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

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

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

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

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

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# Abbreviations for Pediatric Oncology Imaging Guidelines

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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AFP</td>
<td>Alpha-fetoprotein (tumor marker)</td>
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<tr>
<td>ALCL</td>
<td>Anaplastic Large Cell Lymphoma</td>
</tr>
<tr>
<td>ALL</td>
<td>Acute Lymphoblastic Leukemia</td>
</tr>
<tr>
<td>AML</td>
<td>Acute Myelogenous Leukemia</td>
</tr>
<tr>
<td>β-hCG</td>
<td>human chorionic gonadotropin beta-subunit (tumor marker)</td>
</tr>
<tr>
<td>BKL</td>
<td>Burkitt's lymphoma</td>
</tr>
<tr>
<td>BWT</td>
<td>bilateral Wilms tumor</td>
</tr>
<tr>
<td>CCSK</td>
<td>Clear Cell Sarcoma of the Kidney</td>
</tr>
<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>COG</td>
<td>Children's Oncology Group</td>
</tr>
<tr>
<td>CPT®</td>
<td>Current Procedural Terminology; trademark of the American Medical Association</td>
</tr>
<tr>
<td>CSF</td>
<td>cerebrospinal fluid</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>CXR</td>
<td>chest x-ray</td>
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<tr>
<td>DAWT</td>
<td>diffuse anaplasia Wilms tumor</td>
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<tr>
<td>ESFT</td>
<td>Ewing Sarcoma Family of Tumors</td>
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<tr>
<td>FAWT</td>
<td>focal anaplasia Wilms tumor</td>
</tr>
<tr>
<td>FHWT</td>
<td>favorable histology Wilms tumor</td>
</tr>
<tr>
<td>HL</td>
<td>Hodgkin lymphoma</td>
</tr>
<tr>
<td>HSCT</td>
<td>hematopoietic stem cell transplant (bone marrow or peripheral blood)</td>
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<tr>
<td>HVA</td>
<td>homovanillic acid</td>
</tr>
<tr>
<td>LL</td>
<td>lymphoblastic lymphoma</td>
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<tr>
<td>MIBG</td>
<td>metaiodobenzylguanidine (nuclear scan using $^{123}$I or $^{131}$I)</td>
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<tr>
<td>MPNST</td>
<td>malignant peripheral nerve sheath tumor</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
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<tr>
<td>NBL</td>
<td>neuroblastoma</td>
</tr>
<tr>
<td>NED</td>
<td>no evidence of disease</td>
</tr>
<tr>
<td>NHL</td>
<td>non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>NPC</td>
<td>nasopharyngeal carcinoma</td>
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<td>NRSTS</td>
<td>nonrhabdomyosarcomatous soft tissue sarcomas</td>
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<tr>
<td>OS</td>
<td>osteosarcoma</td>
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<tr>
<td>PET</td>
<td>positron emission tomography</td>
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<tr>
<td>PMBCL</td>
<td>primary mediastinal B-cell lymphoma</td>
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<tr>
<td>PNET</td>
<td>primitive neuroectodermal tumor</td>
</tr>
<tr>
<td>RCC</td>
<td>renal cell carcinoma</td>
</tr>
<tr>
<td>RMS</td>
<td>rhabdomyosarcoma</td>
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<td>US</td>
<td>ultrasound</td>
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<tr>
<td>VMA</td>
<td>vannilylmandelic acid</td>
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<tr>
<td>WBC</td>
<td>white blood cell count</td>
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<td>XRT</td>
<td>radiation therapy</td>
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**PEDONC-1.1: Age Considerations**

- The majority of malignancies occurring in the pediatric population are different diagnoses than those occurring in the adult population.

- For those diseases which occur in both pediatric and adult populations, minor differences may exist in management between pediatric and adult medical oncologists due to the following:
  - Age of the individual
  - Comorbidities
  - Differences in disease natural history between children and adults

- Individuals who are < 18 years old at initial diagnosis should be imaged according to the Pediatric Oncology Imaging Guidelines.

- Individuals who are ≥ 18 years at initial diagnosis should be imaged according to the adult Oncology Imaging Guidelines, except where directed otherwise by a specific guideline section.
  - Individuals who are 15 to 39 years old at initial diagnosis are defined as Adolescent and Young Adult (AYA) Oncology individuals.
  - There is significantly more overlap between cancer types in this age group.
  - When unique guidelines for a specific cancer type exist only in either Oncology or Pediatric Oncology, AYA individuals should be imaged according to the guideline section for their specific cancer type, regardless of the individual’s age.
  - When unique guidelines for a specific cancer type exist in both Oncology and Pediatric Oncology, AYA individuals should be imaged according to the age rule in the previous bullet.
PEDONC-1.2: Appropriate Clinical Evaluations

In general, a recent (within 60 days) detailed history and physical examination and appropriate laboratory studies should be performed prior to considering advanced imaging, unless the individual is undergoing guideline-supported scheduled off-therapy surveillance evaluation.

- Because of the relatively small number of childhood cancer treatment centers, it is common to combine off-therapy visits with imaging and other subspecialist visits to accommodate families traveling long distances for their child’s care.

The majority of pediatric oncology imaging indications are listed in the diagnosis-specific guideline sections.

- Rare malignancies and other circumstances not specifically addressed elsewhere in the Pediatric Oncology guidelines, the following general principles apply:
  - Routine imaging of brain, spine, neck, chest, abdomen, pelvis, bones, or other body areas is not indicated in the absence of:
    - Localizing symptoms or
    - Abnormalities on plain radiography or ultrasound

The overwhelming majority of pediatric oncology individuals treated in the United States will be enrolled on or treated according to recent Children’s Oncology Group (COG) protocols.

- COG is a National Cancer Institute (NCI) supported clinical trials group
- These imaging guidelines are consistent with evaluations recommended by COG protocols commonly used for direct individual care (whether formally enrolled on study or not)

For individuals enrolled on a COG study, imaging recommended by COG protocols should generally be approved unless the imaging is being performed solely to address a study objective and would not be indicated in usual clinical care.
Phases of Pediatric Oncology Imaging:

- **Screening:**
  - All imaging studies requested for individuals at increased risk for a particular cancer in the absence of any clinical signs or symptoms
  - Screening using advanced imaging is only supported for conditions listed in **PEDONC-2: Screening Imaging in Cancer Predisposition Syndromes**

- **Initial Staging:**
  - All imaging studies requested from the time cancer is first clinically suspected until the initiation of specific treatment (which may be surgical resection alone)
  - Pediatric malignancies in general behave more aggressively than adult cancers, and the time from initial suspicion of cancer to specific therapy initiation can be measured in hours to days for most pediatric cancers
    - It is recommended that children with pediatric solid tumors undergo CT evaluation of the Chest prior to general anesthesia for biopsy or resection due to the risk of post-operative atelectasis mimicking pulmonary metastasis resulting in inaccurate staging and/or delay in therapy initiation
    - If CTs of other body areas are indicated, (neck, abdomen, pelvis), they should be performed concurrently with CT Chest to avoid overlapping fields and the resulting increase in radiation exposure
    - Metastatic CNS imaging and nuclear medicine imaging are generally deferred until after a histologic diagnosis is made, with the exception of aggressive Non-Hodgkin lymphomas

- **Treatment Response:**
  - All imaging studies completed during any type of active treatment (chemotherapy or other medications, radiation therapy, or surgery), including evaluation at the end of planned active treatment
  - Unless otherwise stated in the diagnosis-specific guidelines, imaging for treatment response can be approved after every 2 cycles, which is usually 6 weeks of therapy for solid tumors and usually 8 to 12 weeks for CNS tumors

- **Surveillance:**
  - All routine imaging studies requested for an individual who is not receiving any active treatment, even if residual imaging abnormalities are present
  - Unlike adult cancers, in most pediatric cancers surveillance does not begin until all planned multimodal therapy is completed
  - Pediatric cancers where surgical resection is considered curative are listed in the diagnosis-specific guideline sections
  - The recommended timing for surveillance imaging studies in these guidelines refers to individuals who:
    - Are asymptomatic or
    - Have stable chronic symptoms
  - Certain tumor types do not require surveillance with advanced imaging as individual outcomes following relapse are not improved by surveillance imaging. See diagnosis-specific guideline sections for details
  - PET imaging is not supported for surveillance imaging unless specifically stated elsewhere in the diagnosis-specific guideline sections
Individuals with new or changing clinical signs or symptoms suggesting recurrent disease should have symptom-appropriate imaging requests approved even when surveillance timing recommendations are not met

Recurrence:
- All imaging studies completed at the time a recurrence or progression of a known cancer is documented or is strongly suspected based on the following:
  - Clinical signs or symptoms or
  - Laboratory findings or
  - Results of basic imaging studies such as plain radiography or ultrasound
- Following documented recurrence of childhood cancer, any studies recommended for initial staging of that cancer type in the diagnosis-specific imaging guideline section should be approved
- During active treatment for recurrent pediatric cancer, conventional imaging evaluation (CT or MRI, should use the same modality for ongoing monitoring as much as possible) of previously involved areas should be approved according to the treatment response imaging in the diagnosis-specific guideline section:
  - Imaging may be indicated more frequently than recommended by guidelines with clinical documentation that the imaging results are likely to result in a treatment change for the individual, including a change from active treatment to surveillance
- Unless otherwise specified for a specific cancer type, PET is generally not indicated for routine treatment response evaluation during active treatment for recurrent pediatric cancer
  - In rare circumstances, PET may be appropriate when results are likely to result in a treatment change for the individual, including a change from active treatment to surveillance
  - These requests will be forwarded for Medical Director review
- If an individual with recurrent pediatric cancer completes active treatment with no evidence of disease (NED), she/he should be imaged according to the diagnosis-specific surveillance guideline sections
Cardiac Function Assessment in Pediatric Oncology during Active Treatment:

- Echocardiography (CPT® 93306, CPT® 93307, or CPT® 93308) is preferred for evaluation of cardiac function prior to cardiotoxic chemotherapy and can be performed as often as each chemotherapy cycle at the discretion of the treating pediatric oncologist based on:
  - Cumulative cardiotoxic therapy received to date
  - Individual's age and gender
  - Most recent echocardiogram results
  - New or worsening cardiac symptoms

- MUlti-Gated Acquisition (MUGA, CPT® 78472) blood pool nuclear medicine scanning should be approved for cardiac function monitoring in pediatric oncology individuals only if one of the following applies:
  - Echocardiography yielded a borderline shortening fraction (< 30%) and additional left ventricular function data are necessary to make a chemotherapy decision
  - Echocardiography windowing is suboptimal due to body habitus or tumor location

Background and Supporting Information

Immunosuppression during Pediatric Cancer therapy and imaging ramifications:

- Individuals may be severely immunocompromised during active chemotherapy treatment and any conventional imaging request to evaluate for infectious complications during this time frame should be approved immediately
  - Imaging requests for infectious disease concerns for all individuals with absolute neutrophil count (ANC) < 500 or
  - Inconclusive findings on chest x-ray or US at any ANC during active treatment should be approved as requested
  - Individuals may have therapy-induced hypogammaglobulinemia which requires supplemental intravenous immune globulin (IVIG) during maintenance therapy. These individuals receiving supplemental IVIG should be treated similarly to individuals with ANC < 500 with regards to imaging for infectious disease

- Some individuals are treated with very intensive chemotherapy regimens (including autologous stem cell transplantation) and spend the majority of their chemotherapy treatment phase in the hospital. See ONC-29: Hematopoietic Stem Cell Transplantation.

- Due to the high risk of invasive infections, frequent CT may be indicated to evaluate known sites of invasive fungal infection, and in general these should be approved as requested
  - Surveillance imaging of asymptomatic individuals to detect invasive fungal infection has not been shown to impact individual outcomes
    - Imaging requests are indicated when acute clinical decisions will be made based on the imaging
Hematopoietic Stem Cell Transplant (HSCT) in Pediatric Oncology:

- Transplantation of hematopoietic stem cells from bone marrow, peripheral blood, or cord blood is commonly used in the following clinical situations:
  - High risk or recurrent leukemia (allogeneic)
  - Recurrent lymphoma (allogeneic or autologous)
  - Hemophagocytic lymphohistiocytosis (allogeneic)
  - High risk sickle cell disease (allogeneic)
  - High risk neuroblastoma (autologous)
  - High risk CNS tumors (autologous)
  - Recurrent Ewing sarcoma family of tumors (autologous, rarely allogeneic)
- Imaging considerations for HSCT should follow guidelines in: ONC-29: Hematopoietic Stem Cell Transplantation.
PEDONC-1.3: Modality General Considerations

- Plain radiography
  - CXR can provide a prompt means to evaluate primary intrathoracic tumors and continues to be the initial imaging study recommended to detect complications, such as suspected infection, in symptomatic individuals undergoing treatment.
  - CXR continues to be the initial imaging study recommended for pulmonary surveillance for some pediatric cancers. See diagnosis-specific guideline sections for details.
  - Plain radiography continues to be the initial imaging study recommended for evaluation of lesions involving the appendicular skeleton, both during and after completion of treatment. See diagnosis-specific guideline sections for details.
  - Plain abdominal radiographs have largely been replaced by ultrasound, CT, or MRI.

- Ultrasound
  - Ultrasound is not widely used in pediatric oncology for staging, but is frequently used for surveillance in individuals who have successfully treated (primarily abdominal or pelvic) tumors with little or no residual disease.
  - See diagnosis-specific guideline sections for details.

- CT
  - CT with contrast is the imaging study of choice in pediatric individuals with lymphomas or solid tumors of the neck, thorax, abdomen, and/or pelvis.
  - If CT contrast use is contraindicated due to allergy or impaired renal function, either CT without contrast or MRI with and without contrast may be substituted at the discretion of the ordering physician.

- MRI
  - MRI without and with contrast is the study of choice for CNS tumors and musculoskeletal tumors.
    - If MRI without contrast is contraindicated due to allergy or impaired renal function, MRI without contrast may be substituted at the discretion of the ordering physician.
    - Due to the length of time for image acquisition and the need for stillness, anesthesia is required for almost all infants and young children (age < 7 years), as well as older children with delays in development or maturity. In this population, MRI imaging sessions should be planned with a goal of avoiding a short-interval repeat anesthesia exposure due to insufficient information using the following considerations:
      - MRI should always be performed without and with contrast unless there is a specific contraindication to gadolinium use since the individual already has intravenous access for anesthesia.
        - Recent evidence-based literature demonstrates the potential for gadolinium deposition in various organs including the brain, after the use of MRI contrast.
- The U.S. Food and Drug Administration (FDA) has noted that there is currently no evidence to suggest that gadolinium retention in the brain is harmful and restricting gadolinium-based contrast agents (GBCAs) use is not warranted at this time
- It has been recommended that GBCA use should be limited to circumstances in which additional information provided by the contrast agent is necessary and the necessity of repetitive MRIs with GBCAs should be assessed
- If requesting clinicians indicate that a non-contrast study is being requested due to concerns regarding the use of gadolinium, the exam can be approved
- If multiple body areas are supported by eviCore Guidelines for the clinical condition being evaluated, MRI of all necessary body areas should be obtained concurrently in the same anesthesia session

- **Nuclear Medicine**
  - General PET imaging considerations can be found in **PEDONC-1.4: PET Imaging** in Pediatric Oncology
  - Bone scan is frequently used for evaluation of bone metastases in pediatric oncology during initial treatment, treatment response, and surveillance
  - For the purposes of these guidelines, any of the following codes can be approved where “bone scan” is indicated:
    - CPT® 78300
    - CPT® 78305
    - CPT® 78306
    - CPT® 78320
    - CPT® 78305 and CPT® 78320
    - CPT® 78306 and CPT® 78320
    - If CPT® 78300 and CPT® 78320 are requested together, only CPT® 78320 should be approved
    - CPT® 78315 has no specific indications for evaluation of malignant disease
  - $^{123}$I-Metaiodobenzylguanidine (MIBG) scintigraphy is the preferred metabolic imaging for neuroblastoma and is positive in 90 to 95% of neuroblastomas, and is also used for evaluation of pheochromocytomas, paragangliomas, ganglioneuromas, and ganglioneuroblastomas
  - For the purposes of these guidelines, any of the following codes can be approved where “MIBG” is indicated:
    - CPT® 78800
    - CPT® 78801
    - CPT® 78802
    - CPT® 78803
    - CPT® 78804
  - Octreotide and gallium scans use the same CPT® codes as MIBG
PEDONC-1.4: PET Imaging in Pediatric Oncology

Throughout these guidelines, the term “PET” refers specifically to $^{18}$F-FDG-PET imaging and also applies to PET/CT fusion studies.

- PET imaging in pediatric oncology should use PET/CT fusion imaging (CPT® 78815 or CPT® 78816) unless there is clear documentation that the treating facility does not have fusion capacity, in which case PET alone (CPT® 78812 or CPT® 78813) can be approved along with the appropriate CT studies. Unbundling PET/CT imaging into separate PET and diagnostic CT codes is otherwise not supported.

- The decision whether to use skull base to mid-femur (“eyes to thighs”) procedure code for PET (CPT® 78812 or CPT® 78815) or whole body PET (CPT® 78813 or CPT® 78816) is addressed in the diagnosis-specific guideline sections.

- PET imaging is not reliable for the detection of anatomic lesions smaller than 8 mm in size.

