdomen are supported every 2 cycles. Pelvic imaging may be added for signs and symptoms of peritoneal/ pelvic disease or known pelvic/peritoneal disease as noted in the initial staging section. The same logic applies to any patients with signs and symptoms of recurrence.
For patients receiving induction chemotherapy, CT chest and abdomen (with pelvis if previously reviewed indications are present) are supported at end of induction. Response is categorized by validated mRECIST criteria on CT. If there is no metastatic disease, this may again be confirmed with PET/CT prior to attempted resection,

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

ensuring the patient is not subjected to futile invasive surgery when RT or further systemic therapy may be more appropriate. If CT chest is inconclusive, MRI chest without and with contrast is supported. MRI chest may differentiate between treatment-related changes (fibrosis) and persistent mesothelioma, which is not well-differentiated on PET/CT as both may have unpredictable FDG uptake.

Malignant Pleural Mesothelioma – Surveillance (ONC-10.4)

ON.OT.0010.4.A
v2.0.2025

Indication	Imaging Study
All	• CT Chest with contrast (CPT® 71260) and previously involved regions every 3 months for 2 years, then annually thereafter

Evidence Discussion

There is no clear consensus for surveillance imaging for malignant pleural mesothelioma, and the NCCN offers no guidance on this topic. The European Society of Medical Oncology (ESMO) advises CT for surveillance without a specific timeframe. Given the known value of CT in assessing primary mesothelioma and abdomino/peritoneal metastatic disease, these guidelines support CT for surveillance. The timeframe is based on National Cancer Database survival statistics for malignant pleural mesothelioma. In review of 40,000+ patients treated between 2004 and 2020, patients undergoing surgery had a median survival time for 19.8 months, compared with 7.9 moths in those who had not undergone surgery. The 2 year survival for those who underwent surgery was 44%, with 18% 2 year survival in unresectable patients. 5-year survival is 5% in unresected patients, and 16% in those who underwent surgery. These guidelines support CT Chest and Abdomen with contrast every 3 months for the first 2 years, then annually. As noted in the restaging section, CT imaging is always supported for new signs and symptoms.

Thymoma and Thymic Carcinoma – Suspected/Diagnosis (ONC-10.5)

ON.OT.0010.5.A

v2.0.2025

- See: **Mediastinal Mass (CH-20.1)** in the Chest Imaging Guidelines for evaluation of suspected thymic malignancies.
- See: **Bronchopulmonary or Thymic Carcinoid – Initial Staging (ONC-15.6)** for imaging guidelines for thymic carcinoid.

Thymoma and Thymic Carcinoma – Initial Work-up/Staging (ONC-10.6)

ON.OT.0010.6.A
v2.0.2025

Indication	Imaging Study
Encapsulated or invasive limited disease	• CT Chest with contrast (CPT® 71260)
Extensive mediastinal involvement on CT Chest	• CT Abdomen with contrast (CPT® 74160) • CT Neck with contrast (CPT® 70491)
Inconclusive finding on CT	ONE of the following: • PET/CT (CPT® 78815) • MRI Chest without and with contrast (CPT® 71552)
Preoperative planning	• MRI Chest without and with contrast (CPT® 71552)
Thymic Carcinomas	• Image according to **Non-Small Cell Lung Cancer - Initial Work-up/Staging (ONC-8.3)**

Evidence Discussion

Thymomas and thymic carcinomas originate in the thymus and are epithelial tumors. Thymomas are rare tumors (though most common primary tumor of anterior mediastinum) that typically spread locally with 5 year survival rates of 90% while thymic carcinomas are very rare, more invasive and often present with metastases with 5 year survival rates of 55%. Initial imaging for thymoma includes CT Chest with contrast that usually shows a well-defined rounded or oval mass without adenopathy. If there is extensive mediastinal involvement, CT Neck/Abdomen with contrast can be performed. If CT imaging is inconclusive, PET/CT or MRI Chest with and without contrast may be indicated, with MRI preferred in thymic carcinoma. For preoperative planning, MRI Chest is also indicated.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Thymoma and Thymic Carcinoma – Restaging (ONC-10.7)

ON.OT.0010.7.A
v2.0.2025

Indication	Study
Adjuvant therapy following surgical resection	• Follow surveillance imaging
Following induction chemotherapy prior to surgical resection, if no evidence of metastatic disease	• PET/CT (CPT® 78815)
For suspected recurrence	• CT Chest with contrast (CPT® 71260)
Recurrence with extensive mediastinal involvement on CT Chest	• CT Abdomen with contrast (CPT® 74160) • CT Neck with contrast (CPT® 70491)
Inconclusive finding on CT	ONE of the following: • PET/CT (CPT® 78815) • MRI Chest without and with contrast (CPT® 71552)
Metastatic disease on chemotherapy	• CT Neck (CPT® 70491), CT Chest (CPT® 71260), and CT Abdomen (CPT® 74160) with contrast, every 2 cycles of therapy
Thymic carcinomas	• See: **Non-Small Cell Lung Cancer Restaging/ Recurrence (ONC-8.4)**

Evidence Discussion

If induction chemotherapy is given, PET/CT can be obtained prior to surgical resection as studies have shown a correlation of radiographic response to pathologic response to help guide resectability. For recurrence, CT Chest with CT Neck/Abdomen as clinically indicated. PET/CT or MRI Chest indicated if CT Chest is inconclusive. For individuals

on chemotherapy for metastatic disease, CT Neck/Chest/Abdomen with contrast can be given every 2 cycles.

Thymoma and Thymic Carcinoma – Surveillance (ONC-10.8)

ON.OT.0010.8.A
v2.0.2025

Indication	Study
Thymoma	• CT Chest with contrast (CPT® 71260) and previously involved regions every 6 months for 2 years, then annually for next 10 years
Thymic carcinomas	• CT Chest with contrast (CPT® 71260) every 6 months for 2 years and then annually for next 5 years

Evidence Discussion

Thymoma surveillance should be with CT Chest with contrast and any previously involved areas every 6 months for 2 years then annually for 10 years due to the risk of late recurrence. Thymic carcinoma surveillance includes CT Chest with contrast every 6 months for 2 years then annually for the next 5 years.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-10)

v2.0.2025

1. Ettinger DS, Wood DE, Stevenson J, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – November 21, 2023. Mesothelioma: Pleural, available at: https://www.nccn.org/professionals/physician_gls/pdf/meso_pleural.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Mesothelioma: Pleural V1.2024 – November 21, 2023. ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Ettinger DS, Wood DE, Stevenson J, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – November 21, 2023. Mesothelioma: Peritoneal, available at: https://www.nccn.org/professionals/physician_gls/pdf/meso_peritoneal.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Mesothelioma: Peritoneal V1.2024 – November 21, 2023. ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Ettinger DS, Wood DE, Riely GJ, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – November 21, 2023. Thymoma and Thymic carcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Thymoma and Thymic carcinoma, V1.2024 – November 21, 2023. ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
4. Sørensen JB, Ravn J, Loft A, Brenøe J, Berthelsen AK, Nordic Mesothelioma Group. Preoperative staging of mesothelioma by 18F-fluoro-2-deoxy-D-glucose positron emission tomography/computer tomography fused imaging and mediastinoscopy compared to pathological findings after extrapleural pneumonectomy. *Eur J Cardiothorac Surg*. 2008;34:1090-1096. doi:10.1016/j.ejcts.2008.07.050.
5. Wilcox BE, Subramaniam RM, Peller PJ, et al. Utility of computed tomography-positron emission tomography for selection of operable malignant pleural mesothelioma. *Clin lung cancer*. 2009;10:244-248. doi: 10.3816/CLC.2009.n.033.
6. Marom EM. Imaging thymoma. *J Thorac Oncol*. 2010;5(10 Suppl 4):S296-S303. doi:10.1097/JTO.0b013e3181f209ca.
7. Marom EM. Advances in thymoma imaging. *J Thorac Imaging*. 2013;28(2):69-80. doi:10.1097/RTI.0b013e31828609a0.
8. Hayes SA, Huang J, Plodkowski AJ, et al. Preoperative computed tomography findings predict surgical resectability of thymoma. *J Thorac Oncol*. 2014;9(7):1023-1030. doi:10.1097/JTO.0000000000000204.
9. Mineo TC, Ambrogi V. Malignant pleural mesothelioma: factors influencing the prognosis. *Oncology.* 2012;26(12):1164-75.
10. Cox CW, Chung JH, Ackman JB, et al. ACR Appropriateness Criteria® Occupational Lung Diseases. *J Am Coll Radiol*. 2020;17(5S):S188-S197. doi:10.1016/j.jacr.2020.01.022.
11. Tsao AS, Pass HI, Rimner A, Mansfield AS. New era for malignant pleural mesothelioma: updates on therapeutic options. *J Clin Oncol*. 2022;40(6):681692. doi:10.1200/JCO.21.01567.
12. Sugarbaker PH. Intra-abdominal manifestations of pleural mesothelioma. *Ann Transl Med*. 2017;5(11):231. doi:10.21037/atm.2016.11.44.
13. Popat S, Baas P, Faivre-Finn C, et al. ESMO Guidelines Committee.Malignant pleural mesothelioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2022;33(2):129-142. doi:10.1016/j.annonc.2021.11.005.
14. Sadohara J, Fujimoto K, Muller NL et al. Thymic epithelial tumors: comparison of CT and MR imaging findings of low-risk thymomas, high-risk thymomas, and thymic carcinomas. *Eur J Radiol*. 2006;60:7079.
15. Treglia G, Sadeghi R, Giovanella L, et al. Is (18)F-FDG PET useful in predicting the WHO grade of malignancy in thymic epithelial tumors? A meta-analysis. *Lung Cancer.* 2014;86:5-13.

16. Lococo F, Chiapetta M, Triumbari E. et al. Current roles of PET/CT in thymic epithelial tumors: which evidences and which prospects? A pictorial review. *Cancers*. 2021;13(23).
17. Bou-Samra P, Chang A, Azari F,et al. Epidemiological, therapeutic, and survival trends in malignant pleural mesothelioma: A review of the National Cancer Database. *Cancer Med*. 2023;12(11):12208-12220. doi:10.1002/cam4.5915.

Breast Cancer (ONC-11)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Breast Cancer – General Considerations (ONC-11.0)

ON.BC.0011.0.A

v2.0.2025

- This guideline applies to invasive carcinoma and ductal carcinoma in situ histologies of breast cancer.
- Advanced imaging to evaluate for distant metastases is not indicated for asymptomatic individuals with invasive carcinoma or ductal carcinoma in situ (DCIS).
- High-risk lesions, such as LCIS, ADH, and ALH are discussed in **Breast MRI Indications (BR-5.1)**.
- Bone scan has a high concordance rate with PET for detecting bone metastases.
- Scintimammography and Breast Specific Gamma Imaging (BSGI) are considered experimental, investigational, or unproven.

Breast Cancer – Suspected/Diagnosis (ONC-11.1)

ON.BC.0011.1.A
v2.0.2025

- See: **Breast MRI Indications (BR-5.1)** in the Breast Imaging Guidelines for evaluation of suspected breast cancer.

Breast Cancer – Initial Work-Up/Staging (ONC-11.2)

ON.BC.0011.2.C
v2.0.2025

Indication	Imaging Study
All newly diagnosed breast cancer or ductal carcinoma in situ	• Diagnostic bilateral mammogram and/or Ultrasound Breast (CPT® 76641 or CPT® 76642) are imaging modalities of choice • MRI Breast bilateral without and with contrast (CPT® 77049)
ANY of the following: • Atypical ductal hyperplasia (ADH) • Atypical lobular hyperplasia (ALH) • Lobular carcinoma in situ (LCIS)	See: **Breast MRI Indications (BR-5.1)**
ANY of the following: • Ductal carcinoma in situ • Stage I-III	• For sentinel lymph node evaluation: Lymph system imaging (lymphoscintigraphy, CPT® 78195 ◦ SPECT/CT (CPT® 78830) if requested
Stages I, II, and operable stage III (N1 disease)	• Routine systemic imaging is not indicated for initial staging of non-metastatic breast cancer in the absence of signs or symptoms

Indication	Imaging Study
ANY of the following: • Clinically suspected or biopsy-proven distant metastases/ Stage IV disease (not locally advanced disease with three or less positive axillary nodes) • Signs or symptoms of systemic disease • Elevated liver function tests or tumor markers • Inflammatory breast cancer (stage T4d) • 4 or more axillary lymph nodes positive for cancer involvement (i.e., N2 disease)	ANY or ALL of the following: • CT Chest (CPT® 71260) **and** CT Abdomen and Pelvis (CPT® 74177) with contrast • Bone scan (CPT® 78306) (if PET/CT is not being performed)
ANY of the following: • Stage III N2 disease • T4 disease • Inflammatory breast cancer (stage T4d) • Inconclusive CT and/or bone scan	In addition to the above: • FDG PET/CT (CPT® 78815)
Bone pain	• Bone scan (CPT® 78306) • PET/CT (CPT® 78815) with Sodium Fluoride radiotracer may be obtained if CT, MRI, Bone scan and FDG PET/CT scan are inconclusive for bone metastases • See: **Bone (Non-Vertebral) Metastases (ONC-31.5)** • See: **Spinal/Vertebral Metastases (ONC-31.6)**

Evidence Discussion

Evaluation of disease in the breast/axilla with breast MRI:

National Comprehensive Cancer Network (NCCN) guidelines state that breast MRI "may be used for staging evaluation to define extent of cancer or presence of multifocal or

multicentric cancer in the ipsilateral breast, or to screen the contralateral breast at the time of initial diagnosis" (NCCN, 2024). Disagreement continues to exist as to whether the benefit of breast MRI in initial staging outweighs the drawbacks. Detractors cite evidence of increased time-to-surgery, high false-positive rates among the reasons to avoid universal usage of breast MRI in initial staging (Chapar et al., 2022; Cozzi et al., 2023). The American Society of Breast Surgeons Consensus (ASBrS) statement recommend against the use of routine MRI in the preoperative workup of patients with breast cancer (ASBrS: Consensus Guideline on Diagnostic and Screening Magnetic Resonance Imaging of the Breast, 2017). MRI may be helpful in elucidating whether disease exists in the intervening breast tissue thereby aiding in tumor size estimation and the decision to opt for mastectomy vs. lumpectomy. NCCN cautions that "surgical decisions should not be based solely on MRI findings" (NCCN, 2024). Breast MRI has been shown to find occult primary cancers in roughly two thirds of patients who present with positive axillary lymph nodes, allowing for definitive surgical management. (de Bresser, de Vos, van der Ent, & Hulsewe, 2010). In patients with inconclusive conventional imaging, MRI may be a useful adjunct (Lee, Smith, Levine, Troiano, & Tocino, 1999). NCCN states that breast MRI "may be helpful for evaluation before and after preoperative systemic therapy to define extent of disease, response to treatment, and potential for breast-conservation therapy" (NCCN, 2024). Breast MRI has also been shown to more accurately predict tumor size in patients with invasive lobular carcinoma than conventional imaging (Hovis et al., 2021). While data are limited on the use of breast MRI in the setting of Paget's disease of the breast, one study found that for patients with a histologic diagnosis of Paget's disease and a negative mammogram, MRI was able to detect occult cancer in 4/8 (50%) patients. (Morrogh et al., 2008). NCCN guidelines note that there is considerable controversy in the use of MRI based on breast density (NCCN, 2024). They note that MRI advocates argue that it has a high sensitivity to find occult disease in "dense breasts where mammographically occult disease is more likely to elude preoperative detection"; however, MRI detractors note the high percentage of false- positive findings, resulting in further workup, overestimation of extent of disease and increased frequency of mastectomy. Given the recommendation by NCCN that breast MRI may be useful for specific circumstances in initial staging, these guidelines allow for the approval of breast MRI in initial staging to empower patients and providers to discuss the risks and benefits of this modality and move forward with the most advantageous choice for the patient's specific circumstances.

Lymphatic mapping with lymphoscintigraphy and/or SPECT/CT:

Sentinel node biopsy is important in the staging of patients with breast cancer. However, lymphoscintigraphy has limited utility in this setting (Chagpar et al., 2005). In patients with recurrent disease who have had previous axillary surgery, lymphoscintigraphy with SPECT/CT may be helpful in delineating alternate drainage pathways.(Borrelli et al., 2017) In patients who have had a positive axillary node prior to neoadjuvant chemotherapy, some authors have also found the technique to be helpful in identifying

the previously positive clipped node, which may not be subsequently identified as a sentinel node.(Christin, Kuten, Even-Sapir, Klausner, & Menes, 2019).

Systemic staging with CT Chest, Abdomen, Pelvis, and bone scan vs. PET/CT:

The NCCN guidelines state to "consider additional imaging studies only in the presence of signs and symptoms of metastatic disease and for patients who are clinically high risk" (NCCN, 2024). This is in keeping with the ACR Appropriateness Criteria which states that systemic staging is "usually not appropriate" for all newly diagnosed clinical Stage I-IIA (early stage) breast cancer patients, and clinical Stage IIB-III (late stage) patients with ER+/HER2- breast cancer (American College of Radiology (ACR) Appropriateness Criteria Imaging of Invasive Breast Cancer, 2023). Over a third of patients with inflammatory breast cancer will have distant metastatic disease at presentation (Kleer, van Golen, & Merajver, 2000) and NCCN does recommend staging studies in these patients (NCCN, 2024).

NCCN guidelines recommend CT scan for the work up for distant metastatic disease (NCCN, 2024). NCCN also states that the "routine use of FDG PET/CT is not recommended in the staging of clinical stage I, II, or operable III (T3,N1) breast cancer (NCCN, 2024). However, NCCN indicates that PET/CT may be performed at the same time as diagnostic CT and can be helpful as a problem-solving tool when conventional imaging is suspicious or inconclusive. It is also noted to be "helpful in identifying unsuspected regional nodal disease and/or distant metastases when used in addition to standard staging studies". (NCCN, 2024) Bone imaging is not recommended if FDG PET/CT is already going to be performed. (NCCN, 2024) Given the above, these guidelines allow for the selected use of concomitant PET/CT for initial staging in specific clinical circumstances.

Breast Cancer – Restaging/Recurrence (ONC-11.3)

ON.BC.0011.3.C
v2.0.2025

- For imaging related to breast reconstruction, see: **Breast Reconstruction (BR-3.1)** in the Breast Imaging Guidelines

Indication	Imaging Study
ANY of the following: • End of planned neoadjuvant chemotherapy to determine resectability • Biopsy proven local recurrence • Suspicion of recurrence with inconclusive mammogram and/or ultrasound (BIRADS 0) • Mammogram and ultrasound conflicts with physical exam	• MRI Breast Bilateral without and with contrast (CPT® 77049)
After neoadjuvant chemotherapy, if sentinel lymph node evaluation is planned	• Lymph system imaging (lymphoscintigraphy, CPT® 78195) ◦ SPECT/CT (CPT® 78830) if requested
ANY of the following: • Assessing for residual disease after surgery • Assessing response to neoadjuvant chemotherapy • After lumpectomy or mastectomy, prior to adjuvant therapy	• Neither PET nor CT are indicated for systemic restaging after neoadjuvant chemotherapy or after surgery

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
• Treatment response in individuals with metastatic disease and measurable disease on imaging: ◦ For individuals receiving chemotherapy, imaging is indicated after every 2 cycles ◦ For individuals receiving hormonal or endocrine therapy, imaging is indicated every 3 months	• CT Chest with contrast (CPT® 71260); and CT Abdomen and Pelvis with contrast (CPT® 74177) • Bone scan (CPT® 78306) In addition to the above options, for individuals receiving systemic treatment for brain metastases: • MRI Brain without and with contrast (CPT® 70553)
ANY of the following: • Elevated LFTs • Elevated tumor markers • Signs or symptoms of recurrence • Biopsy proven recurrence	Any or all of the following: • CT Chest with contrast (CPT® 71260); **and** CT Abdomen and Pelvis with contrast (CPT® 74177) • Bone scan (CPT® 78306) For individuals with prior history of brain metastases or current signs or symptoms of brain metastasis: • MRI Brain without and with contrast (CPT® 70553)
• Inconclusive CT, MRI, and/or bone scan • Treatment response assessment for bone-only metastases (excluding brain metastases) and a prior bone scan has not been performed for serial comparison	• ^{18}F-FDG PET/CT (CPT® 78815)
Individuals with known or suspected bone metastases AND inconclusive bone findings on ALL of the following: CT, MRI, bone scan, and FDG PET/CT scan	• ^{18}F Sodium Fluoride PET/CT (CPT® 78815)

Indication	Imaging Study
To determine the ER-status of suspected/ known metastatic recurrence noted on CT/ bone scan and any one of the following: • Biopsy of metastatic site is non-diagnostic/inconclusive • Biopsy of metastatic site is risky & cannot be performed (metastatic sites in the brain, spine or near vascular structures)	• ^{18}F-FES (fluoroestradiol) PET/CT scan (CPT® 78815 or CPT® 78816)

Evidence Discussion

Evaluation of disease in the breast/axilla with breast MRI:

Breast MRI has been shown to predict extent of pathological tumor response in the breast and lymph nodes after neoadjuvant systemic therapy better than conventional imaging, although may over- or under-estimate residual tumor size (Yeh et al., 2005).

While some authors have found the use of MRI to be helpful in terms of estimating size of ipsilateral breast tumor recurrences and finding multifocal or multicentric disease, (Walstra et al., 2020) others have found that the addition of MRI in this context did not significantly change management and increased time to definitive therapy.(Sutherland et al., 2022) However, as previously noted, MRI may be a useful adjunct in situations where conventional imaging is inconclusive.

Systemic staging with CT Chest, Abdomen, Pelvis, and bone scan vs. PET/CT:

As patients with symptoms for distant metastatic disease would have had systemic staging prior to neoadjuvant chemotherapy and/or surgery, there is no indication to repeat these until treatment is completed. However, for patients with metastatic disease, NCCN guidelines recommend CT Chest, Abdomen, and Pelvis with contrast every 2-4 cycles of chemotherapy or every 2-6 months of endocrine therapy and bone scan is recommended every 4-6 cycles of chemotherapy or every 2-6 months of endocrine therapy. Restaging using these modalities is also advised if there is concern for progression of disease. They note that PET/CT is not routinely indicated for restaging "because of the absence of a reproducible, validated, and widely accepted set of standards for disease activity assessment". PET is instead preferred to be reserved as a problem-solving tool when conventional imaging is inconclusive. Additionally, NCCN notes sodium fluoride PET/CT may be helpful to detect bone metastases where other imaging is inconclusive (NCCN, 2024).

Breast Cancer – Surveillance/Follow-Up (ONC-11.4)

ON.BC.0011.4.C
v2.0.2025

Indication	Imaging Study
Measurable metastatic disease on maintenance therapy or being monitored off therapy	ANY or ALL of the following, every 3 months for up to 5 years after completion of active treatment: • CT Chest (CPT® 71260) **and** CT Abdomen and Pelvis (CPT® 74177) with contrast • Bone scan (CPT® 78306)
• Asymptomatic non-metastatic disease • Individuals receiving post-operative adjuvant therapy	• No advanced imaging indicated

Indication	Imaging Study
Breast surveillance in an individual with prior history of breast cancer (not treated with bilateral mastectomy) AND any one of the following: • Known high risk genetic mutations: ◦ Li-Fraumeni Syndrome/TP53 Syndrome ◦ BRCA1 ◦ BRCA2 ◦ Peutz-Jehgers Syndrome (STK11/LKB1 gene variations) ◦ PTEN Mutation/Cowden Syndrome ◦ CDH1 ◦ NF1 ◦ PALB2 ◦ ATM ◦ CHEK2 ◦ NBN ◦ BARD1 ◦ RAD51C ◦ RAD51D • Clinical lifetime risk estimated to be ≥20% using genetic or clinical risk estimator, calculated prior to the initial diagnosis of breast cancer • Extremely dense breast tissue (breast density category D) on mammography • Age at diagnosis ≤50 years • Invasive lobular carcinoma (ILC) • Individuals with a prior history of high-risk lesions, including: atypical ductal hyperplasia	• Bilateral MRI Breast without and with contrast (CPT® 77049) annually • See also: **Breast MRI Indications (BR-5.1)**

Indication	Imaging Study
(ADH), atypical lobular hyperplasia (ALH), or lobular carcinoma in situ (LCIS)	
• Individuals treated with bilateral mastectomy • All other individuals with no high risk features (as stated above)	• Breast MRI is not indicated for routine surveillance of asymptomatic individuals

Evidence Discussion

Evaluation of disease in the breast/axilla with breast MRI:

NCCN guidelines suggest that "the utility of MRI in follow-up screening of most patients with prior breast cancer is undefined", but recommend annual MRI in patients with a personal history of breast cancer who were either younger than age 50 or who have dense breasts (NCCN, 2024). However, as breast cancer patients may have residual breast tissue in the ipsilateral or contralateral breast for which certain genetic mutations may increase the risk of subsequent cancers, breast MRI would also be indicated in such patients (NCCN, 2024). Patients with a clinical lifetime risk estimated to be ≥ 20% lifetime risk prior to their diagnosis of breast cancer and/or who had a history of ADH or lobular neoplasia would have been candidates for breast cancer screening with breast MRI regardless (see BR 5.1) and therefore, would equally be eligible for this screening modality after breast cancer treatment, as long as they had not had bilateral mastectomies. Patients who have had bilateral mastectomies have little residual tissue, and therefore, surveillance with breast imaging would be of little value. A recent metaanalysis found that the rate of occult cancer in patients with mastectomy and the rate at which MRI detected cancer in patients after mastectomy was well below the current BIRADS benchmark for women with genetic predispositions to cancer (Smith, Sepehr, Karakatsanis, Strand, & Valachis, 2022).

Systemic surveillance with CT Chest, Abdomen, Pelvis, and bone scan vs. PET/CT:

The NCCN guidelines state "In the absence of clinical signs and symptoms suggestive of recurrent disease, there is no indication for laboratory or imaging studies for metastases screening" (NCCN, 2024). This is in keeping with ASCO's Choosing Wisely guideline which similarly recommends against surveillance testing with biomarkers or imaging for asymptomatic breast cancer patients who have been treated with curative intent (ASCO, 2021). Several studies have shown no benefit from routine imaging which can result in unnecessary radiation exposure and biopsies, and lead to misdiagnosis and treatment related complications (Jochelson M, 2013). A recent study also found that

more intensive screening for metastasis did not result in improved survival (Cheun et al., 2021).

References (ONC-11)

v2.0.2025

1. Gradishar WJ, Moran MS, Abraham J, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 6.2024 – November 11, 2024. Breast cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Breast Cancer V6.2024 – November 11, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Cardoso F, Costa A, Norton L, et al. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). *Ann Oncol*. 2014;25(10):1871-1888. doi:10.1093/annonc/mdu385.
3. Khatcheressian JL, Hurley P, Bantug E, et al. Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol.* 2013;31:961-965. doi:10.1200/JCO.2012.45.9859.
4. Puglisi F, Follador A, Minisini AM, et al. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications. *Ann Oncol*. 2005;16(2):263-266. doi:10.1093/annonc/mdi063.
5. Rong J, Wang S, Ding Q, Yun M, Zheng Z, Ye S. Comparison of 18 FDG PET-CT and bone scintigraphy for detection of bone metastases in breast cancer patients. A meta-analysis. *Surg Oncol*. 2013;22(2):86-91. doi:10.1016/j.suronc.2013.01.002.
6. Hong S, Li J, Wang S. 18FDG PET-CT for diagnosis of distant metastases in breast cancer patients. A meta-analysis. *Surg Oncol*. 2013;22(2):139-143. doi:10.1016/j.suronc.2013.03.001.
7. Cheng X, Li Y, Liu B, Xu Z, Bao L, Wang J. 18F-FDG PET/CT and PET for evaluation of pathological response to neoadjuvant chemotherapy in breast cancer: a meta-analysis. Acta Radiol. 2012;53(6):615-627. doi:10.1258/ar.2012.110603.
8. Simos D, Catley C, van Walraven C, et al. Imaging for distant metastases in women with early-stage breast cancer: a population-based cohort study. *CMAJ*. 2015;187(12):E387-E397. doi:10.1503/cmaj.150003.
9. Crivello ML, Ruth K, Sigurdson ER, et al. Advanced imaging modalities in early stage breast cancer: preoperative use in the United States Medicare population. *Ann Surg Oncol*. 2013;20(1):102-110. doi:10.1245/s10434-012-2571-4.
10. Heller SL, Lourenco AP, Niell BL, et. al. ACR Appropriateness Criteria® - Imaging after Mastectomy and Breast Reconstruction. Available at https://acsearch.acr.org/docs/3155410/Narrative/. American College of Radiology.
11. Landercasper J, Bailey L, Berry TS, et. al. Don't routinely order breast MRI in new breast cancer patients. American Society of Breast Surgeons. https://www.choosingwisely.org/clinician-lists/breast-surgeons-mris-in-new-breast-cancer-patients/
12. Chagpar AB, Howard-McNatt M, Chiba A, et. al. Factors affecting time to surgery in breast cancer patients. *Am Surg*. 2022;88(4):648-652. doi:10.1177/00031348211054714.
13. Peters NHGM, van Esser S, van den Bosch MAAJ, et. al. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: the MONET – randomized controlled trial. *Eur J Cancer*. 2011;47(6):879-886. doi:10.1016/j.ejca.2010.11.035
14. Turnbull L, Brown S, Harvey I, et. al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomized controlled trial. *Lancet*. 2010;375(9714):563-571. doi:10.1016/S0140-6736(09)62070-5.
15. Daly MB, Pal T, AlHilli Z, et. al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – November 7, 2024. Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate, available at: https://www.nccn.org/professionals/physician_gls/pdf/genetics_bopp.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate V2.2025 – November 7, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.

16. Moncrieff M, Pywell S, Snelling A, et. al. Effectiveness of SPECT/CT imaging for sentinel node biopsy staging of primary cutaneous melanoma and patient outcomes. *Ann Surg Oncol*. 2022;29(2):767-775. doi:10.1245/s10434-021-10911-4.
17. Quartuccio N, Garau LM, Arnone A, et. al. Comparsion of 99mTc-labeled colloid SPECT/CT and planar lymphoscintigraphy in sentinel lymph node detection in patients with melanoma: a meta-analysis. *J Clin Med*. 2020;9(6):1680. doi:10.3390/jcm9061680.
18. Bennie G, Vorster M, Buscombe J, Sathekge M. The added value of a single-photon emission computed tomography-computed in sentinel lymph node mapping in patients with breast cancer and malignant melanoma. *World J Nucl Med.* 2015;14(01):41-46. doi:10.4103/1450-1147.150543
19. Ulaner GA, Mankoff DA, Clark AS, et al. Appropriate use criteria for estrogen receptor-targeted pet imaging with 16α-18f-fluoro-17β-fluoroestradiol. *J Nucl Med.* 2023;64(3):351-354. doi:10.2967/jnumed.123.265420.
20. Borrelli P, Donswijk ML, Stokkel MP, et al. Contribution of SPECT/CT for sentinel node localization in patients with ipsilateral breast cancer relapse. *Eur J Nucl Med Mol Imaging*. 2017;44(4): 630-637. doi:10.1007/s00259-0163545-8.
21. Chagpar, AB, Kehdy F, Scoggins CR, et al. Effect of lymphoscintigraphy drainage patterns on sentinel lymph node biopsy in patients with breast cancer. *Am J Surg*. 2005;190(4):557-562. doi:10.1016/j.amjsurg.2005.06.010.
22. Cheun JH, Jung J, Lee ES, et al. Intensity of metastasis screening and survival outcomes in patients with breast cancer. *Sci Rep*. 2021;11(1):2851. doi:10.1038/s41598-021-82485-w.
23. Christin OL, Kuten J, Even-Sapir E, Klausner J, Menes TS. Node positive breast cancer: Concordance between baseline PET/CT and sentinel node assessment after neoadjuvant therapy. *Surg Oncol*. 2021;30:1-5. doi:10.1016/j.suronc.2019.05.006.
24. Jochelson MHD, Ganz PA. Surveillance and monitoring in breast cancer survivors: maximizing benefit and minimizing harm. *ASCO Educational Book*. 2013;33(33). doi:https://doi.org/10.14694/EdBook_AM.2013.33.e13.
25. Smith D, Sepehr S, Karakatsanis A., Strand F, Valachis A. Yield of surveillance imaging after mastectomy with or without reconstruction for patients with prior breast cancer: a systematic review and meta-analysis. *JAMA Network Open*. 2021;5(12):e2244212-e2244212. doi:10.1001/jamanetworkopen.2022.44212.
26. Sutherland A, Huppe A, Wagner JL. The clinical impact of MRI on surgical planning for patients with in-breast tumor recurrence. *Breast Cancer Res Treat*. 2022;193(2):515-522. doi:10.1007/s10549-022-06589-1.
27. Walstra C, Schipper RJ, Winter-Warnars GA, et al. Local staging of ipsilateral breast tumor recurrence: mammography, ultrasound, or MRI? *Breast Cancer Res Treat*. 2020;184(2), 385-395. doi:10.1007/s10549-020-05850-9.
28. ASCO. 2021. *Choosing Wisely.* Retrieved from: https://old-prod.asco.org/news-initiatives/current-initiatives/cancer-care-initiatives/value-cancer-care/choosing-wisely.

Sarcomas – Bone, Soft Tissue, and GIST (ONC-12)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Bone and Soft Tissue Sarcomas – General Considerations (ONC-12.1)

ON.SS.0012.1.A
v2.0.2025

- Sarcomas are tumors of mesenchymal origin, classified as high-, intermediate-, and low-grade (G) tumors (sometimes described as “spindle cell” cancers). They can arise in any bony, cartilaginous, smooth muscle, skeletal muscle, or cardiac muscle tissue.
- Malignant nerve sheath tumor cell types should be imaged as high-grade sarcoma.
- Sarcomas occur in both adult and pediatric individuals, but some are more common in one age group than the other. Unless specified below, individuals age ≥18 years old should be imaged according to this guideline section.
- Exceptions include:
  - Rhabdomyosarcoma in individuals of all ages should be imaged according to guidelines in **Rhabdomyosarcoma (RMS) (PEDONC-8.2)** in the Pediatric Oncology Imaging Guidelines.
  - Osteogenic sarcoma (Osteosarcoma) in individuals of all ages should be imaged according to guidelines in **Osteogenic Sarcoma (OS) (PEDONC-9.3)** in the Pediatric Oncology Imaging Guidelines.
  - Ewing sarcoma and Primitive Neuroectodermal Tumor in individuals of all ages should be imaged according to guidelines in **Ewing Sarcoma and Primitive Neuroectodermal Tumors (ESFT) (PEDONC-9.4)** in the Pediatric Oncology Imaging Guidelines.
  - Kaposi’s sarcoma in individuals of all ages should be imaged according to guidelines in **Kaposi’s Sarcoma (ONC-31.10)**.
  - See: **Uterine Cancer (ONC-22)** for imaging recommendations for uterine sarcoma.
  - Desmoplastic small round cell tumor in individuals of all ages should be imaged according to guidelines in **Non-Rhabdomyosarcoma Soft Tissue Sarcomas (NRSTS) (PEDONC-8.3).**

Evidence Discussion

The choice of imaging modality is driven by the primary tumor site. Cross sectional imaging of the primary site with MRI with and without contrast or CT with contrast is recommended for best illustration of anatomic detail and vascular and nodal involvement and provides flexibility for clinician discretion for choice of modality for all sites for maximum tumor definition with consideration of minimizing radiation exposure. CT is superior for evaluation for metastatic disease of the lung, which is supported for all patients with a newly diagnosed malignant sarcoma. Imaging both with and without

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

contrast for evaluation of metastatic disease to the lung is not supported as this exposes patients to higher radiation doses without significant clinical benefit.

Soft Tissue Sarcomas – Initial Work-up/ Staging (ONC-12.2)

ON.SS.0012.2.C
v2.0.2025

Indication	Imaging Study
All individuals	• CT Chest with (CPT® 71260) or CT Chest without (CPT® 71250) contrast • MRI without and with contrast of involved area ◦ CT of involved area if contraindication to MRI
ANY of the following: • Angiosarcoma • Alveolar soft part sarcoma • Clear cell sarcoma • Epithelioid sarcoma • Hemangiopericytoma • Leiomyosarcoma • Liposarcoma • Retroperitoneal or intra-abdominal primary site (including pelvic primary site) • Other histologies documented to have propensity for lymphatic spread and deep-seated tumors	In addition to the above, one of the following combinations: • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast • MRI Abdomen (CPT® 74183) with and without contrast and CT Pelvis (CPT® 72193) with contrast • CT Abdomen (CPT® 74160) with contrast and MRI Pelvis (CPT® 72197) without and with contrast
ANY of the following: • Myxoid round cell liposarcoma • Angiosarcoma • Alveolar soft part sarcoma • Cardiac sarcoma • Neurologic signs or symptoms raising suspicion of CNS metastases	In addition to the above: • MRI Brain without and with contrast (CPT® 70553) • MRI Cervical/Thoracic/Lumbar Spine without and with contrast (CPT® 72156, CPT® 72157, and CPT® 72158)

Indication	Imaging Study
Leiomyosarcoma	In addition to the above: • Bone scan (CPT® 78306)
ANY of the following: • Grade of tumor in doubt following biopsy • Conventional imaging suggests solitary metastasis amenable to surgical resection • Inconclusive conventional imaging • Prior to planned neoadjuvant therapy	• PET/CT (CPT® 78815 or CPT® 78816)
Desmoid Tumors	ONE of the following: • CT without contrast or with contrast of the affected body part • MRI without contrast or without and with contrast of the affected body part • Imaging of lung, lymph node, and metastatic site for these tumors is not indicated
Dermatofibrosarcoma Protuberans (DFSP)	ONE of the following: • CT without contrast or with contrast of the affected body part • MRI without contrast or without and with contrast of the affected body part • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast for: ◦ Pulmonary symptoms ◦ Abnormal chest x-ray ◦ Sarcomatous differentiation

Evidence Discussion

- PET/CT is supported where the grade of tumor is in doubt following biopsy or to confirm oligometastatic disease amenable to local treatment, to support treatment decision making. NCCN also supports the use of PET/CT for initial staging prior to planned neoadjuvant therapy (von Mehren, NCCN 2024). It is also a useful tool to follow inconclusive conventional imaging.

- Different subtypes of soft tissue sarcomas have different patterns of spread; thus a histologic diagnosis is essential to determine imaging strategy.
- Abdominal and pelvic imaging is not supported for extremity, trunk or head and neck primary sites, unless documented histologies with propensity for lymphatic spread (Zagars, 2003). Due to the propensity of myxoid and round cell liposarcomas for leptomeningeal spread, initial evaluation of the spine with MRI is supported. MRI of the brain is supported for those with CNS signs and symptoms, and for all patients with angiosaroma, alveolar soft part sarcomas, and cardiac sarcoma (von Mehren, NCCN 2024).
- For Desmoid tumors, disease biology and patterns of recurrence do not support metastatic disease workup, CT Chest or body areas outside of the primary site subject patients to additional radiation and incidental finding risk (Peng, 2012).
- For Dermatofibrosarcoma Protuberans (DFSP), CT Chest is supported for sarcomatous differentiation as noted for other sarcoma histologies above, or for pulmonary symptoms. In the absence of these features, CT exposes to risk with no statistically significant clinical benefit (Schmultz, NCCN 2024, Akram 2014).

Soft Tissue Sarcomas – Restaging/ Recurrence (ONC-12.3)

ON.SS.0012.3.A
v2.0.2025

Indication	Imaging Study
ANY of the following: • After preoperative radiotherapy • After surgical resection • After adjuvant radiotherapy	• MRI without and with contrast or CT with contrast of affected body area • Chest or lymph node imaging is not indicated if no abnormality on previous imaging
Baseline end of therapy evaluation	• Same studies as indicated during initial work-up
ANY of the following: • Differentiate tumor from radiation or surgical fibrosis • Determine response to neoadjuvant therapy • Confirm oligometastatic disease prior to curative intent surgical resection	• PET/CT (CPT® 78815 or CPT® 78816) ◦ If treated with radiation therapy, PET/CT no sooner than 12 weeks (3 months) post completion of radiation therapy
Chemotherapy response for individuals with measurable disease	• CT with contrast or MRI without and with contrast of affected body area every 2 cycles
Recurrence suspected	• Repeat all imaging for initial workup of specific histology and/or primary site and other symptomatic areas
Preoperative planning prior to resection	ANY or ALL of the following: • MRI without contrast or without and with contrast of involved area • CT (contrast as requested) of involved area

Indication	Imaging Study
Dermatofibrosarcoma Protuberans (DFSP)	• CT without contrast or with contrast of the affected body part or MRI without contrast or without and with contrast of the affected body part • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast for: ◦ Known prior thoracic disease ◦ New or worsening pulmonary symptoms ◦ New or worsening chest x-ray ◦ Sarcomatous differentiation

Evidence Discussion

- Local therapy is a cornerstone of treatment for sarcomas. Cross-sectional imaging of primary site, with modality used at diagnosis specific to tumor site, is supported after pre-operative radiotherapy, and after resection of adjuvant radiotherapy to determine response, as well as for pre-operative planning prior to resection and every two cycles of treatment during active therapy. NCCN supports imaging for a baseline at the end of therapy. In the absence of known lung involvement or pulmonary symptoms, restaging of lung on active treatment does not provide benefit in most histologies and exposes patient to additional radiation and risk of incidental findings (von Mehren, NCCN 2024).
- NCCN indicates that PET/CT may be useful for therapy response. Patients with baseline tumor SUVmax ≥6 and <40% decrease in FDG avidity after neoadjuvant therapy are at high risk for disease recurrence. Pretreatment tumor SUVmax and change in SUV max after neoadjuvant therapy has been shown to identify patients at high risk of tumor recurrence and may be used to identify patients most likely to benefit from additional chemotherapy (Schuetze, 2005). PET/CT is supported to assess neoadjuvant therapy response, to differentiate scarring from disease, or to confirm oligometastatic disease prior to resection (von Mehren, NCCN 2024, Schuetze SM, et al. 2005).

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Soft Tissue Sarcomas Surveillance/ Follow-up (ONC-12.4)

ON.SS.0012.4.A
v2.0.2025

Indication	Imaging Study
For any of the following: • Retroperitoneal/intra-abdominal primary site (including pelvic primary site) • Angiosarcoma • Epithelioid sarcoma	ANY or ALL of the following every 3 months for 3 years, then every 6 months for 2 more years, then annually: • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast or MRI without and with contrast of any other involved body areas
Myxoid/round cell liposarcoma	ANY or ALL of the following every 3 months for 2 years, then every 6 months for 2 more years, then annually: • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast or MRI without and with contrast of any other involved body areas • MRI Cervical/Thoracic/Lumbar Spine without and with contrast (CPT® 72156, CPT® 72157, and CPT® 72158)
Low-grade/Stage I extremity or trunk, primary site	ANY or ALL of the following every 6 months for 2 years, then annually thereafter: • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) • CT with contrast, MRI without contrast, or MRI without and with contrast of primary site

Indication	Imaging Study
ANY of the following: • Extremity/trunk primary site - grade II/stage II or higher • Head/neck primary site	ANY or ALL of the following every 3 months for 2 years, then every 6 months for 2 more years, then annually: • CT with contrast, MRI without contrast, or MRI without and with contrast of primary site • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT with contrast or MRI without and with contrast of any other involved body areas
ANY of the following: • Angiosarcoma • Alveolar soft part sarcoma • Cardiac sarcoma	In addition to the above studies: • MRI Brain without and with contrast (CPT® 70553) annually For surveillance of individuals with known brain metastases, see: **Brain Metastases (ONC-31.3)**
Desmoid tumors	ONE of the following every 3 months for 3 years, then every 6-12 months: • CT without contrast or with contrast of the affected body part • MRI without contrast or without and with contrast of the affected body part
Dermatofibrosarcoma Protuberans	• No routine imaging unless clinical signs/symptoms of recurrence

Evidence Discussion

Time frames, modality, and body site for surveillance by histology are based on tumor recurrence patterns specific to primary site and tumor biology (von Mehren, NCCN 2024, Peng 2012, Akram 2014). PET/CT is not supported for asymptomatic surveillance, as this can lead to unnecessary radiation exposure and invasive procedures or excess treatment.

Gastrointestinal Stromal Tumor (GIST) (ONC-12.5)

ON.SS.0012.5.A
v2.0.2025

General Considerations

- GISTs are mesenchymal neoplasms of the gastrointestinal (GI) tract, mostly found in the stomach and upper small bowel, commonly metastasizing to the liver and abdominal cavity and primarily treated with surgery.
- Recurrence risk of GIST is estimated by prognostic model based on location, size of primary tumor, and mitotic rate per high power field (HPF). High-risk category includes any tumor >5 cm with >5 mitoses/50 HPF and any tumors >10 cm in size regardless of mitotic rate.

Indication	Imaging Study
Suspected/Diagnosis	• CT Abdomen and Pelvis with contrast (CPT® 74177)
Initial Work-up/Staging	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • MRI Abdomen without and with contrast (CPT® 74183) is indicated for evaluation of liver lesions that are equivocal on CT imaging or for preoperative assessment of liver • PET (CPT® 78815) is indicated for evaluation of inconclusive findings on conventional imaging
Monitoring response to treatment (every 8 to 12 weeks) in either of the following: • Unresectable primary disease • Metastatic disease	EITHER of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Known or suspected recurrence	• CT Abdomen and Pelvis with contrast (CPT® 74177)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Any of the following: • Prior evidence of chest disease • Signs or symptoms of chest disease	• CT Chest with contrast (CPT® 71260)
Evaluation of inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)
Surveillance for any of the following: • Incompletely resected • Metastatic disease • High-risk disease	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 3 months for 3 years, then every 6 months for 2 years, and then annually
Surveillance for all others	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 6 months for 5 years, then annually

Evidence Discussion

Suspected/Diagnosis

CT Abdomen and Pelvis are recommended by NCCN (von Mehren, 2024) for suspected GIST. While CT Chest is supported to rule out metastatic disease in biopsy proven GIST, advanced imaging prior to confirmation of diagnosis may expose patient to unnecessary radiation and increased irrelevant incidental findings.

Initial staging

CT is preferred for initial staging of GIST over MRI as it is easier to access, faster, and less costly while MRI is not viewed as superior (von Mehren, 2024). MRI should be used to clarify inconclusive liver findings. The NCCN notes that PET/CT is not a substitute for diagnostic CT, which has superior sensitivity for this tumor site, but PET/CT is supported for inconclusive CT findings, aligning with NCCN recommendations (von Mehren, 2024).

Restaging

Abdominal/pelvic imaging every 8-12 weeks to assess response to TKI is appropriate given the typical response timeframe for this treatment (Kelly, 2021). More frequent imaging may lead to premature or incorrect treatment decisions. Chest imaging in the absence of prior chest findings or signs and symptoms of chest involvement is low-yield and not recommended by the NCCN (von Mehren, 2024), it poses potential for risk of increased incidental findings and increased radiation exposure.

Surveillance

Surveillance guidelines align with NCCN recommendations with regard to modality, body site and timeframe. FDG PET/CT is supported only to clarify ambiguous findings on other advanced imaging (von Mehren, 2024).

Bone Sarcomas - Initial Work-Up/Staging (ONC-12.6)

ON.SS.0012.6.C
v2.0.2025

- Osteogenic sarcoma (Osteosarcoma) in individuals of all ages should be imaged according to guidelines in **Osteogenic Sarcoma (OS) (PEDONC-9.3)** in the Pediatric Oncology Imaging Guidelines.
- Ewing sarcoma and Primitive Neuroectodermal Tumor in individuals of all ages should be imaged according to guidelines in **Ewing's Sarcoma Family of Tumors (PEDONC-9.4)** in the Pediatric Oncology Imaging Guidelines.

Indication	Imaging Study
Chondrosarcoma • Low-grade intra-compartmental • High-grade (grade II or grade III) • Clear cell • Extra-compartmental	ANY or ALL of the following: • MRI without contrast or without and with contrast of involved area • CT (contrast as requested) of involved area • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast
Dedifferentiated chondrosarcoma	See: **Osteogenic Sarcoma (OS) (PEDONC-9.3)** for imaging recommendations
Mesenchymal chondrosarcoma	See: **Ewing's Sarcoma Family of Tumors (PEDONC-9.4)** for imaging recommendations
Chordoma	ANY or ALL of the following: • MRI without contrast or without and with contrast of involved area • CT (contrast as requested) of involved area • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Cervical (CPT® 72156), Thoracic (CPT® 72157), and Lumbar (CPT® 72158) Spine without and with contrast • Bone scan (CPT® 78306)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Chordoma with inconclusive findings on conventional imaging	PET/CT (CPT® 78815 or CPT® 78816)

Evidence Discussion

The choice of imaging modality is driven by the primary tumor site. Cross sectional imaging of the primary site with MRI with and without contrast or CT with contrast is recommended for best illustration of anatomic detail and vascular and nodal involvement. Our guideline provides flexibility for provider discretion for choice of modality for all sites. Providers should choose modality expected to offer maximum primary tumor definition with consideration of minimizing radiation exposure (von Mehren, Biermann, NCCN 2024). CT is more sensitive and specific than MRI for evaluation for metastatic disease of the lung and is supported for all patients with a newly diagnosed malignant sarcoma. Imaging both with and without contrast for evaluation of metastatic disease to the lung is not supported as this exposes patients to higher radiation doses without significant clinical benefit. CT either with or without contrast should be selected at discretion of the provider (ACR, 2024).

Chordomas have a propensity for the distant disease at presentation including spine, so unlike other bone sarcomas, imaging of the abdomen and pelvis with contrasted CT as well as bone scan and MRI of the spine are supported. FDG PET/CT is supported only for inconclusive conventional imaging. PET is not generally supported for initial staging of other histologies discussed in this section due to low sensitivity and specificity (Biermann, NCCN 2024).

Bone Sarcomas - Restaging/Recurrence (ONC-12.7)

ON.SS.0012.7.C
v2.0.2025

Indication	Imaging Study
Chondrosarcoma • Low-grade intra-compartmental • High-grade (grade II or grade III) • Clear cell • Extra-compartmental	ANY or ALL of the following, after completion of radiotherapy or every 2 cycles of chemotherapy: • MRI without contrast or without and with contrast of involved area • CT (contrast as requested) of involved area • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast
Suspected recurrence of atypical cartilaginous tumor (low-grade intra-compartmental appendicular tumor)	• MRI without contrast or without and with contrast of involved area of CT (contrast as requested) of involved area • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • Bone scan (CPT® 78306)
Dedifferentiated chondrosarcoma	See: **Osteogenic Sarcoma (OS) (PEDONC-9.3)** for imaging recommendations
Mesenchymal chondrosarcoma	See: **Ewing's Sarcoma Family of Tumors (PEDONC-9.4)** for imaging recommendations
Chordoma	ANY or ALL of the following, after completion of radiotherapy or every 2 cycles of chemotherapy: • MRI without contrast or without and with contrast of involved area • CT (contrast as requested) of involved area • Bone scan (CPT® 78306)

Indication	Imaging Study
Chordoma with inconclusive findings on conventional imaging	PET/CT (CPT® 78306 OR CPT® 78816)

Evidence Discussion

CT Chest is supported for restaging for all bone sarcomas, as well as MRI of primary site. CT of other body areas is driven by clinical symptoms and patterns of spread at primary site and not routine across all cell types (Biermann, NCCN 2024). PET/CT for restaging is not routinely supported but may be used for inconclusive conventional imaging (Biermann, NCCN 2024).

