CLINICAL APPROPRIATENESS GUIDELINES

ADVANCED IMAGING

Appropriate Use Criteria: Oncologic Imaging

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Proprietary
# Table of Contents

Description and Application of the Guidelines .......................................................... 4
Administrative Guidelines ......................................................................................... 5
    Ordering of Multiple Studies ................................................................................. 5
        Simultaneous Ordering of Multiple Studies ......................................................... 5
        Repeated Imaging ............................................................................................. 5
    Pre-Test Requirements ......................................................................................... 6
History ....................................................................................................................... 6
Oncologic Imaging ..................................................................................................... 7
    General Information/Overview .............................................................................. 7
        Scope ................................................................................................................. 7
        Technology Considerations ................................................................................ 7
        Definitions ....................................................................................................... 8
        References ...................................................................................................... 9
Clinical Indications .................................................................................................... 11
    Cancer Screening ................................................................................................ 11
        Breast Cancer Screening .................................................................................... 11
        Colorectal Cancer Screening ........................................................................... 12
        Lung Cancer Screening ..................................................................................... 12
    Anal Cancer ......................................................................................................... 16
    Bladder, Renal, Pelvis, and Ureter Cancers ............................................................. 18
    Brain and Spinal Cord Cancers .............................................................................. 21
    Breast Cancer ...................................................................................................... 23
    Cancers of Unknown Primary .............................................................................. 27
    Cervical Cancer .................................................................................................... 28
    Colorectal Cancer ................................................................................................ 31
    Esophageal and Gastroesophageal Junction Cancers ............................................ 35
    Gastric Cancer ...................................................................................................... 37
    Germ Cell Tumors ................................................................................................. 40
    Head and Neck Cancer ........................................................................................ 43
    Kidney Cancer/Renal Cell Carcinoma ................................................................. 46
    Lung Cancer – Non-Small Cell .............................................................................. 48
    Lung Cancer – Small Cell ..................................................................................... 51
    Lymphoma – Hodgkin .......................................................................................... 53
    Lymphoma – Non-Hodgkin .................................................................................. 55
    Melanoma – Cutaneous ....................................................................................... 59
    Melanoma – Mucosal ............................................................................................ 61
    Merkel Cell Carcinoma ......................................................................................... 63
    Multiple Myeloma ................................................................................................. 64
    Neuroendocrine Tumors ....................................................................................... 67
    Ovarian Cancer (Epithelial) ............................................................................... 69
Description and Application of the Guidelines

The AIM Clinical Appropriateness Guidelines (hereinafter “the AIM 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. As used by AIM, the Guidelines establish objective and evidence-based criteria for medical necessity determinations where possible. In the process, multiple functions are accomplished:

- 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 advocate for patient safety concerns
- To enhance the quality of health care
- To promote the most efficient and cost-effective use of services

The AIM guideline development process complies with applicable accreditation 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. Relevant citations are included in the References section attached to each Guideline. AIM reviews all of its Guidelines at least annually.

AIM makes its Guidelines publicly available on its website twenty-four hours a day, seven days a week. Copies of the AIM Clinical Appropriateness Guidelines are also available upon oral or written request. Although the Guidelines are publicly-available, AIM considers the Guidelines to be important, proprietary information of AIM, which cannot be sold, assigned, leased, licensed, reproduced or distributed without the written consent of AIM.

AIM 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 AIM 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. If requested by a health plan, AIM will review requests based on health plan medical policy/guidelines in lieu of the AIM Guidelines.

The Guidelines may also be used by the health plan or by AIM 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.
Administrative Guidelines

Ordering of Multiple Studies

Requests for multiple imaging studies to evaluate a suspected or identified condition and requests for repeated imaging of the same anatomic area are subject to additional review to avoid unnecessary or inappropriate imaging.

Simultaneous Ordering of Multiple Studies

In many situations, ordering multiple imaging studies at the same time is not clinically appropriate because:

- Current literature and/or standards of medical practice support that one of the requested imaging studies is more appropriate in the clinical situation presented; or
- One of the imaging studies requested is more likely to improve patient outcomes based on current literature and/or standards of medical practice; or
- Appropriateness of additional imaging is dependent on the results of the lead study.

When multiple imaging studies are ordered, the request will often require a peer-to-peer conversation to understand the individual circumstances that support the medically necessity of performing all imaging studies simultaneously.

Examples of multiple imaging studies that may require a peer-to-peer conversation include:

- CT brain and CT sinus for headache
- MRI brain and MRA brain for headache
- MRI cervical spine and MRI shoulder for pain indications
- MRI lumbar spine and MRI hip for pain indications
- MRI or CT of multiple spine levels for pain or radicular indications
- MRI foot and MRI ankle for pain indications
- Bilateral exams, particularly comparison studies

There are certain clinical scenarios where simultaneous ordering of multiple imaging studies is consistent with current literature and/or standards of medical practice. These include:

- Oncologic imaging – Considerations include the type of malignancy and the point along the care continuum at which imaging is requested
- Conditions which span multiple anatomic regions – Examples include certain gastrointestinal indications or congenital spinal anomalies

Repeated Imaging

In general, repeated imaging of the same anatomic area should be limited to evaluation following an intervention, or when there is a change in clinical status such that imaging is required to determine next steps in management. At times, repeated imaging done with different techniques or contrast regimens may be necessary to clarify a finding seen on the original study.

Repeated imaging of the same anatomic area (with same or similar technology) may be subject to additional review in the following scenarios:

- Repeated imaging at the same facility due to motion artifact or other technical issues
- Repeated imaging requested at a different facility due to provider preference or quality concerns
- Repeated imaging of the same anatomic area (MRI or CT) based on persistent symptoms with no clinical change, treatment, or intervention since the previous study
- Repeated imaging of the same anatomical area by different providers for the same member over a short period of time
Pre-Test Requirements

Critical to any finding of clinical appropriateness under the guidelines for specific imaging exams is a determination that the following are true with respect to the imaging request:

- A clinical evaluation has been performed prior to the imaging request (which should include a complete history and physical exam and review of results from relevant laboratory studies, prior imaging and supplementary testing) to identify suspected or established diseases or conditions.

- **For suspected diseases or conditions:**
  - Based on the clinical evaluation, there is a reasonable likelihood of disease prior to imaging; and
  - Current literature and standards of medical practice support that the requested imaging study is the most appropriate method of narrowing the differential diagnosis generated through the clinical evaluation and can be reasonably expected to lead to a change in management of the patient; and
  - The imaging requested is reasonably expected to improve patient outcomes based on current literature and standards of medical practice.

- **For established diseases or conditions:**
  - Advanced imaging is needed to determine whether the extent or nature of the disease or condition has changed; and
  - Current literature and standards of medical practice support that the requested imaging study is the most appropriate method of determining this and can be reasonably expected to lead to a change in management of the patient; and
  - The imaging requested is reasonably expected to improve patient outcomes based on current literature and standards of medical practice.

- 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 supersede the pre-test requirements set forth above. During the peer-to-peer conversation, factors such as patient acuity and setting of service may also be taken into account.

### History

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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.

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. 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.

Functional imaging studies such as positron emission tomography (PET) provide information about the metabolic activity of tumor. 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. Its utility may be improved by overlaying the areas of high uptake with CT images in order to provide anatomic detail. PET 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. Other PET tracers including C-11 choline and F-18 fluciclovine are not addressed the guidelines, as AIM does not review them at this time.
There are a large number of 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 signs or symptoms of disease
- **Diagnosis** – testing based on a reasonable suspicion of a particular condition or disorder, usually due to the presence of signs or symptoms
- **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
- **Surveillance** – periodic assessment following completion of therapy, or for monitoring known disease that is stable or asymptomatic

**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** – 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** – 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** – 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** – a cancer staging and classification system for gynecologic malignancies developed by the International Federation of Gynecology and Obstetrics.

- **Lugano classification** – 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.


**References**


Clinical Indications

CT and MRI imaging is appropriate for symptom-directed management or perioperative evaluation of an established malignancy when not specifically excluded under individual cancer diagnoses.

Indications are presented in the following sections by tumor type.

Cancer Screening

Advanced imaging is indicated for screening of breast cancer, colorectal cancer, and lung cancer.

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
- Individuals known to have ANY of the following genetic mutations:
  - ATM
  - CDH1
  - CHEK2
  - PALB2
- History of lobular carcinoma in situ, atypical ductal hyperplasia, or atypical lobular hyperplasia on biopsy
- Lifetime risk ~20% or greater as defined by BRCAPRO 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%.\(^1\)\(^2\) Falsepositives are commonly seen in average-risk women screened for breast cancer with MRI, particularly those with dense breasts.\(^3\) In a systematic review for the U.S. Preventive Services Task Force, the authors concluded that the effect of supplemental screening on breast cancer outcomes remains unclear.\(^4\) However, additional imaging with MRI breast has been found to be beneficial in higher-risk groups.\(^5\)\(^-\)\(^12\)

MRI mammography has been shown to be more sensitive but less specific than mammography.\(^6\)\(^)\(^-\)\(^16\) 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.\(^17\) 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.\(^18\) Benefits in survival may also be seen, particularly in patients with BRCA1 and BRCA2 mutations.\(^19\)\(^20\) 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.\textsuperscript{21}

AIM Oncologic Imaging guidelines pertaining to breast cancer screening are in concordance with the National Comprehensive Cancer Network, American Cancer Society, and American College of Radiology recommendations.\textsuperscript{22-24}

Colorectal cancer screening

CT colonography is indicated in ANY of the following scenarios:

- **Screening CT colonography** is indicated as an alternative to conventional colonoscopy or double contrast barium enema at 5-year intervals, beginning at age 50

- **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

Rationale

Although CT colonography allows noninvasive screening of the colon, it also carries the risk of radiation exposure and detection of clinically insignificant extracolonic disease. A study by Chung et al. reported sensitivities of CT colonography for detecting polyps of 5 mm or smaller, of 6-9 mm, and of 10 mm or larger were 84%, 94%, and 100%, respectively.\textsuperscript{25} In an update and systematic review of colorectal cancer screening for the U.S. Preventive Services Task Force, CT colonography with bowel preparation had sensitivity to detect adenomas 6 mm and larger, which was comparable with colonoscopy.\textsuperscript{26} As reviewed in a meta-analysis of 24 studies (N = 4181), CT colonography appeared sensitive and specific in the detection of large and medium polyps: 86% and 86%.\textsuperscript{27} In a review comparing primary CT colonography and optical colonoscopy, both screening strategies result in similar detection rates for advanced neoplasia (3%), although the numbers of polypectomies and complications were considerably higher in the optical colonoscopy group.\textsuperscript{28}

In patients with positive fecal occult blood test and incomplete optical colonoscopy, CT colonography was able to identify either polyps or colorectal cancer in 50% of cases (21/42).\textsuperscript{29} Another small study showed that CT colonography detected an additional 33% more lesions and had a sensitivity and specificity of 100% and 96% in patients with clinically suspected colorectal cancer and incomplete optical colonoscopy.\textsuperscript{30} Based on the low sensitivity for detecting polyps, optical colonoscopy should be the preferred modality for cancer surveillance in patients with a history of colorectal cancer.\textsuperscript{31}

AIM 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.\textsuperscript{32, 33}

Lung cancer screening

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

- Age equal to or greater than 55 and less than or equal to 80
- 30 or greater pack-year history* of cigarette smoking
- Current smoker or quit date within the past 15 years
- 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

Screening for lung cancer can be beneficial; however, these benefits must be weighed against the risks of radiation exposure, overdiagnosis, and false positives.34 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 low-dose helical CT than with standard screening chest X-rays,35 but those screened also experience higher overall rates of false positive results, invasive procedures, and serious complications.36

At the end of 2013, the U.S. Preventive Services Task Force released the following recommendation summary: "The USPSTF [U.S. Preventive Services Task Force] recommends annual screening for lung cancer with low-dose CT in adults aged 55 to 80 years who have a 30 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."37

AIM AIM 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.34,37-39

References


Oncologic Imaging

Anal Cancer

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven anal cancer.