- PET imaging using isotopes other than $^{18}$F-FDG and $^{68}$Ga-DOTATATE is considered investigational at this time. Please see the table below for the most commonly used isotopes and their corresponding codes:

  - **Covered:**
    - $^{18}$F-FDG
    - $^{68}$Gallium DOTATATE (NETSPOT®) for localization of somatostatin receptor positive neuroendocrine tumors in adult and pediatric population
  
  - **Not covered:**
    - PET/CT imaging using isotopes other than those specified above

<table>
<thead>
<tr>
<th>CPT/HCPCS Code</th>
<th>Code Description</th>
<th>Brand or common name</th>
<th>FDA-approved?</th>
<th>Code reviewed by eviCore for Cigna?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A9552</td>
<td>fluorine-18 (F-18) fluorodeoxyglucose (FDG), diagnostic, per study dose, up to 45 millicuries</td>
<td>FDG</td>
<td>Yes, to assess abnormal glucose metabolism</td>
<td>No</td>
</tr>
<tr>
<td>A9587</td>
<td>Gallium GA-68, dotatate, diagnostic, 0.1 millicurie</td>
<td>NETSPOT®</td>
<td>Yes, for localization of somatostatin receptor positive neuroendocrine tumors in adult and pediatric population</td>
<td>No</td>
</tr>
</tbody>
</table>

- PET has not been shown to be diagnostically useful in all forms of childhood cancer. PET is supported for pediatric malignancies with significant published evidence regarding its diagnostic accuracy and importance in accurately directing individual care decisions. See diagnosis-specific guideline sections for details.

- PET imaging is not specific to cancer, and has a high rate of false positivity. Inflammation, infection (especially granulomatous), trauma, and post-operative healing may show high levels of FDG update and be false-positive for malignant lesions.
PET for rare malignancies not specifically addressed by eviCore guidelines is generally not indicated, due to lack of available evidence regarding diagnostic accuracy of PET in the majority of rare cancers. Conventional imaging studies should be used for initial staging and treatment response for these diagnoses.

PET can be approved if all of the following apply:

- Conventional imaging (CT, MRI, US, plain film) reveals findings that are equivocal or suspicious
- No other specific metabolic imaging (MIBG, octreotide, technetium, etc.) is appropriate for the cancer type
- The submitted clinical information describes a specific decision regarding the individual’s care that will be made based on the PET results
- These requests will be forwarded for Medical Director review

PET imaging for surveillance imaging only when specifically stated elsewhere in the diagnosis-specific guideline sections.

Unless otherwise specified for a specific cancer type, once PET has been documented to be negative for a given individual’s cancer or all PET-avid disease has been surgically resected, PET should not be used for continued disease monitoring or surveillance unless one of the following applies:

- Conventional imaging (CT, MRI, US, plain film) reveals findings that are inconclusive or suspicious for recurrence
  - Residual mass that has not changed in size since the last conventional imaging does not justify PET imaging
  - PET avidity in a residual mass at the end of planned therapy is not an indication for PET imaging during surveillance
- Very rare circumstances where tumor markers or obvious clinical symptoms show strong evidence suggesting recurrence and PET would replace conventional imaging modalities
- The individual is undergoing salvage treatment for a recurrent solid tumor with residual measurable disease on conventional imaging and confirmed repeat negative PET imaging will allow the individual to transition from active treatment to surveillance
- These requests will be forwarded for Medical Director review
PEDONC-1.5: Diagnostic Radiation Exposure in Pediatric Oncology

- Young children are presumed to be at increased risk for malignancy from diagnostic radiation exposure, most commonly from CT and nuclear medicine imaging. They are more sensitive to radiation than adults and generally live longer after receiving radiation doses from medical procedures, resulting in a larger number of years during which to manifest a cancer.

- Because of this presumed increased risk in young children, requests to substitute MRI without and with contrast for CT with contrast to avoid radiation exposure if all of the following criteria apply:
  - The individual is presently a young child and the ordering physician has documented the reason for MRI, rather than CT, is to avoid radiation exposure.
  - The disease-specific guidelines do not list CT as superior to MRI for the current disease and time point, meaning the MRI will provide equivalent or superior information relative to CT.
  - The request is for a body area other than chest as MRI is substantially inferior to CT for detection of small pulmonary metastases.

- The guidelines listed in this section for certain specific indications are not intended to be all-inclusive; clinical judgment remains paramount and variance from these guidelines may be appropriate and warranted for specific clinical situations.


21. Coccia PF, Pappo AS, Beaupin L et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2018—October 11, 2017, Adolescent and Young Adult (AYA) Oncology, available at: https://www.nccn.org/professionals/physician_gls/pdf/aya.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Adolescent and Young Adult (AYA) Oncology V2.2018 10/11/17. ©2017 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
# PEDONC-2: Screening Imaging in Cancer Predisposition Syndromes

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PEDONC-2.1: General Considerations

- This section is intended to give guidance for screening imaging prior to diagnosis with a specific malignancy. Once an individual with a cancer predisposition syndrome has been diagnosed with a malignant disease, future imaging decisions should be guided by the appropriate disease-specific guidelines except as explicitly stated elsewhere in this section.

- This section’s guidelines are limited to cancer predisposition syndromes with screening imaging considerations. Syndromes requiring only clinical or laboratory screening are not discussed here.

- In general, a recent (within 60 days) detailed history and physical examination and appropriate laboratory studies should be performed prior to considering advanced imaging, unless the individual is undergoing guideline-supported scheduled screening evaluation identified in this section.

- Many of these cancer predisposition syndromes also affect adults as survival continues to improve for these individuals. Adults with syndromes covered in this section may follow these imaging guidelines except where contradicted by specific statements in the adult imaging guideline.
PEDONC-2.2: Li-Fraumeni Syndrome (LFS)

- MRI Brain (CPT® 70553) without and with contrast annually
- Ultrasound Abdomen (CPT® 76700) and Ultrasound Pelvis (CPT® 76856) every 3 months
- MRI Breast (CPT® 77059) annually alternating every 6 months with Ultrasound Breast (CPT® 76641) for breast cancer surveillance is appropriate for LFS individuals beginning at age 20 to 25. See BR-6: Breast MRI Indications
- Targeted MRI imaging without and with contrast of any body area(s) with documented signs or symptoms suggestive of possible malignancy. When a specific malignancy is suspected, the individual should be imaged according to the eviCore imaging guideline specific to the suspected cancer type
- Studies ordered as part of a screening imaging program based on specific family cancer history that has been developed for an individual in conjunction with a multidisciplinary team including at least genetics and oncology
  - Specifics of the program should be obtained and available for the medical director reviewing the case
  - Even in this setting, whole body MRI is not supported for LFS

Background and Supporting Information

- LFS - syndrome inherited in an autosomal dominant manner (50% risk to offspring) associated with germline mutations in TP53 resulted in an increased susceptibility to a variety of cancers.
  - Eighty percent of individuals will have germline TP53 mutation:
  - Tumor-specific TP53 mutations are much more common than germline TP53 mutations and are not associated with an increased risk for subsequent cancers.
  - If TP53-negative, formal diagnosis of LFS should be assigned by a physician with significant training and/or experience in LFS (most commonly a geneticist or oncologist) based on specified clinical criteria prior to beginning a screening imaging program.
    - TP53 mutations may be present in 50 to 80% of pediatric adrenocortical carcinoma, 10% of pediatric rhabdomyosarcoma, and 10% of pediatric osteogenic sarcoma individuals.
- Individuals with LFS have an increased sensitivity to ionizing radiation, so screening strategies resulting in significant radiation exposure are not appropriate (CT and nuclear medicine).
- Because of the wide variety of possible malignancies, there is not to date a standard approach for screening that is supported by evidence:
  - Several longitudinal trials are ongoing to establish an optimal screening protocol for LFS individuals.
    - Whole body MRI (WBMRI) is frequently studied in these protocols13-19
    - Several studies have demonstrated the ability to detect cancers using WBMRI, but only a small percentage of the cancers are detected using WBMRI alone
The false positive rates are extremely variable, and range up to 87%.\(^{17}\)

- A recent meta-analysis\(^{16}\) reported that 31% of 578 screened LFS patients had investigable lesions but only 7% of patients were subsequently diagnosed with a new malignant neoplasm.

- False negatives also occur with WBMRI, most frequently in the brain, but also include tumors such as osteosarcoma and adrenocortical carcinoma. This is felt to be primarily due to the limited images used for WBMRI approaches.

- Substantial variation continues to exist in WBMRI techniques, with lack of consensus around even such basic principles as which anatomic views to use (coronal, sagittal, and/or axial) and whether contrast is important, and a CPT code for WBMRI has not yet been assigned.

- At this time, the evidence remains too contradictory to support WBMRI as a standard of care for screening of LFS individuals outside the clinical trial setting.

- Annual complete detailed physical examinations, complete blood counts, and urinalyses form the backbone of LFS cancer screening.
**PEDONC-2.3: Neurofibromatosis 1 and 2 (NF1 and NF2)**

**NF1:**
- CT and/or nuclear medicine studies in some acute clinical situations. These requests will be forwarded for Medical Director review
- MRI Brain (CPT® 70553) and Orbits (CPT® 70543) without and with contrast can be approved one time to clarify the diagnosis of NF1
- Routine follow-up imaging of unidentifed bright objects (UBOs, T2-weighted signal abnormalities) only in the presence of acute symptoms suggesting new or worsening intracranial disease
- Individuals with NF1 and documented optic pathway gliomas should be imaged according to **PEDONC-4.2: Interacranial Low Grade Gliomas (LGG)**
- MRI imaging without and with contrast is appropriate for any clinical symptoms suggestive of change in a known PN in an individual with NF1
- PET imaging for evaluating indiviudals with NF1 with clinical symptoms concerning for malignant transformation of a known PN when **all** of the following conditions exist:
  - Recent MRI is inconclusive regarding transformation or progression
  - Negative PET will result in a decision to avoid biopsy in a difficult or morbid location
- Inconclusive PET findings should lead to biopsy of the concerning lesion
- Individuals with NF1 and known plexiform neurofibromas should be imaged according guidelines in **PEDPN-2.1: Neurofibromatosis 1**
- Individuals with NF1 and new soft tissue masses should be imaged according to **ONC-12: Sarcomas – Bone, Soft Tissue and Gist** or **PEDONC-8.3: Non-Rhabdomyosarcoma Soft Tissue Sarcomas (NRSTS)**, depending on the individual's age at the time the mass is discovered
- Individuals with NF1 and new bone masses should be imaged according to **PEDONC-9: Bone Tumors**
Background and Supporting Information

- Common syndrome inherited in an autosomal dominant manner (50% risk to offspring) affecting 1 in 2500 people. The diagnosis is commonly made based on established clinical criteria including café-au-lait spots, lisch nodules of the iris, axillary freckling, family history, and the presence of NF-associated tumors.

- The majority of tumors are benign in nature, but malignant degeneration can occur.

- NF1-affected persons have increased sensitivity to ionizing radiation, so CT and nuclear medicine imaging are not appropriate screening or surveillance studies for these individuals. CT and/or nuclear medicine studies may be indicated for acute clinical situations and should be forwarded for Medical Director review.

- Annual ophthalmology evaluation is recommended beginning at the time of diagnosis of NF1 to evaluate for optic pathway abnormalities:
  - Screening MRIs of the Brain (CPT® 70553) and Orbits (CPT® 70543) for asymptomatic individuals are not generally recommended due to the ~60% rate of unidentified bright objects (UBOs, T2-weighted signal abnormalities) which mostly disappear by age 30
  - Routine follow up imaging of UBOs is not warranted in the absence of acute symptoms suggesting new or worsening intracranial disease
  - Children with negative brain and orbital screening at age 15 months generally do not develop optic pathway gliomas

- NF1 individuals are at increased risk for plexiform neurofibromas (PN) and malignant peripheral nerve sheath tumors (MPNST—a high grade sarcoma)
  - Screening imaging of asymptomatic individuals for these tumors is not supported by evidence. PET imaging is not supported for PN surveillance in asymptomatic individuals at this time as the positive predictive value is only 60 to 65% even in symptomatic individuals
  - Although PET imaging has a positive predictive value of only 61 to 63% in NF1 individuals with suspected transformation to MPNST, the negative predictive value is high (96 to 99%)

- Repeat PET studies are not indicated due to the poor positive predictive value in this setting

NF2:

- Individuals with NF2 and known vestibular schwannomas should be imaged according to guidelines in PEDPN-2.2: Neurofibromatosis 2

- Individuals with NF2 and known meningioma should be imaged according to guidelines in ONC-2.8: Meningiomas (Intracranial and Intraspinal)

- Individuals with NF2 and known ependymoma should be imaged according to guidelines in PEDONC-4.8: Ependymoma
Recommended cancer screening imaging includes:

- MRI Brain without and with contrast (CPT® 70553) annually beginning at age 10 years
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) every 3 years beginning at age 10 for individuals without spinal tumors and annually for individuals with NF2 and a history of spinal tumors

Additional appropriate imaging requests include:

- MRI Brain without and with contrast (CPT® 70553) for any individual with NF2 and clinical symptoms of intracranial mass or vestibular disease
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) should be approved for any individual with NF2 and:
  - Clinical symptoms suggestive of spinal or paraspinal tumors, including uncomplicated back pain or radiculopathy
  - Recent diagnosis with a meningioma or vestibular schwannoma

Background and Supporting Information

NF2 is substantially less common than NF1. It is inherited in an autosomal dominant manner (50% risk to offspring) affecting ~1 in 25000 people. NF2 is associated with increased risk for Meningiomas (50% of affected individuals), vestibular schwannomas, and spinal tumors (75% of affected individuals)
PEDONC-2.4: Beckwith-Wiedemann Syndrome (BWS)

**Recommended cancer screening imaging includes:**

- Ultrasound Abdomen (CPT® 76700) every 3 months from birth to the 8th birthday
  - Individuals found to have adrenal masses on screening ultrasound should receive additional imaging as follows:
    - Ultrasound screening every 3 months without additional imaging for those with purely cystic masses
    - Age 0 to 5 months:
      - MIBG imaging and either CT or MRI Abdomen (contrast as requested) for solid or mixed mass 0 to 3 cm in diameter and ultrasound Abdomen every 6 weeks for 2 years if no evidence of malignancy based on MIBG, CT or MRI, Urine HVA/VMA, and serum ACTH
      - MIBG imaging and MRI Abdomen (contrast as requested) for solid or mixed mass > 3 cm in diameter:
    - Age 6 months or greater:
      - MIBG imaging prior to biopsy or resection for solid or mixed mass
      - Ultrasound Abdomen (screening) every 3 months resumed if no evidence of malignancy on biopsy or resection

- Individuals with BWS and known renal tumors should be imaged according guidelines in **PEDONC-7: Pediatric Renal Tumors**

- Individuals with BWS and known hepatoblastoma should be imaged according guidelines in **PEDONC-11.2: Hepatoblastoma**

- Individuals with BWS and known neuroblastoma should be imaged according guidelines in **PEDONC-6: Neuroblastoma**

- Individuals with BWS and known adrenocortical carcinoma should be imaged according guidelines in **PEDONC-14: Pediatric Adrenocortical Carcinoma**

- Individuals with BWS and known pheochromocytoma should be imaged according guidelines in **ONC-15: Neuroendocrine Cancers and Adrenal Tumors**

**Background and Supporting Information**

- Inherited syndrome characterized by macroglossia, hemihypertrophy, macrosomia, organomegaly, and neonatal hypoglycemia. Individuals with isolated hemihypertrophy are also imaged according to this guideline

- Caused by mutation at chromosome 11p15, affected children are predisposed to Wilms tumor, hepatoblastoma, rhabdomyosarcoma, and adrenal tumors
**PEDONC-2.5: Denys-Drash Syndrome (DDS)**

**Recommended cancer screening imaging includes:**
- Ultrasound Abdomen (CPT® 76700) every 3 months from birth to the 8th birthday
- Individuals with DDS and known renal tumors should be imaged according to guidelines in **PEDONC-7: Pediatric Renal Tumors**

**Background and Supporting Information**
Characterized by pseudohermaphroditism, early renal failure, and > 90% risk of Wilms tumor development in each kidney. Associated with mutations at 11p13, risk of renal failure after detection of symptomatic Wilms tumor is 62%, so early detection may allow for renal-sparing surgical approaches
**PEDONC-2.6: Wilms Tumor-Aniridia-Growth Retardation (WAGR)**

**Recommended cancer screening imaging includes:**
- Ultrasound Abdomen (CPT® 76700) every 3 months from birth to the 8th birthday
- Individuals with WAGR and known renal tumors should be imaged according to guidelines in **PEDONC-7: Pediatric Renal Tumors**

**Background and Supporting Information**
Named for the components of the disorder, it is associated with mutations at 11p13. As the name suggests, individuals are predisposed to Wilms tumor, with 57% of individuals in one cohort developing Wilms tumor. Risk of renal failure after detection of symptomatic Wilms tumor is 38%, so early detection may allow for renal-sparing surgical approaches
**PEDONC-2.7: Familial Adenomatous Polyposis (FAP) and Related Conditions**

**Recommended cancer screening imaging includes:**
- Ultrasound Abdomen (CPT® 76700) every 3 months from birth to the 6th birthday, and annually for life after age 6 with family history of desmoid tumors
- Annual thyroid ultrasound (CPT® 76536) beginning at age 12
- Annual pelvic ultrasound (CPT® 76856) beginning at age 30
- Individuals with FAP and known colorectal tumors should be imaged according to guidelines in **ONC-16: Colorectal Cancer**
- Individuals with FAP and known desmoid tumors should be imaged according to guidelines in **PEDONC-8.3: Non-Rhabdomyosarcoma Soft Tissue Sarcomas (NRSTS)**
- Individuals with Lynch, Gardner, and Turcot syndromes should also be imaged according to these guidelines

**Background and Supporting Information**
- Inherited in an autosomal dominant manner (50% risk to offspring), it is also known as Adenomatous Polyposis Coli (APC). It is associated with the development of thousands of colonic polyps by age 20 and > 90% risk of colorectal carcinoma. Prophylactic total colectomy is recommended by age 20 for most individuals. FAP is also associated with hepatoblastoma, tumors of the pancreas and small bowel, medulloblastoma, and thyroid cancer
- Recommended cancer screening includes:
  - Serum AFP every 3 months to the 6th birthday
  - Annual colonoscopy beginning at age 7
  - Annual esophagastroduodenoscopy beginning at age 10
PEDONC-2.8: Multiple Endocrine Neoplasias (MEN)

Recommended cancer screening imaging includes:

- **MEN1**
  - MRI Brain without and with contrast (CPT® 70553) annually beginning at age 5
  - MRI Abdomen without and with contrast (CPT® 74183), CT Abdomen with contrast (CPT® 74160), or Ultrasound Abdomen (CPT® 76700) annually beginning at age 5
  - MRI Chest without and with contrast (CPT® 71552) or CT Chest with contrast (CPT® 71260) annually beginning at age 15
  - Octreotide study (CPT® codes: CPT® 78800, CPT® 78801, CPT® 78802, CPT® 78803, or CPT® 78804) annually beginning at age 5

- Individuals with MEN1 and known thyroid cancer should be imaged according to guidelines in **ONC-6: Thyroid Cancer**

- Individuals with MEN1 and known pheochromocytoma should be imaged according to guidelines in **ONC-15: Neuroendocrine Cancers and Adrenal Tumors**

- **MEN2a and MEN2b**
  - MRI Abdomen without and with contrast (CPT® 74183) can be approved every 3 years beginning at age 5
  - Octreotide study (CPT® codes: CPT® 78800, CPT® 78801, CPT® 78802, CPT® 78803, or CPT® 78804) or Adrenal nuclear imaging (CPT® 78075) can be approved for elevated catecholamines or inconclusive adrenal mass on MRI.

