Status: Revised
Doc ID: RBM07-0325.1

Effective Date: 03/23/2025
Last Review Date:07/16/2024

Approval and implementation dates for specific health plans may vary. Please consult the applicable health plan for more details.

Clinical Appropriateness Guidelines

Advanced Imaging

Appropriate Use Criteria: Oncologic Imaging

Proprietary

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Description and Application of the Guidelines

The Carelon Clinical Appropriateness Guidelines (hereinafter “the Carelon Clinical Appropriateness Guidelines” or the “Guidelines”) are designed to assist providers in making the most appropriate treatment decision for a specific clinical condition for an individual. The Guidelines establish objective and evidence-based criteria for medical necessity determinations, where possible, that can be used in support of the following:

- To establish criteria for when services are medically necessary
- To assist the practitioner as an educational tool
- To encourage standardization of medical practice patterns
- To curtail the performance of inappropriate and/or duplicate services
- To address patient safety concerns
- To enhance the quality of health care
- To promote the most efficient and cost-effective use of services

The Carelon guideline development process complies with applicable accreditation and legal standards, including the requirement that the Guidelines be developed with involvement from appropriate providers with current clinical expertise relevant to the Guidelines under review and be based on the most up-to-date clinical principles and best practices. Resources reviewed include widely used treatment guidelines, randomized controlled trials or prospective cohort studies, and large systematic reviews or meta-analyses. Carelon reviews all of its Guidelines at least annually.

Carelon makes its Guidelines publicly available on its website. Copies of the Guidelines are also available upon oral or written request. Additional details, such as summaries of evidence, a list of the sources of evidence, and an explanation of the rationale that supports the adoption of the Guidelines, are included in each guideline document.

Although the Guidelines are publicly available, Carelon considers the Guidelines to be important, proprietary information of Carelon, which cannot be sold, assigned, leased, licensed, reproduced or distributed without the written consent of Carelon.

Carelon applies objective and evidence-based criteria, and takes individual circumstances and the local delivery system into account when determining the medical appropriateness of health care services. The Carelon Guidelines are just guidelines for the provision of specialty health services. These criteria are designed to guide both providers and reviewers to the most appropriate services based on a patient’s unique circumstances. In all cases, clinical judgment consistent with the standards of good medical practice should be used when applying the Guidelines. Guideline determinations are made based on the information provided at the time of the request. It is expected that medical necessity decisions may change as new information is provided or based on unique aspects of the patient’s condition. The treating clinician has final authority and responsibility for treatment decisions regarding the care of the patient and for justifying and demonstrating the existence of medical necessity for the requested service. The Guidelines are not a substitute for the experience and judgment of a physician or other health care professionals. Any clinician seeking to apply or consult the Guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment.

The Guidelines do not address coverage, benefit or other plan specific issues. Applicable federal and state coverage mandates take precedence over these clinical guidelines, and in the case of reviews for Medicare Advantage Plans, the Guidelines are only applied where there are not fully established CMS criteria. If requested by a health plan, Carelon will review requests based on health plan medical policy/guidelines in lieu of the Carelon Guidelines. Pharmaceuticals, radiotracers, or medical devices used in any of the diagnostic or therapeutic interventions listed in the Guidelines must be FDA approved or conditionally approved for the intended use. However, use of an FDA approved or conditionally approved product does not constitute medical necessity or guarantee reimbursement by the respective health plan.

The Guidelines may also be used by the health plan or by Carelon for purposes of provider education, or to review the medical necessity of services by any provider who has been notified of the need for medical necessity review, due to billing practices or claims that are not consistent with other providers in terms of frequency or some other manner.

General Clinical Guideline

Clinical Appropriateness Framework

Critical to any finding of clinical appropriateness under the guidelines for a specific diagnostic or therapeutic intervention are the following elements:

- Prior to any intervention, it is essential that the clinician confirm the diagnosis or establish its pretest likelihood based on a complete evaluation of the patient. This includes a history and physical examination and, where applicable, a review of relevant laboratory studies, diagnostic testing, and response to prior therapeutic intervention.
- The anticipated benefit of the recommended intervention is likely to outweigh any potential harms, including from delay or decreased access to services that may result (net benefit).
- Widely used treatment guidelines and/or current clinical literature and/or standards of medical practice should support that the recommended intervention offers the greatest net benefit among competing alternatives.
- There exists a reasonable likelihood that the intervention will change management and/or lead to an improved outcome for the patient.

Providers may be required to submit clinical documentation in support of a request for services. Such documentation must a) accurately reflect the clinical situation at the time of the requested service, and b) sufficiently document the ordering provider's clinical intent.

If these elements are not established with respect to a given request, the determination of appropriateness will most likely require a peer-to-peer conversation to understand the individual and unique facts that would justify a finding of clinical appropriateness. During the peer-to-peer conversation, factors such as patient acuity and setting of service may also be taken into account to the extent permitted by law.

Simultaneous Ordering of Multiple Diagnostic or Therapeutic Interventions

Requests for multiple diagnostic or therapeutic interventions at the same time will often require a peer-to-peer conversation to understand the individual circumstances that support the medical necessity of performing all interventions simultaneously. This is based on the fact that appropriateness of additional intervention is often dependent on the outcome of the initial intervention.

Additionally, either of the following may apply:

- Current literature and/or standards of medical practice support that one of the requested diagnostic or therapeutic interventions is more appropriate in the clinical situation presented; or
- One of the diagnostic or therapeutic interventions requested is more likely to improve patient outcomes based on current literature and/or standards of medical practice.

Repeat Diagnostic Intervention

In general, repeated testing of the same anatomic location for the same indication should be limited to evaluation following an intervention, or when there is a change in clinical status such that additional testing is required to determine next steps in management. At times, it may be necessary to repeat a test using different techniques or protocols to clarify a finding or result of the original study.

Repeated testing for the same indication using the same or similar technology may be subject to additional review or require peer-to-peer conversation in the following scenarios:

- Repeated diagnostic testing at the same facility due to technical issues

- Repeated diagnostic testing requested at a different facility due to provider preference or quality concerns
- Repeated diagnostic testing of the same anatomic area based on persistent symptoms with no clinical change, treatment, or intervention since the previous study
- Repeated diagnostic testing of the same anatomic area by different providers for the same member over a short period of time

Repeat Therapeutic Intervention

In general, repeated therapeutic intervention in the same anatomic area is considered appropriate when the prior intervention proved effective or beneficial and the expected duration of relief has lapsed. A repeat intervention requested prior to the expected duration of relief is not appropriate unless it can be confirmed that the prior intervention was never administered. Requests for on-going services may depend on completion of previously authorized services in situations where a patient's response to authorized services is relevant to a determination of clinical appropriateness.

Oncologic Imaging

General Information/Overview

Scope

These guidelines address advanced imaging for oncologic conditions in both adult and pediatric populations. For interpretation of the Guidelines, and where not otherwise noted, “adult” refers to persons age 19 and older, and “pediatric” refers to persons age 18 and younger. Where separate indications exist, they are specified as **Adult** or **Pediatric**. Where not specified, indications and prerequisite information apply to persons of all ages. In addition, these guidelines for oncologic conditions will address the following aspects of the care continuum:

- Screening for cancer
- Diagnosis of breast and prostate cancer
- Diagnostic workup, management, and surveillance of documented malignancy: typically requires biopsy unless imaging findings are an accepted alternative to biopsy (hepatobiliary cancer, brain cancer or spinal cord cancer) OR are highly suspicious for cancer when biopsy is contraindicated or non-diagnostic.

For all other imaging related to tumor evaluation, please refer to the Carelon Guidelines for Advanced Imaging of the anatomic region of concern.

See the Coding section for a list of modalities included in these guidelines.

Technology Considerations

Advanced imaging for oncologic conditions includes both anatomic and functional modalities. Judicious use of advanced imaging is important to minimize risk and to avoid duplication of information. Testing should be performed in a stepwise fashion, with follow-up imaging studies performed based on the need for information not provided by the initial study.

Computed tomography (CT) and **magnetic resonance imaging (MRI)** are the most widely used modalities to visualize anatomic detail. CT provides rapidly obtained, high-resolution images that yield information on lesion morphology, size, and location. CT is less prone to motion artifact than MRI, and is useful for evaluation of bones and soft tissue. Improved techniques such as multi-slice technology and enhanced image processing refine image quality and resolution. **Helical CT** may be preferable to conventional axial CT for oncologic imaging due to increased speed of image acquisition and ability to perform **computed tomography angiography (CTA),** which is useful to assess vascular structures associated with tumors. Disadvantages of CT include exposure to ionizing radiation and risks associated with infusion of iodinated contrast media, including allergic reactions or renal compromise. MRI provides similar information to CT; however, image acquisition is slower and thus more prone to motion artifact. MRI has higher resolution and is better able to detect subtle abnormalities in soft tissue. For this reason, it is often preferable for visualizing infiltrative tumors. The term MRI spine in these guidelines specifically references MRI cervical spine, thoracic spine, and/or lumbar spine. **Magnetic resonance angiography (MRA)** is the MR analog of CTA and is also useful to assess tumor blood supply. The presence of implantable devices such as pacemakers or defibrillators, a potential need for sedation in pediatric patients, and claustrophobia are the main limitations of MRI. Infusion of gadolinium may also confer an unacceptable risk in persons with advanced renal disease.

Multiparametric MRI (mpMRI) of the prostate utilizes detailed anatomical imaging (T2-weighted imaging) as well as at least two functional imaging sequences (diffusion-weighted imaging, diffusion weighted imaging with apparent diffusion coefficient, and/or dynamic intravenous contrast-enhanced imaging) for detailed visualization and characterization of the prostate.

Magnetic resonance spectroscopy (MRS) provides a biochemical profile of metabolic constituents in tissues and may be used as an adjunct in cases where standard MRI fails to distinguish between diseased and healthy tissue. In oncologic imaging, it is used primarily to differentiate between residual brain tumor and necrotic tissue following treatment.

Positron emission tomography (PET) or positron emission tomography with computed tomography (PET-CT) (collectively PET/CT) provide functional information about metabolic activity.

PET imaging requires the use of radiotracers. Carelon guidelines cover PET imaging performed with any Food and Drug Administration (FDA) approved radiotracer. The most common radiotracer is fluorodeoxyglucose (FDG) and all references to PET or PET-CT in this guideline assume use of FDG. PET imaging is sometimes performed using non FDG radiotracers.

PET utilizes a radiotracer, typically 2-(fluorine-18) fluoro-2-deoxy-D-glucose (fluorodeoxyglucose or FDG), which accumulates in areas of high metabolic activity such as tumor cells. The utility of PET may be improved by overlaying the areas of high uptake with CT images in order to provide anatomic detail (PET-CT). PET/CT is most useful in detecting tumors with a high metabolic rate; tumors that are indolent or slow growing are less likely to be detected using this modality. The lack of specificity for oncologic processes also results in FDG uptake occurring in benign etiologies such as physiologic lymphoid tissue uptake, infection, and benign tumors. Therefore, radiotracers have been in development that target cancer-specific cell surface transporters. 11C-choline and 18F-fluciclovine (Axumin) were approved by the U.S. Food and Drug Administration (FDA) in 2012 and 2016, respectively, for the detection of suspected prostate cancer recurrence. 68Ga-dotatate (NETSPOT) was approved by the FDA in 2016 as the first in-class PET/CT radiotracer for detection of well-differentiated neuroendocrine tumors (NET).

Where evidence based specific criteria for a particular non-FDG radiotracer exists, it will be called out in the Carelon guidelines as a modifier to PET or PET-CT. See, for example, 18F Fluciclovine PET/CT or 11C Choline PET/CT.

Where evidence based specific criteria for a particular non-FDG radiotracer does not exist, the medical necessity criteria to be applied in adjudicating the use of the non-FDG radiotracer will be the Clinical Appropriateness Framework.

There are many radiotracers currently under development which target specific tumor types, and several are already in clinical use. As these continue to be evaluated in clinical practice, the use of this technology is expected to evolve and grow.

Definitions

Phases of the care continuum are broadly defined as follows:

- **Screening** – testing in the absence of an established or clinically suspected diagnosis
- **Diagnosis** - testing based on a reasonable clinical suspicion of a particular condition or disorder
- **Diagnostic Workup** – initial staging of documented malignancy
- **Management** – testing to direct therapy of an established condition, which may include preoperative or postoperative imaging, or imaging performed to evaluate the response to nonsurgical intervention. In oncologic imaging, management applies to patients with measurable disease and to imaging performed before or after planned treatment intervention, therapy response, restaging or clinically suspected recurrence.
- **Surveillance** – periodic assessment following completion of therapy. In oncologic imaging, surveillance applies to asymptomatic patients in remission and/or without measurable disease

Other terms used in this guideline:

- **Documented malignancy**: Established cancer diagnosis, usually by biopsy. Biopsy may not be required when imaging findings are an accepted alternative (for instance hepatobiliary cancer, brain cancer or spinal cord cancer) OR are highly suspicious for cancer when biopsy is contraindicated or nondiagnostic.

- **Indicated** – Evidence supports use and is considered medically necessary and consistent with Carelon's clinical appropriateness framework. Scenarios that follow "Indicated" are required by the clinical guideline. Scenarios that follow "Indicated" with a note are suggested but not required to establish medical necessity.
- **Not indicated** – Evidence does not support use and/or is not considered medically necessary and consistent with Carelon's clinical appropriateness framework
- **Indeterminate lesion** – focal mass or mass-like finding identified on prior imaging that has not been confidently diagnosed as either benign or malignant based on imaging appearance and/or biopsy
- **Cannot be performed or is nondiagnostic – applies when the test:**
    - Is positive or indeterminate for clinically significant pathology when the information provided about the abnormality by the test is not sufficient to direct subsequent management
    - Is negative when the negative likelihood ratio of the test is both insufficient to confidently exclude the absence of suspected disease and unable to direct subsequent management. This typically applies in scenarios with moderate to high clinical pretest probability with negative testing or low pretest probability with clear evidence for net benefit
    - Has been previously nondiagnostic because of a persistent clinical factor (e.g., body habitus, immobility) that is very likely to make retesting nondiagnostic as well
    - Cannot be performed due to a medical contraindication (e.g., contrast nephrotoxicity, allergy, or in highly radiation sensitive populations such as pediatrics and pregnancy) or reasonable unavailability related to lack of local expertise or service availability.
- **Standard or conventional imaging**: Refers to imaging that does not require a PET/CT. Depending on the clinical scenario and individual patient circumstances, this may include computed tomography, magnetic resonance imaging, ultrasound and/or scintigraphy.
- **Clinical suspicion**: Documented signs, symptoms, lab and/or other diagnostic test results that sufficiently increase the pre-test likelihood of disease to warrant further advanced imaging evaluation to direct management. Includes symptom directed staging.

Statistical terminology

- **Confidence interval (CI) –** range of values which is likely to contain the cited statistic. For example, 92% sensitivity (95% CI, 89%-95%) means that, while the sensitivity was calculated at 92% on the current study, there is a 95% chance that, if a study were to be repeated, the sensitivity on the repeat study would be in the range of 89%-95%.
- **Diagnostic accuracy –** ability of a test to discriminate between the target condition and health. Diagnostic accuracy is quantified using sensitivity and specificity, predictive values, and likelihood ratios.
- **Hazard ratio –** odds that an individual in the group with the higher hazard reaches the outcome first. Hazard ratio is analogous to odds ratio and is reported most commonly in time-to-event analysis or survival analysis. A hazard ratio of 1 means that the hazard rates of the 2 groups are equivalent. A hazard ratio of greater than 1 or less than 1 means that there are differences in the hazard rates between the 2 groups.
- **Likelihood ratio –** ratio of an expected test result (positive or negative) in patients *with* the disease to an expected test result (positive or negative) in patients *without* the disease. Positive likelihood ratios, especially those greater than 10, help rule in a disease (i.e., they substantially raise the post-test probability of the disease, and hence make it very likely and the test very useful in identifying the disease). Negative likelihood ratios, especially those less than 0.1, help rule out a disease (i.e., they substantially decrease the post-test probability of disease, and hence make it very unlikely and the test very useful in excluding the disease).
- **Odds ratio –** odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure. An odds ratio of 1 means that the exposure does

not affect the odds of the outcome. An odds ratio greater than 1 means that the exposure is associated with higher odds of the outcome. An odds ratio less than 1 means that the exposure is associated with lower odds of the outcome.

- **Predictive value –** likelihood that a given test result correlates with the presence or absence of disease. Positive predictive value is defined as the number of true positives divided by the number of test positives. Negative predictive value is defined as the number of true negatives divided by the number of test negative patients. Predictive value is dependent on the prevalence of the condition.
- **Pretest probability –** probability that a given patient has a disease prior to testing. May be divided into very low (less than 5%), low (less than 20%), moderate (20%-75%), and high (greater than 75%) although these numbers may vary by condition.
- **Relative risk –** probability of an outcome when an exposure is present relative to the probability of the outcome occurring when the exposure is absent. Relative risk is analogous to odds ratio; however, relative risk is calculated by using percentages instead of odds. A relative risk of 1 means that there is no difference in risk between the 2 groups. A relative risk of greater than 1 means that the outcome is more likely to happen in the exposed group compared to the control group. A relative risk less than 1 means that the outcome is less likely to happen in the exposed group compared to the control group.
- **Sensitivity –** conditional probability that the test is positive, given that the patient has the disease. Defined as the true positive rate (number of true positives divided by the number of patients with disease). Excellent or high sensitivity is usually greater than 90%.
- **Specificity –** conditional probability that the test is negative, given that the patient does not have the disease. Defined as the true negative rate (number of true negatives divided by the number of patients without the disease). Excellent or high specificity is usually greater than 90%.

Staging systems referred to in the Guidelines:

- **AJCC staging**[1] – classification system developed by the American Joint Committee on Cancer for describing the extent of disease progression in cancer patients. It utilizes the TNM scoring system which takes into account Tumor size, the lymph Nodes affected, and Metastases.
- **Ann Arbor staging**[2] – system for staging Hodgkin lymphoma and non-Hodgkin lymphoma based on location of malignant tissue and on systemic symptoms due to the lymphoma.
- **Deauville criteria**[3] – internationally accepted response assessment criteria utilizing a five-point scoring system for the FDG avidity of a Hodgkin lymphoma or non-Hodgkin lymphoma tumor mass as seen on FDG-PET.
- **FIGO system**[4] – a cancer staging and classification system for gynecologic malignancies developed by the International Federation of Gynecology and Obstetrics.
- **Lugano classification**[5] – staging and response assessment system used for patients with non-Hodgkin lymphoma based on the Ann Arbor staging system. The Lugano criteria takes into account FDG-PET in response assessment.
- **RECIST**[6] (response evaluation criteria in solid tumors) – set of published rules jointly developed by the European Organization for Research and Treatment of Cancer, National Cancer Institute of the U.S., and the National Cancer Institute of Canada Clinical Trials Group to assess tumor response during treatment.

Clinical Indications

The following sections include indications for which advanced imaging is considered medically necessary, along with prerequisite information and supporting evidence where available. Indications, diagnoses, or imaging modalities not specifically addressed are considered not medically necessary.

Indications are presented in the following sections by tumor type.

Cancer Screening

Advanced imaging is indicated for the following screening scenarios.

Breast cancer screening

Annual MRI breast is indicated in **ANY** of the following scenarios:

- Individuals who received radiation to the chest between ages 10 and 30
- Individuals with a genetic predisposition to breast cancer, in either themselves or a first-degree relative, which may include **ANY** of the following:
    - Bannayan-Riley-Ruvalcaba syndrome
    - *BRCA1* and *BRCA2* mutations
    - Cowden syndrome
    - Li-Fraumeni syndrome (TP53)
- Individuals known to have **ANY** of the following established genetic mutations:
    - ATM
    - BARD1
    - CDH1
    - CHEK2
    - NF-1
    - PALB2
    - PTEN
    - RAD51C or RAD51D
    - STK11 (Peutz-Jeghers syndrome)
- History of lobular carcinoma in situ (LCIS), atypical ductal hyperplasia (ADH), or atypical lobular hyperplasia (ALH) on biopsy
- Lifetime risk of 20% or greater as defined by the GAIL model, BOADICEA, BRCAPRO, Claus, Tyrer-Cuzick or other models that are largely dependent on family history

Rationale

While several recent studies have shown breast MRI to improve cancer detection in women with a personal history of breast cancer, the false positive rate remains extremely high, with one study reporting a false positive rate of 61%.[7, 8] False positives are commonly seen in average-risk women screened for breast cancer with MRI, particularly those with dense breasts.[9] In a systematic review for the U.S. Preventive Services Task Force (USPSTF), the authors concluded that the current evidence is insufficient to assess the balance of benefits and harms of supplemental MRI screening in women identified to have dense breasts on an otherwise negative screening mammogram.[10] However, additional imaging with MRI breast has been found to be beneficial in higher-risk groups.[11-17] The American College of Radiology Appropriate Use Criteria for supplemental screening based on breast density note that there is limited data regarding the use of MRI for screening average-risk patients with dense breast tissue. They report some evidence supporting MRI for supplemental screening of patients with dense breast tissue and intermediate risk for breast cancer, specifically in patients with a personal history of breast cancer or LCIS, though those studies included all breast densities. Additionally, the ACR recommends MRI for breast cancer screening in transmasculine patients age 25 to 30 or older and who are at high risk for breast cancer (based on genetic predisposition, first-

degree relative with genetic predisposition, chest irradiation between age 10 and 30 years, or 20% or greater lifetime risk of breast cancer).[18]

MRI has been shown to be more sensitive but less specific than mammography.[11, 19-22] In a review of 11 prospective, nonrandomized studies comparing screening MRI to mammography in women at high risk for breast cancer, the sensitivity of MRI was higher than mammography: 77% vs 39%, respectively. Similar to previous studies, the specificity of MRI was lower than mammography: 86% vs 95%. Comparing diagnostic odds ratios (positive defined as BI-RADS 3 or higher), the diagnostic odds ratio was 14.7 (6.1-35.6) for mammogram, 18.3 (11.7-28.7) for MRI, and 45.9 (17.5-120.9) for the MRI-mammogram combination. The combined modalities were superior in terms of sensitivity (94%) and specificity (77%) to either modality alone.[23] A prospective randomized trial showed that when MRI was added to screening ultrasound and mammography for high-risk patients, the sensitivity was 100% as compared to 44% for mammography and ultrasound alone.[24] Benefits in survival may also be seen, particularly in patients with *BRCA1* and *BRCA2* mutations.[25, 26] In a prospective trial using both mammography and MRI breast for screening of high-familial-risk women for breast cancer (N = 649), 19 cancers were detected by MRI only, 6 by mammography only, and 8 by both modalities combined, with 2 found on serial imaging. In patients with lobular carcinoma in situ and atypical hyperplasia, MRI was significantly more sensitive than mammography, but resulted in 3 times more benign biopsies.[27]

Carelon Oncologic Imaging guidelines pertaining to breast cancer screening are in concordance with the USPSTF, American Cancer Society, and American College of Radiology recommendations.[28-31]

Colorectal cancer screening

CT colonography (CTC) is indicated in **ANY** of the following scenarios:

- **Screening CT colonography** is indicated for average risk individuals* as an alternative to conventional colonoscopy at 5-year intervals, beginning at age 45

**Average risk:*

- No personal history of colonic adenoma, serrated sessile polyp/lesion (SSP/SSL), or colorectal cancer (CRC)

- No personal history of inflammatory bowel disease, high-risk CRC genetic syndromes, cystic fibrosis, or childhood cancer

- Negative family history for CRC, confirmed advanced adenoma (i.e. high-grade dysplasia, ≥ 1 cm, villous or tubulovillous histology or an advanced SSP/SSL)

- **Diagnostic CT colonography** is indicated when **ANY** of the following conditions are present:
    - Coagulopathy
    - Complications from prior fiberoptic colonoscopy
    - Diverticulitis with increased risk of perforation
    - Failed or incomplete fiberoptic colonoscopy of the entire colon, due to inability to pass the colonoscope proximally (may be secondary to obstructing neoplasm, spasm, redundant colon, altered anatomy or scarring from previous surgery, stricture, or extrinsic compression)
    - Increased sedation risk, such as chronic obstructive pulmonary disease or previous adverse reaction to anesthesia
    - Known colonic obstruction when standard fiberoptic colonoscopy is contraindicated
    - Lifetime or long-term anticoagulation with increased patient risk if discontinued
    - Following screening CTC demonstrating 1-2 polyps which are 6-9 mm in size, for 3 year follow-up CTC