Initial treatment strategy

- CT chest, abdomen, and pelvis
- PET imaging when standard imaging studies are equivocal or nondiagnostic for metastatic disease

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

Radiation planning

- PET imaging for definitive treatment only

Subsequent treatment strategy

- CT chest, abdomen, and pelvis as clinically indicated
- PET imaging in **EITHER** of the following scenarios:
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - Restaging of local recurrence when salvage surgery is planned

Surveillance

- CT chest, abdomen, and pelvis as clinically 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

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.

INITIAL TREATMENT STRATEGY

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.

PET/CT scan in initial staging and radiation planning allows for better assessment of nodal metastases which may alter the radiation plan for curative combined modality therapy. 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.1 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 78% for detecting nodal disease. A total of 5.1% to 37.5% of patients were upstaged and 8.2% to 26.7% were downstaged with 12.5% to 59.3% of patients requiring treatment changes. However, the majority of the changes in treatment were in radiation planning.2

SUBSEQUENT TREATMENT STRATEGY

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 to 12 weeks after treatment. Patients with persistent disease but without evidence of progression may be managed with close followup for up to 6 months. 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.3 The 5-year overall survival was 64% in a small study of 39 patients treated with radical salvage surgery.4
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, abdomen, and pelvis with contrast annually for a duration of 3 years per the NCCN guidelines. However, due to the lack of prospective trials and because most recurrences are locoregional, the European Society of Medical Oncology, European Society of Surgical Oncology, and the European Society for Radiotherapy and Oncology do not endorse routine advanced imaging.

References

Bladder, Renal Pelvis, and Ureter Cancer

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven bladder, renal pelvis, and ureter cancer.

Initial treatment strategy

- Noninvasive bladder/urothelial cancer
  - CT abdomen and pelvis
  - MRI pelvis for local staging for sessile or high-grade tumors (as an adjunct to CT imaging)
- Invasive bladder cancer/urothelial cancer
  - CT abdomen and pelvis
  - CT chest for abnormal chest X-ray in high-risk patients, or as clinically indicated
  - MRI pelvis for local staging (as an adjunct to CT imaging)
  - MRI brain for symptomatic or high-risk patients
  - PET imaging in ANY of the following scenarios:
    - Evaluation of stage II or stage III bladder cancer prior to surgery
    - When bone metastasis is suspected based on signs and symptoms and standard imaging has not demonstrated bone lesions

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

Subsequent treatment strategy

- Noninvasive bladder/urothelial cancer
  - CT abdomen and pelvis
- Invasive bladder cancer/urothelial cancer
  - CT abdomen and pelvis
  - PET imaging in ANY of the following scenarios:
    - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
    - When objective signs or symptoms of disease are present and CT or MRI has not clearly demonstrated recurrence or progression

Surveillance

- Noninvasive bladder/urothelial cancer
  - CT abdomen and pelvis
  - Chest imaging generally not required
- Invasive bladder/urothelial cancer
  - CT abdomen and pelvis with or without CT chest (chest radiograph preferred over CT)

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 urinary tract, including kidney, renal pelvis, ureter, bladder, and urethra, comprise the sixth most common cancer in men and women. Outside of the kidney, 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.

INITIAL TREATMENT STRATEGY

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 is the preferred study for the staging of invasive locally advanced bladder cancer. 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 for local staging of bladder cancer. In clinical situations where CT abdomen and pelvis with excretory imaging is inadequate, an MRI pelvis may be indicated. 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%. Both CT and MRI have comparable accuracy for staging lymph nodes: 73% to 90%. In the event that iodinated or gadolinium-based contrast cannot be used, renal ultrasound and/or CT without contrast (particularly when PET/CT is not utilized) may be used in conjunction with retrograde urography.

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 scans had similar specificities of 97% and 98%. 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. 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 pooled sensitivity and specificity of PET/CT for staging or restaging metastatic lesions of bladder cancer were 82% and 89%, 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. Another review and meta-analysis by Soubra et al. showed a slightly lower sensitivity and specificity at 58% and 95%, respectively, for detecting lymph node metastases. Although PET shows promise as a useful clinical tool for staging of bladder cancer, especially outside of the pelvis, it should only be used to confirm resectability prior to planned surgical intervention for stage II and III bladder/urothelial cancers, and currently its use is a National Comprehensive Cancer Network (NCCN) category 2B recommendation.

Additional metastatic workup with MRI of the brain and bone scan should not be routinely ordered unless localizing labs or symptoms are present. 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.

SUBSEQUENT TREATMENT STRATEGY

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. 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. 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. Early detection of asymptomatic recurrence has been shown to positively impact survival. To completely assess these areas for potential metastases, chest X-ray and CT abdomen and pelvis with excretory imaging are the imaging modalities recommended by NCCN. CT scan of the abdomen and pelvis with and without contrast may replace CT abdomen and pelvis with excretory imaging after 2 years.

References


Brain and Spinal Cord Malignancy

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven primary central nervous system cancer.

**Initial treatment strategy**
- CT chest, abdomen, and pelvis when systemic involvement is clinically suspected
- MRI brain and/or MRI spine
- fMRI for preoperative neurosurgical planning, as a replacement for a Wada test or direct electrical stimulation mapping
- PET brain imaging for primary central nervous system cancer

**Subsequent treatment strategy**
- MR perfusion/angiography for evaluation of vascular supply to tumor
- MRI brain and/or MRI spine
- fMRI for preoperative neurosurgical planning, as a replacement for a Wada test or direct electrical stimulation mapping
- MRS to differentiate recurrent or residual brain tumor from post-therapy changes, such as delayed radiation necrosis
- PET brain imaging may be used as an alternative modality to differentiate posttreatment scarring from residual or recurrent disease

**Surveillance**
- MRI brain and/or MRI spine

*Notes:*
Spine imaging is indicated for intracranial and spinal ependymoma, medulloblastoma, primary spinal cord tumors, leptomeningeal disease, and symptomatic or cerebrospinal fluid-positive primary central nervous system lymphoma.

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

*Commonly used radiolabeled tracers for PET brain are not currently reviewed at AIM.*

**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. 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.

**INITIAL TREATMENT STRATEGY**
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 primary central nervous system lymphoma. Systemic imaging is also indicated for central nervous system lymphomas; one study found that PET/CT had a significantly higher sensitivity (94%-98%) than CT imaging and resulted in change in management in 34% of patients. However, the evidence to date is limited and PET imaging is currently a National Comprehensive Cancer Network (NCCN) level 2B recommendation.

**SUBSEQUENT TREATMENT STRATEGY**
MR perfusion/angiography, fMRI, MRS, or PET scan may be used to differentiate radiation necrosis from active tumor. Limited data have confirmed the utility of MR perfusion in identifying tumor response in high-grade gliomas. 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. In a meta-analysis comparing the accuracy of MRS to PET, there was no significant difference between the two modalities.

SURVEILLANCE

AIM 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.

References

Breast Cancer

Advanced imaging is considered medically necessary for initial treatment strategy and subsequent treatment strategy of biopsy-proven breast cancer. Routine surveillance imaging following completion of therapy is not considered medically necessary.

Suspected cancer

- MRI breast in ANY of the following scenarios:
  - Single follow-up MRI at 6 months following a breast MRI with BI-RADS category 3 findings
  - Differentiation of palpable mass from surgical scar tissue
  - Lesion characterization when other imaging examinations, such as ultrasound and mammography, and physical examination are inconclusive for the presence of breast cancer, and biopsy cannot be performed
  - Metastatic cancer of unknown primary and suspected to be of breast origin and/or axillary adenopathy and no mammographic or physical findings of primary breast carcinoma

Initial treatment strategy

- CT chest, abdomen and/or pelvis for stage IIIA-IV or as clinically indicated
- MRI breast in ANY of the following scenarios:
  - To determine the extent of disease in biopsy-proven invasive carcinoma and ductal carcinoma in situ
  - 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
  - To assess response to neoadjuvant chemotherapy prior to surgery
- MRI brain with contrast for central nervous system symptoms
- MRI spine with contrast for back pain or symptoms of cord compression
- PET imaging in ANY of the following scenarios:
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - Locally advanced disease (stage IIIA-IIIC) has been established and standard imaging does not clearly demonstrate metastatic disease
  - Symptom directed staging has been performed and is equivocal or suspicious for metastatic disease

Subsequent treatment strategy

- CT chest, abdomen and/or pelvis as clinically indicated
- MRI breast in ANY of the following scenarios:
  - Post-lumpectomy with close or positive margins to evaluate for residual disease
  - Suspected recurrence in patients with tissue transfer flaps (rectus, latissimus dorsi, and gluteal) post-reconstruction
  - Suspected recurrence in women with a prior history of breast cancer when clinical, mammographic, and/or sonographic findings are inconclusive
• PET imaging in ANY of the following scenarios:
  o Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  o Suspected worsening of disease based on objective signs or symptoms (such as rising tumor markers), when standard imaging has not clearly identified a site of recurrence or progression

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

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. 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 should be biopsied. MRI breast may be indicated in high-risk patients without a positive biopsy. MRI breast has been shown to have improved sensitivity over conventional mammographic imaging; however, limited data exists to support the use of MRI in patients with a lumpy, dense, clinically negative breast exam and normal conventional imaging. 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.