- Individuals with MEN2a or MEN2b and known pheochromocytoma should be imaged according to guidelines in **ONC-15: Neuroendocrine Cancers and Adrenal Tumors**

**Background and Supporting Information**

- Inherited in an autosomal dominant manner (50% risk to offspring).

- MEN1 is characterized by parathyroid, pancreatic islet cell, and pituitary gland tumors (3 P’s), as well as carcinoid tumors in the chest and abdomen, and 28% of individuals will develop at least one tumor by age 15.

- MEN2a is characterized by medullary thyroid carcinoma, parathyroid adenomas, and pheochromocytomas.

- MEN2b is characterized by ganglioneuromas of the GI tract and skeletal abnormalities presenting in infancy.

**Recommended cancer screening:**

MEN2a and MEN2b: Annual measurement of catecholamines for pheochromocytoma screening
**PEDONC-2.9: Tuberous Sclerosis Complex (TSC)**

**Recommended cancer screening imaging includes:**
- Brain MRI without and with contrast (CPT® 70553) annually beginning at age 3
- Renal US (CPT® 76770) annually beginning at age 3. MRI Abdomen without and with contrast (CPT® 74183) can be substituted for Renal US annually in individuals with documented renal lesions
- Echocardiography annually beginning at age 4
- CT Chest without contrast (CPT® 71250) every 5 years beginning at age 18 years
  - CTs may be approved every 1 year for individuals with documented abnormalities
  - CT Chest without contrast should be approved for evaluation of any new pulmonary symptoms or worsening pulmonary function testing
- Individuals with TSC and known SEGA tumors should be imaged according to **PEDONC-4.2: Intracranial Low Grade Gliomas (LGG)**
- Individuals with TSC and known renal cell carcinoma should be imaged according to **PEDONC-7.4: Pediatric Renal Cell Carcinoma (RCC)**

**Background and Supporting Information**
- Inherited in an autosomal dominant manner (50% risk to offspring), affecting ~1 in 6000 individuals, it is associated with benign tumors, hypopigmented skin macules (ash leaf spots), pulmonary lymphangioleiomyomatosis, developmental delay, and epilepsy
- Malignancies associated with this syndrome include:
  - Subependymal giant cell astrocytomas (SEGA tumors)
    - Historically, early surgery was important to reduce morbidity related to these tumors
    - More recently, everolimus has been successfully used to treat these tumors without surgery, and early detection remains an important feature for success
  - Renal cell carcinoma
  - Cardiac rhabdomyosarcoma
  - Pulmonary lymphangioleiomyomatosis

**Recommended cancer screening includes:**
Ophthalmologic evaluation annually
**PEDONC-2.10: Von Hippel-Lindau Syndrome (VHL)**

**Recommended cancer screening imaging includes:**

- Octreotide study (CPT® 78800, CPT® 78801, CPT® 78802, CPT® 78803, or CPT® 78804) or Adrenal nuclear imaging (CPT® 78075) for elevated catecholamines or inconclusive adrenal mass on MRI

- MRI Brain without and with contrast (CPT® 70553) with attention to internal auditory canals if frequent ear infections are present

- MRI Brain without and with contrast (CPT® 70553)
  - Every 2 years beginning at age 12
  - Annually for any new or worsening symptoms or in individuals with known hemangioblastoma that has not been resected

- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, and Lumbar-CPT® 72158)
  - Every 2 years beginning at age 16
  - Annually for any new or worsening symptoms or in individuals with known hemangioblastoma that has not been resected

- Abdominal US (CPT® 76700) annually beginning at age 5

- MRI Abdomen without and with contrast (CPT® 74183) every 2 years beginning at age 16

- Individuals with VHL and known CNS hemangioblastoma should be imaged according to **PEDONC-4.2: Intracranial Low Grade Gliomas (LGG)**

- Individuals with VHL and known renal cell carcinoma should be imaged according to **PEDONC-7.4: Pediatric Renal Cell Carcinoma (RCC)**

- Individuals with VHL and known pheochromocytoma or other neuroendocrine tumors should be imaged according to guidelines in **ONC-15: Neuroendocrine Cancers and Adrenal Tumors**

**Background and Supporting Information**

Inherited in an autosomal dominant manner (50% risk to offspring), it is associated with CNS hemangioblastomas, retinal angiomas, endolymphatic sac tumors, renal cell carcinoma, pheochromocytomas, and other neuroendocrine tumors.

**Recommended cancer screening includes:**

- Annual ophthalmologic evaluation

- Annual measurement of catecholamines beginning at age 2

- Audiology assessment every 2 to 3 years beginning at age 5
**PEDONC-2.11: Rhabdoid Tumor Predisposition Syndrome**

Targeted advanced imaging (CT, MRI, PET) for any individual with this syndrome and any clinical symptoms to suggest malignancy.

**Background and Supporting Information**

- Inherited in an autosomal dominant manner (50% risk to offspring), it is associated with malignant rhabdoid tumors of the kidney and extrarenal locations, and atypical teratoid/rhabdoid tumors of the CNS. It is caused by a germline mutation in *INI1* or *SMARCB1*, and is associated with a more variable prognosis than de novo rhabdoid tumors.

- There is insufficient evidence to date to provide screening recommendations for advanced imaging.
PEDONC-2.12: Familial Retinoblastoma Syndrome

Ultrasound or MRI should be used if at all possible in lieu of CT or nuclear imaging, when advanced imaging is necessary, to avoid radiation exposure in these individuals.

**Background and Supporting Information**

- This syndrome is inherited in an autosomal dominant manner (50% risk to offspring). As the name suggests, it is associated with retinoblastoma, as well as osteosarcoma, pediatric melanoma, and a significantly increased risk for radiation-related malignancies.

- Regular physical and ophthalmologic evaluations under anesthesia are the hallmark of surveillance strategies for these individuals, and asymptomatic screening imaging does not have a defined role at this time.
PEDONC-2.13: Hereditary Paraganglioma-Pheochromocytoma Syndromes

The following recommended imaging can be approved:

- All individuals with \textit{SDHx} mutations:
  - MIBG imaging, see \textit{PEDONC-1.3: Modality General Considerations} for evaluation of elevated catecholamines
    - MRI without and with contrast or CT with contrast to evaluate abnormal MIBG findings

- Individuals with \textit{SDHC} or \textit{SDHD} mutations:
  - MRI Orbits/Face/Neck without and with contrast (CPT® 70543) every 2 years
  - MIBG imaging every 4 years, see \textit{PEDONC-1.3: Modality General Considerations}
    - MRI without and with contrast or CT with contrast to evaluate abnormal MIBG findings

- Individuals with \textit{SDHB} mutations:
  - CT chest (CPT® 71260) and CT Abdomen/Pelvis with contrast (CPT® 74177) or MRI chest (CPT® 71552), Abdomen (CPT® 74183), and Pelvis (CPT® 72197) without and with contrast, and every 2 years
  - MIBG imaging every 4 years, see: \textit{PEDONC-1.3: Modality General Considerations}

- Individuals with multiple endocrine neoplasias should not use this guideline and should be imaged according to: \textit{PEDONC-2.8: Multiple Endocrine Neoplasias (MEN)}

- Individuals with VHL and known pheochromocytoma or other neuroendocrine tumors should be imaged according to guidelines in \textit{ONC-15: Neuroendocrine Cancers and Adrenal}

\textit{Background and Supporting Information}

- Caused by mutations in SDHx genes, this syndrome is inherited in an autosomal dominant manner (50% risk to offspring), and is associated with pheochromocytomas and paragangliomas

- Cancer screening should begin at age 10 or at least 10 years before the youngest age at pheochromocytoma or paraganglioma diagnosis in the family history, whichever is earlier
**Recommended cancer screening:**

- All individuals with *SDHx* mutations:
  - Annual measurement of catecholamines
  - MIBG imaging, see [PEDONC-1.3: Modality General Considerations](#) for evaluation of elevated catecholamines

- For individuals with *SDHC* or *SDHD* mutations there is no documented role for PET/CT imaging in screening for these individuals

- For individuals with *SDHB* mutations there is no documented role for PET/CT imaging in screening for these individuals

- For individuals with *SDHA* or *SDH5* mutations, no specific imaging screening has been shown to improve individual outcomes to date
**PEDONC-2.14: Costello Syndrome**

**Recommended screening imaging includes:**

- Following initial diagnosis, any or all of the following:
  - Echocardiogram (CPT® 93306)
  - MRI Brain (CPT® 70553) without and with contrast
  - MRI Cervical (CPT® 72156) and Thoracic Spine (CPT® 72157) without and with contrast

- Ultrasound of the Abdomen (CPT® 76700) and Pelvis (CPT® 76856) every 3 months from birth to the 10\(^{th}\) birthday

- Echocardiogram (CPT® 93306) as requested for individuals with Costello Syndrome and known cardiac disease

- Individuals with Costello Syndrome and known rhabdomyosarcoma should be imaged according to guidelines in **PEDONC-8.2: Rhabdomyosarcoma (RMS)**

- Individuals with Costello Syndrome and known neuroblastoma should be imaged according to guidelines in **PEDONC-6: Neuroblastoma**

**Background and Supporting Information**

Caused by mutations in HRAS genes, this syndrome is inherited in an autosomal dominant manner (50% risk to offspring), and is associated with rhabdomyosarcoma and neuroblastoma in early childhood, and transitional cell cancer of the bladder in older children and adults.
References


45. Provenzale D, Gupta S, Ahnen DJ et al, National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2017—October 10, 2017, Genetic/Familial High-Risk Assessment: Colorectal, available at: https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf, Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Genetic/Familial High-Risk Assessment: Colorectal V3.2017 10/10/17. ©2017 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org


## PEDONC-3: Pediatric Leukemias

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PEDONC-3.1: Pediatric Leukemia General Considerations

- MRI Brain without and with contrast (CPT® 70553) for:
  - Individuals exhibiting CNS symptoms and
  - Individuals found to have high tumor burden on CSF cytology
- See ONC-29: Hematopoietic Stem Cell Transplantation for imaging guidelines related to transplant

Background and Supporting Information

- The overwhelming majority of leukemias occurring in children are acute. Chronic myelogenous leukemia (CML) is rare in children, and the occurrence of chronic lymphocytic leukemia (CLL) appears to have only been reported once in pediatric individuals to date
- There is not sufficient evidence to support the use of PET imaging for any indication in the management of acute lymphoblastic leukemia, acute myeloid leukemia, chronic myeloid leukemia
- Routine advanced imaging is not indicated in the evaluation and management of chronic myeloid leukemia in the absence of specific localizing clinical symptoms or clearance for hematopoietic stem cell transplantation
**PEDONC-3.2: Acute Lymphoblastic Leukemia (ALL)**

- **CXR** should be performed to evaluate for mediastinal mass in suspected cases or upon initial diagnosis.
  - CT Chest with contrast (CPT® 71260) immediately to evaluate for airway compression and anesthesia safety prior to attempting histologic diagnosis if mediastinal widening is seen on CXR.
  - Individuals with known or strongly suspected T-cell histology or other suspected lymphoblastic lymphoma involvement EITHER of the following for initial staging purposes:
    - CT Neck (CPT® 70491), CT Chest (CPT® 71260) and CT Abdomen and Pelvis (CPT® 74177) with contrast OR
    - PET/CT (CPT® 78815 or CPT® 78816)
- MRI Brain without and with contrast (CPT® 70553) for individuals exhibiting CNS symptoms and for individuals found to have high tumor burden on CSF cytology.

**Additional imaging in lymphoblastic lymphoma:**

- CT to assess response to therapy **only** for individuals with known bulky nodal disease (usually with T-cell histology) at the end of induction (4 to 6 weeks). Individuals with residual masses can be evaluated with every new therapy phase (consolidation, interim maintenance, etc., generally every 8 to 12 weeks) until disease resolution is seen.
- PET/CT (CPT® 78815) when residual mass ≥ 8 mm in diameter is present on recent CT imaging **and** there is documentation of how PET findings will affect immediate treatment decision making. These requests should be forwarded for Medical Director review.
- CXR or Abdominal ultrasound (CPT® 76700) **only**, as indicated by site(s) of bulky disease present at diagnosis, for further surveillance, once CT imaging shows no evidence of disease.
- CT of all involved bulky nodal areas for individuals with persistent residual masses performed as part of an end of therapy evaluation.

**Immunosuppression during ALL therapy:**

- Imaging requests for infectious disease concerns **for individuals with ALL with:**
  - Absolute neutrophil count (ANC) < 500 **or**
  - Inconclusive findings on chest x-ray **or** US at any ANC during active treatment.
Imaging during therapy for relapsed ALL:

- Frequent CT to evaluate known or suspected new sites of invasive fungal or other aggressive infections
- Surveillance imaging of asymptomatic individuals to detect invasive fungal infection only when acute clinical decisions will be made based on the imaging

Imaging of known or suspected osteonecrosis in ALL:

- MRI without contrast or without and with contrast of the affected joint(s) with symptoms suggesting osteonecrosis
  - CT without contrast when MRI is contraindicated or unavailable or for diagnosis of suspected subchondral fracture
- MRI Bilateral Hips (CPT® 73721 or CPT® 73723 with modifier -50) once at 6 to 9 months after diagnosis for individuals age ≥ 11 years
- Repeat MRI without contrast of the affected joint(s) every 2 cycles of maintenance (every 6 months) if reintroduction of corticosteroids is being considered in individuals whose symptoms have resolved and are still receiving active treatment
- MRI without contrast of the affected joint(s) for preoperative planning for individuals undergoing core decompression
- See PEDONC-19.4: Osteonecrosis in Long Term Cancer Survivors for information on osteonecrosis in ALL individuals who have completed therapy

Background and Supporting Information

- The majority of individuals with ALL have B-precursor ALL and routine advanced imaging is not necessary
- Individuals with B-precursor or T-cell lymphoblastic lymphoma without bone marrow involvement are treated similarly to leukemia individuals of the same cell type and should be imaged according to this guideline section
- This section does not apply to individuals with mature B-cell histology (primarily Burkitt’s in children). See PEDONC-5.3: Pediatric Aggressive Mature B-Cell Non-Hodgkin Lymphomas (NHL) for guidelines for these individuals
- Individuals with ALL are severely immunocompromised during the first 4 to 6 weeks of treatment (Induction) and any conventional imaging request to evaluate for infectious complications during this time frame should be approved immediately
- Individuals with ALL who relapse are treated with very intensive chemotherapy regimens and most spend the majority of their chemotherapy treatment phase in the hospital
- Individuals may have therapy-induced hypogammaglobulinemia which requires supplemental intravenous immune globulin (IVIG) during maintenance therapy. Those receiving supplemental IVIG should be treated similarly to those with ANC < 500 with regards to imaging for infectious disease
Osteonecrosis (ON) in individuals with ALL is a relatively common complication of ALL and its treatment, primary corticosteroids. Approximately 3% of younger children and 12 to 15% of adolescents are affected by ON at some point during therapy. The peak incidence occurs approximately one year from the time of diagnosis.

Screening MRI of asymptomatic individuals age ≤ 10 years to detect osteonecrosis has not been shown to impact outcomes, and it is not standard to alter treatment based on imaging findings alone without symptoms.