Rationale

CT Colonography (CTC) has the advantages of being noninvasive and not requiring sedation, but carries the risk of radiation exposure and detection of potentially clinically insignificant extracolonic findings; a positive finding by CTC still requires subsequent optical colonoscopy evaluation. However, CTC may be an acceptable screening alternative for many individuals at average risk for colorectal cancer. In the National CT Colonography trial (ACRIN 6664) organized by the American College of Radiology (ACR) Imaging Network, 2531 participants underwent CTC followed by traditional optical colonoscopy.[32] CTC detected 90% of patients who had lesions measuring 10 mm of larger found by colonoscopy (sensitivity 90%, specificity 86%). In a review comparing CTC and optical colonoscopy, both screening strategies resulted in comparable detection rates for advanced neoplasia (3.2% for CTC, 3.4% for colonoscopy), although the numbers of polypectomies and complications were considerably higher in the optical colonoscopy group.[33] A population based study of 93 individuals with one or two polyps (6-9 mm) examined with 3 year surveillance CTC suggested that polyps of this size are unlikely to progress to advanced neoplasia within 3 years.[34]

Carelon Oncologic Imaging guidelines pertaining to colorectal cancer screening are in concordance with the U.S. Preventive Services Task Force and National Comprehensive Cancer Network recommendations.[35, 36]

Lung cancer screening

Annual low-dose CT is indicated when **ALL** of the following criteria are met:

- Age equal to or greater than 50 and less than or equal to 80
- 20 or greater pack-year history* of cigarette smoking (current smoker, or quit date within the past 15 years), or established asbestosis-related lung disease
- No signs or symptoms suggestive of underlying cancer
- No health problems that would be expected to substantially limit life expectancy or the ability to undergo an intervention with curative intent

**One pack-year of smoking equals smoking 1 pack (20 cigarettes) per day for 1 year or 7300 cigarettes annually.*

Rationale

Low dose CT (LDCT) is an annual lung cancer screening exam which utilizes specific protocols to image the lungs at an ultra-low dose of radiation. Screening CT for lung cancer can be beneficial; however, these benefits must be weighed against the risks of radiation exposure, over diagnosis, and false positives.[37] Previous studies have shown that screening with standard chest X-rays does not reduce the mortality rate from lung cancer. A 2011 National Cancer Institute-sponsored National Lung Screening Trial showed that people ages 55 to 74 with a history of heavy smoking were 20% less likely to die from lung cancer if they were screened with LDCT than with standard screening chest X-rays,[38] but those screened also experience higher overall rates of false positive results, invasive procedures, and serious complications.[39]

In 2021, the U.S. Preventive Services Task Force released the following updated recommendation summary: “The USPSTF [U.S. Preventive Services Task Force] recommends annual screening for lung cancer with LDCT in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.”[40] (Note: Centers for Medicare & Medicaid Services (CMS) requests follow national coverage determination (NCD) eligibility criteria, for which the screening upper age limit is 77 years). One multi-center study also found that in subjects with past asbestos exposure, the presence of smoking history, fibrotic plus emphysema changes, and pleural effusion were correlated with an increased prevalence of lung cancer. [41]

Carelon Oncologic Imaging guidelines pertaining to lung cancer screening are in concordance with the American Cancer Society, American College of Chest Physicians, American Society of Clinical Oncology, and U.S. Preventive Services Task Force recommendations.[37, 40, 42]

Pancreatic cancer screening

Annual CT or MRI (preferred) Abdomen is indicated as an alternative to endoscopic ultrasound in **ANY** of the following scenarios:

- Peutz-Jeghers syndrome (LKB1/STK11 mutations), starting at age 30-35 or 10 years earlier than youngest affected relative
- Familial Atypical Multiple Melanoma and Mole syndrome (FAMMM; CDKN2A, p16 mutation), starting at age 40 or 10 years earlier than youngest affected relative
- BRCA1, BRCA2, PALB2, ATM, EPCAM, TP53, or MLH1/MSH2/MSH6 (Lynch syndrome) gene mutation and at least one first- or second- degree relative* with pancreatic cancer, starting at age 50 or 10 years earlier than the youngest affected relative
- Hereditary pancreatitis gene mutation (PRSS1 or SPINK1) with personal or family history of recurrent acute pancreatitis, starting at age 40 or 20 years after the initial onset of pancreatitis
- Family history of pancreatic cancer in ≥ 1 first-degree and ≥ 1 second-degree relatives*, starting at age 50 or 10 years earlier than the youngest affected relative

**Relative(s) with exocrine pancreatic cancer, on the same side of the family as the gene mutation or history of pancreatic cancer*

Rationale

Emerging data regarding the efficacy of pancreatic cancer screening in select individuals has largely been limited to individuals with known pathogenic/likely pathogenic germline variants in a pancreatic cancer susceptibility gene (as listed above) or those with strong family history, utilizing contrast MRI/MRCP and/or EUS. Potential benefits of screening include a suggestion of tumor downgrading and improved mortality, compared to historical data, with 75%-90% of screen-detected malignancy being surgically resectable at diagnosis.[43, 44] Longer term studies are needed to determine if this downstaging translates to improved survival, as evidence suggests that long term survival is common in patients presenting with stage I sporadic ductal adenocarcinoma, and further data is needed to better define the threshold for biopsy and surgical intervention given the frequency with which pancreatic abnormalities are seen (42% of high risk individuals in one study had at least one pancreatic mass/cyst and/or duct abnormality).[45]

Carelon Oncologic Imaging guidelines pertaining to pancreatic cancer screening are based on the National Comprehensive Cancer Network.[46]

Hepatocellular carcinoma (HCC) screening

CT or MRI Abdomen is indicated every 6 months as an alternative to abdominal ultrasound in patients with Hepatitis B or cirrhosis (any etiology) when ultrasound cannot be performed or is nondiagnostic.

Rationale

Hepatocellular cancer (HCC) is the sixth-most common cancer in the world and in the United States, and the third leading cause of cancer-related mortality as of 2020.[47] Pre-existing cirrhosis is found in more than 80% of individuals diagnosed with HCC. Risk factors for HCC include hepatitis B and C virus, alcohol, non-alcoholic fatty liver disease (NAFLD), as well as less prevalent conditions such as hereditary hemochromatosis and Wilson's disease. Hepatitis B is correlated with the development of HCC even in the absence of cirrhosis, as DNA integration occurring in most cases of chronic infection induces genetic damage.

The American Association for the Study of Liver Diseases (AASLD) recommends screening for HCC with abdominal ultrasound every six months in those with cirrhosis (any etiology) or hepatitis B (also National Comprehensive Cancer Network category 2A recommendation).[47, 48] However, ultrasound may be limited due to technical factors like morbid obesity, obscuring intestinal gas, chest wall deformity, or the degree of liver disease itself (advanced cirrhosis causes distortion and heterogeneity of the hepatic parenchyma), resulting in poor liver visualization and lowered sensitivity for detection of early HCC.[49-52] The AASLD notes that CT or MRI may be utilized "in select patients with a high likelihood of having an inadequate US or if US is attempted but inadequate."

Carelon Oncologic Imaging guidelines pertaining to HCC screening are based on the National Comprehensive Cancer Network (NCCN) and the American Association for the Study of Liver Diseases (AASLD) guidelines.[47, 48]

Cancer screening, not otherwise specified

CT or MRI is indicated for cancer screening currently categorized as a 2A recommendation from the National Comprehensive Cancer Network (NCCN).

Rationale

Carelon will adopt all level 1 or 2A single modality and/or preferred modality and frequency recommendations published by the National Comprehensive Cancer Network (NCCN), including any imaging recommended for cancer screening not addressed in other sections.

Anal Cancer

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented anal cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated	Indicated (note: DRE exam of choice)	Indicated no more than annually (stage II-III)
MRI pelvis	Indicated	Indicated	Indicated no more than annually (stage II-III)
FDG-PET/CT	Indicated when standard imaging cannot be performed or is nondiagnostic for metastatic disease	Indicated in **EITHER** of the following scenarios: • Radiation planning for definitive treatment only • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Note: PET/CT does not replace a diagnostic CT scan.

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Anal cancer, which arises from the cells of the anal canal or anal margin, accounts for 3% of all gastrointestinal cancers. The most common histological subtype is squamous cell carcinoma. Risk factors for developing anal cancer include high-risk sexual behavior, tobacco use, and infection with human papillomavirus or human immunodeficiency virus. The most common presentation is rectal bleeding or pain.

DIAGNOSTIC WORKUP

Anal cancer is staged using the American Joint Committee on Cancer TNM system. The vast majority of patients with locoregional disease will undergo concurrent chemoradiation treatment regardless of tumor or nodal staging. Evaluation of pelvic lymph nodes with CT or MRI Pelvis is recommended by the NCCN for initial staging, as is CT of the Chest and Abdomen to assess disseminated disease (since veins of the anal region are part of the venous network associated with systemic circulation).[53] The European Society for Medical Oncology (ESMO) also recommends MRI pelvis and CT chest, abdomen, and pelvis for initial staging, and states that PET-CT may be considered, though they note that further research is needed to validate its utility as a supplement to conventional imaging.[54]

PET/CT can be used to verify staging before treatment, which may alter the radiation plan for curative combined modality therapy. PET/CT has been reported to be useful in the evaluation of pelvic lymph nodes, even when appearing normal-sized by CT. A meta-analysis of 12 studies found that CT and PET had a sensitivity of 60% and 99%, respectively, for the detection of primary disease. Compared with conventional imaging, PET upstaged 15% and downstaged another 15% of nodal disease.

This led to a change in nodal staging in 28% and TNM staging in 41% of patients.[55] A more recent meta-analysis published by Mahmud et al. found a pooled sensitivity of 99% for PET or PET/CT and 67% for CT scan alone. PET imaging also had a sensitivity of 93% and specificity of 76% for detecting nodal disease. A total of 5.1-37.5% of patients were upstaged and 8.2-26.7% were downstaged, with 12.5-59.3% of patients requiring treatment changes. However, the majority of the changes in treatment were in radiation planning.[56]

MANAGEMENT

Following completion of concurrent chemoradiation therapy, the National Comprehensive Cancer Network (NCCN) recommends that initial follow up of anal cancer include digital rectal exam 8-12 weeks after treatment. Patients with persistent disease but without evidence of progression may be managed with close follow-up for up to 6 months to ensure complete response after completion of radiation and chemotherapy. In the event of biopsy-proven progressive disease or recurrence, reimaging can be performed with conventional advanced imaging or PET/CT scan when salvage surgery is indicated.[53] The 5-year overall survival was 64% in a small study of 39 patients treated with radical salvage surgery.[57] ESMO recommends the use of CT chest, abdomen, and pelvis at diagnosis and follow-up. They state that while PET/CT may be considered to assist in radiation therapy planning, there is insufficient evidence to recommend routine PET/CT for assessment of treatment response or follow-up.[54]

SURVEILLANCE

Local recurrence of early stage disease is detectable by exam or anoscopy. For patients at high risk for recurrence (locally advanced [T3/T4], inguinal node positive, or locally persistent/progressive/recurrent anal squamous cell cancer), surveillance may include CT chest, CT or MRI abdomen/pelvis with contrast annually for a duration of 3 years per the NCCN guidelines.[53] However, due to the lack of prospective trials and because most recurrences are locoregional, the European Society of Medical Oncology does not endorse routine advanced imaging.[54]

Bladder and Urothelial Cancers

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented urothelial cancers of the bladder, renal pelvis, ureter, prostate and urethra.

Bladder/Urothelial Cancers: Non-muscle Invasive

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest	Indicated	Indicated	Not indicated
CT abdomen and pelvis*	Indicated	Indicated	Indicated no more than every 12 months
MRI pelvis	Indicated for local staging of sessile or high-grade tumors (as an adjunct to CT imaging)	Not indicated	Not indicated
FDG-PET/CT	Not indicated	Not indicated	Not indicated

**Includes CT urography (CTU) (CT of the abdomen and pelvis without and with IV contrast with excretory imaging).*

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity). MR urography (MRU, requested as MRI Abdomen/MRI Pelvis) may be appropriate in patients with poor renal function or iodinated CT contrast allergy but with GFR >30 and no acute renal failure.

Bladder/Urothelial Cancers: Muscle Invasive

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis*	Indicated	Indicated	Indicated no more than every 6 months
MRI pelvis	Indicated for local staging (as an adjunct to CT imaging)	Not indicated	Not indicated
FDG-PET/CT	Indicated when standard imaging cannot be performed or is nondiagnostic for metastatic disease	Indicated when standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

**Includes CT urography (CTU) (CT of the abdomen and pelvis without and with IV contrast with excretory imaging).*

Note: PET is not indicated in bladder tumors which have not invaded the muscle (stage < cT2).

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity). MR urography (MRU, requested as MRI Abdomen/MRI Pelvis) may be appropriate in patients with poor renal function or iodinated contrast allergy but with GFR >30 and no acute renal failure.

Rationale

Cancers of the urinary tract, including renal pelvis, ureter, bladder, and urethra, comprise the sixth most common cancer in men and women. The most common histology of urinary tract cancer is urothelial carcinoma (also called transitional cell carcinoma), accounting for 90% of tumors. Risk factors for urothelial cancer include tobacco use and occupational exposure to carcinogens. The most common presentation of urinary tract cancer includes hematuria, pain from local or metastatic disease, and voiding symptoms.

DIAGNOSTIC WORKUP

Staging utilizes the American Joint Committee on Cancer TNM system. Bladder cancer is further classified as muscle invasive or non-muscle invasive. Imaging is used to further assess the local tumor, lymph nodes, and distant metastases.

CT abdomen and pelvis with excretory imaging can be used for staging of invasive locally advanced bladder cancer.[58] Although CT provides adequate visualization of tumors and allows for assessment of the upper urinary tract, it does not have the same capability as MRI pelvis for local staging of bladder cancer. Compared to CT, MRI has the added benefit of high soft tissue contrast and direct multiplanar imaging capabilities, allowing for accurate tumor evaluation and better visualization of the bladder dome, trigone, and adjacent structures. The reported accuracy of MRI in overall staging of bladder cancer varies from 60% to 85%, whereas local staging ranges from 73% to 96%.[59] Both CT and MRI have comparable accuracy for staging lymph nodes: 73% to 90%.[60] The European Society for Medical Oncology (ESMO) recommends cross-sectional upper tract imaging with either CT or MR urography to assess for concurrent upper tract urothelial carcinoma. They recommend that, in patients with invasive disease, regional and distant staging should be done with CT chest and either CT or MRI abdomen/pelvis. There was no consensus reached on the utility of PET/CT.[61] The National Comprehensive Cancer Network (NCCN) does not recommend routine evaluation of bone metastases for non-muscle invasive urothelial cancer, and only recommends bone scintigraphy for muscle invasive urothelial cancer in symptomatic, high-risk patients or those with laboratory indicators of bone metastasis.[62]

The utility of PET/CT prior to planned cystectomy has been studied prospectively. In a study by Goodfellow et al., PET/CT was able to detect metastatic disease outside the pelvis with a sensitivity of 54% compared to 41% for the staging CT (N = 207). Both modalities had similar specificities of 97% and 98%.[63] In 2 additional studies, management was changed in 6%-27% of the patients based on new findings on PET/CT not detected by conventional CT.[64, 65] A meta-analysis of PET/CT in urinary bladder cancer showed pooled sensitivity and specificity of PET/CT for primary lesion detection were 90% and 100%, respectively. The authors concluded that diagnostic accuracy of PET/CT was good in metastatic lesions of urinary bladder cancer, but due to the small number of patients and limited number of studies analyzed, the diagnostic capability of FDG-PET or PET/CT in detection of primary bladder wall lesions could not be assessed.[66]

Additional metastatic workup with MRI of the brain and bone scan should not be routinely ordered unless localizing labs or symptoms are present.[67, 68] The imaging recommendations for renal pelvis and urothelial carcinoma of the ureter for ≤ T1 disease should be guided by recommendations for noninvasive bladder cancer and for ≥ T2 disease should be guided by recommendations for invasive bladder cancer.[69, 70]

MANAGEMENT

There is limited evidence to favor one imaging modality over another for tumor evaluation following initial therapy. Results for the bladder cohort from the national oncologic PET registry showed that FDG-PET used for chemotherapy monitoring changed management in 52% of patients.[71] This study included all disease stages and did not report the comparative effects of other imaging modalities on treatment.

SURVEILLANCE

The majority of recurrences after cystectomy are asymptomatic and routine surveillance is indicated. Professional society guidelines including the NCCN and the American College of Radiology Appropriate Use Criteria recommend post-treatment surveillance in patients with muscle-invasive bladder cancer, and those with nonmuscle invasive bladder cancer and symptoms or risk factors.[70, 72] The most common sites of recurrence are the peritoneum, lymph nodes, liver, bone, lungs, and adrenal glands with late recurrences occurring in the upper urinary tract.[73] Early detection of asymptomatic recurrence has been shown to positively impact survival.[74]

Brain and Spinal Cord Malignancy

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented primary central nervous system cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated (note: especially useful when systemic involvement is clinically suspected)	Not indicated	Not indicated
MRI brain	Indicated	Indicated for evaluation of suspected or known primary CNS cancer or brain metastases	Indicated
MRI spine	Indicated (note: especially useful for intracranial and spinal ependymoma, medulloblastoma, primary spinal cord tumors, leptomeningeal disease, and symptomatic or cerebrospinal fluid-positive primary central nervous system lymphoma)	Indicated for evaluation of suspected or known primary CNS cancer or spinal metastases	Indicated for primary CNS cancers affecting the spinal cord
fMRI	Indicated for preoperative neurosurgical planning, as a replacement for a Wada test or direct electrical stimulation mapping	Indicated for preoperative neurosurgical planning, as a replacement for a Wada test or direct electrical stimulation mapping	Not indicated
MR angiography head	Not indicated	Indicated for evaluation of vascular supply to tumor	Not indicated
MR spectroscopy	Not indicated	Indicated to differentiate recurrent or residual brain tumor from post-therapy changes, such as delayed radiation necrosis	Not indicated

Imaging Study	Diagnostic Workup	Management	Surveillance
FDG-PET/CT brain	Not indicated	Indicated for differentiation of posttreatment scarring from residual or recurrent disease	Not indicated
FDG-PET/CT whole body	Indicated for evaluation of possible systemic disease in proven CNS lymphoma	Not indicated	Not indicated

Note: CT head or CT myelogram are imaging alternatives when MRI cannot be performed or is not available.

Rationale

Primary brain and spinal cord tumors encompass a large and heterogeneous group of cancers that range from benign to highly aggressive. Glioblastomas are the most common high-grade primary central nervous system cancer, and comprise about 15% of primary brain cancers.[75] Risk factors for brain and spinal cord cancers include genetic predisposition and radiation exposure. The most common presentation is focal neurological symptoms based on the region of brain involved.

DIAGNOSTIC WORKUP

The World Health Organization Classification of Tumors of the Central Nervous System is used to classify and grade gliomas. All patients require an MRI of the brain for initial evaluation unless contraindicated. Spine imaging is indicated for intracranial and spinal ependymoma, medulloblastoma, primary spinal cord tumors, leptomeningeal disease, and symptomatic or cerebrospinal fluid-positive central nervous system lymphoma. Imaging is also indicated for central nervous system lymphomas to assess for possible systemic involvement; one study found that PET/CT body had a significantly higher sensitivity (94%-98%) than CT and resulted in change in management in 34% of patients.[76] Per NCCN, MRI of the brain and spine (with and without contrast) are gold standard for imaging evaluation.[77]

MANAGEMENT

Per NCCN, the most common use for MR perfusion, MRS, or PET brain is to differentiate radiation necrosis from active tumor.[78, 79] In a study comparing MRI to MRS, MRS plus diffusion-weighted imaging sequences was found to have above 95% sensitivity and specificity for distinguishing bacterial abscess from cystic tumor.[80] In a meta-analysis comparing the accuracy of MRS to PET, there was no significant difference between the two modalities.[81]

SURVEILLANCE

Carelon Oncologic Imaging guidelines for monitoring of primary central nervous system cancers are in concordance with both NCCN Nervous System Cancers guidelines as well as the European Society for Medical Oncology High-Grade Malignant Glioma guidelines.[77, 82]

Breast Cancer

Advanced imaging is considered medically necessary for the diagnostic workup and management of suspected or documented breast cancer. Routine surveillance imaging following completion of therapy is not considered medically necessary.

Imaging Study	Suspected Cancer	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Not indicated	Indicated for at-risk* or clinically suspected metastatic disease	Indicated	Not indicated
MRI breast	Indicated in **ANY** of the following scenarios: • Single follow-up MRI at 6 months following a breast	Indicated in **EITHER** of the following scenarios: • To determine the extent of disease in biopsy-proven breast cancer in **EITHER** of the	Indicated in **ANY** of the following scenarios: • To assess response to neoadjuvant chemotherapy prior to surgery • Post-lumpectomy with close or positive	Indicated annually for a personal history of breast cancer after breast conserving therapy or unilateral mastectomy in **ANY** of the following scenarios:

Imaging Study	Suspected Cancer	Diagnostic Workup	Management	Surveillance
	MRI with BI-RADS category 3 findings ● Differentiation of palpable mass from surgical scar tissue ● Lesion characterization when ultrasound and mammography are inadequate to localize for biopsy ● Suspected breast implant associated anaplastic large cell lymphoma (BIA-ALCL) in patients with textured breast implants when ultrasound is nondiagnostic ● Metastatic cancer suspected to be of breast origin by histology when no mammographic findings of primary breast carcinoma ● Evaluation of pathologic nipple discharge** after nondiagnostic mammography and ultrasound	following scenarios: ○ Ductal carcinoma in situ (DCIS) when the lesion is greater than 2 cm in size ○ Invasive breast carcinoma ● To define the relationship of the tumor to the fascia and its extension into the pectoralis major, serratus anterior, and/or intercostal muscles prior to surgery	margins to evaluate for residual disease ● Suspected recurrence in patients with tissue transfer flaps (rectus, latissimus dorsi, and gluteal) post-reconstruction ● Suspected recurrence of breast cancer when clinical, mammographic, and/or sonographic findings are inconclusive	○ Meets criteria for MRI breast screening ○ Heterogeneously or extremely dense breasts ○ Breast cancer diagnosis before age 50
FDG-PET/CT	Not indicated	Indicated when standard imaging cannot be performed or is nondiagnostic for metastatic disease	Indicated in **ANY** of the following scenarios: ● Radiation planning for treatment of locoregional recurrence ● Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease ● Evaluation of elevated LFTs or rising tumor markers when standard imaging has not clearly identified a site of recurrence or progression ● Restaging/treatment response when bone is the only site of measurable disease in the chest, abdomen, and pelvis	Not indicated

Imaging Study	Suspected Cancer	Diagnostic Workup	Management	Surveillance
18F-fluoroestradiol (18F-FES) PET/CT	Not indicated	Not indicated	Not indicated	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Note: PET mammography will continue to undergo review as new evidence-based studies are published. Interval routine coverage for PET mammography is not considered medically appropriate at this time.

**Tumor size >2 cm (T2), positive lymph nodes, tumor size >1 cm (T1c) and HER2+, or triple-negative disease*

***Pathologic nipple discharge: persistent and reproducible on exam, spontaneous, unilateral, single duct, and clear or bloody*

Rationale

Breast cancer is the most common cancer in women. Invasive ductal carcinoma and invasive lobular carcinoma are the two main histological subtypes of breast cancer, accounting for 91% of all diagnoses.[83] Incidence increases with age and risk factors include family history, use of hormone replacement therapy, use of oral contraceptives and benign breast disease. Most cases of breast cancer are detected by mammographic screening or self-examination.