Bone Sarcomas – Surveillance/Follow-up (ONC-12.8)

ON.SS.0012.8.A
v2.0.2025

Indication	Imaging Study
• Intra-compartmental Chondrosarcoma	ANY or ALL of the following every 6-12 months for 2 years, then annually for 10 years: • Plain x-ray of primary site ◦ MRI without and with contrast is indicated for new findings on plain x-ray or new/worsening clinical symptoms. • Chest x-ray ◦ CT Chest with (CPT® 71260) or without (CPT® 71250) contrast for new findings on chest x-ray, or new/ worsening signs/symptoms
• Grade I, II, or III Chondrosarcoma • Clear Cell Chondrosarcoma • Extra-compartmental Chondrosarcoma • Low-grade extra-compartmental appendicular tumors	ANY or ALL of the following every 6 months for 5 years, then annually for 10 years: • Plain x-ray of primary site ◦ MRI without and with contrast is indicated for new findings on plain x-ray or new/worsening clinical symptoms. • CT Chest with (CPT® 71260) **or** CT Chest without (CPT® 71250) contrast
Dedifferentiated chondrosarcoma	See: **Osteogenic Sarcoma (OS) (PEDONC-9.3)** for imaging recommendations
Mesenchymal chondrosarcoma	See: **Ewing's Sarcoma Family of Tumors (PEDONC-9.4)** for imaging recommendations

Indication	Imaging Study
Chordoma	• Plain x-ray of primary site every 6 months for 5 years and then annually until year 10 ◦ MRI without and with contrast is indicated for new findings on plain x-ray or new/worsening clinical symptoms. • Chest x-ray every 6 months for 5 years and then annually until year 10 ◦ CT Chest with (CPT® 71260) or without (CPT® 71250) contrast may be obtained annually or for evaluation of any new findings on chest x-ray or new/worsening signs/symptoms

Evidence Discussion

Data do not show an overall survival benefit with advanced imaging surveillance of sarcomas. Less than 20% of local recurrences are detected based on advanced imaging surveillance in asymptomatic patients. Sensitivity and specificity of chest imaging are higher in grade two or higher disease (Srinivasan, 2024).

For grades I-III disease, plain x-ray is supported as primary tool for primary site surveillance, with cross sectional advanced imaging for signs and symptoms of progression or changes on x-ray. Chest imaging is supported with either plain imaging or CT. Recurrence beyond 10 years is rare; asymptomatic surveillance imaging beyond 10 years is low yield and is not generally supported (Biermann, 2024).

Benign Bone Tumors – General Considerations (ONC-12.9)

ON.SS.0012.9.A
v2.0.2025

- Variety of diagnoses, including osteoid osteochondroma, chondroblastoma, desmoplastic fibroma, Paget's disease, osteoid osteoma and others.
- Plain x-ray appearance is diagnostic for many benign bone tumors and advanced imaging is generally unnecessary except for preoperative planning.
- MRI without and with contrast is the primary modality for advanced imaging of bone tumors and can be approved to help narrow differential diagnoses and determine whether biopsy is indicated.
- Some benign bone tumor types carry a risk of malignant degeneration over time, but routine advanced imaging surveillance has not been shown to improve outcomes for these individuals.
- MRI without and with contrast can be approved to evaluate new findings on plain x-ray new/worsening clinical symptoms not explained by a recent plain x-ray.
- There are no data to support the use of PET/CT in the evaluation of benign bone tumors, and PET requests should not be approved without biopsy confirmation of a malignancy.
- Other benign bone tumors should be imaged according to guidelines in **Lesion of Bone (MS-10.1)** in the General Musculoskeletal Imaging Guidelines or **Mass Involving Bone (including Lytic and Blastic Metastatic Disease) (PEDMS-3.4)** in the Pediatric Musculoskeletal Imaging Guidelines.

Evidence Discussion

Many benign bone tumors have characteristic appearance on plain x-ray, particularly in conjunction with history, patient age, and size and growth characteristics. Lesions without aggressive appearing characteristics on x-ray generally do not require further evaluation. Advanced imaging modalities are supported when x-ray is indeterminate for malignancy to determine management strategy. Thus, the advanced imaging guidelines in this section pertain to enchondromas, which often appear indeterminate on plain x-ray, and giant cell tumor of bone (GCTB), which have potential for malignant degeneration and metastasis.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Benign Bone Tumors - Initial Work-Up/ Staging (ONC-12.10)

ON.SS.0012.10.C
v2.0.2025

Indication	Imaging Study
Giant Cell Tumor of Bone (GCTB)	ANY or ALL of the following: • MRI without contrast or without and with contrast of involved area • CT (contrast as requested) of involved area • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • Bone scan (CPT® 78306)
Enchondroma	• MRI without contrast or without and with contrast of primary site

Evidence Discussion

- Giant Cell Tumor of Bone
  - MRI can help distinguish malignant transformation, while complex bony anatomy maybe better visualized on CT. To establish management strategy, our guidelines support using both modalities for involved areas in alignment with NCCN and ACR (Biermann 2024, Montgomery 2019).
  - CT Chest and whole-body bone scan are supported at time of initial staging given the malignant and metastatic potential of GCTB. CT abdomen and pelvis are not supported without symptoms in these areas as this would not be a typical pattern of metastasis in the setting of malignant degeneration of GCTB. CT of abdomen and pelvis increases radiation exposure with low yield. (Biermann 2023)
- Enchondroma
  - MRI can help distinguish suspected enchondroma on plain film from other more malignant entities and is supported for initial staging to confirm characteristic appearance.

Benign Bone Tumors - Restaging/ Recurrence (ONC-12.11)

ON.SS.0012.11.C
v2.0.2025

Indication	Imaging Study
Giant Cell Tumor of Bone (GCTB)	ANY or ALL of the following, after completion of radiotherapy or every 2 cycles of chemotherapy: • MRI without contrast or without and with contrast of involved area • CT (contrast as requested) of involved area • Bone scan (CPT® 78306)
Enchondroma	• Plain films of primary site

Evidence Discussion

- GCTB
  - For patients requiring chemotherapy, repeat of all imaging done at initial staging may be done every two cycles to assess treatment response or need to change therapy. For patients treated with radiotherapy, repeat imaging may be done at completion of radiotherapy to verify treatment response and establish baseline for surveillance (Biermann, 2024).
- Enchondroma
  - Once initial staging with advanced imaging has been completed, plain films should be adequate to ensure stability or for suspected recurrence, restaging after local therapy, or surveillance. Further advanced imaging is generally low yield unless there are indeterminate findings on the plain films.

Benign Bone Tumors – Surveillance/ Follow-up (ONC-12.12)

ON.SS.0012.12.A
v2.0.2025

Indication	Imaging Study
Giant Cell Tumor of Bone (GCTB)	ANY or ALL of the following every 6-12 months for 4 years, then annually thereafter: • Plain x-ray of primary site ◦ MRI without and with contrast is indicated for new findings on plain x-ray or new/worsening clinical symptoms. • Chest x-ray ◦ CT Chest with (CPT® 71260) or without (CPT® 71250) contrast for new findings on chest x-ray, or new/worsening signs/ symptoms.
Enchondroma	Plain films of primary site

Evidence Discussion

- GCTB
  - The role of advanced imaging in asymptomatic surveillance is not well established for GCTB. Though late recurrences can occur, there is not strong data to support advanced imaging over plain film in asymptomatic patients. These guidelines allow advanced imaging if there are indeterminate findings on plain film, both for primary site and chest. Time frames for plain films are in alignment with NCCN. (Biermann 2024, Montgomery 2019)
- Enchondroma
  - Once initial staging with advanced imaging has been completed, plain films should be adequate to ensure stability or further imaging for recurrence, restaging after local therapy, or surveillance . Further advanced imaging is generally low yield unless there are indeterminate findings on the plain films.

References (ONC-12)

v2.0.2025

1. Von Mehren M, Kane III JM, Armstrong SA, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – November 21, 2024. Soft Tissue Sarcoma, available at: https://www.nccn.org/ professionals/ physician_gls/pdf/sarcoma.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Soft Tissue Sarcoma V4.2024 – November 21, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Biermann JS, Hirbe A, Agulnik M, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – August 20, 2024. Bone cancer, available at: https://www.nccn.org/professionals/physician_gls/ pdf/bone.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Bone cancer V1.2025 – August 20, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Von Mehren M, Kane III JM, Armstrong SA, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – March 8, 2024. Gastrointestinal Stromal Tumors, available at: https:// www.nccn.org/ professionals/physician_gls/pdf/gist.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Gastrointestinal Stromal Tumors V1.2024 – March 8, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN™ Guidelines, go online to NCCN.org
4. Nishiguchi T, Mochizuki K, Ohsawa M, et al, Differentiating benign notochordal cell tumors from chordomas: radiographic features on MRI, CT, and tomography. *Am Jour Roentgenol*. 2011;196(3):644-650. doi:10.2214/ AJR.10.4460.
5. Van den Abbeele AD. The lessons of GIST-PET and PET/CT: a new paradigm for imaging. *Oncologist*. 2008;13:8-13. doi:10.1634/theoncologist.13-S2-8.
6. Demetri GD, von Mehren M, Antonescu CR, et al. NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. *J Natl Compr Canc Netw.* 2010;8(Suppl 2):S42-44.
7. Peng PD, Hyder O, Mavros MN, et al. Management and recurrence patterns of desmoids tumors: a multi-institutional analysis of 211 patients. *Ann Surg Oncol*. 2012;19(13):4036-4042. doi:10.1245/s10434-012-2634-6.
8. Tseng WW, Amini B, Madewell JE. Follow-up of the soft tissue sarcoma patient. *J Surg Oncol.* 2015;111(5):641-645. doi:10.1002/jso.23814.
9. Grotz TE, Donohue JH. Surveillance strategies for gastrointestinal stromal tumors. *J Surg Oncol*. 2011;104(8):921-927. doi:10.1002/jso.21862.
10. Akram J, Wooler G, Lock-Andersen J. Dermatofibrosarcoma protuberans: clinical series, national Danish incidence data and suggested guidelines. *J Plast Surg Hand Surg*. 2014;48(1):67-73. doi:10.3109/2000656X.2013.812969.
11. Puri A, Gulia A, Hawaldar R, Ranganathan P, Badwe RA. Does intensity of surveillance affect survival after surgery for sarcomas? Results of a randomized noninferiority trial. *Clin Orthop Relat Res*. 2014;472(5):1568-1575. doi:10.1007/s11999-013-3385-9.
12. Biermann JS, Adkins DR, Aqulnik M, et al. Bone cancer. *J Natl Compr Canc Netw*. 2013;11(6):688-723.
13. Schuetze SM, Rubin BP, Vernon C, et al. Use of positron emission tomography in localized extremity soft tissue sarcoma treated with neoadjuvant chemotherapy. *Cancer*. 2005;103(2):339-48. doi:10.1002/cncr.20769.
14. Zagars GK, Ballo MT, Pisters PW, et al. Prognostic factors for patients with localized soft-tissue sarcoma treated with conservation surgery and radiation therapy: an analysis of 1225 patients. *Cancer*. 2003;97(10):253043. doi:10.1002/cncr.11365.
15. Bordeaux J, Blitzblau R, Aasi SZ, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – October 11, 2024. Dermatofibrosarcoma protuberans, available at: https://www.nccn.org/professionals/ physician_gls/pdf/dfsp.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology

(NCCN Guidelines™) for Dermatofibrosarcoma protuberans V1.2025– October 11, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.

16. Montgomery C, Couch C, Emory CL, Nicholas R. Giant cell tumor of bone: review of current literature, evaluation, and treatment options. *J Knee Surg*. 2019;32(4):331336. doi:10.1055/s-0038-1675815.
17. Kelly CM, Gutierrez Sainz L, Chi P. The management of metastatic GIST: current standard and investigational therapeutics. *J Hematol Oncol.* 2021;14(1):2. doi:10.1186/s13045-02001026-6.
18. Srinivasan S, Keerthivasagam S, Kumar S, Puri A. Impact of surveillance imaging in detecting local and metastatic lung recurrences among patients with sarcomas of the extremities: a systematic review and meta-analysis. *Ann Surg Oncol*. 2024;31(1):213227. doi: 10.1245/s10434-023-14429-9.

Pancreatic Cancer (ONC-13)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Pancreatic Cancer – General Considerations (ONC-13.0)

ON.PC.0013.0.A

v2.0.2025

- This guideline refers only to adenocarcinoma of the exocrine pancreas, which accounts for over 90% of pancreatic malignancies. This guideline may also be used for cancer of the Ampulla of Vater.
- Neuroendocrine and carcinoid tumors of the pancreas are not included in this guideline, see: **Neuroendocrine Cancers and Adrenal Tumors (ONC-15)**.

Pancreatic Cancer – Screening Studies for Pancreatic Cancer (ONC-13.1)

ON.PC.0013.1.A
v2.0.2025

- Detailed history of any known inherited syndrome in the individual and detailed family history in first- and second-degree relatives, including the age and lineage, is essential to guide screening recommendations. See table below for age- and risk-specific screening recommendations.
- New onset of diabetes in individuals older than 50 has been recognized as a potential indicator of the development of pancreatic cancer. Approximately 1% of individuals in this category are diagnosed with cancer within 3 years. A prediction model has been established which identifies those individuals at greatest risk for pancreatic malignancy. The scoring system, known as ENDPAC (Enriching New-Onset Diabetes for Pancreatic Cancer) is based on 3 discriminatory factors, including change in blood glucose, change in weight, and age of onset at the time of the new diagnosis of diabetes. A score of >3 imparts an elevated risk of pancreatic cancer (3.6%), and these individuals should be screened. Screening is not indicated at this time for scores of 0-2.

Indications	Imaging Study
Individuals who meet **BOTH** of the following criteria: • One or more first- or second-degree relative affected with pancreatic cancer **AND** • Known mutation carrier of ONE of the following genes: ◦ Lynch Syndrome (MLH1, MSH2, or MSH6 gene mutations) ◦ BRCA1 ◦ PALB2 mutation ◦ EPCAM ◦ TP53	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) starting at age 50 or 10 years earlier than the youngest affected family member, repeat annually

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indications	Imaging Study
Individuals with family history of pancreatic cancer but no known genetic mutation: • Individuals with 2 relatives with pancreatic cancer where one is a first-degree relative • Individuals with 3 or more relatives with pancreatic cancer	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) starting at age 45 or 10 years earlier than the youngest affected family member, repeat annually
Pancreatic Cancer Kindred (individuals who have at least one first-degree relative with pancreatic cancer who in turn also has a first-degree relative with pancreatic cancer) and NO known genetic germline mutations	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) starting at age 50 or 10 years earlier than the youngest affected family member, repeat annually
Hereditary Pancreatitis (PRSS1, CPA1, and CTRC gene mutations)	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) beginning at age 40 or 20 years after the first pancreatitis attack, repeat annually.
Peutz-Jeghers Syndrome (LKB1/STK11 gene mutation)	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) starting at age 30 or 10 years earlier than the youngest affected family member, repeat annually ◦ Family history is not required to begin imaging at age 30
CDKN2A mutation (also known as p16, p16INK4a, and MTS1, FAMM-Familial Atypical Multiple Melanoma and Mole Syndrome)	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) beginning at age 40 or 10 years earlier than the youngest affected family member, repeat annually. ◦ Family history is not required to begin imaging at age 40

Indications	Imaging Study
• BRCA2 • ATM (Ataxia-Telangiectasia)	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) starting at age 50 or 10 years earlier than the youngest affected family member, repeat annually. ◦ Family history is not required to begin imaging at age 50
Screening MRI reveals cystic lesion of the pancreas	• Repeat MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) in 6 months
Screening MRI reveals indeterminate solid lesion	• CT Abdomen with contrast – pancreatic protocol (CPT® 74160) • May repeat MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) in 3 months after the CT scan
Screening MRI reveals pancreatic stricture and/or dilation ≥6 mm without a mass	• CT Abdomen with contrast – pancreatic protocol (CPT® 74160) • May repeat MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) in 3 months after the CT scan
New onset diabetes in adults with ENDPAC score of ≥3	• CT Abdomen without and with contrast (CPT® 74170) or MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) at baseline; if negative, can be repeated once after 6 months

Evidence Discussion

International Cancer of the Pancreas Screening Consortium (CAPS) recommends screening for those with an estimated lifetime risk of pancreatic cancer >5%, to facilitate early detection, as the survival of patients diagnosed with advanced disease at presentation is extremely poor. Patients may be high risk due to family history of

2-3 relatives with pancreatic adenocarcinoma with first degree relative affected, or those with known deleterious genetic mutations in conjunction with one first- or second-degree relative with pancreatic adenocarcinoma (Canto 2013, Abe 2019, Daly 2025). Asymptomatic screening has not been shown to improve outcomes in those without an established lifetime risk of >5%, including those with only more distant relatives affected, a single relative affected and no known high-risk mutation, or those with mutations whose risk is unknown (Canto 2013, Abe 2019).

The lifetime risk and age at presentation varies with each genetic mutation. Updated CAPS recommendations generally support imaging at age 50 or ten years younger than the age of the youngest relative with pancreatic adenocarcinoma. These guidelines align with CAPS and NCCN with multiple exceptions to this to allow screening at younger ages for patients with mutations known to be higher risk or present at younger ages (Daly 2025, Goggins 2020). US Preventative Services Task Force (USPSTF) does not generally recommend pancreatic cancer screening, though they did not evaluate patients with high-risk criteria in this data. The USPSTF notes that screening has moderate risk due to unnecessary imaging and management of incidental findings (Owens, 2019). These findings further support that screening for those that do not meet the clearly defined risk factors listed in the guideline is not indicated.

MRI without and with contrast shows up to 93% sensitivity for pancreatic lesions and better illustrates pancreatic ducts, which may indirectly identify pancreatic malignancy, and is the preferred modality for screening for most patients in these guidelines. This is superior to both CT and endoscopic ultrasound, which may not detect smaller lesions (Khayat, 2024). CT pancreatic protocol is supported in these guidelines if indeterminate findings on MRI in the interest of early detection.

A unique group is patients with new onset diabetes and ENDPAC score >3. These patients are at an elevated risk of developing pancreatic cancer within 6 months even in the absence of family history or known deleterious mutations. MRI or CT is supported in this population at diagnosis of diabetes and again in 6 months (Hajibandeh S 2023, Sharma 2018).

Pancreatic Cancer – Suspected/ Diagnosis (ONC-13.2)

ON.PC.0013.2.A
v2.0.2025

Indication	Imaging Study
For any suspected symptoms only (e.g., epigastric pain, weight loss, pain radiating to back, etc.)	• Ultrasound (CPT® 76700 or CPT® 76705) • Also see: **Epigastric Pain and Dyspepsia (AB-2.5)**
Symptoms suspicious for pancreatic cancer AND any one of the following: • Abnormal labs (e.g., elevated CA 19-9, ALKP, bilirubin, or GGTP) • Abnormal physical exam findings (e.g., abdominal mass) • Abnormal or non-diagnostic ultrasound/ERCP	Any ONE of the following: • CT Pancreatic Protocol (CT Abdomen with contrast with dual phase imaging, CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377)
Preoperative studies for potentially resectable tumors without confirmed histologic diagnosis	• See: **Pancreatic Cancer – Initial Work-up/ Staging (ONC-13.3)**

Evidence Discussion

For patients with symptoms suspicious for pancreatic cancer with abnormal labs and physical findings or abnormal or non-diagnostic ultrasound or ERCP, CT pancreatic protocol (abdomen without and with contrast) or MRI abdomen without and with contrast are supported. CT pancreatic protocol has a sensitivity and specific or 90 and 87 percent respectively (Toft 2017, Kato 2020). Sensitivity and specificity of MRI and 89 and 90% respectively (Toft 2017, Kato 2020). CT has the advantage of being less costly, more accessible, and faster, but exposes to more radiation. MRI may be more sensitive for visualization of pancreatic ducts and has less radiation exposure, but can be less accessible, more costly, takes longer, and can pose difficulties with claustrophobia and has more contraindications (Kato, 2020). Given their similar sensitivity and specificity, these guidelines allow flexibility for providers and patients to weigh risks and benefits for each patient for suspected disease.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Pancreatic Cancer – Initial Work-up/ Staging (ONC-13.3)

ON.PC.0013.3.A
v2.0.2025

Indication	Imaging Study
All individuals	• CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with (CPT® 74177) or CT Abdomen and Pelvis without and with contrast (CPT® 74178)
For any of the following: • Preoperative planning • CT insufficient to determine resectability • Evaluation of indeterminate liver lesions	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377)
No evidence of metastatic disease on CT or MRI AND any of the following: • Borderline resectable disease • Equivocal or indeterminate conventional imaging findings • Markedly elevated CA 19-9 • Large primary tumor(s) • Enlarged regional lymph nodes • Planned neoadjuvant therapy	• PET/CT (CPT® 78815)

Evidence Discussion

For biopsy proven pancreatic adenocarcinoma, evaluation for metastatic disease with contrasted CTs of the chest, abdomen and pelvis are supported, given that approximately 80% of patients have metastatic or locally advanced disease at presentation (NCI, 2024). Resectability has a dramatic impact on prognosis, and MRI abdomen with and without contrast is supported in addition to CT if CT insufficient to determine resectability, for preoperative planning, or to evaluate indeterminate liver lesions (Tempero, 2024). Given the high incidence of metastatic disease at presentation,

if high-risk features are noted but no metastatic disease is visible on conventional imaging, a PET/CT is supported to assess for occult extra-pancreatic metastatic disease, in alignment with the NCCN. This is not a substitute for a diagnostic-quality contrasted CT or MRI, which is superior for detecting pancreatic disease (Tempero 2024, Toft 2017). PET/MRI has a weak expert consensus without sufficient data, and as such these guidelines do not routinely support this modality (Tempero 2024, Rijtkers 2014, Wang 2013, Sohal 2016).

Pancreatic Cancer – Restaging/ Recurrence (ONC-13.4)

ON.PC.0013.4.A
v2.0.2025

Indication	Imaging Study
For ANY of the following: • After neoadjuvant therapy • Post-operative baseline • Suspected recurrence	• CT Chest with contrast (CPT® 71260) • Abdominal imaging with one of the following, using same modality as used at initial evaluation: ◦ CT Abdomen and Pelvis with (CPT® 74177) ◦ CT Abdomen and Pelvis without and with contrast (CPT® 74178) ◦ MRI Abdomen without and with contrast (CPT® 74183) ◦ MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377) • CT with contrast of other involved or symptomatic areas
Unresectable disease or metastatic disease on chemotherapy	Every 2 cycles of treatment (commonly every 6 to 8 weeks): • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with (CPT® 74177) or CT Abdomen and Pelvis without and with contrast (CPT® 74178) • CT with contrast of other involved or symptomatic areas
Unexplained elevated liver enzymes or inconclusive recent CT abnormality	• MRI Abdomen without and with contrast (CPT® 74183) or MRCP with 3D rendering (CPT® 74183 and CPT® 76376 or CPT® 76377)
If complete surgical resection was initial therapy	• See: **Pancreatic Cancer – Surveillance/Follow-up for surveillance imaging (ONC-13.5)**
Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

For patients with unresectable or metastatic disease on chemotherapy, imaging of the chest, abdomen and pelvis with contrast (or without and with contrast for the abdomen and pelvis) are supported every 2 cycles of treatment, given the high rate of progression and metastases, to allow for prompt consideration of changes in treatment. CT of any involved or symptomatic area is also supported. The same imaging is supported after neoadjuvant chemoradiation to assess resectability and rule out metastatic disease. Resection is the mainstay of curative therapy in pancreatic cancer, but only 20% of patients achieve this status. Patients with unresectable or metastatic disease are unlikely to benefit from surgery, thus pre-operative evaluation for metastasis is essential to minimize unnecessary surgical risk (NCI 2024, Tempero 2024). As noted in the initial staging section, both CT and MRI have advantages and disadvantages. MRI is more specific for liver disease and offers better soft tissue differentiation for inconclusive findings (Tempero 2024, Sohal 2016). The same imaging guidance applies to suspected recurrence of disease. Restaging studies are also supported as a post-operative baseline, to ensure the absence of residual disease and make decisions regarding adjuvant treatment, and to ensure accurate comparison for surveillance imaging.

Pancreatic Cancer – Surveillance/Follow-up (ONC-13.5)

ON.PC.0013.5.A
v2.0.2025

Indication	Imaging Study
All individuals	Every 3 months for 2 years, then annually: • CT Chest with contrast (CPT® 71260) And ANY ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Measurable metastatic disease on maintenance therapy or being monitored off therapy	Every 3 months for up to 5 years after completion of definitive treatment, then annually: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)

Evidence Discussion

Data on the role of surveillance in pancreatic cancer are limited, due to the poor prognosis and small numbers of patients with long-term follow up. The NCCN recommendations for surveillance are based on consensus rather than data, and SEER-Medicare data shows no significant survival benefit for patients who received regular surveillance scans/no improved outcome with earlier detection of recurrence (Tempero 2024, Witkowski 2012). The role of ongoing imaging in patients with metastatic disease on maintenance or observation is also unclear. There is no clear data on length of time for maintenance therapy in those with metastatic disease, and treatment 'holidays' are often interjected in therapy. Outside of situations where there is a clear impact on management decisions, ASCO states that imaging should be supplanted by clinical evaluation (Sohal, 2016). However, the NCCN offers several second and third-line treatment options. These guidelines provide some flexibility for patient-centricity and provider preference in this setting, allowing for CT Chest, Abdomen and Pelvis every 3 months for up to 5 years and then annually after completion of definitive treatment (Tempero, 2024).

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-13)

v2.0.2025

1. Tempero MA, Malafa MP, Benson III AB, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – December 20, 2024. Pancreatic Adenocarcinoma, available at: https://www. nccn.org/professionals/physician_gls/pdf/pancreatic.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Pancreatic Adenocarcinoma V1.2025 – December 20, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am. J. Gastroenterol*. 2015;110(2):223-262. doi:10.1038/ajg.2014.435.
3. Canto MI, Harinck F, Hruban RH, et al. International Cancer of the Pancreas Screening (CAPS) consortium summit on the management of patients with increased risk for familial pancreatic cancer. *Gut.* 2013;62(3):339-347. doi:10.1136/gutjnl-2012-303108.
4. U.S. Preventive Services Task Force. *Screening for pancreatic cancer: recommendation statement.* Rockville, Maryland: Agency for Healthcare Research and Quality (AHRQ); 2004.
5. Heinrich S, Goerres GW, Schafer M, et al. Positron emission tomography/computed tomography influences on the management of resectable pancreatic cancer and its cost-effectiveness. *Ann Surg*. 2005;242(2):235-243.
6. Gemmel C, Eickhoff A, Helmstädter L, Riemann JF. Pancreatic cancer screening: state of the art. *Expert Rev Gastroenterol Hepatol*. 2009;3(1):89-96. doi:10.1586/17474124.3.1.89.
7. Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. *Gastroenterology*. 2014;146(1):291-304. doi:10.1053/j.gastro.2013.11.004.
8. Tersmette AC, Petersen GM, Offerhaus GJ. Increased risk of incident pancreatic cancer among first-degree relatives of patients with familial pancreatic cancer. *Clin Cancer Res*. 2001;7(3):738-44.
9. Tzeng CW, Abbott DE, Cantor SB et al. Frequency and intensity of postoperative surveillance after curative treatment of pancreatic cancer: a cost-effectiveness analysis. *Ann Surg Oncol*. 2013;20(7):2197-2203. doi:10.1245/s10434-013-2889-6.
10. Furman MJ, Lambert LA, Sullivan ME, Whalen GF. Rational follow-up after curative cancer resection. *Journal of Clinical Oncology*. 2013;31(9):1130-1133. doi:10.1200/JCO.2012.46.4438.
11. Tzeng C, Fleming J, Lee J, et al. Yield of clinical and radiographic surveillance in patients with resected pancreatic adenocarcinoma following multimodal therapy. *HPB*. 2012;14(6):365-372. doi:10.1111/j.1477-2574.2012.00445.x.
12. Sharma, A, Kandlakunta H, Nagpal SJS, et.al. Model to determine risk of pancreatic cancer in patients with new-onset diabetes. *Gastroenterology.* 2018;155(3):730-739.
13. Goggins M, Overbeek KA, Brand R, et. al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening Consortium. *Gut*. 2020;69(1):7-17. doi:10.1136/gutjnl-2019-319352.
14. Abe T, Blackford AL, Tamura K, et al. Deleterious germline mutations are a risk factor for neoplastic progression among high-risk individuals undergoing pancreatic surveillance. *J Clin Oncol.* 2019;37(13):1070-1080. doi:10.1200/JCO.18.01512.
15. Khayat S, Choudhary K, Gurav J, et al. Pancreatic cancer: from early detection to personalized treatment approaches. *Ann Med Surg (Lond)*. 2024;86(5):2866-2872. doi:10.1097/MS9.0000000000002011.
16. Hajibandeh S, Intrator C, Carrington-Windo E, et al. Accuracy of the END-PAC model in predicting the risk of developing pancreatic cancer in patients with new-onset diabetes: a systematic review and meta-analysis. *Biomedicines*. 2023;11(11):3040. doi:10.3390/biomedicines11113040.
17. Daly MB, Pal T, AlHilli Z, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version V2.2025 – November 7, 2024. Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate available at: https://www.nccn.org/professionals/physician_gls/pdf/bopp.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate V2.2025 – November 7, 2024. ©2024 National

18. Kato S, Honda K. Use of biomarkers and imaging for early detection of pancreatic cancer. *Cancers (Basel).* 2020;12(7):1965. doi:10.3390/cancers12071965.
19. Toft J, Hadden WJ, Laurence JM, et al. Imaging modalities in the diagnosis of pancreatic adenocarcinoma: A systematic review and meta-analysis of sensitivity, specificity and diagnostic accuracy. *Eur J Radiol*. 2017;92:17-23. doi:10.1016/j.ejrad.2017.04.009.
20. PDQ® Adult Treatment Editorial Board. PDQ. Bethesda, MD: National Cancer Institute. Pancreatic Cancer Treatment (PDQ®)–Health Professional Version. Available at Pancreatic Cancer Treatment (PDQ®) - NCI.
21. Rijkers AP, Valkema R, Duivenvoorden HJ, van Eijck CH. Usefulness of F-18-fluorodeoxyglucose positron emission tomography to confirm suspected pancreatic cancer: a meta-analysis. *Eur J Surg Oncol.* 2014;40(7):794-804. doi:10.1016/j.ejso.2014.03.016.
22. Wang Z, Chen JQ, Liu JL, Qin XG, Huang Y. FDG-PET in diagnosis, staging and prognosis of pancreatic carcinoma: a meta-analysis. *World J Gastroenterol*. 2013;19(29):4808-17. doi:10.3748/wjg.v19.i29.4808.
23. Witkowski ER, Smith JK, Ragulin-Coyne E, Ng SC, Shah SA, Tseng JF. Is it worth looking? Abdominal imaging after pancreatic cancer resection: a national study. *J Gastrointest Surg*. 2012;16(1):121-8. doi:10.1007/s11605-011-1699-z.
24. Sohal DP, Mangu PB, Khorana AA, et al. Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol*. 2016;34(23):2784-96. doi:10.1200/JCO.2016.67.1412.

Upper GI Cancers (ONC-14)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Hepatocellular Carcinoma (HCC) – General Considerations (ONC-14.1)

ON.GI.0014.1.A

v2.0.2025

- A biopsy is not always required for the diagnosis of Hepatocellular carcinoma (HCC). A dedicated triple-phase CT or MRI may be obtained. MRI with contrast is the test of choice for the evaluation of liver masses. It offers soft tissue contrast resolution superior to CT as well as the possibility of using two different contrast agents, one of which if more blood flow based and the other which also is blood flow based and demonstrates hepatobiliary function (Eovist). Classical imaging findings include:
  - arterial phase hyper-enhancement
  - venous phase washout appearance
  - capsule appearance
  - threshold growth
- For individuals who are high-risk for developing HCC (cirrhosis, chronic Hepatitis B or current or prior HCC), if the liver lesion is >1 cm with 2 classic enhancements on triple-phase CT or MRI, the diagnosis is confirmatory and biopsy is not needed.
- For lesions less than 1 cm or with less than 2 classical enhancements or for any liver lesions in individuals who are not high-risk, a biopsy is needed for histological confirmation. PET/CT scan is considered not medically necessary for the diagnosis or staging of HCC.

Evidence Discussion

HCC does not necessarily require a biopsy for diagnosis as a triple phase CT or MRI can support the diagnosis in the absence of biopsy as these lesions are characterized by arterial hypervascularity and "wash out" on portal venous phases unlike the surrounding liver. For individuals who are high-risk for developing HCC (cirrhosis, chronic Hepatitis B or current or prior HCC), if the liver lesion is >1 cm with 2 classic enhancements on triple-phase CT or MRI, the diagnosis is confirmatory and biopsy is not needed. For lesions less than 1 cm or with less than 2 classical enhancements or for any liver lesions in individuals who are not high-risk, a biopsy may be needed for histological confirmation. Serum biomarkers such as AFP are not sensitive or specific enough to establish a diagnosis. PET/CT scan is not medically necessary for the diagnosis or staging of HCC due to limited sensitivity.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Hepatocellular Carcinoma (HCC) – Suspected/Diagnosis (ONC-14.2)

ON.GI.0014.2.A

v2.0.2025

- See: **Chronic Liver Disease, Cirrhosis and Screening for HCC (AB-26.1)** in the Abdomen Imaging Guidelines.
- See: **Liver Lesion Characterization (AB-29.1)** in the Abdomen Imaging Guidelines.

Hepatocellular Carcinoma (HCC) – Initial Work-up/Staging (ONC-14.3)

ON.GI.0014.3.A
v2.0.2025

Indication	Imaging Study
All individuals	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) And ONE of the following: • CT Abdomen with contrast (CPT® 74160) • CT Abdomen without and with contrast (CPT® 74170) • CT Abdomen and Pelvis with contrast (CPT® 74177) or without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast

Evidence Discussion

All newly diagnosed individuals require a CT chest with or without contrast in addition to abdominal +/- pelvic imaging that includes CT with or with/without contrast or MRI Abdomen/Pelvis with and without contrast. Common sites of metastases include lung, adrenal glands, peritoneum and bone.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Hepatocellular Carcinoma (HCC) - Restaging/Recurrence (ONC-14.4)

ON.GI.0014.4.C
v2.0.2025

Indication	Imaging Study
ONE of the following: • After initial therapy • For suspected recurrence • Individuals receiving systemic therapy (every 2 cycles)	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) ONE of the following: • CT Abdomen with contrast (CPT® 74160) • CT Abdomen without and with contrast (CPT® 74170) • CT Abdomen and Pelvis with contrast (CPT® 74177) or CT Abdomen and Pelvis without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Hepatocellular Carcinoma treated with local therapy (ablation, embolization)	• See: **Liver Metastases (ONC-31.2)** for imaging studies indicated prior to and post-procedure
Hepatocellular Carcinoma awaiting liver transplant	• See: **Liver Transplant, Pre-Transplant (AB-42.1)** in the Abdomen Imaging Guidelines

Evidence Discussion

After initial therapy, for suspected recurrence or new liver lesions, or individuals receiving systemic therapy (every 2 cycles), CT Chest with or without contrast in addition to abdominal +/- pelvic imaging that includes CT with or with/without contrast or MRI Abdomen/Pelvis with and without contrast is indicated. For individuals undergoing liver embolization, CTA Abdomen can be obtained immediately prior to this procedure. In addition, either MRI or CT of the Abdomen with and without contrast can be obtained immediately prior and 1 month post-ablation. ONC-31.2 provides a broader description of additional appropriate studies prior to and after embolization for liver metastases.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Hepatocellular Carcinoma (HCC) – Surveillance/Follow-up (ONC-14.5)

ON.GI.0014.5.A
v2.0.2025

Indication	Imaging Study
Hepatocellular Carcinoma: • Treated with surgical resection • Treated with embolization • Being monitored off therapy	Every 3 months for 2 years, then every 6 months until year 5: • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) And ONE of the following: • CT Abdomen with contrast (CPT® 74160) • CT Abdomen without and with contrast (CPT® 74170) • CT Abdomen and Pelvis with contrast (CPT® 74177) or without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and Pelvis (CPT® 72197) without and with contrast
Hepatocellular Carcinoma treated with liver transplant	• See: **Liver Transplant, Post-transplant Imaging (AB-42.3)** in the Abdomen Imaging Guidelines

Evidence Discussion

Individuals treated with surgical resection, embolization or being monitored off therapy, recommendation is to obtain CT chest with or without contrast every 3 months for 2 years then every 6 months until year 5 as well as one of the following: CT Abdomen with or with/without contrast, CT Abdomen/Pelvis with or with/without contrast or MRI Abdomen/Pelvis with and without contrast. Multiphasic cross-sectional imaging with CT or MRI is preferred due to its reliability in assessing arterial vascularity, which is associated with increased risk of recurrence following treatment. HCC treated with transplant is addressed in AB-42.3, Liver Transplant and Post-Transplant Imaging.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Gallbladder and Biliary Tumors – Initial Work-up/Staging (ONC-14.6)

ON.GI.0014.6.A
v2.0.2025

Indication	Imaging Study
All individuals	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) And ONE of the following: • CT Abdomen with contrast (CPT® 74160) • CT Abdomen without and with contrast (CPT® 74170) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Inconclusive liver findings on CT (if MRI not already performed)	MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Inconclusive findings on MRI Abdomen	• PET/CT (CPT® 78815)

Evidence Discussion

CT Chest with or without contrast plus one of the following: CT Abdomen with or with/without contrast, CT Abdomen/Pelvis with contrast and MRI Abdomen/Pelvis with and without contrast. High-quality contrast-enhanced cross-sectional imaging (CT and/or MRI) of the chest, abdomen, and pelvis is recommended to evaluate tumor penetration through the wall of the gallbladder and the presence of nodal and distant metastases, and to detect the extent of direct tumor invasion of other organs/biliary system or major vascular invasion. PET/CT for inconclusive findings on CT/MRI keeping in mind false positives related to an inflamed gallbladder are problematic.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Gallbladder and Biliary Tumors – Restaging/Recurrence (ONC-14.7)

ON.GI.0014.7.A
v2.0.2025

Indication	Imaging Study
ANY of the following: • After initial therapy • For suspected recurrence or new liver lesions • Individuals receiving systemic chemotherapy (every 2 cycles)	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) And ONE of the following: • CT Abdomen with contrast (CPT® 74160) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Inconclusive liver findings on CT (if MRI not already performed for restaging)	• MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Inconclusive findings on MRI Abdomen	• PET/CT (CPT® 78815)

Evidence Discussion

CT Chest with or without contrast plus one of the following: CT Abdomen with or with/without contrast, CT Abdomen/Pelvis with contrast and MRI Abdomen/Pelvis with and without contrast. High-quality contrast-enhanced cross-sectional imaging (CT and/or MRI) of the chest, abdomen, and pelvis is recommended to evaluate tumor penetration through the wall of the gallbladder and the presence of nodal and distant metastases, and to detect the extent of direct tumor invasion of other organs/biliary system or major vascular invasion. PET/CT for inconclusive findings on CT/MRI keeping in mind false positives related to an inflamed gallbladder are problematic.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Gallbladder and Biliary Tumors – Surveillance/Follow-up (ONC-14.8)

ON.GI.0014.8.A
v2.0.2025

Indication	Imaging Study
All individuals	Every 6 months for 2 years, and then annually up to year 5: • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) And ONE of the following: • CT Abdomen with contrast (CPT® 74160) • CT Abdomen without and with contrast (CPT® 74170) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Biliary carcinoma treated with liver transplant	See: **Liver Transplant, Post-transplant Imaging (AB-42.3)** in the Abdomen Imaging Guidelines

Evidence Discussion

Same imaging options in ONC-14.6 to be performed every 6 months for 2 years then annually up to year 5. Biliary cancer treated with liver transplant would follow AB-42.3, Liver Transplant, Post-transplant Imaging.

Gastric Cancer – Initial Work-up/Staging (ONC-14.9)

ON.GI.0014.9.A
v2.0.2025

Indication	Imaging Study
All individuals	• CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Gastric cancer ≥T2 or higher with no metastatic disease by conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

All individuals should get CT Chest/Abdomen/Pelvis with contrast. For T2 or higher stage disease with no metastatic disease by CT, PET/CT recommended to complete staging. FDG-PET alone is not an adequate diagnostic procedure in the detection and preoperative staging of gastric cancer, but can be helpful when used in conjunction with CT.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Gastric Cancers - Restaging/Recurrence (ONC-14.10)

ON.GI.0014.10.C
v2.0.2025

Indication	Imaging Study
• After initial therapy for presumed surgically resectable disease • Post curative chemoradiation being treated without surgery • For suspected recurrence	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)
Monitoring response to chemotherapy (every 2 cycles, ~every 6-8 weeks) for: • Unresected primary disease • Metastatic disease	• CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Chest with contrast (CPT® 71260) for: ◦ Known prior thoracic disease ◦ New or worsening pulmonary symptoms ◦ New or worsening chest x-ray findings
New liver lesion(s) and primary site controlled	• CT Abdomen without and with contrast (CPT® 74170) **or** MRI Abdomen without and with contrast (CPT® 74183)
ONE of the following: • After neoadjuvant therapy for presumed surgically resectable disease or • Post curative chemoradiation being treated without surgery	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)
Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

CT Chest/Abdomen/Pelvis should be obtained after initial therapy for presumed resectable disease, post curative chemoradiation (no surgery) and for suspected recurrence. Monitoring chemotherapy response should include CT Abdomen/Pelvis and include CT Chest for known disease, new/worsening pulmonary symptoms or abnormal

chest x-ray. PET/CT can be considered with inconclusive findings on conventional imaging.

Gastric Cancer – Surveillance/Follow-up (ONC-14.11)

ON.GI.0014.11.A
v2.0.2025

Indication	Imaging Study
Stage I (treated with resection alone)	• No routine imaging unless clinical signs/ symptoms of recurrence
ANY of the following: • Stage I treated with systemic therapy • Stages II-III • Stage IV - Metastatic disease with no measurable disease post definitive treatment	Every 6 months for 2 years, and then annually for 3 more years: • CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)
Measurable metastatic disease on maintenance therapy or being monitored off therapy	Every 3 months for up to 5 years after completion of active treatment: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)

Evidence Discussion

Stage I treated with resection alone does not require routine imaging in the absence of signs/symptoms of recurrence. Stage I treated with systemic therapy, Stages II-III and Stage IV s/p definitive treatment of all measurable disease or being observed off therapy should undergo CT Chest/Abdomen/Pelvis every 6 months for 2 years then annually up to 5 years. Measurable metastatic disease on maintenance therapy or being monitored off therapy should undergo CT Chest/Abdomen/Pelvis every 3 months for up to 5 years after completion of active treatment.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-14)

v2.0.2025

1. Ajani JA, D'Amico TA, Barzi A, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2024 – May 29, 2024. Gastric cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Gastric cancer V2.2024 – May 29, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Benson AB, D'Angelica MI, Abrams T, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2024—July 2, 2024, Hepatocellular Carcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf, Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Hepatocellular Carcinoma V2.2024 July 2, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Benson AB, D'Angelica MI, Abrams T, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024—July 2, 2024, Biliary Tract Cancers, available at: https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf, Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Biliary Tract Cancers V3.2024 July 2, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org
4. Vallböhmer D, Hölscher AH, Schnieder PM, et al. [18F]-fluorodeoxyglucose-positron emission tomography for the assessment of histopathologic response and prognosis after completion of neoadjuvant chemotherapy in gastric cancer. *J Surg Oncol*. 2010;102(2):135-140. doi:10.1002/jso.21592.
5. Zou H, Zhao Y. 18FDG PET-CT for detecting gastric cancer recurrence after surgical resection: a meta-analysis. *Surg Oncol*. 2013;22(3):162-166. doi:10.1016/j.suronc.2013.05.001.
6. Bridgewater J, Galle PR, Khan SA, et al. Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma. *J Hepatol*. 2014;60(6):1268-1289. doi:10.1016/j.jhep.2014.01.021.
7. Khan SA, Davidson BR, Goldin RD, et al. Guidelines for the diagnosis and treatment of cholangiocarcinoma: an update. *Gut.* 2012;61(12):1657-1669. doi:10.1136/gutjnl-2011-301748.
8. Natsuizaka M, Omura T, Akaike T, et al. Clinical features of hepatocellular carcinoma with extrahepatic metastases. *J Gastroenterol Hepatol.* 2005;20:1781-1787.
9. Roayaie S, Blume IN, Thung SN, et al. A system of classifying microvascular invasion to predict outcome after resection in patients with hepatocellular carcinoma. *Gastroenterology*. 2009;137:850-855.
10. Sumie S, Nakashima O, Okuda K, et al. The significance of classifying microvascular invasion in patients with hepatocellular carcinoma. *Ann Surg Oncol.* 2014;21:1002-1009.
11. Furlan A, Ferris JV, Hosseinzadeh K, Borhani AA. Gallbladder carcinoma update: multimodality imaging evaluation, staging, and treatment options. *AJR Am J Roentgenol*. 2008;191:1440-1447.
12. Lamarca A, Barriuso J, Chander A, et al. (18)F-fluorodeoxyglucose positron emission tomography ((18)FDG-PET) for patients with biliary tract cancer: Systematic review and meta-analysis. *J Hepatol*. 2019;71:115-129.
13. Dassen AE, Lips DJ, Hoekstra CJ, et al. FDG-PET has no definite role in preoperative imaging in gastric cancer. *Eur J Surg Onco*l 2009;35:449- 455.
14. Lim JS, Yun MJ, Kim M-J, et al. CT and PET in stomach cancer: preoperative staging and monitoring of response to therapy. *Radiographics*. 2006;26:143-156.
15. Farinati F, Marino D, De Giorgio M, et al. Diagnostic and prognostic role of alpha-fetoprotein in hepatocellular carcinoma: both or neither? *Am J Gastroenterol.* 2006;101:524-532.

Neuroendocrine Cancers and Adrenal Tumors (ONC-15)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

General Considerations (ONC-15.1)

ON.NA.0015.1.A
v2.0.2025

This guideline includes low-grade or well-differentiated carcinoid and endocrine tumors of the lung, thymus, pancreas, gastrointestinal tract or unknown primary site; including insulinoma, glucagonoma, VIPoma, gastrinoma, somatostatinoma and others as well as catecholamine-secreting tumors of the adrenal gland such as pheochromocytoma, paraganglioma, adrenocortical carcinoma, and others.

- For poorly-differentiated or high-grade small cell or large cell neuroendocrine tumors arising outside the lung or from an unknown primary site, see: **Extrathoracic Small Cell and Large Cell Neuroendocrine Tumors (ONC-31.8)**.
- For poorly-differentiated or high grade neuroendocrine tumors of the lung, see: **Small Cell Lung Cancer (ONC-7)**.
- Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma occurring in adults should be imaged according to **Neuroblastoma (PEDONC-6)** in the Pediatric Oncology Imaging Guidelines.
- Many are associated with Multiple Endocrine Neoplasia (MEN) familial syndromes.
  – See: **Multiple Endocrine Neoplasias (MEN) (PEDONC-2.8)** in the Pediatric Oncology Imaging Guidelines for screening recommendations.
- Somatostatin receptor (SSR) based imaging is more sensitive and specific for evaluation of well-differentiated neuroendocrine tumors and may be performed using ^{111}In DTPA Octreotide scintigraphy or PET/CT scan with SSR radiotracers (such as ^{68}Ga–DOTATATE, ^{68}Ga-DOTATOC, or ^{64}Cu-DOTATATE). This study is not part of evaluation of poorly-differentiated or high-grade neuroendocrine tumors, which are imaged according to: **Extrathoracic Small Cell and Large Cell Neuroendocrine Tumors (ONC-31.8)**.

Evidence Discussion

This guideline includes low-grade or well-differentiated (Grade 1, 2 or 3; Ki-67 > 20% and < 55%) carcinoid and endocrine tumors of the lung, thymus, pancreas, gastrointestinal tract or unknown primary site; including insulinoma, glucagonoma, VIPoma, gastrinoma, somatostatinoma and others as well as catecholamine-secreting tumors of the adrenal gland such as pheochromocytoma, paraganglioma, adrenocortical carcinoma, and others. These tumors are particularly sensitive and specific to somatostatin receptor (SSR) based imaging (nearly 80% express SSR on the cell surface) while poorly differentiated or high-grade tumors typically are not with imaging recommendations being addressed in separate guidelines.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Gastrointestinal/Pancreatic Neuroendocrine Cancers – Suspected/ Diagnosis (ONC-15.2)

ON.NA.0015.2.A
v2.0.2025

Indication	Imaging Study
• Systemic symptoms strongly suggestive of functioning neuroendocrine tumor • Suspicious findings on other imaging studies • Unexplained elevation in ANY of the following: ◦ Chromogranin A ◦ 5HIAA ◦ Insulin ◦ VIP ◦ Glucagon ◦ Gastrin ◦ Substance P ◦ Serotonin ◦ Somatostatin	ANY of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) or without and with contrast (CPT® 74178) **OR** MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) • CT with contrast or MRI without and with contrast of any other symptomatic body areas

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
• Continued suspicion with negative/ inconclusive CT or MRI	ONE of the following: • PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE • If PET/CT is not available, octreotide scan ◦ Any one of the following planar imaging codes - CPT® 78801, 78802, or 78804 **AND** ◦ Any one of the follow SPECT/SPECT-CT codes - CPT® 78803, 78830, 78831, 78832

Evidence Discussion

Neuroendocrine tumors (NETs) arise from cells of the endocrine system that can be found throughout the body. They can occur sporadically or arise in the context of an inherited genetic syndrome. Presentation is usually attributable to hormonal hypersecretion (functional tumors) that can include flushing/diarrhea/wheezing (Carcinoid syndrome), hypertension and hypoglycemia versus being found incidentally on various imaging studies. If these symptoms/signs are suspicious for a NET, appropriate serologic/urinary workup may include chromogranin A, 5HIAA, insulin, VIP, glucagon, gastrin, substance P, serotonin and somatostatin. If these markers are elevated, CT chest with or without contrast as well as CT or MRI of abdomen/pelvis/ any other symptomatic body area is indicated. CT is best for detection of primary small bowel lesions and lymphadenopathy while MRI is preferred for pancreatic NETs and detecting hepatic metastases. If these imaging studies are negative/inconclusive, SSR based imaging with either Octreotide scan or Dotatate/Dotatoc (Gallium-68, Copper-64) may be indicated (SSR PET/CT). All three of these functional imaging modalities are FDA approved and can be performed in individuals on somatostatin analog therapy and are considered to be superior to Octreotide scan. FDG-based PET/CT has limited use as the majority of NETs are metabolically inactive and fail to take up the tracer well.