If osteonecrosis is detected on initial MRI, corticosteroids are often withheld during maintenance chemotherapy (but continued in earlier phases of therapy).
**PEDONC-3.3: Acute Myeloid Leukemia (AML)**

- Frequent CT or MRI imaging to evaluate known sites of invasive fungal infection due to the high risk of invasive infections
- Surveillance imaging of asymptomatic individuals to detect invasive fungal infection **only** when acute clinical decisions will be made based on the imaging

**Background and Supporting Information**

- The majority of AML individuals do not have any bulky disease and routine advanced imaging is not necessary
- Advanced imaging may be indicated for rare individuals with bulky tumor masses (chloromas) noted on physical examination or other imaging such as plain film or ultrasound
- AML individuals are treated with very intensive chemotherapy regimens and spend the majority of their chemotherapy treatment phase in the hospital
References


**PEDONC-4: Pediatric CNS Tumors**

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PEDONC-4.1: Pediatric CNS Tumors General Considerations

- MRI is the preferred imaging modality for all pediatric CNS tumors
  - MRI Brain without and with contrast (CPT® 70553) is the primary imaging study for pediatric brain tumors
  - MRI Brain without contrast (CPT® 70551) if requested for initial evaluation of suspected CNS tumor for children able to undergo MRI without sedation
  - Initial MRI should be performed without and with contrast in order to avoid a second anesthesia exposure in younger children requiring sedation for MRI

- CT for evaluation of ventriculomegaly or other operative considerations, or for children who cannot undergo MRI safely
  - CT for evaluation of headaches related to head trauma or evaluation of skull or facial bone abnormalities
  - MRA or CTA **only** for preoperative planning or to clarify inconclusive findings on MRI or CT

- MRI Brain without and with contrast (CPT® 70553) one time in the immediate preoperative period (even if another study has already been completed) to gain additional information which can be important in optimizing individual outcomes, such as:
  - Completion of additional specialized MRI sequences such as diffusion-tensor imaging, perfusion imaging, tractography, or other sequences not reported under a separate CPT® code but not part of a routine MRI Brain series
  - Repeat MRI Brain that is being requested solely for loading into operative navigation software should not be requested as a diagnostic code, but can be approved under a treatment planning code (CPT® 76498). These requests should be forwarded for Medical Director review

**MR Spectroscopy (MRS, CPT® 76390)**

- MRS is **only** supported for use in brain tumors of specified histologies where diagnostic accuracy has been established in peer-reviewed literature. See diagnosis-specific guidelines for MRS indications

- Requests for MRS should be forwarded for Medical Director review

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

- PET Brain Metabolic imaging (CPT® 78608) is **only** supported for use in brain tumors of specified histologies where diagnostic accuracy has been established in peer-reviewed literature. See diagnosis-specific guidelines for PET indications

- Requests for PET Brain Metabolic should be forwarded for Medical Director review
Background and Supporting Information

- Central nervous system tumors are the second most common form of childhood cancer, accounting for ~20% of all pediatric malignancies.

### Red Flag Symptoms Raising Suspicion for CNS Tumors Include:

<table>
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<td>Any headache complaint from a child age ≤ 5 years</td>
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<td>Headaches awakening from sleep</td>
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<td>Clumsiness (common description of gait or coordination problems in young children)</td>
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<td>New onset of seizure activity with focal features</td>
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- CT is not a recommended study for evaluation of pediatric headache when brain tumor is clinically suspected because of its limited diagnostic accuracy in this area. MRI should be used as first line imaging in these cases.

- CT should not be used in place of MRI to avoid sedation in young children when red flag symptoms for CNS tumors are present.

- Definitive imaging should be completed prior to considering biopsy given the high degree of morbidity associated with operating on the CNS.
  - Occasionally biopsy is not necessary because the imaging findings provide a definitive diagnosis. Examples include diffuse intrinsic pontine gliomas and optic pathway gliomas in an individual with known neurofibromatosis.

- Perioperative Imaging Frequency
  - Children may undergo very frequent imaging in the immediate perioperative period around resection or debulking of a CNS tumor due to the small anatomic spaces involved.
    - Requests for imaging during this time period to specifically evaluate postoperative course or ventriculoperitoneal shunt functioning should, in general, be approved as requested.

- MRS is considered investigational/experimental for all other histologies and indications not listed in a diagnosis-specific guideline section.

- MR Spectroscopy is not indicated for routine surveillance.

- PET Brain Metabolic imaging is considered investigational/experimental for all other histologies and indications not listed in a diagnosis-specific guideline section.

- PET Brain Perfusion imaging (CPT® 78609) is not indicated in the evaluation or management of primary CNS tumors.

- Fusion PET/CT studies (CPT® 78814, CPT® 78815, or CPT® 78816) are not indicated in the evaluation or management of primary CNS tumors.

- PET Brain Metabolic is not indicated for routine surveillance.
PEDONC-4.2: Intracranial Low Grade Gliomas (LGG)

- PET Brain Metabolic Imaging (CPT® 78608) to:
  - Determine need for biopsy when transformation to high grade glioma is suspected based on clinical symptoms or recent MRI findings
  - Evaluate a brain lesion of indeterminate nature when the PET findings will be used to determine whether biopsy/resection can be safely postponed

- MR Spectroscopy (MRS, CPT® 76390) to:
  - Distinguish low grade from high grade gliomas
  - Evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed
  - Distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy

Low Grade Gliomas Initial Staging:

- MRI Brain without and with contrast (CPT® 70553) for all LGG

- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158)
  - Spinal imaging is particularly recommended for:
    - Multicentric tumors
    - Intracranial leptomeningeal disease
    - Clinical signs or symptoms suggesting spinal cord involvement
    - MRI Spine with contrast (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) only if being performed immediately following a contrast-enhanced MRI Brain

Low Grade Gliomas Treatment Response:

- Children who have resection of the tumor can have:
  - MRI Brain without and with contrast (CPT® 70553) once following resection to establish baseline imaging. Those with a complete resection should then be imaged according to surveillance guidelines
  - MRI Brain without and with contrast (CPT® 70553) once at completion of radiotherapy for individuals age > 10 years with incompletely resected tumors who received adjuvant radiation therapy, then should be imaged according to surveillance guidelines
  - MRI Brain without and with contrast (CPT® 70553) every 2 cycles during active treatment and once at the end of planned chemotherapy for individuals age ≤ 10 years with incompletely resected tumors who received chemotherapy
  - Spinal imaging is only indicated during treatment response for individuals with evidence of spinal cord involvement at initial diagnosis
  - Spinal imaging every 2 cycles during induction chemotherapy for individuals with measurable spinal cord disease on MRI
**Low Grade Gliomas Surveillance**

- MRI Brain without and with contrast (CPT® 70553) after completion of therapy every 3 months for 2 years, and then every 6 months for 3 years, and then annually MRI Spine during surveillance in individuals without prior history of spinal involvement only to evaluate symptoms suspicious for spinal cord recurrence.

- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) with cord involvement at diagnosis after completion of therapy every 3 months for 2 years, then every 6 months for 3 years, and then annually.

- MRI Spine with contrast (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) only if being performed immediately following a contrast-enhanced MRI Brain.

**Background and Supporting Information**

- Low Grade Gliomas
  - Intracranial LGGs account for 40 to 60% of pediatric CNS tumors. These tumors are defined as having a WHO histologic grade of I or II (out of IV), can occur anywhere in the CNS, and includes the following tumors:
    - Pilocytic astrocytoma
    - Fibrillary (or diffuse) astrocytoma
    - Optic Pathway Gliomas
    - Pilomyxoid Astrocytoma
    - Oligodendroglioma
    - Oligoastrocytoma
    - Oligodendrocytoma
    - Subependymal Giant Cell Astrocytoma (SEGA)
    - Ganglioglioma
    - Gangliocytoma
    - Dysembryoplastic infantile astrocytoma (DIA)
    - Dysembryoplastic infantile ganglioglioma (DIG)
    - Dysembryoplastic neuroepithelial tumor (DNT)
    - Tectal plate gliomas
    - Cervicomedullary gliomas
    - Pleomorphic xanthoastrocytoma (PXA)
    - Any other glial tumor with a WHO grade of I or II

- Low Grade Gliomas Initial Staging
  - Children with neurofibromatosis and small optic pathway tumors may not undergo biopsy or resection and will proceed directly to treatment or surveillance.

- Low Grade Gliomas Treatment Response
  - Children with neurofibromatosis and small optic pathway gliomas may be observed without specific treatment and should be imaged according to surveillance guidelines for LGG.
Low Grade Gliomas Surveillance

- MRI Spine is not indicated during surveillance in individuals without prior history of spinal involvement except to evaluate symptoms suspicious for spinal cord recurrence.
- MR Spectroscopy and PET Brain Metabolic are not indicated for routine surveillance.
PEDONC-4.3: High Grade Gliomas (HGG)

PET Brain Metabolic Imaging (CPT® 78608) to:
- Distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy
- Evaluate inconclusive MRI findings when the PET findings will be used to determine need for biopsy or change in therapy, including a change from active therapy to surveillance
- Evaluate a brain lesion of indeterminate nature when the PET findings will be used to determine whether biopsy/resection can be safely postponed

MR Spectroscopy (MRS, CPT® 76390) to:
- Distinguish low grade from high grade gliomas
- Evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed
- Distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy

High Grade Gliomas Initial Staging

MRI Brain without and with contrast (CPT® 70553)

MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) and spinal imaging is particularly recommended for:
- Multicentric tumors
- Intracranial leptomeningeal disease
- Clinical signs or symptoms suggesting spinal cord involvement
- MRI Spine with contrast (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) only if being performed immediately following a contrast-enhanced MRI Brain

High Grade Gliomas Treatment Response

MRI Brain without and with contrast (CPT® 70553) once following resection to establish baseline imaging and those with a complete resection should then be imaged according to surveillance guidelines

MRI Brain without and with contrast (CPT® 70553) once at the end of adjuvant radiotherapy after a complete resection

MRI Brain without and with contrast (CPT® 70553) every 2 cycles during active treatment and at the end of planned chemotherapy for those with incompletely resected tumors treated with chemotherapy

Spinal imaging during treatment response only for individuals with evidence of spinal cord involvement at initial diagnosis

Spinal imaging every 2 cycles during induction chemotherapy for individuals with measurable spinal cord disease on MRI
**High Grade Gliomas Surveillance**

- MRI Brain without and with contrast (CPT® 70553) after completion of therapy every 3 months for 3 years, and then every 6 months
- MRI Spine may be indicated during surveillance in individuals without prior history of spinal involvement to evaluate symptoms suspicious for spinal cord recurrence
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) can be approved for individuals with cord involvement at diagnosis after completion of therapy every 3 months for 3 years, and then every 6 months thereafter
- MRI Spine can be performed with contrast (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) **only** if being performed immediately following a contrast-enhanced MRI Brain
- Individuals with documented residual masses can have annual imaging until 20 years after completion of therapy due to the risk of late transformation of these tumors
- For additional imaging guidelines for individuals in long term follow up after CNS tumor treatment that included radiation therapy, see **PEDONC-19.3: Second Malignant Neoplasms (SMN)**

**Background and Supporting Information**

- High Grade Gliomas (HGG)
  - Rare in children compared with the adult population, but represent 10 to 20% of pediatric CNS tumors. Prognosis is very poor, and survival significantly beyond 3 years from diagnosis is rare, even with complete surgical resection at initial diagnosis
  - These tumors are defined as having a WHO histologic grade of III or IV (out of IV can occur anywhere in the CNS (though the majority occur in the brain), and includes the following tumors:
    - Anaplastic astrocytoma
    - Glioblastoma multiform
    - Diffuse intrinsic pontine glioma (DIPG, or “brainstem glioma”)
    - Gliomatosis cerebri
    - Gliosarcoma
    - Anaplastic oligodendroglioma
    - Anaplastic ganglioglioma
    - Anaplastic mixed glioma
    - Anaplastic mixed ganglioneuronal tumors
    - Any other glial tumor with a WHO grade of III or IV
  - PET Brain is not indicated in gliomas occurring in the brain stem due to poor uptake and lack of impact on individuals outcomes
- High Grade Gliomas Surveillance
  - MR Spectroscopy and PET Brain metabolic are not indicated for routine surveillance
**PEDONC-4.4: Medulloblastoma (MDB), Supratentorial Primitive Neuroectodermal Tumors (sPNET), and Pineoblastoma**

- PET Brain Metabolic Imaging (CPT® 78608) to:
  - Distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy
  - Evaluate inconclusive MRI findings when the PET findings will be used to determine need for biopsy or change in therapy, including a change from active therapy to surveillance
  - Evaluate a brain lesion of indeterminate nature when the PET findings will be used to determine whether biopsy/resection can be safely postponed

- MR Spectroscopy (CPT® 76390) to evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed

**Medulloblastoma, sPNET, Pineoblastoma Initial Staging:**

- MRI Brain without and with contrast (CPT® 70553) preoperatively
- MRI Brain without and with contrast (CPT® 70553) postoperatively (preferably within 48 hours of surgery) to quantify residual tumor volume
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) either preoperatively or within 28 days postoperatively
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
- Medulloblastoma, sPNET, Pineoblastoma Treatment Response: MRI Brain without and with contrast (CPT® 70553) and MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) at the start of adjuvant chemotherapy and every 2 cycles until therapy is completed
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
- MRI Brain without and with contrast (CPT® 70553) and MRI Spine (with or without and with contrast) as part of end-of-treatment evaluation
Medulloblastoma, sPNET, Pineoblastoma Surveillance

- MRI Brain without and with contrast (CPT® 70553) after completion of therapy every 3 months for 2 years, then every 6 months for 3 years, then annually
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) after completion of therapy every 3 months for 2 years, then every 6 months for 3 years, and then annually
- MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain

Background and Supporting Information

Medulloblastoma (MDB), Supratentorial Primitive Neuroectodermal Tumors (sPNET), and Pineoblastoma account for 15 to 25% of pediatric CNS tumors; prognosis is generally favorable. Leptomeningeal spread is common and can occur after initial diagnosis.

Includes the Following Tumors:

- Medulloblastoma and Pineoblastoma
- sPNET
  - Medulloepithelioma
  - Cerebral or cerebellar neuroblastoma
  - Cerebral or cerebellar ganglioneuroblastoma
  - Ependymoblastoma

Risk Assessment is Important in Determining Optimal Treatment

High risk features include the following:

- Spinal metastasis (including cytology positive only)
- Multifocal intracranial tumors
- Anaplastic histology
- All sPNET and pineoblastomas
- > 1.5 cm² residual tumor area on postoperative MRI and age < 3 years

Individuals without any high risk features are considered “Average Risk”

- Individuals generally proceed to chemoradiotherapy within 31 days of surgical resection. All individuals receive adjuvant chemotherapy lasting 6 to 12 months that begins ~6 weeks after completion of chemoradiotherapy
- Children age < 3 years are often treated with multiple cycles of high dose chemotherapy with autologous stem cell rescue in lieu of radiotherapy, and disease evaluations may occur prior to each cycle (every 4 to 6 weeks) if needed for response determination
- MR Spectroscopy and PET Brain Metabolic are not indicated for routine surveillance.
PEDONC-4.5: Atypical Teratoid/Rhabdoid Tumors (ATRT)

- Rhabdoid malignancies occurring outside the CNS should be imaged according to PEDONC-7.6: Malignant Rhabdoid Tumor of the Kidney (MRT) and Other Extracranial Sites

**Atypical Teratoid/Rhabdoid Tumor Initial Staging:**

- MRI Brain without and with contrast (CPT® 70553) preoperatively
- MRI Brain without and with contrast (CPT® 70553) (preferably within 48 hours of surgery) to quantify residual tumor volume postoperatively
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) either preoperatively or within 28 days postoperatively
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
- Renal US (CPT® 76770) to evaluate for renal masses at initial diagnosis
  - CT Abdomen/Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) if a renal lesion is detected on US
  - If a renal lesion is also present, imaging guidelines for MRT should be followed. See: PEDONC-7.6: Malignant Rhabdoid Tumor of the Kidney (MRT) and Other Extracranial Sites
- MR Spectroscopy (CPT® 76390) to evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed

**Atypical Teratoid/Rhabdoid Tumor Treatment Response:**

- MRI Brain without and with contrast (CPT® 70553) and MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) after every 2 cycles of induction chemotherapy
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
- MRI Brain without and with contrast (CPT® 70553) and MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) for children receiving consolidation chemotherapy prior to each cycle (every 4 to 6 weeks) if needed for response determination and following the end of the planned stem cell rescues
- MRI performed at the end of consolidation therapy should serve as the diagnostic MRI prior to radiotherapy (if the individual is receiving radiotherapy after chemotherapy)
- MRI Brain without and with contrast (CPT® 70553) and MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) at the end of all planned therapy
MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain

**Atypical Teratoid/Rhabdoid Tumor Surveillance**
- MRI Brain without and with contrast (CPT® 70553) after completion of therapy every 3 months for 2 years, then every 6 months for 3 years, and then annually thereafter
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) after completion of therapy every 3 months for 2 years, then every 6 months for 3 years, and then annually thereafter
- MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain

**Background and Supporting Information**
- Highly aggressive tumor occurring primarily in very young children that has a clinical presentation very similar to medulloblastoma with a much higher rate of leptomeningeal spread. Metastases can occur outside the CNS, and associated tumors can also arise in the kidneys (Malignant Rhabdoid Tumor of the Kidney, MRT)
- Overall prognosis is poor, with < 20% of individuals surviving beyond 2 years from diagnosis
- PET Brain Metabolic does not have a defined role in the evaluation of ATRT at this time
- Individuals generally proceed to induction chemotherapy shortly following surgical resection or biopsy
- Children with ATRT are often treated using consolidation chemotherapy with 2 to 4 cycles of high dose chemotherapy with autologous stem cell rescue
- Death from recurrent disease later than 8 years from the end of therapy is rare and routine advanced imaging is not warranted for these individuals.
- For additional imaging guidelines for individuals in long-term follow up after CNS tumor treatment that included radiation therapy, see **PEDONC-19.3: Second Malignant Neoplasms (SMN)**
PEDONC-4.6: Pineocytomas

Pineocytomas Initial Staging:
- MRI Brain without and with contrast (CPT® 70553)
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) for:
  - Multicentric tumors
  - Atypical histology including pineoblastoma-like elements
  - Clinical signs or symptoms suggesting spinal cord involvement
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) can be approved if being performed immediately following a contrast-enhanced MRI Brain

Pineocytomas Treatment Response:
- MRI Brain without and with contrast (CPT® 70553) following resection to establish baseline imaging in individuals with a complete resection. Additional imaging: see surveillance guidelines
- MRI Brain without and with contrast (CPT® 70553) for individuals with incomplete resection receiving adjuvant radiotherapy at completion of radiotherapy. Additional imaging: see surveillance guidelines
  - Spinal imaging for treatment response is only indicated with evidence of spinal cord involvement at initial diagnosis
  - Spinal imaging for treatment response at completion of radiotherapy with measurable spinal cord disease on MRI

Pineocytomas Surveillance:
- MRI Brain without and with contrast (CPT® 70553) after completion of therapy every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, then annually thereafter MRI Spine during surveillance only with prior history of spinal involvement to evaluate symptoms suspicious for spinal cord recurrence
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) with cord involvement at diagnosis after completion of therapy then every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, then annually
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
Background and Supporting Information