SUSPECTED CANCER

Imaging cannot replace tissue diagnosis, and suspicious lesions detected by screening mammography should be evaluated with diagnostic mammography and breast ultrasound to further characterize and direct potential biopsy. MRI breast may be indicated when these modalities are unable to localize a lesion for biopsy. Although the risk of malignancy with a mammogram designated as BI-RADS 3 is relatively low (0.3%-2%), some experts recommend follow-up with MRI in this scenario. MRI can also assess possible mammographically-occult primary breast cancer when presenting with supraclavicular or axillary nodal metastases.[84]

DIAGNOSTIC WORKUP

Breast cancer is staged using the American Joint Committee on Cancer TNM system. Advanced imaging should be guided by stage and other presenting symptoms. Based on the poor sensitivity and specificity of imaging in asymptomatic early stage breast cancer, imaging should be reserved for evaluation of specific signs or symptoms suggestive of metastatic disease.[85, 86]

The use of PET or PET/CT is not indicated in the routine staging of clinical stage I, stage II or operable stage III (T3 N1) breast cancer, supported by studies detailing the high false-negative rate in the detection of lesions that are small (<1 cm), low sensitivity for detecting axillary nodal metastases, low probability of these patients having detectable metastatic disease, and high rate of false-positive scans.[87-90] In the setting of metastatic disease found on conventional imaging, there is insufficient data and limited evidence to show PET scan alters treatment. In a prospective study (N=178) by Jeong et al., patients without clinically detected axillary node metastases had virtually no benefit from PET/CT scan; management was changed in only 1.7% of patients.[91] The NCCN notes PET/CT to be most beneficial and accurate for advanced (stage III) disease and invasive ductal histology, and may be useful when standard staging studies are equivocal.[31]

The utility of preoperative MRI breast is controversial and is not universally recommended. In 2 prospective trials, the rate of postoperative re-excision was unaffected by preoperative MRI.[92, 93] In a meta-analysis of 4 studies by Houssami et al., (N=3169 patients), there was no difference in the rate of local recurrence or disease-free survival at 8 years for patients receiving a preoperative breast MRI compared with those without preoperative imaging.[94] The NCCN designates MRI breast as an optional imaging test.[31] The American College of Radiology states that MRI breast with and without contrast “may be appropriate” prior to treatment of newly diagnosed breast cancer in some scenarios, including for lesions greater than 2 cm in size, or for lesions 2 cm or smaller when there is clinical evidence of nodal involvement. However, they also note that much of the evidence regarding diagnostic accuracy of breast MRI relate to evaluating tumor within the breast, not to evaluation of axillary nodal involvement.[95]

MANAGEMENT

For evaluation of the axilla, both in newly diagnosed breast cancer and in post-treatment evaluation, ultrasound is generally the initial study of choice. However, the American College of Radiology states that MRI breast with and without contrast “may be appropriate” after completion of therapy or in the setting of local recurrence (following diagnostic mammography or digital

breast tomosynthesis). For newly diagnosed local recurrence, the ACR also indicates that FDG-PET/CT imaging "may be appropriate," but that the primary supporting evidence consists of a systematic review in which analysis was limited due to the heterogeneity of the included studies.[95]

Response to therapy based on PET/CT imaging has been correlated with longer time to progression but whether this translates into improved patient outcomes is unknown.[96] In a comparative study of 17 single-institution, nonrandomized, observational studies, PET/CT response correlated with changes in tumor volume as determined by bone scan, MRI, and/or CT; however, performance compared to conventional modalities and overall clinical impact could not be determined.[97] The NCCN recommends conventional imaging for systemic restaging.[31] In the unique scenario of bone-only metastases, the Carelon External Expert Advisory Board allows for disease monitoring with PET imaging, as restaging with CT or MRI is expected to result in suboptimal distinction between treated and residual/recurrent bone disease.

The FDA approved CERIANNA (18F-fluoroestradiol, 18F-FES) for use as an adjunct to biopsy in metastatic or recurrent breast cancer.[98] There is a high correlation between 18F-FES uptake and estrogen receptor (ER) expression on immunohistochemistry.[99] Appropriate use criteria from the Society of Nuclear Medicine and Molecular Imaging (SNMMI) state that FES-PET imaging is appropriate for assessment of ER status when biopsy is nondiagnostic or in lesions difficult to biopsy, as well as when other imaging tests are equivocal or suggestive. They further state that FES-PET is appropriate when considering endocrine therapy in newly diagnosed metastatic disease and when considering second-line endocrine therapy after progression of metastatic disease, citing multiple prospective trials using FES-PET as a predictive biomarker for response to therapy.[100] However, decisions regarding initial therapy rely on both ER status as well as HER2 status, and evidence regarding outcomes when used to direct management remains limited. In a retrospective data review from the TRANSCAN project, a prospective multicenter clinical trial, the authors reported that while FES-PET can reveal more lesions than FDG-PET, it should not be used as a first-line technique for detection of metastatic disease in patients with ductal ER-positive disease due to lower sensitivity compared to FDG-PET, on patient-based analysis. The authors state, "although some encouraging data are available, conflicting results have been reported and the real predictive value of this imaging procedure in terms of patient outcome has never been proved by large prospective studies."[101]

SURVEILLANCE

Both the American Society of Clinical Oncology and the NCCN discourage the use of advanced imaging for routine surveillance of treated, asymptomatic breast cancer.[31, 102] Early detection has not been shown to provide an advantage in survival or the ability to palliate recurrent disease and there is no evidence to support the use of CT, MRI, or PET scan.[88]

The NCCN recommends annual mammography surveillance, and notes that while MRI surveillance is of undefined utility, it should be considered for those with dense breasts treated with breast conservation + radiation, those diagnosed before age 50, and those whose lifetime risk of a second primary cancer is >20% (based on models largely dependent on family history) .[31] The American College of Radiology (ACR) Appropriateness Criteria considers MRI and other advanced imaging modalities usually inappropriate for the mastectomy or reconstruction side(s) in patients with a history of breast cancer.[103]

Cancers of Unknown Primary / Cancers Not Otherwise Specified

The following imaging criteria may be utilized for cancers not addressed elsewhere in the Oncologic Imaging guidelines, including cancers of unknown primary.

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented malignancy.

Imaging Modality	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated based on specific cancer or cancer type suspected	Indicated based on specific cancer or cancer type suspected	Indicated based on specific cancer or cancer type suspected
MRI imaging	Indicated based on specific cancer or cancer type suspected	Indicated based on specific cancer or cancer type suspected	Indicated based on specific cancer or cancer type suspected
FDG-PET/CT	Indicated when standard imaging cannot be performed or is nondiagnostic in	Indicated when standard imaging cannot be performed or is	Not indicated

	determining the extent of disease	nondiagnostic in determining the extent of disease	

Note: For malignancy of unknown origin involving the cervical lymph nodes, please see "Head and Neck Cancer"

Rationale

Cancer of unknown primary (CUP) describes findings of malignancy by histopathology, without confirmation of tumor origin. CUP can be subdivided into four categories: adenocarcinoma, squamous cell carcinoma, neuroendocrine carcinomas, and poorly differentiated carcinomas. Further testing should be guided by patient history and physical, pattern of disease spread, and clinical factors. In the majority of CUP, the underlying malignancy is never identified and treatment often is empiric based on histopathologic subtype. As CUP often present as metastatic disease, prognosis is poor with 80% of patients having a median overall survival of only 6 months.[104] This section addresses both cancers of unknown primary as well as cancers not otherwise specified in Carelon Clinical Appropriateness Guidelines section for Oncologic Imaging.

DIAGNOSTIC WORKUP

For malignancy of unknown origin involving the cervical lymph nodes but suspected to be of Head/Neck origin, please see "Head and Neck Cancer" guidelines.

The initial work-up for cancers of unknown primary should include a history and physical, laboratory evaluation, and imaging studies. CT of the chest, abdomen, and pelvis is commonly used to identify the primary cancer, assess extent of disease, and select for sites amenable to biopsy.[105] PET imaging is increasingly being used as part of the diagnosis of CUP. A meta-analysis and systematic review on the use of PET/CT in patients with CUP found that primary tumors were detected in 37% of 433 patients from 11 studies, with pooled sensitivity and specificity both at 84%.[106] Another study found that PET/CT detected more primary sites (24%-40%) than CT or MRI (20%-27%).[107] NCCN, however, does not recommend routine use of PET imaging for CUP due to a lack of prospective randomized studies comparing PET imaging to conventional imaging.[84] Special consideration should be given to patients presenting with a solitary metastasis where localized intervention is planned and to cervical nodal metastases of unknown origin. In a comprehensive review of patients with a solitary metastasis, PET imaging changed management in 34% of patients relative to conventional imaging. Fourteen percent of patients underwent surgery with curative intent.[108] In a systematic review and meta-analysis of patients with cervical nodal metastases of unknown origin, the primary tumor detection rate, sensitivity, and specificity of PET-CT were 0.44 (95% CI, 0.31-0.58), 0.97 (95% CI, 0.63-0.99), and 0.68 (95% CI, 0.49-0.83). Area under the curve was 0.83 (95% CI, 0.80-0.86).[109]

The initial work-up of patients with cancer not otherwise specified should include imaging of the primary neoplastic process and assessment for systemic involvement if warranted. Specific imaging recommendations vary with underlying pathologic diagnosis, staging, and patient factors. Because of the many nuances associated with cancer evaluation, peer-to-peer discussions will often be necessary to determine appropriateness of advanced imaging.

MANAGEMENT

For patients with either active disease or localized disease in remission, follow-up frequency should be determined by clinical need with additional diagnostic tests based on symptomatology.[84]

Subsequent imaging strategy for cancer not otherwise specified varies with underlying pathologic diagnosis and staging. In general terms, imaging used in the initial detection of the cancer may be used to assess for treatment response.

SURVEILLANCE

For patients with either active disease or localized disease in remission, follow-up frequency should be determined by clinical need with additional diagnostic tests based on symptomatology.[84]

The type and frequency of surveillance imaging for cancer not otherwise specified is dependent on the underlying pathologic diagnosis and staging. When indicated, CT imaging can be used in most cancers, with PET rarely indicated for surveillance.

Cervical Cancer

Advanced imaging is considered medically necessary for diagnostic workup and management of documented cervical cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest	Indicated (note: CXR usually sufficient for Stage I)	Indicated (note: especially useful 3-6 months after	Not indicated

CT abdomen and pelvis		completion of therapy if PET imaging not done)	
MRI pelvis	Indicated	Indicated (note: especially useful 3-6 months after completion of therapy **OR** in patients who have undergone fertility-sparing surgery)	Not indicated
FDG-PET/CT	Indicated for patients with stage IB1 or higher disease, or small cell neuroendocrine carcinoma of the cervix, as an alternative to CT chest, abdomen, and pelvis	Indicated in **ANY** of the following scenarios: • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease • Single treatment response evaluation following radiation or chemoradiation when performed at least 12 weeks following completion of therapy • Signs or symptoms concerning for recurrent or metastatic disease	Indicated for small cell neuroendocrine carcinoma of the cervix only

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Ninety-five percent of cervical cancers are classified as either squamous cell carcinomas (the majority) or adenocarcinomas.[110] Other rare histologies include neuroendocrine carcinoma, small cell carcinoma, lymphoma, and rhabdomyosarcoma. Risk factors for cervical cancer include immunosuppression, high-risk sexual behavior and infection with human papillomavirus.

DIAGNOSTIC WORKUP

Cervical cancer is staged using the FIGO system. Pelvis MRI is most useful for determination of tumor location, size, invasion, and presence of regional nodal disease.[111] A systematic review of 57 single-institution trials showed MRI was more accurate than CT for overall staging of cervical cancer.[112] A retrospective American College of Radiology Imaging Network/Gynecology Oncology Group (ACRIN/GOG) study comparing MRI and CT for early-stage cervical cancer found that contrast-enhanced multi-detector CT was equivalent to MRI for overall preoperative staging, but MRI performed significantly better for visualization of the primary tumor and detection of parametrial invasion.[113] In a second ACRIN/GOGIntergroup Study, MRI was superior to CT and clinical examination for evaluating uterine body involvement and measuring tumor size.[114] This benefit was also seen for preoperative selection of women for fertility-sparing surgery and for evaluation of residual tumor in the cervix after a cone biopsy with negative margins. In a small retrospective study in patients with negative margins after conization, MRI was 100% concordant in showing no residual cancer.[115] MRI may also play a role in radiation planning to aid with CT contouring.[116]

PET/CT is a useful modality for evaluating for extrauterine disease.[117, 118] Lin et al. reported a PET sensitivity of 85.7%, specificity of 94.4%, and accuracy of 92% for detecting para-aortic lymph node metastasis in CT-negative advanced cervical cancer patients.[119] Another review also concluded that PET/CT appeared better than conventional imaging for detection of metastatic lymph nodes with a reported sensitivity of 78%-84% for PET/CT, 72% for MRI, and only 47% for CT alone.[120] Per NCCN, whole body PET/CT is preferred for stage IB1/IB2 disease prior to fertility sparing treatment, and for stage IB3 and higher disease as part of initial work-up (level of evidence category 2A).[121]

MANAGEMENT

PET imaging is preferred for patients with high risk stage IB2 or above disease treated with adjuvant radiation or chemoradiation therapy. Early data suggest PET/CT during and/or after concurrent chemoradiation therapy may be a useful test for predicting local and distant failures and overall survival.[122] In the setting of recurrent disease, PET/CT has reported sensitivities ranging from 90.3%-92.7% and specificities ranging from 81%-100%.[123] NCCN recommends whole-body PET/CT for suspected recurrent/metastatic disease.[121]

SURVEILLANCE

In the setting of fertility-sparing surgery, MRI is commonly used for postoperative follow up. In a single-institution study, serial MRI follow up detected recurrent cervical cancer at a rate of 4%. Review of the literature shows that the recurrence rate after trachelectomy varies from 0%-25%.[124, 125]

Routine surveillance is not indicated in cervical cancer patients treated with radical hysterectomy, radiation, or concurrent chemotherapy, in accordance with NCCN guidelines.[121]

Colorectal Cancer

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented colorectal cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis	Indicated	Indicated	Indicated annually for Stage II or III colorectal cancer, and no more than every 6 months for Stage IV colorectal cancer
MRI pelvis	Indicated for rectal cancer	Indicated for rectal cancer	Indicated no more than every 6 months for rectal cancer treated with transanal local excision or nonoperative management
FDG-PET/CT	Indicated when standard imaging (CT Chest, Abdomen and Pelvis) cannot be performed or is non-diagnostic for surgically curable metastatic disease	Indicated in **ANY** of the following scenarios: • CT/MRI is equivocal for metastatic disease and lesion(s) is/are greater than 1 cm in diameter • CT demonstrates recurrence that is potentially curable with surgery • CT does not demonstrate a focus of recurrence, but carcinoembryonic antigen (CEA) level is rising • Signs or symptoms are suggestive of recurrence and CT is contraindicated	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Colorectal cancer is the third most common cancer in both men and women. Over 90% of cancers originating from the colon and rectum are adenocarcinomas. Incidence is higher in males and increases with age; other risk factors include alcohol use, dietary factors, obesity, smoking, and lack of physical exercise. There is a strong association with inflammatory bowel disease, and up to 10% of colorectal cancers are due to genetic factors. Tumors may be discovered on screening colonoscopy. Other presentations include bloody stool, abdominal pain, anemia, and obstructive symptoms.

DIAGNOSTIC WORKUP

Colorectal cancer is staged using the American Joint Committee on Cancer TNM system. For colon cancer, the NCCN recommends CT chest, abdomen, and pelvis for initial staging.[126] Additionally, the European Society for Medical Oncology (ESMO) states, “staging is carried out primarily with imaging techniques, such as a contrast-enhanced CT of the thorax, abdomen, and pelvis.”[127] In a meta-analysis of 19 studies evaluating CT imaging in preoperative colorectal staging, the pooled

sensitivity and specificity for detection of tumor invasion were 86% (95% CI, 78%-92%) and 78% (95% CI, 71%-84%). Similarly, the values for nodal detection were 70% (95% CI, 63%-73%) and 78% (95% CI, 73%-82%). In a subgroup analysis, studies utilizing multi-detector CT fared better than conventional CT.[128] Results from this meta-analysis are consistent with the findings of several other studies.[129-134]

MRI pelvis or endoscopic rectal ultrasound (ERUS) is indicated for the initial staging of rectal cancer, in addition to CT chest and abdomen.[135] In the prospective MERCURY II trial, MRI pelvis was able to accurately assess the low rectal plane which resulted in avoidance of overtreatment through selective preoperative therapy and substantially fewer pathologically positive circumferential resection margins.[136]

PET/CT does not supplant a diagnostic contrast enhanced CT, and should only be used to evaluate an equivocal finding or in patients with strong contraindications to IV contrast. Two studies found that PET/CT was not superior to CT for routine preoperative staging of colorectal cancer. In a study by Furukawa et al., PET/CT findings resulted in treatment changes in only 2% of patients who had bone and distant lymph node metastases detected only by PET/CT. In one case, CT imaging detected lung metastases that were not demonstrated on PET.[137]

PET/CT may be useful in identifying additional sites of extrahepatic metastases, but a positive impact on overall management and survival has not been definitively established. In the setting of resectable M1 disease, Moulton et al. found that PET/CT compared with CT alone did not influence survival. Surgical management was affected in 8% of patients, in which only 2.7% were deemed to no longer be surgical candidates. In addition, the false positive rate of PET/CT was 8.4%.[138] However, a meta-analysis of 18 studies suggests that FDG PET/CT is highly accurate for the detection of liver metastases on a per-patient basis but less accurate on a per-lesion basis. Compared to MRI, PET was less sensitive but more specific, and impacted management in about 25% of patients.[139]

MANAGEMENT

Response to neoadjuvant therapy can be seen in as many as 60% and complete response in as many as 18% of patients with rectal cancer.[140, 141] In the prospective MERCURY study, MRI assessment of tumor response and circumferential resection margin was correlated with positive survival outcomes. [142] A recent meta-analysis by de Jong et al., however, concluded that MRI, CT, and ERUS could not be used to predict complete response of locally advanced rectal cancer, and had poor accuracy for predicting lymph node involvement and tumor invasion in the circumferential resection margin.[143]

Chemotherapy may reduce the sensitivity of PET for the detection of liver metastases, likely due to metabolic inhibition caused by cytotoxic therapies.[144, 145] False negative rates of 87% have been reported for PET scans performed within 4 weeks of chemotherapy.[146] False positive PET/CT scans may also result from tissue inflammation after surgery.

In the uncommon setting of a rising carcinoembryonic antigen (CEA) and CT scans which have not identified a site of recurrence, PET/CT is a consideration; however, surgically curable recurrent disease may not be identified. It is notable that almost half of elevated CEAs after R0 resection are false positives and serial CTs at 3-month intervals until CEA stabilizes or normalizes or until disease is identified is often the preferred approach. When the CEA level is above 15ng/mL, false negatives are rare.[147] Based on a pooled analysis for detection of colorectal cancer recurrence, the sensitivity of CEA ranges from 68% for a threshold of 10 µg/L to 82% for a threshold of 2.5 µg/L and the specificity ranges from 97% for a threshold of 10 µg/L to 80% for a threshold of 2.5 µg/L.[148] A meta-analysis of 11 studies estimated sensitivity and specificity and positive and negative likelihood ratios of FDG-PET/CT in the detection of tumor recurrence in colorectal cancer patients with elevated CEA to be 94.1%, 77.2%, 4.70, and 0.06, respectively.[149]

SURVEILLANCE

Surveillance CT chest, abdomen and pelvis is indicated for stage II and higher colon cancer per the NCCN at variable intervals depending on stage of disease.[126] For patients who have undergone local transanal excision of rectal cancer, the NCCN recommends surveillance imaging with MRI or EUS of the rectum every 3-6 months for 2 years, then every 6 months for a total of 5 years.[135]

Although PET/CT detects recurrence earlier in some patients, these benefits are offset by both false positive and false negative results. A trial randomizing patients (N = 130) treated with curative resection to conventional surveillance alone or conventional surveillance plus PET/CT scan found no significant difference in detection of recurrence between the 2 groups. The use of PET/CT in the setting of metastatic colorectal cancer treated with definitive therapy is also not indicated. A recent retrospective study failed to show a correlation with frequency of imaging and effect on time to second procedure or median survival duration.[150]

For surveillance of colorectal cancer, Carelon Oncologic Imaging guidelines are in concordance with the American Society of Clinical Oncology recommendations, National Comprehensive Cancer Network (NCCN) Guidelines for Colon Cancer, and NCCN Guidelines for Rectal Cancer.[126, 135, 151]

Esophageal and Gastroesophageal Junction Cancers

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented esophageal and gastroesophageal junction cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen**	Indicated	Indicated (note: especially useful if PET imaging not done)	Indicated no more than every 6 months (T1b or greater)
CT pelvis	Indicated based on clinical suspicion for pelvic disease	Indicated based on clinical suspicion for pelvic disease	Indicated based on clinical suspicion for pelvic disease
FDG-PET/CT	Indicated when standard imaging cannot be performed or does not demonstrate distant (M1) metastatic disease	Indicated in **ANY** of the following scenarios: • Radiation planning for preoperative or definitive treatment only • Single assessment of response to primary (neoadjuvant) treatment when performed at least 5 weeks after completion of therapy • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Esophageal cancer is the seventh most common cause of cancer-related mortality in men. Over 90% of esophageal cancers are either squamous cell carcinoma or adenocarcinoma.[152] Risk factors for squamous cell carcinoma include tobacco and alcohol use, while adenocarcinoma is associated with gastroesophageal reflux disease and Barrett's esophagus. The most common presentation is symptoms due to obstruction (such as dysphagia or odynophagia), or symptoms caused by distant metastases.

DIAGNOSTIC WORKUP

Esophageal cancer is staged using the American Joint Committee on Cancer TNM system. The role of endoscopic ultrasound is to evaluate tumor depth and lymph node involvement. The overall accuracy of endoscopic ultrasound (EUS) for this component of staging is in the 80% to 90% range. In a meta-analysis which also included high grade esophageal dysplasia, surgical or endoscopic mucosal resection pathologic staging compared to EUS had a T-stage concordance of only 65%.[153] Nonetheless, EUS is still considered superior to CT, MRI, and PET for locoregional staging.[154-156] The National Comprehensive Cancer Network (NCCN) recommends chest/abdominal CT with oral and IV contrast for initial workup; pelvic CT with contrast only as clinically indicated.[157]

While CT is the most widely used modality for detection of distant metastases (M1 disease), the addition of FDG-PET improves detection of lesions that may remain occult on CT, allowing proper patient selection for surgical resection. A meta-analysis of 31 articles found PET/CT to be more accurate than CT for identifying metastatic disease: sensitivity and specificity were 71% (95% CI, 0.62-0.79) and 93% (95% CI, 0.89-0.97) for FDG-PET and 52% (95% CI, 0.33-0.71) and 91% (95% CI, 0.86-0.96) for CT, respectively.[154] In the prospective American College of Surgeons Oncology Group trial Z0060, PET scan identified an additional 5% of biopsy-confirmed distant metastatic disease as compared to conventional imaging.[158] In 2 additional studies, PET/CT resulted in avoidance of futile surgery in up to 17% of patients and change in management of 38.2% of cases.[159]

MANAGEMENT

Metabolic response by PET/CT has been suggested as a surrogate marker for prognosis. In the largest of these studies, the prospective MUNICON phase II trial (N=110) showed that post-treatment PET correlated with treatment response and event-free survival (29.7 months in metabolic responders and 14.1 months in nonresponders, Hazard Ratio, 2.18, P = .002).[160] Conversely, in a review from 2017 that included 13 studies (N = 697), Cremonesi et al. noted that 8 studies supported interim PET, while 5 studies found no benefit in terms of pathological complete response and/or outcome.[161] The NCCN recommends PET/CT as a preferred modality after preoperative or definitive chemoradiation (level 2A recommendation), at least 5-8 weeks after completion of therapy.[157]

SURVEILLANCE

The majority of esophageal and gastroesophageal junction cancer recurrences present as distant metastases within the first 1 to 3 years. Based on the NCCN Guidelines, surveillance imaging can be considered for up to 5 years.[157]

Gastric Cancer

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented gastric cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated	Indicated	Indicated no more than every 6 months
FDG-PET/CT	Indicated for tumors initially stage IB or higher when standard imaging cannot be performed or does not demonstrate distant (M1) metastatic disease, and the patient is a candidate for curative surgery	Indicated in **ANY** of the following scenarios: • Radiation planning for preoperative or definitive treatment only • Single assessment of response to primary (neoadjuvant) treatment, when performed at least 5 weeks after completion of therapy • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

The incidence of gastric cancer has declined over the past 10 years, but it remains one of the leading causes of death worldwide. The most common histologic type is adenocarcinoma. Presenting symptoms may include weight loss, pain, bleeding, or dysphagia. More advanced disease can manifest as ascites and symptoms related to distant metastases.