INITIAL TREATMENT STRATEGY

Breast cancer is staged using the American Joint Committee on Cancer TNM system. Advanced imaging should be guided by stage and other presenting symptoms. In a large single-institution retrospective study of newly diagnosed asymptomatic breast cancer, bone scan detected bony metastases in 6% of patients (stage I 5%, stage II 6%, and stage III 14%), liver ultrasound detected hepatic metastases in 0.7% of patients (stage I or II 0% and stage III 6%), and chest X-ray detected lung metastases in 0.9% of patients (stage I or II 0% and stage III 7%). However, there was an unacceptably high rate of false positives: 6% for bone scans, 6% for liver ultrasounds, and 3% for chest X-rays.2 Ravaiolí et al. reported the rate of metastases detection in asymptomatic breast cancer patients was 1.46% for stage I and II versus 10.68% for stage III.4 A review of 20 studies similarly showed that bone scan detected skeletal metastases in 0.5%-6.8% of those with stage I, 2.4%-8.8% with stage II, and 8.3%-24.5% with stage III breast cancer. The detection of liver and bone metastases ranged from 0%-1.7% in stage I-II patients and 1.7%-2% for stage III patients. False-positive rates were 10%-22% for bone scan, 33%-66% for liver ultrasonography, and 0%-23% for chest radiography. 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.

In the setting of metastatic disease found on conventional imaging, there is insufficient data and limited evidence to show PET scan alters treatment. Recent studies have found that PET/CT imaging changed the initial treatment in 1%-8% of patients with early-stage breast cancer. 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.5 For locally advanced disease, a higher proportion, 7%-13% had changes in management based on PET/CT imaging.6 Additionally, a prospective multicenter study evaluating the use of PET/CT in detecting axillary metastases found sensitivity and specificity to be 61% and 80%, respectively.7 A review of 21 studies showed that PET/CT had equivalent specificity when compared to MRI but had a substantially worse sensitivity, 64% versus 82%, respectively.8 In advanced breast cancer, a handful of studies have shown potential benefit to PET imaging in detecting distant metastases over conventional imaging.9,10 In the largest of the prospective studies, the overall sensitivity and specificity of PET/CT for detecting distant metastases were 100% and 98%, respectively, whereas the sensitivity and specificity of conventional imaging were 60% and 83%, respectively. PET/CT led to a change in the initial staging in 42% of patients.11 In a recent meta-analysis of six studies, Sun et al. found PET/CT had a sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of 99%, 95%, 21.1, and 0.02 compared to conventional imaging 57%, 88%, 4.8, and 0.49 for detecting distant metastases.12 The National Comprehensive Cancer Network (NCCN) has designated PET/CT scan as a category 2B option.13

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.14,15 In a meta-analysis of 4 studies by Nehmat 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.16 The NCCN designates MRI breast as an optional imaging test.13

SUBSEQUENT TREATMENT STRATEGY
MRI breast been shown to inaccurately estimate the size of the residual tumor. 17 In the phase III INTENS trial, ultrasound was able to more accurately predict pathological residual tumor as compared to MRI. 18 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. 19 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. 20 PET imaging is designated category 2B by the NCCN. 13 In the unique scenario of bone-only metastases, the AIM External Expert Advisory Board allows for disease monitoring with PET imaging.

SURVEILLANCE

Both the American Society of Clinical Oncology and the NCCN discourage the use of advanced imaging for surveillance of asymptomatic breast cancer. 13, 21 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. 22

References


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 initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven malignancy.

Initial treatment strategy
- CT based on specific cancer
- MRI based on specific cancer
- PET when standard imaging studies are equivocal or nondiagnostic in determining the extent of disease

Subsequent treatment strategy
- CT based on specific cancer
- MRI based on specific cancer
- PET when standard imaging studies are equivocal or nondiagnostic in determining recurrence or progression of disease

Surveillance
- CT may be indicated based on specific cancer

References
No references cited
Cervical Cancer

Advanced imaging is considered medically necessary for initial treatment strategy and subsequent treatment strategy of biopsy-proven cervical cancer.

Initial treatment strategy

- CT chest, abdomen and/or pelvis
  
  *Note: Chest radiograph is generally adequate for patients with stage I cervical cancer.*

- MRI pelvis for stage IB2 cervical cancer and prior to fertility-sparing surgery to assess local disease extent and proximity of tumor to the internal cervical os or as clinically indicated
  
  *Note: MRI pelvis is optional for stage II-IV cervical cancer and after total hysterectomy with incidentally found cervical cancer.*

- PET imaging for patients with a definitive diagnosis of stage IB2 or higher

Subsequent treatment strategy

- CT chest, abdomen, and pelvis

- MRI pelvis (optional)

- PET imaging in either of the following scenarios (preferred for stage IB2-IV cervical cancer):
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - Assessment of response to definitive chemoradiation when performed at least 12 weeks following therapy

Rationale

Ninety-five percent of cervical cancers are classified as either squamous cell carcinomas (the majority) or adenocarcinomas. 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.

INITIAL TREATMENT STRATEGY

Cervical cancer is staged using the FIGO system. MRI is most useful for determination of tumor location, size, invasion, and presence of nodal disease. A systematic review of 57 single-institution trials showed MRI was more accurate than CT for overall staging of cervical cancer. However, 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. MRI performed significantly better for visualization of the primary tumor and detection of parametrial invasion. In a second ACRIN 6651/GOG 183 Intergroup Study, MRI was superior to CT and clinical examination for evaluating uterine body involvement and measuring tumor size. 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. MRI may also play a role in radiation planning to aid with CT contouring.

CT and PET/CT are both useful modalities for evaluating for extraterine disease. The results of studies comparing PET/CT to CT alone for evaluation of nodal involvement are mixed, although PET/CT performs better in advanced disease. In the prospective ACRIN 6671/GOG 0233 trial, PET/CT did not show significantly higher specificity in detecting abdominal lymph node metastasis in advanced cervical cancer when compared to CT alone and showed only marginally higher sensitivity (P = .05). 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. 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. Pretreatment PET/CT may also play a role in radiation planning with respect to nodal volume. In a Phase III randomized trial, pretreatment PET imaging and detection of para-aortic lymph nodes decreased the need for extended-field concurrent
chemoradiation therapy, but did not improve overall survival, disease-free survival, or freedom from extrapelvic metastasis.15

SUBSEQUENT TREATMENT STRATEGY

PET imaging is preferred for patients with high risk stage IB2 or above disease treated with definitive 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.16 It is still unclear whether PET/CT affects overall management with resultant improvements in outcome. In the setting of recurrent disease, PET/CT has reported sensitivities ranging from 90.3%-92.7% and specificities ranging from 81%-100%.17

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%.18 19 Routine surveillance is not indicated in cervical cancer patients treated with radical hysterectomy, radiation, or concurrent chemotherapy, in accordance with National Comprehensive Cancer Network guidelines and Society of Gynecologic Oncology recommendations.20 21

References


Colorectal Cancer

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven colorectal cancer.

Initial treatment strategy

- CT chest, abdomen, and pelvis
- MRI pelvis for rectal cancer only
- PET imaging in ANY of the following scenarios:
  - Standard imaging (CT or ultrasound) suggests resectable metastatic disease and confirmation will impact the decision regarding curative surgery
  - Indeterminate lesions greater than 1 cm in diameter are identified on standard imaging and are not amenable to biopsy (or biopsy is considered high risk)

Radiation planning (Rectal cancer only)

- PET imaging for preoperative treatment only

Subsequent treatment strategy

- CT chest, abdomen, and pelvis
- MRI pelvis for rectal cancer only
- PET imaging in ANY of the following scenarios:
  - CT 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

Surveillance

- CT chest, abdomen, and pelvis for colon cancer with ANY of the following high-risk features:
  - Lymphatic or venous invasion
  - Lymph node involvement
  - Perineural invasion
  - Poorly differentiated tumor
  - T4 tumor
  - Associated with bowel obstruction
  - Close, indeterminate, or positive margins
  - Fewer than 12 nodes examined at surgery
  - Localized perforation

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.

INITIAL TREATMENT STRATEGY

Colorectal cancer is staged using the American Joint Committee on Cancer TNM system. CT is used for locoregional assessment of the primary tumor to assess degree of invasion and lymph node involvement as well as metastatic disease. 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. Results from this meta-analysis are consistent with the findings of several other studies.

The initial staging evaluation for rectal cancer requires the addition of a MRI pelvis or endoscopic rectal ultrasound (ERUS). 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. Although CT is commonly ordered preoperatively, it often does not impact management. A retrospective study of 180 patients reported that preoperative CT only changed management in 2% of patients. In a review of CT chest preoperative imaging, 9% were discovered to have indeterminate lung lesions with only 1% of the total population found to have metastatic cancer. Two studies found that PET/CT was not superior to CT for routine preoperative staging of colorectal cancer. 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. Another study comparing pretreatment CT to PET/CT in the setting of locally advanced rectal cancer receiving preoperative chemoradiation resulted in PET/CT detecting all 10 patients with confirmed metastatic disease while CT alone detected 9 of them.

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%. 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.

SUBSEQUENT TREATMENT STRATEGY

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. In the prospective MERCURY study, MRI assessment of tumor response and circumferential resection margin was correlated with positive survival outcomes. 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.

Chemotherapy may reduce the sensitivity of PET for the detection of liver metastases, likely due to metabolic inhibition caused by cytotoxic therapies. False negative rates of 87% have been reported for PET scans performed within 4 weeks of chemotherapy. 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, it is very unlikely that surgically curable recurrent disease will be identified. It is notable that almost half of elevated CEA 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. 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. 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 0.98, respectively.

SURVEILLANCE

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. For surveillance of colorectal cancer, AIM 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.
References


Esophageal and Gastroesophageal Junction Cancers

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven esophageal and gastroesophageal junction cancer.

Initial treatment strategy
- CT chest and abdomen
- CT pelvis as clinically indicated
- PET imaging when standard imaging studies are equivocal or nondiagnostic for metastatic disease

Radiation planning
- PET imaging for preoperative or definitive treatment only

Subsequent treatment strategy
- CT chest and abdomen
- CT pelvis as clinically indicated
- PET imaging in EITHER of the following scenarios:
  - Assessment of response to chemoradiation (as definitive treatment or prior to surgery) when performed at least 5 weeks after completion of therapy
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease

Surveillance
- CT chest and abdomen

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. 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.

INITIAL TREATMENT STRATEGY
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%. Nonetheless, EUS is still considered superior to CT, MRI, and PET for locoregional staging.