- Low grade malignancy that is similar in presentation to LGG
- PET Brain Metabolic imaging and MR Spectroscopy do not have a defined role in the evaluation of pineocytoma
- Surgical resection is curative for most individuals
- As late progression can occur surveillance continues for the life of the individual
- For additional imaging guidelines for individuals in long term follow up after CNS tumor treatment that included radiation therapy, see PEDONC-19.3: Second Malignant Neoplasms (SMN)
**PEDONC-4.7: CNS Germinomas and Non-Germinomatous Germ Cell Tumors (NGGCT)**

- MR Spectroscopy (CPT® 76390) to evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed

**CNS Germinoma & NGGCT Initial Staging**

- MRI Brain without and with contrast (CPT® 70553)
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158)
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain

**CNS Germinoma & NGGCT Treatment Response:**

- Individuals receiving chemotherapy following surgical resection or biopsy:
  - MRI Brain without and with contrast (CPT® 70553) after every 2 cycles of induction chemotherapy
  - MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) at the end of induction chemotherapy for localized intracranial tumors
    - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
    - Spinal imaging is appropriate every 2 cycles during induction chemotherapy for individuals with measurable spinal cord disease on MRI
- MRI of all known sites of measurable disease prior to planned second-look surgery and/or prior to radiotherapy following completion of chemotherapy
- MRI Brain without and with contrast (CPT® 70553) and MRI Spine (with OR without and with contrast) at the end of all planned therapy
CNS Germinoma & NGGCT Surveillance:
- MRI Brain without and with contrast (CPT® 70553) every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, and then annually until 5 years after completion of therapy
  - For additional imaging guidelines for individuals in long-term follow up after CNS tumor treatment that included radiation therapy, see PEDONC-19.3: Second Malignant Neoplasms (SMN)
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, and then annually until 5 years after completion of therapy
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain

Background and Supporting Information
- More common in older school age children and younger adolescents, but can occur throughout the pediatric age range. Although leptomeningeal spread is common, prognosis is excellent due to high sensitivity to chemotherapy and radiotherapy

Includes the Following Tumors:
- CNS Germinoma
- Non-Germinomatous Germ Cell Tumors (NGGCT)
  - Embryonal carcinoma
  - Yolk sac tumor
  - Choriocarcinoma
  - Teratoma
  - Mixed germ cell tumor

- PET Metabolic Brain imaging does not have a defined role in the evaluation of CNS GCT
- Individuals generally proceed to chemotherapy shortly following surgical resection or biopsy and will usually receive 2 to 4 cycles.
PEDONC-4.8: Ependymoma

MR Spectroscopy (CPT® 76390) to evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed

Ependymoma Initial Staging:
- MRI Brain without and with contrast (CPT® 70553)
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158)
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if performed immediately following a contrast-enhanced MRI Brain

Ependymoma Treatment Response:
- MRI Brain or involved spinal level(s) without and with contrast (CPT® 70553) once following resection to establish baseline imaging:
  - In individuals with complete resection for subsequent requests: see surveillance guidelines
  - In individuals with incomplete resection or high risk histology receiving adjuvant radiation therapy:
    - MRI Brain or involved spinal level(s) without and with contrast (CPT® 70553) once at the completion of radiotherapy. For subsequent requests: see surveillance guidelines
    - MRI Brain or involved spinal level(s) without and with contrast (CPT® 70553) in individuals receiving chemotherapy:
      - Every 2 cycles during active treatment
      - At the end of planned chemotherapy
    - MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) at the end of induction chemotherapy for localized intracranial tumors
    - MRI Brain without and with contrast (CPT® 70553) at the end of induction chemotherapy for localized intraspinal tumors
      - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
- MRI of all known sites of measurable disease prior to planned second-look surgery and/or prior to radiotherapy following completion of chemotherapy
- MRI Brain without and with contrast (CPT® 70553) and MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) at the end of all planned therapy
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
**Ependymoma Surveillance:**

- For individuals with primary **intracranial** ependymoma:
  - MRI Brain without and with contrast (CPT® 70553) after completion of therapy every 3 months for 1 year, then every 6 months for 1 year, then annually thereafter
  - MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) annually for 2 years after completion of therapy with no history of spinal cord involvement
  - MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) for individuals with metastatic cord involvement at diagnosis after completion of therapy, every 3 months for 1 year, then every 6 months for 1 year, then annually thereafter
    - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain

- For individuals with primary **intraspinal** ependymoma:
  - MRI without and with contrast of the involved spinal level(s) after completion of therapy every 3 months for 1 year, then every 6 months for 1 year, and then annually
  - MRI Brain without and with contrast (CPT® 70553) annually for 2 years after completion of therapy with no history of intracranial involvement
  - MRI Brain without and with contrast (CPT® 70553) for metastatic intracranial involvement at diagnosis after completion of therapy every 3 months for 1 year then every 6 months for 1 year, and then annually

**Background and Supporting Information**

- Occur primarily intracranially, roughly 2/3 in the posterior fossa. Overall prognosis is very good, with supratentorial tumors faring better. Primary spinal tumors can also occur, and are more common in adults than children and adolescents
- Surgery is the primary treatment modality. Radiotherapy +/- chemotherapy is used for:
  - Incompletely resected tumors
  - Anaplastic histology
  - Infratentorial location
- PET Brain Metabolic imaging does not have a defined role in the evaluation of ependymoma
- MR Spectroscopy is not indicated for routine surveillance
PEDONC-4.9: Malignant Tumors of the Spinal Cord

- MRI Spine without and with contrast of all involved levels of the primary site(s) (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158)
  - Entire spine imaging may be indicated based on the histologic type
- MRI Brain without and with contrast (CPT® 70553) at initial diagnosis, but may be not be necessary during treatment response and surveillance

Background and Supporting Information

- Treatment principles are the same as tumors of the brain, and should follow imaging guidelines according to the specific histologic type
- Multiple spinal cord tumors should raise suspicion for neurofibromatosis
- Common histologies of primary spinal cord tumor in children include:
  - Low Grade Glioma, see PEDONC-4.2: Intracranial Low Grade Gliomas (LGG) for guidelines
  - Ependymoma, see PEDONC-4.8: Ependymoma for guidelines
- Any type of malignant spinal cord tumor can occur, but other histologies are rare
- Given the rarity of primary spinal cord tumors in children, MRI Brain requests should, in general, be approved for surveillance after recent evaluation by a physician with significant training and/or experience in pediatric spinal cord tumors (most commonly a pediatric neurosurgeon or pediatric oncologist) as the need for intracranial surveillance is highly individualized.
- Asymptomatic surveillance imaging should generally end at the time point appropriate for the specific tumor type
**PEDONC-4.10: Craniopharyngioma and Pituitary Tumors**

**Craniopharyngioma Initial Staging:**
- MRI Brain without and with contrast (CPT® 70553)
- CT imaging can demonstrate calcifications but is usually unnecessary if MRI is completed
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) for:
  - Multicentric tumors
  - Clinical signs or symptoms suggesting spinal cord involvement
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain

**Craniopharyngioma Treatment Response:**
- MRI Brain without and with contrast (CPT® 70553) following resection to establish baseline imaging for individuals with a complete resection. Additional imaging: see surveillance guidelines
- MRI Brain (CPT® 70553) at completion of radiotherapy for individuals with incomplete resection receiving adjuvant therapy. Additional imaging: see surveillance guidelines
- MRI Brain without and with contrast (CPT® 70553) for the rare individual treated with chemotherapy every 2 cycles during active treatment and at the end of planned chemotherapy
  - Spinal imaging every 2 cycles during induction chemotherapy with measurable spinal cord disease on MRI

**Craniopharyngioma Surveillance:**
- MRI Brain without and with contrast (CPT® 70553) every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, and then annually until 10 years after completion of therapy as late progressions can occur
- For additional imaging guidelines for individuals in long-term follow up after CNS tumor treatment that included radiation therapy, see **PEDONC-19.3: Second Malignant Neoplasms (SMN)**
- MRI Spine is only indicated during surveillance with prior history of spinal involvement to evaluate symptoms suspicious for spinal cord recurrence
Background and Supporting Information

- Imaging guidelines and treatment approaches for pediatric pituitary tumors other than craniopharyngioma are consistent with those used for adults with pituitary tumors. For these tumors follow guidelines in **HD-19: Pituitary**
- Craniopharyngiomas are less common, accounting for 6 to 8% of pediatric CNS tumors. Most commonly affects children in the preadolescent ages
- PET Brain Metabolic imaging and MR Spectroscopy do not have a defined role in the evaluation of Craniopharyngioma
PEDONC-4.11: Primary CNS Lymphoma

- Primary CNS lymphoma imaging indications in pediatric individuals are identical to those for adult individuals. See ONC-2.7: CNS Lymphoma (also known as Mircoglioma) for imaging guidelines.

- CNS Lymphomas also involving bone marrow and/or lymph nodes should be imaged according to: PEDONC-5.3: Pediatric Aggressive Mature B-Cell Non-Hodgkin Lymphomas (NHL)

**Background and Supporting Information**

Primary CNS Lymphoma is a solitary or multifocal mass occurring in the brain without evidence of systemic (bone marrow or lymph node) involvement. Usually associated with immunodeficiency, this is a very rare entity in pediatrics accounting for < 0.1% of pediatric malignancies, so age-specific guidelines have not been established.
**PEDONC-4.12: Meningiomas**

- Meningioma imaging indications in pediatric individuals are identical to those for adult individuals. See **ONC-2.8: Meningiomas (Intracranial and Intraspinal)** for imaging guidelines.

**Background and Supporting Information**

- Account for 1 to 3% of pediatric CNS tumors. Usually associated with neurofibromatosis type 2 (NF-2) or prior therapeutic radiation exposure to the brain. Lifetime risk may be as high as 20% for young children receiving whole brain radiotherapy, most commonly occurring 15 to 20 years after radiation exposure.
**PEDONC-4.13: Choroid Plexus Tumors**

MR Spectroscopy (CPT® 76390) to evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed

**Choroid Plexus Papilloma:**
- MRI Brain without and with contrast (CPT® 70553)
- MRI Brain without and with contrast (CPT® 70553) may be repeated if return of hydrocephalus is suspected or seen on CT imaging

**Choroid Plexus Adenoma or Atypical Choroid Plexus Papilloma:**
- MRI Brain without and with contrast (CPT® 70553)
- Spinal imaging if requested at initial diagnosis
- MRI Brain without and with contrast (CPT® 70553) may be repeated if return of hydrocephalus is suspected or seen on CT imaging

**Choroid Plexus Carcinoma Initial Staging:**
- MRI Brain without and with contrast (CPT® 70553)
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158)
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
**Choroid Plexus Carcinoma Treatment Response:**

- MRI Brain without and with contrast (CPT® 70553) once following resection to establish baseline imaging in an individual with **complete** resection. Additional imaging: see surveillance guidelines.

- MRI Brain without and with contrast (CPT® 70553) once at the completion of radiotherapy in an individual with **incomplete** resection and receiving adjuvant radiation therapy. Additional imaging: see surveillance guidelines.

- MRI Brain without and with contrast (CPT® 70553) for individuals treated with chemotherapy every 2 cycles during active treatment at the end of planned chemotherapy.

  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain.
  - Spinal imaging every 2 cycles during induction chemotherapy for measurable spinal cord disease on MRI.

- MRI of all known sites of measurable disease following completion of chemotherapy prior to second-look surgery and prior to radiotherapy.

- MRI Brain without and with contrast (CPT® 70553) and MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) at the end of all planned therapy.
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain.

**Choroid Plexus Carcinoma Surveillance**

- MRI Brain without and with contrast (CPT® 70553) every 4 months for 3 years, then every 6 months for 2 years after completion of therapy.

- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) with no history of spinal cord involvement at 12 and 24 months after completion of therapy.

- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) every 4 months for 3 years, then every 6 months for 2 years after completion of therapy for cord involvement at diagnosis.
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain.
**Background and Supporting Information**

As a group these account for 1 to 4% of pediatric CNS tumors, and 70% of choroid plexus tumors present within the first 2 years of life.

- Includes the following tumors:
  - Choroid plexus papilloma
  - Choroid plexus adenoma, or atypical choroid plexus papilloma
  - Choroid plexus carcinoma

- PET Metabolic Brain imaging does not have a defined role in the evaluation of choroid plexus tumors.

- Choroid Plexus Papillomas outnumber other choroid plexus tumors by 4 to 5 times. These ventricular tumors commonly present with hydrocephalus caused by increased CSF production, resulting in signs of increased intracranial pressure. Appearance on MRI Brain without and with contrast (CPT® 70553) is typical, and they are usually treated by excision.

- Choroid Plexus Adenomas or Atypical Choroid Plexus Papillomas are extremely rare tumors with features midway in the malignant spectrum between papillomas and carcinomas. They are more prone to local invasion, but rarely to metastasis. Presenting symptoms are similar to papillomas. Appearance on MRI Brain without and with contrast (CPT® 70553) is typical, and they are usually treated by excision.

- Choroid Plexus Carcinoma is a very aggressive malignancy, with high rates of metastasis to other parts of the CNS. Prognosis is significantly less favorable than for papillomas with overall survival rates of 35 to 40%.

- Surgical resection is curative for many individuals with Choroid Plexus Carcinoma.

- For additional imaging guidelines for individuals in long-term follow up after CNS tumor treatment that included radiation therapy, see PEDONC-19.3: Second Malignant Neoplasms (SMN).

- MR Spectroscopy is not indicated for routine surveillance.
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### PEDONC-5: Pediatric Lymphomas

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**PEDONC-5.1: Pediatric Lymphoma General Considerations**

- Pediatric lymphomas are generally Hodgkin Lymphomas, Aggressive B-Cell Non-Hodgkin Lymphomas, Lymphoblastic Lymphomas, or Anaplastic Large Cell Lymphomas.

- Individuals with Lymphoblastic Lymphoma (even those with bulky nodal disease) are treated using the leukemia treatment plan appropriate to the cell type (B or T cell).
  - These individuals should be imaged using guidelines in **PEDONC-3.2: Acute Lymphoblastic Leukemia (ALL)**

- Other histologies are rare in pediatric individuals, and should be imaged according to the following guidelines:
  - Follicular lymphoma: **ONC-27.3: Follicular Lymphoma**
  - Marginal zone or MALT lymphomas: **ONC-27.4: Marginal Zone Lymphoma**
  - Mantle cell lymphomas: **ONC-27.5: Mantle Cell Lymphoma**
  - Cutaneous lymphomas: **ONC-27.8: Cutaneous Lymphoma and T Cell Lymphomas**
    - Exception: Cutaneous B-Lymphoblastic Lymphoma should be imaged using guidelines in **PEDONC-3.2: Acute Lymphoblastic Leukemia (ALL)**
  - Castleman's Disease: **ONC-31.11: Castleman's Disease (Unicentric and Multicentric)**

- All CT imaging recommended in this section refers to CT with contrast only.
  - Noncontrast CT imaging has not been shown to be beneficial in the management of pediatric lymphomas.
  - Given the limited utility of noncontrast CT imaging in pediatric lymphomas, MRI without or without and with contrast is recommended in place of CT for individuals who cannot tolerate CT contrast due to allergy or impaired renal function.

- MRI without and with contrast of symptomatic or previously involved bony areas can be approved in known lymphoma individuals without prior plain x-ray or bone scan evaluation.
  - Bone scan is inferior to MRI for evaluation of known or suspected bone metastases in lymphoma.

- MRI Brain without and with contrast (CPT® 70553) is the preferred study for evaluation of suspected brain metastases in pediatric lymphoma.
  - CT Head with (CPT® 70460) or without and with contrast (CPT® 70470) can be approved when MRI is contraindicated.
PEDONC-5.2: Pediatric Hodgkin Lymphoma (HL)

Pediatric Hodgkin Lymphoma Initial Staging

- CT Neck (CPT® 70491), CT Chest (CPT® 71260), and CT Abdomen/Pelvis (CPT® 74177), and CT with contrast or MRI without and with contrast for any other symptomatic body area. See: PEDONC-5.1: Pediatric Lymphoma General Considerations

- PET/CT (CPT® 78815) for initial staging and can be performed prior to biopsy if necessary
  - Whole body PET/CT (CPT® 78816) if there is clinical suspicion of skull or distal lower extremity involvement

- Rarely, CT or MRI of other body areas based on physical findings or PET/CT results. See: PEDONC-5.1: Pediatric Lymphoma General Considerations

Pediatric Hodgkin Lymphoma Treatment Response

- Restaging for treatment response as often as every 2 cycles of chemotherapy

- Both CT Neck (CPT® 70491), CT Chest (CPT® 71260), and CT Abdomen/Pelvis (CPT® 74177) and other previously involved areas and PET/CT (CPT® 78815) during early treatment response evaluations as decisions about chemotherapy drug selection and radiation treatment are frequently made based on both anatomic (CT-based) and metabolic (PET/CT-based) responses
  - PET/CT for treatment response after cycles 1 and 3 instead of cycles 2 and 4 for low risk (stage IA or IIA) mixed cellularity Hodgkin lymphoma,

- Once an individual has a negative PET/CT (either Deauville or Lugano 1, 2 or 3 as reported in formal radiology interpretation), all subsequent treatment response evaluations should use CT only, including end of therapy evaluation

Pediatric Hodgkin Lymphoma Surveillance:

- CT Neck (CPT® 70491), CT Chest (CPT® 71260), CT Abdomen and Pelvis (CPT® 74177) and other previously involved or currently symptomatic areas OR PET/CT (CPT® 78815 or CPT® 78816) for any individual with clinical symptoms suggesting recurrence

- Stage I or II HL
  - CT Neck/Chest (CPT® 70491 and CPT® 71260) and other previously involved areas at 6 months and 12 months after completing therapy

- Stage III or IV HL:
  - CT Neck (CPT® 70491), CT Chest (CPT® 71260), and CT Abdomen/Pelvis (CPT® 74177) and other previously involved areas at 6 months and 12 months after completing therapy

- Recurrent HL with no evidence of disease following successful treatment
  - CT of the Neck/Chest/Abdomen/Pelvis every 3 months for 1 year after completing therapy for recurrence
PET/CT can be approved to clarify inconclusive findings on conventional imaging to evaluate the need for biopsy to establish recurrence. These requests should be forwarded for Medical Director review.