Gastrointestinal/Pancreatic Neuroendocrine Cancers – Initial Work-up/Staging (ONC-15.3)

ON.NA.0015.3.A
v2.0.2025

- For undifferentiated neuroendocrine tumors, see: **Extrathoracic Small Cell and Large Cell Neuroendocrine Tumors ONC-31.8**

Indication	Imaging Study
ANY of the following: • Jejunal • Ileal • Colon • Gastric type 3 • Neuroendocrine tumors of unknown primary • Grade 3 well-differentiated tumors	If not already done, ANY or ALL of the following are indicated: • PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ 68Ga-DOTATATE ◦ 68Ga-DOTATOC ◦ 68Cu-DOTATATE • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) • And ONE of the following: ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) ◦ CT Abdomen and Pelvis without and with contrast (CPT® 74178) ◦ MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
All other GI or pancreatic neuroendocrine (carcinoid) tumors	If not already done: • CT Abdomen and Pelvis with contrast (CPT® 74177) or without and with contrast (CPT® 74178) OR MRI Abdomen (CPT® 74183) and Pelvis (CPT® 72197) without and with contrast is indicated • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250)
Inconclusive CT or MRI scans	ONE of the following: • PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE • If PET is not available, octreotide scan (ANY one of the following): ◦ Any one of the following planar imaging codes - CPT® 78801, 78802, or 78804 AND ◦ Any one of the following SPECT/SPECT-CT codes - CPT® 78803, 78830, 78831, 78832
ANY of the following: • Markers fail to normalize after complete resection AND CT/MRI and somatostatin-receptor based study are negative • Biopsy-proven neuroendocrine tumor of unknown primary site AND CT/MRI and somatostatin-receptor based study are negative	• FDG-PET/CT (CPT® 78815)

Evidence Discussion

For initial evaluation of all neuroendocrine tumors, the National Comprehensive Cancer Network (NCCN) recommends that cross-sectional imaging be performed of the primary site of disease utilizing either CT or MRI. Imaging with chest CT is also an NCCN recommended consideration. For certain disease types including neuroendocrine tumors of the jejunum, ileum, and colon, as well as gastric type 3, neuroendocrine tumors of unknown primary, and grade 3 well-differentiated tumors, the NCCN recommends that a PET/CT or PET/MRI utilizing SSR radiotracers be performed in addition to diagnostic CT or MRI imaging. Brain imaging is not generally recommended for well-differentiated NET without signs and symptoms of neurologic involvement. The NCCN states octreotide scans are "much less sensitive for defining SSTR-positive disease than PET". Thus, these guidelines reserve octreotide scans as a problem-solving tool if PET is inconclusive or not available. (NCCN, 2025)

Gastrointestinal/Pancreatic Neuroendocrine Cancers – Restaging/ Recurrence (ONC-15.4)

ON.NA.0015.4.A
v2.0.2025

Indication	Imaging Study
All after surgical resection	• See: **Gastrointestinal/Pancreatic Neuroendocrine Cancers – Surveillance (ONC-15.5)**
Unresectable/metastatic disease on treatment with somatostatin analogues	• CT or MRI of involved body area no more frequently than every 3 months
Unresectable/metastatic disease on treatment with chemotherapy	• CT or MRI of involved body area every 2 cycles (6 to 8 weeks)
Suspected recurrence	• PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE • CT Chest without contrast (CPT® 71250) or CT Chest with contrast (CPT® 71260) And ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen and Pelvis without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Continued suspicion for recurrence with negative or inconclusive CT or MRI, and PET not available	• Octreotide scan: ◦ Any one of the following planar imaging codes - CPT® 78801, 78802, or 78804 **AND** ◦ Any one of the following SPECT/SPECT-CT codes - CPT® 78803, 78830, 78831, 78832
To assess candidacy for peptide receptor radionuclide therapy (PRRT) with Lutetium ^{177}Lu-dotatate	• PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE

Evidence Discussion

NCCN recommends that for any suspected recurrence of disease, PET/CT or PET/MRI be performed in addition to systemic diagnostic imaging. For individuals with unresectable/metastatic disease, NCCN states that "anatomic imaging should generally be performed every 12 weeks-12 months based on clinical or pathologic signs of aggressiveness". Thus, CT imaging of involved body area is recommended every 3 months if on somatostatin therapy versus every 2 cycles (6-8 weeks) if on chemotherapy. To assess for candidacy for peptide receptor radionuclide therapy (PRRT) with Lutetium Lu-177 dotatate (Lutathera), any of the 3 SSR PET/CT or PET/MRI options are supported. The NCCN states octreotide scans are "much less sensitive for defining SSTR-positive disease than PET". Thus, these guidelines reserve octreotide scans as a problem-solving tool if PET is inconclusive or not available. (NCCN, 2025)

Gastrointestinal/Pancreatic Neuroendocrine Cancers – Surveillance (ONC-15.5)

ON.NA.0015.5.A
v2.0.2025

Indication	Imaging Study
ANY of the following: • Appendix carcinoid <1 cm, completely resected • Rectal carcinoid <1 cm, completely resected • Gastric carcinoid treated with complete endoscopic resection	• Advanced imaging is not routinely indicated for surveillance
Rectal carcinoid 1-2 cm, completely resected	• MRI Pelvis without and with contrast (CPT® 72197) at 6 and 12 months post resection. No further routine surveillance imaging indicated
All other GI neuroendocrine tumors (stomach, large and small intestine)	• CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast once at 3 to 12 months postoperatively and every 12-24 months up to year 10
Unresected GI neuroendocrine tumors being monitored with observation alone	• CT Abdomen with contrast (CPT® 74160) once at 3 to 12 months from initial diagnosis, then every 3 months for 1 year, then every 6 months in year 2, and then annually up to year 10
Pancreatic neuroendocrine tumors	• CT Abdomen with contrast (CPT® 74160) once at 3 to 12 months postoperatively then annually up to year 10
Unresected pancreatic neuroendocrine tumors being monitored with observation alone	• CT Abdomen with contrast (CPT® 74160) once at 3 to 12 months from initial diagnosis then annually up to year 10

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Measurable metastatic disease on maintenance treatment or off therapy	• CT of involved body area no more frequently than every 3 months

Evidence Discussion

In the absence of signs/symptoms of recurrence, advanced imaging is not routinely indicated for completely resected appendiceal carcinoid <1 cm, completely resected rectal carcinoid <1 cm, and gastric carcinoid treated with complete endoscopic resection due to their excellent prognosis and low risk of recurrence. For completely resected rectal carcinoid 1-2 cm, MRI pelvis with and without contrast at 6 and 12 months post-resection and if clear, no further imaging. Due to the indolent nature of NETs, long term follow-up is recommended. For all other GI NETs, CT or MRI abdomen/pelvis once 3-12 months postoperatively and then every 12-24 months for 10 years is supported by NCCN. Unresected GI NETs on observation should undergo CT abdomen with contrast once at 3-12 months from initial diagnosis then annually up to year 10. Resected pancreatic NETs should undergo CT abdomen with contrast once at 3-12 months postoperatively then annually up to year 10. Unresected pancreatic NETs should undergo CT Abdomen with contrast once at 3-12 months from initial diagnosis then annually up to year 10. For individuals with measurable metastatic disease on maintenance or off therapy, CT of involved body area no more frequently than every 3 months. After 10 years, surveillance should be as clinically indicated. (NCCN, 2025)

Bronchopulmonary or Thymic Carcinoid – Initial Staging (ONC-15.6)

ON.NA.0015.6.A
v2.0.2025

Indication	Imaging Study
Initial diagnosis	If not already done: • CT Chest with contrast (CPT® 71260) • CT Abdomen with contrast (CPT® 74160) or without and with contrast (CPT® 74170) or MRI Abdomen (CPT® 74183) without and with contrast
Inconclusive CT or MRI scans	ONE of the following: • Octreotide scan (ANY ONE of the following): ◦ Any one of the following planar imaging codes - CPT® 78801, 78802, or 78804 **AND** ◦ Any one of the following SPECT/SPECT-CT codes - CPT® 78803, 78830, 78831, 78832 • PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE

Indication	Imaging Study
ANY of the following: • Markers fail to normalize after complete resection AND CT/MRI and somatostatin-receptor based study are negative • Biopsy-proven neuroendocrine tumor of unknown primary site AND CT/MRI and somatostatin-receptor based study are negative	• FDG-PET/CT (CPT® 78815) OR PET/MRI (CPT® 78813 and CPT® 76498)

Evidence Discussion

More than 80% of lung carcinoids are diagnosed at Stage I or II with the most common sites of metastases being liver, bone, and lung. Most thymic carcinoids are diagnosed at Stage III or IV with the most common sites of metastases being pleura, pericardium, bone, lung, and liver. Recommended initial imaging includes CT Chest with contrast and CT or MRI of the abdomen. Imaging of the brain, pelvis or osseous structures is based on signs/symptoms of disease. If the CT/MRI is inconclusive, Octreotide scan or SSR-based PET can be completed. In the setting where markers fail to normalize after surgery AND CT/MRI and SSR based study are negative OR there is biopsy proven NET of unknown origin AND CT/MRI and SSR based study are negative, FDG-based PET is indicated for the concern of a higher-grade NET being present.

Bronchopulmonary or Thymic Carcinoid – Restaging/Recurrence (ONC-15.7)

ON.NA.0015.7.A
v2.0.2025

Indication	Imaging Study
All after surgical resection	• See: **Bronchopulmonary or Thymic Carcinoid - Surveillance (ONC-15.8)**
Unresectable/metastatic disease on treatment with somatostatin analogues	• CT or MRI of involved body area no more frequently than every 3 months
Unresectable/metastatic disease on treatment with chemotherapy	• CT or MRI of involved body area every 2 cycles (6 to 8 weeks)
Progression of symptoms or elevation of tumor markers	• CT Chest without (CPT® 71250) or CT Chest with contrast (CPT® 71260) And ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen and Pelvis without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and Pelvis (CPT® 72197) without and with contrast

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Continued suspicion for recurrence with negative or inconclusive CT or MRI	ONE of the following: • Octreotide scan ◦ Any one of the following planar imaging codes - CPT® 78801, 78802, or 78804 **AND** ◦ Any one of the following SPECT/SPECT-CT codes - CPT® 78803, 78830, 78831, 78832 • PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498)with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE

Evidence Discussion

For individuals with unresectable/metastatic disease, CT imaging of involved body area is recommended every 3 months if on somatostatin therapy versus every 2 cycles (6-8 weeks) if on chemotherapy. CT Chest and CT/MRI Abdomen/Pelvis is indicated for progression of symptoms or elevation of tumor markers while Octreotide scan or SSR PET if conventional imaging is negative/inconclusive.

Bronchopulmonary or Thymic Carcinoid – Surveillance (ONC-15.8)

ON.NA.0015.8.A
v2.0.2025

Indication	Imaging Study
Carcinoid tumors of lung or thymus	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) and CT Abdomen with contrast (CPT® 74160) once at 3 to 12 months post resection and then annually up to year 10
Unresected primary tumors being monitored with observation alone	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) and CT Abdomen with contrast (CPT® 74160) once at 3 to 12 months from initial diagnosis then annually up to year 10
Asymptomatic lung or thymus distant metastasis on observation alone	Every 3 months for 1 year, and then every 6 months: • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) • CT Abdomen and Pelvis with contrast (CPT® 74178) or MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Measurable metastatic disease on maintenance treatment or off therapy	• CT Chest with contrast (CPT® 71260) • CT of involved body area no more frequently than every 3 months

Evidence Discussion

For carcinoid tumors of the lung or thymus, prognosis varies. In typical lung carcinoid, 5-year and 10-year overall survival (OS) is approximately 81-96% and 74-91% respectively for both node negative and node positive disease. With atypical histology, 5-year OS is 82-90% in node negative disease and 58-71% in node positive disease. Thymic carcinoid 5-year OS is <50%. Due to lack of long-term follow-up imaging studies, it is recommended to minimize risk of radiation exposure using CT or MRI. In individuals with resected disease, CT Chest 3-12 months post resection and then annually for up to 3 years then every 2 years up to year 10. Unresected primary tumors on observation follow a similar schedule with CT Chest 3-12 months from initial diagnosis and then annually for up to 3 years then every 2 years up to year 10. Measurable metastatic disease on maintenance therapy or observation undergoes CT of involved body area no

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

more frequently than every 3 months. After 10 years, surveillance should be as clinically indicated.

Adrenal Tumors – Suspected/Diagnosis (ONC-15.9)

ON.NA.0015.9.A
v2.0.2025

- See: **Adrenal Cortical Lesions (AB-16.1)** in the Abdomen Imaging Guidelines for evaluation of indeterminate adrenal masses.
- Adrenal tumors that involve the adrenal medulla or neural crest tissue outside the adrenal gland include pheochromocytoma, paraganglioma, and paraganglioneuroma.
  - These tumors are imaged according to sections **ONC-15.10 through ONC-15.12**.
  - Malignant adrenal tumors that involve the adrenal cortex are addressed in **Adrenocortical Carcinoma (ONC-15.13).**
- Adrenocortical carcinoma is imaged according to **Adrenocortical Carcinoma (ONC-15.13)**.
- If concern for genetic predisposition syndrome such as MEN, neurofibromatosis, or Von Hippel-Lindau disease, see screening recommendations in **Screening Imaging and Cancer Predisposition Syndromes (PEDONC-2)** in the Pediatric Oncology Imaging Guidelines.

Adrenal Tumors – Initial Work-up/Staging (ONC-15.10)

ON.NA.0015.10.A
v2.0.2025

- This guideline can be applied to **any primary site** (including beyond adrenal gland) for pheochromocytoma, paraganglioma, or paraganglioneuroma.

Indication	Imaging Study
For ANY of the following: • Pheochromocytoma • Paraganglioma • Paraganglioneuroma	If not already done: • CT Chest without (CPT® 71250) or CT Chest with contrast (CPT® 71260) And ONE of the following (if not already done): • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen and Pelvis without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast • CT with contrast or MRI without and with contrast of any other symptomatic body areas
Hypercortisolemia with ANY of the following: • Tumor greater than 4 cm • Inhomogeneous • Irregular margins • Local invasion • Other malignant imaging characteristics	ANY or ALL of the following: • FDG PET/CT (CPT® 78815) • CT Abdomen with contrast (CPT® 74160) or CT Abdomen without and with contrast (CPT® 74170) or MRI Abdomen without and with contrast (CPT® 74183)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Continued suspicion with negative/ inconclusive CT or MRI	ONE of the following: • Octreotide or MIBG scan: ◦ Any one of the following planar imaging codes - CPT® 78801, 78802, 78804 **AND** ◦ Any one of the following SPECT/SPECT-CT codes - CPT® 78803, 78830, 78831, 78832 • PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE
All above studies done and negative/ inconclusive	• FDG PET/CT scan (CPT® 78815)

Evidence Discussion

Radiologic evaluation of adrenal tumors should follow biochemical conformation of the diagnosis of pheochromocytoma and paraganglioglioma. Ninety-five percent of this group of tumors occur in the abdomen and pelvis. Paragangliomas account for 15% of this group of tumors. The initial work-up/staging of this group of tumors includes CT Chest (with contrast or without contrast) as approximately 10% of paragangliomas are found in the chest and pheochromocytoma has a potential to metastasize to chest. CT imaging with or without and with contrast or MRI imaging without and with contrast of the abdomen, pelvis and any other symptomatic body areas are indicated for initial staging. Hypercortisolemia can be caused by benign and malignant tumors. NCCN states, "Malignancy should be suspected if the tumor is larger than 4 centimeters or is inhomogeneous with irregular margins and/or has local invasion and other malignant imaging characteristics" and goes on to recommend imaging with PET/CT, CT Chest, and CT or MRI abdominal imaging (Bergsland, 2025).

Functional imaging is a valuable problem-solving tool when there is continued suspicion for this group of tumors with inconclusive or negative findings on CT/MRI. ^{123}I/^{131}I-MIBG sensitivity is higher for detecting pheochromocytoma than for detecting paraganglioma, at 88% and 67%, respectively. Another approach to functional imaging utilizes ^{68}Ga-DOTA-somatostatin analogs including DOTATOC, DOTANOC, and DOTATATE (SSR-PET/CT. In meta-analyses, the sensitivity of 68Ga-DOTA-somatostatin analogs (93%) is

superior to ^{18}F-FDG (74%), and^{123}I/^{131}I-MIBG (38%). Imaging with ^{111}In-pentetreotide (octreotide) (24%) is less sensitive that imaging with ^{68}Ga-DOTA-somatostatin analogs. Of note, functional imaging using ^{18}F-FDG PET/CT can be useful for evaluation in the scenario that CT/MRI and other functional imaging studies are negative/inconclusive.

Adrenal Tumors – Restaging/Recurrence (ONC-15.11)

ON.NA.0015.11.A
v2.0.2025

- This guideline can be applied to **any primary site** (including beyond adrenal gland) for pheochromocytoma, paraganglioma, or paraganglioneuroma.

Indication	Imaging Study
If surgery is primary therapy	See: **ONC-15.12** for surveillance recommendations
Recurrence, progression of symptoms, or elevation of tumor markers	• CT Chest without contrast (CPT® 71250) or CT Chest with contrast (CPT® 71260) • CT with contrast of involved areas And ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen and Pelvis without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Continued suspicion for recurrence with negative or inconclusive CT or MRI	ONE of the following: • Octreotide or MIBG scan (ANY ONE of the following): ◦ Any one of the following planar imaging codes - CPT® 78801, 78802, or 78804 **AND** ◦ Any one of the following SPECT/SPECT-CT codes - CPT® 78803, 78830, 78831, 78832 • PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: ◦ ^{68}Ga-DOTATATE ◦ ^{68}Ga-DOTATOC ◦ ^{64}Cu-DOTATATE

Indication	Imaging Study
To assess candidacy for peptide receptor radionuclide therapy (PRRT) with Lutetium ^{177}Lu-dotatate	• PET/CT (CPT® 78815) or PET/MRI (CPT® 78813 and CPT® 76498) with any ONE of the following SSR radiotracers: • ^{68}Ga-DOTATATE • ^{68}Ga-DOTATOC • ^{64}CU-DOTATATE
For ANY of the following: • All above studies done and negative/ inconclusive • Hypercortisolemia with inconclusive findings on CT • Pheochromocytoma bone-dominant disease • Paraganglioma bone-dominant disease	• FDG-PET/CT scan (CPT® 78815)

Evidence Discussion

In individuals who underwent surgery for resection of localized disease, CT Abdomen with contrast is supported within the first year post resection. Follow-up imaging is based on surveillance recommendations noted in Adrenal Tumors – Surveillance (ONC 15.12). In individuals who develop recurrence, progression of symptoms or elevation of tumor markers, the extent of disease must be determined with CT/MRI imaging. CT chest (with contrast or without contrast), CT imaging with or without and with contrast or MRI imaging without and with contrast of the abdomen, pelvis and any any other symptomatic body areas are indicated. Functional imaging with ^{111}In-pentetreotide (octreotide scan) or ^{68}Ga-DOTA-somatostatin analog PET is a valuable problem solving tool when there is continued suspicion of recurrence with inconclusive or negative findings on CT/MRI. Further evaluation using ^{18}F-FDG PET/CT can be useful for evaluation in the scenario that CT/MRI and other functional imaging studies are negative/inconclusive. ^{18}F-FDG PET/CT is also supported by NCCN for the evaluation of hypercortisolemia with inconclusive findings on CT, pheochromocytoma bone-dominant disease, and paraganglioma bone-dominant disease.

Adrenal Tumors – Surveillance (ONC-15.12)

ON.NA.0015.12.A
v2.0.2025

- This guideline can be applied to **any primary site** (including beyond adrenal gland) for pheochromocytoma, paraganglioma, paraganglioneuroma, or hypercortisolemia.

Indication	Imaging Study
All individuals	Once within 3-12 months post resection and then annually for 10 years: • CT Chest with contrast (CPT® 71260) or without contrast (CPT® 71250) • CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and 72197) • CT with contrast of other involved body areas
Measurable metastatic disease being observed off therapy or on maintenance treatment	• CT of involved body area no more frequently than every 3 months for up to 5 years after completion of definitive therapy and annually thereafter

Evidence Discussion

In individuals who had resectable disease. CT Chest (with contrast or without contrast), CT imaging with or without and with contrast or MRI imaging without and with contrast of the abdomen, pelvis and any other previously involved body areas are indicated once within 3-12 months post resection then annually for 10 years. In individuals with measurable metastatic disease being observed off therapy or on maintenance therapy are at greater risk for recurrence. In addition to the imaging schedule noted above, imaging of the involved body area is indicated with greater frequency (3 months) for up to 5 years followed by annual imaging.

Adrenocortical Carcinoma (ONC-15.13)

ON.NA.0015.13.A
v2.0.2025

Indication	Imaging Study
Initial Staging	• FDG PET/CT (CPT® 78815) • CT Chest without (CPT® 71250) or CT Chest with contrast (CPT® 71260) <u>And ONE of the following (if not already done)</u>: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen and Pelvis without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Suspected recurrence	• CT Chest without (CPT® 71250) or CT Chest with contrast (CPT® 71260) <u>And ONE of the following</u>: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen and Pelvis without and with contrast (CPT® 74178) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
• Inconclusive findings on conventional imaging	• FDG PET/CT (CPT® 78815)
Surveillance after complete response to definitive treatment	<u>Annually for 5 years</u>: • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) • CT Abdomen with contrast (CPT® 74160) or MRI Abdomen (CPT® 74183) without and with contrast • CT of other involved body areas with contrast

Indication	Imaging Study
Measurable metastatic disease on maintenance therapy or being monitored off therapy	Every 3 months for up to 5 years after completion of definitive therapy: • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) • CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast • CT with contrast of other involved body areas

Evidence Discussion

Adrenocortical Carcinoma (ACC) is a rare, aggressive tumor arising from the adrenal cortex. Most cases of ACC are sporadic; however, ACC has been described as a component of hereditary cancer syndromes that include Li-Fraumeni syndrome, Beckwith Weidemann syndrome and multiple endocrine neoplasia type 1 (MEN1). Recommended imaging guidelines for screening of individuals with these syndromes are summarized in Screening Imaging in Cancer Predisposition Syndromes (PEDONC-2). ACCs that secrete excess adrenal hormones are classified as functional tumors and occur in 15-30% of cases in adults. Those patients with functional tumors present with Cushing's syndrome and/or virilization. The majority of adults with non-functioning ACCs present symptomatically with abdominal pain or flank pain; however, these tumors may present asymptomatically as a large palpable intra-abdominal mass or incidentally as a small adrenal mass. Approximately 30% of ACCs present with metastatic disease in lymph nodes, lung, live and bone. ACCs may also present with invasion of adjacent structures and with venous extension.

CT and MRI cross-sectional imaging are the standard imaging modalities used for the evaluation of ACC. Due to the measurable risk for widely metastatic disease at initial presentation, cross-section imaging of the chest and abdomen/pelvis is indicated. CT Chest (with contrast or without contrast) is indicated to evaluate for lung metastases. Cross-sectional imaging of the abdomen/pelvis using CT Abdomen/Pelvis (with or with and without contrast) or MRI Abdomen as well as MRI Pelvis (with and without contrast) are indicated for characterization of the primary tumor and evaluation for metastatic disease. If recurrence is suspected, the same imaging studies should be completed as was done for initial staging. Additional imaging may be needed to assess other suspicious sites of disease based on clinical signs/symptoms.

NCCN endorses the use of FDG PET/CT in addition to diagnostic CT or MRI for initial imaging of suspected adrenocortical carcinoma. FDG PET/CT scan is a valuable

problem-solving tool; thus, FDG PET/CT is supported to characterize inconclusive findings CT/MRI.

CT imaging is the standard approach in surveillance. In individuals who had complete response to definitive therapy, the recommendation is annual imaging for 5 years after completion of treatment as the rate of recurrence is < 25% and overall survival rate approaches 74-95% at 5 years. In individuals with metastatic disease on maintenance therapy or being monitored off treatment, the frequency of CT imaging is shortened and repeated at 3 month intervals for up to 5 years.

References (ONC-15)

v2.0.2025

1. Bergsland E, Rose JB, Benson III AB, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – January 17, 2025. Neuroendocrine and Adrenal tumors, available at: https://www. nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Neuroendocrine and Adrenal tumors V4.2024 – January 17, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Qadan M, Ma Y, Visser BC, et al. Reassessment of the current American Join Committee on Cancer staging system for pancreatic neuroendocrine tumors. *J Am Coll Surg*. 2014;218(2):188-195. doi:10.1016/j.jamcollsurg.2013.11.001.
3. Lenders JWM, Duh Q-Y, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915-1942. doi:10.1210/jc.2014-1498.
4. Ruys AT, Bennink RJ, van Westreenen HL, et al. FDG-positron emission tomography/computed tomography and standardized uptake value in the primary diagnosis and staging of hilar cholangiocarcinoma. *HPB (Oxford)*. 2011;13(4):256-262. doi:10.1111/j.1477-2574.2010.00280.x.
5. Ter-Minassian M, Chan JA, Hooshmand SM, et al. Clinical presentation, recurrence, and survival in patients with neuroendocrine tumors: results from a prospective institutional database. *Endocr Relat Can*. 2013;20(2):187-196. doi:10.1530/ERC-12-0340.
6. Murray SE, Lloyd RV, Sippel RS, Chen H, Oltmann SC. Postoperative surveillance of small appendiceal carcinoid tumors. *Am J Surg*. 2014;207(3):342-345. doi:10.1016/j.amjsurg.2013.08.038.
7. Thakker RV, Newey PJ, Walls GV, et al. Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). *J Clin Endocrinol Metab*. 2012;97(9):2990-3011. doi:10.1210/jc.2012-1230.
8. Singh S, Moody L, Chan DL, et al. Follow-up recommendations for completely resected gastroenteropancreatic neuroendocrine tumors. *JAMA Oncol*. 2018;4(11):1597-1604. doi:10.1001/jamaoncol.2018.2428.
9. Zhang J, Kunz P. Making sense of a complex disease: a practical approach to managing neuroendocrine tumors. *JCO Oncology Practice*. 2022;18(4):258-264.
10. Maxwell J, Howe J. Imaging in neuroendocrine tumors: an update for the clinician. *Int J Endocr Oncol*. 2015;2(2):159-168.
11. Galgano S, Iravani A, Bodei L, et al. Imaging of neuroendocrine neoplasms: monitoring treatment response—AJR expert panel narrative review. *AJR*. 2022;218(5):767-780.
12. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 trial of Lu-177 dotatate for midgut neuroendocrine tumors. *New England Journal of Medicine*. 2017;376(2):125-135.
13. Chi Y, Du F, Zhao H, et al. Characteristics and long-term prognosis of patients with rectal neuroendocrine tumors. *World Journal of Gastroenterology*. 2014;20(43):16252-16257.
14. Baudin E, Caplin M, Garcia-Carbonero R, et al. Lung and thymic carcinoids: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2021;32(4):439-451.
15. Carrasquillo JA, Chen CC et al. Imaging of pheochromocytoma and paraganglioma. *J Nucl Med*. 2021;62(8):1033–1042.
16. Fishbein L, Del Rivero J, et al. The North American Neuroendocrine Tumor Society consensus guidelines for surveillance and management of metastatic and/or unresectable pheochromocytoma and paraganglioma. *Pancreas*. 2021;50(4):469-493. doi:10.1097/MPA.0000000000001792.
17. Han S, Suh CH, Woo S, Kim YJ, Lee JJ. Performance of 68Ga-DOTA-conjugated somatostatin receptor-targeting peptide PET in detection of pheochromocytoma and paraganglioma: a systematic review and metaanalysis. *J Nucl Med*. 2019;60:369–376.
18. Leung K, Stamm M, Raja A, Low G. Pheochromocytoma: the range of appearances on ultrasound, CT, MRI, and functional imaging. *AJR*. 2013;200(2).237-468. doi:10.2214/AJR.12.9126.
19. Bharwani N, Rockall AG, Sahdev A, et al. Adrenocortical carcinoma: the range of appearances on CT and MRI. *AJR*. 2011;196(6): w706-714. doi:10.2214/AJR.10.5540.

20. Fassnacht M, Dekkers O, Else T, et al. European Society of Endocrinology clinical practice guidelines on the management of adrenocortical carcinoma in adults, in collaboration with the European Network for the Study of Adrenal Tumors. *Eur J Endocrinol.* 2018;179(4)G1-G46. doi:1.1530/EJE-18-0608.
21. Fassnacht M, Johanssen S, Fenske W, et al. Improved survival in patients with stage II adrenocortical carcinoma followed up prospectively by specialized centers. *J Clin Endocrinol Metab*. 2010;95(11):4925. doi:10.1210/jc.2010-0803.
22. Sidhu S, Sywak M, Robinson B, Delbridge L. Adrenocortical cancer: recent clinical and molecular advances. *Curr Opin Oncol*. 2004;16(1):13. doi:10.1097/00001622-200401000-00004.

Colorectal and Small Bowel Cancer (ONC-16)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Colorectal Cancer – General Considerations (ONC-16.0)

ON.CC.0016.0.A
v2.0.2025

- Neuroendocrine tumors of the bowel are covered in: **Neuroendocrine Cancers and Adrenal Tumors (ONC-15)**.
- Appendiceal adenocarcinoma (including pseudomyxoma peritonei) follows imaging guidelines for colorectal cancer.
- For squamous cell carcinoma of the rectum, see: **Anal Carcinoma (ONC-24)**.

Colorectal Cancer – Suspected/ Diagnosis (ONC-16.1)

ON.CC.0016.1.A
v2.0.2025

- See: **GI Bleeding (AB-22)** or **CT Colonography (CTC) (AB-25.1)** in the Abdomen Imaging Guidelines for evaluation of suspected colorectal malignancies.
- See: **Abnormal Findings on Endoscopy/Colonoscopy (AB-13.3)** in the Abdomen Imaging Guidelines for evaluation of abnormal findings on endoscopy/colonoscopy.
- If findings on colonoscopy are suspicious for colon cancer, see: **Colorectal Cancer – Initial Work-up/Staging (ONC-16.2)**.

Colorectal Cancer – Initial Work-up/ Staging (ONC-16.2)

ON.CC.0016.2.A
v2.0.2025

Indication	Imaging Study
Carcinoma within a polyp that is completely removed	• No advanced imaging needed
• Biopsy proven invasive adenocarcinoma • Colonoscopy findings suspicious for colon cancer	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)
• Further evaluation of an inconclusive liver lesion seen on CT • Potentially resectable liver metastases	• MRI Abdomen without and with contrast (CPT® 74183)
Rectal adenocarcinoma	• MRI Pelvis without and with contrast (CPT® 72197) or MRI Pelvis without contrast (CPT® 72195) (can be obtained in addition to CT scans for initial staging)
Rectal adenocarcinoma with ANY one of the following: • Rectal MRI is contraindicated • Rectal MRI is inconclusive • Superficial lesions	• Endorectal ultrasound (CPT® 76872)
ONE of the following: • Isolated metastatic lesion(s) on other imaging and individual is a candidate for aggressive surgical resection or other localized treatment to metastasis for curative intent • Inconclusive conventional imaging	• PET/CT (CPT® 78815)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

- Carcinoma within a polyp that is completed resected does not require advanced imaging.
- Invasive cancer at any stage requires advanced imaging with CT of CAP with contrast needed to adequately visualize lung, nodal and especially liver lesions with MRI of abdomen appropriate in the event of unclear liver lesions. The chest CT can identify lung metastases, which occur in approximately 4% to 9% of patients with colon and rectal cancer.
- Rectal cancer requires additional dedicated imaging with MRI pelvis that is superior to CT imaging to locally stage this form of colon cancer with endorectal/ endoscopic ultrasound (EUS) providing additional staging information when MRI is contraindicated/inconclusive/superficial. MRI is considered superior to EUS due to the latter's limitations in regard to high/bulky tumors, tumor deposits or vascular invasion.
- PET/CT is reserved for inconclusive CT/MRI imaging and to confirm isolated metastases that are amenable to definitive localized treatment with curative intent.

Colorectal Cancer – Restaging/ Recurrence (ONC-16.3)

ON.CC.0016.3.A
v2.0.2025

Indication	Imaging Study
• Complete resection • Individuals receiving post-operative adjuvant chemotherapy	• See: **Surveillance/Follow-up (ONC-16.4)**
Recurrence suspected (i.e., signs or symptoms, elevated CEA)	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast
After completion of planned neoadjuvant therapy	Prior to surgical resection in individuals with non-metastatic rectal cancer: • CT Chest with contrast (CPT® 71260) and Any ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) and MRI Pelvis without and with contrast (CPT® 72197)
Unresected primary disease or metastatic disease on chemotherapy	Every 2 cycles of chemotherapy treatment and at the completion of chemoradiotherapy: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of other involved or symptomatic areas
• Further evaluation of an inconclusive liver lesion seen on CT • Potentially resectable liver metastases	• MRI Abdomen without and with contrast (CPT® 74183)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
ONE of the following: • Postoperative elevated or rising CEA or LFTs with negative recent conventional imaging • Isolated metastatic lesion(s) on other imaging and individual is a candidate for aggressive surgical resection or other localized treatment to metastasis for curative intent • Differentiate local tumor recurrence from postoperative and/or post-radiation scarring	• PET/CT (CPT® 78815)
New or worsening pelvic pain and recent CT imaging negative or inconclusive	• MRI Pelvis without and with contrast (CPT® 72197)

Evidence Discussion

- If recurrence is suspected, CT Chest/Abdomen/Pelvis with contrast is the first line of imaging
- NCCN states that ctDNA is not recommended for surveillance (Benson III, 2025).
- Upon completion of neoadjuvant therapy, to insure the cancer has not progressed prior to definitive surgery, repeat imaging of the chest, abdomen and pelvis is indicated
- With measurable disease or unresected primary disease on chemotherapy, CT imaging is indicated every 2 cycles of treatment to assess response and appropriateness to continue the same treatment or change to new therapy.
- MRI Abdomen is indicated for inconclusive liver lesion or to better define resectability.
- PET/CT may be used in specific situations to better determine cancer recurrence if CT/MRI is inconclusive. These results may allow aggressive interventions (surgery, radiation, liver directed therapy) to take place with goal of cure, explain elevated or rising CEA level or LFTs with negative conventional imaging and can also be useful to differentiate surgical/radiation scarring from cancer. A systemic review and meta-analysis of 11 studies using PET/CT with elevated CEA and negative CT Chest/Abdomen/Pelvis showed a sensitivity of 94% and specificity of 77% in detection of tumor recurrence.

Colorectal Cancer – Surveillance/Follow-Up (ONC-16.4)

ON.CC.0016.4.C
v2.0.2025

Indication	Imaging/Lab Study
Colon and rectal adenocarcinoma: • Stage I	• No routine advanced imaging indicated
Colon and rectal adenocarcinoma: • Stage II-III	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177) after completion of surgery and then every 6 months for 5 years
Colon and rectal adenocarcinoma: • Stage IV or distant metastatic disease (post definitive treatment of all measurable disease or being observed off therapy)	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177) every 3 months for 2 years and then every 6 months for 3 years
Measurable metastatic disease on maintenance therapy	Every 3 months for up to 5 years after completion of active treatment: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Rectal cancer treated with transanal excision alone	Any one of the following every 6 months for 5 years: • Endorectal ultrasound (CPT® 76872) • MRI Pelvis without and with contrast (CPT® 72197)
Stage II-III rectal cancer treated with chemoradiation alone (no surgical treatment)	In addition to the above stage-specific surveillance: • MRI Pelvis (CPT® 72197) without and with contrast every 6 months for 3 years

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging/Lab Study
Pseudomyxoma peritonei	ONE of each of the following, every 3 months for first year, then every 6 months for 4 more years: • CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) • CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast

Evidence Discussion

- Up to 95% of recurrences occur in the first 5 years after surgery with 80% occurring in the first 3 years, many of which can still be cured supporting the need for CT imaging.
- Given the >90% cure rate with Stage I cancer, routine imaging is not usually indicated.
- Given the recurrence rate between 20-30% in Stage II-III disease, CT Chest/Abdomen/Pelvis is indicated after completion of surgery (new baseline) and annually for 5 years. More frequent imaging has a lower level of support based on the following trials: FACS, COLOFOL, CEAwatch, and PRODIGE 13.
- For Stage IV cancer s/p definitive treatment or being observed off therapy, CT imaging is recommended every 6 months for 2 years then annually for 3 years.
- For Stage IV cancer that is measurable and on maintenance therapy, CT imaging is recommended every 3 months for up to 5 years after completion of active treatment.
- For rectal cancer treated with transanal excision alone, due to higher risk of local recurrence, endorectal ultrasound (EUS) should be performed every 6 months for 5 years with pelvic MRI reserved for abnormal findings on EUS or EUS can't be performed as well as new signs/symptoms concerning for local recurrence.
- Treatment with chemoradiation alone (no surgery) is becoming more common in the setting of rectal cancer in the presence of a complete response to therapy with 5 year survival rates exceeding 80% in several trials. These members require additional follow-up studies to include MRI Pelvis every 6 months for 3 years as well as DRE/endoscopy every 3-4 months for 2 years and every 6 months for 3 more years to assess for local recurrence even without s/s of recurrence.
- Pseudomyxoma peritonei is a condition associated with appendiceal cancer and requires close imaging follow-up due to high risk of recurrence thus imaging with CT/MRI is indicated every 3 months for year 1 and every 6 months for 4 more years.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Small Bowel Cancer – Initial Work-up/ Staging (ONC-16.5)

ON.CC.0016.5.A
v2.0.2025

This section provides imaging guidelines for small bowel adenocarcinoma arising from the duodenum, jejunum, and ileum.

Indication	Imaging/Lab Study
Carcinoma within a polyp that is completely removed	• No advanced imaging needed
Invasive adenocarcinoma	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast ◦ MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197) if CT is inconclusive or cannot be performed

Evidence Discussion

- Cancerous polyps that are completely removed do not require imaging.
- Invasive cancer at any stage requires advanced imaging with CT of Chest/Abdomen/ Pelvis with contrast needed to adequately visualize lung, nodal and especially liver lesions with MRI of abdomen/pelvis appropriate in the event the CT is inconclusive or cannot be performed.

Small Bowel Cancer – Restaging/ Recurrence (ONC-16.6)

ON.CC.0016.6.A
v2.0.2025

Indication	Imaging Study
Complete resection	• See Surveillance below
Recurrence suspected	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast
Unresected primary disease or metastatic disease on chemotherapy	Every 2 cycles of chemotherapy: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Further evaluation of an inconclusive liver lesion seen on CT	• MRI Abdomen without and with contrast (CPT® 74183)
ONE of the following: • Postoperative elevated or rising CEA or LFTs with negative recent conventional imaging • Isolated metastatic lesion(s) on other imaging and individual is a candidate for aggressive surgical resection or other localized treatment to metastasis for curative intent	• PET/CT (CPT® 78815)

Evidence Discussion

- If recurrence is suspected, CT Chest/Abdomen/Pelvis with contrast is the first line of imaging.
- With measurable disease or unresected primary disease on chemotherapy, CT imaging is indicated every 2 cycles of treatment to assess response and appropriateness to continue the same treatment or change to new therapy.
- MRI Abdomen is indicated for inconclusive liver lesion on CT

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

- PET/CT may be used in specific situations to better determine cancer recurrence if CT/MRI is inconclusive. These results may allow aggressive interventions (surgery, radiation, liver directed therapy) to take place with goal of cure and also explain elevated or rising CEA level or LFTs with negative conventional imaging.

Small Bowel Cancer – Surveillance/ Follow-up (ONC-16.7)

ON.CC.0016.7.A
v2.0.2025

Indication	Imaging/Lab Study
Stage I-III	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast after completion of surgery, and then annually for 5 years
Stage IV - Metastatic disease (post definitive treatment of all measurable disease, or being observed off therapy)	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast every 6 months for 2 years and then annually for 3 years
Measurable metastatic disease on maintenance therapy	Every 3 months for up to 5 years after completion of active treatment: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)

Evidence Discussion

- Stage I, II and III cancers undergo CT CAP at completion of surgery then annually for 5 years, similar to Colorectal guidelines due to lack of data regarding optimal approach.
- For Stage IV cancer s/p definitive treatment or being observed off therapy, CT imaging is recommended every 6 months for 2 years then annually for 3 years.
- For Stage IV cancer that is measurable and on maintenance therapy, CT imaging is recommended every 3 months for up to 5 years after completion of active treatment.

References (ONC-16)

v2.0.2025

1. Benson III AB, Venook AP, Adam M, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – February 6, 2025. Colon cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Colon cancer V1.2025 – February 6, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Benson III AB, Venook AP, Adam M, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – February 7, 2025. Rectal cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Rectal cancer V1.2025 – February 7, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Benson AB, Venook AP, Pedersen K, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – January 17, 2025. Small Bowel Adenocarcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/small_bowel.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Small Bowel Adenocarcinoma V1.2025 – January 17, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
4. ACR Appropriateness Criteria. Pretreatment Staging of Colorectal Cancer. Rev. 2011.
5. Bailey CE, Hu C-Y, You YN et al. Variation in positron emission tomography use after colon cancer resection. *J Oncol Pract*. 2015;11(3):e363-e372. doi:10.1200/JOP.2014.001933.
6. Lu YY, Chen JH, Ding HJ, Chien CR, Lin WY, Kao CH. A systematic review and meta-analysis of pretherapeutic lymph node staging of colorectal cancer by 18F-FDG PET or PET/CT. *Nucl Med commun*. 2012;33(11):1127-1133. doi:10.1097/MNM0b013e328357b2d9.
7. Moulton CA, Gu CS, Law CH, et al. Effect of PET before liver resection on surgical management for colorectal adenocarcinoma metastases: a randomized clinical trial. *JAMA*. 2014;311(18):1863-1869. doi:10.1001/jama.2014.3740.
8. Steele SR, Chang GJ, Hendren S, et al. Practice guideline for the surveillance of patients after curative treatment of colon and rectal cancer. *Dis Colon Rectum*. 2015;58(8):713-725. doi:10.1097/DCR.0000000000000410.
9. van de Velde CJ, Boelens PG, Borras JM, et al. EURECCA colorectal: multidisciplinary management: European concensus conference colon & rectum. *Eur J Cancer*. 2014;50(1):e1-e34. doi:10.1016/j.ejca.2013.06.048.
10. Akce M, El-Rayes BF. Nonsurgical management of rectal cancer. *Journal of Oncology Practice*. 2019;15(3):123-131. doi:10.1200/JOP.18.00769.
11. Qiu M, Hu J, Yang D, et al. Pattern of distant metastases in colorectal cancer: a SEER based study. *Oncotarget*. 2015;6:38658-38666. doi:10.18632/oncotarget.6130.
12. Balyasnikova S, Brown G. Optimal imaging strategies for rectal cancer staging and ongoing management. *Curr Treat Options Oncol*. 2016;17:32. doi:10.1007/s11864-016-0403-7.
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*. 2013;28:1039-1047. doi:10.1007/s00384-013-1659-z.
14. Byun HK, Koom WS. A practical review of watch-and-wait approach in rectal cancer. *Radiat Oncol Jl*. 2023;41:4-11. doi:10.3857/roj.2023.00038.
15. Hardiman KM, Felder SI, Friedman G, et al. The American Society of Colon and Rectal Surgeons clinical practice guidelines for the surveillance and survivorship care of patients after curative treatment of colon and rectal cancer. *Diseases of the Colon & Rectum*. 2021;64(5):517-533. doi:10.1097/DCR.0000000000001984.

Renal Cell Cancer (RCC) (ONC-17)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Renal Cell Cancer (RCC) – General Considerations (ONC-17.0)

ON.RC.0017.0.A

v2.0.2025

- PET is considered not medically necessary for initial diagnosis, staging or restaging of renal cell cancer.
- A minority of adult individuals with renal cell cancer (RCC) will have translocations in TFE3 or TFEB, which have a different natural history than “adult type” RCC. Individuals of any age with TFE3 or TFEB translocated RCC should be imaged according to guidelines in **Pediatric Renal Cell Carcinoma (RCC) (PEDONC-7.4)** in the Pediatric Oncology Imaging Guidelines.
- Individuals of any age with Wilms tumor should be imaged according to guidelines in section **Unilateral Wilms Tumor (UWT) (PEDONC-7.2)** or **Bilateral Wilms Tumor (BWT) (PEDONC-7.3)** in the Pediatric Oncology Imaging Guidelines.
- Oncocytoma in individuals of all ages should be imaged according to these guidelines.

Renal Cell Cancer (RCC) – Suspected/ Diagnosis (ONC-17.1)

ON.RC.0017.1.A
v2.0.2025

Indication	Imaging Study
• Solitary renal mass suspicious for renal cell cancer	• See: **Indeterminate Renal Lesion (AB-35.1)** in the Abdomen Imaging Guidelines for evaluation of suspected renal malignancies • CT Chest with contrast with (CPT® 71260) or without contrast (CPT® 71250)

Renal Cell Cancer (RCC) – Initial Work-Up/Staging (ONC-17.2)

ON.RC.0017.2.C
v2.0.2025

Indication	Imaging Study
All individuals	If not done previously: • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT Abdomen and Pelvis, contrast as requested
ANY of the following: • Extension of tumor into the vena cava by other imaging • Inconclusive findings on CT	• MRI Abdomen without and with contrast (CPT® 74183)
Bone pain	• Bone scan (CPT® 78306)
EITHER of the following: • Signs/symptoms suspicious for brain metastases • Newly diagnosed stage IV/metastatic RCC	• MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

American Urological Association (AUA) and the National Comprehensive Cancer Network (NCCN) guidelines state that pre- and post-contrast enhanced axial imaging, either CT or MRI, is the ideal imaging technique for the diagnosis and staging of clinically localized renal masses. Contrast-enhanced abdominal imaging best characterizes the mass, provides information regarding both the affected and unaffected renal unit, can assess extrarenal tumor spread (venous invasion or regional lymph nodes), and evaluates the adrenal glands and other abdominal organs for visceral metastasis.

Masses initially diagnosed by ultrasound should be confirmed with pre- and postcontrast enhanced imaging.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

In patients with RCC or suspicion of RCC, complete staging is typically completed with chest radiography (CXR) or chest CT. Bone scans should be reserved primarily for patients with bone pain as the prevalence of osseous metastasis for localized renal cell cancer has been shown to be low in patients without symptoms suggestive of osseous metastasis. Brain imaging is reserved for patients with neurologic symptoms, as most patients with metastasis to the central nervous system are symptomatic, or patients with newly diagnosed metastatic disease.

Renal Cell Cancer (RCC) – Restaging/ Recurrence (ONC-17.3)

ON.RC.0017.3.A
v2.0.2025

Indication	Imaging Study
Unresectable disease or metastatic disease on systemic therapy	Every 2 cycles of treatment (commonly every 6 to 8 weeks): • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis, contrast as requested (CPT® 74177, CPT® 74178, or CPT® 74176) • CT with contrast of other involved or symptomatic areas
Recurrence suspected	• CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis, contrast as requested (CPT® 74177, CPT® 74178, or CPT® 74176)
EITHER of the following: • Biopsy-proven recurrent/ metastatic disease • Signs or symptoms concerning for brain metastases	• MRI Brain without and with contrast (CPT® 70553)

Evidence Discussion

Patients presenting with findings suggesting a new renal primary or local recurrence of renal malignancy, should undergo metastatic evaluation including chest and abdominal imaging. The most common sites of distant metastasis include lung, bone, retroperitoneal and mediastinal nodes, liver, brain, or multiple sites.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Renal Cell Cancer (RCC) – Surveillance (ONC-17.4)

ON.RC.0017.4.C
v2.0.2025

Indication	Imaging Study
RCC on active surveillance of renal mass <1 cm	ALL of the following, once within 6 months of surveillance initiation and annually thereafter: • CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, or CPT® 74150) or MRI Abdomen without and with contrast (CPT® 74183) • Chest x-ray ◦ CT Chest with contrast (CPT® 71260) or without contrast (CPT® 71250) is indicated instead of chest x-ray for any of the following: ▪ Known prior thoracic disease ▪ New or worsening pulmonary symptoms ▪ New or worsening chest x-ray findings
RCC on active surveillance of renal mass ≥1 cm	ALL of the following, every 3 months for year 1, every 6 months for years 2 and 3 and annually thereafter: • CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, or CPT® 74150) OR MRI Abdomen without and with contrast (CPT® 74183) • Chest x-ray ◦ CT Chest with contrast (CPT® 71260) or without contrast (CPT® 71250) is indicated instead of chest x-ray for any of the following: ▪ Known prior thoracic disease ▪ New or worsening pulmonary symptoms ▪ New or worsening chest x-ray findings

Indication	Imaging Study
Follow up after post-ablation therapy of RCC	EITHER of the following, at 1 to 3 months, 6 months, and 12 months post-ablation and then annually thereafter: • CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, or CPT® 74150) or MRI Abdomen without and with contrast (CPT® 74183) AND Annually for 5 years: • Chest x-ray (in addition to abdominal imaging) or CT Chest with contrast (CPT® 71260) or without contrast (CPT® 71250)
Stage I RCC, after partial or radical nephrectomy	ONE of each of the following, 3 to 12 months post-resection: • CT Chest with (CPT® 71260) or CT Chest without (CPT® 71250) contrast • CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, or CPT® 74150) or MRI Abdomen without and with contrast (CPT® 74183) ONE of each of the following, annually for 5 years: • Chest x-ray or CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • Abdominal imaging with any ONE of the following: ◦ CT Abdomen with (CPT® 74160) or without (CPT® 74150) contrast ◦ MRI Abdomen without and with contrast (CPT® 74183) or CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, or CPT® 74150)

Indication	Imaging Study
Stage II RCC, post-nephrectomy	ONE of each of the following, 3 to 6 months post-resection: • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, CPT® 74150) or MRI Abdomen without and with contrast (CPT® 74183) ONE of each of the following, every 6 months for 2 years, then annually until year 5: • Chest x-ray or CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • MRI Abdomen without and with contrast (CPT® 74183) or CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, or CPT® 74150)
Stage III RCC, post-nephrectomy	ONE of each of the following, 3 to 6 months post-resection: • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, CPT® 74150) or MRI Abdomen without and with contrast (CPT® 74183) ONE of each of the following, every 3 months for 3 years, then annually to year 5: • CT Chest with (CPT® 71260) or without (CPT® 71250) contrast • CT Abdomen, contrast as requested (CPT® 74170, CPT® 74160, or CPT® 74150) or MRI Abdomen without and with contrast (CPT® 74183)
Stage IV/metastatic disease on maintenance therapy or being observed off therapy	Every 3 months for up to 5 years after completion of active treatment: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis contrast as requested (CPT® 74177, CPT® 74176, CPT® 74178) • CT with contrast of other involved or symptomatic areas

Evidence Discussion

Active surveillance Stage T1a

Active surveillance entails serial abdominal imaging in order to study the growth rate of the tumor and it is recommended that abdominal imaging (CT or MRI with contrast) within 6 months from initiation of active surveillance; subsequent imaging (with CT, MRI, or ultrasound [US]) may be performed annually thereafter. CT and MRI have both been found to accurately predict pathologic tumor size in a retrospective analysis. Therefore, best clinical judgment should be used in choosing the imaging modality. A chest x-ray or chest CT at baseline and annually as clinically indicated to assess for pulmonary metastases. Repeat chest imaging can be considered if intervention is being contemplated.