CT is being replaced as the sole modality for detection of metastatic disease. 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. 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.
studies, PET/CT resulted in avoidance of futile surgery in up to 17% of patients and change in management of 38.2% of cases.\textsuperscript{7}

**SUBSEQUENT TREATMENT STRATEGY**

The benefit of PET/CT over standard CT following neoadjuvant therapy has not been clearly shown. Both modalities allow for detection of new metastatic disease as well as for assessment of tumor response. PET/CT has been used to assess metabolic response, which has been suggested as a surrogate marker for prognosis. In the largest of these studies, the prospective MUNICON (Metabolic response evalUatIon for Individualisation of neoadjuvant Chemotherapy in oesOpHageal and oesophagoGastric adeNocarcinoma) 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).\textsuperscript{8} 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.\textsuperscript{9} Several studies have demonstrated that PET/CT has poor accuracy in determining local tumor response, especially at the microscopic level. The National Comprehensive Cancer Network (NCCN) recommends that PET/CT should not be the sole determinant for selection of patients after neoadjuvant chemoradiation therapy and categorizes PET/CT as a Level 2B recommendation.\textsuperscript{10} There is, however, general agreement that PET/CT is useful in detecting metastases prior to potentially curative surgery, and this remains the primary indication for its use.\textsuperscript{11-13}

**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 for Esophageal and Esophagogastric Junction Cancers, surveillance imaging is appropriate for stage T1b or higher disease.\textsuperscript{10}

**References**

Gastric Cancer

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven gastric cancer.

Initial treatment strategy

- CT chest, abdomen, and pelvis
- PET for tumors initially stage IB or higher when standard imaging does not clearly demonstrate metastatic disease and the patient is a candidate for curative surgery

Radiation planning

- PET for preoperative or definitive treatment only

Subsequent treatment strategy

- CT chest, abdomen, and pelvis
- PET in EITHER of the following scenarios:
  - To determine resectability of residual disease following completion of primary (neoadjuvant) treatment, when follow-up evaluation with standard modalities does not demonstrate metastatic disease
  - Evaluation of suspected recurrence based on signs or symptoms when standard modalities are equivocal for recurrent disease

Surveillance

- CT chest, abdomen, and pelvis as clinically 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.

INITIAL TREATMENT STRATEGY

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 63% and 67%, respectively.¹ 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%.² 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.³

The accuracy of CT for assessing primary tumor is only 50%-70% and for nodal staging 50%-64%⁴.⁵ CT performs better with regard to metastatic disease, with an accuracy of 79%-84%.⁶

In general, PET is less useful for staging of gastric cancer than for other tumor types. Compared to CT, FDG-PET has significantly lower sensitivity in the detection of local lymph node involvement (78% vs 56%), but with higher specificity (62% vs. 92%).⁷ Moreover, the use of PET has not led to improved survival in patients with detectable tumors vs those with nondetectable tumors (P = .85).⁸ 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. However, the decision to proceed to surgery was not significantly impacted by PET/CT. The major advantage conferred by PET is improved specificity over CT for the detection of distant metastases. 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.

SUBSEQUENT TREATMENT STRATEGY

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. In another study, survival of patients without FDG-avid disease was not significantly different from FDG-avid non-responders. 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.

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. In a review of 5 articles that included 810 patients, intense surveillance with CT imaging did not show an improvement in survival. Based on the National Comprehensive Cancer Network Guidelines for Gastric Cancer, surveillance imaging for patients with stage II or greater gastric cancer is indicated for up to 5 years following completion of therapy.

References


Germ Cell Tumors: Testis and Ovary

This section primarily addresses imaging of seminomatous and nonseminomatous germ cell tumors of the testis. Imaging recommendations for ovarian germ cell tumors are based on available society guidelines and extrapolation of testicular germ cell tumor data. Specific imaging considerations are addressed below.

Advanced imaging is indicated for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven germ cell tumors of the ovary and testis.

Initial treatment strategy

- Seminoma
  - CT abdomen and pelvis
  - CT chest for positive abdominal CT or abnormal chest radiographs, or as clinically indicated
  - MRI brain if clinically indicated or high risk for metastases (beta-hCG > 5000 IU/L or extensive lungs metastases)

- Nonseminoma
  - CT chest, abdomen, and pelvis
  - MRI brain when clinically indicated or high risk for metastases (beta-hCG > 5000 IU/L, AFP > 10000 ng/mL, extensive lung metastases, nonpulmonary visceral metastases, or choriocarcinoma)

- Malignant ovarian germ cell cancer
  - CT chest, abdomen, and pelvis
  - MRI abdomen and pelvis as clinically indicated

- PET imaging in the following scenario (all tumor types):
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease

Subsequent treatment strategy

*Note: For nonseminomatous germ cell tumors, a residual mass greater than 1 cm should be surgically resected.*

- Seminoma
  - CT chest, abdomen, and pelvis for IIA, IIB, IIC, III after chemotherapy, or as clinically indicated

- Nonseminoma
  - CT chest, abdomen, and pelvis for IIA, IIB, IIC, III after chemotherapy, or as clinically indicated

- Malignant ovarian germ cell cancer
  - CT chest, abdomen, and pelvis, or as clinically indicated

- MRI abdomen and pelvis as clinically indicated

- PET imaging in **EITHER** of the following scenarios (all tumor types):
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
Residual mass greater than 3 cm and with normal tumor markers

Surveillance

- Seminoma
  - Chest radiographs
  - CT abdomen and/or pelvis

- Nonseminoma
  - Chest radiographs
  - CT abdomen and/or pelvis

- Malignant ovarian germ cell cancer
  - CT chest, abdomen, and pelvis unless tumor markers are normal at initial presentation, or as clinically 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

Testicular cancer is the most common cancer in men between ages 15 and 35.1 Germ cell tumors are the most common type of testicular cancer and are broadly divided into seminomatous and nonseminomatus. Risk factors include cryptorchidism, family history, and ethnicity. The most common presentation is testicular pain or a palpable mass.

Limited data is available for the initial work up of patients with ovarian germ cell tumors, but due to their histologic similarity, recommendations are extrapolated from testicular germ cell tumor data.

INITIAL TREATMENT STRATEGY

Germ cell tumors 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.2 In direct comparisons, MRI has not shown an advantage over CT for accuracy of staging.3,4 In a prospective study, the accuracy of PET for stage I and II nonseminomatous germ cell tumors (NSGCT) was 83%, compared to 71% accuracy of CT. 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 of testicular cancer.5 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.6

SUBSEQUENT TREATMENT STRATEGY

PET/CT has higher positive and negative predictive values for identifying residual viable tumors compared to CT. 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%).7

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 tumor from radiation necrosis and fibrosis. 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%).8

AIM guidelines are in accordance with the National Comprehensive Cancer Network (NCCN) Guidelines for Testicular Cancer.9

SURVEILLANCE

Seminomas tend to recur within the first 14 months and nonseminomas within the first 2 years.10 AIM guidelines are in accordance with the NCCN Guidelines for Testicular Cancer, NCCN Guidelines for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, and European Society for Medical Oncology guidelines.9,11,12

References


Head and Neck Cancer

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven head and neck cancer.

Initial treatment strategy

- CT primary site (if outside the neck, also include CT neck)
- CT chest for advanced disease and for lung cancer screening in smokers or as clinically indicated
- CT abdomen and pelvis for occult primary with Level IV or lower V lymph nodes if PET not performed or as clinically indicated
- MRI primary site preferred for nasopharyngeal carcinoma
- PET imaging in ANY of the following scenarios:
  - Evaluation of stage III and IV cancers (tumors greater than 4 cm in size, or any evidence of regional node involvement) 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 epithelial tumor) when CT or MRI evaluation of the neck has not detected a primary site of tumor

  Note: PET is not generally indicated for initial evaluation of lip and salivary gland cancers, regardless of stage.

Radiation planning

- PET for preoperative or definitive treatment only

  Note: PET imaging is not indicated for adjuvant radiation therapy planning when all known disease has been removed.

Subsequent treatment strategy

- CT or MRI primary site and neck to assess response to neoadjuvant treatment or after concurrent chemoradiotherapy
- PET in ANY of the following scenarios:
  - Evaluation of disease following clinical response to treatment, no sooner than 12 weeks after completion of therapy
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - Follow up of an equivocal post-treatment PET scan, no sooner than 4 weeks after the study, to determine need for further intervention such as neck dissection

Surveillance

- CT chest as clinically indicated for patients with smoking history
- CT or MRI primary site and neck within 6 months of completed treatment for baseline 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).
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.

INITIAL TREATMENT STRATEGY

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. 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, but up to 67% of pathologic lymph nodes may still be missed. MRI may be indicated as an adjunct to CT, particularly in the management of nasopharyngeal cancers. In general, MRI is not as sensitive as CT for evaluation of nodal metastases although advanced techniques are improving the ability to differentiate benign from malignant adenopathy. 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%.

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. In a meta-analysis of 8 studies, sensitivity and specificity of PET/PET-CT for detecting distant metastatic disease were 85% and 96% compared with conventional anatomic imaging, 44% and 96%, respectively. The accuracy of PET for evaluation of patients with 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.

SUBSEQUENT TREATMENT STRATEGY

A prospective randomized trial by Mehnana et al. found that PET/CT performed 12 weeks after chemoradiation therapy for assessment of treatment response for patients with N2/3 disease resulted in substantially fewer neck dissections with no adverse impact on survival. 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. A negative PET/CT corresponds with a 90% chance of disease eradication. These findings were corroborated by 2 additional retrospective studies.

SURVEILLANCE

Most recurrences are discovered by patients and not by serial imaging or physical exam. AIM guidelines are in accordance with NCCN Guidelines for Head and Neck Cancers.

References


Kidney Cancer/Renal Cell Carcinoma

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven kidney cancer.

Initial treatment strategy

- CT chest when clinically indicated
- CT abdomen and/or pelvis
- MRI brain when clinically indicated
- PET imaging to evaluate extent of disease when curative resection of primary tumor or limited metastatic disease is planned and standard imaging is equivocal for additional sites of disease

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

Subsequent treatment strategy

- CT abdomen and/or pelvis
- PET imaging when **ALL** of the following are true:
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - Biopsy cannot be performed
  - Tumor has been shown to be PET avid (if a prior PET scan has been performed)

Surveillance

- CT chest (radiographs often sufficient)
- CT abdomen
- CT pelvis as clinically 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 the 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).

INITIAL TREATMENT STRATEGY

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. In another prospective study, accuracy of MRI was 78%-87%, and the accuracy of CT was 80%-83%. 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.

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. Current evidence suggests that imaging of the pelvis is of low yield and does not affect overall management. For chest imaging, radiography is preferred, although CT is more sensitive in patients with symptoms, advanced-stage disease, anemia, or thrombocytopenia.
AIM guidelines are in accordance with recommendations from the National Comprehensive Cancer Network Guidelines for Kidney Cancer, American College of Radiology ACR Appropriateness Criteria® for Renal Cell Carcinoma Staging, and European Association of Urology.10,11

SUBSEQUENT TREATMENT STRATEGY

A pooled analysis of 15 studies found PET/CT to have combined sensitivity of 86% and specificity of 88%. Comparison across studies found similar sensitivity but markedly higher specificity with PET imaging.12

SURVEILLANCE

Survveillance of asymptomatic renal cell cancer generally should not go beyond 5 years. All recommendations are level of evidence category 2B as designated by the National Comprehensive Cancer Network.10

References

Lung Cancer – Non-Small Cell

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven non-small cell lung cancer.