**Background and Supporting Information**

- Most individuals experiencing recurrence are detected based on physical findings, and frequent CT surveillance imaging of Hodgkin lymphoma after completion of therapy does not improve post-recurrence overall survival.
- Advanced imaging may include multiple fields as pediatric individuals have a high rate of neck and Waldeyer’s ring involvement with Hodgkin lymphoma.
- Surveillance except at 6 months and 12 months from the end of therapy should use physical exam and CXR only.
**PEDONC-5.3: Pediatric Aggressive Mature B-Cell Non-Hodgkin Lymphomas (NHL)**

**Pediatric Aggressive Mature B-Cell NHL Initial Staging**
- CT Neck (CPT® 70491), CT Chest (CPT® 71260), and CT Abdomen/Pelvis (CPT® 74177) and CT with contrast or MRI without and with contrast for any other symptomatic body areas. See PEDONC-5.1: Pediatric Lymphoma General Considerations.
- MRI Brain without and with contrast (CPT® 70553) if symptoms or extent of disease suggest intracranial extension (skull base involvement, for example) or metastasis.
- PET/CT (CPT® 78815) for initial staging
  - Whole body PET/CT (CPT® 78816) if there is clinical suspicion of skull or distal lower extremity involvement.
- PET/CT should be approved for treatment response in these cases as these lymphomas are nearly universally FDG-avid.

**Pediatric Aggressive Mature B-Cell NHL Treatment Response**
- CT with contrast or MRI without and with contrast of previously involved areas can be performed around Day 6 of low intensity therapy to evaluate response and to determine the next steps in therapy.
- CT with contrast or MRI without and with contrast (should be same modality as initial diagnosis if possible) of previously involved areas and PET/CT can be performed following initial response evaluation
  - Restaging for treatment response as often as every cycle of chemotherapy (~every 3 weeks).
- Once an individual has a negative PET/CT (either Deauville or Lugano 1, 2 or 3 as reported in formal radiology interpretation), all subsequent treatment response evaluations should use CT imaging only, including end of therapy evaluation
  - PET/CT to assess disease activity in inconclusive residual masses seen on conventional imaging.

**Pediatric Aggressive Mature B-Cell NHL Surveillance**
- CXR and Ultrasound Abdomen (CPT® 76700) and Ultrasound Pelvis (CPT® 76856) are sufficient to follow asymptomatic individuals with residual masses in the chest or abdomen/pelvis.
- CT Neck (CPT® 70491), CT Chest (CPT® 71260), CT Abdomen and Pelvis (CPT® 74177) and other previously involved or currently symptomatic areas OR PET/CT (CPT® 78815 or CPT® 78816) for any individual with clinical symptoms or laboratory findings suggesting recurrence
  - PET/CT (CPT® 78815) can be approved for suspected PTLD recurrence with documentation of new palpable nodes, rising LDH, or rising quantitative EBV PCR.
PET/CT to clarify inconclusive findings on conventional imaging to evaluate the need for biopsy to establish recurrence. These requests should be forwarded for Medical Director review.

**Background and Supporting Information**

- Aggressive Mature B-Cell NHL includes all of the following diagnoses, all of which should be imaged according to this section:
  - Burkitt’s lymphoma/leukemia (BL)
  - Diffuse Large B-Cell Lymphoma (DLBCL)
  - Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
  - Post-transplant lymphoproliferative disorder (PTLD): most commonly occurs following solid organ transplantation
  - Viral-associated lymphoproliferative disorders: most commonly occurs following hematopoietic stem cell transplantation or in individuals with primary immunodeficiency

- Due to the extremely aggressive nature of this group of tumors (the doubling time can be as short as 8 hours), it may not be possible to obtain PET/CT prior to therapy initiation.

- Initial treatment is 7 days of low intensity therapy, with early response evaluation determining next steps in therapy using CT with contrast or MRI without and with contrast of previously involved areas performed around Day 6.
  - Individuals are customarily still inpatient for this evaluation so outpatient requests should be rare for this time point.

- Routine asymptomatic surveillance with advanced imaging has not been found to impact outcomes as the majority of these individuals present clinically at relapse due to the highly aggressive nature of these lymphomas

- Surveillance imaging with CT or MRI has not been shown to improve outcomes following recurrence and is not the standard of care.
PEDONC-5.4: Anaplastic Large Cell Lymphoma (ALCL)

**Anaplastic Large Cell Lymphoma Initial Staging:**
- CT Neck/Chest/Abdomen/Pelvis (CPT® 70491, CPT® 71260, and CPT® 74177) and CT with contrast or MRI without and with contrast of any other symptomatic body area. See PEDONC-5.1: Pediatric Lymphoma General Considerations
- PET/CT (CPT® 78815) for initial staging can be performed prior to biopsy if necessary to accommodate scheduling
  - Whole body PET/CT (CPT® 78816) if there is clinical suspicion of skull or distal lower extremity involvement
- CT or MRI of other body areas for individuals based on physical findings or PET/CT results
  - Rarely individuals will have primary tumor sites outside the Neck→Pelvis region, and MRI without and with contrast may be substituted for soft tissue extremity or paraspinal primary masses as necessary

**Anaplastic Large Cell Lymphoma Treatment Response:**
- CT with contrast or MRI without and with contrast for restaging for treatment response of previously involved areas (should be same modality as initial diagnosis if possible) at the end of induction chemotherapy (commonly 4 to 6 weeks)
- CT or PET/CT of previously involved areas for individuals treated with cytotoxic chemotherapy to assess treatment response as often as every 2 cycles of chemotherapy as decisions about chemotherapy drug selection and radiation treatment can be made based on either anatomic or metabolic responses
  - If CT is performed for primary treatment response, PET/CT can be approved to clarify inconclusive findings detected on conventional imaging
  - If PET/CT is performed for primary treatment response, CT or MRI can be approved to clarify inconclusive findings detected on PET imaging
- Once an individual has a negative PET/CT (either Deauville or Lugano 1, 2 or 3 as reported in formal radiology interpretation), all subsequent treatment response evaluations should use CT imaging only, including end of therapy evaluation

**Anaplastic Large Cell Lymphoma Surveillance**
- CT Neck (CPT® 70491), CT Chest (CPT® 71260), CT Abdomen/Pelvis (CPT® 74177) and other previously involved or currently symptomatic areas for clinical symptoms suggesting recurrence
- CT with contrast or MRI without and with contrast of all previously involved areas after therapy is completed at 3 months, 6 months, 12 months and, 18 months
- PET/CT to clarify inconclusive findings on conventional imaging to evaluate the need for biopsy to establish recurrence. These requests should be forwarded for Medical Director review
References


PEDONC-6: Neuroblastoma

- PET imaging is rarely indicated in neuroblastoma but is indicated in the following situations:
  - Whole Body PET (CPT® 78816) rather than MIBG for metabolic tumor assessment for individuals with MIBG-negativity documented at initial diagnosis,
  - MIBG should be continued for individuals who are MIBG positive at diagnosis and then become MIBG negative in response to treatment (See PEDONC-1.3: Modality General Considerations) for metabolic imaging indications
    - PET at major decision points, such as hematopoietic stem cell transplantation or surgery if MIBG and CT/MRI findings are inconclusive.
  - Individuals currently receiving medications that may interfere with MIBG uptake and that cannot safely be discontinued prior to imaging, including:
    - Tricyclic antidepressants (amitriptyline, imipramine, etc.)
    - Selective serotonin reuptake inhibitors (SSRI’s, sertraline, paroxetine, escitalopram, etc.)
    - Neuroleptics (risperidone, haloperidol, etc.)
    - Antihypertensive drugs (alpha or beta blockers, calcium channel blockers)
    - Decongestants (phenylephrine, ephedrine, pseudoephedrine)
    - Stimulants (methylphenidate, dextroamphetamine, etc.)
  - PET should only be approved for this indication when specific documentation of the medication interaction is included with the current PET imaging request. These requests will be forwarded for Medical Director review.

Neuroblastoma Initial Staging

- CT Neck/Chest/Abdomen/Pelvis with contrast (CPT® 70491, CPT® 71260, and CPT® 74177) or MRI Neck/Chest/Abdomen/Pelvis without and with contrast (CPT® 70543, CPT® 71552, CPT® 74183, and CPT® 72197)
- MRI without and with contrast is preferred for evaluation of paraspinal tumors where cord compression is a possibility
- Metabolic imaging in neuroblastoma:
  - Adrenal nuclear imaging (CPT® 78075) when CT or MRI is inconclusive, for evaluation of suspected adrenal neuroblastoma, ganglioneuroblastoma, or ganglioneuroma
  - Occasionally MIBG cannot be performed prior to initiation of therapy in this circumstance MIBG should be completed within 3 weeks of therapy initiation as the reduction in MIBG avidity in response to chemotherapy is not immediate
- MRI Brain without and with contrast (CPT® 70553) is preferred for evaluation of brain metastases (rare) if clinical signs/symptoms suggest brain involvement

Neuroblastoma Treatment Response Imaging (Risk Group Dependent)
Risk Grouping will not be known at the time of initial staging, but is critical for all imaging decisions after initial staging is complete (see Background and Supporting Information – Staging and Risk Grouping – Neuroblastoma for details)
**Very Low Risk and Low Risk Neuroblastoma not receiving chemotherapy:**
- CT with contrast or MRI without and with contrast of the primary tumor site 6 to 8 weeks after diagnosis to determine if additional treatment is necessary

**All Intermediate Risk Neuroblastoma and Very Low Risk or Low Risk Neuroblastoma receiving chemotherapy**
- Treatment response assessment every 2 cycles of chemotherapy (~every 6 weeks and at the end of planned treatment):
  - CT Chest/Abdomen/Pelvis (CPT® 71260, and CPT® 74177) with contrast or MRI without and with contrast (CPT® 71552, CPT® 74183, and CPT® 72197), and other sites with prior measurable disease
  - MIBG scan every 4 cycles and at the end of planned treatment. See **PEDONC-1.3: Modality General Considerations**

**High Risk Neuroblastoma:**
- Treatment response assessment every 2 cycles of chemotherapy, monoclonal antibody (mAb), or biologic therapy (~every 6 weeks):
  - CT Chest/Abdomen/Pelvis (CPT® 71260, and CPT® 74177) with contrast or MRI without and with contrast (CPT® 71552, CPT® 74183, and CPT® 72197), and other sites with prior measurable disease
  - MIBG scan see **PEDONC-1.3: Modality General Considerations**
  - MIBG scan is also indicated following ¹³¹I-MIBG therapy
  - Treatment response assessment at every change in modality (prior to surgery, HSCT, XRT, and mAb therapy).
  - More frequent imaging around the time of surgery if needed for preoperative planning.

**Neuroblastoma Surveillance Imaging (Risk Group Dependent):**

**Very Low Risk and Low Risk Neuroblastoma:**
- CT with contrast or MRI without and with contrast of the primary tumor site 3, 6, 9, 12, 18, 24, and 36 months after surgery
  - If negative at 36 months, no further advanced imaging is necessary
    - Ultrasound may be sufficient to evaluate the primary tumor site for certain individuals and may be approved if requested to replace CT or MRI

**Intermediate Risk Neuroblastoma:**
- CT with contrast or MRI without and with contrast of the primary tumor and known metastatic sites at 3, 6, 9, 12, 18, 24, and 36 months after completion of therapy
  - If negative at 36 months, no further advanced imaging is necessary
    - Ultrasound may be sufficient to evaluate the primary tumor site for certain individuals and may be approved if requested to replace CT or MR
  - MIBG scan at 3, 6, 9, 12, 24, and 36 months after completion of therapy for all individuals with stage 4 or M disease or individuals with stage 4S or MS disease and positive MIBG at completion of therapy
    - See **PEDONC-1.3: Modality General Considerations**
      - If negative at 36 months, no further MIBG imaging is necessary
**High Risk Neuroblastoma:**
- CT with contrast or MRI without and with contrast of the primary tumor site at 3, 6, 9, 12, 18, 24, 30, 36, 42, 48, 54, and 60 months then annually until 10 years after completion of therapy. If negative at 10 years, no further advanced imaging is necessary
- MIBG scan at 3, 6, 9, 12, 18, 24, 30, and 36 months after completion of therapy
  - See PEDONC-1.3: Modality General Considerations
  - If negative at 36 months, no further MIBG or PET imaging is necessary.

**Background and Supporting Information**
- Neuroblastoma is the most common extracranial solid tumor of childhood, and may be divided into very low, low, intermediate, and high risk disease based on International Neuroblastoma Risk Group (INRG) Staging System. The treatments for each disease group vary widely and have distinct imaging strategies
- 90 to 95% of neuroblastomas secrete the catecholamine metabolites homovanillic acid (HVA) and vannilylmandelic acid (VMA) in the urine, and Urine HVA/VMA should be performed at every disease evaluation for individuals with positive HVA or VMA at diagnosis
- Esthesioneuroblastoma should be imaged according to guidelines in ONC-3: Squamous Cell Carcinomas Of The Head And Neck

**Neuroblastoma Initial Staging**
- MIBG scintigraphy is the preferred metabolic imaging for neuroblastoma and is positive in 90 to 95% of neuroblastomas
- MIBG provides superior sensitivity and sensitivity for detecting viable osseous disease compared with bone scintigraphy so technetium bone scan is not necessary when MIBG is utilized
- Most MIBG imaging studies are SPECT/CT studies using CT for localization only. Separate diagnostic CT codes should not be approved for this purpose
- Inability to complete MIBG before starting therapy is not an indication to approve PET imaging
- MRI Brain of asymptomatic individuals with no history of brain metastases is not indicated for neuroblastoma

**Neuroblastoma Treatment Response Imaging (Risk Group Dependent)**
- Risk Grouping will not be known at the time of initial staging, but is critical for all imaging decisions after initial staging is complete. The treating oncologist should always know the individual’s risk grouping. It is not possible to establish the appropriate imaging plan for an individual with neuroblastoma without knowing his/her risk group

**Very Low Risk and Low Risk Neuroblastoma Not Receiving Chemotherapy**
- Many individuals will be treated with surgical resection only without adjuvant therapy, so individuals enter immediately into surveillance
**All Intermediate Risk Neuroblastoma and Very Low Risk or Low Risk**

- Individuals generally receive 2 to 12 cycles of moderate-intensity chemotherapy depending on response to treatment
- Surgical resection may occur prior to or following chemotherapy depending on disease stage. Restaging prior to surgery is appropriate
- Treatment response in addition to imaging with:
  - Urine HVA/VMA if positive at diagnosis
  - Bone marrow aspiration/biopsy if positive at diagnosis

**High Risk Neuroblastoma:**

- This group of individuals receives highly aggressive therapy using sequential chemotherapy, surgery, stem cell rescue, radiotherapy, monoclonal antibody (mAb) therapy, and biologic therapy
- Treatment response with:
  - Urine HVA/VMA (if positive at diagnosis)
  - Bone marrow aspiration/biopsy if positive at diagnosis
- Treatment response assessment is necessary at every change in modality (prior to surgery, HSCT, XRT, and mAb therapy)
- More frequent imaging can be approved around the time of surgery if needed for preoperative planning

**Neuroblastoma Surveillance Imaging (Risk Group Dependent):**

**Very Low Risk and Low Risk Neuroblastoma:**

- Urine HVA/VMA (if positive at diagnosis) at 1, 2, 3, 6, 9, 12, 18, 24, 36, 48, and 60 months after surgery
- MIBG is not indicated for surveillance of low risk neuroblastoma, but can be used to clarify findings suspicious for disease recurrence
- CT Chest is not indicated in asymptomatic surveillance imaging of neuroblastoma individuals with no prior history of thoracic disease

**Intermediate Risk Neuroblastoma:**

- Urine HVA/VMA (if positive at diagnosis) every month until 12 months after completion of therapy, then at 14, 16, 18, 21, 24, 30, and 36 months after completion of therapy, and then annually until 10 years after completion of therapy
- With the exception of individuals with stage 4 or M disease or those with stage 4S or MS disease and positive MIBG at the complete of therapy MIBG (or PET, if MIBG-negative at initial diagnosis) during surveillance is not indicated for individuals with intermediate risk neuroblastoma
- CT Chest is not indicated in asymptomatic surveillance imaging of neuroblastoma individuals with no prior history of thoracic disease.
**High Risk Neuroblastoma:**
- Urine HVA/VMA (if positive at diagnosis) at 3, 6, 9, 12, 18, 24, 30, 36, 42, 48, 54, and 60 months after completion of therapy, then annually until 10 years after completion of therapy.
- Early detection of recurrence with $^{123}$I-MIBG has been shown to improve post-relapse outcomes in high risk neuroblastoma
- CT Chest is not indicated in asymptomatic surveillance imaging of neuroblastoma individuals with no prior history of thoracic disease