Follow up after ablative therapy for Stage T1a

An abdominal imaging either CT or MRI with and without IV contrast (unless otherwise contraindicated) at 1 through 6 months to assess treatment response, followed by annual abdominal CT or MRI (preferred) for 5 years or longer as clinically indicated. If the patient cannot receive IV contrast, MRI is preferred.

Follow up after partial or radical nephrectomy for Stages 1-2

Stage I RCC, it is recommended that abdominal CT or MRI (preferred) within 3 to 12 months following renal surgery, then annually for up to 5 years or longer as clinically indicated. For patients with stage II RCC, it is recommended to increase in abdominal imaging frequency, with baseline abdominal CT or MRI (preferred) every 6 months for 2 years, then annually for up to 5 years or longer, as clinically indicated.

It is also recommended that yearly chest x-ray or CT for at least 5 years and as clinically indicated thereafter.

Follow up for patients with Stage 3 RCC

It is recommended to obtain a baseline abdominal CT or MRI within 3 to 6 months following surgery, followed by CT, MRI (preferred), or US every 3 to 6 months for at least 3 years, and annually thereafter for up to 5 years.

A baseline chest CT within 3 to 6 months following surgery, is also recommended as well as continued imaging (CT preferred) every 3 to 6 months for at least 3 years, and annually thereafter for up to 5 years.

CT is the preferred modality for those with a high risk of recurrence.

Follow up for patient with relapse or unresectable disease or Stage 4 RCC It is recommended to obtain chest, abdominal and pelvic imaging at baseline and then as clinically indicated based on clinical status, and therapeutic schedule.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-17)

v2.0.2025

1. Motzer RJ, Jonasch E, Agarwal N, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2025 – January 9, 2025. Kidney cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Kidney cancer V3.2025 – January 9, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. ACR Appropriateness Criteria. *Post-treatment follow up of renal cell carcinoma*. Rev. 2013.
3. Herts BR, Silverman SG, Hindman NM, et al. *Management of the incidental renal mass on CT: a white paper of the ACR incidental findings committee*. J Am Coll Radiol. 2018;15(2):264-273. doi:10.1016/j.jacr.2017.04.028.
4. Finelli A, Ismaila N, Bro B, et al. Management of small renal masses. American Society of Clinical Oncology clinical practice guideline. *Journal of Clinical Oncology*. 2017;35(6):668-680. doi:10.1200/JCO.2016.69.9645.
5. Davenport MS, Caoili EM, Cohan RH, et al. MRI and CT characteristics of successfully ablated renal masses: imaging surveillance after radiofrequency ablation. *AJR Am J Roentgenol.* 2009;192:1571-1578. doi:10.2214/AJR.08.1303.
6. Clark TW, Millward SF, Gervais DA, et al. Reporting standards for percutaneous thermal ablation of renal cell carcinoma. *J Vasc Interv Radiol*. 2009;20(7 Suppl):S409-S416. doi:10.1016/j.jvir.2009.04.013.
7. Rais-Bahrami S, Guzzo TJ, Jarrett TW, Kavoussi LR, Allaf ME. Incidentally discovered renal masses: oncological and perioperative outcomes in patients with delayed surgical intervention. *BJU Int*. 2009;103(10):1355-1358. doi:10.1111/j.1464-410X.2008.08242.x.
8. Wang HY, Ding HJ, Chen JH, Chao CH, Lu YY, Lin WY, Kao CH. Meta-analysis of the diagnostic performance of [18F]FDG-PET and PET/CT in renal cell carcinoma. *Cancer Imaging*. 2012 October;12:464-474. doi:10.1102/1470-7330.2012.0042.
9. Kim EH, Strope SA. Postoperative surveillance imaging for patients undergoing nephrectomy for renal cell carcinoma. *Urol Oncol*. 2015;33(12):499-502. doi:10.1016/j.urolonc.2015.08.008.
10. Sankineni S, Brown A, Cieciera M, Choyke PL, Turkbey B. Imaging of renal cell carcinoma. *Urol Oncol*. 2016;34(3):147-155. doi:10.1016/j.urolonc.2015.05.020.
11. ACR Appropriateness Criteria. *Renal cell carcinoma staging*. Rev. 2015.
12. Campbell S, Uzzo R, Allaf M, et al. Renal mass and localized renal cancer: AUA guideline. *J Urol*. 2017:198(3):520-529. doi:10.1016/j.juro.2017.04.100.
13. Kutikov A, Fossett LK, Ramchandani P, et al. Incidence of benign pathologic findings at partial nephrectomy for solitary renal mass presumed to be renal cell carcinoma on preoperative imaging. *Urology*. 2006;68:737.
14. Lane BR, Babineau D, Kattan MW, et al. A preoperative prognostic nomogram for solid enhancing renal tumors 7 cm or less amenable to partial nephrectomy. *J Urol*. 2007;178:429.
15. Johnson DC, Vukina J, Smith AB, et al. Preoperatively misclassified, surgically removed benign renal masses: a systematic review of surgical series and United States population level burden estimate. *J Urol*. 2015;193:30.
16. Davenport MS, Perazella MA, Yee J, et al. Use of intravenous iodinated contrast media in patients with kidney disease: Consensus statements from the American College of Radiology and the National Kidney Foundation. *Radiology*. 2020;294:660.
17. Mano R, Vertosick E, Sankin AI, et al. Subcentimeter pulmonary nodules are not associated with disease progression in patients with renal cell carcinoma. *J Urol*. 2015;193:776.
18. Weinreb JC, Rodby RA, Yee J, et al. Use of intravenous gadolinium-based contrast media in patients with kidney disease: Consensus statements from the American College of Radiology and the national kidney foundation. *Radiology*. 2021;298:28.
19. Koga S, Tsuda S, Nishikido M, et al. The diagnostic value of bone scan in patients with renal cell carcinoma. *J Urol*. 2001;166:2126.
20. Campell SC, Clark PE, Chang SS, et al. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline part I. *J Urol.* 2021;206:199.

21. Campbell SC, Uzzo RG, Karam JA, et al Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: Part II. *J Urol*. 2021;206:209.
22. Park JW, Jo MK, Lee HM. Significance of 18F-fluorodeoxyglucose positron-emission tomography/computed tomography for the postoperative surveillance of advanced renal cell carcinoma. *BJU Int*. 2009;103:615-619.
23. Dabestani S, Beisland C, Stewart GD, et al. Long-term outcomes of follow-up for initially localised clear cell renal cell carcinoma: RECUR database analysis. *Eur Urol Focus*. 2019;5:857-866.
24. Koga S, Tsuda S, Nishikido M, et al. The diagnostic value of bone scan in patients with renal cell carcinoma. *J Urol*. 2001;166:2126-8.
25. Mano R, Vertosick E, Sankin AI, et al. Subcentimeter pulmonary nodules are not associated with disease progression in patients with renal cell carcinoma. *J Urol.* 2015;193:776-82.
26. Thompson RH, Hill JR, Babayev Y, et al. Metastatic renal cell carcinoma risk according to tumor size. *J Urol.* 2009;182:41-5.
27. Umbreit EC, Shimko MS, Childs MA, et al. Metastatic potential of a renal mass according to original tumour size at presentation. *BJU Int*. 2012;109:190-4; discussion 94
28. Winter H, Meimarakis G, Angele MK, et al. Tumor infiltrated hilar and mediastinal lymph nodes are an independent prognostic factor for decreased survival after pulmonary metastasectomy in patients with renal cell carcinoma. *J Urol*. 2010;184:1888-94
29. Flanigan RC, Campbell SC, Clark JI, Picken MM. Metastatic renal cell carcinoma. *Curr Treat Options Oncol*. 2003;4:385-90.
30. Griffin N, Gore ME, Sohaib SA. Imaging in metastatic renal cell carcinoma. *AJR Am J Roentgenol*. 2007;189:360-70.

Transitional Cell Cancer (ONC-18)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Transitional Cell Cancer – General Considerations (ONC-18.0)

ON.TS.0018.0.C

v2.0.2025

- Transitional cell cancers can include: tumors of the bladder, ureters, prostate, urethra, or renal pelvis. For primary cancer of the kidney, see: **Renal Cell Cancer (RCC) (ONC-17)**.
- The most common histology of bladder cancer is transitional cell (TCC) or urothelial carcinoma (UCC). Rare histologies include adenocarcinoma, squamous cell (imaged according to: **Transitional Cell Cancer (ONC-18)**), or small cell (imaged according to: **Extrathoracic Small Cell and Large Cell Neuroendocrine Tumors (ONC-31.8)**).
- Urachal cancer is a rare type of bladder cancer; the most common histology is adenocarcinoma. These are imaged according to muscle invasive bladder cancer.

Transitional Cell Cancer – Suspected/ Diagnosis (ONC-18.1)

ON.TS.0018.1.A

v2.0.2025

- See: **Hematuria and Hydronephrosis (AB-39)** in the Abdomen Imaging Guidelines for evaluation of suspected transitional cell malignancies.

Transitional Cell Cancer – Initial Work-up/Staging (ONC-18.2)

ON.TS.0018.2.C
v2.0.2025

Indication	Imaging Study
All individuals	ONE of the following: • CT Abdomen and Pelvis without and with contrast (CPT® 74178) ◦ MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast if contraindication to CT contrast • CT Abdomen and Pelvis without contrast (CPT® 74176) with retrograde pyelogram or renal ultrasound (CPT® 76770 or CPT® 76775) in individuals who cannot receive either CT or MRI contrast
Sessile or high-grade tumors	In addition to the imaging above, if not already performed: • MRI Pelvis without and with contrast (CPT® 72197)
ANY of the following: • Muscle invasive bladder carcinoma • Urethral carcinoma • Urothelial carcinoma of the prostate	• CT Chest without (CPT® 71250) or with (CPT® 71260) contrast
Individuals without metastatic disease, when requested by operating surgeon for operative planning	• CT with contrast or MRI without and with contrast of all operative sites

Indication	Imaging Study
Evaluation of suspected bone metastasis: • Individuals with symptoms of bone metastasis • Laboratory indicators of bone metastasis • Individuals with muscle invasive disease • Suspected sites of extra-osseous metastatic disease	Any ONE of the following: • Bone scan (CPT® 78306) • MRI without and with contrast of areas of suspected involvement • FDG PET/CT (CPT® 78815)
To evaluate inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)
Suspected brain metastases	See: **Brain Metastases (ONC-31.3)**

Evidence Discussion

Initial staging of non-muscle invasive bladder cancer (NMIBC)

A clinician should perform upper tract imaging as a component of the initial evaluation of a patient with bladder cancer, NCCN guidelines recommend CT urography CTU (CT of the abdomen and pelvis without and with IV contrast with excretory imaging), which is an imaging study that is tailored to improve visualization of both the upper and lower urinary tracts. CT scan can require a significant dose of ionizing radiation but the speed of image acquisition reduces the potential for motion artifact.

MR urography (MRU) may be appropriate, especially in patient with poor renal function or iodinated contrast allergy but with GFR >30 and no acute renal failure. MRU can be degraded due to motion artifact, but there is no ionizing radiation with this imaging modality.

CTU and MRU allow for comprehensive evaluation of the genitourinary tract, as well as assessment of retroperitoneal and pelvic lymph nodes.

Renal ultrasound (US) or CT without contrast may be utilized in conjunction with retrograde ureteropyelograpy in patients who cannot receive either iodinated or gadolinium-based contrast material. Ultrasound requires no ionizing radiation, but is not sufficient for evaluation alone, and must be combined with either retrograde ureteropyelography or ureteroscopy to completely evaluate the upper urinary tract.

NCCN guidelines states that chest imaging may not be necessary in the initial staging of non-invasive disease, as the risk of chest metastasis in patient with TA or T1 NMBIC is low.

FDG PET/CT is not recommended to delineate the anatomy of the upper urinary tract as it does not provide detailed imaging of the bladder. Thus, it is reserved as a problem-solving tool when other imaging studies are inconclusive.

Initial staging of non-metastatic muscle-invasive bladder cancer (MIBC)

Prior to muscle-invasive bladder cancer management, clinicians should perform a complete staging evaluation, including imaging of the chest and cross-sectional imaging of the abdomen and pelvis with intravenous contrast if not contraindicated. Laboratory evaluation should include a comprehensive metabolic panel (complete blood count, liver function tests, alkaline phosphatase, and renal function).

All patient with MIBC require imaging of the thorax. Chest radiography is an effective screening exam. Any abnormality should be followed up with a CT exam.

For sessile or high-grade tumors, it is recommended that MRI Pelvis be performed in addition to CTU for local staging (NCCN, 2024).

NCCN indicates that bone imaging is indicated if there are clinical indications of bone metastases or in individuals with muscle-invasive disease (NCCN, 2024).

FDG PET/CT is not recommended to delineate the anatomy of the upper urinary tract as it does not provide detailed imaging of the bladder. Thus, it is reserved as a problem-solving tool when other imaging studies are inconclusive.

Initial staging of Urothelial Carcinoma of the prostate/primary carcinoma of the urethra

Initial work up is similar to non-metastatic muscle invasive bladder cancer and should include Chest CT, CTU or MRU.

Transitional Cell Cancer – Restaging/ Recurrence (ONC-18.3)

ON.TS.0018.3.A
v2.0.2025

Indication	Imaging Study
After definitive surgery	• CT Abdomen and Pelvis with contrast (CPT® 74177) or CT Abdomen and Pelvis without and with contrast (CPT® 74178) for post-operative baseline
Recurrence suspicion	• CT Abdomen and Pelvis with contrast (CPT® 74177) or with and without contrast (CPT® 74178) • CT Chest with contrast (CPT® 71260) for ANY of the following: ◦ Known prior thoracic disease ◦ New or worsening pulmonary symptoms ◦ New or worsening chest x-ray findings ◦ Known prior or suspected muscle invasive disease
After neoadjuvant therapy and before resection	• CT Chest with contrast (CPT® 71260) and CT Urogram (CPT® 74178)
Monitoring therapy for metastatic disease	Every 2 cycles of therapy: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Chest with contrast (CPT® 71260) for ANY of the following: ◦ Known prior thoracic disease ◦ New or worsening pulmonary symptoms ◦ New or worsening chest x-ray findings
To evaluate inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

Patients presenting with findings suggesting a new primary or local recurrence of malignancy, should undergo metastatic evaluation including abdominal and pelvic

imaging. The most common sites for metastasis include lymph nodes, bone, lung, liver, and peritoneum. The recommended imaging for restaging of suspected recurrence mirrors that which is performed in initial staging.

Transitional Cell Cancer – Surveillance/ Follow-up (ONC-18.4)

ON.TS.0018.4.A
v2.0.2025

Indication	Imaging Study
ANY of the following: • Papillary urothelial neoplasm of low malignant potential • Low risk lesions ◦ Solitary Ta lesions ≤3cm • Intermediate risk lesions ◦ Low-grade >3 cm ◦ Low-grade multifocal ◦ T1 lesions ◦ High-grade solitary Ta ≤3cm	One-time baseline imaging at the end of therapy: • CT Urogram (CPT® 74178) or MR Urogram (CPT® 74183 and CPT® 72197) • Further advanced imaging is not routinely indicated for surveillance
ANY of the following high-risk non-muscle invasive transitional cell carcinoma of the bladder or upper tracts: • Multifocal high-grade lesions • High-grade lesions >3 cm • Superficial and minimally invasive (Tis and T1) • BCG unresponsive • Lymphovascular invasion • Prostatic urethral invasion	• CT Urogram (CPT® 74178) or MR Urogram (CPT® 74183 and CPT® 72197) (imaging as performed at initial staging) every 1-2 years for 10 years
Non-muscle-invasive transitional carcinoma of the bladder treated with cystectomy	• CT Urogram (CPT® 74178) or MR Urogram (CPT® 74183 and CPT® 72197) (imaging as performed at initial staging) at 3 and 12 months post-cystectomy, and then annually for years 2-5

Indication	Imaging Study
Muscle invasive lower and upper genitourinary tumors treated with cystectomy, nephrectomy, or chemoradiation	Every 3-6 months for 2 years, then annually for 3 more years: • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250), and CT Abdomen and Pelvis with contrast (CPT® 74177) or without and with contrast (CPT® 74178) OR • CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250), and MR Urogram (CPT® 74183 and CPT® 72197)
Measurable metastatic disease on maintenance therapy or being monitored off therapy	Every 3 months for up to 5 years after completion of active treatment: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177), CT Urogram (CPT® 74178), or MR Urogram (CPT® 74183 and CPT® 72197) (imaging as performed at initial staging)
Urethral cancers (high-risk T1 or greater) and urothelial carcinoma of the prostate	Every 3-6 months for 2 years, then annually: • CT Abdomen and Pelvis with contrast (CPT® 74177) or without and with contrast (CPT® 74178) OR • MR Urogram (CPT® 74183 and CPT® 72197) AND • Chest x-ray ◦ CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) for any of the following: ▪ Signs/symptoms of pulmonary disease ▪ Abnormal chest x-ray ▪ Prior involvement of the chest

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

Surveillance of non-muscle invasive bladder cancer

In an asymptomatic patient with a history of low-risk NMIBC a clinician should not perform routine surveillance upper tract imaging, after the initial baseline.

For an intermediate or high-risk patient, a clinician should consider performing surveillance upper tract imaging at one-to-two-year intervals. Initially obtaining imaging at 12 months, then every 1-2 years up to 10 years. CT urography (CTU), MRU, or retrograde ureteropyelography with non-contrast CT or US or ureteroscopy with a non-contrast CT or US.

Routine chest imaging is not appropriate for patients with NMBIC unless an abnormality is identified with chest radiography.

Surveillance of non-metastatic muscle-invasive bladder cancer

Clinicians should obtain chest imaging and cross-sectional imaging of the abdomen and pelvis with CT or magnetic resonance imaging (MRI) at 6-12 month intervals for 2-3 years and then may continue annually.

References (ONC-18)

v2.0.2025

1. Flaig TW, Spiess PE, Abern M, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 5.2024 – October 28, 2024. Bladder cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Bladder cancer V5.2024, October 28, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Verma S, Rajesh A, Prasad SR et al, Urinary bladder cancer: role of MR imaging. *Radiographics*. 2012;32(2):371-387. doi:10.1148/rg.322115125.
3. Lu YY, Chen JH, Liang JA. Clinical value of FDG PET or PET/CT in urinary bladder cancer: a systematic review and meta-analysis. *Eur J Radiol*. 2012;81(9):2411-2416. doi:10.1016/j.ejrad.2011.07.018.
4. Gakis G, Witjes JA, Comperat E, et al. EAU guidelines on primary urethral carcinoma. *Eur Urol.* 2013;64(5):823-830. doi:10.1016/j.eururo.2013.03.044.
5. Rouprêt M, Babjuk M, Compérat E, et al. European guidelines on upper tract urothelial carcinomas: 2013 update. *Eur Urol*. 2013;63(6):1059-1071. doi:10.1016/j.eururo.2013.03.032.
6. Holzbeierlein J, Bixler BR, Buckley DI, et al. Treatment of non-metastatic muscle-invasive bladder cancer: AUA/ASCO/SUO guideline (2017; amended 2020, 2024). *J Urol*. 2024. doi:10.1097/JU.0000000000003981.
7. Holzbeierlein J, Bixler BR, Buckley DI, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline: 2024 amendment. *J Urol*. 2024. doi:10.1097/JU.0000000000003846.
8. Coleman JA, Clark PE, Bixler BR, et al. Diagnosis and management of non-metastatic upper tract urothelial carcinoma: AUA/SUO guideline. *J Urol*. 2023;209(6):1071-1081.
9. Juri H, Koyama M, Azuma H, Narumi Y. Are there any metastases to the chest in non-muscle invasive bladder cancer patients on follow-up computed tomography? *Int Urol Nephrol*. 2018;50:1771-78.
10. Wang D, Zhang WS, Xiong MH, Yu M, Xu JX. Bladder tumors: dynamic contrast-enhanced axial imaging, multiplanar reformation, three-dimensional reconstruction and virtual cystoscopy using helical CT. *Chin Med J (Engl)*. 2004;117:62-6.
11. Witjes JA, Bruins HM, Carrión A, et al. EUA guidelines on muscle-invasive and metastatic bladder cancer. *European Association of Urology*. 2024;6-97. https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer.
12. Powles T, Bellmunt J, Comperat E, et al. Bladder cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2022;33:244-58.

Prostate Cancer (ONC-19)

Guideline Page

Prostate Cancer – General Considerations (ONC-19.0)

ON.PR.0019.0.C

v2.0.2025

- Prostate cancer screening begins at age 45 for individuals at average risk of prostate cancer. However, individuals at high-risk may begin screening at age 40. High-risk features include:
  - African ancestry
  - germline mutations (BRCA1 or 2, HOXB13, ATM, CHEK2, or mismatch repair genes - MLH1, MSH2, MSH6, PMS2) that increase the risk of prostate cancer
  - family history of first or second-degree relative with prostate, male breast, colorectal, pancreatic, endometrial or female breast cancer at age <45 years
- Treatment of benign prostatic hyperplasia with 5-alfa reductase inhibitors (such as finasteride and dutasteride) can falsely reduce the measured PSA levels by 50%. Thus, the reported PSA level should be doubled when prostate cancer is suspected in individuals on these medications
- Individuals with high-risk adverse clinical and pathological factors may benefit from a more aggressive diagnostic and therapeutic approach at the time of relapse after initial treatment. These factors include pre-treatment Gleason score of ≥8, pre-treatment clinical stage of cT3b or higher, positive surgical margins, post-treatment PSA doubling time of <3 months, and an interval to biochemical failure of <3 years after initial treatment.
- PET/CT scans using ^{18}F-FDG radiotracer are considered not medically necessary for evaluation of prostate cancer.
- ^{11}C Choline, ^{18}F-Fluciclovine (AXUMIN®), and PSMA-specific radiopharmaceuticals have recently gained FDA approval for evaluation of prostate cancer. Optimal detection rates for these radiotracers vary greatly with PSA levels. False positive rate is high and histological confirmation of positive sites is recommended.
- PSMA-specific PET radiopharmaceuticals that are currently FDA-approved and indicated in prostate cancer are: ^{68}Ga PSMA-11 (UCSF & UCLA), ^{18}F Piflufolastat (Pylarify®), ^{18}F Flotufolastat (Posluma®), and ^{68}Ga Gozetotide (Illuccix® and Locametz®).
- While early detection of low-volume recurrence after treatment of prostate cancer using PET/CT scans may influence therapeutic decisions; there is lack of evidence that this approach has any meaningful impact on overall survival.
- MR Spectroscopy (CPT® 76390) is considered not medically necessary in the evaluation of prostate cancer at this time.

- As laser prostate ablation is considered investigational and experimental at this time, advanced imaging for treatment planning and/or surveillance of laser prostate ablation is considered not medically necessary.
- Monitoring an elevated prostate-specific antigen level (PSA) with serial MRI is not indicated for suspected prostate cancer.
- Requests for imaging based on PSA must provide a recent PSA.

ISUP Prostate Cancer Grade Groups[30]

Grade Group	Gleason Score	Gleason Pattern
1	≤6	≤3+3
2	7	3+4
3	7	4+3
4	8	4+4, 3+5, 5+3
5	9 or 10	4+5, 5+4, or 5+5

NCCN Initial Risk Stratification

- Very Low Risk
  - ALL of the following features are present:
    - Tumor not clinically palpable, but present on one or both lobes on biopsy (cT1a, cT1b, or cT1c)
    - PSA (ng/mL) <10
    - Gleason Grade Group = 1
    - <3 prostate biopsy cores positive, ≤50% cancer in each core
    - PSA Density <0.15 ng/mL/g
- Low Risk
  - ALL of the following features are present but does not qualify for very low risk:
    - Clinical T Stage = cT1-cT2a (palpable tumor limited to ≤1/2 of one side)
    - PSA (ng/mL) <10
    - Gleason Grade Group = 1
- Intermediate Risk
  - No "high-risk" or "very high-risk" features and one or more of the following intermediate risk factors (IRFs):
    - cT2b-cT2c
    - Grade group 2 or 3

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

        - PSA 10-20 ng/mL
    - Favorable Intermediate Risk
        - ALL of the following features must be present:
            - Only 1 IRF
            - Gleason Grade Group = 1 or 2
            - <50% biopsy cores positive (e.g., <6 of 12 cores)
    - Unfavorable Intermediate Risk
        - One or more of the following must be present:
            - 2 or 3 IRFs
            - Gleason grade group = 3
            - ≥50% biopsy cores positive (e.g., ≥6 of 12 cores)
- High-Risk
    - Only ONE of the following high-risk features is present:
        - Clinical T Stage = cT3a (unilateral or bilateral extra-prostatic extension that is not fixed and does not invade the seminal vesicles)
        - PSA (ng/mL) >20
        - Gleason Grade Group = 4 or 5
- Very High-Risk
    - At least ONE of the following features is present:
        - Clinical T stage = cT3b-cT4 (extension into the seminal vesicles or invasion into adjacent structures)
        - Primary Gleason Pattern = 5
        - Gleason Grade Group = 4 or 5 in >4 cores
        - Presence of 2 or 3 high-risk features (noted above)

3D Rendering of MRI for MRI/Ultrasound Fusion Biopsy:

- When specific target lesion(s) is (are) detected on mpMRI (multi-parametric MRI) and classified as PIRADS 4 or 5, 3D Rendering (CPT® 76377) to generate prostate segmentation data image set for target identification on MRI/Transrectal ultrasound (TRUS) fusion biopsy is approvable as:
    - Subsequent separate standalone request; or
    - As retrospective request for medical necessity.
- For MRI/TRUS fusion biopsy of a PIRADS 1-3 lesion, approval of 3D rendering at independent workstation (CPT® 76376 or CPT® 76377) can be considered on a case-by-case basis.
- If there is no target lesion identified on MRI then 3D rendering and MRI/TRUS fusion biopsy is not generally indicated.

- 3D Rendering for the TRUS component of a fusion is a part of the UroNav Fusion Equipment Software and an additional CPT® code CPT® 76377 should not be approved.

Evidence Discussion

Screening can begin as early as age 40 for high-risk patients (Black/African-American identity, certain germline mutations, and concerning family history) and 45 for individuals with average risk. Those with a first-degree relative diagnosed at age less than 60 years have a more than 2 fold increase in likelihood of prostate cancer diagnosis. Individuals with African ancestry have a 60% higher incidence of prostate cancer. Individuals with high-risk adverse clinical and pathologic factors may benefit from a more aggressive diagnostic and therapeutic approach at the time of relapse after initial treatment.

Suspected Prostate Cancer (ONC-19.1)

ON.PR.0019.1.A
v2.0.2025

Indication	Imaging Study
ANY of the following: • Age 40-75 years with PSA >3 ng/ml or very suspicious DRE and ONE of the following high-risk features: ◦ African ancestry ◦ Germline mutations that increase the risk of prostate cancer ◦ Family history of first- or second-degree relative with prostate, male breast, pancreatic, or ovarian cancer ◦ Family history of first- or second-degree relative diagnosed at age ≤45 years with female breast cancer ◦ Family history of first- or second-degree relative diagnosed at age ≤50 years with colorectal or endometrial cancer • Age 45-75 years and ONE of the following: ◦ PSA >3 ng/ml ◦ Very suspicious DRE • Age >75 years and ONE of the following: ◦ PSA ≥4 ng/ml ◦ Very suspicious DRE • At least one negative/non-diagnostic TRUS biopsy and ANY of the following: ◦ Rising PSA ◦ Abnormal DRE ◦ Need for confirmatory MR/US fusion biopsy	ANY of the following: • Transrectal ultrasound (CPT® 76872) • TRUS-guided biopsy (CPT® 76942) • MRI Pelvis without and with contrast (CPT® 72197) or MRI Pelvis without contrast (CPT® 72195) if an MR/US guided fusion biopsy is planned • MRI/US fusion biopsy (CPT® 76942)
• PIRADS 4 or 5 lesion identified on recent diagnostic MRI Pelvis (CPT® 72195 or CPT® 72197) and planning for biopsy to be done by MRI/TRUS fusion technique	• 3D Rendering (CPT® 76376 or CPT® 76377)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
ANY of the following: • Multifocal (3 or more lesions) high-grade prostatic intraepithelial neoplasia (PIN) • Atypia on biopsy	• Extended pattern re-biopsy within 6 months by TRUS-guided biopsy (CPT® 76942)
• Focal PIN (1-2 lesions)	ONE of the following: • MRI Pelvis without contrast (CPT® 72195) • MRI Pelvis without and with contrast (CPT® 72197) • MRI/US fusion biopsy (CPT® 76942) • MRI guided biopsy (CPT® 77021)

Evidence Discussion

Based on the high-risk factors outlined above along with age, digital rectal exam (DRE) findings and PSA level, further imaging work-up may be indicated to include transrectal ultrasound with or without biopsy, MRI of the pelvis without and/or with contrast as well as MRI/US fusion biopsy is indicated. These interventions will help dictate the appropriate therapy for each individual diagnosed with prostate cancer.

Prostate Cancer – Initial Work-up/ Staging (ONC-19.2)

ON.PR.0019.2.C
v2.0.2025

Indication	Imaging Study
Localized prostate cancer with any of the following risk groups (see: **Prostate Cancer – General Considerations (ONC-19.0)** for definition of risk groups): • Very low risk • Low risk • Favorable intermediate risk	Advanced imaging is not routinely indicated for initial staging If not already performed prior to biopsy, MRI Pelvis without and with contrast (CPT® 72197) is appropriate for any of the following: • Prior to planned treatment (surgery and/ or radiation therapy) • To establish candidacy for active surveillance

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Localized prostate cancer with any of the following risk groups (see: **Prostate Cancer – General Considerations (ONC-19.0)** for definition of risk groups): • Unfavorable intermediate risk • High-risk • Very high-risk	Any ONE of the following combinations, not all (may be obtained in addition to mpMRI prostate): • CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and Bone scan (CPT® 78306) • CT Chest with contrast (CPT® 71260), CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197) if not previously performed, and Bone scan (CPT® 78306) • PSMA PET/CT scan (CPT® 78815 or CPT® 78816) using any one of the following radiotracers: ◦ ^{68}Ga-PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®) ◦ ^{18}F Flotufolastat (Posluma®)

Indication	Imaging Study
Known or clinically suspected oligo- or low volume metastatic prostate cancer (including prior to prostate biopsy)	Any ONE of the following combinations, not all: • CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and Bone scan (CPT® 78306) • CT Chest with contrast (CPT® 71260), CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197) if not previously performed, and Bone scan (CPT® 78306) • PSMA PET/CT (CPT® 78815 or CPT® 78816) or PSMA PET/MRI (CPT® 78816 and CPT® 76498) with any of the following radiotracers: ◦ ^{68}Ga-PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{18}F Flotufolastat (Posluma®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®)
Known or clinically suspected diffuse metastatic prostate cancer (including prior to prostate biopsy)	Any ONE of the following combinations, not all: • CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and Bone scan (CPT 78306) • CT Chest with contrast (CPT® 71260), CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197) if not previously performed, and Bone scan (CPT® 78306

Indication	Imaging Study
Inconclusive bone scan	Any ONE of the following: • CT with contrast of involved body site • MRI without and with contrast of involved body site • PET/CT (CPT® 78815 or CPT® 78816) or PET/MRI (CPT® 78816 and CPT® 76498) using any one of the following radiotracers: ◦ ^{18}F Fluciclovine ◦ ^{11}C Choline ◦ ^{68}Ga-PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{18}F Flotufolastat (Posluma®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®) ◦ ^{18}F sodium fluoride

Evidence Discussion

Risk stratification uses a minimum of stage, Gleason grade, and PSA to assign individuals to risk groups that in turn help select the imaging options and predict the probability of biochemical recurrence after definitive local therapy. The current prostate cancer grading system was adopted from the ISUP 2014 consensus conference with the goal to limit overtreatment. The grading system is divided into 6 risk groups.

The goal of imaging is to detect and characterize disease in order to guide disease management. Very low risk, low risk, and favorable intermediate risk does not routinely require advanced imaging. NCCN states that "conventional bone scans are rarely positive in asymptomatic patients with PSA <10 ng/mL". Very low risk, low risk, and favorable intermediate risk groups have very low risk of positive bone scan or CT scan.

Unfavorable intermediate risk, high-risk, and very high-risk do require imaging that can be a combination of CT/MRI Pelvis or PSMA PET using specific radiotracers. In individuals with known or suspected metastatic disease, CT Chest, Abdomen, and Pelvis along with bone scan are indicated. MRI Pelvis is an acceptable choice in lieu of CT Pelvis due to MRI's ability to provide detailed soft tissue characterization and contrast. NCCN supports bone imaging for those at high risk for skeletal metastases.

For inconclusive bone findings, NCCN states that additional imaging using CT, MRI, PSMA-PET/CT or PSMA-PET/MRI, or PET/CT or PET/ MRI with F-18 sodium fluoride,

C-11 choline, or F-18 fluciclovine can be considered. For conventional imaging suggesting oligo- or low-volume metastatic disease, PET/CT using specific radiotracers can be performed to confirm the individual is a candidate for localized treatment.

F18-FDG PET/CT scans are considered not medically necessary for evaluation of prostate cancer, because, per NCCN, there is a lack of data surrounding the use of this radiotracer in indivduals with prostate cancer. Other radiotracers (C11 choline, F18-Fluciclovine, PSMA-specific) are FDA approved and have influenced treatment planning but the impact on long-term survival remains to be studied. However, data does indicate that PSMA-PET has a high sensitivity for metastatic disease and small-volume disease compared to conventional imaging and therefore it has become a useful tool for the evaluation of individuals with prostate cancer.

Prostate Cancer – Restaging/Recurrence (ONC-19.3)

ON.PR.0019.3.C
v2.0.2025

Indication	Imaging Study
For ANY of the following: • Obvious progression by DRE with plans for prostatectomy or radiation therapy • Repeat TRUS biopsy for rising PSA shows progression to a higher Gleason's score with plans for prostatectomy or radiation therapy • Inconclusive findings on CT scan	• MRI Pelvis without and with contrast (CPT® 72197)
Non-metastatic prostate cancer previously treated with prostatectomy, radiation therapy, ablation, hormonal therapy or chemotherapy **and** any one of the following: • Clinical suspicion of relapse/recurrence • PSA fails to become undetectable post prostatectomy • Palpable anastomotic recurrence • PSA rises above post-treatment baseline to >0.2 ng/mL but <0.5 ng/mL on two consecutive measurements	Any ONE of the following combinations: • CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and Bone scan (CPT® 78306) • CT Chest with contrast (CPT® 71260), CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197), and Bone scan (CPT® 78306)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Non-metastatic prostate cancer previously treated with prostatectomy and **all** of the following are met: • Persistent detectable PSA after prostatectomy, or • Undetectable PSA that subsequently becomes detectable with two consecutive increases in PSA (to any amount), or • Any increase in PSA to 0.1 ng/mL or higher AND: • Individual is a candidate for salvage local therapy	Any ONE of the following: • PSMA PET/CT scan (CPT® 78815 or CPT® 78816) or PET/MRI (CPT® 78816 and CPT® 76498) with any of the following radiotracers: ◦ ^{68}Ga-PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{18}F Flotufolastat (Posluma®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®) • CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and Bone scan (CPT® 78306) • CT Chest with contrast (CPT® 71260), CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197), and Bone scan (CPT® 78306)

Indication	Imaging Study
Non-metastatic prostate cancer previously treated with radiation therapy and **all** of the following are met: • Two consecutive increases in PSA above nadir AND • Individual is a candidate for salvage local therapy	Any ONE of the following: • PSMA PET/CT scan (CPT® 78815 or CPT® 78816) or PET/MRI (CPT® 78816 and CPT® 76498) with any of the following radiotracers: ◦ ^{68}Ga-PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{18}F Flotufolastat (Posluma®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®) • CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and Bone scan (CPT® 78306) • CT Chest with contrast (CPT® 71260), CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197), and Bone scan (CPT® 78306)
Non-metastatic prostate cancer previously treated with prostatectomy or radiation therapy, and **all** of the following are met: • PSA rises on two consecutive measurements above post-treatment baseline **and** • PSA ≥1 ng/mL **and** • Recent CT scan and bone scan are negative for metastatic disease **and** • Individual is a candidate for salvage local therapy	• PET/CT scan (CPT® 78815 or CPT® 78816) using any **ONE** of the following radiotracers: ◦ ^{18}F-Fluciclovine ◦ ^{11}C Choline
Suspected progression of known metastatic disease based on: • New or worsening signs/symptoms • Rising PSA levels	• CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and Bone scan (CPT® 78306) • CT with contrast of any involved or symptomatic body part

Indication	Imaging Study
Metastatic prostate cancer receiving treatment with chemotherapy	One of the following combinations, every 2 cycles (6 to 8 weeks), while on chemotherapy: • CT Abdomen and Pelvis with contrast (CPT® 74177) and CT scan with contrast of any involved body part OR • CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197) AND, every 3-6 months: • Bone scan (CPT® 78306)
Metastatic prostate cancer receiving anti-androgen therapy	One of the following combinations, every 3 months, while on anti-androgen therapy: • CT Abdomen and Pelvis with contrast (CPT® 74177) and CT scan of any involved body part OR • CT Abdomen with contrast (CPT® 74160), MRI Pelvis without and with contrast (CPT® 72197) AND, every 3-6 months: • Bone scan (CPT® 78306)
Previously treated metastatic prostate cancer progressed on conventional imaging and being considered for ^{177}Lu-PSMA-617 (Pluvicto®) treatment[31, 32]	• PSMA PET/CT scan (CPT® 78815 or CPT® 78816) with one of the following agents: ◦ ^{68}Ga PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®) ◦ ^{18}F Flotufolastat (Posluma®)
Prior to start of Xofigo (Radium-223) therapy	• ONE time CT Chest, Abdomen and Pelvis with contrast (CPT® 71260 and CPT® 74177)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Inconclusive bone scan	Any ONE of the following: • CT with contrast of involved body site • MRI without and with contrast of involved body site • PET/CT (CPT® 78815 or CPT® 78816) or PET/MRI (CPT® 78816 and CPT® 76498) using any one of the following radiotracers: ◦ ^{18}F Fluciclovine ◦ ^{11}C Choline ◦ ^{68}Ga-PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{18}F Flotufolastat (Posluma®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®) ◦ ^{18}F sodium fluoride
Conventional imaging studies (CT and bone scan) suggests oligo- or low volume metastatic disease that needs further confirmation	• PET/CT scan (CPT® 78815 or CPT® 78816) using any one of the following radiotracers: ◦ ^{18}F Fluciclovine ◦ ^{11}C Choline ◦ ^{68}Ga-PSMA-11 ◦ ^{18}F Piflufolastat (Pylarify®) ◦ ^{68}Ga Gozetotide (Illuccix® and Locametz®) ◦ ^{18}F Flotufolastat (Posluma®)

Evidence Discussion

The use of PSMA PET radiotracers has been shown to impact treatment planning but more research is needed on the impact to long-term outcomes. However, the benefit to patients of initiating treatment earlier for recurrent disease detected on PSMA PET outweighs the disadvantages of possible false-positives. For non-metastatic prostate cancer previously treated with prostatectomy, NCCN states that PET can be used without prerequisite conventional imaging for suspected biochemical recurrence. This recommendation is due to "increased sensitivity and specificity of PSMA-PET tracers for detecting micrometastatic disease compared to conventional imaging". Conventional imaging is also noted as useful for workup of recurrence or progression. For individuals

treated with radiation therapy, NCCN states that suspected recurrence can also be imaged using these modalities. In the setting of distant metastatic disease, CT imaging along with bone scan is the mainstay of imaging with PET/CT reserved for inconclusive conventional imaging or oligo-/low volume disease that needs confirmation. NCCN states "CT provides a high level of anatomic detail, and may detect gross extracapsular disease, nodal metastatic disease, and/or visceral metastatic disease". PSMA imaging at baseline is indicated for individuals being considered for 177Lu-PSMA-617 (Pluvicto) treatment. (NCCN, 2024)

Prostate Cancer – Follow-up On Active Surveillance (ONC-19.4)

ON.PR.0019.4.A
v2.0.2025

Active surveillance is being increasingly utilized in prostate cancer, and this therapeutic option involves regimented monitoring of an individual with known diagnosis of low risk prostate cancer for disease progression, without specific anticancer treatment. While being treated with active surveillance, an individual is generally considered a potential candidate for curative intent treatment approaches in the event that disease progression occurs.

It is important to distinguish active surveillance from watchful waiting (or observation), which is generally employed in individuals with limited life expectancy. Watchful waiting involves cessation of routine monitoring and treatment is initiated only if symptoms develop.

Current active surveillance guidelines suggest the following protocol:

- PSA every 6 months
- Digital Rectal Exam (DRE) every 12 months
- Repeat prostate biopsy every 12 months
- Repeat mpMRI (CPT® 72195 or CPT® 72197) no more often than every 12 months

Indication	Imaging Study
Routine monitoring on active surveillance protocol	• MRI Pelvis without (CPT® 72195) or without and with contrast (CPT® 72197) at initiation of active surveillance, and every 12 months thereafter
Planning for re-biopsy to be done by MRI/US fusion technique	• 3D Rendering (CPT® 76376 or CPT® 76377)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
For ANY of the following: • Progression is suspected based on DRE changes or rising PSA and a recent TRUS biopsy was negative • Repeat TRUS biopsy shows progression to a higher Gleason score	• MRI Pelvis without (CPT® 72195) or MRI Pelvis without and with contrast (CPT® 72197)
Individuals on active surveillance who are noted to have progression and have plans to initiate treatment	• Imaging studies for initial staging as per **ONC-19.2**

Evidence Discussion

For certain individuals who fall into a low risk category, close monitoring in the absence of treatment can be pursued with the intent to offer curative therapy in the event progression occurs. Current guidelines include PSA every 6 months, DRE every 12 months, repeat prostate biopsy every 12 months and repeat mpMRI no more often than every 12 months. NCCN states that a metastatic staging evaluation is not indicated for those on active surveillance. With progression and the decision to pursue treatment, imaging is performed according to the same principles as stated in initial staging.

Surveillance/Follow-up For Treated Prostate Cancer (ONC-19.5)

ON.PR.0019.5.C
v2.0.2025

Indication	Imaging/Lab Study
An individual with ALL of the following: • Asymptomatic or stable chronic symptoms • Stable DRE findings • Stable PSA levels	• Advanced imaging not routinely indicated
An individual with ANY of the following: • New or worsening symptoms • Change in DRE findings • Rising PSA	ANY of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Pelvis without contrast (CPT® 72195) or without and with contrast (CPT® 72197)

Evidence Discussion

For individuals who are asymptomatic or have chronic stable findings to include DRE and PSA, advanced imaging is not routinely indicated. This form of monitoring is also referred to as observation. NCCN states that the advantages of observation avoidance of "possible side effects of unnecessary confirmatory testing and definitive therapy" (Schaeffer, 2024).

References (ONC-19)

v2.0.2025

1. Schaeffer E, Srinivas S, Adra N, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – May 17, 2024. Prostate cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Prostate cancer V4.2024 – May 17, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Moses KA, Sprenkle PC, Bahler C, et al. National Comprehensive Cancer Network (NCCN) Guidelines V2.2024 – March 6, 2024. Prostate Cancer Early Detection available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate detection.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Prostate Cancer Early Detection V2.2024 – March 6, 2024 ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Jadvar H, Calais J, Fanti S, et. al. Appropriate use criteria for prostate-specific membrane antigen PET imaging, Society for Nuclear Medicine and Molecular Imaging. https://www.snmmi.org/ClinicalPractice/content.aspx?ItemNumber=38657.
4. Hofman MS, Lawrentschuk N, Francis RJ, et. al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. *Lancet*. 2020;395(10231):1208-1216. doi:10.1016/S0140-6736(20)30314-7.
5. Pienta KJ, Gorin MA, Rowe SP, et. al. A phase 2/3 prospective multicenter study of the diagnostic accuracy of prostate specific membrane antigen PET/CT with ^{18}F-DCFPyL in prostate cancer patients (OSPREY). *J Urol*. 2021;206(1):52-61. doi:10.1097/JU.0000000000001698.
6. Artibani W, Porcaro AB, De Marco V, et. al. Management of biochemical recurrence after primary curative treatment for prostate cancer: A review. *Urol Int*. 2018;100:251–262. doi:10.1159/000481438.
7. Zumsteg ZS, Spratt DE, Romesser PB, et. al. The natural history and predictors of outcome following biochemical relapse in the dose escalation era for prostate cancer patients undergoing definitive external beam radiotherapy. *Eur Urol*. 2015;67(6):1009-1016. doi:10.1016/j.eururo.2014.09.028.
8. Trabulsi EJ, Rumble RB, Jadvar H, et al. Optimum imaging strategies for advanced prostate cancer: ASCO guideline. *J Clin Oncol*. 2020 Jan 15. doi:10.1200/JCO/19.02757 (Epub ahead of print).
9. Andriole G, Siegel B, LOCATE Study Group. PD60-12 Sites of prostate cancer recurrence delineated with 18F-Flucicloved positron emission tomography in patients with negative or equivocal conventional imaging. *Journal of Urology*. 2019;201(4):e1100-e1101. doi:10.1097/01.JU.0000557289.21741.20.
10. ACR Appropriateness Criteria. Prostate cancer – pretreatment detection, surveillance, and staging. Rev. 2016.
11. Schoots IG, Nieboer D, Giganti F, Moore CM, Bangma CH, Roobol MJ. Is magnetic resonance imaging-targeted biopsy a useful addition to systematic confirmatory biopsy in men on active surveillance for low risk prostate cancer? A systematic review and meta-analysis. *BJU Int*. 2018;122(6):946-958. doi:10.1111/bju.14358.
12. Mullins J, Bodenkamp D, Landis P, et al. Multiparametric magnetic resonance imaging findings in men with low-risk prostate cancer followed by active surveillance. *BJU Int.* 2013;111(7):1037-1045. doi:10.1111/j.1464-410X.2012.11641.x.
13. Sanda MG, Chen RC, Crispino T, et al. *AUA/ASTRO/SUO guidelines for clinically localized prostate cancer.* Linthicum, MD: American Urological Association; 2017.
14. Lu-Yao GL, Albertsen PC, Moore DF, et al. Outcomes of localized prostate cancer following conservative management. *JAMA*. 2009;302(11):1202-1209. doi:10.1001/jama.2009.1348.
15. Chen RC, Rumble RB, Loblaw DA, et al. Active surveillance for the management of localized prostate cancer (Cancer Care Ontario guideline): American Society of Clinical Oncology clinical practice guideline endorsement. *J Clin Oncol*. 2016;34(18):2182-2190. doi:10.1200/JCO.2015.65.7759.
16. Liu D, Lehmann HP, Frick KD, Carter HB. Active surveillance versus surgery for low risk prostate cancer: a clinical decision analysis. *J Urol*. 2012;187(4):1241-1246. doi:10.1016/j.juro/2011.12.015.

17. Klotz L, Zhang L, Lam A, Nam R, Mamedov A, Loblaw A. Clinical results of long-term follow-up of a large, active surveillance cohort with localized prostate cancer. *J Clin Oncol*. 2010;28(1):126-131. doi:10.1200/JCO.2009.24.2180.
18. Blomqvist L, Carlsson S, Gjertsson P, et al. Limited evidence for the use of imaging to detect prostate cancer: a systematic review. *Eur J Radiol*. 2014;83(9):1601–1606. doi:10.1016.j.ejrad.2014.06.028.
19. Schoots IG, Petrides N, Giganti F, et al. Magnetic resonance imaging in active surveillance of prostate cancer: a systematic review. *Eur Urol*. 2015;67(4):627-636. doi:10.1016/j.eururo.2014.10.050.
20. Quentin M, Blondin D, Arsov C, et al. Prospective evaluation of magnetic resonance imaging guided in-bore prostate biopsy versus systematic transrectal ultrasound guided prostate biopsy in biopsy naïve men with elevated prostate specific antigen. *J Urol*. 2014;192(5):1374-1379. doi:10.1016/j.juro.2014.05.090.
21. Klotz L, Vesprini D, Sethukavalan P, et al. Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. *J Clin Oncol*. 2015;33(3):272-277. doi:10.1200/JCO.2014.55.1192.
22. Cooperberg MR. Long-term active surveillance for prostate cancer: answers and questions. *J Clin Oncol*. 2015;33(3):238-240. doi:10.1200/JCO.2014.59.2329.
23. Risko R, Merdan S, Womble PR, et al. Clinical predictors and recommendations for staging CT scan among men with prostate cancer. *Urology*. 2014;84(6):1329-1334. doi:10.1016.j.urology.2014.07.051.
24. Heck MM, Souvatzoglou M, Retz M, et al. Prospective comparison of computed tomography, diffusion-weighted magnetic resonance imaging and [11C]choline positron emission tomography/computed tomography for preoperative lymph node staging in prostate cancer patients. *Eur J Nucl Med Mol Imaging*. 2014;41(4):694-701. doi:10.1007/s00259-013-2634-1.
25. Armstrong JM, Martin CR, Dechet C, et al. ^{18}F-fluciclovine PET CT detection of biochemical recurrent prostate cancer at specific PSA thresholds after definitive treatment. *J Urol Onc*. 2020;38(7):636.e1-636.e6. doi:10.1016/j.urolonc.2020.03.021.
26. Baruch B, Lovrec P, Solanki A, et al. Fluorine 18 labeled fluciclovine PET/CT in clinical practice: factors affecting the rate of detection of recurrent prostate cancer. *AJR*. 2019;213(4):851-858. doi:10.2214/AJ.19.21153.
27. Marcus C, Butler P, Bagrodia A, et al. Fluorine-18-labeled fluciclovine PET/CT in primary and biochemical recurrent prostate cancer management. *AJR*. 2020:1-10. doi:10.2214/AJR.19.22404.
28. Trabulsi EJ, Rumble BR, Jadvar H, et. al. Optimum imaging strategies for advanced prostate cancer: ASCO guideline. J Clin Oncol. 2020;38:1963-1996. doi:10.1200/JCO.19.02757.
29. Lowrance WT, Breau RH, Chou R, et. al. Advanced Prostate Cancer: AUA/ASTRO/SUO Guideline PART I. *J Urol*. 2021;205:14.
30. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA. The 2014 International Society of Urological Pathology (ISUP) consensus conference on gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system. *Am J Surg Pathol.* 2016;40(2):244-52. doi:10.1097/PAS.0000000000000530.
31. FDA Oncology Center of Excellence. FDA approves Pluvicto for metastatic castration-resistant prostate cancer. 2022. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pluvicto-metastatic-castration-resistant-prostate-cancer.
32. Sartor O, de Bono J, Chi KN, et. al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. *N Engl J Med*. 2021;385:1091-1103. doi:10.1056/NEJMoa2107322.