DIAGNOSTIC WORKUP

Gastric cancer is staged using the American Joint Committee on Cancer TNM system. Endoscopic ultrasound (EUS) is used to obtain pathologic confirmation of malignancy and local tumor staging, with advanced imaging used to assess lymph nodes and metastases. In a meta-analysis of 50 studies, EUS for assessment of locoregional disease showed sensitivity and specificity rates for distinguishing T1 from T2 cancers of 85% and 90%, respectively. Sensitivity and specificity for distinguishing T1/2 from T3/4 tumors were 86% and 90%, respectively. When used to evaluate lymph nodes, EUS had a lower diagnostic yield with sensitivity and specificity of 83% and 67%, respectively.[162] A second meta-analysis reported accuracy rates for tumor staging at 75% and nodal staging at 64% with a sensitivity of 74% and specificity of 80%.[163] In a third systematic review comparing EUS, CT, and MRI, the diagnostic accuracy of overall T staging for EUS, multidetector CT, and MRI varied between 65% to 92.1%, 77.1% to 88.9%, and 71.4% to 82.6%, respectively. The authors concluded that although efficacy was similar, EUS remains the standard of care.[164] The American College of Radiology Appropriate Use Criteria for epigastric pain state that endoscopy is the reference standard for diagnosis of gastric cancer, though they note that patients

often present with nonspecific symptoms leading to advanced imaging such as CT; they further state that CT may be ordered in the setting of suspected gastric outlet obstruction.[165]

Combining PET and CT leads to improved accuracy in preoperative staging (68%) compared to PET (47%) or CT (53%) alone, and in a single-institution retrospective study, changed management in 38% of patients.[166] The major advantage conferred by PET is improved specificity over CT for the detection of distant metastases (M1 disease). Smyth et al. reported in a prospective study that PET/CT identified an additional 10% occult metastatic lesions in patients with locally advanced disease, compared to preoperative CT imaging, EUS, and laparoscopy.[167] FDG PET/CT is recommended for locally advanced or metastatic disease (may not be appropriate for T1 disease) by National Comprehensive Cancer Network (NCCN) (level of evidence category 2A).[168]

MANAGEMENT

The results of studies showing response to therapy as evidenced by FDG-PET have been mixed. A prospective observation trial by Vallbohmer et al. showed no correlations between interval PET findings and change in FDG avidity to response or prognosis.[169] In another study, survival of patients without FDG-avid disease was not significantly different from FDG-avid non-responders.[170] In the setting of recurrent disease, a retrospective study showed overall sensitivity and specificity of 78% and 82% for PET compared to 74% and 85% for CT, respectively.[171] Therefore, NCCN recommends chest/abdominal/pelvic CT scan for medically fit patients after the completion of preoperative therapy (chemotherapy or chemoradiation) and before surgical intervention, with PET as clinically indicated.[168]

SURVEILLANCE

The majority of gastric cancer recurrences occur locoregionally in the lymph nodes and peritoneum, followed by the liver. A retrospective Italian trial, which included patients with T1-4 N0-3 M0 gastric cancer who had undergone D2 dissection, found that 94% recurred within 2 years and 98% recurred within 3 years. Of the recurrences, only 3.2% were treated with curative intent.[172] In a review of 5 articles that included 810 patients, intense surveillance with CT imaging did not show an improvement in survival.[173] Based on the NCCN Guidelines for Gastric Cancer, surveillance imaging for patients with stage II or greater gastric cancer can be done every 6 months for the first 2 years, then annually up to 5 years; after 5 years, additional follow-up may be considered based on risk factors and comorbidities.[168]

Head and Neck Cancer

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented head and neck cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT or MRI primary site and neck	Indicated	Indicated to assess response to neoadjuvant treatment or after concurrent chemoradiotherapy	Indicated
CT chest CT abdomen and pelvis	Indicated	Indicated	Indicated
FDG-PET/CT	Indicated in **EITHER** of the following scenarios: • Evaluation of locoregionally advanced cancers (T3-T4 primary or ≥ N1 nodal staging) of the oral cavity, oropharynx, hypopharynx, nasopharynx, larynx, and sinus • Following biopsy suggestive of a head and neck primary tumor (squamous cell cancer, adenocarcinoma, or anaplastic undifferentiated	Indicated in **ANY** of the following scenarios: • Radiation planning for preoperative or definitive treatment only • Single treatment response evaluation, no sooner than 12 weeks after completion of radiation therapy or chemoradiation • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease • Follow up of equivocal post-treatment PET scan, no	Not indicated

Imaging Study	Diagnostic Workup	Management	Surveillance
	epithelial tumor) when CT or MRI evaluation of the neck has not detected a primary site of tumor	sooner than 12 weeks after the last study	

Note: PET is not generally indicated for initial evaluation of lip and salivary gland cancers, regardless of stage. PET imaging is not indicated for adjuvant radiation therapy planning when all known disease has been removed.

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Head and neck cancers comprise 3% of all cancers in the U.S. Squamous cell carcinoma accounts for more than 90% of these tumors. Tobacco and alcohol use in addition to human papillomavirus infection are primary risk factors. The most common presenting symptoms are pain, dysphagia, or neck mass. Early mucosal lesions may be found incidentally on oral examination.

DIAGNOSTIC WORKUP

Head and neck cancers are staged using the American Joint Committee on Cancer TNM system. When compared to physical exam alone, CT results in a change of stage in 54% of patients.[174] However, CT is relatively poor at identifying invasion of non-osseous cartilage. Newer techniques have improved sensitivity and specificity of CT to almost 90% and 96%, respectively,[175] but up to 67% of pathologic lymph nodes may still be missed.[176] MRI may be indicated as an adjunct to CT, particularly in the management of nasopharyngeal cancers. In a meta-analysis of 10 studies, diffusion-weighted MRI for evaluation of head and neck squamous cell carcinomas improved overall accuracy from 66% to 86%.[177]

In a retrospective study conducted by Fleming et al., PET/CT had an accuracy of 90%, true positive rate of 82.9%, and false positive rate of 12.2%. In patients with unknown primary, PET/CT was able to identify the primary site in 72.7% of patients. Distant metastases were detected in 15.4% of patients, and overall treatment was altered in 30.9% of patients.[178] In a meta-analysis of 8 studies, sensitivity and specificity of PET/PET-CT for detecting distant metastatic disease were 83% and 96% compared with conventional anatomic imaging, 44% and 96%, respectively.[179] The accuracy of PET in early stage head and neck cancers without lymph node involvement is less clear. Multiple small studies have shown relatively poor sensitivity ranging from 25% to 63% for detecting occult lymph node metastases.[180, 181]

MANAGEMENT

A prospective randomized trial by Mehanna et al. found that PET/CT performed 12 weeks after chemoradiation therapy for treatment response for patients with N2/3 disease resulted in substantially fewer neck dissections with no adverse impact on survival.[182] A meta-analysis of 23 studies looking at accuracy of PET/CT found a pooled sensitivity and specificity of 92% and 87%, respectively, for detection of recurrence. A second meta-analysis of 27 studies confirmed these results, with pooled sensitivity and specificity of PET for detecting residual or recurrent head and neck squamous cell carcinoma reported to be 94% and 82%, respectively. However, sensitivity was adversely affected when PET/CT imaging was done within 10 weeks of completion of treatment.[183] A negative PET/CT corresponds with a 90% chance of disease eradication.[184] These findings were corroborated by 2 additional retrospective studies.[185, 186]

SURVEILLANCE

Most recurrences are discovered by patients and not by serial imaging or physical exam. Carelon guidelines are in accordance with National Comprehensive Cancer Network Guidelines for Head and Neck Cancers.[187]

Hepatocellular and Biliary Tract Cancers

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented hepatocellular and biliary tract cancers.

Imaging Study	Diagnostic Workup and Diagnosis	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated	Indicated	Indicated no more than every 6 months

Imaging Study	Diagnostic Workup and Diagnosis	Management	Surveillance
MRI abdomen with or without MRCP	Indicated for **EITHER** of the following scenarios: • Known cirrhosis or hepatitis B, with positive or rising serum alpha fetoprotein (AFP)* • Documented hepatobiliary cancer	Indicated	Indicated no more than every 6 months
FDG-PET/CT	Indicated when standard imaging cannot be performed or is nondiagnostic regarding the extent of disease	Indicated when standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

**Positive AFP ≥ 200 ng/mL (American Association for the Study of Liver Disease)*

Rationale

DIAGNOSTIC WORKUP

Hepatobiliary cancer (including gallbladder cancer, cholangiocarcinoma and hepatocellular carcinoma) is staged using the American Joint Committee on Cancer TNM system.

Hepatocellular Carcinoma (HCC)

The initial staging evaluation of suspected HCC should include either a multiphasic abdominal CT or MRI to establish the diagnosis and assess the burden of disease. The National Comprehensive Cancer Network (NCCN) also recommends CT or MRI if positive or rising serum AFP is found during HCC screening.[48]

A diagnosis of HCC can be made based on imaging criteria in patients at high risk for developing HCC; the most commonly used guidelines are published by the American Association for the Study of Liver Disease (AASLD)[47], which incorporates the American College of Radiology (ACR) Liver Imaging Reporting and Data System (LI-RADS).[188] In a systematic review and meta-analysis evaluating the diagnostic performance of multidetector CT and MRI, the overall per-patient sensitivity of MR imaging was 88% (95% CI, 83%-92%) and per-patient specificity was 94% (95% CI, 85%-98%). An insufficient number of studies disallowed pooled analysis of CT for diagnostic accuracy and comparison to MRI, but the overall per-lesion sensitivity of MR imaging was higher than that of multidetector CT when the paired data of the 11 available studies were pooled (80% vs 68%, P = .0023). In addition, MRI sensitivity was further improved when gadoxetic acid-enhanced MR imaging was used. Sensitivity tends to be worse in both modalities for lesions < 1cm.[189]

Extrahepatic imaging should include CT of the chest and pelvis if not already done. Bone scan may be useful when clinical suspicion of bone metastases is high. In a retrospective study comparing PET and conventional imaging for initial diagnosis of HCC, PET identified additional metastases in 2.7% of patients with T2, 5.3% of patients with T3a (5.3%), and 4.8% of patients with T3b tumor classifications.[190] In a systematic review and meta-analysis, the pooled estimates of sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of FDG PET for the detection of metastatic hepatocellular carcinoma were 76.6%, 98.0%, 14.68, and 0.28, respectively.[191] Although PET imaging may provide prognostic information on the biological aggressiveness of the cancer, the low sensitivity restricts its usefulness.[192]

Cholangiocarcinoma and Gallbladder Cancer

In patients with suspected cholangiocarcinoma/gallbladder cancer, CT chest and multi-detector, multiphasic CT of the abdomen and pelvis should be performed to assess local disease, lymph nodes, and sites of distant metastases. If an intervention is not required and accurate imaging of the pancreatobiliary tract is needed to assess surgical resectability, an MRI abdomen with magnetic resonance cholangiopancreatography (MRCP) should be considered. MRCP has largely replaced endoscopic retrograde cholangiopancreatography (ERCP) as it provides better anatomical imaging, a non-invasive alternative with lower risk of complications, and at least equivalent accuracy.[193-197] In a systematic review and meta-analysis comparing CT, MRI, and PET to assess for resectability of hilar cholangiocarcinoma, CT had the highest pooled sensitivity at 95% (95% CI, 91%-97%) and a pooled specificity of 69% (63%-75%). MRI had a pooled sensitivity of 94% (90%-97%) and a pooled specificity of 71% (60%-81%), whereas PET/CT had a pooled sensitivity of 91% (84%-96%), and the highest pooled specificity at 81% (95% CI, 69%-90%). The area under the curves (AUC) of CT, MRI, and PET/CT were 0.9269, 0.9194, and 0.9218, respectively. Overall, CT and MRI are comparable imaging modalities to assess resectability. [198] The data to support

use of PET/CT for initial staging of cholangiocarcinoma is mixed, although some studies show a change in management of 17%-25%.[199-201] Overall, PET imaging has limited sensitivity for local evaluation of cholangiocarcinoma, although high specificity for detection of nodal and distant metastatic disease. Per NCCN recommendations, PET/CT may be considered when equivocal findings are seen.[202] The European Society for Medical Oncology (ESMO) recommends MRI as the reference examination for local extension of cholangiocarcinoma and for hepatic metastases, and recommends thoraco-abdomino-pelvic CT for evaluation of nodal disease and other metastases.[203]

MANAGEMENT

Response to treatment can be assessed with multiphasic CT or MRI of the abdomen, as both can assess intra-nodular arterial vascularity, a key feature of residual or recurrent tumor. Overall nodule size does not reliably indicate treatment response since a variety of factors may cause a successfully treated lesion to appear stable in size or even larger after treatment. The NCCN notes for hepatocellular cancer “PET/CT has limited sensitivity but high specificity, and may be considered when there is an equivocal finding.”[48]

SURVEILLANCE

In patients treated with curative intent, follow-up for HCC includes CT or MRI imaging of the liver, and consideration for CT chest imaging. Monitoring of AFP is appropriate for HCC. Carelon Oncologic Imaging guidelines are in concordance with the NCCN Guidelines for Hepatocellular Carcinoma and for Biliary Tract Cancers and the ESMO Clinical Practice Guideline for biliary tract cancer.[48, 202 203]

Histiocytic Neoplasms

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of Langerhans cell histiocytosis (LCH), Erdheim-Chester disease (ECD), and Rosai-Dorfman disease (RDD).

Imaging Study	Diagnostic Workup	Management	Surveillance
MRI or CT (any)	Indicated when categorized as 2A recommendation by NCCN	Indicated when categorized as 2A recommendation by NCCN	Indicated when categorized as 2A recommendation
FDG-PET/CT	Indicated in **p**atients with LCH, ECD, or RDD	Indicated for **ANY** of the following scenarios: • Following radiation therapy • Treatment response after 2-3 cycles of systemic therapy and at completionCT • After completion of surgical curettage • Treatment response of ECD	Indicated for **EITHER** of the following scenarios: • LCH: every 3-6 months for first 2 years following treatment completion, then annually • ECD/RDD: every 3-6 months after starting therapy until stabilization of disease

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

DIAGNOSTIC WORKUP

Histiocytic neoplasms are rare neoplasms (annual incidence of < 5 cases per million population) originating from cells of the myeloid lineage. Clinical overlap is observed among the three most commonly seen disorders: Erdheim-Chester disease (ECD), Langerhans cell histiocytosis (LCH), and Rosai-Dorfman disease (RDD). These neoplasms may present clinically as focal or diffuse multiple organ disease, with the disease spectrum varying from incidental lesions on imaging studies to critical illness arising from severe organ dysfunction. Common sites of involvement include the axial/appendicular skeleton and skull, hypothalamus/pituitary gland, lungs, skin, heart, kidneys/retroperitoneum and less commonly arterial blood vessels, spleen, and liver.

A presumptive diagnosis (without tissue diagnosis) is typically made with characteristic radiographic/clinical findings (e.g., typical pattern of lung nodules, cysts, and cavitated nodules on high-resolution Chest CT), but definitive diagnosis requires tissue examination and immunohistochemistry stains. Because neoplastic cells are often sparsely distributed amongst fibrosis

and inflammatory cells, biopsy and histologic evaluation can be challenging. Whole-body PET/CT is recommended by several guidelines (including the National Comprehensive Cancer Network, NCCN) as part of the workup/evaluation of histiocytic neoplasms, to assess both presence and extent of disease.[204]

MANAGEMENT

NCCN recommends PET/CT as the preferred modality for treatment response assessment, including post radiation therapy, systemic therapy, and completion of surgical curettage.

SURVEILLANCE

Carelon Oncologic Imaging guidelines are in concordance with the National Comprehensive Cancer Network (NCCN) Guidelines for Histiocytic Neoplasms.

Kidney Cancer

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented kidney cancer (including renal cell carcinoma, Wilms tumor/nephroblastoma).

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest	Indicated	Indicated	Indicated for **ANY** of the following: • Ablation: no more than annually • Partial or total nephrectomy: no more than every 6 months • Stage III or IV disease
CT abdomen +/- pelvis **MRI abdomen**	*See "Renal mass" in Abdominal Imaging*	Indicated for **EITHER** of the following: • Baseline imaging after ablation, partial or total nephrectomy • Active surveillance of stage I renal cancer: within 6 months of initiation, then annually	Indicated for **ANY** of the following: • After ablation, partial or total nephrectomy: no more than every 6 months • Stage III or IV disease
FDG PET/CT	Not indicated	Not indicated	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Kidney cancer is the sixth most common cancer in men and the tenth most common cancer in women. The most common tumor type is renal cell carcinoma, which arises from renal parenchyma. Primary nephrectomy is indicated in most forms of kidney cancer. Until recently, fully resected renal cell carcinoma has been managed with surveillance only. Treatment options for metastatic renal cell carcinoma have greatly expanded in the last decade with immunosuppressive therapies such as cell cycle checkpoint inhibitors (PD-1 agents), mechanistic target of rapamycin (mTOR) inhibitors, and tyrosine kinase inhibitors (TKI).

DIAGNOSTIC WORKUP

Kidney cancer is staged using the American Joint Committee on Cancer TNM system. In a study comparing triphasic helical CT and fast MRI, renal cell carcinoma was correctly staged 67% of the time.[205] In another prospective study, accuracy of MRI was 78%-87%, and the accuracy of CT was 80%-83%.[206] Both modalities, however, are poor at detecting invasion of perinephric fat and assessing tumor extension into the renal veins or inferior vena cava. For the evaluation of renal vein involvement, MRI and CT appear to have approximately the same accuracy of 72%-76% and 78%-88%, respectively.[207]

In the evaluation of primary renal cell carcinoma, PET accuracy was only 50%. The utility of PET/CT is adversely affected by poor FDG avidity and background uptake from the kidney. Although a poor staging modality, specificity of PET was found to approach 100% in 2 separate studies.[208, 209] The NCCN and ACR notes that the value of PET in renal cell carcinoma remains to be determined.[210] [211] Current evidence suggests that imaging of the pelvis is of low yield and does not affect overall

management.[212, 213] For chest imaging, radiography is preferred, although CT is more sensitive in patients with symptoms, advanced-stage disease, anemia, or thrombocytopenia.[214, 215]

Carelon guidelines are in accordance with recommendations from the National Comprehensive Cancer Network Guidelines for Kidney Cancer.[210,]

MANAGEMENT

Imaging (CT or MRI) with contrast can be done when clinically indicated following ablative techniques, and as baseline imaging after partial or radical nephrectomy (NCCN level of evidence category 2B).[210, 216]

SURVEILLANCE

Active surveillance can be considered in select T1b patients. Imaging (CT or MRI) should be done with contrast when clinically indicated if no contraindication. Active surveillance entails serial abdominal imaging with timely intervention should the mass demonstrate growth (e.g. tumor size, growth rate, infiltrative pattern) indicative of increasing metastatic potential. No single follow-up plan is appropriate for all patients. Follow-up frequency and duration should be individualized based on patient requirements, and may be extended beyond 5 years at the discretion of the physician. The choice to perform imaging follow-up is level of evidence category 2B as designated by the National Comprehensive Cancer Network.[210, 216]

Lung Cancer – Non-Small Cell

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented non-small cell lung cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis	Indicated	Indicated	Indicated (note: usually only CT chest needed with contrast for 1st 2 years followed with non-contrast thereafter)
MRI chest	For Pancoast tumors when CT is nondiagnostic	Not indicated	Not indicated
FDG-PET/CT	Indicated for evaluation of extent of disease following biopsy confirmation of non-small cell lung cancer, if not previously performed	Indicated in **ANY** of the following scenarios: • Radiation planning for preoperative or definitive treatment • Evaluation following induction or neoadjuvant therapy, to determine eligibility for resection • Assessment of response to definitive chemoradiation when performed at least 12 weeks following therapy • Standard imaging cannot be performed, or is nondiagnostic for recurrent or progressive disease • Surveillance CT Chest demonstrates recurrence	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Lung cancer is the second most common cancer in both men and women but accounts for the largest number of cancer deaths. The two most common types of lung cancer are non-small cell lung cancer and small cell lung cancer. Non-small cell lung cancer accounts for 85%-90% of lung cancers and is further subdivided into adenocarcinoma, squamous cell carcinoma, and other large cell carcinomas. Risk factors for developing non-small cell lung cancer include tobacco use, radon exposure, asbestos exposure, and other environmental factors. Adenocarcinoma is unique as this lung cancer is most often seen in nonsmokers and light smokers. Presenting symptoms may include cough, hemoptysis, dyspnea, and chest pain.

DIAGNOSTIC WORKUP

Non-small cell lung cancer is staged using the American Joint Committee on Cancer TNM system. CT can accurately evaluate the primary tumor and detect metastatic disease, but is less accurate than PET/CT in identifying mediastinal lymphadenopathy.[217, 218] Studies comparing CT and PET/CT for staging of mediastinal nodes have found accuracy rates of 80%-84% for PET/CT versus 76%-77% for CT alone.[219, 220] In one prospective trial, PET/CT prevented unnecessary surgery in 17% of patients.[221]

PET/CT can be used for planning treatment volumes as well as determination of the need for extranodal irradiation. The Radiation Therapy Oncology Group 0151 showed that PET/CT-derived tumor volumes were smaller than those derived by CT alone with only a small number of patients developing nodal failures.[222] Involved field irradiation has been shown to improve overall survival in patients over extranodal irradiation in a prospective study by Yuan et al. In this prospective study, the involved field irradiation arm achieved better overall response and local control than the extranodal irradiation arm, and it allowed a dose increase from 68 to 74 Gy to be safely administered.[223]

MANAGEMENT

Following treatment with concurrent chemoradiation therapy for superior sulcus non-small cell lung cancer, restaging with either CT or PET/CT is appropriate for detection of metastatic disease. For definitive treatment with chemoradiation therapy, the most appropriate follow-up imaging modality is not clear. A prospective study looking at PET/CT versus CT for the restaging of stage IIIA non-small cell lung cancer after neoadjuvant chemoradiation therapy showed PET/CT scan was more accurate than CT alone for restaging at all pathologic stages (stage 0, 92% vs 39%, P = .03; stage I, 89% vs 36%, P = .04). The authors, however, concluded that nodal biopsies are required since a persistently high maximum standardized uptake value does not equate to residual cancer.[224] Two other studies which evaluated post-treatment PET for locally advanced non-small cell lung cancer after treatment with concurrent chemoradiation therapy found PET was able to accurately predict local control and tumor response.[225, 226] Pan et al. compared conventional CT to PET/CT for locally advanced non-small cell lung cancer performed at 9 months after completion of therapy. Although PET/CT was able to identify progression of disease and recurrence in 48% of patients, no difference in survival could be demonstrated (21.6 months in CT group vs. 23.5 months in PET/CT, P = .89).[227] PET/CT may remain FDG-avid up until 2 years after radiation therapy.[228] Any suspected recurrence should be biopsied for pathologic confirmation.

SURVEILLANCE

NCCN recommends surveillance imaging with CT chest every 6 months for 2 to 3 years followed by annual low-dose technique CT chest for stage I/II treated with surgery. All others should undergo CT chest every 3 to 6 months for 3 years, then every 6 months for 2 years. Timing of CT scans within Guideline parameters is a clinical decision.[229]

Lung Cancer – Small Cell

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented small cell lung cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen with or without pelvis	Indicated	Indicated	Indicated
FDG-PET/CT	Indicated prior to definitive therapy when standard imaging is nondiagnostic for extent of disease	Indicated for **EITHER** of the following scenarios: • Prior to initiation of radiation therapy	Not indicated

Imaging Study	Diagnostic Workup	Management	Surveillance
		• Standard imaging cannot be performed, or is nondiagnostic for recurrent or progressive disease	

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Lung cancer is the second most common cancer in both men and women but accounts for the largest number of cancer deaths. The two most common types of lung cancer are small cell lung cancer and non-small cell lung cancer. Small cell lung cancer is classified as limited stage small cell lung cancer or extensive stage small cell lung cancer. Small cell lung cancer accounts for 10% to 15% of lung cancers and is most commonly found in smokers. Presenting symptoms may include cough, hemoptysis, dyspnea, and chest pain.