**Staging and Risk Grouping - Neuroblastoma**
- Risk Grouping will not be known at the time of initial staging, but is critical for all imaging decisions after initial staging is complete. **The treating oncologist should always know the individual's risk grouping.** It is not possible to establish the appropriate imaging plan for an individual with neuroblastoma without knowing his/her risk group.
- Most recent treatment protocols are using the recently validated International Neuroblastoma Risk Group (INRG) Staging System, which is primarily defined by the complexity of local tumor extension and the presence or absence of distant metastases:
  - **L1:** Localized tumor not involving vital structures as defined by the list of image-defined risk factors and confined to one body compartment
    - **Image-defined risk factors** include a list of specific imaging findings defining individuals less likely to be candidates for complete surgical resection these risk factors involve the encasement of any of the following:
      - Major blood vessels
      - Airway
      - Skull base
      - Costovertebral junction
      - Brachial plexus
      - Spinal canal
      - Major organs or structures
  - **L2:** Logoregional tumor with presence of one or more image-defined risk factors
  - **M:** Distant metastatic disease (except stage MS)
  - **MS:** Metastatic disease in children younger than 18 months with metastases confined to skin, liver, and/or bone marrow with $< 10\%$ involvement (MIBG must be negative in bone and bone marrow)
- Neuroblastoma was historically staged according to the International Neuroblastoma Staging System (INSS) which uses age, histology, sites of disease, and MYCN status to determine appropriate therapy, and some standard protocols for neuroblastoma treatment still use this staging system:
  - **Stage 1:** Localized tumor with complete gross excision, with or without microscopic residual disease; representative ipsilateral lymph nodes negative for tumor microscopically (nodes attached to and removed with the primary tumor may be positive)
- Stage 2A: Localized tumor with incomplete gross resection; representative ipsilateral non-adherent lymph nodes negative for tumor microscopically
- Stage 2B: Localized tumor with or without complete gross excision, with ipsilateral non-adherent lymph nodes positive for tumor; enlarged contralateral lymph nodes must be negative microscopically
- Stage 3: Localized tumor with or without complete gross excision, with ipsilateral non-adherent lymph nodes positive for tumor; enlarged contralateral lymph nodes must be negative microscopically
  - The midline is defined as the vertebral column. Tumors originating on one side and crossing the midline must infiltrate to or beyond the opposite side of the vertebral column
- Stage 4: Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs (except as defined for Stage 4S)
- Stage 4S: Infants < 1 year of age with localized primary tumor (as defined for Stage 1, 2A or 2B) with dissemination limited to skin, liver, and/or bone marrow with < 10% involvement
## INRG Neuroblastoma Risk Grouping

### Very Low Risk Neuroblastoma (28% of individuals, event-free survival > 85%)
- Stage L1 or L2 maturing ganglioneuroma or intermixed ganglioneuroblastoma
- Stage MS individuals meeting all of the following:
  - Age < 18 months
  - Without MYCN amplification
  - Without 11q aberration

### Low Risk Neuroblastoma (27% of individuals, event-free survival > 75 to ≤ 85%)
- Stage L2 individuals age < 18 months meeting all of the following:
  - Any histology except maturing ganglioneuroma or intermixed ganglioneuroblastoma
  - Without MYCN amplification
  - Without 11q aberration
- Stage L2 individuals age ≥ 18 months meeting all of the following:
  - Differentiating neuroblastoma or nodular ganglioneuroblastoma
  - Without MYCN amplification
  - Without 11q aberration
- Stage M individuals meeting all of the following:
  - Age < 18 months
  - Without MYCN amplification
  - With hyperdiploidy (tumor DNA index > 1)

### Intermediate Risk Neuroblastoma (9% of individuals, event-free survival ≥ 50 to ≤ 75%)
- Stage L2 individuals age < 18 months meeting all of the following:
  - Any histology except maturing ganglioneuroma or intermixed ganglioneuroblastoma
  - With 11q aberration
- Stage L2 individuals age ≥ 18 months meeting all of the following:
  - Neuroblastoma or nodular ganglioneuroblastoma
  - Without MYCN amplification
  - With 11q aberration
- Stage M individuals meeting all of the following:
  - Age < 18 months
  - Without MYCN amplification
  - With diploidy (tumor DNA index = 1)

### High Risk Neuroblastoma (36% of individuals, event-free survival < 50%, includes the following)
- All individuals age ≥ 18 months with stage M disease regardless of other factors
- All individuals with neuroblastoma and MYCN amplification regardless of other factors
- All stage MS individuals with 11q aberration regardless of other factors
<table>
<thead>
<tr>
<th>INSS Neuroblastoma Risk Grouping</th>
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<tbody>
<tr>
<td><strong>Low Risk Neuroblastoma</strong> (overall survival 99%, includes the following)</td>
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<tr>
<td>- All stage 1 individuals regardless of other factors</td>
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<tr>
<td>- Stage 2A/2B individuals meeting all of the following:</td>
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<tr>
<td>- Without MYCN amplification</td>
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<tr>
<td>- With $\geq 50%$ tumor resection</td>
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<tr>
<td>- No clinical symptoms</td>
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<tr>
<td>- Stage 4S individuals meeting all of the following:</td>
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<tr>
<td>- Without MYCN amplification</td>
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<tr>
<td>- With favorable INPC histology,</td>
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<tr>
<td>- Tumor DNA index &gt; 1</td>
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<tr>
<td>- No clinical symptoms</td>
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<tr>
<th>Intermediate Risk Neuroblastoma (overall survival 96%, includes the following)</th>
</tr>
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<tbody>
<tr>
<td>- Stage 2A/2B individuals with any of the following:</td>
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<tr>
<td>- $&lt; 50%$ tumor resection or</td>
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<td>- With clinical symptoms</td>
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<tr>
<td>- Stage 3 individuals with any of the following:</td>
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<tr>
<td>- Age $&lt; 18$ months with no high risk features</td>
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<tr>
<td>- Age $\geq 18$ months with favorable INPC histology</td>
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<tr>
<td>- Stage 4 individuals with any of the following:</td>
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<tr>
<td>- Age $&lt; 12$ months with no high risk features</td>
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<tr>
<td>- Age $\geq 12$ and $&lt; 18$ months with favorable INPC histology and tumor DNA index &gt; 1</td>
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<tr>
<td>- Stage 4S individuals with any of the following:</td>
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<tr>
<td>- Without MYCN amplification</td>
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<tr>
<td>- With unfavorable INPC histology</td>
</tr>
<tr>
<td>- Tumor DNA index = 1</td>
</tr>
<tr>
<td>- Clinical symptoms</td>
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</tbody>
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<tr>
<th>High Risk Neuroblastoma (overall survival $\sim40%$, includes the following)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- All individuals age $\geq 18$ months with stage 4 disease regardless of other factors</td>
</tr>
<tr>
<td>- All individuals with stages 2-4 or 4S disease and MYCN amplification regardless of other factors</td>
</tr>
<tr>
<td>- All stage 3 individuals age $\geq 18$ months with unfavorable INPC histology</td>
</tr>
<tr>
<td>- All stage 4 individuals age $\geq 12$ months with unfavorable INPC histology or tumor DNA index = 1</td>
</tr>
</tbody>
</table>
References


## PEDONC-7: Pediatric Renal Tumors

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PEDONC-7.1: Pediatric Renal Tumors General Considerations

A variety of tumors can occur in the pediatric kidney, and include the following:

- Wilms Tumor
  - Favorable histology (FHWT)
  - Focal anaplasia (FAWT)
  - Diffuse anaplasia (DAWT)
  - Bilateral Wilms Tumor (BWT)
- Renal Cell Carcinoma (RCC)
- Clear Cell Sarcoma of the Kidney (CCSK)
- Malignant Rhabdoid Tumor of the Kidney (MRT)
- Congenital Mesoblastic Nephroma (CMN)
- Other Cancers occurring in the Kidney:
  - Neuroblastoma
  - Primitive Neuroectodermal Tumor
  - Rhabdomyosarcoma
  - Non-Rhabdomyosarcoma Soft Tissue Sarcomas

These and other rare tumors have been reported occurring primarily in the kidney and should be imaged according to the guidelines for the specific histologic diagnosis.
**PEDONC-7.2: Unilateral Wilms Tumor (UWT)**

### Unilateral Wilms Tumor Initial Staging:
- CT Abdomen/Pelvis with contrast (CPT® 74177)
  - If bilateral renal lesions are noted on ultrasound or CT, MRI Abdomen (CPT® 74183) and Pelvis (CPT® 72197) without and with contrast should be strongly considered for better characterization
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) should be completed prior to anesthesia exposure if possible
- MRI Brain without and with contrast (CPT® 70553) for initial staging for neurologic signs or symptoms raising suspicion of CNS metastases
  - Bone scan (See PEDONC-1.3: Modality General Considerations) for any individual with signs or symptoms raising suspicion of bony metastases

### Unilateral Wilms Tumor Treatment Response:
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned therapy
- CT Abdomen/Pelvis with contrast (CPT® 74177) or MRI Abdomen (CPT® 74183) and Pelvis (CPT® 72197) without and with contrast every 2 cycles during treatment and at the end of planned therapy
- PET may be indicated to assess treatment response in Wilms tumor in rare circumstances to establish the presence of active disease only when a major therapeutic decision depends on PET avidity. These requests will be forwarded for Medical Director review.

### Unilateral Wilms Tumor Surveillance Imaging:
- Very low risk FHWT treated with nephrectomy only:
  - CT Chest with (CPT® 71260), CT Chest without contrast (CPT® 71250) or chest x-ray at 3, 6, 12, and 18 months after nephrectomy
  - CT Abdomen and Pelvis with contrast (CPT® 74177) or Abdomen and Pelvis ultrasound (CPT® 76700 and CPT® 76506) at 3, 6, 12, and 18 months after nephrectomy
  - Surveillance pelvic imaging in this group due to higher risk of recurrence in surgery only treatment
  - Other surveillance imaging should be by Abdominal US (CPT® 76700) and CXR
- FHWT treated with chemotherapy with or without XRT:
  - CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 6 months for 3 years after completion of all therapy
  - CT Abdomen with contrast (CPT® 74160), MRI Abdomen without and with contrast (CPT® 74183), or Abdominal ultrasound (CPT® 76700) every 6 months for 3 years after completion of all therapy
  - Pelvic imaging is only indicated for surveillance when prior pelvic involvement has been documented or there was tumor rupture at diagnosis
  - Other surveillance imaging should be by Abdominal US and CXR
FAWT or DAWT treated with chemotherapy with or without XRT:
- CT Chest with (CPT® 71260) or Chest CT without contrast (CPT® 71250) every 3 months for 2 years after completion of all therapy
- CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) every 3 months for 2 years after completion of all therapy
- Abdominal US (CPT® 76700) and CXR for other surveillance imaging

Surveillance imaging with CT of the Chest/Abdomen/Pelvis (CPT® 71260 and CPT® 74177) following successful treatment for recurrent unilateral Wilms Tumor every 3 months for 1 year after completing therapy for recurrence. Surveillance imaging later than 12 months after completing therapy for recurrence should follow the standard timing listed in this surveillance section

**Background and Supporting Information**
- Many individuals will present with an asymptomatic abdominal mass and will undergo ultrasound as a primary evaluation. Doppler ultrasound to evaluate for tumor thrombus is no longer necessary unless CT findings are inconclusive, and should not be performed if CT is already completed
- MRI Brain without and with contrast (CPT® 70553) for initial staging for neurologic signs or symptoms raising suspicion of CNS metastases as only ~0.5% of Wilms Tumor individuals will ever develop brain metastases
  - Bone scan (See [PEDONC-1.3: Modality General Considerations](#)) for signs or symptoms raising suspicion of bony metastases
- PET is not indicated in the initial staging of any pediatric renal tumor
- A very low risk subset of stage I FHWT will be observed after nephrectomy and enter directly into surveillance
- The majority of individuals will receive chemotherapy with or without XRT, beginning within 14 days of initial surgery
- There are no data to support the use of PET imaging for routine surveillance in any individual with Wilms Tumor
**PEDONC-7.3: Bilateral Wilms Tumor (BWT)**

**Bilateral Wilms Tumor Initial Staging:**
- MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197)
  - CT Abdomen and Pelvis with contrast (CPT® 74177) is often performed prior to discovery of bilateral lesions and should not prevent MRI from being approved
  - CT Abdomen and Pelvis with contrast (CPT® 74177) may be used for individuals with a contraindication to MRI
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) during the initial workup of all pediatric renal tumors and should be completed prior to anesthesia exposure if possible
- MRI Brain without and with contrast (CPT® 70553) for initial staging with neurologic signs or symptoms raising suspicion of CNS metastases
  - Bone scan (See **PEDONC-1.3: Modality General Considerations**) for any individual with signs or symptoms raising suspicion of bony metastases

**Bilateral Wilms Tumor Treatment Response:**
- MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) every 2 cycles during treatment and at the end of planned therapy
  - CT Abdomen and Pelvis with contrast (CPT® 74177) for individuals with a contraindication to MRI
  - Advanced imaging for disease evaluation at week 6, if treating with chemotherapy without a biopsy:
    - If either tumor has not shrunk 50%, then open biopsy to confirm favorable histology
    - If partial nephrectomy still not feasible at week 6, the next disease evaluation is at week 12
    - Surgical resection should occur no later than week 12
- CT Chest with (CPT® 71260) or without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned therapy
- PET to assess treatment response in Wilms tumor in rare circumstances to establish the presence of active disease only when a major therapeutic decision depends on PET avidity. These requests will be forwarded for Medical Director review
**Bilateral Wilms Tumor Surveillance Imaging:**
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 6 months for 3 years after completion of all therapy
- CT Abdomen with contrast (CPT® 74160) or MRI Abdomen without and with contrast (CPT® 74183):
  - Every 6 months for 3 years after completion of therapy
  - “Extra” one-time imaging at 3 months after completion of all therapy
  - Pelvic imaging for surveillance only if prior pelvic involvement has been documented or there was tumor rupture at diagnosis
- Abdominal US (CPT® 76700) and CXR for other surveillance
  - Screening Abdominal US every 3 months until age 8 when CT or MRI Abdomen are no longer indicated individuals with bilateral Wilms Tumor
- CT of the Chest/Abdomen/Pelvis (CPT® 71260 and CPT® 74177) for surveillance following successful treatment for recurrent bilateral Wilms Tumor:
  - Every 3 months for 1 year after completing therapy for recurrence
  - Surveillance imaging more than 12 months after completing therapy for recurrence should follow the standard timing listed in this surveillance section

**Background and Supporting Information**
- Many individuals will present with an asymptomatic abdominal mass and will undergo ultrasound as a primary evaluation. Doppler ultrasound to evaluate for tumor thrombus is no longer necessary unless CT findings are inconclusive, and should not be performed if CT is already completed
- Individuals with bilateral Wilms Tumor may begin therapy without a histologic diagnosis to preserve a localized disease stage and attempt to shrink the tumors to allow for renal-sparing surgical approaches
- MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) is the preferred imaging modality for individuals with bilateral Wilms tumor
- MRI Brain without and with contrast (CPT®70553) for initial staging for neurologic signs or symptoms raising suspicion of CNS metastases as only ~0.5% of Wilms Tumor individuals will ever develop brain metastases
- Avoidance of anesthesia exposure is not a contraindication to MRI for these individuals
  - Bone scan (See PEDONC-1.3: Modality General Considerations) for any individual with signs or symptoms raising suspicion of bony metastases
- PET is not indicated in the initial staging of any pediatric renal tumor
- PET is not routinely utilized to assess treatment response in Wilms tumor
- Extra” one-time imaging is supported at 3 months after completion of all therapy because close surgical margins occur frequently in individuals undergoing nephron-sparing surgical approaches, and the risk for early local recurrence is higher
**PEDONC-7.4: Pediatric Renal Cell Carcinoma (RCC)**

**Pediatric Renal Cell Carcinoma Initial Staging:**
- CT Abdomen and Pelvis with contrast (CPT® 74177)
  - MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) should be strongly considered if bilateral renal lesions are noted on ultrasound or CT
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) should be completed prior to anesthesia exposure if possible
- Other staging imaging should be deferred until a histologic diagnosis is made by complete nephrectomy for most unilateral renal tumors and biopsy for bilateral renal tumors or inoperable unilateral tumors
- MRI Brain without and with contrast (CPT® 70553) with neurologic signs or symptoms raising suspicion of CNS metastases

**Pediatric Renal Cell Carcinoma Treatment Response:**
- CT Chest with (CPT® 71260) or Chest CT without contrast (CPT® 71250) and CT Abdomen with contrast (CPT® 74160) every 2 cycles during active treatment for individuals with residual measurable disease after initial surgery and receiving adjuvant medical therapy
- Pelvic imaging only when prior pelvic involvement has been documented
- PET to assess treatment response in Pediatric RCC to establish the presence of active disease only when a major therapeutic decision depends on PET avidity. These requests will be forwarded for Medical Director review

**Pediatric Renal Cell Carcinoma Surveillance Imaging:**
- All Pediatric RCC individuals:
  - MRI Brain without and with contrast (CPT® 70553) every 6 months for 2 years after completion of all therapy only with documented CNS metastases or new signs/symptoms suggestive of CNS recurrence
- TFE3 or TFEB subtype:
  - CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 3 months for 2 years, then every 6 months for 2 years after completion of all therapy
  - CT Abdomen with contrast (CPT® 74160) or MRI Abdomen without and with contrast (CPT® 74183) every 3 months for 2 years, then every 6 months for 2 years after completion of all therapy
  - Pelvic imaging for surveillance when prior pelvic involvement has been documented
- All other histologies:
  - Surveillance imaging is appropriate as listed in the adult Oncology Imaging Guidelines: **ONC-17.4: Surveillance**
Background and Supporting Information

- A majority of pediatric cases have a novel subtype involving TFE3 or TFEB translocations, which have a different natural history than "adult type" RCC. Individuals of any age with TFE3 or TFEB translocated RCC should be imaged according to this guideline section.

- 40 to 45% of pediatric RCC cases have similar histologies to adult RCC (clear cell, papillary, chromophobe, etc.) and imaging decisions will be similar to adult oncology guidelines. Individuals with all other subtypes of RCC should be imaged according to ONC-17: Renal Cell Cancer (RCC).

- Many individuals will present with an asymptomatic abdominal mass and will undergo ultrasound as a primary evaluation. Doppler ultrasound to evaluate for tumor thrombus is no longer necessary unless CT findings are inconclusive, and should not be performed if CT is already completed.