Initial treatment strategy

- CT chest and abdomen
- MRI brain
- MRI chest for stage IIIB (T3 invasion N0) and stage IIIA (T4 extension N0-1, T3 N1, T4N0-1) with superior sulcus lesions abutting the spine or subclavian vessels
- MRI spine as clinically indicated
- PET imaging in **EITHER** of the following scenarios:
  - Diagnosis in patients with a strong clinical or radiographic suspicion of non-small cell lung cancer
  - Evaluation of the extent of disease following biopsy confirmation of non-small cell lung cancer

Radiation planning

- PET imaging for preoperative or definitive treatment only

Subsequent treatment strategy

- CT chest and abdomen
- MRI brain as clinically indicated for evaluation of suspected or known brain metastases
- MRI chest as clinically indicated for reevaluation of superior sulcus lesions abutting the spine or subclavian vessels
- MRI spine as clinically indicated for evaluation of suspected or known spinal metastases
- PET imaging in **ANY** of the following scenarios:
  - 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
  - Evaluation of signs or symptoms of disease when CT or MRI has not clearly demonstrated recurrence or progression
  - Differentiation of tumor from benign conditions (atelectasis, consolidation, or radiation fibrosis) when CT clearly delineates the abnormal findings

Surveillance

- CT chest

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.

INITIAL TREATMENT STRATEGY

Non-small cell lung cancer is staged using the American Joint Committee on Cancer TNM system.

CT accurately evaluates the primary tumor and detects metastatic disease but is less accurate in identifying mediastinal lymphadenopathy.\textsuperscript{1,2} 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.\textsuperscript{3,4} In one prospective trial, PET/CT prevented unnecessary surgery in 17% of patients.\textsuperscript{5}

An added benefit of PET/CT is detection of distant metastases, although its superiority over conventional CT has not been definitively shown. In a retrospective analysis of 217 patients, PET/CT showed a sensitivity and specificity of 92% and 98%, respectively, for the detection of malignant extrapulmonary lesions.\textsuperscript{6} 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.\textsuperscript{7} 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.\textsuperscript{8}

Asymptomatic metastatic central nervous system disease is seen in as many as 12% of patients, and brain imaging should always be performed for stage II or higher.\textsuperscript{9} MRI chest with contrast should be considered to assess the spine/thoracic inlet for superior sulcus lesions abutting the spine and/or subclavian vessels in patients with stage IIB (T3 invasion N0) and stage IIIA (T4 extension N0-1; T3 N1; T4N0-1).

SUBSEQUENT TREATMENT STRATEGY

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.\textsuperscript{10} 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.\textsuperscript{11,12} 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, \(P = .89\)).\textsuperscript{13} PET/CT may remain FDG-avid up until 2 years after treatment.\textsuperscript{14} Any suspected recurrence should be biopsied for pathologic confirmation.

SURVEILLANCE

Surveillance imaging should include CT chest every 6 months for 2 to 3 years followed by annual low-dose 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.\textsuperscript{15}

References


Lung Cancer – Small Cell

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven small cell lung cancer.

Initial treatment strategy

- CT chest and abdomen
- MRI brain
- PET imaging prior to definitive therapy when standard imaging suggests limited stage disease

Radiation planning

- PET imaging prior to initiation of radiation therapy

Subsequent treatment strategy

- CT chest and abdomen
- MRI brain prior to prophylactic cranial irradiation

Surveillance

- CT chest and abdomen as clinically indicated
- MRI brain every 3 to 4 months for 1 to 2 years when prophylactic cranial irradiation not given or as clinically 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 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.

INITIAL TREATMENT STRATEGY

Asymptomatic metastatic central nervous system disease is seen in up to 15% of patients and MRI brain with contrast is indicated regardless of stage.1,2 If CT and MRI are negative for metastatic disease then a PET/CT is also indicated. 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 has a high sensitivity for detecting lymph node involvement and distant metastases 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.3 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 planning and upstaging to extensive stage small cell lung cancer with PET staging.4 Another review found an 84% concordance between PET and CT for staging; however, 19% were upstaged to extensive stage small cell lung cancer and 11% were downstaged to limited stage small cell lung cancer when PET was performed.5 Ruben et al. published data from a second review of 22 studies showing PET sensitivity approaching 100% and specificity exceeding 90%. PET altered the treatment plan in at least 26% of cases, with 6% deemed appropriate for curative treatment and 9% in which radiation was deemed no longer appropriate.6 In studies where PET/CT was used for staging and targetting of lymph nodes for radiation, the local recurrence rates have been reported to be less than 3%.6,7

SUBSEQUENT TREATMENT STRATEGY

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.2
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.\(^8\)

References

Lymphoma – Hodgkin

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven Hodgkin lymphoma.

Initial treatment strategy
- CT chest, abdomen, and pelvis
- CT neck when radiation of neck planned or PET positive disease
- PET imaging as an adjunct to CT

Radiation planning
- PET imaging for definitive or consolidative treatment

Subsequent treatment strategy
- CT neck, chest, abdomen, and pelvis
- PET imaging in **ANY** of the following scenarios:
  - Evaluation of response following 2-4 cycles of treatment
  - Post-treatment evaluation at least 3 weeks following completion of all cycles of chemotherapy or 12 weeks following completion of radiation therapy
  - Evaluation of suspected recurrence or progression of disease based on standard imaging or objective signs/symptoms

Surveillance
- CT neck, chest, abdomen, and pelvis with contrast as clinically indicated

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.

INITIAL TREATMENT STRATEGY
Hodgkin lymphoma is staged using the Lugano classification system. Response to treatment uses the 5-point Deauville criteria for assessment of metabolic response. PET/CT can result in changing of clinical stage in 20% of patients. In the RATHL (Response-Adapted Therapy in Advanced Hodgkin Lymphoma) study, PET/CT resulted in upstaging 14% and downstaging 6%. 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.

SUBSEQUENT TREATMENT STRATEGY
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. 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). Cercil et al. found 3-year event-free survival was 53.4% for PET positive and 90.5% for PET negative (P < 0.001). 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.

SURVEILLANCE
There is limited data to support routine surveillance 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%; \( P = .01 \)).

Although PET/CT negative patients had a high likelihood of being disease free, PET/CT also produced false positive rates as high as 20%. A systematic review found no retrospective or prospective data demonstrating a survival advantage associated with the use of surveillance imaging for patients with Hodgkin lymphoma who achieved remission after first-line therapy.

References
Lymphoma – Non-Hodgkin

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven chronic lymphocytic leukemia/small lymphocytic lymphoma and non-Hodgkin lymphomas.

**Initial treatment strategy**

- Chronic lymphocytic leukemia or small lymphocytic lymphoma
  - CT chest, abdomen, and pelvis with contrast
  - PET imaging for suspicion of Richter’s transformation when PET is utilized to direct biopsy
- Indolent non-Hodgkin lymphoma
  - CT neck
  - CT chest, abdomen, and pelvis
  - PET imaging 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
- Intermediate and high grade non-Hodgkin lymphoma
  - CT chest, abdomen, and pelvis
  - PET imaging in ANY of the following scenarios:
    - Initial evaluation of suspected lymphoma when lymph nodes are not amenable to biopsy
    - As an adjunct to CT for initial staging

**Radiation planning**

- PET imaging prior to definitive or consolidative treatment for indolent, aggressive, and highly-aggressive non-Hodgkin lymphoma

**Subsequent treatment strategy**

- Chronic lymphocytic leukemia or small lymphocytic lymphoma
  - CT based on symptoms or to evaluate bulky disease
  - PET for suspicion of Richter’s transformation when PET is utilized to direct biopsy

*Note: Suspicion of Richter’s transformation is most commonly based on a presentation of rapidly enlarging lymph nodes, onset of B symptoms, hepatosplenomegaly, and elevated serum lactate dehydrogenase levels.*
Indolent non-Hodgkin lymphoma
- CT chest, abdomen, and pelvis
- PET imaging in ANY of the following scenarios:
  - Post-treatment response evaluation, when initial PET scan has 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

Aggressive and highly aggressive non-Hodgkin lymphoma
- CT chest, abdomen, and pelvis and/or CT of affected area
- PET imaging in ANY of the following scenarios:
  - Evaluation of response following 2 to 4 cycles of treatment for stage III and IV disease
  - Post-treatment evaluation
  - Evaluation of suspected recurrence or progression of disease based on standard imaging or objective signs/symptoms

**Surveillance**

- Chronic lymphocytic leukemia or small lymphocytic lymphoma
  - CT chest, abdomen, and pelvis as clinically indicated based on symptoms or to evaluate bulky disease

- Indolent non-Hodgkin lymphoma
  - CT chest, abdomen, and pelvis as clinically indicated (not to exceed 2 years following completion of treatment)

- Aggressive and highly aggressive non-Hodgkin lymphoma
  - CT chest, abdomen, and pelvis as clinically indicated (not to exceed 2 years following completion of treatment)

*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**

Non-Hodgkin lymphoma is the seventh most common cancer in both men and women. Lymphomas are divided into Hodgkin and non-Hodgkin lymphomas. 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 non-Hodgkin lymphomas, symptoms resulting from local tumor growth or systemic metabolic derangements.

**INITIAL TREATMENT STRATEGY**

Lymphoma is staged using the Lugano classification system. The 5-point Deauville criteria are used for assessment of treatment response. For chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), CT chest, abdomen, and pelvis is not indicated. PET/CT is most accurate for staging and interim assessment of lymphomas with high FDG avidity like diffuse large B-cell lymphoma, follicular non-Hodgkin lymphoma, and nodal marginal zone lymphoma, but may be less accurate for CLL/SLL, marginal zone lymphoma, and hairy cell leukemia.

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For staging of indolent non-Hodgkin lymphomas, 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. 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.

For aggressive and highly aggressive non-Hodgkin lymphomas, 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 non-Hodgkin lymphoma, 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.

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). Change in treatment has been reported in as many as 9% of cases with the addition of PET/CT scan.

**SUBSEQUENT TREATMENT STRATEGY**

In general, advanced imaging is not necessary for routine monitoring of treatment response or progression of chronic lymphocytic leukemia or small lymphocytic lymphoma. 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.

For indolent non-Hodgkin lymphomas, CT or PET/CT is indicated; 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). In the analysis of the PRIMA trial, patients with remaining PET-positive disease had a significantly inferior progression-free survival at 42 months compared with those who became PET negative (33% vs 71%, P < .001).

Multiple studies have confirmed that PET positivity correlates with active tumor. However, there is insufficient evidence that post-treatment PET/CT improves outcomes to recommend its routine use. 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). 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).