DIAGNOSTIC WORKUP

Asymptomatic metastatic central nervous system disease is seen in up to 15% of patients and MRI brain with contrast is indicated regardless of stage.[230, 231] Most of the available data regarding PET in lung cancer is for non-small cell lung cancer, but limited data does suggest that PET/CT can increase staging accuracy in small cell lung cancer. In a small prospective trial (N = 24) evaluating PET versus CT in limited stage small cell lung cancer, FDG-PET had a lesion-based sensitivity relative to CT of 100% and upstaged 2/24 (8.3%) patients. In addition, 25% of patients (6/24) were discovered to have unsuspected regional nodal metastasis.[232] Survival benefit was seen in a retrospective study using pre-treatment PET in patients with limited stage small cell lung cancer. Three-year overall survival was 47% for PET versus 19% for CT (P = .03). The authors attributed the difference in survival to improved radiation field planning and disease upstaging.[233] Another review found an 84% concordance between PET and CT for staging; however, 19% were upstaged to extensive stage small cell lung cancer and 8% were downstaged to limited stage small cell lung cancer when PET was performed.[230] In studies where PET/CT was used for staging and targeting of lymph nodes for radiation, the local recurrence rates have been reported to be less than 3%.[234, 235] Pathologic staging is still required for PET/CT-detected lesions that would result in upstaging.[236]

MANAGEMENT

The NCCN recommends assessment of treatment response following systemic therapy with or without subsequent radiation therapy using chest/abdomen/pelvis CT (level of evidence category 2A); NCCN does not recommend PET/CT for routine follow-up.[236] Three small prospective trials (N = 36) evaluated the use of PET for response assessment in small cell lung cancer. Although metabolic response was associated with better prognosis, no patient benefit was observed.[231]

SURVEILLANCE

National Comprehensive Cancer Network Guidelines for Small Cell Lung Cancer recommend imaging surveillance with a CT of the chest and abdomen every 3 to 4 months as clinically indicated. There is no role for PET/CT in surveillance of treated small cell lung cancer.[236]

Lymphoma – Hodgkin

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented Hodgkin lymphoma, as below.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck **CT chest** **CT abdomen and pelvis**	Indicated (note: may consider omitting if PET/CT has been completed)	Indicated (note: may consider omitting if PET/CT done to assess disease response to chemotherapy)	Indicated not to exceed 2 years following completion of treatment
FDG-PET/CT	Indicated (note: especially useful as an adjunct to CT imaging)	Indicated in **ANY** of the following scenarios: • Radiation planning for definitive or consolidative treatment	Not indicated

Imaging Study	Diagnostic Workup	Management	Surveillance
		• Interim restaging following 2-4 cycles of treatment • Baseline post-treatment evaluation at least 3 weeks following completion of all cycles of chemotherapy or 12 weeks following completion of radiation therapy • Single follow up when first post-treatment baseline PET showed Deauville 4 or 5 findings* • Clinical suspicion for recurrence or progression of disease based on standard imaging or objective signs/symptoms	

**Deauville 4 (uptake moderately increased compared to the liver at any site); Deauville 5 (uptake markedly increased compared to the liver at any site)*

Rationale

Hodgkin lymphoma accounts for about 10% of all lymphomas. Risk factors include Epstein-Barr viral infection, immunosuppression, autoimmune disorders, and genetic predisposition. The most common presentation is painless lymphadenopathy, although many patients also present with B (systemic) symptoms (fevers, chills, night sweats, and weight loss). In more advanced disease, symptoms result from local tumor growth affecting organ function or causing systemic metabolic derangements.

DIAGNOSTIC WORKUP

Hodgkin lymphoma is staged using the Lugano classification system. PET/CT can result in changing of clinical stage in 20% of patients.[237] In the RATHL (Response-Adapted Therapy in Advanced Hodgkin Lymphoma) study, PET/CT resulted in upstaging 14% and downstaging 6%.[238] In a meta-analysis of 20 studies, the pooled sensitivity for PET/CT was 90.9% (95% CI, 88.0-93.4), and the pooled false positive rate was 10.3% (95% CI, 7.4-13.8) for staging and restaging.

MANAGEMENT

Response to treatment uses the 5-point Deauville criteria for assessment of metabolic response. For early stage favorable Hodgkin lymphoma, the value of interim PET/CT has been mixed although more recent data supports the use of interim PET for response-adapted treatment.[239, 240] For early stage unfavorable Hodgkin lymphoma or stage III and IV Hodgkin lymphoma, Gallamini et al. found that following a negative interim PET scan, the 2-year progression-free survival was 12.8% for PET positive and 95.0% for PET negative (P < .0001).[241] Cercil et al. found 3-year event-free survival was 53.4% for PET positive and 90.5% for PET negative (P < 0.001).[242] Three large randomized trials have confirmed that a risk-adapted approach to chemotherapy after negative interim PET is safe and did not result in poorer outcomes.[243, 244]

SURVEILLANCE

National Comprehensive Cancer Network (NCCN) Guidelines include consideration of CT every 3-6 months up to 2 years following completion of therapy as clinically indicated.[245] There is limited data to support routine PET/CT imaging in Hodgkin lymphoma. A randomized study comparing PET/CT to ultrasound and chest radiography for routine surveillance of patients with advanced Hodgkin lymphoma showed that sensitivity was equal in both groups. The conventional imaging arm had a higher specificity (96% vs 86%; P = .02) and positive predictive value (91% vs 73%; P = .01).[246] Although PET/CT negative patients had a high likelihood of being disease free, PET/CT also produced false positive rates as high as 20%.[5, 247, 248]

Lymphoma – Non-Hodgkin and Leukemia

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented acute leukemia, chronic lymphocytic leukemia/small lymphocytic lymphoma and non-Hodgkin lymphomas.

Acute Leukemia

Advanced imaging is considered medically necessary for diagnostic workup and management of documented acute leukemias.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck CT chest CT abdomen and pelvis	Indicated	Indicated for clinical suspicion or treatment response to extramedullary disease (chloromas)	Not indicated
PET/CT	Indicated in **EITHER** of the following scenarios: • Clinical suspicion for extramedullary disease or lymphadenopathy • When standard imaging cannot be performed or is nondiagnostic	Indicated in **ANY** of the following scenarios: • Relapsed or refractory extramedullary disease • Treatment response of ALL with lymphomatous extramedullary disease • When standard imaging cannot be performed or is nondiagnostic	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Chronic lymphocytic leukemia or small lymphocytic lymphoma

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis	Indicated	Indicated based on symptoms or to evaluate bulky disease	Not indicated
FDG-PET/CT	Indicated for suspicion of Richter's transformation when PET is utilized to direct biopsy	Indicated for suspicion of Richter's transformation when PET is utilized to direct biopsy	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Lymphoma – Non-Hodgkin: Indolent non-Hodgkin lymphoma

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck CT chest CT abdomen and pelvis	Indicated	Indicated	Indicated in **EITHER** of the following scenarios: • Follicular, marginal zone/MALT, or mantle cell lymphoma: Every 6 months, up to 2 years following completion of treatment and every 12 months thereafter • All other subtypes: Every 6 months, up to 2 years following completion of treatment

Imaging Study	Diagnostic Workup	Management	Surveillance
FDG-PET/CT	Indicated in **ANY** of the following scenarios: • Initial evaluation of suspected lymphoma when lymph nodes are not amenable to biopsy • Evaluation of suspected transformation to a more aggressive lymphoma based on clinical signs or symptoms • Prior to initiation of therapy	Indicated in **ANY** of the following scenarios: • Radiation planning prior to definitive or consolidative treatment • Evaluation at completion of therapy, when initial PET scan demonstrated FDG uptake • Evaluation of suspected recurrence or progression of disease based on standard imaging when there is an indication to resume systemic treatment • Evaluation of suspected transformation to a more aggressive lymphoma based on clinical signs or symptoms	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Lymphoma – Non-Hodgkin: Intermediate and high grade non-Hodgkin lymphoma

Includes Castleman Disease, Post-Transplant Lymphoproliferative Disorders

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck **CT chest** **CT abdomen and pelvis**	Indicated (note: may consider omitting if PET/CT has been completed)	Indicated	Indicated in **EITHER** of the following scenarios: • Follicular, marginal zone/MALT, or mantle cell lymphoma: Every 6 months, up to 2 years following completion of treatment, and every 12 months thereafter • All other subtypes: Every 6 months, up to 2 years following completion of treatment
FDG-PET/CT	Indicated in **EITHER** of the following scenarios: • Initial evaluation of suspected lymphoma when lymph nodes are not amenable to biopsy • Initial staging (often used as an adjunct to CT chest/abdomen/pelvis)	Indicated in **ANY** of the following scenarios: • Radiation planning prior to definitive or consolidative treatment • Interim restaging following 2-4 cycles of treatment • Evaluation at completion of therapy • Evaluation of suspected recurrence or progression of disease based on	Not indicated

Imaging Study	Diagnostic Workup	Management	Surveillance
		standard imaging or objective signs/symptoms	

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Lymphomas are divided into Hodgkin and non-Hodgkin lymphomas. Non-Hodgkin lymphoma (NHL) is the seventh most common cancer in both men and women. Non-Hodgkin lymphoma is further subdivided into indolent, aggressive, and highly aggressive. Aggressive and highly aggressive lymphomas generally present over weeks to months, while indolent lymphomas may be undiagnosed for years due to their slow rate of growth. Common presenting symptoms include enlarged lymph nodes, B symptoms (fevers, chills, night sweats, weight loss), or in the case of more aggressive NHL, symptoms resulting from local tumor growth or systemic metabolic derangements.

Acute leukemias include acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and acute promyelocytic leukemia (APL). Risk factors for developing ALL include older age (> 70 years), exposure to chemotherapy or radiation therapy, and certain genetic disorders. The clinical presentation of ALL is typically nonspecific, and may include fatigue, B symptoms, dyspnea, and easy bruising or bleeding. Approx. 20% of patient have lymphadenopathy, splenomegaly and/or hepatomegaly.[249] Extramedullary disease (including CNS involvement) is uncommon in AML; presentation of solitary extramedullary disease is currently referred to as myeloid sarcoma (historically as chloroma).[250]

DIAGNOSTIC WORKUP

Lymphoma is staged using the Lugano classification system. For chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), CT chest, abdomen, and pelvis is not routinely indicated unless clinically indicated.[251] PET/CT is most accurate for staging and interim assessment of lymphomas with high FDG avidity like diffuse large B-cell lymphoma, follicular NHL, and nodal marginal zone lymphoma, but may be less accurate for CLL/SLL, marginal zone lymphoma, and hairy cell leukemia.[252, 253]

For staging of indolent NHL, the evidence comparing the accuracy of PET/CT to CT alone is mixed. In a recent prospective trial, both modalities performed equally well at initial staging for both indolent and intermediate grade lymphomas.[254] However, multiple retrospective trials have found significantly higher sensitivity for PET/CT (94%-98%) and a resultant change of management based on PET findings in 34% of patients.[255, 256]

For aggressive and highly aggressive NHL, a PET/CT with or without CT chest, abdomen and pelvis with contrast is indicated. In a retrospective study comparing CT to PET for Hodgkin lymphoma and high-grade NHL, the sensitivity of PET/CT versus contrast-enhanced CT was 94% vs. 88% respectively. For evaluation of organ involvement, sensitivity of PET/CT versus contrast-enhanced CT was 88% vs. 50%, respectively. Statistically, PET/CT and CT were equivalent for nodal disease, but PET/CT was more accurate for extranodal disease.[257] In a meta-analysis of 20 studies, PET/CT had a pooled sensitivity of 90.9% (95% CI, 88.0-93.4) and the pooled false-positive rate was 10.3% (95% CI, 7.4-13.8).[258] Change in treatment has been reported in as many as 9% of cases with the addition of PET/CT scan.[259]

For acute leukemia, CT scans of the neck, chest, and abdomen/pelvis with IV contrast and CT or MRI head are recommended as indicated by signs/symptoms at diagnosis; PET/CT may be considered if any extramedullary involvement is suspected.[249, 250]

MANAGEMENT

In general, advanced imaging is not necessary for routine monitoring of treatment response or progression of CLL/SLL. A meta-analysis of the German CLL study group phase 3 trials (CLL4, CLL5, and CLL8) found that 77% of recurrent/progressive disease were detected by clinical symptoms or laboratory testing; CT detected an additional 9% with only a 1% effect on management decisions.[260]

The 5-point Deauville criteria are used for assessment of treatment response. In a retrospective study, PET/CT outperformed CT for response assessment for follicular non-Hodgkin lymphoma. The accuracy of PET/CT for response assessment was superior to CT (0.97 vs 0.64) and also predicted improvement in progression-free survival (48 months vs 17 months, P < .01).[261]

Multiple studies have confirmed that PET positivity correlates with active tumor for both NHL and lymphomatous extramedullary disease in ALL. In a representative study, patients who had negative PET imaging after 2 cycles of therapy had a higher rate of complete remission (83% vs 58%) and greater estimated 2 year overall survival (90% vs 61%, P < .001).[262] A more recent prospective study, however, showed that a positive interim PET scan predicted worse event-free survival (48% vs 74%, P =.004), but was unable to predict differences in 2 year overall survival (88% vs 91%, P < .001).[263]

SURVEILLANCE

For CLL/SLL, routine use of CT is not indicated. Management changes resulting from CT imaging only occurred in 1% of patients.[260]

National Comprehensive Cancer Network Guidelines (NCCN) for B-Cell Lymphomas recommend surveillance imaging with chest, abdominal/pelvic CT no more than every 6 months up to 2 years post treatment, then no more than annually thereafter (for certain subtypes) or as clinically indicated.[253]

Melanoma

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented cutaneous or mucosal (including uveal/choroidal) melanoma.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck **CT chest** **CT abdomen and pelvis**	Indicated	Indicated	Indicated for stage IIB or higher
MRI Abdomen	*See "Suspected or Known Metastases"*	*See "Suspected or Known Metastases"*	Indicated for uveal melanoma when liver ultrasound cannot be performed or nondiagnostic
FDG-PET/CT	Indicated in **ANY** of the following scenarios: • To determine the extent of involvement in mucosal melanoma or stage III and IV cutaneous melanoma, when used in place of CT chest, abdomen, and pelvis • Standard imaging cannot be performed or is nondiagnostic for metastatic disease • When the primary site is unknown and standard imaging is negative	Indicated in **ANY** of the following scenarios: • Radiation planning for definitive treatment • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease • To assess treatment response in mucosal melanoma or unresectable stage III and IV cutaneous melanoma, when used in place of CT chest, abdomen, and pelvis	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Melanoma, which arises from the pigment-producing cells of the epidermis, is the sixth most common cancer in men and women. Incidence increases with age and is higher in Caucasians. Risk factors include excessive sun exposure, family history, and immunosuppression. The most common initial manifestation of melanoma is a darkly pigmented lesion that changes in size, shape, or color.

Mucosal melanoma is an aggressive type of noncutaneous melanoma arising from melanocytes in mucosal cells, and includes uveal or choroidal melanomas of the eye. The most common site is the head and neck. The incidence of mucosal melanoma is higher in females and persons of African descent, and increases with age. Lesions are most often found incidentally on exam, although they can present with local symptoms such as vision loss/changes, epistaxis, loss of smell, bleeding, or ulceration. Unlike other solid cancers, all mucosal melanomas are considered stage III at a minimum. Resectable disease is treated with surgery and neck dissection followed by adjuvant radiation. For advanced stage (IVB/C) disease, treatment may include radiation and/or systemic treatment.

DIAGNOSTIC WORKUP

Cutaneous melanoma

Melanoma is staged using the American Joint Committee on Cancer TNM system. Imaging for patients with stage I/II disease is insensitive and has a high rate of false positive findings. In a study of 344 patients with T1b-T3b melanoma who had preoperative imaging, the false positive rates were 88% for CT chest, 91% for CT abdomen and pelvis, and 60% for PET/CT.[264] Among patients with positive sentinel lymph nodes, routine imaging resulted in 48% of patients having indeterminate findings, of these less than 4% had confirmed systemic metastases. All patients with true positive metastatic disease had thick melanomas and/or lymph node macrometastases.[265] Older studies evaluating the accuracy of CT for detection of metastases in stage III disease have found rates approaching 4%, with false positives ranging from 3%-8%.[266, 267]

In a systematic review evaluating PET/CT imaging, sensitivity ranged from 68% to 87% and specificity from 92% to 98% for stage III/IV melanomas. These results were similar to another meta-analysis showing an overall sensitivity of 89.4% and specificity of 88.8%. Management changed in 22% of patients when PET imaging was utilized. Comparing across modalities, a meta-analysis of 74 studies showed that the sensitivity, specificity, and odds ratio of CT were 51%, 69%, and 2.29, respectively, for detection of distant metastases compared to PET/CT which were 80%, 87%, and 25.23, respectively.[268]

Mucosal melanoma

Staging studies for tumors arising in the head and neck should include CT/MRI to determine extent of the primary tumor, resectability, and lymph node involvement. Despite the lack of treatment options for patients with uveal melanoma and distant metastatic disease, NCCN favors staging before primary treatment.[269] The most frequent sites of uveal melanoma metastasis are liver, lungs, skin/soft tissue and bones. As such, NCCN recommends at minimum that these patients have contrast MRI or ultrasound of the liver, with modality preference determined by expertise at the treating institution.[269] Bone scintigraphy is generally not required, especially if a FDG-PET/CT is planned. Evidence to support the use of PET is limited, but given the behavior of these tumors, Carelon's panel of external experts has recommended in favor of its use.

MANAGEMENT

In most cases, conventional imaging with CT is adequate for assessment of treatment response. If radiation is planned either for definitive therapy or consolidative therapy, PET imaging may be used to assess for metastatic disease. After complete surgical resection, additional imaging should follow guidelines for surveillance.

SURVEILLANCE

The majority of cutaneous melanoma recurrences are either detected by the patient or on physical examination. Surveillance imaging is of low yield and not indicated for early stage disease. In surveillance imaging for stage III melanoma, studies have found detection rates were widely variable, ranging between 7%-56%.[270-273] The National Comprehensive Cancer Network (NCCN) follow-up recommendations for stage IIB-IV (no evidence of disease) melanoma include consideration of imaging every 3-12 months for 2 years, then every 6-12 months for another 3 years (level 2B recommendation).[274] Surveillance imaging of asymptomatic patients should not continue beyond 3-5 years due to the risk of radiation exposure and based on expected patterns of recurrence.[275] For patients with uveal melanoma who elect surveillance imaging, options include contrast MRI or ultrasound of the liver, with modality preference determined by expertise at the treating institution.[269]

Merkel Cell Carcinoma

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented Merkel cell carcinoma.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck **CT chest** **CT abdomen and pelvis**	Indicated (note: may consider omitting if PET imaging done)	Indicated (note: may consider omitting if PET imaging done)	Indicated (note: most useful with high-risk patients)
FDG-PET/CT	Indicated	Indicated	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Merkel cell carcinoma (MCC) is a very rare and aggressive type of skin cancer arising from cells in the basal layer of the epidermis and hair follicles. Incidence increases with age and is higher in Caucasians; other risk factors include sun exposure, immunosuppression, and Merkel cell polyomavirus.

DIAGNOSTIC WORKUP AND MANAGEMENT

MCC is staged using the American Joint Committee on Cancer TNM system. MCC is a highly aggressive cancer and up to 8% of patients will present with metastases.[276] Results from a single institution study showed that PET resulted in upstaging in 17% and downstaging in 5% of patients with an overall management change in 37% of patients. A second single institution study also found that PET resulted in upstaging of 16% of patients.[277] A meta-analysis of 6 studies (N = 92 patients) showed PET had a sensitivity of 90% (95% CI, 80%-96%) and specificity of 98%.[278] Asymptomatic brain metastases are fairly rare and routine use of MRI is not recommended.[279]

The NCCN recommends imaging in most cases of MCC as clinically indicated (whole-body PET/CT or PET/MRI or chest/abdomen/pelvis CT), with several studies indicating whole-body PET with fused axial imaging is more sensitive for detecting occult metastatic disease at baseline. [280]

SURVEILLANCE

Most recurrences of MCC occur within the first 2 years. In high-risk patients, routine surveillance with CT neck, chest, abdomen, and pelvis with contrast can be considered for the first 3 years although there is limited data to support this recommendation.

Multiple Myeloma

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented solitary plasmacytoma and multiple myeloma.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated for multiple myeloma, smoldering myeloma, or solitary plasmacytoma*	Indicated	N/A
MRI (bone marrow blood supply)	Indicated for multiple myeloma, smoldering myeloma, or solitary plasmacytoma*	Indicated for **ANY** of the following scenarios: • Multiple myeloma • Smoldering myeloma or solitary plasmacytoma: restaging/treatment response, or follow-up every 12 months	N/A
MRI dedicated body part	Indicated for evaluation of focal bone lesions	Indicated for evaluation of focal bone lesions	N/A
FDG-PET/CT	Indicated for multiple myeloma or solitary plasmacytoma*	Indicated for **ANY** of the following scenarios: • Multiple myeloma • Smoldering myeloma or solitary plasmacytoma: restaging/treatment response, or follow-up every 12 months	N/A

**Includes provisional diagnosis supported by initial diagnostic workup including but not limited to labs, serum/urine protein electrophoresis, serum free light chain (FLC) assay, and bone marrow aspirate/biopsy*

Rationale

Multiple myeloma arises from plasma cells in the bone marrow. The disease disseminates widely and often produces antibodies and other proteins that interfere with normal function of bone, kidney, and other organ systems. Incidence increases with age and is higher in males and persons of African descent. The most common presenting symptoms include generalized fatigue, anemia, bone pain, hypercalcemia, and renal dysfunction.

Plasmacytoma is a related tumor which, unlike multiple myeloma, remains localized in bone or soft tissue. Once systemic involvement is excluded (by laboratory testing or bone marrow evaluation), solitary plasmacytoma is typically treated with radiation therapy alone; however, close surveillance is required as these tumors may recur or evolve into multiple myeloma.

DIAGNOSTIC WORKUP

MRI is the most sensitive modality for detection of bone lesions; when compared head to head, MRI detected lesions in 74% of patients compared to 56% with whole body X-ray. In patients with negative skeletal surveys, MRI detected lesions in 52% of patients, while 20% of patients with a negative MRI were discovered to have focal lesions on skeletal survey.[281] In patients thought to have a solitary plasmacytoma, MRI detected additional disease and led to a change of management in 25% of those studied.[282] In a similar study of indolent myeloma, MRI detected 28% more lesions.[283]

While MRI is superior for detection of bone disease, PET/CT may be more sensitive for extramedullary involvement. The majority of patients with active myeloma will have positive results on PET scan, and PET imaging may detect early bone marrow involvement in patients with solitary plasmacytoma.[284, 285] In a prospective study using PET/CT to stage solitary plasmacytoma and multiple myeloma, 14% of patients had a change in management as a result of information gleaned from PET imaging.[284] NCCN recommends either WBCT or FDG PET/CT for initial workup of patients suspected of having multiple myeloma or solitary plasmacytoma (level of evidence category 2A); if negative, whole body MRI with contrast can be considered to discern smoldering from multiple myeloma.[5] The European Society for Medical Oncology (ESMO) similarly recommends WBCT (FDG PET/CT deemed optional if carried out instead of WBCT, if available) and whole body MRI for WBCT-negative cases (if FDG PET/CT not carried out).[286]

MANAGEMENT

MRI may be able to detect early treatment response based on the pattern of marrow response, but false positive results are common due to persistent nonviable lesions.[287] In one study, the overall accuracy of whole body MRI was 79% with a sensitivity of 64%, specificity of 86%, positive predictive value of 70%, and negative predictive value of 83%. MRI had only moderate agreement with routinely performed laboratory tests for determining remission.[288]

PET imaging, however, does provide early assessment of response as well as prognostic information for lesions smaller than 5 mm.[289] In a head-to-head study comparing MRI and PET/CT for treatment evaluation of multiple myeloma, PET/CT was less accurate but was able to detect treatment responses earlier.[290] In the IMAJEM study, normalization of PET following induction therapy with lenalidomide/bortezomib/dexamethasone (RVD) regimen was associated with improved progression-free survival (30-month progression-free survival, 78.7% vs 56.8%, respectively)[291] whereas normalization of MRI findings was not found to correlate with improved outcome measures. The NCCN panel recommends considering using the same imaging modality used during the initial workup for the follow-up assessment.[61] The ESMO recommends FDG PET/CT to confirm imaging minimum residual disease (MRD) at treatment response assessment, and every 12 months for follow-up of bone marrow MRD-negative patients.[286]

Since the risk of progression of solitary plasmacytoma into multiple myeloma or relapse is relatively high (14%-48% within first 3 years of diagnosis), the NCCN recommends yearly follow-up with the same imaging used at first diagnosis for the first 5 years; the NCCN also recommends advanced whole body imaging (ie MRI, low-dose CT, FDG PET/CT) annually for follow-up of smoldering myeloma.[61]

Carelon guidelines are in accordance with the NCCN Guidelines for Multiple Myeloma and the European Society for Medical Oncology (ESMO).[61, 286]

Neuroendocrine Tumors

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented neuroendocrine tumors.