Testicular, Ovarian and Extragonadal Germ Cell Tumors (ONC-20)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Testicular, Ovarian and Extragonadal Germ Cell Tumors – General Considerations (ONC-20.0)

ON.TO.0020.0.A

v2.0.2025

- This section applies to primary germ cell tumors occurring outside the central nervous system if individual's age >15 years at the time of initial diagnosis. Individuals age ≤15 years at diagnosis should be imaged according to pediatric guidelines in: **Pediatric Germ Cell Tumors (PEDONC-10)** in the Pediatric Oncology Imaging Guidelines.
- These guidelines are for germ cell tumors of the testicle, ovary and extragonadal sites as well as malignant sex cord stromal tumors (granulosa cell and Sertoli-Leydig cell tumors).
- Requests for imaging must state the histologic type of the cancer being evaluated.
- Classified as pure seminomas (dysgerminomas, 40%) or non-seminomatous germ cell tumors (NSGCT, 60%):
  - Pure seminomas are defined as pure seminoma histology with a normal serum concentration of alpha fetoprotein (AFP). Seminomas with elevated AFP are by definition mixed.
  - Required for TNM staging are the tumor marker levels indicated by "S" (TNMS)
  - Mixed tumors are treated as NSGCTs, as they tend to be more aggressive.
  - The NSGCT histologies include:
    - yolk-sac tumors
    - immature (malignant) teratomas
    - choriocarcinomas (<1%)
    - embryonal cell carcinomas (15% to 20%)
    - endodermal Sinus Tumors (ovarian)
    - combinations of all of the above (mixed)
- MRI in place of CT scans to reduce risk of secondary malignancy is not supported by the peer-reviewed literature. CT scans are indicated for surveillance and are the preferred modality of imaging to assess for recurrence.
- PET/CT is considered not medically necessary for evaluation of non-seminomatous germ cell tumors
- Active surveillance in testicular cancer refers to treatment with surgery (orchiectomy) alone without any additional post-operative treatment such as chemotherapy or radiotherapy.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Testicular, Ovarian and Extragonadal Germ Cell Tumors – Initial Work-Up/ Staging (ONC-20.1)

ON.TO.0020.1.A
v2.0.2025

Indication	Imaging Study
Orchiectomy/oophorectomy is both diagnostic and therapeutic	For all individuals, following orchiectomy or oophorectomy, EITHER of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) or • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Suspicious testicular mass on ultrasound	EITHER of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) or • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Pelvic mass suspicious for ovarian etiology	See: **Ovarian Cancer - Suspected/Diagnosis (ONC-21.2)**
For ANY of the following: • Non-seminoma histology • Ovarian germ cell tumor • Abdominal lymphadenopathy noted on CT scan • Abnormal chest x-ray or signs/ symptoms suggestive of chest involvement	• CT Chest with contrast (CPT® 71260)
Extragonadal Germ Cell Tumor	• CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Testicular, Ovarian and Extragonadal Germ Cell Tumors – Restaging/ Recurrence (ONC-20.2)

ON.TO.0020.2.A
v2.0.2025

Indication	Imaging Study
Treatment response for stage II-IV individuals with measurable disease on CT	• CT with contrast of previously involved body areas every 2 cycles
Seminoma with residual mass >3 cm after completion of chemotherapy	• PET/CT (CPT® 78815)
End of therapy evaluation for NSGCT post chemotherapy or post retroperitoneal lymph node dissection (RPLND)	• CT Abdomen and Pelvis with contrast (CPT® 74177)
Recurrence suspected, including increased tumor markers	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • Ultrasound (CPT® 76856 or CPT® 76857) of the remaining gonad if applicable
Unexplained pulmonary symptoms despite a negative chest x-ray, or new findings on chest x-ray	• CT Chest with contrast (CPT® 71260)
All others	• See: **Surveillance (ONC-20.3)**

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Testicular, Ovarian and Extragonadal Germ Cell Tumors – Surveillance (ONC-20.3)

ON.TO.0020.3.A
v2.0.2025

Indication	Imaging Study
Stage I Seminoma treated with orchiectomy alone (no radiotherapy or chemotherapy, also called active surveillance)	ONE of the following, once at 4-6 months and 12 months post-orchiectomy, then every 6 months for years 2 and 3, and then annually until year 5: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Stage I Seminoma treated with radiotherapy and/or chemotherapy	ONE of the following, annually for 3 years: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Stage IIA and non-bulky Stage IIB Seminomas treated with radiotherapy or chemotherapy	ONE of the following, once at 3 months, then once at 9-12 months after completion of therapy, then annually for 2 additional years: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)

Indication	Imaging Study
Bulky Stage IIB, IIC, and III Seminomas treated with chemotherapy	For individuals with ≤3 cm residual mass, ONE of the following every 4 months for 1 year, every 6 months for 1 year, and then annually for 2 additional years: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197) For individuals with >3 cm residual mass and negative PET scan, ONE of the following 6 and 12 months after completion of therapy, then annually until year 5: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197) For individuals with thoracic disease: • CT Chest with contrast (CPT® 71260) every 2 months for 1 year, then every 3 months for 1 year, then annually until year 5 after completion of therapy

Indication	Imaging Study
Stage IA Non-Seminomatous germ cell tumors treated with orchiectomy alone (without risk factors)	ONE of the following, every 4 months for one year, every 6 months in the second year, and then annually for years 3, 4, and 5: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Stage IB Non-Seminomatous germ cell tumors treated with orchiectomy alone (with risk factors – lymphovascular invasion or invasion into spermatic cord/ scrotum)	ONE of the following, every 4 months for years 1 and 2, then every 6 months for year 3, and then annually in years 4 and 5: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Stage IA/IB Non-Seminomatous germ cell tumors treated with chemotherapy and/or primary RPLND	ONE of the following, annually for 2 years: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)

Indication	Imaging Study
Stage II-III Non-Seminomatous germ cell tumors with complete response to chemotherapy +/- post-chemotherapy RPLND	ONE of the following, every 4 months in year 1, every 6 months in year 2, and then annually in year 3: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197) For individuals with known thoracic disease or thoracic symptoms, every 4 months in year 1, every 6 months in year 2, then annually until year 4 after completion of therapy: • CT Chest with contrast (CPT® 71260)
Stage IIA or IIB Non-Seminomatous germ cell tumors treated with post-primary RPLND and adjuvant chemotherapy	ONE of the following, once at 4 months after completion of RPLND: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Stage IIA or IIB Non-Seminomatous germ cell tumors treated with post-primary RPLND without adjuvant chemotherapy	ONE of the following, once at 3 to 4 months after completion of therapy and repeat annually for 1 additional year: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) • MRI Abdomen without and with contrast (CPT® 74183) • MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)

Indication	Imaging Study
All stages of ovarian dysgerminoma germ cell tumors	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 4 months for 1 year, every 6 months for 1 year and then annually for 3 years after completion of therapy
All ovarian non-dysgerminoma germ cell tumors: • Embryonal tumor • Endodermal sinus tumor • Immature teratoma • Non-gestational choriocarcinoma	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 4 months for 1 year, every 6 months for 1 year and then annually for 3 years after completion of therapy • CT Chest with contrast (CPT® 71260) every 4 months for 1 year and every 6 months for 1 year after completion of therapy
• Sex cord stromal tumors (male and female) • Mature teratoma	• No routine advanced imaging indicated
Extragonadal germ cell tumors	• CT of the involved region every 3 months for one year and every 6 months for one year.

Evidence Discussion - ONC-20

Initial Evaluation

- American Urological Association guideline recommends scrotal ultrasound with Doppler should be obtained in patients with a unilateral or bilateral scrotal mass suspicious for neoplasm and that magnetic resonance imaging (MRI) should not be used in the initial evaluation and diagnosis of a testicular lesion suspected of being a neoplasm.
- Ultrasound requires no ionizing radiation and is readily available. Overall ultrasound is relatively quick and non-invasive modality to evaluate a testicular lesion. There are relatively few disadvantages of ultrasound for testicular lesions and primarily relate to sonographer experience.
- As advanced imaging modalities, computer tomography (CT) and magnetic resonance imaging (MRI) offer excellent 3-dimensional resolution. CT scan can require a significant dose of ionizing radiation but the speed of image acquisition reduces the potential for motion artifact. MRI yields better soft contrast resolution than CT and does not expose individuals to ionizing radiation, but due to longer image time is motion artifact-prone and may require sedation.

Seminoma:

- NCCN recommends CT of the abdomen and pelvis with contrast or MRI of the abdomen and pelvis with and without contrast, and a chest x-ray. Chest CT with contrast is recommended if there is a positive finding on abdomen CT or abnormal chest x-ray.

Nonseminoma:

- NCCN recommends CT of the abdomen, pelvis and chest with contrast or MRI of the abdomen and pelvis with and without contrast in addition to a chest CT with contrast.

Surveillance

Pure seminoma:

- Chest radiography is sufficient when compared with CT for follow-up of stage 1 pure seminoma and is recommended by NCCN. While CT is more sensitive than radiography for detecting recurrent disease in the chest, this added sensitivity is offset by lower specificity and a higher false positive detection rate for abnormalities that are not metastatic.
- Scrotal US does not have a role in the restaging of men with testicular cancer that has been established by orchiectomy, unless there is concern for contralateral tumor or equivocal clinical exam.
- CT Abdomen and Pelvis is the reference standard imaging test used for assessing the retroperitoneum. It is rapid, reproducible, and provides excellent imaging of the para-aortic and paracaval regions, but does expose patients to significant ionizing radiation.
- MRI of the abdomen and pelvis
    - MRI has comparable accuracy with CT for the detection of metastatic retroperitoneal lymph nodes and has the benefit of no ionizing radiation. The disadvantage of MRI is longer imaging time which can lead to motion artifact.
- CT of the abdomen and pelvis is the standard imaging test used for assessing the retroperitoneum for nodal metastasis but does expose the patient to high levels of ionizing radiation.
- NCCN guidelines recommend chest radiography for the surveillance of stage 1 nonseminomatous testicular cancer but chest CT with contrast is preferred in the presence of thoracic symptoms.
- MRI of the abdomen and pelvis shows comparable accuracy with CT in the detection of metastatic retroperitoneal lymph nodes and does not have high levels of ionizing radiation but is subject to motion artifact due to longer imaging time.
- Scrotal US does not have a role in the restaging of men with testicular cancer that has been established by orchiectomy, unless there is concern for contralateral tumor or equivocal clinical exam.

Nonseminoma:

- CT of the abdomen and pelvis is the standard imaging test used for assessing the retroperitoneum for nodal metastasis but does expose the patient to high levels of ionizing radiation.
- NCCN guidelines recommend chest radiography for the surveillance of stage 1 nonseminomatous testicular cancer but chest CT with contrast is preferred in the presence of thoracic symptoms.
- MRI of the abdomen and pelvis shows comparable accuracy with CT in the detection of metastatic retroperitoneal lymph nodes and does not have high levels of ionizing radiation but is subject to motion artifact due to longer imaging time.
- Scrotal US does not have a role in the restaging of men with testicular cancer that has been established by orchiectomy, unless there is concern for contralateral tumor or equivocal clinical exam.

References (ONC-20)

v2.0.2025

1. Gilligan T, Lin DW, Adra N, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – January 17, 2025. Testicular cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/testicular.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Testicular cancer V1.2025 – January 17, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Armstrong DK, Alvarez RD, Backes FJ, et. al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – July 15, 2024. Ovarian cancer, including fallopian tube cancer and primary peritoneal cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Ovarian cancer V3.2024 – July 15, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines ™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Salani R, Backes FJ, Fung MF, et al. Post treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations. *Am J Obstet Gynecol*. 2011;204(6):466-478. doi:10.1016/j.ajog.2011.03.008.
4. Gershenson DM. Management of ovarian germ cell tumors. *J Clin Oncol*. 2007;25(20):2938-2943. doi:10.1200/JCO.2007.10.8738.
5. Colombo N, Parma G, Zanagnolo V, Insinga A. Management of ovarian stromal cell tumors. *J Clin Oncol*. 2007;25(20):2944-2951. doi:10.1200/JCO.2007.11.1005.
6. Cadron I, Leunen K, Van Gorp T, Amant F, Neven P, Vergote I. Management of Borderline Ovarian Neoplasms. *J Clin Oncol*. 2007;25(20):2928-2937. doi:10.1200/JCO/2007.10.8076.
7. del Carmen MG, Birrer M, Schorge JO. Carcinosarcoma of the ovary: a review of the literature. *Gynecol Oncol*. 2012;125(1):271-277. Doi:10.1016/j.ygyno.2011.12.418.
8. Kollmannsberger C, Tandstad T, Bedard PL, et al. Patterns of relapse in patients with clinical stage I testicular cancer managed with active surveillance. *J Clin Oncol*. 2015;33(1):51-57. doi:10.1200/JCO.2014.56.2116.
9. Oechsle K, Hartmann M, Brenner W, et al. [18F]Fluorodeoxyglucose positron emission tomography in nonseminomatous germ cell tumors after chemotherapy: the German multicenter positron emission tomography study group. *J Clin Oncol*. 2008;26(36):5930-5935. doi:10.1200/JCO.2008.17.1157.
10. Daugard G, Gundgaard MG, Mortensen MS, et al. Surveillance for stage I non seminoma testicular cancer: outcomes and long term follow-up in a population based cohort. *J. Clin Oncol*. 2014;32(34):3817-3823. doi:10.1200/JCO.2013.53.5831.
11. Zuniga A, Kakiashvilli D, Jewett MA. Surveillance in stage I nonseminomatous germ cell tumours of the testis. *BJU Int*. 2009;104:1351-1356. doi:10.1111/j.1464-410X.2009.08858.x.
12. Stephenson A, Bass EB, Bixler BR, et al. Diagnosis and treatment of early-stage testicular cancer: AUA Guideline amendment 2023. *J Urol*. 2023;10.1097/JU.0000000000003694. doi:10.1097/JU.0000000000003694.
13. Harvey ML, Geldart TR, Duell R, Mead GM, Tung K. Routine computerised tomographic scans of the thorax in surveillance of stage I testicular non-seminomatous germ-cell cancer--a necessary risk? *Ann Oncol*. 2002;13:237-42.
14. Horan G, Rafique A, Robson J, Dixon AK, Williams MV. CT of the chest can hinder the management of seminoma of the testis; it detects irrelevant abnormalities. *Br J Cancer*. 2007;96:882-5.
15. Meyer CA, Conces DJ. Imaging of intrathoracic metastases of nonseminomatous germ cell tumors. *Chest Surg Clin N Am*. 2002;12:717-38.
16. Horan G, Rafique A, Robson J, Dixon AK, Williams MV. CT of the chest can hinder the management of seminoma of the testis; it detects irrelevant abnormalities. *Br J Cancer*. 2007;96:882-5.
17. Laukka M, Mannisto S, Beule A, Kouri M, Blomqvist C. Comparison between CT and MRI in detection of metastasis of the retroperitoneum in testicular germ cell tumors: a prospective trial. *Acta Oncol*. 2020;59:660-65.

Ovarian Cancer (ONC-21)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Ovarian Cancer – General Considerations (ONC-21.0)

ON.OC.0021.0.A

v2.0.2025

- Ovarian cancers include: epithelial ovarian cancers, ovarian cancers of low malignant potential and mixed Müllerian tumors, primary peritoneal and fallopian tube cancers.
  - There are five main types of epithelial ovarian cancers:
    - High-grade serous carcinoma (HGSC) (70%)
    - Endometrioid carcinoma (EC) (10%)
    - Clear cell carcinoma (CCC) (10%)
    - Mucinous carcinoma (MC) (3%)
    - Low-grade serous carcinoma (LGSC) (<5%)
- Borderline tumors (formerly referred to as tumors of low malignant potential) usually have some feature of carcinoma when they recur.
- Fallopian tube and primary peritoneal are usually serous carcinoma.
- Germ cell tumors and sex cord stromal tumors (granulosa cell tumors), are imaged according to **Testicular, Ovarian and Extragonadal Germ Cell Cancer (ONC-20)**.

Screening for Ovarian Cancer (ONC-21.1)

ON.OC.0021.1.C

v2.0.2025

- The use of advanced imaging in ovarian cancer screening is not recommended by the USPSTF, and is considered not medically necessary.

Ovarian Cancer – Suspected/Diagnosis (ONC-21.2)

ON.OC.0021.2.C
v2.0.2025

Indication	Imaging/Lab Study
• Pelvic signs or symptoms • Palpable pelvic mass	• Transvaginal (TV) ultrasound (CPT® 76830) and/or Pelvic ultrasound (CPT® 76856 or CPT® 76857)
• Ultrasound shows complex and/or solid adnexal mass suspicious for ovarian malignancy or • Any suspicious signs/symptoms for ovarian malignancy (ascites, abdominal symptoms such as distension or tenderness, elevated CA-125, elevated LFTs, obstructive uropathy*	ANY of the following: • MRI Pelvis without and with contrast (CPT® 72197) ◦ MRI Pelvis without contrast (CPT® 72195) if contrast is contraindicated • CT Abdomen and Pelvis with contrast (CPT® 74177) ◦ CT Abdomen and Pelvis without and with contrast (CT Urogram – CPT® 74178) only for symptoms of obstructive uropathy*

Evidence Discussion

Since staging of ovarian cancer is primarily surgical, routine imaging is not indicated pre-operatively. If there is a question about the pelvic mass evaluation by ultrasound, transvaginal or pelvic ultrasound using O-RADS or IOTA is indicated to clarify risk before surgery.

Ovarian Cancer – Initial Work-Up/Staging (ONC-21.3)

ON.OC.0021.3.A
v2.0.2025

Indication	Imaging Study
Clinical stage II disease or higher	• CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Chest with contrast (CPT® 71260) for: ◦ Abnormal signs/symptoms of pulmonary disease ◦ Abnormal chest x-ray
ANY of the following: • Primary peritoneal disease with biopsy-proven malignancy consistent with ovarian carcinoma • Elevated tumor markers with negative or inconclusive CT imaging	• PET/CT (CPT® 78815)

Evidence Discussion

Once surgical staging is completed, CT Chest, Abdomen, and Pelvis would be needed for stage II or higher. Only if surgical proof of primary peritoneal disease or inconclusive CT findings would PET/CT be needed.

Ovarian Cancer – Restaging/Recurrence (ONC-21.4)

ON.OC.0021.4.A
v2.0.2025

Indication	Imaging Study
Completely resected or definitively treated with chemotherapy and normal(ized) tumor markers	• No advanced imaging needed
ANY of the following: • Unresected disease • Unknown preoperative markers • Difficult or abnormal examination • Elevated LFTs • Elevated tumor markers (CA-125, inhibin) • Signs or symptoms of recurrence	• CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Chest with contrast (CPT® 71260) for ANY of the following: ◦ Known prior thoracic disease ◦ New or worsening pulmonary symptoms ◦ New or worsening chest x-ray findings ◦ Rising tumor markers (CA-125, inhibin)
Monitoring response to treatment (every 2 cycles, or ~every 6 to 8 weeks)	• CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Chest with contrast (CPT® 71260) for ANY of the following: ◦ Known prior thoracic disease ◦ New or worsening pulmonary symptoms ◦ New or worsening chest x-ray findings
• CT negative or inconclusive and CA-125 continues to rise or elevated LFTs • Conventional imaging failed to demonstrate tumor or if persistent radiographic mass with rising tumor markers	• PET/CT (CPT® 78815)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

If disease was completely resected and normal CA-125 or other markers normal, then no imaging is needed. If there any question or signs or symptoms of recurrence then CT is appropriate with chest included if there are symptoms there or rising tumor markers. To monitor response to treatment CT is appropriate every two cycles. PET is only indicated if there is a question on CT.

Ovarian Cancer – Surveillance (ONC-21.5)

ON.OC.0021.5.A
v2.0.2025

Indication	Imaging Study
Stages I-III	• Advanced imaging is not routinely indicated for surveillance
Measurable metastatic disease on maintenance therapy or being monitored off therapy	Every 3 months for up to 5 years after completion of active treatment: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved body areas

Evidence Discussion

Stages I to III there is no need for advanced imaging if there are no signs or symptoms. If on maintenance or if there is measurable disease present, CT of the areas involved every three months for up to 5 years.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-21)

v2.0.2025

1. Armstrong DK, Alvarex RD, Backes FJ, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – July 15, 2024. Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer V3.2024 – July 15, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Daly MB, Pal T, AlHilli Z, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version V3.2024 – February 12, 2024. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic available at: https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Ovarian cancer V3.2024 – February 12, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Moyer VA, U.S. Preventive Services Task Force. Screening for ovarian cancer: U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med*. 2012;157(12):900-904. doi:10.7326/0003-4819-157-11-201212040-00539.
4. Cadron I, Leunen K, Van Gorp T, Amant F, Neven P, Vergote I. Management of borderline ovarian neoplasms. *J Clin Onco*l. 2007;25(20):2928-2937. doi:10.1200/JCO.2007.10.8076.
5. ACR Appropriateness Criteria. *Ovarian cancer screening*. Rev. 2017.
6. Rosenthal AN, Fraser LSM, Phipott S. Evidence of stage shift in women diagnosed with ovarian cancer during phase II of the United Kingdom familial ovarian cancer screening study. *J Clin Oncol*. 2017;35(13):13:1411-1420. doi:10.1200/JCO.2016.69.9330.
7. Shinagare AB, O'Neill AC, Cheng S, et al. Advanced high-grade serous ovarian cancer: frequency and timing of thoracic metastases and the implications for chest imaging follow-up. *Radiology*. 2015;277(3):733-740. doi:10.1148/radiol.2015142467.
8. Musto A, Grassetto G, Marzola MC, et al. Management of epithelial ovarian cancer from diagnosis to restaging: an overview of the role of imaging techniques with particular regard to the contribution of 18F-FDG PET/CT. *Nucl Med Commun*. 2014;35(6):588-597. doi:10.1097/MNM.0000000000000091.
9. Fischerova D, Burgetova A. Imaging techniques for the evaluation of ovarian cancer. *Best Pract Res Clin Obstet Gynaecol*. 2014;28(5):697-720. doi:10.1016/j.bpobgyn.2014.04.006.
10. Andriotti, RT, Timmerman, D, Strachowski, LM, et al, O-RADS US risk stratification and management system a concensus guideline from ACR ovarian-adnexal reporting and data system committee. *Radiology*. 2020; 294(1):168-185.
11. Lu KH, Skales S, Hernandez MA, et al. A 2 Stage ovarian cancer screening strategy using the Risk of Ovarian Cancer Algorithm (ROCA) identifies early-stage incident cancers and demonstrates high positive predictive values. *Cancer*. 2013;119(19) 3454-3461.

Uterine Cancer (ONC-22)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Uterine Cancer – General Considerations (ONC-22.0)

ON.UC.0022.0.C

v2.0.2025

- Gestational trophoblastic neoplasia (GTN) – see: **Molar Pregnancy and Gestational Trophoblastic Neoplasia (GTN) (PV-16.1)** in the Pelvic Imaging Guidelines.
- Imaging not routinely indicated pre-operatively for laparoscopic/minimally invasive surgery unless initial staging criteria are met. Pelvic and para-aortic lymphadenectomy can still be performed.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Uterine Cancer – Suspected/Diagnosis (ONC-22.1)

ON.UC.0022.1.A

v2.0.2025

- See: **Abnormal Uterine Bleeding (PV-2.1)** in the Pelvic Imaging Guidelines for evaluation of suspected uterine malignancies.

Uterine Cancer – Initial Work-Up/Staging (ONC-22.2)

ON.UC.0022.2.A
v2.0.2025

Indication	Imaging Study
ANY of the following: • Extra-uterine disease suspected • To assess local extent of tumor prior to fertility-sparing surgery for well-differentiated Stage IA (grade 1) uterine cancer • Poor surgical candidate (due to medical comorbidities) considering medical therapy	• MRI Pelvis without and with contrast (CPT® 72197) • Transvaginal ultrasound (CPT® 76830) if MRI is contraindicated • Chest x-ray ◦ CT Chest with contrast (CPT® 71260) for: ▪ New or worsening pulmonary symptoms ▪ New or worsening chest x-ray findings In addition, for surgical staging: • Lymph system imaging (lymphoscintigraphy, CPT® 78195) ◦ SPECT/CT (CPT® 78830) if requested
ANY of the following: • Abdominal symptoms or abnormal examination findings • Elevated LFTs • Other imaging studies suggest liver involvement	ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160)

Indication	Imaging Study
ANY of the following high-risk histologies: • Papillary serous • Clear cell • High-grade/poorly differentiated endometrioid carcinoma • Uterine sarcomas: ◦ Carcinosarcoma ◦ Soft tissue sarcoma of the uterus ◦ Leiomyosarcoma ◦ Rhabdomyosarcoma ◦ Undifferentiated sarcoma ◦ Endometrial stromal sarcoma	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • Lymph system imaging (lymphoscintigraphy, CPT® 78195) ◦ SPECT/CT (CPT® 78830) if requested
Tumors detected incidentally or incompletely staged surgically ***and*** ANY of the following high-risk features: • Myoinvasion >50% • Cervical stromal involvement • Lymphovascular invasion • Tumor >2 cm	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast
Inconclusive findings on conventional imaging	• PET/CT scan (CPT® 78815)

Evidence Discussion

- The National Comprehensive Cancer Network guidelines (NCCN) for non-fertility sparing treatment recommend considering chest imaging with chest x-ray. If an abnormality is seen on chest x-ray, or if there are symptoms of chest involvement, then chest CT may be performed. Both NCCN and the American College of Radiology note that MRI of the pelvis is the preferred imaging modality when pretreatment assessment of local tumor extent is indicated due to suspected extra-uterine disease or prior to fertility sparing treatment.
- Transvaginal ultrasound can be done if MRI is contraindicated or unavailable.
- If distant metastatic disease is suspected based on abnormal physical examination findings, or for high-grade endometrioid carcinoma, serous, clear cell or

carcinosarcoma, cross-sectional imaging with CT Chest and CT Abdomen and Pelvis can be considered.

- For incidental findings of endometrial cancer after hysterectomy or incompletely surgically staged with uterine risk factors (myoinvasion of over 50%, cervical stromal involvement or tumor larger than 2 cm), consideration should be given to CT Chest/ Abdomen and Pelvis to evaluate for distant metastatic disease per NCCN guidelines.
- FDG-PET/CT in select patients if metastases is suspected and other cross-sectional imaging is inconclusive.
- Although endometrial cancer is surgically staged, preoperative imaging can help tailor surgery and medical treatment in cases as outlined by NCCN and ACR. MRI or transvaginal ultrasound is valuable to assess local tumor extent. CT and/or PET-CT is valuable to assess lymph node metastases and distant spread. Preoperative imaging may identify deep myometrial invasion, cervical stromal involvement and metastatic disease. Although these imaging methods may provide information about likely tumor stage, the reported accuracies for preoperative staging of endometrial cancer by conventional imaging have not yet been good enough to replace surgical staging.
- MRI Pelvis has long been established as a valuable imaging method in the preoperative staging of endometrial cancer because it allows the most accurate evaluation of the extent of the pelvis tumor. A meta-analysis showed that the efficacy of contrast-enhanced MRI is significantly better than that of non-contrast MRI and US, and tended toward better results than CT, in evaluating the depth of myometrial invasion in patients with EC.
- Transvaginal ultrasound may be used if MRI is contraindicated. A study found this imaging modality to have a 79.5% sensitivity and an 89.6% specificity for detecting deep myometrial invasion. However, MRI showed greater accuracy than ultrasound and ultrasound is limited in the setting of concomitant benign disease.
- CT Chest, Abdomen and Pelvis may be used for detection of lymph node metastases, if distant metastatic disease is suspected as per NCCN and ACR listed above.
- FDG-PET/CT may be indicated if distant metastatic disease is suspected and CT scans are inconclusive. A meta-analysis reported that the overall pooled sensitivity, specificity, and accuracy of using FDG-PET/CT for detection of lymph node metastasis in EC was 72.0%, 94.0%, and 88.0%, respectively.

Uterine Cancer – Restaging/Recurrence (ONC-22.3)

ON.UC.0022.3.A
v2.0.2025

Indication	Imaging Study
• Unresected disease • Medically inoperable disease • Incomplete surgical staging • Difficult or abnormal examination • Elevated LFTs or rising tumor markers • Signs or symptoms of recurrence	• CT Chest (CPT® 71260) **and** • CT Abdomen and Pelvis with contrast (CPT® 74177)
Monitoring response to chemotherapy (every 2 cycles, ~every 6-8 weeks) for: • Unresected primary disease • Metastatic disease	• CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Chest with contrast (CPT® 71260) for: ◦ Known prior thoracic disease ◦ New or worsening pulmonary symptoms ◦ New or worsening chest x-ray findings
Any of the following: • After fertility sparing treatment • Inconclusive CT scan findings	• MRI Pelvis without and with contrast (CPT® 72197)
• Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

- Recurrence rates for low- or intermediate-risk patients with endometrial cancer are infrequent. A recent review of post-treatment surveillance and diagnosis of recurrence in women with gynecologic cancers sponsored by the Society of Gynecologic Oncology recommends that radiologic evaluation be used only to investigate suspicion of recurrent disease because of symptoms or physical exam and not for routine surveillance after treatment.
- CT Chest, Abdomen and Pelvis is useful for suspected recurrence of disease based on abnormal physical examination findings and/or new pelvis, abdominal or pulmonary symptoms. A study reported that 45 asymptomatic women had routine

CT scans, and recurrence was diagnosed by CT in only 2 (4.4%), whereas 37 symptomatic women had CT scans for suspicion of recurrence, and it was confirmed by CT in 17 (46%).

- MRI of the pelvis may be done after fertility sparing treatment for persistent endometrial carcinoma. In patients with persistent endometrial carcinoma after 6 months of failed hormonal therapy, pelvic MRI to exclude myoinvasion and nodal/ovarian metastasis is recommended before continuing fertility-sparing therapy.
- FDG-PET/CT may give further clinically applicable information in cases where conventional imaging is inconclusive. As per the prior meta-analysis, the overall pooled sensitivity, specificity, and accuracy of using FDG-PET/CT for detection of lymph node metastasis in EC was 72.0%, 94.0%, and 88.0%, respectively.

Uterine Cancer – Surveillance (ONC-22.4)

ON.UC.0022.4.A
v2.0.2025

Indication	Imaging Study
Stage I-III of uterine carcinoma	Advanced imaging is not routinely indicated for surveillance
Measurable metastatic disease on maintenance therapy or being monitored off therapy	Every 3 months for up to 5 years after completion of definitive treatment: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved body areas
All stages of uterine sarcoma: • Soft tissue sarcoma of the uterus • Leiomyosarcoma • Adenosarcoma • Carcinosarcoma • Rhabdomyosarcoma • Undifferentiated sarcoma • Endometrial stromal sarcoma	CT Chest (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177) every 3 months for 2 years, every 6 months for 3 years, and then every 1-2 years until year 10

Evidence Discussion

- Advanced imaging is not routinely indicated for surveillance for non-metastatic, asymptomatic disease in endometrial cancer. A recent review of post-treatment surveillance and diagnosis of recurrence in women with gynecologic cancers sponsored by the Society of Gynecologic Oncology recommends that radiologic evaluation be used only to investigate suspicion of recurrent disease because of symptoms or physical exam and not for routine surveillance after treatment.
- Measurable metastatic disease can be followed with CT Abdomen and Pelvis and CT of previously involved body areas every 3 months for 5 years after treatment.
- All stages of uterine sarcoma, CT Chest, Abdomen and Pelvis every 3 months for 2 years, every 6 months for 3 years and then every 1-2 years until year 10.

Gestational Trophoblastic Neoplasia (GTN) (ONC-22.5)

ON.UC.0022.5.A
v2.0.2025

- The most common form of gestational trophoblastic disease (GTD) is hydatidiform mole (HM), a benign form, also known as molar pregnancy.
  - See: **Molar Pregnancy and GTN (PV-16.1)**
- Gestational trophoblastic neoplastic disorders including a malignant form of GTD, and can present as invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT), or epithelioid trophoblastic tumor (ETT). GTN cells are malignant and can metastasize to other organs such as lungs, brain, bone and vagina. These tumors have a high likelihood of cure and treatment with methotrexate usually allows for fertility preservation.
- Surveillance is generally with serial monitoring of HCG levels, and advanced imaging is reserved for high-risk histologies where HCG levels may not be a reliable marker.

Indication	Imaging Study
Initial staging	• CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
EITHER of the following: • Pulmonary metastases noted on CT scan • Signs/symptoms of CNS involvement	• MRI Brain without and with contrast (CPT® 70553)
EITHER of the following: • Monitoring response to systemic therapy (every 2 cycles, i.e., 6-8 weeks) • Suspected progression	• CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)

Indication	Imaging Study
Surveillance for any of the following high risk histologies: • Placental site trophoblastic tumor (PSTT) • Epithelioid trophoblastic tumor (ETT)	Annually for 2 years: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)

Evidence Discussion

- The most common form of GTD is hydatidiform mole (HM), also known as molar pregnancy. HMs are considered a benign, premalignant disease.
- Initial determination of suspected HM is often made based on ultrasound findings in combination with clinical symptoms and hCG levels.
- Gestational trophoblastic neoplastic disorders include a malignant form of GTD, and can present as invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT), or epithelioid trophoblastic tumor (ETT). GTN cells are malignant and can metastasize to other organs such as lungs, brain, bone and vagina.
- Initial staging of GTN includes a CT of chest and CT of abdomen and pelvis.
- If pulmonary metastases are noted on CT chest or for signs or symptoms of central nervous system (CNS) involvement, MRI brain is indicated to evaluate for metastatic disease. Rates of CNS metastases are low with post-molar GTN, but approximately 20% of patients with choriocarcinoma have CNS involvement.
- For monitoring response to treatment or for suspected progression CT Chest, Abdomen and Pelvis is performed.
- Post-treatment surveillance in general is done with monitoring of hCG levels in patients with post-molar GTN or choriocarcinoma, where hCG is a reliable tumor marker.
- Surveillance imaging for placental site or epithelioid trophoblastic tumor can be done with CT Chest, Abdomen, and Pelvis annually for 2 years. Post-treatment imaging is indicated for follow-up after treatment of PSTT and ETT, where hCG is a less reliable tumor marker.

References (ONC-22)

v2.0.2025

1. Abu-Rustum NR, Campos SM, Arend R, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – January 31, 2025. Uterine Neoplasms, available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Uterine Neoplasms 2.2025 – January 31, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Fader AN, Boruta D, Olawaiye AB, Gehrig PA. Updates on uterine papillary serous carcinoma. *Expert Rev Obstet Gynecol*. 2009;4(6):647-657. doi:10.1586/eog.09.49.
3. Boruta DM 2nd, Gehrig PA, Fader AN, Olawaiye AB. Management of women with uterine papillary serous cancer: A Society of Gynecologic Oncology (SGO) review. *Gynecol Oncol*. 2009;115(1):142-153. doi:10.1016/j.ygyno.2009.06.011.
4. Olawaiye AB, Boruta DM 2nd. Management of women with clear cell endometrial cancer: a Society of Gynecologic Oncology (SGO) review. *Gynecol Oncol*. 2009;113(2):277-283. doi:10.1016/j.ygyno.2009.02.003.
5. Salani R, Backes FJ, Fung MF et al. Post treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations. *Am J Obstet Gynecol.* 2011;204(6):466-478. doi:10.1016/j.ajog.2011.03.008.
6. Reinhold C, Ueno Y, Akin EA, et. al. ACR Appropriateness Criteria® - Evaluation and follow-up of endometrical cancer. Available at https://acsearch.acr.org/docs/69459/Narrative/. American College of Radiology. Accessed 7/29/2020.
7. Abu-Rustum NR, Campos SM, Arend R, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – January 31, 2025. Gestational Trophoblastic Neoplasia, available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™ for Gestational Trophoblastic Neoplasia, V2.2025 January 31, 2025. ®2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
8. Haldorsen IS, Salvesen HB. What is the best preoperative imaging for endometrial cancer? *Curr Oncol Rep*. 2016;18:25.

Cervical Cancer (ONC-23)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Cervical Cancer – General Considerations (ONC-23.0)

ON.CV.0023.0.A

v2.0.2025

- Primary histology for cervical cancer is squamous cell. Other, less common histologies are adenosquamous and adenocarcinoma. If biopsy is consistent with one of these less common histologies, it is necessary to clarify that tumor is not of primary uterine origin.
- If the primary histology is uterine in origin, follow imaging recommendations for uterine cancer, see: **Uterine Cancer (ONC-22)**.

Cervical Cancer – Suspected/Diagnosis (ONC-23.1)

ON.CV.0023.1.A
v2.0.2025

Indication	Imaging Study
All	• Biopsy should be performed prior to imaging

Cervical Cancer – Initial Work-Up/ Staging (ONC-23.2)

ON.CV.0023.2.A
v2.0.2025

Indication	Imaging Study
Stage IB1 or higher stages	ANY of the following combinations, not both: • PET/CT (CPT® 78815) or • CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)
Any size cervical cancer incidentally found in a hysterectomy specimen	• CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
ANY of the following: • To assess local extent of disease • To assess residual pelvic disease post-operatively • Inconclusive CT findings	• MRI Pelvis without and with contrast (CPT® 72197)
Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

- For clinical stage IB1 or higher, imaging with PET/CT or CT Chest, Abdomen and Pelvis is indicated as per American College of Radiology and National Comprehensive Cancer Network guidelines.

- Imaging is indicated to assess for lymphadenopathy and distant metastases.
- MRI pelvis is an appropriate test prior to fertility sparing treatment and to assess extent of local disease and residual disease post operatively.
- Definitive surgery with radical hysterectomy with lymph node sampling is the treatment of choice for smaller, locally confined invasive cervical cancers. Alternatively, trachelectomy can be considered for patients with stage IA2 or IB1 tumors who wish to maintain fertility.
- Meta-analyses have shown CT with intravenous (IV) contrast to have 43% to 55% sensitivity and 71% specificity for parametrial invasion, and 41% sensitivity and 92% specificity for bladder invasion In comparison, MRI demonstrated 71% specificity (95% confidence interval [CI], 62%-79%) and 91% sensitivity (95% CI, 88%-93%) for parametrial invasion, and 84% sensitivity (95% CI, 57%-95%) and 95% specificity (95% CI, 87%-98%) for bladder invasion.
- PET/CT can also be considered for inconclusive findings on conventional imaging.

Cervical Cancer – Restaging/Recurrence (ONC-23.3)

ON.CV.0023.3.A
v2.0.2025

Indication	Imaging Study
Stage I treated with definitive surgery	• See: **Cervical Cancer – Surveillance (ONC-23.4)**
Stage I-III treated with primary radiation therapy ± chemotherapy (no surgery)	ANY of the following, not both: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast OR, at least 12 weeks after completion of treatment: • PET/CT (CPT® 78815)
• After completion of primary non-surgical treatment (radiation therapy +/- chemotherapy) • Inconclusive findings on CT scan	MRI Pelvis without and with contrast (CPT® 72197)
Unresectable disease or metastatic disease on systemic treatment	Every 2 cycles of treatment (commonly every 6 to 8 weeks): • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of other involved or symptomatic areas
Suspected or biopsy proven recurrence	ANY of the following, not both: • PET/CT (CPT® 78815) OR • CT Chest (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Evidence Discussion

- If primary therapy was surgery, surveillance pathway should be utilized.
- If primary treatment was rad/chemo (no surgery), PET/CT or CT Chest/Abdomen/Pelvis can be utilized.
- Unresectable or metastatic disease on systemic treatment, CT Chest/Abdomen/Pelvis every 2 cycles is appropriate.
- With recurrence: PET/CT or CT Chest/Abdomen/Pelvis is recommended.
- Inconclusive CT can extend imaging to pelvic MRI for better soft tissue resolution.

Cervical Cancer – Surveillance (ONC-23.4)

ON.CV.0023.4.A
v2.0.2025

Indication	Imaging Study
Stage I disease treated with fertility sparing approach	• MRI Pelvis without and with contrast (CPT® 72197) at 6 months after surgery and then annually for 2-3 years
All individuals	• No routine advanced imaging needed in asymptomatic individuals.

Evidence Discussion

With stage I post fertility-sparing treatment, MRI Pelvis is supported by NCCN for surveillance imaging at 6 months post-operatively and then annually for 2-3 years.

References (ONC-23)

v2.0.2025

1. Abu-Rustum NR, Campos SM, Yashar CM, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – January 31, 2025. Cervical Cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Cervical Cancer V2.2025 – January 31, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Salani R, Backes FJ, Fung MF et al. Post treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations. Am J Obstet Gynecol. 2011;204(6):466-478. doi:10.1016/j.ajog.2011.03.008.
3. Zanagnolo V, Ming L, Gadducci A, et al. Surveillance procedures for patients with cervical carcinoma: a review of the literature. *Int J Gynecol Cancer.* 2009;19(3):194-201. doi:10.1111/IGC.0b013e3181a130f3.
4. Elit L, Fyles AW, Devries MC, et al. Follow-up for women after treatment for cervical cancer: A systematic review. *Gynecol Oncol.* 2009;114(3):528-535. doi:10.1016/j.ygyno.2009.06.001.
5. Schwarz JK, Siegel BA, Dehdashti F, Grigsby PW. Association of posttherapy positron emission tomography with tumor response and survival in cervical carcinoma. *JAMA*. 2007;298(19):2289-2295. doi:10.1001/jama.298.19.2289.
6. Meads C, Davenport C, Malysiak S, et al. Evaluating PET-CT in the detection and management of recurrent cervical cancer: systematic reviews of diagnostic accuracy and subjective elicitation. *BJOG*. 2014;121(4):398-407. doi:10.1111/1471-0528.12488.
7. Chu Y, Zheng A, Wang F, et al. Diagnostic value of 18F-FDG-PET or PET-CT in recurrent cervical cancer: a systematic review and meta-analysis. *Nucl Med Commun*. 2014; 35(2):144-150. doi:10.1097/MNM.0000000000000026.

Anal Cancer & Cancers of the External Genitalia (ONC-24)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Anal Carcinoma – General Considerations (ONC-24.0)

ON.AN.0024.0.A

v2.0.2025

- Most are squamous cell carcinomas, although some transitional and cloacogenic carcinomas are seen.
- Adenocarcinoma of the anal canal is managed as rectal cancer according to **Colorectal and Small Bowel Cancer (ONC-16)**.
- Squamous cell carcinoma of the perianal region (up to 5 cm radius from the anal verge) are imaged according to anal carcinoma guidelines.
- Bowen's disease and Paget's disease of the perianal and perigenital skin are considered non-invasive/in-situ conditions and do not routinely require advanced imaging. See: **Non-Melanoma Skin Cancers – Initial Work-up/Staging (ONC-5.6)**.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Anal Carcinoma – Suspected/Diagnosis (ONC-24.1)

ON.AN.0024.1.A
v2.0.2025

Indication	Imaging Study
All	• Advanced imaging prior to biopsy is not needed

Evidence Discussion

Advanced imaging prior to biopsy is not indicated as most tumors are staged clinically by direct examination and microscopic confirmation (biopsy).

Anal Carcinoma – Initial Work-up/ Staging (ONC-24.2)

ON.AN.0024.2.A
v2.0.2025

Indication	Imaging Study
All individuals	• CT Chest with contrast (CPT® 71260) and Any ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT Abdomen with contrast (CPT® 74160) and MRI Pelvis without and with contrast (CPT® 72197)
• Stage II-III Squamous Cell Carcinoma of the Anal Canal and no evidence of metastatic disease by conventional imaging • Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

All individuals undergo CT Chest with contrast and either CT Abdomen and Pelvis with contrast or CT Abdomen with contrast and MRI Pelvis with/without contrast. CT allows information on whether there is other organ involvement or possible disease spread. PET/CT is supported in stage II-III disease with no evidence of distant metastatic disease by conventional imaging or if conventional imaging is inconclusive. PET/CT is useful in assessing pelvic nodes and has been shown to change the nodal status/ TNM stage in up to 41% of patients. PET/CT does not replace a diagnostic CT in initial staging.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Anal Carcinoma – Restaging/Recurrence (ONC-24.3)

ON.AN.0024.3.A
v2.0.2025

Indication	Imaging Study
Stage I treated with complete surgical resection	• See: **Anal Carcinoma – Surveillance (ONC-24.4)** for surveillance guidelines
Stages I, II and III – post chemoradiation evaluation	Any ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Metastatic (stage IV) disease	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 2 cycles (generally 6 to 8 weeks) on treatment • CT Chest with contrast (CPT® 71260) if chest x-ray is abnormal or if symptoms of chest involvement
• Difficult or abnormal examination • Elevated LFTs • Signs or symptoms of recurrence • Biopsy proven recurrence	Preferably using same imaging studies as used in initial imaging: • CT Chest (CPT® 71260) with contrast and Any ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

Due to low risk of recurrence, stage I treated with complete surgical resection would follow surveillance guidelines that do not recommend any routine imaging. For stages I, II, and III treated with chemoradiation, CT Abdomen and Pelvis, or MRI Abdomen and Pelvis should be obtained upon completion of therapy. Stage IV disease on treatment should undergo CT Abdomen and Pelvis every 2 cycles with imaging of the chest if chest x-ray is abnormal or symptoms develop. If recurrence is suspected, CT Chest

with either CT Abdomen and Pelvis or MRI Abdomen and Pelvis should be performed. NCCN states that imaging for recurrence is preferred to mirror the same imaging studies as used in initial imaging (NCCN, 2025). PET/CT is indicated for inconclusive findings on conventional imaging.

Anal Carcinoma – Surveillance (ONC-24.4)

ON.AN.0024.4.A
v2.0.2025

Indication	Imaging Study
Stage I	• Advanced imaging is not routinely indicated for surveillance
• Stage II • Stage III • Local recurrence treated definitively	• CT Chest (CPT® 71260) with contrast or CT Chest without contrast (CPT® 71250) annually for 3 years • And ANY one of the following annually for three years: ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) ◦ MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Stage IV – measurable metastatic disease on maintenance treatment or being observed off treatment	Every 3 months for up to 5 years after completion of all treatment: • CT Chest (CPT® 71260) with contrast • CT Abdomen and Pelvis with contrast (CPT® 74177)

Evidence Discussion

For individuals with Stage II-III disease or had definitive treatment of a local recurrence, CT Chest with or without contrast plus either CT Abdomen and Pelvis with contrast or MRI Abdomen and Pelvis with/without contrast is indicated annually for 3 years. NCCN states that FDG PET/CT is not indicated for surveillance of local recurrence treated definitively (NCCN, 2025).

Cancers of External Genitalia – General Considerations (ONC-24.5)

ON.AN.0024.5.A

v2.0.2025

- These imaging guidelines are applicable for squamous cell carcinomas arising from the vulva, vagina, penis, urethra, and scrotum.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Cancers of External Genitalia – Initial Work-Up/Staging (ONC-24.6)

ON.AN.0024.6.A
v2.0.2025

Indication	Imaging Study
Clinical node negative vulvar cancer with ANY of the following: • Lesion >2 cm • Any size with stromal invasion >1 mm	• For planned sentinel lymph node evaluation: Lymph system imaging (lymphoscintigraphy, CPT® 78195) ◦ SPECT/CT (CPT® 78830) if requested
For stage II or higher vulvar or penile carcinoma	ONE of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) OR • CT Abdomen with contrast (CPT® 74160) and MRI Pelvis without and with contrast (CPT® 72197) • CT Chest with contrast (CPT® 71260) is indicated only for: ◦ Signs/symptoms suggestive of chest involvement ◦ Abnormal findings on chest x-ray
For any stage primary vaginal carcinoma	• CT Abdomen and Pelvis with contrast (CPT® 74177) OR • CT Abdomen with contrast (CPT® 74160) and MRI Pelvis without and with contrast (CPT® 72197) AND • CT Chest with contrast (CPT® 71260)
Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

Lymphoscintigraphy is appropriate since the disease spreads through skin layer and into the lymph system. FIGO surgical staging is used after superficial removal of the lesion. If it is a large (>2 cm) or stromal invasion (>1 mm) then spread is evaluated with CT.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Cancers of External Genitalia – Restaging/Recurrence (ONC-24.7)

ON.AN.0024.7.A
v2.0.2025

Indication	Imaging Study
• Difficult or abnormal examination • Elevated LFTs • Signs or symptoms of recurrence • Biopsy proven recurrence	• CT Chest with contrast (CPT® 71260) And ANY one of the following: • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast
Individuals receiving systemic treatment	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 2 cycles (generally 6 to 8 weeks) during treatment and at the end of planned chemotherapy treatment • CT Chest with contrast (CPT® 71260) if chest x-ray is abnormal or if symptoms of chest involvement
Vaginal primary tumor treated with upfront radiation therapy	• PET/CT (CPT® 78815) at least 12 weeks after completion of radiation therapy ◦ MRI Pelvis without and with contrast (CPT® 72197) is indicated if PET/CT not available (can be performed sooner than 12 weeks after completion of therapy) ◦ MRI Pelvis without and with contrast (CPT® 72197) is indicated for clarification of PET/CT findings
Inconclusive findings on conventional imaging	• PET/CT (CPT® 78815)

Evidence Discussion

Any recurrence is followed with CT of the areas involved. PET is only needed to clarify questions on conventional imaging.

Cancers of External Genitalia – Surveillance (ONC-24.8)

ON.AN.0024.8.A
v2.0.2025

Indication	Imaging Study
• All stages of vulvar and vaginal cancers	• Routine advanced imaging is not indicated for asymptomatic surveillance
• Penile Cancer: stage I-IIIA	• Routine advanced imaging is not indicated for asymptomatic surveillance
• Penile cancer: stages IIIB and higher	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 3 months for year 1, and then every 6 months for year 2, then no further routine advanced imaging indicated

Evidence Discussion

If no symptoms or findings on recent physical examination then advanced imaging is not indicated for all stages of vulvar and vaginal cancer. Stages IIIB and higher penile cancer may be followed with CT Abdomen and Pelvis.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

References (ONC-24)

v2.0.2025

1. Benson III AB, Venook AP, Adam M, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – January 17, 2025. Anal Carcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Anal Carcinoma V2.2025 – January 17, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Flaig TW, Spiess PE, Abern M. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – October 25, 2023. Penile Cancer, available at: https://www.nccn.org/professionals/physician_gls/ pdf/penile.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Penile Cancer V1.2024 – October 25, 2023. ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Abu-Rustum NR, Campos SM, Yashar CM. et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – May 1, 2024. Vulvar Cancer (Squamous Cell Carcinoma), available at: htt ps://www.nccn.org/professionals/physician_gls/pdf/vulvar.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Vulvar Cancer (Squamous Cell Carcinoma) V4.2024 – May 1, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
4. Bhuva NJ, Glynne-Jones R, Sonoda L, Wong WL, Harrison MK. To PET or not to PET? That is the question. Staging in anal cancer. *Ann Oncol*. 2012;23(8):2078-2082. doi:10.1093/annonc/mdr599.
5. Mistrangelo M, Pelosi E, Bellò M, et al. Role of positron emission tomography-computed tomography in the management of anal cancer. *Int J Radiat Oncol Biol Phys*. 2012;84(1):66-72. doi:10.1016/j.ijrobp.2011.10.048.
6. Jones M, Hruby G, Solomon M, Rutherford N, Martin J. The role of FDG-PET in the initial staging and response assessment of anal cancer: a systematic review and meta-analysis. *Ann Surg Oncol*. 2015;22(11):3574-3581. doi:10.1245/s10434-015-4391-9.
7. Moncrieff M, Pywell S, Snelling A, et. al. Effectiveness of SPECT/CT imaging for sentinel node biopsy staging of primary cutaneous melanoma and patient outcomes. *Ann Surg Oncol*. 2022;29(2):767-775. doi:10.1245/s10434-021-10911-4.
8. Quartuccio N, Garau LM, Arnone A, et. al. Comparsion of 99mTc-labeled colloid SPECT/CT and planar lymphoscintigraphy in sentinel lymph node detection in patients with melanoma: a meta-analysis. *J Clin Med.* 2020;9(6):1680. doi:10.3390/jcm9061680.
9. Bennie G, Vorster M, Buscombe J, Sathekge M. The added value of a single-photon emission computed tomography-computed in sentinel lymph node mapping in patients with breast cancer and malignant melanoma. *World J Nucl Med*. 2015;14(01):41-46. doi:10.4103/1450-1147.150543.
10. 10. Cummings BJ, Ajani JA, Swallow CJ. Cancer of the anal region. In: DeVita Jr. VT, Lawrence TS, Rosenberg SA, et al., eds. Cancer: Principles & Practice of Oncology, Eighth Edition. Philadelphia, PA: Lippincott, Williams & Wilkins; 2008.
11. 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.* 2015;22:3574-3581.
12. Kim KW, Schenagre AB, Krajewski KM, et al, Update on imaging of vulvar squamous cell carcinoma. *AJR Am. J. Roentgenol.* 2013;201:W147-157.
13. Del Pino M, Rodriquez-Carunchio L, Ordi J. Pathways of vulvar intraepithelial neoplasia and squamous cell carcinoma. *Histopathology*. 2013;62:161-175.
14. Abu-Rustum N, Gaillared S, Nekhlyudov L. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – August 8, 2024. Vaginal Cancer. available at https://www.nccn.org/professionals/physician_gls/pdf/vaginal.pdf: Referenced with permission from the NCCN Clinical Practice Guidelines in

Multiple Myeloma and Plasmacytomas (ONC-25)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Multiple Myeloma and Plasmacytomas – General Considerations (ONC-25.0)

ON.MM.0025.0.A

v2.0.2025

- Multiple myeloma (MM) is a neoplastic disorder characterized by the proliferation of a single clone of plasma cells derived from B cells which grows in the bone marrow and adjacent bone, producing skeletal destruction.
- Multiple myeloma group of disorders can be classified as below, which influence imaging modality of choice.