**SURVEILLANCE**

For CLL/SLL, routine use of CT is not indicated. Management changes resulting from CT imaging only occurred in 1% of patients. There is limited data to support routine surveillance imaging in indolent non-Hodgkin lymphoma. A retrospective study assessing CT for patients who had achieved complete remission found that only 4% of relapses were detected on surveillance imaging. In a study looking at the use of PET/CT surveillance, relapse was found in 30% of asymptomatic patients. Sixteen percent of patients had no evidence of relapse by CT imaging. The value of PET for early detection of relapse is still under active investigation.

There is limited data to support routine surveillance imaging in aggressive or highly aggressive non-Hodgkin lymphoma. A retrospective study assessing CT in patients who had achieved complete remission found that only 6% of relapses were detected on surveillance imaging. In a prospective trial including patients with indolent, intermediate, and aggressive non-Hodgkin lymphoma, PET/CT surveillance detected relapses in 27% of patients. In a recent population-based study, PET/CT only detected 2% of asymptomatic relapse. Cohen et al. found that surveillance imaging did not detect most relapses prior to clinical signs and symptoms, and the imaging findings did not result in improved survival.

**References**

Melanoma – Cutaneous

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven malignant melanoma.

Initial treatment strategy

- CT neck, chest, abdomen, and pelvis (generally indicated for stage III and above)
- MRI brain for stage IIIC and above or as clinically indicated
- PET imaging in ANY of the following scenarios:
  - To determine the extent of involvement in stage III and IV disease when used in place of CT chest, abdomen, and pelvis
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - When the primary site is unknown and standard imaging is negative

Radiation planning

- PET imaging for definitive treatment only

Subsequent treatment strategy

- CT neck, chest, abdomen, and pelvis for patients not receiving definitive surgical treatment as clinically appropriate
- PET imaging in EITHER of the following scenarios:
  - Evaluation of objective signs or symptoms of metastatic disease when CT or MRI has not clearly demonstrated recurrence or progression
  - To assess treatment response in unresectable stage III and IV disease when used in place of CT chest, abdomen, and pelvis

Surveillance

- CT chest, abdomen, and pelvis (generally indicated for stage IIB or higher)

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 cell 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.

INITIAL TREATMENT STRATEGY

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. 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. 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%.
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.5

SUBSEQUENT TREATMENT STRATEGY

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 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%.

The National Comprehensive Cancer Network considers imaging for stage IIB-IV (no evidence of disease) melanoma a level 2B recommendation.10 Surveillance imaging of asymptomatic patients should not continue beyond 3 to 5 years due to the risk of radiation exposure and based on expected patterns of recurrence.11

References

Melanoma – Mucosal

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven mucosal melanoma.

Initial treatment strategy
- CT or MRI primary site; include neck as clinically indicated
- CT chest, abdomen, and pelvis as indicated
- MRI brain should be considered
- PET/CT

Radiation planning
- PET imaging for preoperative or definitive treatment only

Subsequent treatment strategy
- CT or MRI primary site; include neck as clinically indicated
- CT chest, abdomen, and pelvis as clinically indicated
- PET imaging in ANY of the following scenarios:
  - Evaluation of disease following clinical response to treatment, no sooner than 12 weeks after completion of therapy
  - Evaluation of signs or symptoms of metastatic disease when standard imaging studies are equivocal or nondiagnostic for metastatic disease

Surveillance
- CT chest, abdomen, and pelvis as clinically indicated
- CT or MRI primary site and neck with contrast within 6 months of completed treatment for baseline 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).

Rationale
Mucosal melanoma is an aggressive type of noncutaneous melanoma arising from melanocytes in mucosal cells. 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 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.

INITIAL TREATMENT STRATEGY
Mucosal melanoma is staged using the American Joint Committee on Cancer TNM system. Staging studies for tumors arising in the head and neck should include CT or MRI to determine extent of the primary tumor, resectability, and lymph node involvement. Chest and brain imaging should also be considered. Evidence to support the use of PET is limited, but given the behavior of these tumors, AIM’s panel of external experts has recommended in favor of its use.

Mucosal melanomas arising outside of the head and neck region are rare, but recommendations may be extrapolated from those for head and neck tumors and cutaneous melanomas.

SUBSEQUENT TREATMENT STRATEGY
In most cases, conventional imaging with CT or MRI is adequate for assessment of treatment response and for subsequent strategy planning. If radiation is planned either for preoperative or definitive therapy, PET may be used for radiation planning. Evaluation of response should be done no sooner than 12 weeks after completion of therapy.

SURVEILLANCE

The follow-up protocol for mucosal melanoma is based on recommendations for squamous cell carcinoma of the head and neck and cutaneous melanomas. The National Comprehensive Cancer Network (NCCN) Guidelines for Head and Neck Cancer include follow-up imaging of the primary and neck within 6 months of definitive treatment as a category 2B recommendation.\(^1\) The NCCN Guidelines for Melanoma consider surveillance imaging a level 2B recommendation.\(^2\)

References

Merkel Cell Carcinoma

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven Merkel cell carcinoma.

**Initial treatment strategy**
- CT neck, chest, abdomen, and pelvis
- MRI brain as clinically indicated
- PET imaging as clinically indicated

**Subsequent treatment strategy**
- CT chest, abdomen, and pelvis for biopsy-proven progressive, persistent, or recurrent disease
- PET imaging as clinically indicated

**Surveillance**
- CT neck, chest, abdomen, and pelvis as clinically indicated or in high-risk patients

*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 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.

**INITIAL AND SUBSEQUENT TREATMENT STRATEGIES**

Merkel cell carcinoma is staged using the American Joint Committee on Cancer TNM system. Merkel cell carcinoma is a highly aggressive cancer and up to 8% of patients will present with metastases. 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. A meta-analysis of 6 studies (N = 92 patients) showed PET had a sensitivity of 90% (95% CI, 80%-96%) and specificity of 98%. Asymptomatic brain metastases are fairly rare and routine use of MRI is not recommended.

**SURVEILLANCE**

Most recurrences of Merkel cell carcinoma 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.

**References**

Multiple Myeloma

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven solitary plasmacytoma and multiple myeloma.

Initial treatment strategy

- Whole body or skeletal MRI (bone marrow blood supply) when no lytic bone lesions are identified on whole body radiography
  
  \textit{Note}: A dedicated MRI should be used for characterization of equivocal bone lesions seen on whole body radiography.

- PET imaging to differentiate smoldering myeloma from active myeloma when skeletal survey and/or whole body MRI is negative for bone involvement

Subsequent treatment strategy

- Dedicated MRI as indicated for evaluation of focal bone lesions

- PET imaging when routine evaluation with laboratory findings or bone survey suggests recurrence or progression of disease

Surveillance

- MRI as clinically indicated for focused bone evaluation

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.

INITIAL TREATMENT STRATEGY

The International Staging System and the Durie-Salmon Staging System are both used in staging. Recent advances in low dose CT technology have improved detection rates of lytic bone lesions with a radiation dose comparable to that of a skeletal survey.\(^1\)\(^2\) In a prospective study comparing whole body low-dose CT and whole body X-ray, CT performed markedly better and resulted in a change in management in 18% of patients.\(^3\) In a recent large retrospective study, whole body low-dose CT detected 25% more lytic lesions than conventional bone radiography.\(^4\) Currently the National Comprehensive Cancer Network (NCCN) Guidelines for Multiple Myeloma recommend either a skeletal survey or whole body low-dose CT.\(^5\)

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.\(^6\) In patients thought to have a solitary plasmacytoma, MRI detected additional disease and led to a change of management in 25% of those studied.\(^7\) In a similar study of indolent myeloma, MRI detected 28% more lesions.\(^8\)

While MRI is superior for detection of bone disease, PET/CT may be more sensitive for extramedullary involvement. 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.\(^9\) However, a meta-analysis of 5 studies comparing PET to MRI did not show significant clinical benefit of PET imaging.\(^10\)

SUBSEQUENT TREATMENT STRATEGY

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.\(^11\) 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.\textsuperscript{12} PET imaging, however, does provide early assessment of response as well as prognostic information for lesions smaller than 5 mm.\textsuperscript{13} 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.\textsuperscript{14} 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)\textsuperscript{15} whereas normalization of MRI findings was not found to correlate with improved outcome measures. In a study by Zammagni et al., patients post autologous stem cell transplant with FDG-avid disease had a lower 4-year estimated progression-free survival and overall survival when compared to the PET/CT negative cohorts, 47\% and 79\% (P = .02) versus 32\% and 66\% (P = .02), respectively.\textsuperscript{16}

SURVEILLANCE

Routine follow-up evaluation includes quantitative immunoglobulins and M protein (serum and urine), complete blood count (CBC), kidney function, calcium levels, and bone survey. MRI and PET/CT are not indicated in the absence of signs or symptoms of progressive disease.

AIM guidelines are in accordance with the NCCN Guidelines for Multiple Myeloma.\textsuperscript{5}

References


Neuroendocrine Tumors

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven neuroendocrine cancer.

Initial treatment strategy

- CT head, chest, abdomen, and pelvis
- MRI brain for high-risk patients
- PET imaging when standard imaging studies are equivocal or nondiagnostic for metastatic disease

Subsequent treatment strategy

- CT chest, abdomen, and pelvis with contrast
- PET imaging as clinically indicated

Surveillance

- CT chest, abdomen, and pelvis with contrast

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

Neuroendocrine cancers are a rare type of cancer in which tumors arise from neuroendocrine cells, but may also 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.

INITIAL TREATMENT STRATEGY

Neuroendocrine cancer is staged using the American Joint Committee on Cancer TNM system. As an adjunct to TNM staging, the World Health Organization classification scheme also takes into account proliferation rate (Ki-67) in grading of tumors. Carcinoid is a highly vascular tumor and multiphasic imaging should be used to improve detection.\(^1\) MRI is more sensitive than CT for detection of liver metastases; however, one study found no statistically significant difference between the 2 modalities for this indication.\(^2\) Smaller lesions, especially in the small bowel and appendix, may be difficult to visualize with either modality. Somatostatin receptor-based imaging should also be considered in well-differentiated neuroendocrine tumors. MRI brain with contrast is indicated for poorly differentiated tumors arising from the thorax.

FDG-PET for staging of poorly differentiated neuroendocrine cancer 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.\(^3\)\(^5\)

SUBSEQUENT TREATMENT STRATEGY

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, abdomen, and pelvis with or without contrast is sufficient.

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.

References


Ovarian Cancer (Epithelial)

Advanced imaging is considered medically necessary for initial treatment strategy and subsequent treatment strategy of biopsy-proven ovarian cancer.