Well-differentiated neuroendocrine tumor

Including carcinoid tumors of the gastrointestinal tract, lung or thymus, and pheochromocytoma or paraganglioma.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated	Indicated	Indicated
MRI abdomen **MRI pelvis**	Indicated	Indicated	Indicated
Somatostatin receptor (SSR)-PET/CT*	Indicated in **EITHER** of the following scenarios:	Indicated in **EITHER** of the following scenarios: • Prior to planned peptide receptor radioligand therapy (PRRT) for	Not indicated

Imaging Study	Diagnostic Workup	Management	Surveillance
	• Biopsy-proven well-differentiated neuroendocrine tumor • Suspected well-differentiated neuroendocrine tumor based on endoscopy, conventional imaging[1], or biochemical markers[2] not amenable to biopsy	well-differentiated neuroendocrine tumor • When identification of more extensive disease will change management and **ANY** of the following criteria are met: ○ Equivocal findings of disease progression on conventional imaging ○ Clinical or biochemical progression with negative conventional imaging ○ When the original disease was only detectable by somatostatin receptor-based imaging.	

1 Conventional imaging includes MRI or contrast-enhanced CT.

2 Biochemical evidence for suspected neuroendocrine tumors may include elevated levels of chromogranin A, pancreatic polypeptide, neuron-specific enolase, vasoactive intestinal polypeptide, serotonin (urinary 5-HIAA), gastrin, somatostatin, catecholamines, metanephrines, calcitonin, fasting insulin, C-peptide (proinsulin), or glucagon.

*Somatostatin receptor-based PET/CT includes PET with 68Ga dotatate or 64Cu dotatate radiotracers.

Poorly-differentiated neuroendocrine tumor

For poorly differentiated neuroendocrine tumors of the lung, refer to Small Cell Lung Cancer section

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated	Indicated	Indicated
MRI abdomen **MRI pelvis**	Indicated	Indicated	Indicated
FDG-PET/CT	Indicated when standard imaging cannot be performed or is nondiagnostic for metastatic disease	Indicated to assess treatment response when PET used for initial staging	Not indicated

Rationale

Neuroendocrine tumors are rare tumors arising from neuroendocrine cells, which may occur anywhere in the body. The most common neuroendocrine tumors are carcinoid tumors, the majority of which occur in the gastrointestinal tract. Well-differentiated neuroendocrine tumors are known to have a hereditary component. Poorly differentiated tumors are classically nonsecretory and tend to cause symptoms related to local tumor growth or metastatic disease, whereas secretory tumors such as carcinoid most often present with symptoms such as diarrhea, flushing, and wheezing due to excessive production of hormones.

DIAGNOSTIC WORKUP

Neuroendocrine tumor is staged using the American Joint Committee on Cancer TNM system. The World Health Organization classification scheme also takes into account proliferation rate (Ki-67) in grading of tumors. Neuroendocrine tumors of the GI tract, lung and thymus are highly vascular tumors and multiphasic imaging (abdominal ± pelvic multiphasic CT or MRI per NCCN), including arterial phase imaging, should be used to improve detection.[292, 293] There is no definitive preference between CT and MRI; although the resolution on CT is often better, MRI is generally more sensitive for detecting vascular invasion or liver metastases.[294, 295] Smaller lesions, especially in the small bowel and appendix, may be difficult to visualize with either modality.

Somatostatin receptor (SSR) imaging is recommended by multiple professional societies including ACR, NCCN, and ENTS as a part of initial staging of well-differentiated neuroendocrine tumors when indicated. SSR-PET/CT is generally preferred. A 2018 systematic review of 15 studies with 679 patients comparing the diagnostic accuracy of SSR-PET with OctreoScan, 18FDG PET or CT/MRI, reported that SSR-PET was associated with greater sensitivity than OctreoScan (difference in sensitivity ranged from 14% to 56%) as well as CT and/or MRI (differences in sensitivity ranged from 12% to 49%).[296] Multiple prospective trials confirm the overall superiority of 68Ga DOTATATE PET to somatostatin receptor scintigraphy. Several systematic reviews, a meta-analysis, and prospective studies of variable quality have consistently shown that 68Ga dotatate has a moderate to high diagnostic accuracy for the staging of de novo, recurrent, or suspected neuroendocrine cancer with a moderate to high positive likelihood ratio and a high negative likelihood ratio to exclude neuroendocrine cancer.[296-301]

64Cu-DOTATATE was also found to have non-inferior diagnostic accuracy (corrected sensitivity/specificity of 100% and 96.8%, respectively) compared to 68Ga-DOTATATE.[302, 303]

FDG-PET for staging of poorly differentiated neuroendocrine tumor remains controversial. In a limited number of small studies, FDG-PET appears to be useful in detecting poorly differentiated neuroendocrine tumors and well-differentiated neuroendocrine tumors with high Ki-67.[304-306]

MANAGEMENT

Imaging to assess disease response to therapy should be performed with the same modality used to detect the initial abnormality and the same modality should be used over time. For most cases, CT chest and abdominal ± pelvic multiphasic CT or MRI is sufficient. There is limited evidence for the use of SRT-PET for monitoring disease during treatment.

Somatostatin analog receptor imaging is vital prior to PRRT. Based on the increased sensitivity for detection of somatostatin receptors and expected change in management, 68Ga dotatate also appears to play a role prior to therapy. 68Ga dotatate changed management in 13%-60% of patients, with a wide variation depending on the clinical scenario in which the radiotracer is used. No study has compared the utility of SSTR-PET with alternative imaging modalities for predicting response to PRRT or somatostatin analog therapy.[307]

SURVEILLANCE

Poorly differentiated tumors have a higher risk of recurrent disease after definitive treatment; therefore, routine surveillance imaging may include CT chest, abdomen, and pelvis. Limited evidence supports the use of SRT-PET for monitoring disease after completion of treatment. The North American Neuroendocrine Tumor Society states, that SSTR PET should not be used routinely for surveillance.[294]

Ovarian Cancer - All Variants

Advanced imaging is considered medically necessary for the diagnostic workup and management of documented ovarian cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis	Indicated	Indicated	Indicated when tumor markers or exam are considered unreliable and/or there is a high risk of recurrence.
MRI abdomen and pelvis	Indicated	Indicated	Indicated when tumor markers or exam are considered unreliable and/or there is a high risk of recurrence.
FDG-PET/CT	Indicated to direct management of indeterminate lesions detected by other imaging modalities	Indicated when standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Ovarian cancer is the fifth most common cause of cancer-related death in women in the U.S. Ovarian tumors may arise from epithelial cells, germ cells, and sex cord-gonadal stroma. Epithelial ovarian cancers make up over 95% of ovarian cancers and are further classified as serous, mucinous, endometrioid, or clear cell carcinoma. Incidence increases with age; other risk factors include cigarette smoking, and BRCA gene mutations. Ovarian cancer most commonly presents with pain, bloating, or gastrointestinal symptoms, while more acute presentations from disseminated disease may include bowel obstruction, pulmonary complaints from pleural effusions, or venous thromboembolic disease.

DIAGNOSTIC WORKUP

Ovarian cancer is most commonly staged using the FIGO system, although the American Joint Committee on Cancer TNM system may also be utilized. Until more conclusive data is available, CT abdomen and pelvis with contrast remains the preferred imaging modality for staging. CT abdomen and pelvis has a reported accuracy of 77%. The positive predictive value for cancer nonresectability was 100% and the negative predictive value was 92%. Results of CT are comparable to MRI in terms of accuracy, positive predictive value, and negative predictive value: 78%, 91%, and 99%. In one study, no difference was seen between MRI and CT in detection of abdominal disease.[308] In a second prospective study comparing ultrasound, CT, and MRI, CT and MRI were again found to be equivalent in detecting stage III/IV disease.[309] In a smaller study, MRI outperformed CT for detection of small tumors in extrahepatic sites and was particularly advantageous for evaluating the peritoneum, mesentery, and bowel.[310]

FDG-PET/CT or MRI may be useful for indeterminate lesions if results will alter management.[311] The use of PET for initial staging is not universally supported; sensitivity and specificity have been reported at 86% and 54%, respectively. False negatives can be seen with borderline tumors, early carcinomas, and adenocarcinomas and false positives occur in some benign conditions.[312]

MANAGEMENT

For stage I-IV after primary treatment, the NCCN recommends CT, MRI, PET/CT or PET as clinically indicated without modality preference (level of evidence category 2A).[311] Imaging should be performed with oral and IV contrast (unless contraindicated) and rectal contrast as needed.

SURVEILLANCE

Based on a review of the Surveillance Epidemiology & End Results database, up to 95% of recurrences are detected by physical exam or rising cancer antigen (CA) 125.[313] Studies using radiographic surveillance for ovarian cancer have reported the sensitivity and specificity of CT 40%-93% and 50%-98%, respectively.[314] In a retrospective Italian study, recurrence in asymptomatic patients was detected by physician exam in 14.8%, by serum CA 125 in 23%, and by imaging in 27.2%. No difference was seen in survival with symptomatic or asymptomatic presentation at time or relapse.[315] In a post-hoc analysis of the AURELIA trial (Avastin [Bevacizumab] Use in Platinum-Resistant Epithelial Ovarian Cancer), progression-free survival was improved with earlier recurrence detection, but no difference in overall survival was demonstrated.[316] Additionally, Rustin et al. reported in a randomized trial that there was no evidence of a survival benefit with early treatment of relapse on the basis of a raised CA 125 concentration alone.[317] While the Society of Gynecologic Oncology and the NCCN do not recommend routine use of surveillance imaging, it may be indicated when tumor markers are considered unreliable, the physical exam is unreliable, and/or there is a high risk of recurrence.[311, 314]

Pancreatic Cancer

The following criteria address all cancers originating in the pancreas other than neuroendocrine tumors.

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented pancreatic cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest	Indicated	Indicated	Indicated
CT abdomen and pelvis	Indicated (note: usually CT abdomen pancreatic protocol is needed)	Indicated	Indicated
MRI abdomen	Indicated in **ANY** of the following scenarios: • CT contraindicated or expected to be suboptimal • Characterization of CT-indeterminate liver lesions	Not indicated	Not indicated

Imaging Study	Diagnostic Workup	Management	Surveillance
	• Need to further establish resectability in borderline resectable patients when CT imaging provides insufficient information		

FDG-PET/CT	Indicated when **ALL** of the following are true:
	• Dedicated, high-quality imaging of the pancreas has been performed
	• Extra-pancreatic disease has not been clearly identified
	• ANY of the following high-risk features are present:
	  ○ Cancer antigen 19-9 level greater than 100 U/ml
	  ○ Primary tumor greater than 2 cm in size
	  ○ Enlarged regional nodes
	  ○ Tumor is considered borderline resectable
		Indicated in **EITHER** of the following scenarios:
		• Radiation planning for preoperative or definitive treatment in patients without distant metastasis
		• Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease
			Not indicated

Note: Imaging of the pancreas should include a dedicated pancreatic protocol CT (multi-detector computed tomography angiography using a dual-phase pancreatic protocol, with images obtained in the pancreatic and portal venous phase of contrast enhancement) or MRI if CT is contraindicated. MRI may also be used to clarify CT-indeterminate liver lesions or suspected pancreatic tumors not visible on CT.

Rationale

Pancreatic cancer is the fourth leading cause of cancer mortality in the U.S. The most common type of pancreatic cancer is adenocarcinoma, which accounts for 85% of pancreatic cancers. Diagnosis is rare prior to the age of 45 and the rate is slightly higher in females. Risk factors include genetic predisposition, smoking, and obesity. Presentation is variable and may include pain, jaundice, and cancer anorexia/cachexia syndrome.

DIAGNOSTIC WORKUP

Pancreatic cancer is staged using the American Joint Committee on Cancer TNM system. The Society of Abdominal Radiology and the American Pancreatic Association recommend a dedicated pancreatic CT, performed with multidetector CT angiography using a dual-phase pancreatic protocol.[318] CT using this protocol has demonstrated sensitivity of 89%-97% for diagnosis and a positive predictive value for assessing resectability of 89%-100%. Although a high-quality CT abdomen may suffice in some circumstances, comparison studies have found that scans performed with pancreatic protocol have changed staging and management in up to 56% of cases.[319]

MRI is most commonly used as a problem-solving tool, particularly for CT-indeterminate liver lesions, when CT-occult pancreatic tumors are suspected or when contrast enhanced CT cannot be done.[318] Accuracy of MRI abdomen is similar to that for CT with pancreatic protocol. In a 2016 meta-analysis reviewing different imaging modalities, the pooled sensitivity was 89% and the specificities were 90% and 89% for MRI and CT, respectively.[320]

PET/CT has been studied as an adjunctive staging modality. The sensitivity of detecting metastatic disease for PET/CT alone, standard CT alone, and the combination of PET/CT and CT were 61%, 57%, and 87%, respectively. PET/CT influenced the clinical management in 11% of cases.[321] Treadwell et al. reported no statistically significant difference in sensitivity or specificity in a pooled analysis of six studies comparing PET scan to CT scan for initial treatment staging.[320] A 2017 meta-analysis of 16 articles concluded that high pretreatment PET standardized uptake values predicted poorer event-free survival and overall survival.[322]

MANAGEMENT

There is limited data comparing imaging modalities for post-treatment assessment. One study found that multidetector CT underestimates resectability, but no additional studies exist assessing accuracy for evaluation of lymph node and systemic metastases. Limited information is available for MRI or PET/CT in this setting.[323] In a pooled analysis of the phase III MPACT (Molecular Profiling-based targeted therapy in treating patients with Advanced solid Tumors) trial, response by PET after chemotherapy was associated with improved survival regardless of regimen used (11.3 vs 6.9 months; HR 0.56; P < .001).[324]

SURVEILLANCE

NCCN recommends surveillance every 3-6 months for 2 years, then every 6-12 months as clinically indicated, including CT chest and CT or MRI of abdomen and pelvis with contrast (category 2A recommendation).[325]

Paraneoplastic Syndrome

Advanced imaging is considered medically necessary for the diagnostic workup of paraneoplastic disease. Periodic surveillance of paraneoplastic disease is indicated when initial evaluation has not detected a primary tumor.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck CT chest CT abdomen and pelvis	Indicated	Further management based on primary cancer identified	Further management based on primary cancer identified
FDG-PET/CT	Indicated for initial evaluation of individuals with paraneoplastic syndrome	Further management based on primary cancer identified	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Paraneoplastic disease is a rare manifestation of cancer that is not related directly to tumor involvement, metastases, or metabolic derangements. Autoantibodies have been identified as a cause in up to 60% of the recognized syndromes attributed to paraneoplastic disease.[326] In many cases, symptoms occur prior to discovery of the primary tumor. The most common presentations are neurologic (central or peripheral), but paraneoplastic disease also manifests in muscle and other soft tissue. The most common malignancies associated with paraneoplastic disease are small cell lung cancer, thymoma, and hematologic cancers.[327]

DIAGNOSTIC WORKUP

PET/CT has been found to be more accurate than CT in the detection of occult malignancy associated with paraneoplastic syndrome. In a retrospective study, PET outperformed CT by 50%. The sensitivity and specificity of PET compared to CT were 80% and 67%, vs 30% and 71%, respectively.[328] Another retrospective study from the same institution found that PET/CT detected an additional 18% of cancers in patients with CT-negative paraneoplastic disease.[329] In a review and meta-analysis of 21 studies, PET imaging demonstrated high diagnostic accuracy and moderate to high sensitivity (81%) and specificity (86%) for detection of underlying malignancy in suspected paraneoplastic syndrome.[330]

SURVEILLANCE

The benefit of advanced imaging for surveillance of paraneoplastic syndrome without an identified malignancy has not been demonstrated. The European Federation of Neurological Sciences endorses continued surveillance with repeat screening every 6 months for up to 4 years.[331]

Penile, Vaginal, and Vulvar Cancers

Note: The following information primarily addresses squamous cell carcinomas of the vagina, vulva, and penis; however, applicability and coverage include all cancers originating in the vagina, vulva, and penis unless expressly addressed elsewhere in Oncologic Imaging. Specific imaging considerations are addressed below.

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented vaginal, vulvar, or penile cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis	Indicated (note: for penile cancer especially useful with T1b or higher or palpable inguinal LN; for vulvar cancer especially useful with T2 or	Indicated	Indicated for penile cancer

Imaging Study	Diagnostic Workup	Management	Surveillance
	higher. Chest imaging can be performed either with CT or radiograph.)		
MRI pelvis	Indicated for vaginal or vulvar cancer	Indicated for vaginal or vulvar cancer	Not indicated
FDG-PET/CT	Indicated in **ANY** of the following scenarios: • Standard imaging cannot be performed or is nondiagnostic for metastatic disease • Staging of penile cancer when pelvic lymph nodes are enlarged on CT or MRI and needle biopsy is not technically feasible • Staging of vaginal cancer	Indicated in **ANY** of the following scenarios: • Radiation planning for preoperative or definitive treatment only • Single treatment response assessment following radiation when performed at least 12 weeks after completion of therapy • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease • Restaging of local recurrence when pelvic exenteration surgery is planned	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Vaginal, vulvar, and penile cancers are relatively uncommon; the most common histologic subtype is squamous cell carcinoma, although adenocarcinoma is also seen in the vagina. Risk factors for developing genital cancers are human papillomavirus infection, human immunodeficiency virus infection, smoking, and exposure to diethylstilbestrol. The most common presentation is local symptoms such as bleeding, irritation, discharge, or skin changes.

DIAGNOSTIC WORKUP

Vaginal, vulvar, and penile cancers are staged using the American Joint Committee on Cancer TNM system.

In a retrospective study, MRI performed prior to surgery for vulvar cancer had a local staging accuracy of 83% and an overall staging accuracy of 69.4%, which increased to 75%-85% when combined with CT.[332] Comparable findings regarding the utility of MRI for the diagnosis, local staging, and spread of disease of vaginal cancer have been reported in 2 small studies.[333, 334] There is a lack of high-quality prospective studies evaluating PET/CT for staging vaginal and vulvar cancer. Cohn et al. found that PET/CT had sensitivity of 80%, specificity of 90%, and negative predictive value of 80% in identifying lymph node metastases; thus, PET/CT does not obviate the need for surgical staging.[335] In the largest study (N = 50) comparing PET and conventional imaging data for vulvar and vaginal cancer, FDG PET/CT detected nodes suspicious for metastases in 35% of patients, as compared to MRI and CT, 13% and 7%, respectively. Distant metastases were seen in an additional 4% when compared to conventional CT, and overall resultant change in management occurred in 36% of cases.[336] In a small prospective study (N = 23) of patients with vaginal cancer, PET detected lymph node involvement in 35% of patients compared to 17% for CT alone.[337] The American College of Radiology Appropriate Use Criteria for staging and follow-up of vaginal cancer recommend CT abdomen/pelvis, MRI pelvis, or FDG-PET/CT for initial staging of vaginal cancer, and MRI pelvis or FDG-PET/CT for post-treatment evaluation. They state that these procedures are equivalent alternatives, but also note that data related to patients with primary vaginal cancer is limited.[338, 339] For vulvar cancer, they recommend MRI pelvis for patients with tumor >2 cm and >1 mm stromal invasion, or when the tumor involves or is in proximity to the urethra, vagina, or anus. For vulvar cancer recurrence, they recommend FDG-PET/CT as well, to facilitate treatment planning prior to pelvic exenteration.[340]

For penile cancer, imaging is not indicated for low-risk disease (Tis,Ta, T1a). Distant metastatic disease is rare and occurs in less than 4% of cases without bulky disease.[337, 341] For intermediate to high risk (T1b, T2 or greater) and/or palpable inguinal lymph nodes, chest imaging should be performed in addition to CT abdomen and pelvis with contrast. Preoperative CT has a reported sensitivity of 95% and a specificity of 82%. In a study of 10 patients, MRI with lymphotropic nanoparticles had a sensitivity, specificity, positive predictive value, and negative predictive value of 100%, 97%, 81%, and 100%, respectively.[342]

There is insufficient data to support the routine use of PET/CT for staging of penile cancer. In a comparative study, the sensitivity of PET was 80% compared to 100% in MRI and specificities were equivalent.[343] Another trial looking at 13 patients confirmed these findings.[344] In a meta-analysis of 7 studies, PET had a pooled sensitivity and specificity of 80.9% and 92.4%. Sensitivity was 96.4% when inguinal lymph nodes were detected clinically, but fell to 56.5% when nodes were clinically negative.[345]

SURVEILLANCE

As most recurrences of vulvar and vaginal cancer are local, surveillance imaging is not indicated. In concordance with both National Comprehensive Cancer Network and Society of Gynecologic Oncology guidelines, imaging should only be performed when recurrence is suspected based on symptoms or exam findings.[314, 346] For penile cancer, surveillance with CT may be performed.[347]

Prostate Cancer

Note: The following information addresses adenocarcinoma of the prostate; however, applicability and coverage include all cancers originating in the prostate unless expressly addressed in another Carelon imaging guideline. Specific imaging considerations are addressed below.

Advanced imaging is considered medically necessary for diagnostic workup and management of documented prostate cancer.

Imaging Study	Diagnostic Workup and Diagnosis	Management	Surveillance
CT chest CT abdomen and/or pelvis	Indicated for intermediate or high-risk disease	Indicated for intermediate or high-risk disease	Not indicated
MRI pelvis including multiparametric prostate technique	Indicated in **ANY** of the following scenarios: • Persistent and unexplained elevation in PSA levels* or very suspicious DRE • Initial staging of intermediate or high-risk prostate cancer • Risk-stratification of low-risk** cancer for potential active surveillance	Indicated in **ANY** of the following scenarios: • Persistent or recurrent PSA elevation-especially useful if local salvage surgery planned after radiation therapy • Assessment of extracapsular extension prior to radical prostatectomy • Active surveillance annually • Restaging intermediate or high-risk disease	Not indicated
FDG-PET/CT	Not indicated	Not indicated	Not indicated

18F Fluciclovine PET/CT or 11C Choline PET/CT	Not indicated	Indicated when **ALL** of the following criteria are met:
		• Original clinical stage T1-T3 and NX or N0 treated with prostatectomy and/or radiation therapy, with biochemically recurrent/persistent disease[1]
		• Negative or nondiagnostic imaging based on most recent PSA value (if applicable):
		  ○ PSA ≤ 1 ng/ml and rising: Prostate/Pelvic MRI (within past 60 days)
		  ○ PSA ≥ 10 ng/ml: Any conventional imaging[2] (within past 60 days)
		• Patient is a candidate for curative intent salvage therapy[3]
			Not indicated

Imaging Study	Diagnostic Workup and Diagnosis	Management	Surveillance
		• PET/CT with 18F Fluciclovine or 11C Choline has not been performed within the past 3 months	
PET/CT using 68Ga- or 18F-labeled radiotracers targeting prostate-specific membrane antigen (PSMA)	Indicated for unfavorable intermediate or high-risk disease with equivocal or nondiagnostic conventional imaging,[2] when confirmation may inform decisions about prostatectomy and/or radiation therapy	Indicated in **EITHER** of the following scenarios: • When **ALL** of the following criteria are met: ○ Original clinical stage T1-T3 and NX or N0 treated with prostatectomy and/or radiation therapy, with biochemically recurrent/persistent disease[1] ○ If PSA ≥ 10 ng/ml, negative or nondiagnostic conventional imaging2 (within 60 days)*** ○ Patient is a candidate for curative intent salvage therapy[3] ○ PET/CT has not been performed within the past 3 months • Evaluation of metastatic castrate-resistant disease for radioligand therapy when previously treated with taxane-based chemotherapy **AND ANY** of the following androgen-receptor pathway inhibitors: ○ Abiaterone ○ Apalutamide ○ Enzalutamide ○ Darolutamide	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

**Elevated PSA levels defined as > 3 ng/ml in patients 45-75 years or ≥ 4.0 ng/ml in patients 75 years or older*

***Low-risk prostate cancer defined as Gleason score of 6, PSA less than 10 ng/mL, and stage T1 or T2a.*

****If PSA <10 ng/ml, this criterion does not apply*

1 "Biochemical recurrence/persistence" definition depends on prior treatment:

- Post-prostatectomy (PSA should be 0 after surgery):
  - Persistence: Detection of a PSA higher than 0 within the first three months after surgery
  - Recurrence: PSA initially undetectable, then rising PSA ≥ 0.2 ng/ml, with a second confirmatory level ≥ 0.2 ng/mL (American Urological Association definition)
- Post-radiation therapy:
  - Recurrence: rise by ≥ 2 ng/mL above the nadir PSA (Radiation Therapy Oncology Group-American Society of Therapeutic Radiology and Oncology (RTOG-ASTRO) Phoenix Consensus)

2 Conventional imaging: Bone scan, CT Abdomen and/or Pelvis, MRI pelvis, or mpMRI (prostate MRI).
3 External beam radiation therapy ± androgen deprivation therapy after prostatectomy OR radical prostatectomy, cryosurgery, high-intensity focused ultrasound, or brachytherapy after external beam radiation therapy.