Condition	Monoclonal protein	Bone marrow plasma cells	CRAB criteria**
Solitary Plasmacytoma (biopsy proven tumor containing plasma cells)	<3 gm/dL	Absent	Absent
Monoclonal Gammopathy of Unknown Significance (MGUS)	<3 gm/dL	<10%	Absent
Smoldering Myeloma (SMM) (stage I MM or asymptomatic MM)	≥3 gm/dL	10% - 60%	Absent
Multiple Myeloma (MM)	≥3 gm/dL	≥10%	Present

**CRAB criteria = hypercalcemia, renal insufficiency, anemia, lytic bony lesions

- Diagnosis and monitoring of response to therapy is primarily with laboratory studies that include urine and serum monoclonal protein levels, serum free light chain levels, LDH and beta-2 microglobulin. Routine advanced imaging to monitor response to treatment is not indicated.
- Rarely, (<5%), an individual may have nonsecretory myeloma, which does not produce measurable M-protein. These individuals require imaging as primary method to monitor disease.
- Other conditions that may present with monoclonal gammopathy include:
  - POEMS syndrome: Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein and Skin Changes – may also have sclerotic bone lesions and Castleman's disease. See: **Multiple Myeloma and Plasmacytomas – Initial Work-up/Staging (ONC-25.2)** for imaging recommendations.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

- Waldenström's Macroglobulinemia: IgM monoclonal protein along with bone marrow infiltration of small lymphocytes. See: **Waldenström Macroglobulinemia or Lymphoplasmacytic Lymphoma (ONC-27.10)** for imaging recommendations.
- Systemic Light chain Amyloidosis: light chain monoclonal protein in serum or urine with clonal plasma cells in bone marrow, systemic involvement of the kidneys, liver, heart, gastrointestinal tract or peripheral nerves due to amyloid deposition. See: **Multiple Myeloma and Plasmacytomas – Initial Work-up/Staging (ONC-25.2)** and **Cardiac Amyloidosis (CD-3.8)**for imaging recommendations for systemic light chain amyloidosis.

Multiple Myeloma and Plasmacytomas – Suspected/Diagnosis (ONC-25.1)

ON.MM.0025.1.A
v2.0.2025

See: **Initial Work-up/Staging (ONC-25.2)**

Multiple Myeloma and Plasmacytomas – Initial Work-Up/Staging (ONC-25.2)

ON.MM.0025.2.A
v2.0.2025

Indication	Imaging Study
Either of the following: • Confirmed myeloma • Myeloma suspected based on any of the following: ◦ Abnormal skeletal survey or other imaging ◦ Abnormal myeloma labs ◦ Signs/symptoms of multiple myeloma	EITHER of the following: • Whole-body low-dose skeletal CT (CPT® 76497) or • Whole-body FDG PET/CT (CPT® 78816)
Inconclusive findings on whole-body low-dose skeletal CT	• PET/CT (CPT® 78815 or CPT® 78816)
To discern smoldering myeloma from active myeloma and whole-body CT or PET are negative or inconclusive	ONE of the following: • MRI Bone Marrow Blood Supply (CPT® 77084) • Whole-body MRI (CPT® 76498) • CT contrast as requested of a specific area to determine radiotherapy or surgical candidacy, or for suspected extra-osseous plasmacytoma
Initial work-up of suspected or known POEMS syndrome	• CT Chest with contrast (CPT® 71260) and • CT Abdomen and Pelvis with contrast (CPT® 74177) • Whole-body FDG PET/CT (CPT® 78816) for sclerotic bone lesions on other imaging

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Initial work-up of suspected or known systemic light chain amyloidosis	• Whole-body low dose skeletal CT (76497) OR Whole-body FDG PET/CT (78816) • Additional imaging, base on suspected organ involvement: ◦ CT Chest with contrast (CPT® 71260) ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) For additional imaging related to cardiac involvement, see: **Cardiac Amyloidosis (CD-3.8)**

Multiple Myeloma and Plasmacytomas – Restaging/Recurrence (ONC-25.3)

ON.MM.0025.3.A
v2.0.2025

Indication	Imaging Study
Extra-osseous plasmacytoma response to initial therapy	Repeat imaging with ONE of the following, whichever modality was used at initial diagnosis: • Whole-body low-dose skeletal CT scan (CPT® 76497) • Whole-body FDG PET/CT (CPT® 78816) • Whole-body MRI (CPT® 76498) • CT of any previously involved area, contrast as requested • MRI of any previously involved area, contrast as requested
Known spine involvement with new neurological signs/symptoms or worsening pain	• MRI Cervical (CPT® 72156), Thoracic (CPT® 72157), Lumbar spine (CPT® 72158) without and with contrast
Treatment response assessment • After completion of primary therapy • Non-secretory multiple myeloma • To determine therapy response with inconclusive labs	Repeat imaging with ONE of the modalities below, whichever was used at initial diagnosis: • Whole-body low-dose skeletal CT scan (CPT® 76497) • Whole-body FDG PET/CT (CPT® 78816)
CAR-T cell therapy	Once before treatment and once 30-60 days after completion of treatment: • PET/CT (CPT® 78815 or CPT® 78816)
ANY of the following: • Suspected relapse/recurrence • Suspected progression of MGUS or SMM to a more malignant form	ONE of the following: • Whole-body low-dose skeletal CT (CPT® 76497)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
ANY of the following: • Negative PET will allow change in management from active treatment to maintenance or surveillance. • Inconclusive findings on conventional imaging • Whole-body low-dose skeletal CT (CPT® 76497) is unfeasible and recurrence or progression is suspected	• PET/CT (CPT® 78815 or CPT® 78816)
To discern smoldering myeloma from active myeloma and whole-body CT or PET are negative or inconclusive	ONE of the following: • MRI Bone Marrow Blood Supply (CPT® 77084) • Whole-body MRI (CPT® 76498) • MRI without contrast, or MRI without and with contrast for any previously involved bony area or symptomatic area (including whole spine for spinal symptoms)
Stem cell transplant recipients	ONE of the following, once before transplant and once within 30-100 days after transplant: Imaging should use same modality as initial diagnosis. • Whole-body low-dose skeletal CT scan (CPT® 76497) • MRI Bone Marrow Blood Supply (CPT® 77084) • Whole-body MRI (CPT® 76498) • PET/CT (CPT® 78815 or CPT® 78816)

Multiple Myeloma and Plasmacytomas – Surveillance (ONC-25.4)

ON.MM.0025.4.A
v2.0.2025

Indication	Study
• Smoldering myeloma • Multiple myeloma	ANY ONE of the following (using same imaging modality used at diagnosis) annually: • Whole-body low-dose skeletal CT (CPT® 76497) • MRI Bone Marrow Blood Supply (CPT® 77084) • Whole-body MRI (CPT® 76498) • Whole-body FDG PET/CT (CPT® 78816)
Solitary plasmacytomas	Any ONE of the following (using same imaging modality used at diagnosis) annually for 5 years: • Whole-body low-dose skeletal CT (CPT® 76497) • MRI Bone Marrow Blood Supply (CPT® 77084) • Whole-body MRI (CPT® 76498) • Whole-body FDG PET/CT (CPT® 78816)

Evidence Discussion - ONC-25

- Bone disease is the most frequent feature of multiple myeloma (MM), occurring in approximately two thirds of patients at diagnosis and in nearly all patients during their disease. Imaging is a key part of the evaluation of all patients with suspected MM. And plays a very important role in the management of MM. It is necessary for detection of lytic bone lesions, which represent a marker of disease-related end-organ damage and are traditionally used to diagnose MM and to establish the need for immediate therapy.
- The detection of bone and bone marrow lesions is crucial in the investigation of multiple myeloma and often dictates the decision to start treatment. Cross-sectional imaging (i.e., CT, PET/CT, and MRI) is preferred because these modalities are more sensitive than plain radiographs for the detection of most skeletal lesions in MM.
- Whole body low dose CT (WBLDCT) can be used as a baseline assessment of bone involvement. CT is quick, convenient, relatively sensitive, and cost effective in this scenario. WBLDCT was introduced to detect osteolytic lesions in the whole skeleton, with high accuracy, no need for contrast agents, and twofold to threefold lower radiation dose exposure compared with standard CT. Low-dose whole-body CT

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

has increased sensitivity compared with conventional skeletal survey in the detection of bone disease, which can reveal information leading to changes in therapy and disease management that could prevent or delay the onset of clinically significant morbidity and mortality as a result of skeletal-related events.

- 18F-FDG PET/CT imaging could identify sites of extra medullary disease (EMD), which represent an unfavorable prognostic feature, and it helps to accurately differentiate between solitary plasmacytoma (SP) and MM, as well as to predict the risk of early progression from smoldering MM (SMM) to active disease. This is more sensitive than CT for the detection of extra medullary disease. The combination of functional imaging with positron emission tomography (PET) plus morphological assessment with CT makes this technique the most effective in identifying potential sites of EMD. The use of FGD PET/CT can also confirm a suspected diagnosis of solitary plasmacytoma and can distinguish between smoldering and active multiple myeloma. Thus, NCCN states that FDG PET/CT is the preferred imaging for initial diagnostic workup.
- Whole-body MRI can distinguish between smoldering and active multiple myeloma, acting as a problem-solving tool when PET/CT or whole-body CT is inconclusive.
- MRI is the elective imaging technique to assess the degree of BM PC infiltration, even before bone destruction is present, owing to its ability to visualize large volumes of BM. MRI is highly sensitive for the detection of bone and bone marrow focal lesions and predictive of progression. Unlike CT and PET/CT, MRI can detect focal bone lesions that are not yet lytic (i.e., without advanced cortical bone destruction). Up to half of patients without other evidence of end-organ damage with normal plain films may demonstrate tumor-related lesions on MRI.
- Whole body diffusion weighted MRI (DW-MRI) - Also known as MRI Bone Marrow Blood Supply CPT 77084 is a non-contrast study that covers from the vertex to the heels. Diffusion-weighted magnetic resonance imaging (DWI or DW-MRI) is the use of specific MRI sequences as well as software that generates images from the resulting data that uses the diffusion of water molecules to generate contrast in MR images. This produces images where the contrast between tissues is based on differences in the motion of water at a cellular level. As cellularity in marrow increases secondary either to disease or increased hematopoietic tissue, the amount of free water increases. The capability of WB DW#MRI to demonstrate both focal and diffuse marrow infiltration throughout the whole skeleton makes this extremely useful as a subjective tool for monitoring disease status and assessment of response.

References (ONC-25)

v2.0.2025

1. Kumar SK, Callander NS, Adekola K, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – September 17, 2024. Myeloma, available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Myeloma V1.2025 – September 17, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Hillengass J, Usmani S, Rajkumar SV, Durie BGM, Mateos M, Lonial S. International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders. The Lancet. 2019:20(6):PE302-E312. doi:10.1016/S1470-2045(19)30309-2.
3. Kyle RA, Remstein ED, Therneau TM, et al. Clinical course and prognosis of smoldering (asymptomatic) multiple myeloma. *N Engl J Med*. 2007;356:2582-2590. doi:10.1056/NEJMoa070389.
4. Dimopoulos M, Terpos E, Comenzo RL, et al. International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple myeloma. *Leukemia*. 2009;23(9):1545-1556. doi:10.1038/leu.2009.89.
5. ACR Committee on Drugs and Contrast Media. ACR Manual on Contrast Media, version 10.3. Reston, VA: American College of Radiology; 2018.
6. Mulligan ME, Badros AZ. PET/CR and MR imaging in myeloma. Skeletal Radiol. 2007;36(1):5-16. doi:10.1007/s00256-006-0184-3.
7. Dimopoulos MA, Hillengrass J, Usmani S, et al. Role of magnetic resonance imaging in the management of patients with multiple myeloma: a consensus statement. *J Clin Oncol.* 2015;33(6):657-664. doi:10.1200/JCO.2014.57.9961.
8. Dimopoulos M, Terpos E, Comenzo RL, et al. International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple myeloma. *Leukemia*. 2009;23(9):1545-1556. doi:10.1038.leu.2008.89.
9. Dammacco F, Rubini G, Ferrari C, Vacca A, Racanelli V. 18F-FDG PET/CT: a review of diagnostic and prognostic features in multiple myeloma and related disorders. *Clin Exp Med*. 2015;15(1):1-18. doi:10.1007/s10238-014-0308-3.
10. Ferraro R, Agarwal A, Martin-Macintosh EL, Peller PJ, Subramaniam RM. MR imaging and PET/CT in diagnosis and management of multiple myeloma. *Radiographics*. 2015;35(2):438-454. doi:10.1148/rg.352140112.
11. Rajkumar SV, Kumar S. Multiple myeloma: diagnosis and treatment. *Mayo Clin Proc*. 2016;91(1):101-119. doi:10.1016/j.mayocp.2015.11.007.
12. Westerland O, Amlani A, Kelly-Morland C, et. al. Comparison of the diagnostic performance and impact on management of 18F-FDG PET/CT and whole-body MRI in multiple myeloma. *Eur J Nucl ed Mol Imaging*. 2021. doi:10.1007/s00259-020-05182-2.
13. Terpos E, Berenson J, Raje N, Roodman GD. Management of bone disease in multiple myeloma. *Expert Rev Hematol.* 2014;7(1):113-125.
14. Zamagni E, Cavo M. The role of imaging techniques in the management of multiple myeloma. *Br J Haematol*. 2012;159(5):499-513.
15. Kyle RA, Rajkumar SV. Multiple myeloma. *N Engl J Med*. 2004;351(18):1860-1873.
16. Hillengass J et al: Whole-body computed tomography versus conventional skeletal survey in patients with multiple myeloma: a study of the International Myeloma Working Group. *Blood Cancer J*. 2017;7(8):e599. doi:10.1038/bcj.2017.78.
17. Pianko MJ, Terpos E, Roodman GD, et al. Whole-body low-dose computed tomography and advanced imaging techniques for multi ple myeloma bone disease. *Clin Cancer Res*. 2014;20(23):5888-5897.
18. Ippolito D, Besostri V, Bonaffini PA, Rossini F, Di Lelio A, Sironi S. Diagnostic value of whole body low-dose computed tomography (WBLDCT) in bone lesions detection in patients with multiple myeloma (MM). *Eur J Radiol*. 2013;82(12):2322-2327.

19. Lu YY, Chen JH, Lin WY, et al. FDG PET or PET/CT for detecting intramedullary and extra medullary lesions in multiple myeloma: a systematic review and meta-analysis. *Clin Nucl Med*. 2012; 37(9):833-837.
20. Cavo M, et al. Role of 18F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group. *Lancet Oncol.* 2017;18(4):e206-e217. doi:10.1016/S1470-2045(17)30189-4.
21. Walker R, Barlogie B, et al. Magnetic resonance imaging in multiple myeloma: diagnostic and clinical implications. *J Clin Oncol*. 2007;25(9):1121-8. doi:10.1200/JCO.2006.08.5803.
22. Ailawadhi S et al: Extent of disease burden determined with magnetic resonance imaging of the bone marrow is predictive of survival outcome in patients with multiple myeloma. *Cancer*. 2010;116(1):84-92. doi:10.1002/cncr.24704.
23. Messiou C, Kaiser M. Whole body diffusion weighted MRI--a new view of myeloma. *Br J Haematol*. 2015;171(1):29-37. doi:10.1111/bjh.13509.
24. Walker R, Barlogie B, Haessler J, et al. Magnetic resonance imaging in multiple myeloma: diagnostic and clinical implications. *J Clin Oncol*. 2007; 25:1121-1128.
25. Bartel TB, Haessler J, Brown TL, et al. F18-fluorodeoxyglucose positron emission tomography in the context of other imaging techniques and prognostic factors in multiple myeloma. *Blood*. 2009;114:2068-2076.
26. Zamagni E, Nanni C, Mancuso K, et al. PET/CT improves the definition of complete response and allows to detect otherwise unidentifiable skeletal progression in multiple myeloma. *Clin Cancer Res*. 2015;21:4384-4390.
27. Moreau P, Attal M, Caillot D, et al. Prospective evaluation of magnetic resonance imaging and [(18)F]fluorodeoxyglucose positron emission tomography-computed tomography at diagnosis and before maintenance therapy in symptomatic patients with multiple myeloma included in the IFM/DFCI 2009 trial: Results of the IMAJEM study. *J Clin Oncol*. 2017; 35:2911-2918.

Leukemias, Myelodysplasia and Myeloproliferative Neoplasms (ONC-26)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Leukemias, Myelodysplasia and Myeloproliferative Neoplasms – General Considerations (ONC-26.1)

ON.LM.0026.1.A

v2.0.2025

- Routine advanced imaging is not indicated for the evaluation and management of Hairy cell leukemia in the absence of specific localizing clinical symptoms.

Acute Leukemias (ONC-26.2)

ON.LM.0026.2.A

v2.0.2025

- Imaging indications for acute lymphoblastic leukemia in adult individuals are identical to those for pediatric individuals. See: **Acute Lymphoblastic Leukemia (ALL) (PEDONC-3.2)** in the Pediatric Oncology Imaging Guidelines.
- Imaging indications for acute myeloid leukemia in adult individuals are identical to those for pediatric individuals. See: **Acute Myeloid Leukemia (AML) (PEDONC-3.3)** in the Pediatric Oncology Imaging Guidelines.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Chronic Myeloid Leukemias, Myelodysplastic Syndrome and Myeloproliferative Disorders (ONC-26.3)

ON.LM.0026.3.A

v2.0.2025

- Routine advanced imaging is not indicated in the evaluation and management of chronic myeloid leukemias, myelodysplastic syndromes or myeloproliferative disorders in the absence of specific localizing clinical symptoms or clearance for hematopoietic stem cell transplantation.
- See: **Hematopoietic Stem Cell Transplantation (ONC-29)** for imaging guidelines related to transplant.
- For work-up of elevated blood counts, see: **Paraneoplastic Syndromes – General Considerations (ONC-30.3)**.

Evidence Discussion

It is not routinely recommended to utilize advanced imaging for chronic myeloid leukemia, myelodysplastic syndromes, and myeloproliferative disorders. In the interest of patient safety such that infectious and iatrogenic complications are assessed in a timely manner, these guidelines provide flexibility for approval of advanced imaging for specific localizing symptoms, and a separate guideline section for imaging related to stem cell transplantation.

Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL) (ONC-26.4)

ON.LM.0026.4.A
v2.0.2025

- PET imaging is not indicated in the evaluation of CLL/SLL with the exception of suspected Richter's transformation (see suspected transformation, below).
- CLL/SLL is monitored with serial laboratory studies. Routine advanced imaging is not indicated for monitoring treatment response or surveillance, except when initial studies reveal bulky disease involvement.
- Bulky disease is defined as lymph node mass >10 cm or spleen >6 cm below costal margin.

Indication	Imaging Study
Initial Staging/Diagnosis	• Advanced imaging is not routinely indicated for initial evaluation of asymptomatic individuals
For ANY of the following: • Bulky lymph node mass (>10 cm) • Splenomegaly >6 cm below costal margin • Presence of B symptoms • Progressive anemia and thrombocytopenia • Prior to planned systemic therapy	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Treatment Response	• For individuals with bulky nodal disease at diagnosis, CT with contrast of previously involved area(s) every 2 cycles of therapy • Routine imaging is not indicated for individuals without bulky nodal disease at diagnosis
End of Therapy Evaluation	• For individuals with bulky nodal disease at diagnosis, CT with contrast of previously involved area(s)

Indication	Imaging Study
Suspected Progression	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)
Suspected transformation (Richter's) from a low-grade lymphoma to a more aggressive type based on one or more of the following: • New B symptoms • Rapidly growing lymph nodes • Extranodal disease develops • Significant recent rise in LDH above normal range	• PET/CT (CPT® 78815 or CPT® 78816)
Surveillance	For individuals with bulky nodal disease at diagnosis, every 6 months for two years, then annually: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s) Routine imaging is not indicated for individuals without bulky nodal disease at diagnosis

Evidence Discussion

Suspected/Diagnosis (whenever applicable)

- Diagnosis is by flow cytometry and biopsy. Aligned with the NCCN no imaging is supported.

Initial staging

- These guidelines are aligned with the NCCN and do not support routine advanced imaging for CLL/SLL. However, in the interest of patient safety, to recognize mass effect as assess risk of tumor lysis syndrome prior to treatment, CT imaging of the

chest, abdomen and pelvis are supported. CT Neck may be added if neck symptoms, per the general oncology guidelines. (Shah 2024)

Restaging

- Routine imaging is not supported unless there is bulky nodal disease, as noted in 'initial staging' section. For Bulky nodal disease, treatment response imaging with CT is supported every 2 cycles or for signs and symptoms of disease progression.
- There is no data-supported benefit to routine monitoring with PET/CT, and PET/CT is significantly more radiation than CT alone. PET/CT is supported only for signs and symptoms of Richter's transformation to high grade lymphoma, where the diagnosis can be made without invasive procedure using this modality (Shah 2024).

Surveillance

- There is no benefit to advanced imaging for surveillance of patients without bulky nodal disease at diagnosis, and there is a risk of increased radiation exposure and invasive pursuit of incidental findings. In patients with bulky disease at diagnosis, flexibility is provided for surveillance imaging every 6months x 2 years to assess for mass effect or progression (Shah 2024).

References (ONC-26)

v2.0.2025

1. Wierda WG, Brown J, Abramson JS, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – March 26, 2024. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma V3.2024 – March 26, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Conte MJ, Bowen DA, Wiseman GA, et al. Use of positron emission tomography-computed tomography in the management of patients with chronic lymphocytic leukemia/small lymphocytic lymphoma. *Leuk Lymphoma*. 2014;55(9):2079-2084. doi:10.3109/10428194.2013.869801.
3. Mauro FR, Chauvie S, Paoloni F, et al. Diagnostic and prognostic role of PET/CT in patients with chronic lymphocytic leukemia and progressive disease. *Leukemia*. 2015;29(6):1360-1365. doi:10.1038/leu.2015.21.
4. Nabhan C, Rosen ST. Chronic lymphocytic leukemia: a clinical review. *JAMA*. 2014;312(21):2265-2276. doi:10.1001/jama.2014.14553.
5. Patnaik MM, Tefferi A. Chronic myelomonocytic leukemia: focus on clinical practice. *Mayo Clin Proc*. 2016;91(2):259-272. doi:10.1016/j.mayocp.2015.11.011.
6. American Society of Hematology. Choosing Wisely: Don't perform baseline or routine surveillance computed tomography (CT) scans in patients with asymptomatic, early-stage chronic lymphocytic leukemia (CLL). 2014. https://www.choosingwisely.org/clinician-lists/american-society-hematology-baseline-or-routine-surveillance-ct-scans-for-asymptomatic-early-stage-chronic-lymphocytic-leukemia/.
7. National Cancer Institute PDQ Cancer Information Summaries: adult treatment. Hairy cell Leukemia. PDQ® Adult Cancer Treatment Summaries - NCI.
8. Troussard X, Maître E, Paillassa J. Hairy cell leukemia 2024: Update on diagnosis, risk-stratification, and treatment-Annual updates in hematological malignancies. *Am J Hematol*. 2024;99(4):679-696. doi:10.1002/ajh.27240.
9. Inaba H, Teachey D, Annesley C , et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 6.2024 – July 19, 2024. Pediatric Acute Lymphoblastic Leukemia, available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Pediatric Acute Lymphoblastic Leukemia V6.2024 – July 19, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
10. Ranta S, Palomäki M, Levinsen M, et al. Role of neuroimaging in children with Acute Lymphoblastic Leukemia and central nervous system involvement at diagnosis. *Pediatr Blood Cancer*. 2016;64:64-70. doi:10.1002/pbc.26182/epdf.
11. Baden LR, Swaminathan S, Almyroudis N, et al. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prevention and Treatment of Cancer-Related Infections © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. To view the most recent and complete version of the guideline, go online to NCCN.org.
12. Ha AS, Chang EY, Bartolotta RJ, et. al. Expert Panel on Musculoskeletal Imaging. ACR Appropriateness Criteria® Osteonecrosis. Am Coll Radiol (ACR); Date of Origin: 2016. Revised: 2022.
13. Shah N, Bhatia R, Altman J, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2024 – December 5, 2023. Chronic Myeloid Leukemia, available at: https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Chronic Myeloid Leukemia V2.2024 – December 5, 2023. ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.

14. Baden LR, Swaminathan S, Almyroudis NG, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – April 30, 2024. Prevention and Treatment of Cancer-Related Infections, available at: https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Prevention and Treatment of Cancer-Related Infections V1.2024 – April 30, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.

Non-Hodgkin Lymphomas (ONC-27)

Guideline Page

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Non-Hodgkin Lymphomas – General Considerations (ONC-27.1)

ON.NH.0027.1.A
v2.0.2025

- Lymphoma is often suspected when individuals have any of the following:
  - Bulky lymphadenopathy (lymph node mass >10 cm in size), hepatomegaly or splenomegaly
  - The presence of systemic symptoms (fever, drenching night sweats or unintended weight loss of >10%, called “B symptoms”)
- Individuals with AIDS-related lymphoma should be imaged according to the primary lymphoma histology.
- See: **Castleman’s Disease (unicentric and multicentric) (ONC-31.11)** for guidelines covering Castleman’s disease.
- See: **Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) (ONC-26.4)** for guidelines covering Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL).

Indication	Imaging Study
• Biopsy proven lymphoma, or • Suspected lymphoma and any one of the following: ◦ Bulky lymphadenopathy (LN mass >10 cm) ◦ Hepatomegaly ◦ Splenomegaly ◦ B symptom: Unexplained fever, drenching night sweats, unintended weight loss >10% total body weight	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast ◦ MRI without and with contrast for individuals who cannot tolerate CT contrast due to allergy or impaired renal function
Signs or symptoms of disease involving the neck	• CT Neck with contrast (CPT® 70491)
Signs or symptoms suggesting CNS involvement with lymphoma.	• MRI Brain without and with contrast (CPT® 70553) • See: **CNS Lymphoma (also known as Microglioma) (ONC-2.7)**

Indication	Imaging Study
Known or suspected bone involvement with lymphoma	• MRI without and with contrast of symptomatic or previously involved bony areas ◦ Bone scan is inferior to MRI for evaluation of known or suspected bone involvement with lymphoma
Determine a more favorable site for biopsy when a relatively inaccessible site is contemplated	• PET/CT (CPT® 78815 or CPT® 78816) ◦ PET/CT is not indicated for all other indications prior to histological confirmation of lymphoma
CAR-T cell therapy	Once before treatment and once 30-60 days after completion of treatment: • PET/CT (CPT® 78815 and CPT® 78816)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Diffuse Large B Cell Lymphoma (DLBCL) (ONC-27.2)

ON.TO.0027.2.A
v2.0.2025

- Grey zone lymphomas, primary mediastinal B cell lymphomas, Grade 3 (high) follicular lymphoma, double-hit or triple-hit lymphomas, and primary cutaneous diffuse large B cell lymphoma should also be imaged according to these guidelines.

Indication	Imaging Study
Initial Staging/ Diagnosis	ONE of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) OR • CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177)
Treatment response for all stage I, and stage II without extensive mesenteric disease	ANY of the following may be approved: • CT with contrast of previously involved area(s) may be approved every 2 cycles (6-8 weeks) of therapy • PET/CT (CPT® 78815 or CPT® 78816) after 3-4 cycles of chemotherapy (in lieu of CT or for inconclusive CT)
Treatment response for stage II WITH extensive mesenteric disease, and stages III-IV	ANY of the following may be approved: • CT with contrast of previously involved area(s) may be approved every 2 cycles (6-8 weeks) of therapy • PET/CT (CPT® 78815 or CPT® 78816) after 2-4 cycles of chemotherapy (in lieu of CT or for inconclusive CT)
End of Chemotherapy and/or Radiation Therapy Evaluation	ANY or ALL of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) may be approved at the end of chemotherapy and again at the end of radiation • CT with contrast of previously involved area(s)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s) • PET/CT can be considered in rare circumstances (e.g., bone involvement).
Biopsy-proven recurrence	• PET/CT (CPT® 78815 or CPT® 78816)
CAR-T cell therapy	Once before treatment and once 30-60 days after completion of treatment: • PET/CT (CPT® 78815 or CPT® 78816)
Surveillance for ANY of the following: • All stages of DLBCL • Relapsed lymphoma • Primary mediastinal large B cell lymphoma • Primary cutaneous diffuse large B cell lymphoma	• Every 6 months for 2 years after completion of treatment: ◦ CT Chest with contrast (CPT® 71260) ◦ CT Abdomen and Pelvis with contrast (CPT® 74177) ◦ CT with contrast of previously involved area(s)

Evidence Discussion

Initial Staging

- These guidelines for initial staging align with NCCN and support either PET/CT or diagnostic CTs. Greater than 97 percent of DLBCL are FDG-avid, though it is not known to be more accurate than CT for DLBCL at initial staging. However, baseline PET may be useful for comparison, as end of treatment remission assessment with PET-CT is more accurate than CT alone in DLBCL (Barrington 2014).

Restaging

- CT is supported by NCCN every 2 cycles for restaging. PET/CT is supported by NCCN for interim restaging after 3-4 cycles of therapy and at the end of

chemotherapy and/or radiation for lower stage disease. For stage II with extensive mesenteric disease, stage III, and stage IV, NCCN supports PET/CT more frequently - after 2-4 cycles of therapy and at the end of therapy. PET/CT remains standard for remission assessment at end of therapy, where its accuracy is greater that CT alone for DLBCL (Barrington 2014, Zelenetz 2024). Documentation of residual tissue at end of therapy is useful for monitoring for relapse, and as such diagnostic, contrast enhanced CT is supported if requested in addition to PET at end of therapy (Barrington 2014, Zelenetz 2024).

- FDG avidity is prognostic for relapsed/refractory DLBCL and may have a role in patient selection for CAR-T therapy and to assess response, so is supported as a baseline before CAR-T and once 30-60 days after completion, to assess response and identify patients who may be candidates for further salvage therapy (Barrington 2014, Zelenetz 2024).

Surveillance

- The false-positive rate with PET scans for surveillance in various studies is 16-20%, potentially leading to unnecessary investigations, radiation exposure, biopsies, expense, and patient anxiety (Cheson 2014, Lynch 2014). Several small studies have failed to note an improvement in relapse detection with CT over clinical observation in DLBCL, however, there is no definitive standard for surveillance imaging with CT (Thompson 2014, ElGalaly 2015). The majority of relapses occur in the first 2 years, and the NCCN supports CT imaging of involved areas and chest, abdomen and pelvis every 6 months for the first two year. In the interest of patient and provider centricity, these guidelines align with the NCCN with respect to surveillance in DLBCL.

Follicular Lymphoma (ONC-27.3)

ON.NH.0027.3.A
v2.0.2025

- This section applies to follicular lymphomas with WHO grade of 1 (low) or 2 (intermediate) and primary cutaneous follicle center lymphoma. Grade 3 (high) follicular lymphomas should be imaged according to guidelines found in: **Diffuse Large B Cell Lymphoma (DLBCL) (ONC-27.2)**.

Indication	Imaging Study
Initial Staging/Diagnosis	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
For ANY of the following: • If radiation therapy is being considered for stage I or II disease • If systemic therapy is planned • Pediatric-type follicular lymphoma in adults	• PET/CT (CPT® 78815 or CPT® 78816)
Treatment Response	• CT with contrast of previously involved area(s) every 2 cycles of therapy
End of Therapy Evaluation	ONE of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) OR • CT Chest with contrast (CPT® 71260) and • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)

Indication	Imaging Study
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)
Suspected transformation (Richter's) from a low grade lymphoma to a more aggressive type based on one or more of the following: • New B symptoms • Rapidly growing lymph nodes • Extranodal disease develops • Significant recent rise in LDH above normal range	• PET/CT (CPT® 78815 or CPT® 78816)
Surveillance for ANY of the following: • After completion of active treatment • On maintenance treatment • Observation without any treatment	For all stages, every 6 months for two years, then annually: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)
Surveillance of pediatric-type follicular lymphoma in adults	Advanced imaging is not indicated routinely after complete response

Evidence Discussion

Initial Staging

Diagnostic quality CT with contrast or PET/CT may be used for initial staging. Clinical stage is modified in only 15-20% of patients with use of PET/CT and results in a change in treatment in only 8% of patients (Zelenetz, 2024). A baseline PET/CT is useful for comparison for treatment response and to determine if further treatment intensification is necessary and is recommended if systemic therapy is planned. PET/CT is particularly important in the setting of localized disease with a plan for RT only, to rule out any other

systemic disease and to serve as a baseline for treatment response (Zelenetz 2024, Barrington 2014, Barrington 2016, Cheson 2014).

Restaging

PET/CT is of unclear utility for interim restaging, as interim PET/CT response shows no association with overall survival, thus conventional CT is supported (Dupuis, 2012). PET/CT does identify patients at risk of progression at end of induction therapy, where initial studies showed that 69% of patients who were classified as not having complete remission on CT were re-classified as complete metabolic remission when staged with PET/CT at end of induction (Barrington 2016 PMID 27095319). This increased sensitivity and specificity more accurately identifies patients at risk of poor progression free survival who may be candidates for consolidative therapy and prevents over and under-treatment. These results only apply to end of induction PET/CT (Barrington 2016, Zelenetz 2024, Barrington 2014).

While PET/CT alone is not sufficient to diagnose transformation of follicular lymphoma to diffuse large B cell lymphoma, when clinical signs and symptoms and lab values suggest transformation, PET/CT can be useful to detect transformation. SUV >10 predicts aggressive lymphoma with 80% certainty and PPV increases at higher SUVs (Noy 2009, Zelentz 2024). FDG avidity is also standard of care to select biopsy site in suspected transformation (Noy 2009, Zelenetz 2024)

Surveillance

There is little data on the role of surveillance imaging in indolent lymphomas including follicular lymphoma. The majority of relapses occur within the first 2 years post completion of therapy, and these guidelines align with the NCCN support of CT no more than every 6 months in the first two years and no more than annually following. Given that indolent lymphoma is considered a chronic condition, there is no endpoint for this imaging if requested (Zelenetz, 2024). The exception is pediatric-type follicular lymphoma, for which there is no survival benefit with detection of recurrence via surveillance imaging vs clinical detection; surveillance imaging is not supported in this population (Lynch 2014, Zelenetz 2024). PET/CT surveillance is generally not supported, due to a false positive rate as high as 20%, with no documented survival benefit, and increased radiation, invasive procedures, anxiety and cost (Zelenetz 2024, Lynch 2014).

Marginal Zone Lymphomas (ONC-27.4)

ON.NH.0027.4.A
v2.0.2025

- MALT lymphomas in any location and primary cutaneous marginal zone lymphoma should also be imaged according to these guidelines.
- Splenic Marginal Zone Lymphoma is diagnosed with splenomegaly, peripheral blood flow cytometry and bone marrow biopsy. Splenectomy is diagnostic and therapeutic. PET scan is not routinely indicated prior to splenectomy.

Indication	Imaging Study
Initial Staging/ Diagnosis	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
EITHER of the following: • If radiation therapy is being considered for stage I or II disease • If systemic therapy is planned	• PET/CT (CPT® 78815 or CPT® 78816)
Treatment Response	• CT with contrast of previously involved area(s) every 2 cycles of therapy
End of Therapy Evaluation	ONE of the following may be approved: • CT with contrast of previously involved area(s) • PET/CT (CPT® 78815 or CPT® 78816)
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Suspected recurrence and ANY of the following: • Symptoms of end organ dysfunction • Clinically significant or progressive cytopenias • Bulky disease (single mass of ≥7 cm or ≥3 or more nodal sites 3 cm in diameter) • Steady or rapid progression	In addition to the CT imaging above: • PET/CT (CPT® 78815 or CPT® 78816)
Surveillance of all stages of nodal marginal zone lymphoma for any of the following: • After completion of active treatment • On maintenance treatment • Observation without any treatment	Every 6 months for two years, then annually: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)
Surveillance of all stages of extranodal marginal zone lymphoma	Advanced imaging is not routinely indicated for surveillance of asymptomatic individuals

Evidence Discussion

Initial Staging

Diagnostic, contrasted CT of chest, abdomen and pelvis is supported for all patients to assess extent of disease in. PET avidity of extranodal marginal zone lymphoma is unreliable, as only 50-75% of these tumors are FDG avid (Barrington, 2014). A baseline

PET/CT is useful for comparison for treatment response and to determine if further treatment intensification is necessary, and so is recommended if systemic therapy is planned. PET/CT is particularly important in the setting of localized disease with a plan for RT only, to rule out any other systemic disease and to serve as a baseline for treatment response (Zelenetz 2024, Barrington 2014, Cheson 2014).

Restaging

There is no clear role for PET in interim restaging of marginal zone lymphoma, CT is supported every 2 cycles in alignment with the NCCN. End of therapy PET/CT is supported to identify patients without a complete metabolic response who are candidates for extended therapy, to prevent over- or under- treatment. (Zelenetz 2024, Barrington 2014).

Surveillance

There is little data on the role of surveillance imaging in indolent lymphomas including marginal zone lymphoma. Extranodal marginal zone lymphoma typically remains localized, and asymptomatic surveillance with advanced imaging is not supported (Zucca, 2020).The majority of relapses occur within the first 2 years post completion of therapy. Our guidelines align with the NCCN support of CT no more than every 6 months in the first two years and no more than annually following. Given that indolent lymphoma is considered a chronic condition, there is no endpoint for this imaging if requested (Zelenetz, 2024). PET/CT surveillance is not universally supported, due to a false positive rate as high as 20%, with no documented survival benefit, and increased radiation, invasive procedures, anxiety, and cost (Lynch, 2014). However, PET/CT is a supported imaging modality for specific circumstances of recurrence; NCCN supports PET/CT in recurrence when there are indications for treatment (Zelenetz, 2024).

Mantle Cell Lymphoma (ONC-27.5)

ON.NH.0027.5.A
v2.0.2025

Indication	Imaging Study
Initial Staging/Diagnosis	ONE of the following may be approved: • CT Chest with contrast (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177) OR • PET/CT (CPT® 78815 or CPT® 78816)
Treatment Response	• CT with contrast of previously involved area(s) every 2 cycles of therapy • PET/CT is not indicated for monitoring treatment response but can be considered in rare circumstances when CT did not show disease (e.g., bone).
End of Therapy Evaluation	ONE of the following may be approved: • CT with contrast of previously involved area(s) • PET/CT (CPT® 78815 or CPT® 78816)
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s) • PET/CT can be considered in rare circumstances (e.g., bone involvement).
Surveillance for all stages	Every 6 months for 2 years, and then annually: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)

Evidence Discussion

Initial Staging

Diagnostic CT with contrast OR PET/CT is supported. PET/CT is the preferred modality particularly when systemic therapy is planned, in order to prevent under treatment (Barrington 2016, Zelenetz 2024).

Restaging

Interim restaging with PET/CT has not been shown to change outcomes, thus CT alone is supported every two cycles unless the sites of disease are only visible on PET/CT. However, PET/CT is supported at end of planned therapy as a lack of complete metabolic response may require maintenance treatment (Zelenetz, 2024).

Surveillance

Late relapses, as far as 15 years out, can occur with mantle cell lymphoma. The benefit of detection of with imaging vs clinical detection remains unclear, and some studies have shown no significant advantage in survival for relapses after first remission detected by surveillance imaging (Guidot, 2018). However, this is still an active point for discussion among treating providers, and the NCCN still supports surveillance imaging with CT scan (Guidot 2018, Zelenetz 2024). Given that most providers consider the NCCN the standard of care, this guideline aligns with the more conservative NCCN recommended timeframe, to acknowledge this data while maintaining a patient and provider centric approach. Surveillance scanning with PET/CT has a positive predictive value of only 24% in this entity and is not supported (Guidot 2018, Zelenetz 2024).

Burkitt's Lymphomas (ONC-27.6)

ON.NH.0027.6.A
v2.0.2025

Indication	Imaging Study
Initial Staging/Diagnosis	ANY or ALL of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Treatment Response	• CT with contrast of previously involved area(s) every 2 cycles of therapy • PET/CT is not indicated for monitoring treatment response but can be considered in rare circumstances when CT did not show disease (e.g., bone).
End of Therapy Evaluation	ANY or ALL of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) may be approved at the end of chemotherapy and again at the end of radiation • CT with contrast of previously involved area(s)
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s) • PET/CT can be considered in rare circumstances (e.g., bone involvement).
Surveillance	Every 6 months for 2 years after completion of treatment: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)

Evidence Discussion

Initial Staging/Diagnosis

In alignment with the NCCN, both diagnostic quality CT scan with contrast and PET/CT are supported in Burkitt's Lymphoma. Diagnostic, contrasted CT is helpful for clarifying

node bulk (individual nodes vs conglomerates), anatomic relationships of bulky disease, abdominal and Waldeyer's ring involvement, as well as abdominal visceral involvement, all of which are relevant to treatment decisions and emergency management in Burkitt's lymphoma. Baseline metabolic activity is useful for comparison at end of therapy, where FDG avidity defines treatment response (Zelenetz 2024, Cheson 2024).

Treatment Response

CT alone (rather than PET/CT) should be used to assess response between cycles, as complete response is not defined until completion of upfront therapy regimen. At the end of all planned upfront therapy a PET/CT is supported, even in addition to diagnostic contrasted CTs. Metabolic response at this time point determines whether therapy can be considered complete or whether local therapy or intensification of treatment will be necessary (Zelenetz 2024, Cheson 2024, Barrington 2024).

Surveillance

The role of surveillance in Burkitt's Lymphoma is somewhat controversial. Clinically evident symptoms of recurrence develop quickly in this aggressive entity, and recurrence is as likely to be diagnosed based on symptoms as by surveillance imaging in some studies (Lynch 2014). PET/CT surveillance of Burkitt's Lymphoma is widely discouraged as it increases false positive findings, radiation exposure, and does not improve outcomes (Lynch 2014, Barrington 2024). The NCCN is considered the standard for care in the U.S. and NCCN supports CT with contrast every 6 months for 2 years, with which our guidelines align for a patient and provider centric approach. Relapse after 2 years is rare, imaging after this point for asymptomatic surveillance has not been shown to improve outcomes (Zelenetz 2024, Lynch 2014).

Lymphoblastic Lymphomas (ONC-27.7)

ON.NH.0027.7.A

v2.0.2025

- Individuals with lymphoblastic lymphoma (even those with bulky nodal disease) are treated using the leukemia treatment plan appropriate to the cell type (B or T cell). Imaging indications in adult individuals are identical to those for pediatric individuals. See: **Acute Lymphoblastic Leukemia (ALL) (PEDONC-3.2)** in the Pediatric Oncology Imaging Guidelines.

T Cell Lymphomas (ONC-27.8)

ON.NH.0027.8.A
v2.0.2025

- Includes Peripheral T-Cell Lymphomas, Mycosis Fungoides/Sézary Syndrome, Anaplastic Large Cell Lymphoma (ALCL) including breast implant-associated ALCL, Angioimmunoblastic lymphoma, and Primary Cutaneous CD30+T Cell Lymphoproliferative Disorders

Indication	Imaging Study
Initial Staging/ Diagnosis	ANY or ALL of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
T-cell lymphoma of nasal cavity, oropharynx, or nasopharynx	In addition to the imaging above: • MRI Orbits, Face, and Neck without and with contrast (CPT® 70543)
Breast implant-associated ALCL	In addition to the above initial staging studies: • Ultrasound Breast (CPT® 76641 or CPT® 76642) ◦ MRI Breast (CPT® 77049) may be indicated for evaluation of inconclusive ultrasound findings
Treatment Response	Any ONE of the following may be approved after 3-4 cycles: • PET/CT (CPT® 78815 or 78816) or • CT Chest with contrast (CPT® 71260), and • CT Abdomen and Pelvis with contrast (CPT® 74177) and • CT with contrast of previously involved area(s)

Indication	Imaging Study
End of Therapy Evaluation	Any ONE of the following may be approved at the end of chemotherapy and again at the end of radiation therapy: • PET/CT (CPT® 78815 or CPT® 78816) or • CT Chest with contrast (CPT® 71260), and • CT Abdomen and Pelvis with contrast (CPT® 74177), and • CT with contrast of previously involved area(s)
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s) • PET/CT can be considered in rare circumstances (e.g., bone involvement).
Surveillance, all stages	Every 6 months for 2 years, then annually for 5 years: • CT Chest with contrast (CPT® 71260), CT Abdomen and Pelvis with contrast (CPT® 74177), and CT of previously involved areas

Evidence Discussion

Initial Staging

FDG PET/CT fusion (PET with attenuation CT) is valuable for initial staging as patients with T cell lymphoma often have extranodal disease, which may be missed on body area specific diagnostic CTs. Noncontiguous nodes, Waldeyer ring, and GI/liver involvement is also common in T cell lymphomas and may be difficult to distinguish on PET/CT fusion studies alone, thus our guidelines support the use of diagnostic quality, contrasted CTs when requested. To ensure correct staging and treatment stratification and prevent under- or over-treatment, in addition to PET/CT fusion imaging (NCI PDQ 2024, Horwitz 2024, Zelenetz 2024).

Treatment Response

Modality for restaging should be determined by which studies best illustrated disease at initial staging. PET/CT fusion imaging OR body area specific diagnostic quality, contrasted CTs are generally adequate for comparison to initial staging to assess response (Horwitz, 2024) after 3-4 cycles and again at end of chemotherapy and at end

of radiation. Imaging prior to 3-4 cycles may result in over- or under-treatment, and thus is not supported (Horwitz 2024, Zelenetz 2024).

Surveillance

There is no evidence illustrating an overall survival advantage in detection of relapse from imaging vs clinical detection, but data suggests better progression free survival after second line treatment in patients undergoing imaging surveillance (Lynch, 2014). Considering these perspectives and to align with the NCCN, CT of viscera and all previously involved areas is supported every 6 months for 2 years, then annually for 5 years (Horwitz, 2024). PET/CT surveillance is not supported as no survival improvement is noted with PET/CT surveillance, and it subjects patients to increased radiation, increased costs, and increased risk of invasive procedures for incidental findings, as the false positive rate in this setting is as high as 20 percent (Lynch 2014, Barrington 2016). CT is generally supported for suspected recurrence as well, with PET reserved for biopsy proven recurrence, by the same rationale.

Post-Transplant Lymphoproliferative Disorders (ONC-27.9)

ON.NH.0027.9.A
v2.0.2025

- Post-transplant lymphoproliferative disorder (PTLD) or viral-associated lymphoproliferative disorder can rarely occur following solid organ or hematopoietic stem cell transplantation, or in primary immunodeficiency. When reduction of immunosuppression is unsuccessful, these are often treated with chemoimmunotherapy similar to high-grade NHL.
- This section applies to Monomorphic (B-cell type) PTLD and Polymorphic PTLD.
- For Hodgkin-lymphoma subtype of PTLD, see: **Hodgkin Lymphomas (ONC-28)** for imaging recommendations.

Indication	Imaging Study
Initial Staging/ Diagnosis	ANY or ALL of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Treatment Response	ANY or ALL of the following may be approved after 4 weeks of reducing immunosuppression or every 2 cycles (6-8 weeks) of chemo/immunotherapy: • CT Chest with contrast (CPT® 71260), and • CT Abdomen and Pelvis with contrast (CPT® 74177), and • CT with contrast of previously involved area(s)
End of Therapy Evaluation	ANY one of the following may be approved at the end of treatment: • PET/CT (CPT® 78815 or CPT® 78816) or • CT Chest with contrast (CPT® 71260), and • CT Abdomen and Pelvis with contrast (CPT® 74177), and • CT with contrast of previously involved area(s)
Suspected recurrence	• CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)

Indication	Imaging Study
Surveillance	Advanced imaging is not routinely indicated for surveillance

Evidence Discussion

Initial staging

FDG PET/CT fusion (PET with attenuation CT) is valuable for initial staging as patients with PTLD often have extranodal and/or multi-site disease, which may be missed on body area specific diagnostic CTs. Patients with single sites of disease may be managed with local treatment alone, thus thorough assessment for systemic disease is essential to prevent under-treatment. Node bulk has prognostic value and is used for treatment stratification, and bulky masses vs noncontiguous nodes may be difficult to distinguish on PET/CT fusion studies alone. These guidelines thus support the use of diagnostic quality, contrasted CTs when requested in addition to PET/CT fusion imaging (NCI PDQ 2024, Zelenetz 2024).

Restaging

Restaging with CT is supported every 2 cycles of chemotherapy as is standard for most disease processes (Zelenetz, 2024). Median time to failure of reduction of immunosuppression as first line therapy, however, is only 45 days, so for patient safety our guidelines support earlier restaging in this scenario as soon as 4 weeks after reduction of immunosuppression (Reshef, 2011). Changing therapy based on interim PET/CT alone is not supported and thus our guidelines support CT alone for interim restaging, with biopsy for concerning findings (Zelenetz 2024, Cheson 2014, Barrington 2014). These guidelines do support PET/CT at end of planned treatment to ensure a complete metabolic response (Zelenetz 2024, Cheson 2014, Barrington 2014). Concurrent diagnostic CTs may be done in lieu of PET/CT if requested, but diagnostic CTs in addition to PET/CT fusion studies do not offer additional information in the setting of a complete metabolic response (Barrington 2014, Cheson 2014).