**Initial treatment strategy**
- CT chest, abdomen, and pelvis
- MRI abdomen and pelvis as clinically indicated
- PET imaging for evaluation of indeterminate lesions detected by other imaging modalities

**Subsequent treatment strategy**
- CT chest, abdomen, and pelvis
- MRI abdomen and pelvis as clinically indicated
- PET imaging in the following scenario:
  - Evaluation of objective evidence of recurrent disease (such as rising tumor markers or increasing ascites) when CT or MRI does not clearly demonstrate recurrence or progression

*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 fourth most common cause of cancer-related death 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 infertility, endometriosis, polycystic ovarian syndrome, 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.

**INITIAL TREATMENT STRATEGY**

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. 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. 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.

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. Other studies have shown sensitivity and specificity of PET/CT as high as 100% and 85%, respectively. A small prospective trial (N = 50) found PET/CT had a 69% correlation with final pathologic staging while the correlation for CT was 53%. CT imaging missed 11% of patients with distant metastasis in the liver, pleura, mediastinum, and in left supraclavicular lymph nodes. In a review of 18 studies, PET was superior to both CT and MRI at detecting involved lymph nodes. PET had a sensitivity of 73.2% and specificity of 96.7%.

Conversely, a small prospective trial showed that PET/CT was not superior to CT for the detection of intra-abdominal disease spread, though it was more effective for the detection of extra-abdominal disease.

**SUBSEQUENT TREATMENT STRATEGY**

If treated with neoadjuvant therapy, reassessment should be performed using the same imaging modality that was used in the original assessment. CT chest, abdomen, and pelvis are preferred. In patients with suspected recurrence, PET may be more accurate at detecting recurrence than CT; in one prospective, multicenter cohort study, PET/CT detected additional sites of disease in 68% of patients compared to conventional imaging and led to a change in management in 60%. A second study in patients with suspected recurrence showed that PET detected recurrence in 66% of patients.
while CT only detected 50%. The sensitivities of CT and PET/CT for diagnosing recurrence were 81% and 97%, respectively, and the specificity was 90% for both modalities. These findings have been validated in 2 large meta-analyses.11, 12

SURVEILLANCE

Based on a review of the Surveillance Epidemiology & End Results database, up to 95% of recurrences are detected by physician exam or rising cancer antigen (CA) 125. Studies using radiographic surveillance for ovarian cancer have reported the sensitivity and specificity of CT 40%-93% and 50%-98%, respectively. 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. 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. 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. Limited data is available for MRI and PET/CT in surveillance of asymptomatic patients. The Society of Gynecologic Oncology and National Comprehensive Cancer Network Guidelines for Ovarian Cancer Including Fallopian Tube and Primary Peritoneal Cancer do not recommend routine use of surveillance imaging.16, 18

References


Pancreatic Cancer

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

Advanced imaging is considered medically necessary for initial treatment strategy, radiation planning, subsequent treatment strategy, and surveillance of biopsy-proven pancreatic cancer.

Initial treatment strategy

- CT chest, abdomen, and pelvis
- MRI abdomen in ANY of the following scenarios:
  - CT contraindicated or expected to be suboptimal
  - Characterization of CT-indeterminate liver lesions
  - Need to further establish resectability in borderline resectable patients, when CT imaging provides insufficient information
- PET imaging for detection of extra-pancreatic disease in patients who are candidates for resection 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

Radiation planning

- PET imaging for preoperative or definitive treatment in patients without distant metastasis

Subsequent treatment strategy

- CT chest
- CT abdomen using pancreatic protocol
- PET imaging to detect recurrent or progressive disease when standard imaging is equivocal or nondiagnostic for metastatic disease

Surveillance

- CT abdomen

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.

INITIAL TREATMENT STRATEGY

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. 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. 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.

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. 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. A 2017 meta-analysis of 16 articles concluded that high pretreatment PET standardized uptake values predicted poorer event-free survival and overall survival.

SUBSEQUENT TREATMENT STRATEGY

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. 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).

SURVEILLANCE

A study using the Surveillance, Epidemiology, and End Results (SEER)-Medicare database showed no survival benefit to annual CT surveillance. National Comprehensive Cancer Network Guidelines for Pancreatic Adenocarcinoma categorize CT abdomen with contrast as level 2B based on consensus.

References

Paraneoplastic Syndrome

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

**Initial treatment strategy**
- CT neck, chest, abdomen and pelvis
- MRI brain
- PET or PET/CT

**Surveillance**
- CT neck, chest, abdomen and pelvis

**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. 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.

**INITIAL TREATMENT STRATEGY**

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. Another retrospective study from the same institution found that PET/CT detected an additional 18% of cancers in patients with CT-negative paraneoplastic disease. 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.

**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.

**References**

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 initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven vaginal, vulvar, or penile cancer.

Initial treatment strategy

- CT chest, abdomen, and pelvis
- MRI pelvis for vaginal or vulvar cancer
- PET imaging in EITHER of the following scenarios:
  - Standard imaging studies are equivocal or 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

Subsequent treatment strategy

- CT chest, abdomen, and pelvis
- MRI pelvis for vaginal or vulvar cancer
- PET imaging in EITHER of the following scenarios:
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - Restaging of local recurrence when pelvic exenteration surgery is planned

Surveillance

- CT chest, abdomen, and pelvis for penile cancer

Rationale

Vaginal, vulvar, and penile cancers are relatively uncommon, accounting for less than 1% of all cancers in the U.S. \(^1\) 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.

INITIAL TREATMENT STRATEGY

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. \(^2\) 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. \(^3, 4\) 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. \(^5\) 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. \(^6\) 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. \(^7\)

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. \(^7, 8\) 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 92%. 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. 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. Another trial looking at 13 patients confirmed these findings. 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.

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. For penile cancer, surveillance with CT may be performed for N2/3 disease, but is not indicated beyond 2 years.

References

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 AIM imaging guideline. Specific imaging considerations are addressed below.

Advanced imaging is considered medically necessary for initial treatment strategy and subsequent treatment strategy of biopsy-proven prostate cancer.

Initial treatment strategy
- CT pelvis and/or abdomen unless low risk
- MRI pelvis and/or abdomen unless low risk
- Multiparametric MRI pelvis for suspected prostate cancer in patients with a rising prostate-specific antigen (PSA) and negative transrectal ultrasound biopsy

Note: Low-risk prostate cancer defined as Gleason score of 6, PSA less than 10 ng/mL, and stage T1 or T2.

Subsequent treatment strategy
- CT chest, abdomen, and pelvis for persistent or recurrent PSA elevation
- MRI pelvis for persistent or recurrent PSA elevation
- Multiparametric MRI if anterior and/or aggressive cancer suspected when PSA increases and systemic prostate biopsies are negative

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

INITIAL TREATMENT STRATEGY
Prostate cancer is staged using the American Joint Committee on Cancer TNM system. Advanced imaging is not indicated for very low and low-risk groups. The prospective multicenter, randomized, noninferiority Phase III PRECISION (PRostate Evaluation for Clinically Important Disease: Sampling Using Image-guidance Or Not?) trial published in the New England Journal of Medicine (2018) compared multiparametric MRI (mpMRI)-targeted biopsy to standard transrectal ultrasound-guided biopsy in 500 men with clinical suspicion of prostate cancer 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). The results of this study suggest that mpMRI may be superior to standard biopsy.1 This strategy has not yet been endorsed by societal guidelines and recommendations. In a systematic review of mainly single institution studies, targeted MRI biopsy did not significantly differ in overall prostate cancer detection as compared to systematic biopsy (sensitivity 0.85, 95% CI [0.80-0.89], and 0.81, 95% CI [0.70-0.88], respectively).2 In addition, 2 randomized trials showed conflicting results for the benefit of using MRI for guided initial assessment and biopsy.2-3 In another prospective study, mpMRI showed increased predictive power over conventional CT or MRI for detecting lesions greater than 5 mm diameter and with Gleason scores higher than 7 (P < 0.05). MpMRI sensitivities ranged from 98%-100%.4 When combined with transrectal ultrasound-guided biopsy, mpMRI was also able to detect higher grade cancers in 32% of patients and detect missed cancers in 14% of patients.5,6

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.7 For detection of lymph node metastases, the differences in performance of CT and MRI were not statistically significant.8 Findings from another prospective study confirmed the equivalency of CT and MRI for lymph node staging.9 For intermediate risk or above, abdominal imaging with contrast should be performed if the risk of pelvic lymph node metastases is greater than 10%. In a meta-analysis of 24 studies, the pooled sensitivity of CT was 42% and pooled specificity was 82%, while the pooled sensitivity for MRI was 39% and pooled specificity was 82%. Bone imaging for detection of metastases has a detection rate of less than 5% in patients with PSA less than 10, as compared to over 50% with PSA greater than 20.10 FDG-PET is not indicated, as activity in the bladder obscures tumor detection.11
SUBSEQUENT TREATMENT STRATEGY

For active surveillance, the National Comprehensive Cancer Network recommends mpMRI be considered for suspected anterior and/or aggressive cancers when PSA increases and prostate biopsies are negative.12 Although there are some studies showing a correlation between MRI stability and Gleason stability, the American Urological Association/American Society for Radiation Oncology/Society of Urologic Oncology 2017 Guidelines for Clinically Localized Prostate Cancer do not currently recommend serial MRI for surveillance.13-16 In a prospective trial, the sensitivity, specificity, positive predictive value and negative predictive value of mpMRI for Gleason progression were 53%, 80%, 53% and 80%, respectively. The number needed to biopsy to detect one Gleason progression was 8.74 for systematic biopsy vs 2.9 for fusion biopsy.17

References
Sarcoma of Bone and Soft Tissue

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven bone, cartilage, connective tissue, and other soft tissue sarcoma.

**Initial treatment strategy**

- Soft tissue sarcoma of the extremity, superficial trunk, head, and neck
  - CT or MRI of primary site
  - CT chest
  - CT abdomen and pelvis (most useful for myxoid/round cell liposarcoma, epithelioid sarcoma, angiosarcoma, and leiomyosarcoma)
  - MRI brain for alveolar soft part sarcoma and angiosarcoma
  - MRI total spine for myxoid/round cell liposarcoma
- Soft tissue sarcoma of the retroperitoneal/intra-abdominal/gastrointestinal stromal tumors
  - CT chest, abdomen, and pelvis
- Bone cancer
  - CT or MRI of primary site
  - CT chest
  - CT abdomen and pelvis (most useful for chordoma)
  - MRI brain for chordoma
  - MRI total spine for chordoma
  - MRI spine and pelvis for Ewing sarcoma
- PET imaging in **ANY** of the following scenarios (all tumor types):
  - Standard imaging studies are equivocal or nondiagnostic for metastatic disease
  - Standard imaging suggests a resectable solitary metastasis
  - Baseline study prior to neoadjuvant chemotherapy for deep tumors larger than 3 cm

**Subsequent treatment strategy**

- Soft tissue sarcoma of the extremity, superficial trunk, head, and neck
  - CT or MRI of primary site
  - CT chest, abdomen, and pelvis
- Soft tissue sarcoma of the retroperitoneal/intraabdominal/gastrointestinal stromal tumors
  - CT chest, abdomen, and pelvis
- Bone cancer
  - CT or MRI of primary site
  - CT chest, abdomen, and pelvis
- PET imaging in the following scenario (all tumor types):
Following completion of neoadjuvant chemotherapy for deep lesions larger than 3 cm

**Surveillance**

- Soft tissue sarcoma of the extremity, superficial trunk, head, and neck
  - CT or MRI of primary site
  - CT chest
  - CT abdomen and pelvis as clinically indicated
- Soft tissue sarcoma of the retroperitoneal/intra-abdominal
  - CT chest, abdomen, and pelvis
- Bone cancer
  - CT or MRI primary site
  - CT chest
  - CT abdomen and pelvis as clinically indicated

**Rationale**

Sarcomas account for fewer than 1% of all adult malignancies. 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. Risk factors are not well characterized but may include genetic predisposition, prior chemotherapy or radiation therapy, and environmental exposure.