Rationale

Prostate cancer is the most common malignancy among men in the U.S. The most common histological subtype is adenocarcinoma.

DIAGNOSIS

Prostate cancer is staged using the American Joint Committee on Cancer TNM system. Professional society guidelines base recommendations for MRI and repeat biopsy on PSA doubling time, thus serial PSA levels are important in clinical decision making. Screening and early detection guidelines are based on a PSA level between 3 and 10 ng/mL.[348]

The prospective multicenter, randomized Phase III PRECISION (PRostate Evaluation for Clinically Important Disease: Sampling Using Image-guidance Or Not?) trial compared mpMRI-targeted biopsy to standard transrectal ultrasound-guided biopsy in 500 men with clinical suspicion of prostate cancer (elevated PSA, abnormal digital rectal exam, or both) who had not undergone biopsy previously. The mpMRI-targeted evaluation was able to detect prostate cancer in 38% of men compared with 26% in the standard biopsy group (P = 0.005). Fewer men in the mpMRI group were diagnosed with clinically insignificant cancers (defined as Gleason 6).[349]

DIAGNOSTIC WORKUP

Advanced imaging is not indicated for very low and low-risk groups. Multiparametric MRI (mpMRI, referring to prostate MRI protocol within this guideline) can be used in the staging and characterization of prostate cancer. CT is generally not sufficient to evaluate the prostate gland but can be used for initial evaluation of nodal and/or visceral metastatic disease. In a meta-analysis of 75 studies comparing CT to MRI for initial staging, the pooled data for extracapsular extension and T3 detection showed sensitivity and specificity of 57% and 91% for CT vs 61% and 88% for MRI.[350] For detection of lymph node metastases, the differences in performance of CT and MRI were not statistically significant.[351] Findings from another prospective study confirmed the equivalency of CT and MRI for lymph node staging.[352] For intermediate risk or above, abdominal imaging with contrast should be performed if the risk of pelvic lymph node metastases is greater than 10%.

While PSMA-PET has been found to be more accurate than CT and bone scan in assessing pelvic nodal and distant metastases, it was not sensitive enough to forego pelvic lymph node dissection in those with high risk disease.[353, 354] Multiple high quality guidelines still endorse conventional imaging for initial staging, acknowledging evidence supporting its use for equivocal findings. A guideline from the American Urological Association (AUA) and the American Society for Radiation Oncology (ASTRO) makes a strong evidence-based recommendation for bone scan and mpMRI or CT scan for initial evaluation, suggesting that molecular imaging may be obtained in high-risk patients with negative conventional imaging.[355] The American Society of Clinical Oncology (ASCO) suggests the use of next-generation imaging “when conventional imaging (defined as CT, bone scan, and/or prostate MRI) is negative in patients with a high risk of metastatic disease,” and also for clarification “when conventional imaging is suspicious or equivocal,” though in both cases they note that prospective data is limited.[356] Additionally, a guideline from EAU, EANM, ESTRO, ISUP, and SIOG states that, while consideration may be given to replacing abdominopelvic CT and bone scan with more sensitive imaging modalities in initial staging of high risk prostate cancer, “in absence of prospective studies demonstrating survival benefit, caution must be used when making therapeutic decisions.” They further state, “The prognosis and ideal management of patients diagnosed as metastatic by these more sensitive tests is unknown. In particular, it is unclear whether patients with metastases detectable only with PET/CT or whole-body MRI should be managed using systemic therapies only, or whether they should be subjected to aggressive local and metastases-directed therapies.” In conclusion, they state, “Results from RCTs evaluating the management and outcome of patients with (and without) metastases detected by choline PET/CT, PSMA PET/CT and MRI are awaited before a recommendation can be made to treat patients based on the results of these tests.” Similarly, though the NCCN Panel “does not feel that conventional imaging is a necessary prerequisite to PSMA-PET” cited evidence related to initial staging is limited while also noting that “PET/CT or PET/MRI results may change treatment but may not change oncologic outcome.”[357]

FDG-PET is not indicated, as physiologic activity in the bladder obscures tumor detection.[358] Additionally, there is limited evidence to support 11C-choline and 18F fluciclovine PET for initial staging of prostate cancer.

MANAGEMENT

For active surveillance, the NCCN recommends mpMRI be considered for suspected anterior and/or aggressive cancers when PSA increases and prostate biopsies are negative.[357]

Studies of 11C-choline, 18F-fluciclovine, and prostate-specific membrane antigen (PSMA) PET support their accuracy in evaluating biochemical recurrence (BCR).[359-361] The prospective FALCON (^{18}F-Fluciclovine PET/CT in biochemicAL reCurrence Of Prostate caNcer) trial found the detection ability of 18F-fluciclovine PET after radical treatment (prostatectomy or radiation therapy/brachytherapy) broadly proportional to PSA level (one-third scans positive when PSA ≤ 1 ng/mL, compared to 93% positive with PSA greater than 2 ng/mL).[362] Results were similar to that of the previous LOCATE study (patient-level detection of 56% with overall 63% management changes, compared with 57% and 59%, respectively), the latter limited to patients with negative or equivocal conventional imaging before 18F-fluciclovine PET/CT. Where 18F-fluciclovine

guided salvage therapy, the PSA response rate was higher than when 18F-fluciclovine was not involved (15 out of 17 [88%] vs 28 out of 39 [72%]).[362] 68-Ga PSMA PET was found to have higher diagnostic accuracy than other radiotracers for biochemical recurrence (overall detection rate of 74%) by one systematic review, especially at low PSA values, resulting in management change in 53% of patients.[359] A systematic review and network meta-analysis of 12 studies encompassing eight radiotracers found comparable performance of 68Ga-PSMA-11 and 18F-DCFPyL.[363] Another systematic review, this including 43 studies and 5832 patients, found no difference in detection rate between PSMA tracers based on PSA level, doubling time, or velocity.[359]

PSMA imaging is needed for patient selection prior to treatment of metastatic castration-resistant prostate cancer (mCRPC) with the radioligand therapeutic agent lutetium Lu 177 vipivotide tetraxetan. In the randomized, multi-center trial demonstrating prolonged imaging-based progression-free survival and overall survival of this treatment, all patients were required to have received at least one AR pathway inhibitor, and 1 or 2 prior taxane-based chemotherapy regimens.[364]

Although there are some studies showing a correlation between MRI stability and Gleason stability, the American Urological Association/American Society for Radiation Oncology 2022 Guidelines for Clinically Localized Prostate Cancer (endorsed by the Society of Urologic Oncology) do not currently recommend serial MRI for surveillance.[355, 365-367]

Sarcomas of Bone/Soft Tissue

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented sarcomas of bone, cartilage, connective tissue, and other soft tissue (including gastrointestinal stromal tumors).

Bone Sarcoma

Imaging Study	Diagnostic Workup	Management	Surveillance
CT or MRI primary site	Indicated	Indicated	Indicated (note: especially useful for Ewing sarcoma and osteosarcoma in first 5 years)
CT chest CT abdomen and pelvis	Indicated	Indicated	Indicated
MRI cervical, thoracic, and lumbar spine	Indicated (note: especially useful for chordoma)	Indicated for evaluation of suspected or known spinal metastases	Not indicated
MRI pelvis	Indicated (note: especially useful for Ewing sarcoma)	Indicated for evaluation of suspected or known pelvic metastases	Not indicated
FDG-PET/CT	Indicated in **ANY** of the following scenarios: • Initial work-up of Ewing sarcoma and osteosarcoma if curative treatment planned • Standard imaging cannot be performed or is nondiagnostic for metastatic disease • Standard imaging suggests a resectable solitary metastasis • Baseline study prior to neoadjuvant chemotherapy	Indicated in **EITHER** of the following scenarios: • Following completion of neoadjuvant chemotherapy • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Soft Tissue Sarcoma

Includes head/neck, extremity/body wall, retroperitoneal or intra-abdominal sites, and desmoid tumors

Imaging Study	Diagnostic Workup	Management	Screening & Surveillance
CT or MRI of primary site	Indicated	Indicated	Indicated (note: especially useful for Stage II/III)
CT chest CT abdomen and pelvis	Indicated	Indicated	Indicated
MRI spine	Indicated (note: especially useful for myxoid/round cell liposarcoma)	Indicated for evaluation of suspected or known spinal metastases	Not indicated
FDG-PET/CT	Indicated in **ANY** of the following scenarios (excluding desmoid tumors): • Standard imaging cannot be performed or is nondiagnostic for metastatic disease • Standard imaging suggests a resectable solitary metastasis • Baseline study prior to neoadjuvant chemotherapy • Initial staging for rhabdomyosarcoma	Indicated in **EITHER** of the following scenarios: • Following completion of neoadjuvant chemotherapy • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Gastrointestinal stromal tumor (GIST)

Imaging Study	Diagnostic Workup	Management	Screening & Surveillance
CT chest, abdomen, and pelvis	Indicated	Indicated	Indicated
MRI of abdomen and/or pelvis	Indicated	Indicated	Indicated
FDG-PET/CT	Indicated in **ANY** of the following scenarios: • Standard imaging cannot be performed or is nondiagnostic for metastatic disease • Standard imaging suggests a resectable solitary metastasis • Baseline study prior to neoadjuvant chemotherapy	Indicated in **EITHER** of the following scenarios: • Assess treatment response following completion of neoadjuvant chemotherapy • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Rationale

Sarcomas are a heterogeneous group of cancers which arise from mesenchymal cells and occur in many different types of tissue, most commonly bone, muscle, and cartilage. Gastrointestinal stromal tumors (GISTs) are the most common soft tissue

sarcomas of the GI tract. Risk factors are not well characterized but may include genetic predisposition, prior chemotherapy or radiation therapy, and environmental exposure.

DIAGNOSTIC WORKUP

Sarcomas are staged using the American Joint Committee on Cancer TNM system. Imaging of the primary tumor is important to assess resectability and local invasion. CT or MRI may be done as part of initial workup. However, MRI is often preferred for imaging the primary tumor due to superior resolution of tumor versus surrounding muscle and neurovascular bundles, and for delineating disease involving the pelvis.[368-373] In a large prospective trial comparing CT and MRI imaging in both soft tissue sarcomas and bone cancer, the accuracy of local staging was not statistically different between the 2 modalities.[374]

Imaging of the lungs is critical, as this is the most common site of metastases. Additional imaging recommendations for soft tissue sarcoma vary by subtype. For Ewing sarcoma and osteosarcoma, NCCN recommends whole body PET/CT and/or bone scan as part of initial workup (level of evidence category 2A).[375] A meta-analysis showed a pooled sensitivity of 96% and pooled specificity of 92% for staging and restaging Ewing sarcoma when PET was combined with conventional imaging.[376] In another meta-analysis of 42 trials, PET had a pooled sensitivity and specificity of 96% and 79% for differentiating primary bone sarcomas from benign lesions, 92% and 93% for detecting recurrence, and 90% and 85% for detecting distant metastasis, respectively.[377]

MANAGEMENT

PET has been shown to be a useful adjunct in assessing treatment response to neoadjuvant therapy, as well as an indicator of prognosis.[377-379] A review and meta-analysis of 11 studies confirmed the prognostic value of PET response to overall survival in soft tissue and bone sarcoma.[378, 379]

SURVEILLANCE

Imaging of the primary site for soft tissue sarcoma is based on the risk of recurrence and the accessibility of the primary cancer site.[380] Particularly for younger patients where the radiation risks from multiple CT examinations might cause some concern, the follow up can be performed with MRI of the abdomen and pelvis supplemented with CT thorax.

Testicular Cancer

Advanced imaging is medically necessary for the diagnostic workup, management, and surveillance of documented testicular cancers.

Seminoma

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis	Indicated (note: chest X-ray usually sufficient but especially useful for positive abdominal CT or abnormal chest radiographs)	Indicated (note: especially useful for IIA, IIB, IIC, III after chemotherapy)	Indicated (note: chest X-ray usually sufficient)
FDG-PET/CT	Indicated when standard imaging cannot be performed or is nondiagnostic for metastatic disease	Indicated in **EITHER** of the following scenarios: • Standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease • Residual mass greater than 3 cm and normal tumor markers after completion of chemotherapy	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Nonseminoma

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest CT abdomen and pelvis	Indicated	Indicated (note: especially useful for IIA, IIB, IIC, III after chemotherapy. Chest X-ray is an option)	Indicated (note: chest X-ray usually sufficient)
FDG-PET/CT	Not indicated	Not indicated	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Germ cell tumors (GCTs) are the most common type of testicular cancer and are broadly divided into seminomatous and nonseminomatous subtypes. Risk factors include cryptorchidism, family history, and ethnicity. The most common presentation is testicular pain or a palpable mass.

DIAGNOSTIC WORKUP

GCTs are staged using the American Joint Committee on Cancer TNM system. CT abdomen and pelvis with contrast is primarily used to evaluate the retroperitoneal lymph nodes.[381] A CT Chest with contrast is indicated if the abdominal/pelvic CT or chest x-ray shows evidence of metastatic disease.

In direct comparisons, MRI has not shown an advantage over CT for accuracy of staging.[382, 383] Per NCCN, PET scans should not be used routinely to stage testicular GCTs. In a prospective study, CT imaging showed sensitivity, specificity, positive predictive value, and negative predictive value of 41%, 95%, 87%, and 67% compared with PET/CT 66%, 98%, 95%, and 78%, respectively. The poor negative predictive value of PET limits its usefulness in initial staging.[384] In another prospective trial in which high risk stage I NSGCT was imaged with PET, only 23 of 110 patients were found to have PET avid disease, and 33 of 88 PET-negative patients had disease relapse.[385]

MANAGEMENT

PET/CT has higher positive and negative predictive values for identifying residual viable seminomatous tumors compared to CT, especially in the setting of a radiographically persistent mass and normal tumor markers. In the prospective multicenter SEMPET trial, patients with seminoma, negative tumor markers, and at least a 1 cm residual mass following completion of chemotherapy were imaged with PET and CT of the abdomen and pelvis. When compared to CT, PET had superior sensitivity and specificity (80% and 100% vs 74% and 70%) as well as positive predictive value and negative predictive value (100% and 96% vs 37% and 92%).[386] Accuracy is improved and false-negative results decreased when PET/CT is used to evaluate residual masses at least 3 cm in size.[387]

In patients with NSGCT and residual mass > 1 cm after primary chemotherapy, retroperitoneal lymph node dissection or surgical resection of the residual mass should be strongly considered as opposed to continued radiographic surveillance. PET has limited ability to differentiate residual non-seminomatous tumor from radiation necrosis and fibrosis. NCCN notes “PET has no role in assessing treatment response and residual masses following chemotherapy in patients with nonseminoma.” In a prospective German multicenter trial, PET used for detection of residual NSGCT after chemotherapy only had an accuracy of 56% (compared to CT scan 55% and serum tumor markers 56%).[388]

Carelon guidelines are in accordance with the National Comprehensive Cancer Network (NCCN) Guidelines for Testicular Cancer.[389]

SURVEILLANCE

Seminomas tend to recur within the first 14 months and nonseminomas within the first 2 years.[390] Carelon guidelines are in accordance with the NCCN Guidelines for Testicular Cancer and European Society for Medical Oncology-EURACAN guidelines.[389, 391]

Cancers of the Pleura, Thymus, Heart, and Mediastinum

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of documented pleural malignancies, cancers of the thymus, heart, and mediastinum.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated	Indicated	Indicated
MRI chest	Indicated (note: for thymoma and thymic carcinoma and as an adjunct to CT chest for malignant pleural mesothelioma)	Indicated (note: for thymoma and thymic carcinoma and as an adjunct to CT chest for malignant pleural mesothelioma)	Not indicated
FDG-PET/CT	Indicated in **EITHER** of the following scenarios: • When surgical resection is being considered and metastatic disease has not been detected by CT or MRI • For surgical evaluation of malignant pleural mesothelioma (clinical stage I-IIIA and epithelioid histology), after CT chest and abdomen	Indicated in **EITHER** of the following scenarios: • Radiation planning for definitive treatment • Restaging after induction chemotherapy if patient is a surgical candidate	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Cancers of the pleura, thymus, heart, and mediastinum represent a heterogeneous group of diseases that can be either benign or malignant. The most common malignancies in this group are malignant pleural mesothelioma, thymoma, and thymic carcinoma. Myasthenia gravis is a paraneoplastic syndrome often associated with thymic neoplasms. Patients with mediastinal masses often present with symptoms resulting from direct compression of mediastinal structures, which may include cough, shortness of breath, superior vena cava syndrome, or Horner's syndrome. Malignant pleural mesothelioma may present with nonspecific pulmonary symptoms or systemic symptoms due to distant metastases.

DIAGNOSTIC WORKUP

MRI has been shown to be superior to CT for evaluating solitary foci of chest wall invasion, endothoracic fascial involvement, and diaphragmatic muscle invasion.[392] MRI should be considered for suspected chest wall, spinal, diaphragmatic, or vascular involvement based on CT. The American College of Radiology Appropriate Use Criteria for imaging of mediastinal masses recommends the use of MRI in the workup of mediastinal masses, citing benefits over CT or PET/CT including more specific tissue characterization and superior detection of invasion across tissue planes.[393] Although not highly accurate at staging T4 disease or N2 lymphadenopathy, PET plays a role in detection of extra-thoracic disease, eliminating the need for surgery in 16%-40% of patients.[394-398] For thymoma or thymic carcinoma, MRI chest may help differentiate benign cysts and thymoma from thymic carcinoma, thus avoiding the need for surgery.[399, 400] PET can be used for initial staging to differentiate low grade thymoma from FDG-avid thymic carcinoma.[400, 401]

MANAGEMENT

The American Society for Clinical Oncology recommends CT with assessment of response of malignant pleural mesothelioma based on the RECIST criteria.

SURVEILLANCE

American Society for Clinical Oncology and the National Comprehensive Cancer Network (NCCN) guidelines do not address surveillance imaging for asymptomatic malignant pleural mesothelioma. In most cases, CT should provide adequate information for routine surveillance.

Carelon Oncologic Imaging guidelines are in concordance with the NCCN Guidelines® for Thymomas and Thymic Carcinomas, NCCN Guidelines® for Malignant Pleural Mesothelioma, and the American Society for Clinical Oncology guidelines for evaluation of malignant pleural mesothelioma.[402-404]

Thyroid Cancer

Advanced imaging is considered medically necessary for the diagnostic workup, management, and surveillance of documented thyroid cancer.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT neck	Indicated	Indicated	Indicated
CT chest **CT abdomen and pelvis**	Indicated (note: especially useful for fixed, bulky, or substernal lesions and anaplastic thyroid cancer)	Indicated (note: especially useful based on known site of metastases or as clinically indicated for medullary thyroid cancer with calcitonin > 150 pg/mL AND anaplastic thyroid cancer)	Indicated
MRI neck	Indicated	Indicated when used in place of CT for initial treatment strategy	Not indicated
FDG-PET/CT	Indicated for **ANY** of the following subtypes: • Anaplastic • Oncocytic carcinoma	Indicated in **ANY** of the following scenarios: • Follow up of anaplastic carcinoma • Suspected recurrent papillary, follicular, or oncocytic carcinoma when I-131 scan is negative (or has been negative in the past) and stimulated thyroglobulin level is > 2 ng/dL • Suspected recurrent medullary carcinoma when detectable basal calcitonin or elevated CEA, and standard imaging is negative	Not indicated
Somatostatin receptor (SSR) PET/CT	Indicated for medullary carcinoma when standard imaging cannot be performed or is nondiagnostic	Indicated for suspected recurrent medullary carcinoma when detectable basal calcitonin or elevated CEA, and standard imaging is negative	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Thyroid cancer is the most common endocrine cancer in the U.S. The most common histologic subtypes are papillary and follicular carcinoma, which together account for 95% of all thyroid cancers. Risk factors include environmental factors, radiation exposure, and genetic predisposition (in medullary thyroid cancer). The most common presentation is a palpable mass.

DIAGNOSTIC WORKUP

Thyroid cancer is staged using the American Joint Committee on Cancer TNM system. Thyroid cancer frequently involves cervical lymph nodes, and the addition of ultrasound can result in detection and alteration in management in up to 40% of patients.[405, 406] Compared to CT, high-resolution ultrasound is more accurate for evaluation of extrathyroidal tumor extension and at least equivalent for evaluation of lateral lymph nodes.[407] Sensitivity, specificity, and diagnostic accuracy of ultrasound were 77%, 70%, and 74%, respectively, while those for CT were 62%, 79%, and 68%.[408] MRI and PET have relatively low sensitivities ranging from 30%-40%.[409, 410] An evidence-based guideline from the American Thyroid Association makes a strong recommendation for cross-sectional imaging in the initial tumor staging workup, including CT neck, chest, abdomen, and pelvis (or MRI). They also recommend the use of FDG-PET/CT, but state that bone scan can be obtained to evaluate for bony metastases in the absence of PET imaging.[411]

For dedifferentiated thyroid cancer, PET is indicated. Although there is a lack of prospective evidence, PET has been shown to detect metastatic disease not identified by conventional imaging in 35% of patients.[412] Change in management based on PET imaging findings can be as high as 25%-50%.[413]

MANAGEMENT

For follow up of well-differentiated thyroid cancer, CT or MRI is not indicated unless there is clinical evidence of recurrence. Patients with high-risk features generally undergo additional imaging and/or treatment with radioactive iodine. For suspected iodine non-avid papillary, follicular, or oncocytic carcinoma, PET may be useful. The overall accuracy, sensitivity, and specificity for PET/CT in I-131 negative patients were 93%, 93%, and 81%, respectively.[414]

For suspected recurrence of medullary thyroid cancer, a study comparing several imaging modalities found that CT was superior to PET for evaluation of metastatic lung and mediastinal lymph node involvement, with a reported sensitivity and specificity for CT of 35% and 31%, respectively, versus 15% and 20% for PET. Detection of liver metastases with MRI, CT, ultrasound, and PET showed accuracy rates of 49%, 44%, 41%, and 27%, respectively, while bone metastases were better detected using bone scan or MRI (40%) as compared to PET (35%).[415] In a review of PET for evaluation of recurrent anaplastic thyroid cancer, higher sensitivity (66% to 100%) and specificity (79% to 90%) were seen when compared to conventional imaging modalities.[416]

Carelon Oncologic Imaging guidelines for thyroid cancer are in concordance with the National Comprehensive Cancer Network Guidelines for Thyroid Carcinoma as well as the American Thyroid Association Practice Guidelines.[417, 418]

SURVEILLANCE

Biochemical monitoring remains the most vital component for surveillance of differentiated thyroid cancer; although conventional imaging may also be considered when clinically indicated. Both the American Thyroid Association and National Comprehensive Cancer Network do give consideration to a single exam after completion of therapy in intermediate and high risk differentiated thyroid cancer patients. The value of continued monitoring if no evidence of disease is seen is controversial.[410, 417]

Uterine Cancer

Advanced imaging is considered medically necessary for the diagnostic workup and management of documented uterine cancer (including uterine sarcoma).