Surveillance

Advanced imaging surveillance is not supported for PTLD (Zelenetz 2024, Lynch 2014). Surveillance imaging has not been shown to improve outcomes for PTLD and it subjects patients to increased radiation, increased costs, and increased risk of invasive procedures for incidental findings (Lynch, 2014). Surveillance is predominantly via EBV PCR (Zelenetz, 2024).

Waldenström Macroglobulinemia or Lymphoplasmacytic Lymphoma (ONC-27.10)

ON.NH.0027.10.A
v2.0.2025

Indication	Imaging Study
Initial Staging/Diagnosis	ANY or ALL of the following are indicated: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • PET/CT (CPT® 78815 or CPT® 78816)
Treatment Response	• CT with contrast of previously involved area(s) every 2 cycles of therapy
End of Therapy Evaluation	• CT with contrast of previously involved area(s)
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)
Surveillance	Advanced imaging is not routinely indicated for surveillance

Evidence Discussion

Initial Staging

NCCN supports contrasted CT of chest, abdomen, and pelvis (Kumar 2025, Dimopoulous 2019). PET/CT fusion is recommended equally with diagnostic CT by the NCCN (Kumar, 2025).

Restaging

NCCN supports contrasted, diagnostic quality CTs every 2 cycles of chemotherapy and at end of treatment to determine response and prevent under-treatment. Diagnostic, contrasted CTs of chest, abdomen, pelvis and previously involved areas are supported for suspected recurrence (Kumar 2025, Dimopoulous 2019). PET/CT is not consistently

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

correlated with monoclonal protein response, which is the primary means of monitoring this entity and PET/CT is not recommended for restaging of this entity (Banwait 2011,Thomas 2019, Kumar 2025).

Surveillance

Surveillance of lymphoplasmacytic lymphoma is based on laboratory monitoring of blood counts and chemistries, serum proteins, and immunoglobulins. There is no established role for imaging surveillance in this entity (Thomas 2019, Kumar 2025).

References (ONC-27)

v2.0.2025

1. Zelenetz AD, Gordon LI, Abramson JS, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – December 20, 2024. B-cell lymphomas, available at: https://www.nccn.org/professionals/physician_gls/pdf/B-CELL.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for B-cell lymphomas V1.2025 – December 20, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Horwitz SM, Ansell S, Ai WZ, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – November 11, 2024. T-cell lymphomas, available at: https://www.nccn.org/professionals/physician_gls/pdf/T-CELL.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for T-cell lymphomas V1.2025 – November 11, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment for Hodgkin and Non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol*. 2014;32(27):3059-3067. doi:10.1200/JCO.2013.54.8800.
4. Barrington SF, Mikhaeel NG, Kostakoglu L, et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. *J Clin Oncol*. 2014;32(27):3048-3058. doi:10.1200/JCO.2013.53.5229.
5. Thompson CA, Ghesquieres H, Maurer MJ, et al. Utility of routine post-therapy surveillance imaging in diffuse Large B-Cell Lymphoma. *J Clin Oncol*. 2014;32(31):3506-3512. doi:10.1200/JCO.2014.55.7561.
6. El-Galaly TC, Jakobsen LH, Hutchings M, et al. Routine imaging for diffuse Large B-Cell Lymphoma in first complete remission does not improve post-treatment survival: a Danish-Swedish population-based study. *J Clin Oncol*. 2015;33(34):3993-3998. doi:10.1200/JCO.2015.62.0229.
7. Huntington SF, Svoboda J, Doshi JA. Cost-effectiveness analysis of routine surveillance imaging of patients with diffuse Large B-Cell Lymphoma in first remission. *J Clin Oncol*. 2015;33(13):1467-1474. doi:10.1200/JCO.2014.58.5729.
8. Mamot C, Klingbiel D, Hitz F, et al. Final results of a prospective evaluation of the predictive value of interim positron emission tomography in patients with diffuse large B-cell lymphoma treated with R-CHOP-14 (SAKK 38/07). *J Clin Oncol*. 2015;33(23):2523-2529. doi:10.1200/JCO.2014.58.9846.
9. Mylam KJ, Nielsen AL, Pedersen LM, Hutchings M. Fluorine-18-fluorodeoxyglucose positron emission tomography in diffuse large B-cell lymphoma. *PET Clin*. 2014;9(4):443-455. doi:10.1016/j.cpet.2014.06.001.
10. Avivi I, Zilberlicht A, Dann EJ, et al. Strikingly high false positivity of surveillance FDG-PET/CT scanning among patients with diffuse large cell lymphoma in the rituximab era. *Am J Hematol*. 2013;88(5):400-405. doi:10.1002/ajh.23423.
11. Ulrich Dührsen, Stefan Müller, Bernd Hertenstein, et al. Positron emission tomography-guided therapy of aggressive non-Hodgkin lymphomas (PETAL): a multicenter, randomized phase III trial. *J Clin Oncol*. 2018;36(20):2024-2034. doi:10.1200/JCO.2017.76.8093.
12. Bijal S, Mattison RJ, Abboud R, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – December 20, 2024. Acute Lymphoblastic Leukemia, available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Acute Lymphoblastic Leukemia V3.2024 – December 20, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
13. Lynch RC, Zelenetz AD, Armitage JO, Carson KR. Surveillance imaging for lymphoma: pros and cons. *Am Soc Clin Oncol Educ Book*. 2014:e388-95. doi:10.14694/EdBook_AM.2014.34.e388.

14. Kumar SK, Callander NS, Adekola K, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2025 –February 6, 2025. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Waldenstrom Macroglobulinemia/ Lymphoplasmacytic Lymphoma V3.2025 – February 6, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
15. Banwait R, O'Regan K, Campigotto F, et al. The role of 18F-FDG PET/CT imaging in Waldenstrom macroglobulinemia. *Am J Hematol*. 2011;86(7):567-72. doi:10.1002/ajh.22044.
16. Thomas R, Braschi-Amirfarzan M, Laferriere SL, Jagannathan JP. Imaging of Waldenström macroglobulinemia: a comprehensive review for the radiologist in the era of personalized medicine. *AJR Am J Roentgenol.* 2019;213(6):W248-W256. doi:10.2214/AJR.19.21493.
17. Dimopoulos MA, Kastritis E. How I treat Waldenström macroglobulinemia. *Blood*. 2019;134(23):2022-2035. doi:10.1182/blood.2019000725.
18. Noy A, Schöder H, Gönen M, et al. The majority of transformed lymphomas have high standardized uptake values (SUVs) on positron emission tomography (PET) scanning similar to diffuse large B-cell lymphoma (DLBCL). *Ann Oncol*. 2009;20(3):508-12. doi:10.1093/annonc/mdn657.
19. Zucca E, Arcaini L, Buske C, et al. Marginal zone lymphomas: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2020;31(1):17-29. doi:10.1016/j.annonc.2019.10.010.
20. Barrington SF, Mikhaeel NG. PET scans for staging and restaging in diffuse large b-cell and follicular lymphomas. *Curr Hematol Malig Rep*. 2016;11(3):185-95. doi:10.1007/s11899-016-0318-1.
21. Dupuis J, Berriolo-Riedinger A, Julian A, et al. Impact of [18F]Fluorodeoxyglucose Positron Emission Tomography response evaluation in patients with high-tumor burden follicular lymphoma treated with immunochemotherapy: a prospective study from the Groupe d'Etudes des Lymphomes de l'Adulte and GOELAMS. *J Clin Oncol.* 2012;30:4317-4322.
22. Reshef R, Vardhanabhuti S, Luskin MR, et al. Reduction of immunosuppression as initial therapy for posttransplantation lymphoproliferative disorder. *Am J Transplant*. 2011;11(2):336-47. doi:10.1111/ j.1600-6143.2010.03387.x.
23. Paquin AR, Oyogoa E, McMurry HS, et al. The diagnosis and management of suspected lymphoma in general practice. *Eur J Haematol*. 2023;110(1):3–13. doi:10.1111/ejh.13863.
24. Kühnl A, Cunningham D, Hutka M, et al. Rapid access clinic for unexplained lymphadenopathy and suspected malignancy: prospective analysis of 1000 patients. *BMC Hematol*. 2018;18:19. doi:10.1186/s12878-018-0109-0.
25. Bosch X, Coloma E, Donate C, et al. Evaluation of unexplained peripheral lymphadenopathy and suspected malignancy using a distinct quick diagnostic delivery model: prospective study of 372 patients. *Medicine (Baltimore)*. 2014;93(16):e95. doi:10.1097/MD.0000000000000095.
26. Nixon S, Bezverbnaya K, Maganti M, et al. Evaluation of lymphadenopathy and suspected lymphoma in a lymphoma rapid diagnosis clinic. *JCO Oncol Pract*. 2020;16(1):e29-e36. doi:10.1200/JOP.19.00202.
27. Tokola S, Kuitunen H, Turpeenniemi-Hujanen T, Kuittinen O. Interim and end-of-treatment PET-CT suffers from high false-positive rates in DLBCL: Biopsy is needed prior to treatment decisions. *Cancer Med*. 2021;10(9):3035-3044. doi:10.1002/cam4.3867.
28. Guidot DM, Switchenko JM, Nastoupil LJ, et al. Surveillance imaging in mantle cell lymphoma in first remission lacks clinical utility. *Leuk Lymphoma*. 2018;59(4):888-895. doi:10.1080/10428194.2017.1361032.
29. National Cancer Institute PDQ® Cancer Treatment Summary, Peripheral T-Cell Non-hodgkin Lymphoma Treatment –Health Professional Version. Peripheral T-Cell Non-Hodgkin Lymphoma Treatment (PDQ®) - NCI (cancer.gov).

Hodgkin Lymphoma (ONC-28)

Guideline Page

Hodgkin Lymphoma – General Considerations (ONC-28.1)

ON.HL.0028.1.A
v2.0.2025

- Lymphoma is often suspected when individuals have any of the following:
  - Bulky lymphadenopathy (lymph node mass >10 cm in size), hepatomegaly or splenomegaly
  - The presence of systemic symptoms (fever, drenching night sweats or unintended weight loss of >10%, called “B symptoms”)
- Individuals with AIDS-related lymphoma should be imaged according to the primary lymphoma histology.
- The **Deauville Criteria** are internationally accepted criteria, which utilize a five-point scoring system for the FDG avidity of a Hodgkin's lymphoma or Non-Hodgkin's lymphoma tumor mass as seen on FDG PET.
  - Score 1: No uptake above the background
  - Score 2: Uptake ≤mediastinum
  - Score 3: Uptake >mediastinum but ≤liver
  - Score 4: Uptake moderately increased compared to the liver at any site
  - Score 5: Uptake markedly increased compared to the liver at any site
  - Score X: New areas of uptake unlikely to be related to lymphoma

Indication	Imaging Study
• Biopsy proven lymphoma, or • Suspected lymphoma and any one of the following: ◦ Bulky lymphadenopathy (LN mass >10 cm) ◦ Hepatomegaly ◦ Splenomegaly ◦ B symptom: Unexplained fever, drenching night sweats, unintended weight loss >10% total body weight	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast ◦ MRI without and with contrast for individuals who cannot tolerate CT contrast due to allergy or impaired renal function
Signs or symptoms of disease involving the neck	• CT Neck with contrast (CPT® 70491)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Signs or symptoms suggesting CNS involvement with lymphoma	• MRI Brain without and with contrast (CPT® 70553) • See: **CNS Lymphoma (also known as Microglioma) (ONC-2.7)**
Known or suspected bone involvement with lymphoma	• MRI without and with contrast of symptomatic or previously involved bony areas ◦ Bone scan is inferior to MRI for evaluation of known or suspected bone involvement with lymphoma
Determine a more favorable site for biopsy when a relatively inaccessible site is contemplated	• PET/CT (CPT® 78815 or CPT® 78816) ◦ PET/CT is medically unnecessary for all other indications prior to histological confirmation of lymphoma
CAR-T cell therapy	Once before treatment and once 30-60 days after completion of treatment: • PET/CT (CPT® 78815 or CPT® 78816)

Classical Hodgkin Lymphoma (ONC-28.2)

ON.HL.0028.2.A
v2.0.2025

- This section applies to nodular sclerosis, mixed cellularity, lymphocyte-depleted and lymphocyte-rich subtypes of Hodgkin lymphoma.

Indication	Imaging Study
Initial Staging/Diagnosis	ANY or ALL of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Treatment Response	• PET/CT (CPT® 78815 or CPT® 78816) as frequently as every 2 cycles
End of Chemotherapy and/or Radiation Therapy Evaluation	• PET/CT (CPT® 78815 or CPT® 78816) may be approved at the end of chemotherapy and again at the end of radiation (at least 12 weeks after completion of radiation therapy)
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)
Biopsy proven recurrence	• PET/CT (CPT® 78815 or CPT® 78816)

Indication	Imaging Study
Surveillance	ANY or ALL of the following may be approved every 6 months for 2 years after completion of therapy: • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s) In addition to the above studies: • A single follow-up PET/CT may be approved at three months if end of therapy PET/CT shows Deauville 4 or 5 FDG avidity

Nodular Lymphocyte – Predominant Hodgkin Lymphoma (ONC-28.3)

ON.HL.0028.3.A
v2.0.2025

Indication	Imaging Study
Initial Staging/Diagnosis	ANY or ALL of the following may be approved: • PET/CT (CPT® 78815 or CPT® 78816) • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177)
Treatment Response	• CT with contrast of previously involved areas as frequently as every 2 cycles
End of Chemotherapy and/or Radiation Therapy Evaluation	• PET/CT (CPT® 78815 or CPT® 78816) may be approved at the end of chemotherapy and again at the end of radiation (at least 12 weeks after completion of radiation therapy)
Suspected Recurrence	ANY or ALL of the following may be approved: • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s)
Biopsy proven recurrence	• PET/CT (CPT® 78815 or CPT® 78816)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Suspected transformation (Richter's) from a low-grade lymphoma to a more aggressive type based on one or more of the following: • New B symptoms • Rapidly growing lymph nodes • Extranodal disease develops • Significant recent rise in LDH above normal range	• PET/CT (CPT® 78815 or CPT® 78816)
Surveillance	ANY or ALL of the following may be approved every 6 months for 2 years after completion of therapy: • CT Neck with contrast (CPT® 70491) • CT Chest with contrast (CPT® 71260) • CT Abdomen and Pelvis with contrast (CPT® 74177) • CT with contrast of previously involved area(s) In addition to the above studies: • A single follow-up PET/CT may be approved at three months if end of therapy PET/CT shows Deauville 4 or 5 FDG avidity

Evidence Discussion - ONC-28

Initial staging and Restaging

PET imaging is useful for staging, prognosis, and treatment stratification in all subtypes of Hodgkin Lymphoma. Staging with PET/CT rather than CT often confirms a higher stage of disease. While overall survival outcome is not clearly improved by staging/ restaging with PET/CT, stratification of treatment based on PET/CT benefits patients by preventing over- and under-treatment. PET is thus supported for initial staging, re-staging every 2 cycles, and at the end of therapy . False positive rates are elevated in the weeks following radiation, reaching up to 20%. Decisions based on scans done in close proximity to radiation may result in over-treatment. Therefore, PET/CT should not be performed until 12 weeks after completion of radiation.

Diagnostic CT with contrast is supported concurrently with PET/CT for initial staging as it may better differentiate nodal conglomerates from individual nodes in close proximity, and node bulk is prognostic and also used for treatment stratification. However, performing diagnostic CTs concurrently with PET/CT at restaging does not provide a benefit, as FDG avidity is highly indicative of response in Hodgkin lymphoma, where CT alone may over- or under- estimate response. FDG avidity guides response assessment and informs subsequent treatment decisions. This includes intensifying therapy if PET avidity persists after 2-4 cycles, or omitting consolidative radiotherapy in cases of good response on PET/CT after 4 cycles for low-stage disease. A complete metabolic response (Deauville score of 3 or less) should be confirmed to determine the end of treatment . If the end-of-therapy PET/CT shows a Deauville score of 4-5, repeating the PET/CT 3 months later is appropriate to confirm the metabolic status of residual masses and to prevent under-treatment.

While PET/MRI shows high concordance with PET/CT at a decreased radiation dose, it is inferior for assessing disease in the lungs, more time-consuming, and more costly. Furthermore, it has not been established as a standard for treatment stratification in adult Hodgkin Lymphoma and is therefore not recommended over PET/CT.

Surveillance

Surveillance imaging with PET/CT is not supported, as the false-positive rate with PET scans in this context is greater than 20%, leading to unnecessary investigations, radiation exposure, biopsies, expense, and patient anxiety. In addition, no statistically significant difference in survival has been noted with CT surveillance imaging in Hodgkin Lymphoma, despite statistically significant increase in radiation exposure and cost. However, given that many existing protocols still require surveillance imaging, the NCCN continues to support CT surveillance every 6 months in the first two years post therapy if requested. Given that the NCCN is viewed as the standard of care in most US Oncology treatment centers, we have chosen to align with this current NCCN recommendation for a patient and provider centric approach.

References (ONC-28)

v2.0.2025

1. Hoppe RT, Advani RH, Ambinder RF, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – March 18, 2024. Hodgkin lymphoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Hodgkins Lymphoma V3.2024 – March 18, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment for Hodgkin and Non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol. 2014;32(27):3059-3067. doi:10.1200/JCO.2013.54.8800.
3. Barrington SF, Mikhaeel NG, Kostakoglu L, et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol. 2014;32(27):3048-3058. doi:10.1200/JCO.2013.53.5229.
4. Pingali SR, Jewell SW, Havlat L, et al. Limited utility of routine surveillance imaging for classical Hodgkin lymphoma patients in first complete remission. *Cancer*. 2014;120:2122-2129.
5. Ha CS, Hodgson DC, Advani R, et al. Follow-up of Hodgkin lymphoma. ACR Appropriateness Criteria® 2014;1-16.
6. Picardi M, Pugliese N, Cirillo, M et al. Advanced-stage Hodgkin lymphoma: US/Chest radiography for detection of relapse in patients in first complete remission—a randomized trial of routine surveillance imaging procedures. *Radiology*. 2014;272:262-274.
7. Gallamini A, and Kostakoglu L. Interim FDG-PET in Hodgkin lymphoma: a compass of a safe navigation in clinical trials? *Blood*. 2012;120(25):4913-4920.
8. Biggi A, Gallamini A, Chauvie S, et al. International validation study for interim PET in ABVD-treated, advanced-stage Hodgkin lymphoma: interpretation criteria and concordance rate among reviewers. *J Nucl Med*. 2013; 54(5):683-690.
9. Gallamini A, Barrington SF, Biggi, et al. The predictive role of interim positron emission tomography for Hodgkin lymphoma treatment outcome is confirmed using the interpretation criteria of the Deauville five-point scale. *Haematologica*. 2014; 99(6):1107-1113.
10. El-Galaly TC, Mylam KJ, Brown P, et al. Positron emission tomography/computed tomography surveillance in patients with Hodgkin lymphoma in first remission has a low positive predictive value and high costs. *Haematologica*. 2012;97(6):931-936.
11. Fuchs M, Goergen H, Kobe C, et al. Positron Emission tomography-guided treatment in early-stage favorable Hodgkin lymphoma: final results of the international, randomized phase III HD16 trial by the German Hodgkin study group. *J Clin Oncol*. 2019;37(31):2835-2845. doi:10.1200/JCO.19.00964.
12. Borchmann P, Plütschow A, Kobe C, et al. PET-guided omission of radiotherapy in early-stage unfavourable Hodgkin lymphoma (GHSG HD17): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol*. 2021;22(2):223-234. doi:10.1016/S1470-2045(20)30601-X.

Hematopoietic Stem Cell Transplantation (ONC-29)

Guideline Page

General Considerations for Stem Cell Transplant (ONC-29.1)

ON.HT.0029.1.A
v2.0.2025

Transplant Types:

Allogeneic ("allo"): The donor and recipient are different people, and there are multiple types depending on the source of the stem cells and degree of match between donor and recipient. This is most commonly used in diseases originating in the hematopoietic system, such as leukemias and lymphomas, and bone marrow failure syndromes or metabolic disorders. Common types are:

- Matched sibling donor (MSD or MRD): Donor and recipient are full siblings and HLA-matched
- Matched unrelated donor (MUD): Donor and recipient are HLA matched but not related to each other
- Cord blood: Donor stem cells come from frozen umbilical cord blood not related to the recipient, sometimes from multiple different donors at once
- Haploidentical transplant (haplo): Donor is a half-HLA match to the recipient, usually a parent

Autologous ("auto"): The donor and recipient are the same person. The process involves delivery of high dose chemotherapy that is ablative to the bone marrow, followed by an infusion of one's own harvested stem cells.

Allogeneic HSCT results in a much greater degree of immunosuppression than autologous HSCT because of the need to allow the new immune system to chimerize with the recipient's body. Immune reconstitution commonly takes more than a year for individuals who receive allogeneic HSCT, and individuals remain at high- risk for invasive infections until that has occurred.

Pre-Transplant Imaging in HSCT:

- Pre-transplant imaging in HSCT generally takes place within 30 days prior to transplant and involves a reassessment of the individual's disease status as well as infectious disease clearance.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging
Immediate pre-transplant period	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) for ANY of the following: ◦ Any individual prior to undergoing allogeneic transplant ◦ New findings on chest x-ray ◦ New/worsening signs/symptoms of chest involvement • CT Sinus (CPT® 70486) for any clinical signs or symptoms • CT of other body areas is not indicated without clinical signs or symptoms of involvement
Assess cardiac function	• Echocardiogram (CPT® 93306, CPT® 93307 or CPT® 93308) ◦ MUGA scan (CPT® 78472) may be indicated in specific circumstances, see: **Oncologic Indications for Cancer Therapeutics-Related Cardiac Dysfunction (CTRCD) (CD-12.1)** in the Cardiac Imaging Guidelines
Assess pulmonary function	• Pulmonary function tests
Assess primary disease status	• See disease-specific guidelines for end of therapy response assessment

Post-Transplant Imaging in HSCT:

- There are many common complications from HSCT, including infection, acute and chronic graft versus host disease (GVHD), hepatic sinusoidal obstruction syndrome, restrictive lung disease, among others.
- Disease response generally takes place at ~Day +30 (autos and some allos) or ~Day +100 (allos) post-transplant.

Indication	Imaging
Assess known or suspected HSCT complications	• Site-specific imaging should generally be approved

Indication	Imaging
Suspected hepatic GVHD (elevated liver enzymes)	• Abdominal US (CPT® 76700 or CPT® 76705)
Suspected Bronchiolitis Obliterans Syndrome (BOS)	• CT Chest without contrast (CPT® 71250)
Assess primary disease status post-transplant	• See disease-specific guidelines for end of therapy evaluation and surveillance
Individuals receiving tandem auto transplants (2-4 autos back-to-back, spaced 6 to 8 weeks apart)	• Guideline recommended imaging can be repeated after each transplant

Evidence Discussion

Pre-Transplant imaging in Hematopoietic Stem Cell Transplant (HSCT)

This refers to imaging in the immediate pre-transplant period, approximately 30 days prior to anticipated HSCT. There is not a clear consensus for pre-transplant infectious screening with imaging, but a CT chest and CT sinus are supported for any clinical signs and symptoms of respiratory or sinus infection. The NCCN does not support CT imaging for infection screening in asymptomatic patients. There is no clear data to support pre-transplant sinus imaging in adult patients; extrapolation from pediatric data shows no change in pre-transplantation management nor prediction of post-transplant sinusitis based on pre-transplant imaging of asymptomatic patients. Screening for infection of abdomen and pelvis with advanced imaging is not supported as it has not been shown to change management or outcomes yet increases cost and radiation exposure. Echocardiogram is supported prior to transplant conditioning for all patients, to assure the safest possible dosing for cardiotoxic agents. MUGA scan is supported to supplement echocardiogram in patients with a previous low ejection fraction (LVEF <50%).

Post-Transplant imaging in HSCT

Timing of post-transplant disease restaging varies by disease process. Generally, repeat imaging follows the disease-specific guidelines for end of therapy evaluation and surveillance. For patients receiving tandem auto transplants, disease-specific imaging can be repeated after each transplant. Imaging for post-transplant complications maximizes patient safety and allows for early intervention.

Reference (ONC-29)

v2.0.2025

1. Loren AW, Mielcarek M, Bolaños-Meade J, et. al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2024 – August 30, 2024. Hematopoietic Cell Transplantation, available at: https://www. nccn.org/professionals/physician_gls/pdf/hct.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hematopoietic Cell Transplantation V2.2024 – August 30, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines®, go online to NCCN.org.
2. Harreld JH, Kaufman RA, Kang G, et al. Utility of pre-hematopoietic cell transplantation sinus CT screening in children and adolescents. *AJNR Am J Neuroradiol*. 2020;41(5):911-916. doi:10.3174/ajnr.A6509.
3. Chan SS, Coblentz A, Bhatia A, et al. Imaging of pediatric hematopoietic stem cell transplant recipients: A COG Diagnostic Imaging Committee/SPR Oncology Committee White Paper. *Pediatr Blood Cancer*. 2023;70 Suppl 4(Suppl 4):e30013. doi:10.1002/pbc.30013.
4. Kaste SC, Kaufman RA, Sunkara A, et al. Routine pre- and post-hematopoietic stem cell transplant computed tomography of the abdomen for detecting invasive fungal infection has limited value. *Biol Blood Marrow Transplant*. 2015;21(6):1132-5. doi:10.1016/j.bbmt.2015.02.023.
5. Plana JC, Galderisi M, Barac A, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal - Cardiovascular Imaging*. 2014;15(10):1063-1093. doi:10.1093/ehjci/jeu192.
6. Peña E, Souza CA, Escuissato DL, et al. Noninfectious pulmonary complications after hematopoietic stem cell transplantation: practical approach to imaging diagnosis. *Radiographics*. 2014;34(3):663-83. doi:10.1148/rg.343135080.
7. Alhomoud M, Chokr N, Gomez-Arteaga A, et a. Screening chest CT prior to allogenic hematopoietic stem cell trasplantation. *Transplant Cell Ther*. 2023;29(5):326.e1-326.e10. doi:10.1016/j.jtct.2023.01.029.
8. McQuinn D, Racki L, Venkre VP, et al. Full body screening computed tomography prior to allogeneic hematopoietic stem cell transplantation: a single institution experience from an academic center. *Blood*. 2023;142:378-379.

Medical Conditions with Cancer in the Differential Diagnosis (ONC-30)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Fever of Unknown Origin (FUO) (ONC-30.1)

ON.MC.0030.1.A
v2.0.2025

- FUO is defined as a persistent fever ≥101^{o}F and ≥3 weeks with unidentified cause.
- While fever is a classic “B” symptom of advanced lymphoma, a cancer-related fever presenting in isolation without any other signs or symptoms of neoplastic disease is rare.

Indication	Imaging Study
If physical examination, Chest X-ray, and laboratory studies are non-diagnostic	• Echocardiogram (CPT® 93306) • Abdominal ultrasound (CPT® 76700) • MRI Brain without and with contrast (CPT® 70553)
Above studies (including PE/ENT exam, pelvic exam, and DRE with laboratory studies) have failed to demonstrate site of infection	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent(s): CPT® 78800, CPT® 78801, or CPT® 78802, CPT® 78804, CPT® 78803 or CPT® 78831 (SPECT), or CPT® 78830, or CPT® 78832 (SPECT/CT)
“B” symptoms	• See: **Non-Hodgkin Lymphomas (ONC-27)**
Any CNS sign/symptom accompanied by fever	• MRI Brain without and with contrast (CPT® 70553)
All individuals	• PET is not indicated in the work-up of individuals with FUO

Evidence Discussion

The widely accepted definition of "Fever of Unknown Origin" is persistent fever of at least 101 degrees F for at least 3 weeks with unidentified cause. Most published recommendations are based on expert consensus rather than data. Malignancy accounts for 20-30% of FUO in adults (David 2022, Wright 2020). The remainder are infectious, inflammatory, and immune mediated. Physical exam, chest x-ray, and

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

laboratory findings including workup for specific infections should guide workup, and all routine age-based cancer screening should be complete. If these are negative, further workup may be indicated. Echocardiogram, abdominal ultrasound, and MRI Brain without and with contrast are supported, with sensitivity rates of 80-86%, as abdominal and pelvic abscess, endocarditis, and viral and bacterial CNS processes remain more common causes of fever than malignancy (David 2022, Bleeker-Rovers 2007, Wright 2020). These modalities limit radiation exposure and are recommended as first line imaging in most algorithms (David 2022, Wright 2020, Bleeker-Rovers 2007).

If the above workup has not demonstrated a source of infection, CT with contrast of the chest, abdomen and pelvis is supported as second line imaging, with sensitivity of up to 90% and specificity up to 70% for determining the cause of fever (Davis 2022, Wright 2020). Technitium-based scans are insensitive but highly specific (93-94%), with the advantage of lower radiation exposure than CT, and are supported to localize infectious or inflammatory foci (David 2022, Hayakawa 2016, Takeuchi 2016). MRI Brain without and with contrast is supported for any CNS symptoms accompanied by fever, as supported by several FUO algorithms and as outlined in HD-14.1 CNS and Head Infection. B symptoms with concern for lymphoma also warrant CTs, with further details outlined in eviCore ONC 27.1. The utility of PET/CT in workup of FUO is emerging, but specificity is variable, ranging from 52-85% (Bleeker-Rovers 2007, Kan 2019, Takeuchi 2016, Minamimoto 2022, Palestro 2023). At this time it is not routinely supported in the workup of FUO.

Unexplained Weight Loss (ONC-30.2)

ON.MC.0030.2.A
v2.0.2025

- Unintentional weight loss is defined as loss of ≥10 lbs. or ≥5% of body weight over 6 months or less, without an identifiable reason.
- Initial workup for all individuals may include appropriate detailed history, physical exam, baseline laboratory studies (e.g., CBC, CMP, HgbA1c, ESR/CRP, infectious workup, stool hemoccult, endocrine evaluation to rule out thyroid, pituitary, or gonadal dysfunction, etc.), chest x-ray, age-appropriate cancer screening, and neurological evaluation to rule out depression/dementia.
- Additional workup is directed to evaluate specific signs, symptoms, red flags, or abnormalities detected on initial workup. See condition-specific imaging guidelines for additional details.
- PET is not appropriate in the work-up of individuals with unexplained weight loss.

Indication	Imaging Study
CNS symptoms or abnormal pituitary hormones	• MRI Brain or Sella Turcica without and with contrast (CPT® 70553)
Abnormal thyroid function	• Thyroid ultrasound (CPT® 76536)
Abnormal liver function	• Abdominal ultrasound (CPT® 76700)
Abnormal kidney function	• Ultrasound kidney and bladder (CPT® 76770 or CPT® 76775)
Suspected cardiac dysfunction	• Echocardiogram (CPT® 93306)
Non-smokers	• Chest x-ray ◦ CT Chest with contrast (CPT® 71260) to evaluate abnormalities on chest x-ray
Current or former smokers	• CT Chest with contrast (CPT® 71260)
Dysphagia or early satiety	• See: **Dysphagia and Esophageal Disorders (NECK-3)**
GI bleeding	• See: **GI Bleeding (AB-22)**
Abdominal pain without red flag signs	See: **Abdominal Pain (AB-2)**

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Suspected pancreatic cancer in individuals aged ≥60 years with weight loss and at least one of the following[13]: • Diarrhea • Back pain • Abdominal pain • Nausea/vomiting • Constipation • New onset diabetes • Abnormal labs (CA 19-9, LFTs) • Non-diagnostic or negative abdominal ultrasound	Any ONE of the following may be obtained: • CT Abdomen with contrast (CPT® 74160) • CT Abdomen and Pelvis with contrast (CPT® 74177) • MRI Abdomen without and with contrast (CPT® 74183) See also: **Epigastric Pain and Dyspepsia (AB-2.5)**
If all of the above do not identify cause of weight loss	Any of the following, if not previously performed: • CT Chest (CPT® 71260) • CT Abdomen and Pelvis (CPT® 74177) with contrast

Evidence Discussion

Gradual weight loss is a common occurrence in the elderly. Unintentional weight loss that is associated with in increased risk of morbidity and mortality is generally defined as a weight loss of percentage5 body weight over a period of 6-12 months (Gaddey 2014, Alibhai 2005). Among patients with unintentional weight loss, a minority are diagnosed with malignancy (Bosch 2017, Nicholson 2018). There is no unified published consensus or guideline to guide the workup for weight loss, but most publications recommend that the primary workup should be symptom- focused and include laboratory studies and age-appropriate cancer screening. Workup for particular symptoms or lab findings should be guided by condition-specific guidelines. Based on symptoms and lab findings, thyroid ultrasound, abdominal/renal ultrasounds, and/or echocardiogram are supported by these guidelines. All patients with CNS symptoms or abnormal pituitary hormones warrant an MRI. A chest x-ray is reasonable in all patients (Gaddey 2014, Alibhai 2005, Metalidis 2007).

A negative baseline evaluation is reassuring; with at least one prospective study showing that no patients with a negative baseline clinical and laboratory evaluation were found to have malignancy on subsequent studies (Metalidis 2007, Gaddey 2014). However, other prospective studies do illustrate that underlying malignancy may be

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

detected on advanced imaging, with the highest predictive value for lung, pancreatic, lymphomas, prostate and colorectal cancers (Bosch 2017, Nicholson 2018). Based on this, these guidelines support contrasted CT chest as part of initial workup for all smokers with clinically significant weight loss. These guidelines also support CT or MRI Abdomen (or CT Abdomen and Pelvis) as part of initial workup for patients age 60+ with clinical significant weight loss and additional signs and symptoms significantly associated with pancreatic cancer (NICE 2015). For all other patients, if the patient has clinically significant unintentional weight loss as defined in paragraph 1, and the initial baseline evaluations above are negative, CT with contrast of the chest, abdomen and pelvis are appropriate and supported by these guidelines (Gaddey 2014, Nicholson 2018, Alibhai 2005).

No published algorithm routinely supports PET/CT in the evaluation of unexplained weight loss, and there are no prospective studies illustrating the sensitivity or specificity of PET in this scenario. There may be patients who meet evidence-based criteria for PET/CT based on their specific signs, symptoms and findings, particularly in the lymphomas (refer to guidelines ONC-27 and 28 and ONC 1.4).

Paraneoplastic Syndromes (ONC-30.3)

ON.MC.0030.3.A
v2.0.2025

- Paraneoplastic syndromes are metabolic and neuromuscular disturbances. These syndromes are not directly related to a tumor or to metastatic disease. There may be a lead time between initial finding of a possible paraneoplastic syndrome and appearance of the cancer with imaging. Limited studies suggest annual imaging for 2 years after diagnosis of possible paraneoplastic syndrome may detect cancer, however benefit after 2 years is not well documented.
- The following are the most common symptoms of paraneoplastic syndromes known to arise from various malignancies:
  - Hypertrophic Pulmonary Osteoarthropathy: Often presents as a constellation of rheumatoid-like polyarthritis, periostitis of long bones, and clubbing of fingers and toes
  - Amyloidosis
  - Hypercalcemia
  - Hypophosphatemia
  - Cushing's Syndrome
  - Somatostatinoma syndrome (vomiting, abdominal pain, diarrhea, cholelithiasis)
  - Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
  - Polymyositis/dermatomyositis
  - Opsoclonus
  - Paraneoplastic sensory neuropathy
  - Subacute cerebellar degeneration
  - Eaton-Lambert syndrome (a myasthenia-like syndrome)
  - Second event of unprovoked thrombosis
  - Disseminated Intravascular Coagulation
  - Migratory thrombophlebitis
  - Polycythemia
  - Chronic leukocytosis and/or thrombocytosis
  - Elevated tumor markers
  - Cryptogenic stroke (see also: **HD-21.3)**
- See: **Muscle Disorders (PN-6)** in the Peripheral Nerve Disorders Imaging Guidelines.
- See: **Multiple Myeloma and Plasmacytomas (ONC-25)** for evaluation of possible multiple myeloma.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Initial evaluation	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast
ANY of the following: • Abnormality on conventional imaging difficult to biopsy • Inconclusive conventional imaging • Documented paraneoplastic antibody and conventional imaging fails to demonstrate primary site	• PET/CT (CPT® 78815 or CPT® 78816)
Subsequent evaluation for known paraneoplastic syndrome	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast may be repeated every 6 months for 2 years after initial imaging for Lambert-Eaton Myasthenia syndrome • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast may be repeated every 6 months for 4 years for all other paraneoplastic syndromes
Systemic mastocytosis	ANY ONE of the following: • CT Abdomen and Pelvis (CPT® 74177) with contrast • MRI Abdomen (CPT® 74183) and MRI Pelvis (CPT® 72197) without and with contrast is indicated • PET/CT scan is not indicated for evaluation of mastocytosis
First episode of unprovoked DVT/VTE	• Imaging to evaluate for malignancy is not indicated
Second unprovoked DVT/PE	• Imaging may be considered in the setting of a negative work-up for inherited thrombophilia and antiphospholipid syndrome
Thyroid US is recommended for elevated CEA, and upper/lower endoscopy is recommended for elevated CEA or CA 19-9.	

Evidence Discussion

Cross sectional imaging with contrasted CT of the chest, abdomen and pelvis is generally considered first-line to look for visceral malignancy in most paraneoplastic syndromes. While sensitivity varies widely (30-82% across studies), specificity is reasonable (71-100%) (Sheikhbahaei 2017). PET/CT is supported in patients with documented paraneoplastic antibodies, inconclusive conventional imaging, or to assess for alternate biopsy sites when an abnormality is found on conventional imaging that is inaccessible for biopsy. The sensitivity and specificity of PET/CT is approximately 80%, when used to evaluate patients who had negative or unclear conventional imaging (Harlos 2019). PET/CT is not supported as first line imaging as PET may miss smaller tumors, and has a false negative rate of approximately 20% in this setting (Sheikhbahaei 2017). While there is a lack of prospective data on monitoring paraneoplastic syndromes, it is known that these phenomena may precede detectable malignancy. In the interest of patient safety, these guidelines support repeat CT imaging every 6 months for 4 years; for Lambert-Eaton Syndrome, 2 years is sufficient as 96% of associated SCLC is detected in the first year, with later reports generally from an era of lesser quality CTs. (Pelosof 2010, Badawy 2023, Titulauer 2011).

Venous thromboembolism in the absence of a hypercoagulable risk factor may suggest occult malignancy. Blood testing, exam and non-advanced imaging have been shown to be helpful in most cancers that present with a first unprovoked DVT, but other advanced imaging is not cost-effective without other symptoms suggesting malignancy in this setting. In the setting of a second unprovoked DVT, cross sectional imaging with contrasted CT may be considered and is supported by eviCore guidelines (Badawy 2023, Rutherford 2007, Schwartzbach 2012).

Systemic mastocyctosis may also develop extramedullary involvement and end-organ dysfunction, particularly involving liver and spleen. CT or MRI of abdomen and pelvis are supported in alignment with the NCCN. There is no NCCN recommendation for PET/CT in systemic mastocytosis.

References (ONC-30)

v2.0.2025

1. Carrier M, Lazo-Langner A, Shivakumar S, et al. Screening for occult cancer in unprovoked venous thromboembolism. *N Engl J Med*. 2015 June;373:697-704. doi:10.1056/NEJMoa1506623.
2. Sioka C, Fotopoulos A, Kyritsis AP. Paraneoplastic neurological syndromes and the role of PET imaging. *Oncology.* 2010;78(2):150–156. doi:10.1159/000312657.
3. Schramm N, Rominger A, Schmidt C, et al. Detection of underlying malignancy in patients with paraneoplastic neurological syndromes: comparison of 18F-FDG PET/CT and contrast-enhanced CT. *Eur J Nucl Med Mol Imaging*. 2013;40(7):1014-1024. doi:10.1007/s00259-013-2372-4.
4. Qiu L, Chen Y. The role of 18F-FDG PET or PET/CT in the detection of fever of unknown origin. *Eur J Radiol*. 2012;81(11):3524-3529. doi:10.1016/j.ejrad.2012.05.025.
5. Pelosof LC, Gerber DE. Paraneoplastic syndromes: an approach to diagnosis and treatment. *Mayo Clin Proc*. 2010;85(9):838-854. doi:10.4065/mcp.2010.0099.
6. Wong CJ. Involuntary weight loss. *Med Clin North Am.*2014;98(3):625-43. doi:10.1016/j.mcna.2014.01.012.
7. Titulaer MJ, Soffieti R, Dalmau J, et al. Screening of tumours in paraneoplastic syndromes: report of an EFNS task force. *Eur J Neurol.* 2011;18(1):19–e3. doi:10.1111/j.1468-1331.2010.03220.x.
8. Lancaster E. Paraneoplastic disorders. *Continuum (Minneap Minn)*. 2017;23(6, Neuro-oncology):1653-1679. doi:10.1212/CON.0000000000000542.
9. Gerds AT, Gotlib J, Abdelmessieh P, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – April 24, 2024. Systemic Mastocytosis, available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Systemic Mastocytosis V3.2024 – April 2, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
10. Saver JL. Cryptogenic stroke. *N Engl J Med.* 2016;374:2065-2074. doi:10.1056/NEJMcp1503946.
11. Schwarzbach CJ, Schaefer A, Ebert A, et. al. Stroke and cancer: the importance of cancer-assocaited hypercoagulation as a possible stroke etiology. *Stroke*. 2012;43(11):3029-3034. doi:10.1161/STROKEAHA.112.658625.
12. Kamel H, Merkler AE, Iadecola C, Gupta A, Navi B. Tailoring the approach to embolic stroke of undetermined source: a review. *JAMA Neurol*. 2019;76(7):855-861. doi:10.1001/jamaneurol.2019.0591.
13. National Institute for Health and Care Excellence (NICE). Upper gastroinestinal tract cancers. In: Suspected cancer: recognition and referral. 2015. https://www.nice.org.uk/guidance/ng12/chapter/Recommendations-organised-by-site-of-cancer#upper-gastrointestinal-tract-cancers.
14. David A, Quinlan JD. Fever of unknown origin in adults. *Am Fam Physician*. 2022;105(2):137-143.
15. Wright WF, Auwaerter PG. Fever and fever of unknown origin: review, recent advances, and lingering dogma. *Open Forum Infect Dis*. 2020;7(5):ofaa132. doi:10.1093/ofid/ofaa132.
16. Bleeker-Rovers CP, Vos FJ, de Kleijn EMHA, et al. A prospective multicenter study on fever of unknown origin: the yield of a structured diagnostic protocol. *Medicine (Baltimore)*. 2007;86(1):26-38. doi:10.1097/MD.0b013e31802fe858.
17. Bleeker-Rovers CP, Vos FJ, Mudde AH, et al. A prospective multi-centre study of the value of FDG-PET as part of a structured diagnostic protocol in patients with fever of unknown origin. *Eur J Nucl Med Mol Imaging*. 2007;34(5):694-703. doi:10.1007/s00259-006-0295-z.
18. Hayakawa K, Ramasamy B, Chandrasekar PH. Fever of unknown origin: an evidence-based review. *Am J Med Sci*. 2012;344(4):307-16. doi:10.1097/MAJ.0b013e31824ae504.
19. Minamimoto R. Optimal use of the FDG-PET/CT in the diagnostic process of fever of unknown origin (FUO): a comprehensive review. *Jpn J Radiol*. 2022;40(11):1121-1137. doi:10.1007/s11604-022-01306-w.
20. Palestro CJ, Brandon DC, Dibble EH, Keidar Z, Kwak JJ. FDG PET in evaluation of patients with fever of unknown origin: AJR expert panel narrative review. *AJR Am J Roentgenol*. 2023;221(2):151-162. doi:10.2214/AJR.22.28726.

21. Takeuchi M, Dahabreh IJ, Nihashi T, Iwata M, Varghese GM, Terasawa T. Nuclear imaging for classic fever of unknown origin: meta-analysis. *J Nucl Med.* 2016;57(12):1913-1919. doi:10.2967/jnumed.116.174391.
22. Kan Y, Wang W, Liu J, Yang J, Wang Z. Contribution of 18F-FDG PET/CT in a case-mix of fever of unknown origin and inflammation of unknown origin: a meta-analysis. *Acta Radiol*. 2019;60(6):716-725. doi:10.1177/0284185118799512.
23. Gaddey HL, Holder K. Unintentional weight loss in older adults. *Am Fam Physician*. 2014;89(9):718-22.
24. Nicholson BD, Hamilton W, O'Sullivan J, Aveyard P, Hobbs FR. Weight loss as a predictor of cancer in primary care: a systematic review and meta-analysis. *Br J Gen Pract*. 2018;68(670):e311-e322. doi: 10.3399/bjgp18X695801.
25. Bosch X, Monclús E, Escoda O, et al. Unintentional weight loss: Clinical characteristics and outcomes in a prospective cohort of 2677 patients. *PLoS One*. 2017;12(4):e0175125. doi:10.1371/journal.pone.0175125.
26. Alibhai SM, Greenwood C, Payette H. An approach to the management of unintentional weight loss in elderly people. *CMAJ*. 2005;172(6):773-80. doi:10.1503/cmaj.1031527.
27. Metalidis C, Knockaert DC, Bobbaers H, Vanderschueren S. Involuntary weight loss. Does a negative baseline evaluation provide adequate reassurance? *Eur J Intern Med*. 2008;19(5):345-9. doi:10.1016/j.ejim.2007.09.019.
28. National Institute for Health and Care Excellence (NICE). Upper gastroinestinal tract cancers. In: Suspected cancer: recognition and referral. 2015. https://www.nice.org.uk/guidance/ng12/chapter/Recommendations-organised-by-site-of-cancer#uppergastrointestinal-tract-ca.
29. Harlos C, Metser U, Poon R, MacCrostie P, Mason W. 18 F-Fluorodeoxyglucose positron-emission tomography for the investigation of malignancy in patients with suspected paraneoplastic neurologic syndromes and negative or indeterminate conventional imaging: a retrospective analysis of the Ontario PET Access Program, with systematic review and meta-analysis. *Curr Oncol*. 2019;26(4):e458-e465. doi:10.3747/co.26.4583.
30. Pelosof LC, Gerber DE. Paraneoplastic syndromes: an approach to diagnosis and treatment. *Mayo Clin Proc*. 2010;85(9):838-54. doi:10.4065/mcp.2010.0099.
31. Badawy M, Revzin MV, Consul N, et al. Paraneoplastic syndromes from head to toe: pathophysiology, imaging features, and workup. *Radiographics*. 2023;43(3):e220085. doi:10.1148/rg.220085.
32. Sundermann B, Schröder JB, Warnecke T, et al. Imaging workup of suspected classical paraneoplastic neurological syndromes: a systematic review and retrospective analysis of 18F-FDG-PET-CT. Acad Radiol. 2017;24(10):1195–1202.
33. Sheikhbahaei S, Marcus CV, Fragomeni RS, Rowe SP, Javadi MS, Solnes LB. Whole-Body 18F-FDG PET and 18F-FDG PET/CT in patients with suspected paraneoplastic syndrome: a systematic review and meta-analysis of diagnostic accuracy. *J Nucl Med*. 2017;58(7):1031–1036.
34. Titulaer MJ, Soffieti R, Dalmau J, et al. Screening of tumours in paraneoplastic syndromes: report of an EFNS task force. *Eur J Neurol*. 2011;18(1):19–e3. doi:10.1111/j.1468-1331.2010.03220.x.
35. Rutherford GC, Dineen RA, O'Connor A. Imaging in the investigation of paraneoplastic syndromes. *Clin Radiol*. 2007;62(11):1021–1035.
36. Schwarzbach CJ, Schaefer A, Ebert A, et. al. Stroke and cancer: the importance of cancer-associated hypercoagulation as a possible stroke etiology. *Stroke*. 2012;43(11):3029-3034. doi:10.1161/STROKEAHA.112.658625.3.

Metastatic Cancer, Carcinoma of Unknown Primary Site, and Other Types of Cancer (ONC-31)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

General Guidelines (ONC-31.0)

ON.UP.0031.0.A

v2.0.2025

- Guideline sections **Lung Metastases (ONC-31.1)** through **Bone (Non-Vertebral) Metastases (ONC-31.5)** should only be used for individuals with metastatic cancer in the following circumstances:
  - The primary diagnosis section does not address a particular metastatic site that is addressed in these sections.
  - The cancer type is rare and does not have its own diagnosis-specific imaging guidelines.

Lung Metastases (ONC-31.1)

ON.UP.0031.1.A
v2.0.2025

Indication	Imaging Study
New or worsening signs or symptoms suggestive of metastatic lung involvement or new or worsening chest x-ray abnormality	• CT Chest with contrast (CPT® 71260) • CT Chest without contrast (CPT® 71250) can be approved if there is a contraindication to CT contrast or only parenchymal lesions are being evaluated
Chest wall or brachial plexus involvement	• MRI Chest without and with contrast (CPT® 71552)
ONE of the following **and** no diagnosis-specific guideline regarding PET imaging: • Lung nodule(s) ≥8 mm • Confirm solitary metastasis amenable to resection on conventional imaging	• PET/CT (CPT® 78815) • When primary cancer known, PET request should be reviewed by primary cancer guideline
Previous or current malignancy and pulmonary nodule(s) that would reasonably metastasize to the lungs	• CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) at 3, 6, 12, and 24 months from the first study

Evidence Discussion

All patients with a history of cancer who have new signs or symptoms suggestive of metastatic disease to the lung, or who have new or worsening findings on chest x-ray, warrant CT chest. Contrast is preferable in most scenarios to include evaluation of soft tissue and nodes, but a non-contrast study may be approved if there is a contraindication to contrast or if only parenchymal lung lesions are being evaluated. CT with contrast (or without if for parenchymal lesion only) is supported to follow up new lung nodules in patients with a history of malignancy (Christensen 2024). There is, however, no clear consensus on a time line for this follow up across all malignancy types. Where guidance is not provided in the disease-specific guidelines, these guidelines suggest a follow up time line of CT at 3,6,12 and 24 months from discovery of nodule, extrapolating from Fleischner and Lung-RADS data that a nodule stable >24 months is exceedingly unlikely to be malignant (MacMahon 2017, Christensen 2024). MRI with and without contrast is supported for suspected malignant infiltration of the

brachial plexus or chest wall infiltration, for better soft tissue delineation (Szaro 2021, 2022).

PET/CT is generally addressed in the guidelines for each specific cancer. If no specific guidance is provided, PET/CT is supported for lung nodules greater than or equal to 8mm (MacMahon 2017). In the interest of patient safety to prevent futile invasive procedures on patients with occult metastatic disease, PET/CT is also supported by these guidelines to confirm solitary metastasis on conventional imaging that may be amenable to curative-intent resection. PET/CT surveillance is not generally supported due to high radiation exposure, financial toxicity, and excess radiation exposure.