**INITIAL TREATMENT STRATEGY**

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. MRI is preferred for imaging of the primary tumor due to superior resolution of tumor versus surrounding muscle and neurovascular bundles. In a large prospective trial comparing CT and MRI imaging in both soft tissue sarcomas and bone cancer, the accuracy of local staging of primary malignant bone and soft tissue tumors was not statistically different between the 2 modalities. Since CT is less susceptible to motion artifact, CT is preferable to MRI for patients with retroperitoneal and intra-abdominal soft tissue sarcomas. Anatomic relationship of the tumor to other abdominal organs is well visualized by CT, as is metastatic disease in the liver or peritoneum.

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. Multiple studies have shown a correlation between FDG uptake and tumor grade, which is a strong indicator of prognosis. However, the evidence has not shown that PET significantly impacts staging or management.

For Ewing sarcoma, MRI of the spine and pelvis is indicated for detection of skeletal metastases. A meta-analysis showed a pooled sensitivity of 96% and pooled specificity of 92% with resultant change in management for staging and restaging when PET was combined with conventional imaging. PET response correlates with histopathologic response, improvement in progression-free survival, and potential change in management. 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.

**SUBSEQUENT TREATMENT STRATEGY**

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

**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. Ultrasound is an underutilized tool for surveillance of soft tissue sarcoma; one study found no discernable difference in detection of local recurrences when comparing ultrasound with MRI.

**References**


Cancers of the Pleura, Thymus, Heart, and Mediastinum

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven pleural malignancies, cancers of the thymus, heart, and mediastinum.

Initial treatment strategy

- CT chest
- CT abdomen and pelvis for malignant pleural mesothelioma or as clinically indicated
- MRI chest for thymoma and thymic carcinoma and as an adjunct to CT chest for malignant pleural mesothelioma
- PET imaging when surgical resection is being considered and metastatic disease has not been detected by CT or MRI

Radiation planning

- PET imaging for definitive treatment only

Subsequent treatment strategy

- CT chest
- CT abdomen and pelvis for malignant pleural mesothelioma or as clinically indicated
- MRI chest for thymoma and thymic carcinoma, and as an adjunct to CT chest for malignant pleural mesothelioma is generally not needed (optional)
- PET imaging for restaging after induction chemotherapy, if patient is a surgical candidate

Surveillance

- CT chest, abdomen, and pelvis as clinically indicated

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.

INITIAL TREATMENT STRATEGY

MRI has been shown to be superior to CT for evaluating solitary foci of chest wall invasion, endothoracic fascial involvement, and diaphragmatic muscle invasion. MRI should be considered for suspected chest wall, spinal, diaphragmatic, or vascular involvement based on CT. 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. For thymoma or thymic carcinoma, MRI chest may help differentiate benign cysts and thymoma from thymic carcinoma, thus avoiding the need for surgery. PET can be used for initial staging to differentiate low grade thymoma from FDG-avid thymic carcinoma. In a small number of patients (6%), PET identified unresectable metastatic disease not detected by CT. In a review of 14 studies, PET/CT was able to consistently differentiate benign and malignant disease and detect extrathoracic metastases. Results were mixed regarding correlation with the Masaoka staging system for thymoma, which is based on tumor invasion and metastases.

SUBSEQUENT TREATMENT STRATEGY

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.

AIM 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.12-14

References

Thyroid Cancer

Advanced imaging is considered medically necessary for initial treatment strategy, subsequent treatment strategy, and surveillance of biopsy-proven thyroid cancer.

Initial treatment strategy

- CT or MRI neck
- CT or MRI chest for fixed, bulky, or substernal lesions or as clinically indicated
- CT chest and abdomen for medullary thyroid cancer
- CT neck, chest, abdomen, and pelvis for anaplastic thyroid cancer
- PET is indicated for the following subtypes:
  - Poorly differentiated papillary
  - Anaplastic
  - Medullary
  - Hurthle Cell

Subsequent treatment strategy

- CT neck, chest, abdomen and/or pelvis based on known site of metastases or as clinically indicated for medullary thyroid cancer with calcitonin > 150 pg/mL
- MRI neck and chest (when used in place of CT for initial treatment strategy)
- PET in EITHER of the following scenarios:
  - Follow up of poorly differentiated papillary, anaplastic, medullary, or Hurthle cell carcinoma
  - Evaluation of suspected recurrence of well-differentiated papillary or follicular thyroid cancer when I 131 scan is negative (or has been negative in the past) and stimulated thyroglobulin level is > 2 ng/dL in the absence of antibodies

Surveillance

- CT neck, chest, abdomen and/or pelvis based on known site of metastases or as clinically indicated

Note: PET is most useful for non-iodine-avid thyroid cancer. Alternative imaging modalities should be considered in those tumor types for which falsely negative PET or PET/CT results are commonly reported, including medullary thyroid carcinoma.

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.

INITIAL TREATMENT STRATEGY

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.\(^1\)\(^,\)\(^2\) 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.\(^3\) Sensitivity, specificity, and diagnostic accuracy of ultrasound were 77%, 70%, and 74%, respectively, while those for CT were 62%, 79%, and 68%.\(^4\) MRI and PET have relatively low sensitivities ranging from 30%-40%\(^5\)\(^,\)\(^6\). When PET was compared to CT, no benefit in detection of nodal disease was seen. In one study, PET/CT showed a sensitivity of 30.4%, a specificity of 96.2% and a diagnostic accuracy of 86.9%; corresponding values for CT were 34.8%, 96.2% and 87.2%.\(^7\) In another study, CT outperformed
PET for detection of lung and mediastinal lymph node disease. Evaluation of the liver was most accurate with MRI and CT while evaluation of bone was most accurate with MRI and bone scan.\(^8\)

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.\(^9\) Change in management based on PET imaging findings can be as high as 25%-50%.\(^10\)

**SUBSEQUENT TREATMENT STRATEGY**

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 or follicular thyroid cancer, PET may be useful. The overall accuracy, sensitivity, and specificity for PET/CT in I-131 negative patients were 93%, 93%, and 81%, respectively.\(^11\)

For suspected recurrence of medullary thyroid cancer, a study comparing several imaging modalities found that ultrasound outperformed CT and PET for detection of locally recurrent disease (56% accuracy for ultrasound vs 42% and 32% for CT and PET, respectively). 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%).\(^11\) 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.\(^12\)

AIM 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.\(^13,14\)

**References**


Uterine Cancer

Advanced imaging is considered medically necessary for initial treatment strategy and subsequent treatment strategy of biopsy-proven uterine cancer.

Initial treatment strategy

- CT chest when chest X-ray is abnormal or as clinically indicated
- CT chest, abdomen, and pelvis in high-risk patients or as clinically indicated
- MRI pelvis prior to fertility-sparing treatment or as clinically indicated
- PET imaging when standard imaging studies are equivocal or nondiagnostic for metastatic disease

Subsequent treatment strategy

- CT chest, abdomen, and pelvis for suspected recurrence
- MRI pelvis in EITHER of the following scenarios:
  - Suspected recurrence with intact uterus
  - Prior fertility-sparing treatment after 6 months of failed medical therapy
- PET imaging when standard imaging studies are equivocal or nondiagnostic for metastatic 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

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.

INITIAL TREATMENT STRATEGY

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.\(^1,2\) 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.\(^3\) When evaluation of lymph nodes is required, both CT and MRI provide similar sensitivity and specificity.\(^4,5\) 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.\(^6-11\)

As the majority of endometrial cancers are confined to the uterus (75%) and lymph nodes (10%), systemic imaging is reserved for high-risk patients.\(^12\) In an international prospective trial, the negative predictive value for low-risk endometrial cancer was 97%.\(^13\) 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.\(^14-16\)

SUBSEQUENT TREATMENT STRATEGY

For patients who have undergone fertility-sparing treatment, MRI pelvis with contrast is preferred after 6 months of failed medical therapy. If recurrence is suspected, pelvic MRI may be used for patients with an intact uterus, and CT abdomen and pelvis should be performed if clinically indicated. 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.\(^17\)
SURVEILLANCE

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. Advanced imaging is not indicated for surveillance. 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. Detection of asymptomatic recurrences ranged from 5% to 33% of patients with physical examination, 15% with CA 125, 0% to 14% with chest X-ray, and 5% to 21% with CT abdomen and pelvis. 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. Limited data is available for MRI and PET/CT in surveillance of asymptomatic patients. In a small prospective study, PET detected asymptomatic uterine cancer recurrence in only 4% of patients. 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. The National Comprehensive Cancer Network, American College of Radiology, and Society of Gynecologic Oncology do not recommend routine use of surveillance imaging for uterine cancer.

References


## Codes

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The following codes may be applicable to oncologic imaging and may not be all inclusive.

### CPT

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<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
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<td>70460</td>
<td>CT head/brain, with contrast</td>
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<td>70470</td>
<td>CT head/brain, without contrast, followed by re-imaging with contrast</td>
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<td>70480</td>
<td>CT of orbit, sella, or posterior fossa and outer, middle or inner ear, without contrast</td>
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<td>CT of orbit, sella, or posterior fossa and outer, middle or inner ear, with contrast</td>
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<td>CT of orbit, sella, or posterior fossa and outer, middle or inner ear, without contrast, followed by re-imaging with contrast</td>
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72197  MRI pelvis without contrast, followed by re-imaging with contrast
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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

HCPCS
G0297  Low-dose CT scan (LDCT) for lung cancer screening
ICD-10 Diagnosis
Refer to the ICD-10 CM manual

History

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<td>01/01/2019</td>
<td>Advanced Imaging guidelines redesigned and reorganized to a condition-based structure</td>
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<td>Reviewed and revised</td>
<td>09/07/2017</td>
<td>Last Independent Multispecialty Physician Panel review and revision</td>
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