Imaging Study	Diagnostic Workup	Management	Surveillance
CT chest **CT abdomen and pelvis**	Indicated (note: chest X-ray usually sufficient unless abnormal chest X-ray OR high-risk patient)	Indicated	Indicated for uterine sarcoma ONLY
MRI pelvis	Indicated (note: especially useful prior to fertility-sparing treatment)	Indicated	Not indicated
FDG-PET/CT	Indicated when standard imaging cannot be performed or is nondiagnostic for extent of metastatic disease	Indicated when standard imaging cannot be performed or is nondiagnostic for recurrent or progressive disease	Not indicated

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Uterine cancer is the most common gynecologic cancer and fourth most common cancer among women in the U.S. The most common type of uterine cancer is endometrial, which originates in the uterine lining. Risk factors include exposure to estrogen, obesity, and genetic predisposition. The most common presentation is abnormal bleeding; the cancer may also be found incidentally on exam. Over 80% of endometrial cancers are confined to the uterus upon discovery. The initial staging of patients with suspected endometrial cancer includes local imaging with endovaginal ultrasound or MRI pelvis.

DIAGNOSTIC WORKUP

The staging system most widely adopted for uterine cancer is the International Federation of Gynecology and Obstetrics (FIGO) system, although the American Joint Committee on Cancer TNM system is also used. MRI pelvis is the preferred

modality for assessing the extent of local disease and extension into the cervix.[111, 419] For fertility-sparing therapy, an MRI pelvis is indicated prior to hormonal therapy and dilatation and curettage; a review comparing MRI to transvaginal ultrasound reported better sensitivity for evaluating myometrial invasion with MRI although statistically the two exams were equivalent.[420] When evaluation of lymph nodes is required, both CT and MRI provide similar sensitivity and specificity.[421, 422] In several small studies, PET has been shown to be equivalent or moderately better for detecting nodal disease when compared to MRI and CT; however, these differences rarely affect the decision for lymphadenectomy.[423-428]

As the majority of endometrial cancers are confined to the uterus (75%) and lymph nodes (10%), systemic imaging is reserved for high-risk patients.[429] In an international prospective trial, the negative predictive value for low-risk endometrial cancer was 97%.[430] There is insufficient data to recommend PET/CT for routine assessment. Based on the National Comprehensive Cancer Network (NCCN) uterine cancer guidelines, European Society for Medical Oncology-European Society of Gynecological Oncology-European Society for Therapeutic Radiology and Oncology Consensus, and American College of Radiology guidelines, additional imaging for metastatic workup is optional.[187, 280, 431]

MANAGEMENT

Follow-up imaging should be guided by patient symptoms, risk assessment, and clinical concern for recurrent or metastatic disease. For patients with endometrial carcinoma who have undergone fertility-sparing treatment, MRI pelvis with contrast is preferred after 6 months of failed medical therapy, especially if considering further fertility-sparing approaches. In a small prospective study from Korea, PET for suspected disease recurrence had a sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of 100%, 83.3%, 96%, 95%, and 100%, respectively. PET/CT detected 3/24 (12.5%) recurrences in patients with elevated tumor markers but negative CT abdomen and pelvis findings.[432]

SURVEILLANCE

Following treatment for uterine sarcoma specifically, the NCCN recommends CT of the Chest, Abdomen and Pelvis every 3-6 months for the first 3 years, and then every 6-12 months for the next 2 years.[14] Otherwise, the National Comprehensive Cancer Network, American College of Radiology, and Society of Gynecologic Oncology do not recommend routine use of surveillance imaging.[280, 314, 431]

The most important component for surveillance of asymptomatic uterine cancer is physician history and physical with vaginal cytology, as the vaginal cuff is the most common site of recurrence. Cancer antigen (CA) 125 may be used if initially elevated. In a systematic review by Fung et al., the overall risk of recurrence was 13% for all patients and 3% or less for patients at low risk. Approximately 70% of all recurrences were symptomatic. [433] In a retrospective study, recurrences in high-grade endometrial carcinomas were discovered by symptoms 56% of the time and physical exam 18% of the time. Surveillance CT only detected 15% of asymptomatic recurrences.[434]

Limited data is available for MRI and PET/CT in surveillance of asymptomatic patients.[314] In a small prospective study, PET detected asymptomatic uterine cancer recurrence in only 4% of patients.[432] A retrospective study evaluating adherence to Society of Gynecological Oncology guidelines resulted in an appreciable decline in CT imaging, CA 125, and clinical exams with no effect on outcomes.[435]

Suspected or Known Metastases

Advanced imaging is considered medically necessary for diagnostic workup, management, and surveillance of patients with a documented malignancy when clinical evaluation suggests metastatic disease.

Imaging Study	Diagnostic Workup	Management	Surveillance
CT or MRI brain	Indicated for suspected brain or skull metastases, including high-risk staging (note: exam should be done with contrast; MRI brain preferred)	Indicated	Not indicated
CT neck **CT chest** **CT abdomen and pelvis**	Indicated (note: refer to specific cancer section for guidance)	Indicated (note: refer to specific cancer section for guidance)	Indicated (note: refer to specific cancer section for guidance)
MRI abdomen	*See "Focal liver lesion" in Abdominal Imaging*	Indicated in **EITHER** of the following scenarios: • Prior to and post-procedural baseline following liver directed therapy or surgery	Not indicated

		• Signs or symptoms suggestive of recurrent or progressive hepatic metastatic disease	
MRI axial skeleton (cervical, thoracic, or lumbar spine)	Indicated for evaluation of suspected or known vertebral or intradural metastases	Indicated for evaluation of suspected or known vertebral or intradural metastases	Not indicated
MRI appendicular skeleton (pelvis, lower or upper extremity)	Indicated for **ANY** of the following: • Evaluation of suspected or known bony pelvic metastases • Evaluation of suspected proximal lower/upper extremity metastasis • Evaluation of suspected distal upper/lower metastasis when radiographs are nondiagnostic	Indicated for **EITHER** of the following: • Evaluation of known bony pelvic metastases • Evaluation of known lower or upper extremity metastasis	Not indicated
FDG-PET/CT	Refer to specific tumor type indications	Refer to specific tumor type indications	Not indicated
NaF PET/CT	When performed as part of coverage under evidence determination (CED) in Medicare beneficiaries	When performed as part of coverage under evidence determination (CED) in Medicare beneficiaries	When performed as part of coverage under evidence determination (CED) in Medicare beneficiaries

Note: Criteria for the evaluation of known or suspected metastasis in specific tumor type indications supersede these criteria. These criteria should be used in patients with documented malignancy and with known or suspected metastatic disease when no criteria exist within the more specific tumor type indication

Note: MRI is considered medically necessary when criteria are met and CT is contraindicated or expected to be suboptimal (due to contrast allergy or anticipated contrast nephrotoxicity).

Rationale

Cancer metastasis is a leading cause of morbidity and accounts for approximately 90% of cancer-related mortality.[436] Metastasis involves the spread of cancer cells from the primary tumor to surrounding tissues and to distant organs through direct extension, blood, or lymphatics. The rate at which cancers metastasize varies greatly based on initial stage and cancer type.

DIAGNOSTIC WORKUP

In patients with biopsy-proven malignancy, a thorough history and physical exam, laboratory evaluation, and/or imaging may prompt concern for metastases. Symptoms may vary according the specific area of organ involvement or biochemical derangement.

- Lymph nodes: lymphadenopathy
- Lungs: cough, hemoptysis, shortness of breath
- Liver: hepatomegaly, nausea, jaundice, pain, elevated liver enzymes
- Bones: pain and fracture
- Brain: focal neurological deficit, cognitive dysfunction, headaches, seizures, ataxia

When metastases are clinically suspected, localized imaging is often warranted. Imaging of the body should be targeted to the suspected area of metastases as opposed to simultaneous ordering of multiple studies. For confirmation and initial management of metastatic disease to the liver (especially when liver-directed therapy or surgery is contemplated), MRI Abdomen (with hepatic contrast protocol) is preferred over CT (and PET/CT) to assess the exact number and distribution of

metastatic foci for local treatment planning.[437] Appropriateness of additional imaging is dependent on the results of the lead study.

In patients with suspected brain metastases, both MRI and CT imaging with contrast may be used to evaluate CNS metastases; however, MRI is the preferred exam. Multiple studies have shown that contrast-enhanced MRI is more sensitive for detection of brain metastases as well as differentiating from primary CNS cancer than both CT imaging and non-contrast MRI.[438] [439, 440]

In patients with suspected bone metastases, imaging studies may include plain radiographs, CT imaging, MRI imaging or PET imaging. Preliminary radiographs should be obtained for the distal extremities (hands/feet) as isolated metastatic disease presenting at these sites is less likely than within the axial and proximal appendicular skeleton, and findings may point to a different source for symptoms. In patients where there is concern for impending non-vertebral fracture or vertebral metastases, imaging should include a CT or MRI. MRI remains the imaging modality of choice due to its greater sensitivity to CT for detection of metastases, better delineation of the extent of tumor, and particularly its usefulness in patients with spine metastases to evaluate the extent of medullary and extraspinal disease.[441-444] MRI can also be used to distinguish benign from malignant compression fractures with a sensitivity and specificity of over 90%.[445, 446] In 2011 and 2017 meta-analyses comparing MRI, CT, PET, and bone scintigraphy, the sensitivity of MRI and PET were both statistically better than CT imaging and bone scintigraphy. On a per-patient basis, the pooled sensitivity and specificity estimates for PET, CT, MRI and BS were 89.7%, 72.9%, 90.6%, 86.0% and 96.8%, 94.8%, 95.4% and 81.4% respectively.[447, 448] In patients where disseminated, non-vertebral metastases are suspected, plain films, bone scintigraphy, and PET are all reasonable choices. Additional guidance may be found in the specific cancer section.

MANAGEMENT

For patients with either active disease or localized disease in remission, follow-up frequency should be determined by clinical need with additional diagnostic tests based on symptomatology. In general terms, imaging used in the initial detection of the cancer may be used to assess for treatment response.

SURVEILLANCE

Refer to specific cancer section for guidance.

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Codes

The following code list is not meant to be all-inclusive. Authorization requirements will vary by health plan. Please consult the applicable health plan for guidance on specific procedure codes.

Specific CPT codes for services should be used when available. Nonspecific or not otherwise classified codes may be subject to additional documentation requirements and review.

CPT/HCPCS

70450	CT head/brain, without contrast
70460	CT head/brain, with contrast
70470	CT head/brain, without contrast, followed by re-imaging with contrast
70480	CT of orbit, sella, or posterior fossa and outer, middle or inner ear, without contrast
70481	CT of orbit, sella, or posterior fossa and outer, middle or inner ear, with contrast
70482	CT of orbit, sella, or posterior fossa and outer, middle or inner ear, without contrast, followed by re-imaging with contrast
70486	CT of maxillofacial area, without contrast
70487	CT of maxillofacial area, with contrast
70488	CT of maxillofacial area, without contrast, followed by re-imaging with contrast
70490	CT, soft tissue neck, without contrast
70491	CT, soft tissue neck, with contrast
70492	CT, soft tissue neck, without contrast, followed by re-imaging with contrast
70540	MRI orbit, face and neck, without contrast
70542	MRI orbit, face and neck, with contrast
70543	MRI orbit, face and neck, without contrast, followed by re-imaging with contrast
70551	MRI brain (including brain stem), without contrast
70552	MRI brain (including brain stem), with contrast
70553	MRI brain (including brain stem), without contrast, followed by re-imaging with contrast
70554	MRI brain functional, not requiring physician or psychologist administration
70555	MRI brain functional, requiring physician or psychologist administration of entire neurofunctional testing
71250	Computed tomography, thorax, diagnostic; without contrast material
71260	Computed tomography, thorax, diagnostic; with contrast material(s)
71270	Computed tomography, thorax, diagnostic; without contrast material, followed by contrast material(s) and further sections
71271	Computed tomography, thorax, low dose for lung cancer screening, without contrast material(s)
71550	MRI chest, without contrast
71551	MRI chest, with contrast
71552	MRI chest, without contrast, followed by re-imaging with contrast
72125	CT cervical spine, without contrast
72126	CT cervical spine, with contrast
72127	CT cervical spine, without contrast, followed by reimaging with contrast
72128	CT thoracic spine, without contrast
72129	CT thoracic spine, with contrast
72130	CT thoracic spine, without contrast, followed by reimaging with contrast
72131	CT lumbar spine, without contrast
72132	CT lumbar spine, with contrast
72133	CT lumbar spine, without contrast, followed by reimaging with contrast
72141	MRI cervical spine, without contrast
72142	MRI cervical spine, with contrast

72146	MRI thoracic spine, without contrast
72147	MRI thoracic spine, with contrast
72148	MRI lumbar spine, without contrast
72149	MRI lumbar spine, with contrast
72156	MRI cervical spine, without contrast, followed by reimaging with contrast
72157	MRI thoracic spine, without contrast, followed by reimaging with contrast
72158	MRI lumbar spine, without contrast, followed by reimaging with contrast
72192	CT pelvis without contrast
72193	CT pelvis with contrast
72194	CT pelvis without contrast, followed by re-imaging with contrast
72195	MRI pelvis without contrast
72196	MRI pelvis with contrast
72197	MRI pelvis without contrast, followed by re-imaging with contrast
73200	CT upper extremity, without contrast
73201	CT upper extremity, with contrast
73202	CT upper extremity, without contrast, followed by re-imaging with contrast
73218	MRI upper extremity non-joint, without contrast
73219	MRI upper extremity non-joint, with contrast
73220	MRI upper extremity non-joint, without contrast, followed by re-imaging with contrast
73221	MRI upper extremity any joint, without contrast
73222	MRI upper extremity any joint, with contrast
73223	MRI upper extremity any joint, without contrast, followed by re-imaging with contrast
73700	CT lower extremity, without contrast
73701	CT lower extremity, with contrast
73702	CT lower extremity, without contrast, followed by re-imaging with contrast
73718	MRI lower extremity non-joint, without contrast
73719	MRI lower extremity non-joint, with contrast
73720	MRI lower extremity non-joint, without contrast, followed by re-imaging with contrast
73721	MRI lower extremity any joint, without contrast
73722	MRI lower extremity any joint, with contrast
73723	MRI lower extremity any joint, without contrast, followed by re-imaging with contrast
74150	CT abdomen without contrast
74160	CT abdomen with contrast
74170	CT abdomen without contrast, followed by re-imaging with contrast
74176	CT abdomen and pelvis without contrast
74177	CT abdomen and pelvis with contrast
74178	CT abdomen and pelvis without contrast in one or both body regions, followed by re-imaging with contrast
74181	MRI abdomen without contrast
74182	MRI abdomen with contrast
74183	MRI abdomen without contrast, followed by re-imaging with contrast
74261	CT colonography diagnostic, including image post-processing, without contrast
74262	CT colonography diagnostic, including image post-processing, with contrast including non-contrast images, if performed
74263	CT colonography screening, including image post-processing
76390	MRI spectroscopy
77046	MRI breast without contrast material(s); unilateral

77047	MRI breast without contrast material(s); bilateral
77048	MRI breast without and with contrast with CAD; unilateral
77049	MRI breast without and with contrast with CAD; bilateral
77084	MRI, bone marrow blood supply
78608	Brain imaging PET, metabolic evaluation
78609	Brain imaging PET, perfusion evaluation
78811	PET imaging, limited area
78812	PET imaging, skull to mid-thigh
78813	PET imaging, whole body
78814	PET imaging, with concurrently acquired CT for attenuation correction and anatomic localization; limited area
78815	PET imaging, with concurrently acquired CT for attenuation correction and anatomic localization; skull base to mid-thigh
78816	PET imaging, with concurrently acquired CT for attenuation correction and anatomic localization; whole body
A9515	Choline c-11, diagnostic, per study dose up to 20 millicuries
A9552	Fluorodeoxyglucose f-18 fdg, diagnostic, per study dose, up to 45 millicuries
A9580	Sodium Fluoride F-18, Diagnostic, Per Study Dose, Up To 30 Millicuries
A9587	Gallium ga-68, dotatate, diagnostic, 0.1 millicurie
A9588	Fluciclovine f-18, diagnostic, 1 millicurie
A9591	Fluoroestradiol f 18, diagnostic, 1 millicurie
A9592	Copper cu-64, dotatate, diagnostic, 1 millicurie
A9593	Gallium ga-68 psma-11, diagnostic, (ucsf), 1 millicurie
A9594	Gallium ga-68 psma-11, diagnostic, (ucla), 1 millicurie
A9595	Piflufolastat f-18, diagnostic, 1 millicurie
A9596	Gallium ga-68 gozetotide, diagnostic, (illuccix), 1 millicurie
A9597	Positron emission tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified
A9598	Positron emission tomography radiopharmaceutical, diagnostic, for non-tumor identification, not otherwise classified
A9800	Gallium ga-68 gozetotide, diagnostic, (locametz), 1 millicurie
C8903	MRI with contrast, breast; unilateral
C8905	MRI without contrast followed by with contrast, breast; unilateral
C8906	MRI with contrast, breast; bilateral
C8908	MRI without contrast followed by with contrast, breast; bilateral
G0219	PET imaging whole body; melanoma for non-covered indications
G0235	PET imaging, any site, not otherwise specified
G0252	PET imaging, full and partial-ring PET scanners only, for initial diagnosis of breast cancer and/or surgical planning for breast cancer (e.g., initial staging of axillary lymph nodes)
S8037	Magnetic resonance cholangiopancreatography (mrcp)
S8085	Fluorine-18 fluorodeoxyglucose (f-18 fdg) imaging using dual-head coincidence detection system (non-dedicated PET scan)
0633T	CT Breast w/3d rendering uni without contrast
0634T	CT Breast w/3d rendering uni with contrast
0635T	CT Brst w/3d rendering uni wo cntrst flwd cntrst
0636T	CT Breast w/3d rendering bi without contrast
0637T	CT Breast w/3d rendering bi with contrast
0638T	CT Brst w/3d rendering bi wo cntrst flwd cntrst

ICD-10 Diagnosis

Refer to the ICD-10 CM manual

History

Status	Review Date	Effective Date	Action
Revised	07/16/2024	03/23/2025	Independent Multispecialty Physician Panel (IMPP) review. Revised indications: Colorectal cancer screening, Pancreatic cancer screening, Hepatocellular cancer screening, Anal cancer, Bladder and Urothelial cancers, Breast cancer, Cervical cancer, Colorectal cancer, Esophageal and Gastroesophageal Junction cancers, Gastric cancer, Head and Neck cancer, Hepatocellular and Biliary Tract cancers, Histiocytic Neoplasms, Kidney Cancer, Lung Cancer- Small Cell, Lymphoma- Non-Hodgkin and Leukemia, Multiple Myeloma, Penile, Vaginal and Vulvar Cancers, and Thyroid Cancer.
Revised	07/18/2023	04/14/2024 for commercial, Medicare, and Medicaid except LA	IMPP review. Revised indications: Breast cancer screening, Lung cancer screening, Pancreatic cancer screening, Breast Cancer, Cervical Cancer, Hepatocellular and Biliary Tract Cancers, Lung Cancer-Non-Small Cell, Lung Cancer- Small Cell, Lymphoma-Non-Hodgkin and Leukemia, Melanoma, Prostate Cancer, and Sarcomas of Bone/Soft Tissue.
Updated	01/23/2024	Unchanged	Expanded guideline rationale. Added required language per new Medicare regulations.
Revised	05/09/2022	04/09/2023 for commercial, Medicare, and Medicaid except LA; 06/18/2023 for LA Medicaid	IMPP review. Revised indications: Cancer screening, Cervical cancer, Head and neck cancer, Histiocytic neoplasms, Lymphoma- Non-Hodgkin and leukemia, Multiple myeloma, Prostate cancer, Cancers of the pleura, thymus, heart, and mediastinum, and Thyroid cancer.
Updated	-	12/18/2022	Added code A9800.
Revised	05/09/2022	11/07/2022 for commercial, Medicare, and non-Anthem Medicaid; 04/09/2023 for Anthem Medicaid except LA Medicaid; 06/18/2023 for LA Medicaid	IMPP review. Revised indications: Prostate cancer.
Updated	-	09/01/2022	Added code A9596.
Revised	05/26/2021	03/13/2022	IMPP review. Revised indications: Cancer screening, Bladder cancer, Breast cancer, Colorectal cancer, Esophageal cancer, Hepatobiliary cancer, Lung cancer-Non-small cell, Lymphoma-Hodgkin, Lymphoma- Non-

Status	Review Date	Effective Date	Action
			Hodgkin and Leukemia, Melanoma, Neuroendocrine tumors, Prostate cancer, Sarcoma of bone and soft tissue, Testicular cancer, Thyroid cancer, and Suspected or known metastases. Added indication: Histiocytic neoplasms. Added codes A9515, A9552, A9580, A9587, A9588, A9591, A9592, A9593, A9594, A9595, A9597, A9598, 0633T, 0634T, 0635T, 0636T, 0637T, and 0638T.
Revised	05/26/2021	11/07/2021	IMPP review. Revised indications: Cancer screening and Prostate cancer.
Revised	03/17/2021	05/01/2021	IMPP review. Revised criteria for Cancer Screening.
Revised	05/11/2020, 07/08/2020	03/14/2021	Independent Multispecialty Physician Panel (IMPP) review. Revised criteria for Cancer Screening, Anal, Bladder/renal pelvis/ureter, Breast, Cervical, Colorectal, Esophageal/gastroesophageal junction, Gastric, Germ Cell (now Testicular), Hepatobiliary, Kidney, Lung, Lymphoma- Hodgkin, Lymphoma- Non Hodgkin, Melanoma, Multiple myeloma, Neuroendocrine, Ovarian, Pancreatic, Penile/vaginal/vulvar, Prostate, Sarcoma of Bone and Soft Tissue, Thyroid, Uterine, and Suspected metastases, not otherwise specified. Added codes C8903, C8905, C8906, C8908, G0219, G0235, G0252, S8037, and S8085.
Revised	-	01/01/2021	Annual CPT code update: added 71271; revised descriptions for 71250, 71260, 71270. Removed code G0297.
Revised	10/28/2019	08/17/2020	IMPP review. Revised criteria for Cancer screening and Breast Cancer.
Revised	01/28/2019, 03/25/2019	11/10/2019	IMPP review. Revised criteria for Anal, Bladder/renal pelvis/ureter, Brain/spinal cord, Breast, Cervical, Colorectal, Esophageal/gastroesophageal junction, Germ cell tumors, Head and neck, Kidney, Lung, Lymphoma-Hodgkin, Lymphoma- Non Hodgkin, Mucosal melanoma, Multiple myeloma, Pancreatic, Penile/vaginal/vulvar, Prostate, and Uterine. New sections added for Hepatobiliary and Suspected metastases, not otherwise specified.
Revised	09/12/2018	07/14/2019	IMPP review. Guidelines for 11C-Choline and 18F-Fluciclovine added for Prostate Cancer. Guideline for 68Ga-Dotatate added for Neuroendocrine Cancer.
Restructured	09/12/2018	01/01/2019	IMPP review. Advanced Imaging guidelines redesigned and reorganized to a condition-based structure.
Revised	07/11/2018	03/09/2019	IMPP review. Renamed the Administrative Guidelines to “General Clinical Guideline.” Retitled Pretest Requirements to “Clinical Appropriateness Framework” to summarize the components of a decision to pursue diagnostic testing. Revised to expand applicability beyond diagnostic imaging, retitled Ordering of Multiple Studies to “Ordering of Multiple Diagnostic or Therapeutic Interventions” and replaced imaging-specific terms with

Status	Review Date	Effective Date	Action
			“diagnostic or therapeutic intervention.” Repeated Imaging split into two subsections, “repeat diagnostic testing” and “repeat therapeutic intervention.”
Revised	09/07/2017	03/12/2018	IMPP review. Revised criteria for Anal, Bladder, Bone/cartilage, Central nervous system, Cervical, Colorectal, Germ cell tumors, Lung cancer, Neuroendocrine tumor, Other cancers, Pancreatic, Skin, Thorax, Thyroid, Uterine, and Vaginal/vulvar/penile cancers.
Created	-	03/30/2005	Original effective date