Liver Metastases (ONC-31.2)

ON.UP.0031.2.A
v2.0.2025

- Yitrium-90 Radioembolization (Y90-RE) is also known either as Selective Internal Radiation Therapy (SIRT) or trans-arterial radioembolization (TARE). (Y90-RE) is indicated for inoperable hepatocellular carcinoma and metastatic disease to the liver. Yitrium-90 resin or glass microsphere is injected into the hepatic vessel which supplies the tumor bed. This delivers high radiation dose to the tumor selectively.
- Yitrium-90 Radioembolization consists of three parts:

1. The pre-treatment planning angiogram with Technetium 99m macroaggregated albumin (Tc-MAA). The TcMAA acts as surrogate for biodistribution of application of Y-90. Planar or SPECT/CT are performed for calculation of lung shunt fraction and identification of extra hepatic uptake. The assessment of hepatopulmonary shunt is important in the determination eventual radiation dose. Presence of extra-hepatic uptake may preclude treatment or require coil embolization.
2. Yitrium-90 Radioembolization treatment typically done 7-10 days after mapping.
3. Post-treatment imaging may be done to confirm tumor localization.

- Ablation of liver metastases or primary HCC may be performed utilizing chemical, chemotherapeutic, radiofrequency, or radioactive isotope. Regardless of the modality of ablation, PET is not indicated for assessing response to this mode of therapy.

Indication	Imaging Study
New or worsening signs or symptoms suggestive of metastatic liver involvement or new elevation in LFTs	• CT Abdomen with (CPT® 74160) or without and with (CPT® 74170) contrast
ANY of the following: • Considering limited resection • Inconclusive CT findings	• MRI Abdomen without and with contrast (CPT® 74183)

Indication	Imaging Study
ONE of the following **and** no diagnosis-specific guideline regarding PET imaging: • Confirm solitary metastasis amenable to resection on conventional imaging • LFT's and/or tumor markers continue to rise and CT and MRI are negative	• PET/CT (CPT® 78815) ◦ When primary cancer known, PET request should be reviewed by primary cancer guideline
Monitoring of liver metastases that have been surgically resected	• Review according to primary cancer guideline
Evaluation of hepatic artery chemotherapy infusion or TACE (transarterial chemoembolization)	• CTA Abdomen (CPT® 74175) is indicated immediately prior to embolization ONE of the following studies immediately prior to and one month post-embolization, if not previously done: • CT Abdomen without and with contrast (CPT® 74170) • MRI Abdomen without and with contrast (CPT® 74183)

Indication	Imaging Study
Evaluation for hepatic artery radioembolization with Y-90 radioactive spheres (TheraSphere or SIR Spheres) for liver metastases or primary liver tumors	<u>To assess hepatic vascular anatomy before the procedure, any ONE of the following</u>: • 3D Rendering (CPT® 76377) if conventional hepatic angiogram is being performed • CTA Abdomen (CPT® 74175) <u>ONE of the following studies may be approved PRE-treatment based upon provider preference</u>: • Radiopharmaceutical Localization Limited Area (CPT® 78800 or CPT® 78801) • SPECT or SPECT/CT (CPT® 78803, 78831, 78830, or 78832) • CPT® 78835 may be approved as an add-on code with SPECT/CT codes only (CPT® 78803, 78831, 78830, or 78832) for calculation of lung shunt fraction if planar imaging (CPT® 78800 or CPT® 78801) not performed. Liver-lung shunt calculation is included in planar scans and does not require additional Lung Perfusion Scan <u>ONE of the following studies may be approved POST-treatment based upon provider preference</u>: • Radiopharmaceutical Localization Limited Area (CPT® 78800 or CPT® 78801) • SPECT or SPECT/CT (CPT® 78803, 78831, 78830, or 78832)
Monitoring of ablated liver metastases or primary tumors	<u>ONE of the following, immediately prior to ablation, 1 month post-ablation, then every 3 months for 2 years, and then every 6 months until year 5</u>: • CT Abdomen without and with contrast (CPT® 74170) • MRI Abdomen without and with contrast (CPT® 74183)

Evidence Discussion

For patients with known malignancy with new symptoms suggestive of metastatic liver involvement or increase in LFTs, these guidelines support CT of the abdomen

with contrast or with and without contrast as first line imaging. This helps differentiate vascular enhancement patterns, number of lesions, and associated abdominal findings. If the CT remains indeterminate, MRI with and without contrast is supported as MRI enables better characterization of the internal features of the lesion (Gore 2017, Maino 2023). For patient safety, MRI is also supported if limited resection is being considered.

PET/CT is less specific than conventional imaging for liver lesions, and is not first line to clarify indeterminate liver findings on CT (Gore 2017). However, if LFTs or tumor markers continue to rise and CT and MRI are negative, PET/CT may be used as a problem-solving tool to look for occult metastatic disease (Gore 2017). In the interest of patient safety, if a curative-intent resection of a liver lesion is planned, PET/CT may be used to confirm the liver metastasis is solitary to prevent subjecting the patient to a futile resection.

Imaging is indicated to evaluate for hepatic artery chemotherapy infusion or transarterial chemoembolization (TACE). Either CT or or MRI with and without contrast may be used for this purpose, per provider preference based on individual tumor characteristics, per the logic note in paragraph 1. These guidelines for imaging for radioembolization align with international working group TheraSphere Global Dosimetry Steering Committee (DSC) recommendations (Salem 2023). Vascular mapping prior to radioembolization with CTA abdomen (with 3d rendering if requested), as well as a single nuclear medicine liver planar study or SPECT/SPECT-CT study, based on provider preference and individual tumor characteristics (Salem 2023). Liver-lung shunt calculations can generally be calculated from pre-treatment scans and an addition lung perfusion scan is not generally supported (Salem 2023). The nuclear imaging used pre-treatment is supported once post-treatment, and cross sectional imaging with CT or MRI to evaluate response is supported 1 month post treatment (Salem 2023).

Monitoring of ablated liver tumors, metastatic or primary, is with cross sectional imaging with CT or MRI abdomen, with and without contrast, per provider preference based on patient and tumor characteristics. In alignment with the NCCN hepatocellular carcinoma surveillance recommendations, this guideline supports this imaging 1 month post ablation, every 3 months for 2 years, then every 6 months until year 5 (Benson 2024). PET is not routinely supported for follow up for ablated liver lesions, regardless of ablation modality (Benson 2024, Barabasch 2015). The sensitivity of PET is only 65% in this setting, compared with 96% for MRI, and the positive and negative predictive values are also significantly superior for MRI vs PET (Barabasch 2015).

Brain Metastases (ONC-31.3)

ON.UP.0031.3.A
v2.0.2025

Indication	Imaging Study
Individual with cancer and signs or symptoms of CNS disease or known brain metastasis with new signs or symptoms.	• MRI Brain without and with contrast (CPT® 70553)
To determine candidacy for SRS, and a diagnostic thin-slice MRI Brain has not been performed in the preceding 30 days	• MRI Brain without and with contrast (CPT® 70553)
Stereotactic radiosurgery planning	• Unlisted MRI for treatment planning purposes (CPT® 76498)
Monitoring of brain metastases treated with surgery or radiation therapy	Post-treatment, then every 3 months for 1 year and every 6 months thereafter: • MRI Brain without and with contrast (CPT® 70553) ***Individuals treated with stereotactic radiosurgery alone may have MRI Brain without and with contrast (CPT® 70553) immediately after stereotactic radiosurgery, then every 2 months for the first year, and then every 6 months thereafter
Brain metastases treated with radiation therapy, with recent MRI Brain indeterminate in distinguishing radiation necrosis vs. tumor progression	• MRI Perfusion imaging (CPT® 70553)

Indication	Imaging Study
Brain metastases treated with radiation therapy, with recent MRI Brain and MR Perfusion studies both unable to distinguish radiation necrosis vs. tumor progression	• PET Metabolic Brain (CPT® 78608)
Any of the following: • Solitary brain metastasis suspected in individual with prior diagnosis of cancer and no diagnosis-specific guideline regarding PET imaging • Brain metastases and no known primary tumor	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • Mammography for female individuals • PET/CT (CPT® 78815 or CPT® 78816) is indicated for ANY of the following: ◦ Inconclusive conventional imaging ◦ Confirm either stable systemic disease or absence of other metastatic disease ◦ When primary cancer known, PET request should be reviewed by primary cancer guideline
Primary brain tumors	See: **Primary Central Nervous System Tumors (ONC-2)**
MR Spectroscopy (CPT® 76390) is considered not medically necessary for evaluation of metastatic brain cancer	

Evidence Discussion

Brain metastases are the most common malignant intracranial tumors with an incidence 10-fold higher than primary central brain tumors. Common presenting signs and symptoms of brain metastases include headache, nausea, vomiting, focal neurologic deficits, and mental status changes. The most common cancer associated with brain metastases is lung cancer approaching 50% of the cases. Melanoma is associated with the highest incidence of brain metastases.

These guidelines support MRI Brain without and with contrast as the standard imaging modality for evaluation of an individual with suspected or known brain metastases. The post-treatment monitoring after surgery or radiation is based on NCCN guidelines. Specifically for stereotactic radiosurgery planning, a diagnostic MRI is not supported and the MRI request is based on an unlisted procedure code. Advanced imaging with MR perfusion imaging is a problem-solving tool, complementing a standard MRI Brain, to distinguish between radiation necrosis and tumor progression. PET Metabolic Brain

imaging is a useful tool to distinguish between radiation necrosis and tumor progression with recent indeterminate MRI Brain and MR Perfusion study.

In individuals who present with brain metastases and no known primary tumor, an evaluation to define a primary cancer is supported. Imaging studies that are supported include CT Chest and CT Abdomen and Pelvis with contrast. Mammography is supported for this staging in female individuals. PET/CT is indicated for inconclusive standard imaging, for evaluation of other metastatic disease or for staging if supported by primary cancer guideline. Biopsy or resection of a suspicious lesion is needed to establish a definitive diagnosis.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Adrenal Gland Metastases (ONC-31.4)

ON.UP.0031.4.A
v2.0.2025

Indication	Imaging Study
Differentiate benign adrenal adenoma from metastatic disease	• See: **Adrenal Cortical Lesions (AB-16.1)** in the Abdomen Imaging Guidelines
Known cancer and no known systemic metastases: • New adrenal mass • Enlarging adrenal mass • Inconclusive findings on recent CT	If not done previously, ANY of the following may be obtained: • CT Abdomen without contrast (CPT® 74150) • CT Abdomen without and with contrast (CPT® 74170, adrenal protocol) • MRI Abdomen without contrast (CPT® 74181) • MRI Abdomen without and with contrast (CPT® 74183) • CT-directed needle biopsy (CPT® 77012)
One of the following and no diagnosis-specific guideline regarding PET imaging: • Biopsy is not feasible or is non-diagnostic • Isolated metastasis on conventional imaging and individual is a candidate for aggressive surgical management	• PET/CT (CPT® 78815) When primary cancer known, PET request should be reviewed by primary cancer guideline
Known extra-adrenal malignancy and undiagnosed adrenal mass being monitored off treatment	See: Phases of **Oncology Imaging and General Phase-Related Considerations (ONC-1.2)**

Evidence Discussion

In patients with known extra-adrenal malignancy and no known systemic metastatic disease who have been found to have a new, enlarging or inconclusive adrenal mass

on other imaging, a non-contrast CT adrenal protocol or CT abdomen with and without contrast adrenal protocol or an MRI abdomen without or without and with contrast are all supported by ACR appropriateness criteria (Mody 2021). Non-contrast images allow for initial attenuation measurements, but contrast-enhanced images with imaging for washout characteristics can help differentiate adenomas from metastatic disease (Mody 2021, Mayo-Smith 2017). Non-contrast chemical shift MRI can help detect intracytoplasmic fat, providing insight into benign vs malignant characteristics, but post-contrast imaging adds further specificity for adenoma (Mody 2021, Mayo-Smith 2017). CT-directed needle biopsy may also be appropriate and is supported by the guidelines if requested (Mody 2021, Mayo-Smith 2017).

The utility of PET-CT varies with histology and type of radiotracer. Generally, the use of PET-CT for a given malignancy is addressed in the disease-specific guidelines. For lesions with no known history of malignancy, there is no primary evidence supporting the use of FDG PET-CT for initial evaluation (Mody 2021). In one study of 1,049 incidental adrenal masses in patients with no known history of cancer, zero were malignant (Song 2008). Mild SUV uptake can also be seen in benign adenomas, bringing the sensitivity of PET-CT to only 85% (Vikram 2008, Metser 2006, Mody 2021). False-positive interpretations potentially result in unnecessary invasive procedures. When other adrenal-specific cross sectional imaging is suspicious for malignancy by size and other criteria, biopsy is preferred. If a biopsy is not feasible or non-diagnostic, PET-CT may show increased SUV uptake in malignant lesions and guide further decision making, and is supported by the ACR in this context (Mody 2021, Mayo-Smith 2017).

Bone (Non-Vertebral) Metastases (ONC-31.5)

ON.UP.0031.5.C
v2.0.2025

Indication	Imaging Study
ANY of the following in an individual with a current or prior malignancy: • Bone pain • Rising tumor markers • Elevated alkaline phosphatase	• Bone scan (CPT® 78306) supplemented by plain x-rays is the initial diagnostic imaging study of choice
Individuals ≥40 years of age with symptomatic bone lesion seen on x-ray	EITHER of the following: • CT Chest with contrast (CPT® 72160), CT Abdomen and Pelvis with contrast (CPT® 74177) and Bone Scan (CPT® 78306) OR • FDG PET/CT (CPT® 78815 or CPT® 78816)
ANY of the following: • Bone scan is not feasible or readily available • Bone scan is equivocal or indeterminate • Continued suspicion despite negative/ inconclusive bone scan or other imaging modalities • Soft tissue component suspected on other imaging modalities • Differentiate neoplastic disease from Paget's disease of the bone	ANY one of the following: • MRI without and with contrast of the involved body site • CT without contrast or with contrast of the involved body site
Bone metastases suspected and **both** bone scan and either CT or MRI are inconclusive	• ^{18}F-FDG-PET/CT (CPT® 78815 or CPT® 78816)

Indication	Imaging Study
Suspected metastatic bone disease and negative work-up for myeloma	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast
No prior cancer history with suspected bone metastatic disease or pathologic fracture on plain x-ray	• See: **Carcinoma of Unknown Primary Site (ONC-31.7)**

Evidence Discussion

Bone scan supplemented by plain x-ray is the generally the first-line modality for patients with current or history of malignancy who have new bone pain, rising tumor markers or elevated alkaline phosphatase. Bone scan is 79-86% sensitive and 81-88% specific for metastatic lesions (Yang 2011, Qu 2012). Bone scan allows rapid whole skeletal evaluation, to ensure additional bony disease is not missed by focusing on a single site of cross-sectional imaging. MRI is a useful problem-solving tool if there is continued suspicion for bony metastatic disease with a negative bone scan (DiPrimio 2023, Yang 2011). MRI is supported when a soft tissue component is suspect to avoid understaging and undertreatment (ACR 2024, DiPrimio 2023). MRI is also the most specific study to supplement plain x-ray to differentiate Paget disease of bone from neoplastic disease (Lombardi, 2022).

MRI is more accurate than CT or bone scan for the evaluation of malignant vertebral compression fractures and additionally can assess for cord compression, edema or leptomeningeal disease (Liu 2017). Patients with known stage IV cancer with new back pain or any sings of neurologic compromise may be immediately evaluated by MRI of the whole spine without or without and with contrast (ACR 2024, Liu 2017). MRI is also indicated for suspected leptomeningeal disease (ACR 2024, Liu 2017). CT has the lower accuracy than MRI or bone scan in this setting and is only supported when MRI is contraindicated (Liu, 2017). New leptomeningeal disease should prompt an MRI of the brain for complete neuroaxis imaging.

Where imaging is suspicious for bony metastatic disease and a workup for multiple myeloma is negative, CT chest, abdomen and pelvis with contrast are supported to look for a primary malignancy (Piccoli 2015).

The sensitivity and specificity of FDG PET/CT for bony metastatic disease varies with the malignancy. For example, for breast cancer, PET may be more sensitive (96% vs 76% for bone scan), but may be less specific (92% vs 95% for bone scan). However for some cancers sensitivity of PET is as low as 56% (Liu 2017, Qu 2012). Given this variability, PET/CT is supported as a problem-solving tool when both bone scan and MRI or CT are inconclusive. NCCN does support the use of FDG PET/CT specifically in

individuals who are 40 years of age or older and who have a symptomatic bone lesion with an abnormal x-ray (Bierrman, 2025). These guidelines allow the flexibility of using FDG PET/CT in this specific scenario if it is desire in lieu of diagnostic CT and bone scan. NaF PET is considered investigational due to varying sensitivity and specificity (Zhang-Yin 2023, Ahmed 2022).

Spinal/Vertebral Metastases (ONC-31.6)

ON.UP.0031.6.A
v2.0.2025

- Individuals with stage IV cancer with new onset back pain can forgo a bone scan (and plain films) in lieu of an MRI with and without contrast of the spine.

Indication	Imaging Study
Known cancer history and spinal cord compression suspected based on signs/ symptoms of neurological compromise, including, but not limited to: • Unexpected, sudden loss of bowel or bladder control • Sudden loss of ability to ambulate • Complete loss of pinprick sensation corresponding to a specific vertebral level • Loss of pain at a site that had previously been refractory to pain management	MRI Cervical (CPT® 72156), MRI Thoracic (CPT® 72157), and MRI Lumbar Spine (CPT® 72158) without and with contrast OR without contrast • CT Cervical (CPT® 72126), CT Thoracic (CPT® 72129), and CT Lumbar (CPT® 72132) Spine if MRI is contraindicated
Individual with a known history of cancer and ANY of the following: • Metastatic or stage IV cancer with new or worsening back pain • Back pain and suspicion of spinal malignancy based on any one of the following: ◦ Night pain ◦ Age >70 years ◦ Uncontrolled or unintentional weight loss ◦ Pain unrelieved by change in position ◦ Severe or worsening spinal pain	ONE of the following: • MRI of the relevant spinal level without contrast • MRI of the relevant spinal level without and with contrast • CT of the relevant spinal level without contrast • CT Myelogram of the relevant spinal level

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Monitoring untreated vertebral metastases	One of the following, every 3 months for 1 year: • MRI without and with contrast of the involved spinal level • CT without or with contrast of the involved spinal level **Imaging beyond 1 year is based on any new clinical signs/symptoms
Monitoring metastases within the spine treated with surgery and/or radiation therapy	One of the following, once within 3 months post-treatment, and then every 3 months for 1 year: • MRI without and with contrast of the involved spinal level • CT without or with contrast of the involved spinal level **Imaging beyond 1 year is based on any new clinical signs/symptoms

Indication	Imaging Study
Leptomeningeal involvement with cancer	Suspected: • MRI Brain without and with contrast (CPT® 70553) and MRI Cervical (CPT® 72156), Thoracic (CPT® 72157), and Lumbar spine (CPT® 72158) without and with contrast • CT Cervical (CPT® 72127), Thoracic (CPT® 72130), and Lumbar Spine (CPT® 72133) without and with contrast can be approved if MRI is contraindicated or not readily available On active treatment: • MRI Brain without and with contrast (CPT® 70553) and MRI Cervical (CPT® 72156), Thoracic (CPT® 72157), and Lumbar spine (CPT® 72158) without and with contrast every 2 cycles • CT with or without contrast of the involved spinal level if MRI is contraindicated Once treatment completed: • Routine advanced imaging not indicated for surveillance in asymptomatic individuals

Evidence Discussion

The incidence of malignant cord compression varies with cancer type but is rarely the first sign of systemic cancer. Back pain is the most common presenting symptoms and is reported in 80-95% of patients. Pain is often refractory to traditional pain medications. Sensory and motor deficits occur in 35-75% of patients, and acute bowel/bladder dysfunction are other red flags for cord compression. Up to 35% of patients have multiple levels of compression, which may be non-contiguous, and as such where symptoms as above suggest cord compression in a patient with a history of malignancy, imaging of the whole spine is warranted. MRI with and without contrast has a sensitivity and specificity of 93 and 97 percent respectively. ACR appropriateness criteria state CT myelogram 'may be appropriate' in this setting, and it may be faster to obtain, and may be necessary to plan surgical intervention, and thus is also supported by these guidelines for suspected malignant cord compression.

Some patients will present with more localized symptoms suggestive of localized nerve root involvement but not consistent with the above symptoms of cord compression. Unilateral symptoms suggest a lower motor neuron lesion. Other symptoms suggestive of nerve root involvement are night pain, refractory pain, and pain unrelieved by a change in position. Elderly patients with a cancer history are also at higher risk for nerve root involvement. Unintentional weight loss without other localizing symptoms may also suggest nerve root involvement. Aligning with ACR appropriateness criteria, in patients with a history of malignancy with any of the above, MRI without and with contrast of the involved spinal level of symptoms is supported. CT is less sensitive than MRI in this setting and is supported only when MRI is contraindicated.

Carcinoma of Unknown Primary Site (ONC-31.7)

ON.UP.0031.7.C
v2.0.2025

General Considerations

- Defined as carcinoma found in a lymph node or in an organ known not to be the primary for that cell type (e.g., adenocarcinoma arising in the brain or in a neck lymph node).
- This guideline also applies to a pathologic fracture that is clearly due to metastatic neoplastic disease in an individual without a previous cancer history.
- Detailed history and physical examination including pelvic and rectal exams and laboratory tests to be performed before advanced imaging.
- Individuals presenting with a thoracic squamous cell carcinoma described as metastatic appearing on chest imaging, or in lymph nodes above the clavicle, should undergo a detailed head and neck examination by a clinician skilled in laryngeal and pharyngeal examinations, especially in smokers.
- Individuals with suspected unknown primary based on only suspicious lytic bone lesions should be considered for serum protein electrophoresis (SPEP); urine protein electrophoresis (UPEP) and serum free light chains prior to consideration of extensive imaging.

Indication	Imaging Study
Carcinoma found in a lymph node or in an organ known not to be primary	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • CT Neck with contrast (CPT® 70491) if cervical or supraclavicular involvement • CT with contrast or MRI without and with contrast of any other symptomatic site • For female individuals: ◦ Diagnostic (not screening) mammogram and full pelvic exam ◦ MRI Breast Bilateral (CPT® 77049) if pathology consistent with breast primary and mammogram is inconclusive

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Sebaceous carcinoma of the skin (can be associated with underlying primary malignancy)	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • CT Neck with contrast (CPT® 70491) if cervical or supraclavicular involvement • CT with contrast or MRI without and with contrast of any other symptomatic site
Axillary adenocarcinoma	• Diagnostic (not screening) mammogram and full pelvic exam • MRI Breast Bilateral (CPT® 77049) if pathology consistent with breast primary and mammogram is inconclusive • If the above are non-diagnostic for primary site: ◦ CT Neck (CPT® 70491), CT Chest (CPT® 71260), and CT Abdomen (CPT® 74160) with contrast ◦ CT with contrast or MRI without and with contrast of any other symptomatic site
Carcinoma found within a bone lesion	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis with contrast (CPT® 74177) • Bone Scan (CPT® 78306) • CT with contrast or MRI without and with contrast of any symptomatic site
ANY of the following: • Above studies have failed to demonstrate site of primary • CT scans reveal isolated metastatic disease for which definitive curative therapy is planned	• PET/CT (CPT® 78815 or CPT® 78816)
Post-treatment surveillance	• Advanced imaging is not indicated for routine surveillance of asymptomatic individuals after treatment completion

Evidence Discussion

Carcinoma of unknown primary site (CUP) is defined as carcinoma found in a lymph node or in an organ known not to be the primary for that cell type (e.g., adenocarcinoma arising in the brain or in a neck lymph node). This guideline also applies to a pathologic

fracture that is clearly due to metastatic neoplastic disease in an individual without a previous cancer history. Individuals with suspected unknown primary based on only suspicious lytic bone lesions should be considered for serum protein electrophoresis (SPEP); urine protein electrophoresis (UPEP) and serum free light chains prior to consideration of extensive imaging.

CUP generally occurs in older adults, the majority 6-75 years, and accounts for 2-9% of all tumors. Median survival is poor, at 3-10 months. 20% of patients fall into a more favorable risk group with median survival >1 year, and imaging may help identify this group (Kramer 2022, Stevenson 2024). The primary step in workup of CUP, before advanced imaging, is a detailed history and physical examination including pelvic and rectal exams and laboratory tests, including basic CBC/Chemistries/LFTS but also tumor markers, immunohistochemistry, and PSA (for men over 40). Endoscopy should also be considered if pathology suggests a GI primary. CT of the chest, abdomen and pelvis with contrast is supported for all individuals where primary site is not suggested on physical and lab evaluation, in alignment with NCCN and the European Society of Medical Oncology (ESMO) (Stevenson 2024, Kramer 2022). CT neck may be included if cervical or supraclavicular involvement, as well as CT or MRI for other symptomatic sites or abnormal sites on physical, with the choice of modality driven by body site of interest. If the site of carcinoma is a bone lesion that is not consistent with multiple myeloma, a bone scan should be added to the workup. Morphology on bone scan can help determine the primary site, where lytic lesions are most suggestive of myeloma, renal cell, GI and melanoma, and blastic lesions most commonly occur with prostate cancer and GI carcinoid. Other morphologic features such as location and expansile nature can also help guide workup and treatment toward a particular primary site. (Piccioli 2015). PET/CT has not been shown to be superior to bone scan for this purpose, and in fact may be less sensitive than bone scan for lesions <1cm (Piccioli 2015, Stevenson 2024)

It is essential that female patients have a diagnostic (not screening), mammogram and full pelvic exam. If pathology is consistent with breast cancer from axillary node or other metastatic site, but mammogram is inconclusive, a bilateral breast MRI with and without contrast is supported, as MRI may identify the breast as the primary site in approximately half of the patients presenting with axillary adenocarcinoma metastases (Buchanan 2005, Stevenson 2024). If a primary site is still not found, CT Neck, Chest, Abdomen and Pelvis are supported.

These guidelines align with the NCCN and support PET-CT can be used as a problem-solving tool to look for a primary site of disease when the studies described above still do not reveal a primary site (Stevenson 2024). PET is of intermediate specificity in this setting and large randomized trials are lacking (Stevenson 2024). A meta-analysis on the use of PET/CT in patients with CUP found that primary tumors were detected in 37% of 433 patients across 11 studies, with pooled sensitivity and specificity of 84% (Kwee 2009, Stevenson 2024). In addition, if CT scans reveal oligometastatic disease

and definitive curative therapy is planned, the absence of other sites of disease may be confirmed with PET-CT to prevent over- or under-treatment (Kramer 2022, Stevenson 2024).

Subsequent imaging and surveillance should follow the guideline for each primary site, once a likely primary has been established. NCCN states follow-up should be with history and physical with subsequent diagnostic testing based on symptoms. In 20-50% of patients, the primary site remains unidentified even after postmortem examination, thus continued imaging is low-yield and may contribute to the significant distress associated with the uncertainty of this condition (Kramer 2022, Stevenson 2024). There is no data-driven algorithm for imaging surveillance when the primary site of disease remains undiscovered (Stevenson, 2024).

Extrathoracic Small Cell and Large Cell Neuroendocrine Tumors (ONC-31.8)

ON.UP.0031.8.C

v2.0.2025

- All poorly-differentiated or high-grade, small cell and large cell neuroendocrine tumors arising outside the lungs or of unknown primary origin are imaged according to these guidelines.
- For intrathoracic poorly differentiated neuroendocrine cancer, see: **Small Cell Lung Cancer (ONC-7)**

Indication	Imaging Study
Initial staging	ONE of the following combinations: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • CT Chest with contrast (CPT® 71260) and MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)
Inconclusive findings on conventional imaging studies	• PET/CT (CPT® 78815)
ANY of the following: • Poorly differentiated neuroendocrine cancers of the head or neck • Signs or symptoms of CNS involvement	• MRI Brain without and with contrast (CPT® 70553)

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Indication	Imaging Study
Restaging during treatment	ONE of the following combinations, every 2 cycles: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) and any CT of known sites of disease with contrast • CT Chest with contrast (CPT® 71260) and MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197) and CT with contrast of any known sites of disease
Suspected Recurrence	ANY or ALL of the following are indicated: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast or CT Chest with contrast (CPT® 71260) and MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197) • MRI Brain without and with contrast (CPT® 70553) • Bone scan (CPT® 78306) • PET imaging is generally **not** indicated but can be considered for rare circumstances.
Surveillance	ONE of the following combinations every 3 months for 1 year, then every 6 months: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • CT Chest with contrast (CPT® 71260) and MRI Abdomen without and with contrast (CPT® 74183) and MRI Pelvis without and with contrast (CPT® 72197)

Evidence Discussion

Poorly differentiated/high grade neuroendocrine tumors (NET) may occur anywhere in the body and exhibit more aggressive behavior than other neuroendocrine tumors. When these tumors occur in the lung, they are managed like small cell lung cancer and the small-cell lung cancer guidelines apply. This section refers to extrathoracic, poorly-differentiated or high-grade NETs.

Initial Staging

Initial staging with contrasted CT of the chest, abdomen and pelvis is supported, with sensitivity and specificity ranging from 82-100% (Półtorak-Szymczak 2021, Bergsland 2023). Metastatic disease, particularly to the liver, is common with this entity within this setting (Walter 2017, NCI 2024). MRI is equally supported by NCCN for imaging of the abdomen and pelvis. Given the undifferentiated nature of these tumors, dotatate

PET/CT is not routinely supported as they do not consistently have somatostatin receptors, with some studies showing this modality missing 50% of tumors (NCI 2024). Sensitivity and specificity of FDG PET/CT is superior to somatostatin-receptor based imaging for undifferentiated tumors, but is still widely variable and is not supported for first line imaging but may be used as a problem-solving tool when conventional imaging is inconclusive (Bergsland 2023, Kaewput 2022). Poorly differentiated NETs do have a propensity for CNS involvement, and MRI brain with and without contrast is supported for initial staging with head and neck primary site or for any signs and symptoms suggestive of CNS involvement (Bergsland 2023, NCI 2024). Suspected bony metastatic disease may be evaluated using guideline ONC-31.5.

Restaging and suspected recurrence

In alignment with NCCN, conventional imaging may be repeated every 2 cycles of treatment. In the case of suspected recurrence, CT chest, abdomen and pelvis with contrast are supported as well and MRI brain and bone scan, in alignment with NCCN (Bergsland, 2023). FDG PET/CT is not routinely supported in this setting for the reasons cited in the section on initial staging but may be utilized in rare circumstances in the interest of patient safety.

Surveillance

Guidelines support conventional imaging studies every 3 months for the first year, then every 6 months for 4 additional years, then annually indefinitely due to the long-term risk of recurrence in this entity (Walter 2023, NCI 2024, Bergsland 2023).

Primary Peritoneal Mesothelioma (ONC-31.9)

ON.UP.0031.9.A
v2.0.2025

Indication	Imaging Study
Initial staging	• CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • PET/CT (CPT® 78815) if there is no evidence of metastatic disease or conventional imaging is inconclusive
Recurrence/ Restaging	• If there is known prior disease, CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • PET for inconclusive finding on conventional imaging
Surveillance	• CT Abdomen and Pelvis with contrast (CPT® 74177) every 3-6 months for 5 years, then annually until year 10

Evidence Discussion

Contrasted CT of chest, abdomen and pelvis is essential to assess the degree of dissemination, verify that peritoneal disease is not metastatic from another primary site, evaluate lymphadenopathy, and to identify metastatic disease. For primary peritoneal mesothelioma, most patients present with advanced locoregional disease (Magge 2014). Spread into pleural space and local lymph nodes are the primary sites of metastatic disease, with more distant/diffuse metastatic disease much less common (Magge 2024,Yan 2009). Sensitivity of CT is superior to MRI for this entity (Anwar 2024). As with other malignancies, if CT shows a liver lesion indeterminate for metastatic disease, MRI may be used for further assessment per guideline section ONC-31.2. The sensitivity of PET-CT for malignant peritoneal mesothelioma ranges from 58-100%, so it is not a primary imaging tool for staging. However, PET/CT may detect small peritoneal implants that are missed on CT and alter management (Anwar 2024, Ettinger 2024). These guidelines support PET-CT when no metastatic disease is detected on conventional imaging to ensure patients are not under-staged.

Contrasted CT of the abdomen and pelvis are supported for restaging, as sensitivity of CT is superior to MRI for this disease process (Anwar 2024). Given that progression to chest disease is rare (Anwar 2024, Magge 2014), CT chest is supported for restaging only if there is known disease in the chest or if new chest symptoms develop. Given the widely variable sensitivity of PET-CT for peritoneal mesothelioma, it is supported only for inconclusive findings on conventional imaging.

NCCN guidelines and outcome data support contrasted CT of the chest/abdomen/pelvis every 3 months for 2 years then annually until year 10 (Ettinger 2024, Magge 2014). Frequent imaging is supported only within the first two years as 68 percent of recurrences occur within the first 2 years (Magge 2014), then annual imaging moving forward.

Kaposi's Sarcoma (ONC-31.10)

ON.UP.0031.10.A
v2.0.2025

Indication	Imaging Study
Kaposi's Sarcoma	• Advanced imaging is not generally indicated since disease is generally localized to skin. • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast can be approved at initial diagnosis. If initial scans are negative then future imaging would be based on signs or symptoms.

Evidence Discussion

Most Kaposi Sarcoma (KS) is most often confined to skin, however it can sometimes be found in viscera, particularly in HIV-associated disease. To prevent under-staging and to assess the need for systemic therapy, CT of the chest, abdomen and pelvis with contrast are supported at initial diagnosis.

Routine advanced imaging is not supported if there is no visceral disease at diagnosis, but restaging CTs may be approved for patients with visceral disease on systemic therapy per the timeframes offered in ONC-1.2. Contrasted CTs may also be approved to evaluate areas with specific signs and symptoms of new involvement.

There is no data or expert consensus that supports routine surveillance imaging for Kaposi Sarcoma.

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924

Castleman's Disease (Unicentric and Multicentric) (ONC-31.11)

ON.UP.0031.11.A
v2.0.2025

Indication	Imaging Study
Initial staging	• Either CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast **or** PET/CT (CPT® 78815) • CT Neck with contrast (CPT® 70491) if cervical or supraclavicular involvement • If CT scans were utilized initially and suggested unicentric disease, and surgical resection is being considered, PET/CT (CPT® 78815) can be approved to confirm unicentric disease • If unicentric disease is surgically removed, proceed to Surveillance section
Restaging: • Multicentric disease or surgically unresected unicentric disease on chemotherapy	ONE of the following every 2 cycles: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • PET/CT (CPT® 78815)
ANY of the following: • Suspected recurrence • Recurrent B symptoms • Rising LDH/IL-6/ VEGF levels	ONE of the following: • CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast • PET/CT (CPT® 78815)
Surveillance	• CT with contrast of involved areas no more than every 6 months up to 5 years

Evidence Discussion

Initial Staging

PET/CT fusion is supported for initial staging of Castleman's Disease (Zelenetz, 2024). PET/CT not only assesses for multicentric disease, but the SUV can be used to determine Castleman's disease vs frank lymphoma (Dispenzieri, 2020). A diagnostic, contrasted CTs of the chest, abdomen, pelvis as well as neck if suspected neck disease may be substituted for PET/CT, but diagnostic CT is not generally supported concurrently with PET (Zelenetz, 2024). However, if diagnostic CTs were utilized initially and surgical resection is being considered, these guidelines allow a PET/CT to be done subsequently in the interest of patient safety, to confirm unicentric disease and prevent understaging.

Restaging/Recurrence

Unicentric disease that is surgically resected is considered to be in surveillance and imaging follows surveillance guidelines. For multicentric disease or unresected unicentric disease on chemotherapy, disease may be monitored every 2 cycles with contrasted CT of the chest, abdomen and pelvis or PET/CT fusion studies, in alignment with the NCCN. The same imaging is supported for suspected recurrence or labs concerning for development of POEMS-associated MCD or HHV-8 MCD, as these entities are rapidly aggressive (Hoffman 2022, Dispenzieri 2020). Concurrent contrasted diagnostic CTs with PET/CT fusion studies do not generally change management and as such are not supported, nor are concurrent scans suggested by NCCN or international consensus recommendations (Zelenetz 2024, Hoffman 2022, Dispenzieri 2020, VanRhee 2018).

Surveillance

There are no clear consensus guidelines for imaging surveillance of Castleman's Disease. In the interest of patient safety given a multitude of curative treatment options for recurrent disease, these guidelines support surveillance imaging with CT with contrast of involved body areas no more than every 6 months up to 5 years. PET/CT is not supported for surveillance in alignment with ASCO Choosing Wisely campaign.

References (ONC-31)

v2.0.2025

1. Stevenson MM, Bowles DW, Ettinger DS, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – September 11, 2024. Occult primary (Cancer of Unknown Primary [CUP]), available at: https://www.nccn.org/professionals/physician_gls/pdf/occult.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Occult Primary V2.2025 – September 11, 2024 ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
2. Nabors BL, Portnow J, Baehring J, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – January 21, 2025. Central Nervous System Cancers, available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for CNS Cancer V4.2024 – January 21, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
3. Zelenetz AD, Gordon LI, Abramson JS, et al, National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – January 21, 2025. B-cell lymphomas, available at: https://www.nccn.org/professionals/physician_gls/pdf/B-CELL.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for B-cell lymphomas V1.2025 – January 21, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
4. ACR Appropriateness Criteria®*Incidentally discovered adrenal mass.* Rev. 2012.
5. Pawaskar AS, Basu S. Role of 2-fluoro-2-deoxyglucose PET/computed tomography in carcinoma of unknown primary. *PET Clin.* 2015;10(3):297-310. doi:10.1016/j.cpet.2015.03.004.
6. Avram AM. Radioiodine scintigraphy with SPECT/CT: an important diagnostic tool for thyroid cancer staging and risk stratification. *J Nucl Med*. 2012;53(5): 754-764. doi:10.2967/jnumed.111.104133.
7. Mayo-Smith WW, Song JH, Boland GL, et al. Management of incidental adrenal masses: a white paper of the ACR Incidental Findings Committee. *J Am Coll Radiol*. 2017;14(8):1038-1044. doi:10.1016/j.jacr.2017.05.001.
8. Vaidya A, Hamrahian A, Bancos I, Fleseriu M, Ghayee HK. The evaluation of incidentally discovered adrenal masses. *Endocrine Practice*. 2019:25(2);178-192. doi: 10.4158/DSCR-2018-0565.
9. Bergsland E, Rose JB, Benson III AB, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – January 17, 2025. Neuroendocrine and Adrenal Tumors, available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Neuroendocrine and Adrenal Tumors V4.2024 – January 17, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
10. Furuse M, Nonoguchi N, Yamada K, et. al. Radiological diagnosis of brain radiation necrosis after cranial irradiation for brain tumor: a systematic review. *Radiat Oncol*. 2019;14(28). doi:10.1186/s13014-019-1228-x.
11. American College of Radiology. ACR practice parameter for the performance of stereotactic radiosurgery. 2016; https://www.acr.org/-/media/ACR/Files/Practice-Parameters/stereobrain.pdf
12. Soffietti R, Abacioglu U, Baumert B, et. al. Diagnosis and treatment of brain metastases from solid tumors: guidelines from the European Assocation of Neuro-Oncology (EANO). *Neuro-Oncology*. 2017;19(2):162-174. doi:10.1093/neuonc/now241.
13. Mehrabian H, Detsky J, Soliman H, Sahgal A, Stanisz GJ. Advanced magnetic resonance imaging techniques in management of brain metastases. *Front Oncol*. 2019;9(440). doi:10.3389/fonc.2019.00440.

14. Murthy R, Nunez R, Szklaruk J, et. al. Yttrium-90 microsphere therapy for hepatic malignancy: devices, indications, technical considerations and potential complications. *RadioGraphics*. 2005;25:S41–S55. doi:10.1148/rg.25si055515.
15. Lencioni R, Petruzzi P, Crocetti L. Chemoembolization of hepatocellular carcinoma. *Semin Intervent Radiol*. 2013;30(1):3-11. doi:10.1055/s-0033-1333648.
16. Tong AK, Kao YH, Too CW, Chin KF, Ng DC, Chow PK. Yttrium-90 hepatic radioembolization: clinical review and current techniques in interventional radiology and personalized dosimetry. *Br J Radiol*. 2016;89(1062):20150943.
17. Lopez B, Mahvash A, Lam MGEH, Kappadath SC. Calculation of lung mean dose and quantification of error for ^{90}Y-microsphere radioembolization using ^{99m}Tc-MAA SPECT/CT and diagnostic chest CT. *Med Phys*. 2019;46(9):3929-3940.
18. Villalobos A, Soliman MM, Majdalany BS, et al. Yttrium-90 Radioembolization Dosimetry: What trainees need to know. *Semin Intervent Radiol*. 2020;37(5):543-554.
19. Torkian P, Ragulojan R, J Woodhead G, et al. Lung shunt fraction quantification methods in radioembolization: What you need to know. *Br J Radiol*. 2022;95(1139):20220470.
20. Graves SA, Bageac A, Crowley JR, Merlino DAM. Reimbursement Approaches for Radiopharmaceutical Dosimetry: Current Status and Future Opportunities. *J Nucl Med*. 2021;62(Suppl 3):48S-59S.
21. Brenner AW, Patel AJ. Review of current principles of the diagnosis and management of brain metastases. *Front Oncol*. 2022;12:857622.
22. Mitchell DK, Kwon HJ et al. Brain metastases: an update on multi-disciplinary approach of clinical management *Neurochirurgie*. 2022;68(1): 69–85. doi:10.1016/j.neuchi.2021.04.001.
23. PDQ® Adult Treatment Editorial Board. PDQ Kaposi Sarcoma Treatment. Bethesda, MD: National Cancer Institute. Updated 09/21/2023. Available at: https://www.cancer.gov/types/soft-tissue-sarcoma/hp/kaposi-treatment-pdq.
24. Lawton AJ, Lee KA, Cheville AL, et al. Assessment and management of patients with metastatic spinal cord compression: a multidisciplinary review. *J Clin Oncol*. 2019;37(1):61-71. doi:10.1200/JCO.2018.78.1211.
25. Agarwal V, Shah LM, Parsons MS, et al. ACR Appropriateness Criteria® Myelopathy: 2021 Update. *J Am Coll Radiol*. 2021;18(5S):S73-S82. doi:10.1016/j.jacr.2021.01.020.
26. Juliano AF, Policeni B, Agarwal V, et al. ACR Appropriateness Criteria® Ataxia. *J Am Coll Radiol*. 2019;16(5S):S44-S56. doi:10.1016/j.jacr.2019.02.021.
27. Song JH, Chaudhry FS, Mayo-Smith WW. The incidental adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. *AJR Am J Roentgenol*. 2008;190(5):1163-8. doi:10.2214/AJR.07.2799.
28. Metser U, Miller E, Lerman H, Lievshitz G, Avital S, Even-Sapir E. 18F-FDG PET/CT in the evaluation of adrenal masses. *J Nucl Med*. 2006;47(1):32-7.
29. Vikram R, Yeung HD, Macapinlac HA, Iyer RB. Utility of PET/CT in differentiating benign from malignant adrenal nodules in patients with cancer. *AJR Am J Roentgenol.* 2008;191(5):1545-51. doi:10.2214/AJR.07.3447.
30. Krämer A, Bochtler T, Pauli C, et al. Cancer of unknown primary: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2023;34(3):228-246. doi:10.1016/j.annonc.2022.11.013.
31. Kwee TC, Kwee RM. Combined FDG-PET/CT for the detection of unknown primary tumors: systematic review and meta-analysis. *Eur Radiol*. 2009;19:731-744.
32. Buchanan CL, Morris EA, Dorn PL, et al. Utility of breast magnetic resonance imaging in patients with occult primary breast cancer. *Ann Surg Oncol*. 2005;12:1045-1053.
33. Piccioli A, Maccauro G, Spinelli MS, Biagini R, Rossi B. Bone metastases of unknown origin: epidemiology and principles of management. *J Orthop Traumatol*. 2015;16(2):81-6. doi:10.1007/s10195-015-0344-0.
34. Ettinger DS, Wood DE, Stevenson J, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – November 21, 2024. Mesothelioma: Peritoneal, available at: https://www.nccn.org/professionals/physician_gls/pdf/meso_peritoneal.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Mesothelioma: Peritoneal V1.2025 – November 21, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
35. Magge D, Zenati MS, Austin F, et al. Malignant peritoneal mesothelioma: prognostic factors and oncologic outcome analysis. *Ann Surg Oncol*. 2014;21(4):1159-65. doi:10.1245/s10434-013-3358-y.

36. Yan TD, Deraco M, Baratti D, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: multi-institutional experience. *J Clin Oncol*. 2009;27(36):6237-42. doi:10.1200/JCO.2009.23.9640.
37. Zelenetz AD, Fayad LE, Mayur N. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025 – January 28, 2025. Castleman disease, available at: https://www.nccn.org/professionals/physician_gls/pdf/castleman.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Castleman Disease V2.2025 – January 28, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
38. Hoffmann C, Hentrich M, Tiemann M, et al. Recent advances in Castleman disease. *Oncol Res Treat*. 2022;45(11):693-704. doi:10.1159/000526640.
39. Dispenzieri A, Fajgenbaum DC. Overview of Castleman disease. *Blood*. 2020;135(16):1353-1364. doi:10.1182/blood.2019000931.
40. Van Rhee F, Voorhees P, Dispenzieri A,et al. International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. *Blood*. 2018;132(20):2115-2124. doi:10.1182/blood-2018-07-862334.
41. Yang HL, Liu T, Wang XM, Xu Y, Deng SM. Diagnosis of bone metastases: a meta-analysis comparing ¹#FDG PET, CT, MRI and bone scintigraphy. *Eur Radiol*. 2011;21(12):2604-17. doi:10.1007/s00330-011-2221-4.
42. Qu X, Huang X, Yan W, Wu L, Dai K. A meta-analysis of ¹#FDG-PET-CT, ¹#FDG-PET, MRI and bone scintigraphy for diagnosis of bone metastases in patients with lung cancer. *Eur J Radiol*. 2012;81(5):1007-15. doi:10.1016/j.ejrad.2011.01.126.
43. Di Primio G, Boyd GJ, Fung CI, et al. Recommendations for the management of incidental musculoskeletal findings on MRI and CT. *Can Assoc Radiol J*. 2023;74(3):514-525. doi:10.1177/08465371231152151.
44. Liu T, Wang S, Liu H, et al. Detection of vertebral metastases: a meta-analysis comparing MRI, CT, PET, BS and BS with SPECT. *J Cancer Res Clin Oncol*. 2017;143(3):457-465. doi:10.1007/s00432-016-2288-z.
45. Lombardi AF, Aihara AY, Fernandes ADRC, Cardoso FN. Imaging of Paget's disease of bone. *Radiol Clin North Am*. 2022;60(4):561-573. doi:10.1016/j.rcl.2022.02.005.
46. Zhang-Yin J, Panagiotidis E. Role of 18F-NaF PET/CT in bone metastases. *Q J Nucl Med Mol Imaging*. 2023;67(4):249-258. doi:10.23736/S1824-4785.23.03534-3.
47. Ahmed N, Sadeq A, Marafi F, Gnanasegaran G, Usmani S. Therapy-induced bone changes in oncology imaging with 18F-sodium fluoride (NaF) PET-CT. *Ann Nucl Med*. 2022;36(4):329-339. doi:10.1007/s12149-022-01730-y.
48. Walter T, Tougeron D, Baudin E, et al. Poorly differentiated gastro-entero-pancreatic neuroendocrine carcinomas: Are they really heterogeneous? Insights from the FFCD-GTE national cohort. *Eur J Cancer*. 2017;79:158-165. doi:10.1016/j.ejca.2017.04.009.
49. NCI PDQ Gastrointestinal neuroendocrine tumors treatment. Gastrointestinal Neuroendocrine Tumors (PDQ®) - NCI (cancer.gov).
50. Kaewput C, Vinjamuri S. Role of Combined 68Ga DOTA-Peptides and 18F FDG PET/CT in the Evaluation of Gastroenteropancreatic Neuroendocrine Neoplasms. *Diagnostics (Basel)*. 2022;12(2):280. doi:10.3390/diagnostics12020280.
51. Półtorak-Szymczak G, Budlewski T, Furmanek MI, et al. Radiological Imaging of gastro-entero-pancreatic neuroendocrine tumors. The review of current literature emphasizing the diagnostic value of chosen imaging methods. *Front Oncol*. 2021;11:670233. doi:10.3389/fonc.2021.670233.
52. Szaro P, McGrath A, Ciszek B, Geijer M. Magnetic resonance imaging of the brachial plexus. Part 1: Anatomical considerations, magnetic resonance techniques, and non-traumatic lesions. *Eur J Radiol Open*. 2021;9:100392. doi:10.1016/j.ejro.2021.100392.
53. Szaro P, Geijer M, Ciszek B, McGrath A. Magnetic resonance imaging of the brachial plexus. Part 2: Traumatic injuries. *Eur J Radiol Open*. 2022;9:100397. doi:10.1016/j.ejro.2022.100397.
54. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. *Radiology*. 2017;284(1):228-243. doi:10.1148/radiol.2017161659.
55. Christensen J, Prosper AE, Wu CC, et al. ACR Lung-RADS v2022: Assessment Categories and Management Recommendations. *Chest*. 2024;165(3):738-753. doi:10.1016/j.chest.2023.10.028.
56. Gore RM, Pickhardt PJ, Mortele KJ, et al. Management of incidental liver lesions on CT: A white paper of the ACR incidental findings committee. *J Am Coll Radiol.* 2017;14(11):1429-1437. doi:10.1016/j.jacr.2017.07.018.

57. Maino C, Vernuccio F, Cannella R, et al. Liver metastases: The role of magnetic resonance imaging. *World J Gastroenterol*. 2023;29(36):5180-5197. doi:10.3748/wjg.v29.i36.5180.
58. Benson AB, D'Angelica MI, Abrams T, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024—September 24, 2024, Hepatocellular Carcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf, Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Hepatocellular Carcinoma V3.2024 September 24, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
59. Salem R, Padia SA, Lam M, et al. Clinical, dosimetric, and reporting considerations for Y-90 glass microspheres in hepatocellular carcinoma: updated 2022 recommendations from an international multidisciplinary working group. *Eur J Nucl Med Mol Imaging*. 2023;50(2):328-343. doi:10.1007/s00259-022-05956-w.
60. Barabasch A, Kraemer NA, Ciritsis A, et al. Diagnostic accuracy of diffusion-weighted magnetic resonance imaging versus positron emission tomography/computed tomography for early response assessment of liver metastases to Y90-radioembolization. *Invest Radiol.* 2015;50(6):409-15. doi:10.1097/RLI.0000000000000144.
61. Reid A, Suneja G, Alexiev B, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2025—January 14, 2025, Kaposi Sarcoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/kaposi.pdf, Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Hepatocellular Carcinoma V2.2025 January 14, 2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
62. Mody RN, Remer EM, Nikolaidis P, et al. ACR Appropriateness Criteria® Adrenal Mass Evaluation: 2021 Update. *J Am Coll Radiol*. 2021;18(11S):S251-S267. doi:10.1016/j.jacr.2021.08.010.
63. Biermann JS, Hirbe A, Ahlawat S, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2025 – August 20, 2024. Bone Cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Bone Cancer V1.2025 – August 20, 2024 ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.