- Most individuals will have surgical resection of all disease at the time of diagnosis and will enter directly into surveillance.

- PET is not routinely utilized to assess treatment response in Pediatric RCC.
**PEDONC-7.5: Clear Cell Sarcoma of the Kidney (CCSK)**

**Clear Cell Sarcoma of the Kidney Initial Staging:**
- CT Abdomen and Pelvis with contrast (CPT® 74177)
  - MRI Abdomen and Pelvis without and with contrast should be strongly considered if bilateral renal lesions are noted on ultrasound or CT
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) should be completed prior to anesthesia exposure if possible
- Other staging imaging should be deferred until a histologic diagnosis is made, by complete nephrectomy for most unilateral renal tumors and biopsy for bilateral renal tumors or inoperable unilateral tumors
- MRI Brain without and with contrast (CPT® 70553) for initial staging
- Bone scan (see **PEDONC-1.3: Modality General Considerations**)

**Clear Cell Sarcoma of the Kidney Treatment Response:**
- CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned therapy
- CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) every 6 weeks during treatment and at the end of planned therapy
- MRI Brain without and with contrast (CPT® 70553) every 2 cycles during treatment for individuals with CNS metastases at initial staging and at the end of planned therapy
  - Bone scan (see **PEDONC-1.3: Modality General Considerations**) at the end of planned therapy
- PET to assess treatment response in rare circumstances to establish the presence of active disease only when a major therapeutic decision depends on PET avidity. These requests will be forwarded for Medical Director review.

**Clear Cell Sarcoma of the Kidney Surveillance Imaging:**
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 3 months for 2 years after completion of all therapy
- CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) every 3 months for 2 years after completion of all therapy
- MRI Brain without and with contrast (CPT® 70553) every 6 months for 3 years after completion of all therapy
  - Bone scan (see **PEDONC-1.3: Modality General Considerations**) every 3 months for 1 year, then every 6 months for 1 year after completion of all therapy and if negative at 36 months, no further advanced imaging is necessary
- Abdominal US (CPT® 76700) and CXR for other surveillance imaging
Background and Supporting Information
- Be careful not to confuse the diagnosis with clear cell RCC. See ONC-17: Renal Cell Cancer (RCC) for imaging guidelines
- Many individuals will present with an asymptomatic abdominal mass and will undergo ultrasound as a primary evaluation. Doppler ultrasound to evaluate for tumor thrombus is no longer necessary unless CT findings are inconclusive, and should not be performed if CT is already completed
- PET is not indicated in the initial staging of any pediatric renal tumor
- PET is not routinely utilized to assess treatment response
PEDONC-7.6: Malignant Rhabdoid Tumor of the Kidney (MRT) and Other Extracranial Sites

Malignant Rhabdoid Tumor Initial Staging:
- CT Abdomen and Pelvis with contrast (CPT® 74177)
  - MRI Abdomen and Pelvis without and with contrast should be strongly considered if bilateral renal lesions are noted on ultrasound or CT
- CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) should be completed prior to anesthesia exposure if possible
- Other staging imaging should be deferred until a histologic diagnosis is made, by complete nephrectomy for most unilateral renal tumors and biopsy for bilateral renal tumors or inoperable unilateral tumors
- MRI Brain without and with contrast (CPT® 70553) with MRT of the kidney or other non-CNS site
  - Bone scan (see PEDONC-1.3: Modality General Considerations)

Malignant Rhabdoid Tumor Treatment Response:
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned therapy
- CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) every 2 cycles during treatment and at the end of planned therapy
- CT with contrast or MRI without and with contrast of primary site in place of abdominal and pelvic imaging if primary site other than kidney
- MRI Brain without and with contrast (CPT® 70553) every 2 cycles during treatment with CNS metastases at initial staging and at the end of planned therapy
- PET may be indicated to assess treatment response to establish the presence of active disease only when a major therapeutic decision depends on PET avidity. These requests will be forwarded for Medical Director review

Malignant Rhabdoid Tumor Surveillance Imaging
- CT Chest with (CPT® 71260) or without contrast (CPT® 71250) every 3 months for 2 years after completion of all therapy
- CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) every 3 months for 3 years after completion of all therapy
  - CT with contrast or MRI without and with contrast of primary site in place of abdominal imaging if primary site other than kidney
- MRI Brain without and with contrast (CPT® 70553) every 3 months for 1 year, then every 6 months for 1 year after completion of all therapy
- Abdominal US (CPT® 76700) and CXR for other surveillance imaging
- Bone scan see [PEDONC-1.3: Modality General Considerations](#) every 3 months for 1 year, then every 6 months for 1 year after completion of all therapy only if positive at initial diagnosis. If negative at 36 months, no further advanced imaging is necessary

**Background and Supporting Information**

- Be careful not to confuse the diagnosis with rhabdomyosarcoma. See [PEDONC-8.2: Rhabdomyosarcoma (RMS)](#) for imaging guidelines
- MRT is a highly aggressive histologic variant that can also occur in other locations and all non-CNS sites should follow these guidelines
- Primary CNS rhabdoid malignancies should be imaged according to [PEDONC-4.5: Atypical Teratoid/Rhabdoid Tumors (ATRT)](#)
  - Many individuals will present with an asymptomatic abdominal mass and will undergo ultrasound as a primary evaluation. Doppler ultrasound to evaluate for tumor thrombus is no longer necessary unless CT findings are inconclusive, and should not be performed if CT is already completed
- PET is not indicated in the initial staging of any pediatric renal tumor
- PET is not routinely utilized to assess treatment response in MRT
**PEDONC-7.7: Congenital Mesoblastic Nephroma (CMN)**

**Congenital Mesoblastic Nephroma Initial Staging:**
- CT Abdomen and Pelvis with contrast (CPT® 74177)
- CT Chest with (CPT® 71260) to evaluate inconclusive findings on chest x-ray

**Congenital Mesoblastic Nephroma Treatment Response:**
- CT Abdomen and Pelvis with contrast (CPT® 74177) once following resection to establish baseline imaging, and those with a complete resection should then be imaged according to surveillance guidelines
- CT Abdomen and Pelvis with contrast (CPT® 74177) for individuals receiving preoperative chemotherapy every 2 cycles until surgery and then should be imaged according to surveillance guidelines after their postoperative baseline imaging study

**Congenital Mesoblastic Nephroma Surveillance Imaging:**
- Ultrasound is the preferred surveillance imaging modality to avoid radiation and anesthesia exposures
- CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) for residual abnormalities present on post-operative imaging or inconclusive findings on ultrasound every 3 months for 1 year after completion of all therapy

**Background and Supporting Information**
- This is the most common primary renal tumor occurring in young infants, and the overall prognosis is very good.
- Complete surgical removal is curative in most cases, and histologically confirmed metastatic disease or bilateral disease has never been reported
- Many individuals will present with an asymptomatic abdominal mass at the time of birth or abnormal prenatal ultrasound and will undergo ultrasound as a primary evaluation
- PET is not indicted in the initial staging of any pediatric renal tumor
- Recurrences are rare, but most occur within 12 months of diagnosis
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PEDONC-8.1: General Considerations

- Unless specified below, individuals age < 18 years old should be imaged according to this guideline section. Exceptions include:
  - Rhabdomyosarcoma individuals of all ages should be imaged according to guidelines in **PEDONC-8.2: Rhabdomyosarcoma (RMS)**
  - Kaposi’s sarcoma individuals of all ages should be imaged according to guidelines in **ONC-31.10: Kaposi’s Sarcoma**

- Evaluation of soft tissue masses of uncertain nature prior to biopsy should follow general imaging guidelines:
  - For individuals age 0 to 17 years see: **PEDMS-3: Soft Tissue and Bone Masses** and for individuals age ≥ 18 years see: **MS-10: Soft Tissue Mass or Lesion of Bone**
**PEDONC-8.2: Rhabdomyosarcoma (RMS)**

**Rhabdomyosarcoma Initial Staging:**
- CT with contrast or MRI without and with contrast for primary site imaging of RMS arising in the abdomen or pelvis
- CT Chest with (CPT® 71260) or without contrast (CPT® 71250) to evaluate for lung metastases in the initial workup of all pediatric soft tissue sarcomas and should be completed prior to anesthesia exposure if possible
- Other staging imaging should be deferred until a histologic diagnosis is made
- Whole body PET/CT (CPT® 78816) is the preferred study for initial staging of RMS
- Bone scan (See **PEDONC-1.3: Modality General Considerations**) may be substituted for PET imaging if PET not available
- CT Abdomen and Pelvis with contrast (CPT® 74177) for initial metastatic staging of pediatric RMS only in the following situations:
  - Evaluation of inconclusive PET findings
  - Primary site of abdomen or pelvis
  - Lower extremity primary sites
- MRI Brain (CPT® 70553) and Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) for initial staging of pediatric RMS only in the following situations:
  - Primary site involving the paraspinal or paravertebral region
  - PET- or bone scan-avid lesions in skull, neck, vertebrae
  - With neurologic signs or symptoms raising suspicion of CNS metastases

**Rhabdomyosarcoma Treatment Response:**
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned therapy
- Primary site imaging:
  - CT with contrast or MRI without and with contrast every 2 cycles during treatment and at the end of planned therapy
  - Restaging imaging after local control surgery (complete or partial resection) is completed
- Metastatic site imaging:
  - Repeat imaging of all known metastatic sites using the same modality as during initial staging whenever primary site imaging is necessary
- PET to assess treatment response in RMS only in the following rare circumstances:
  - Assessment prior to local control surgery or radiation therapy.
  - Evaluation of residual mass visible on conventional imaging as part of end of therapy evaluation
  - Assessment of disease visible on PET but not conventional imaging
Once PET has been documented to be negative for a given individual’s cancer or all PET-avid disease has been surgically resected, PET should not be used for continued disease monitoring or surveillance unless one of the exceptions in section PEDONC-1: General Guidelines applies. These requests will be forwarded for Medical Director review.

PET may be appropriate when results are likely to result in a treatment change for the individual, including a change from active treatment to surveillance. These requests will be forwarded for Medical Director review.

Rhabdomyosarcoma Surveillance Imaging:

- All individuals with localized RMS:
  - CT Chest with contrast (CPT® 71260) or MRI Chest without and with contrast (CPT® 71552) of primary tumor site every 3 months for 1 year, then every 4 months for 2 years, then every 6 months for 1 year after completion of all therapy
  - CXR every 3 months for 1 year, then every 4 months for 2 years, then every 6 months for 1 year after completion of all therapy
  - CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250)
    - for new or worsening clinical symptoms of chest disease or new findings on CXR

- All individuals with metastatic RMS:
  - CT Chest with contrast (CPT® 71260) or MRI Chest without and with contrast (CPT® 71552) of primary tumor site every 3 months for 1 year, then every 4 months for 2 years, then every 6 months for 1 year after completion of all therapy
  - CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250)
    - and all known metastatic sites every 3 months for 1 year, then every 4 months for 2 years, then every 6 months for 1 year after completion of all therapy
  - Nuclear bone scan (See PEDONC-1.3: Modality General Considerations) for surveillance of known bony metastases every 3 months for 1 year, then every 4 months for 2 years, then every 6 months for 1 year after completion of all therapy

- PET for surveillance imaging of RMS only when one of the following applies:
  - Conventional imaging (CT, MRI, US, plain film) reveals findings that are inconclusive or suspicious for recurrence, and PET avidity will determine whether biopsy or continued observation is appropriate
  - Rare circumstances where obvious clinical symptoms show strong evidence suggesting recurrence, and PET would replace conventional imaging modalities. These requests will be forwarded for Medical Director review
Background and Supporting Information

- Soft tissue sarcomas occur in both adult and pediatric individuals, but some are more common in one age group than the other.

- Pediatric soft tissue sarcomas are divided into two groups:
  - Rhabdomyosarcoma (RMS) accounts for ~60% of soft tissue sarcomas in young individuals, but only ~25% of soft tissue sarcomas in adolescents
  - Nonrhabdomyosarcoma soft tissue sarcomas (NRSTS) which encompasses all other histologic subtypes

- Because RMS can arise from any muscle tissue, the presenting symptoms and primary tumor sites vary widely and strongly influence the appropriate imaging decisions

- CT with contrast is the preferred primary site imaging modality for RMS arising in the thoracic cavity (not the chest wall)

- MRI without and with contrast is the preferred primary site imaging modality for RMS occurring in all other anatomic locations, including the chest wall

- PET/CT is superior to conventional imaging for detection of nodal and bony metastases in pediatric RMS and is indicated in the initial staging of all individuals after histologic diagnosis is established

- CT Abdomen and Pelvis with contrast (CPT® 74177) is not routinely indicated in the initial metastatic staging of pediatric RMS

- PET is not routinely utilized to assess treatment response in RMS

- PET is generally not indicated during active treatment for recurrent pediatric cancer

- Residual mass that has not changed in size since the last conventional imaging does not justify PET imaging during surveillance

- PET avidity in a residual mass at the end of planned therapy is not an indication for PET imaging during surveillance
**PEDONC-8.3: Non-Rhabdomyosarcoma Soft Tissue Sarcomas (NRSTS)**

**NRSTS Initial Staging:**

- CT with contrast or MRI without and with contrast for primary site imaging of NRSTS arising in the abdomen or pelvis.
- CT with contrast is the preferred primary site imaging modality for NRSTS arising in the thoracic cavity (not the chest wall).
- MRI without and with contrast is the preferred primary site imaging modality for NRSTS occurring in all other anatomic locations, including the chest wall.
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) for evaluation of lung metastases in the initial workup of all pediatric soft tissue sarcomas and should be completed prior to anesthesia exposure if possible.
- Other staging imaging should be deferred until a histologic diagnosis is made:
  - PET/CT (CPT® 78815) may be considered in the following:
    - Desmoplastic small round cell tumor
    - Prior to neoadjuvant chemotherapy
    - Evaluating inconclusive findings found on conventional imaging
    - Whole body PET/CT (CPT® 78816) if there is clinical suspicion of skull or distal lower extremity involvement
  - Nuclear bone scan (See PEDONC-1.3: Modality General Considerations) to evaluate for bony metastases but should be omitted if PET is performed.
  - CT Abdomen and Pelvis with contrast (CPT® 74177) in the initial metastatic staging of pediatric NRSTS, only in the following situations:
    - Evaluation of inconclusive PET findings
    - Primary site of abdomen or pelvis
    - Lower extremity primary sites
    - Desmoplastic small round cell tumor
  - MRI Brain (CPT® 70553) and Spine (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) without and with contrast for initial staging in the following pediatric NRSTS:
    - Primary site involving the paraspinal or paravertebral region
    - PET- or nuclear bone scan-avid lesions in skull, neck, vertebrae
    - With neurologic signs or symptoms raising suspicion of CNS metastases.
NRSTS Treatment Response:

- CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned therapy

- Primary site imaging:
  - CT with contrast or MRI without and with contrast every 2 cycles during treatment and at the end of planned therapy
  - Restaging imaging after local control surgery (complete or partial resection) is completed

- Metastatic site imaging:
  - Repeat imaging of all known metastatic sites using the same modality as during initial staging whenever primary site imaging is necessary

- PET imaging in only in the following circumstances if positive at initial diagnosis:
  - Assessment prior to local control surgery or radiation therapy
  - Evaluation of residual mass visible on conventional imaging as part of end of therapy evaluation
  - Assessment of disease visible on PET but not conventional imaging
  - Once PET has been documented to be negative for a given individual’s cancer or all PET-avid disease has been surgically resected, PET should only be used for continued disease monitoring or surveillance when one of the exceptions in section PEDONC-1: General Guidelines applies. These requests will be forwarded for Medical Director review.
  - PET imaging during active treatment for recurrent pediatric cancer may be indicated in rare circumstances when results are likely to result in a treatment change for the individual, including a change from active treatment to surveillance. These requests will be forwarded for Medical Director review

NRSTS Surveillance Imaging:

- All individuals with localized NRSTS:
  - CT with contrast or MRI without and with contrast of primary site every 6 months for 5 years after completion of all therapy
  - CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 6 months for 5 years after completion of all therapy

- All individuals with metastatic NRSTS:
  - CT with contrast or MRI without and with contrast of primary site every 6 months for 5 years after completion of all therapy
  - CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) and all known metastatic sites every 6 months for 5 years after completion of all therapy
  - Nuclear bone scan (See PEDONC-1.3: Modality General Considerations) should be used for surveillance of known bony metastases every 6 months for 5 years after completion of all therapy

- Surveillance after recurrence:
  - CT Chest with contrast (CPT® 71260) and CT Chest with contrast or MRI without and with contrast of the primary site following successful treatment for recurrent NRSTS every 3 months for 1 year after completing therapy for recurrence
Surveillance imaging more than 12 months after completing therapy for recurrence should follow the standard timing listed in this surveillance section.

- PET for surveillance imaging of NRSTS only when one of the following applies:
  - Conventional imaging (CT, MRI, US, plain film) reveals findings that are inconclusive or suspicious for recurrence, and PET avidity will determine whether biopsy or continued observation is appropriate.
  - Rare circumstances where obvious clinical symptoms show strong evidence suggesting recurrence and PET would replace conventional imaging modalities. These requests will be forwarded for Medical Director review.

**Background and Supporting Information**

- All soft tissue sarcomas other than RMS fall into this category.
- Because soft tissue sarcomas can arise from any soft tissue, the presenting symptoms and primary tumor sites vary widely and strongly influence the appropriate imaging decisions.
- CT Abdomen and Pelvis with contrast (CPT® 74177) is not routinely indicated in the initial metastatic staging of pediatric NRSTS.
- Many individuals with NRSTS will be treated with surgical resection alone, and these individuals enter immediately into surveillance.
- PET imaging is not routinely utilized to assess treatment response in NRSTS.
- PET imaging is generally not indicated during active treatment for recurrent pediatric cancer.
- Residual mass that has not changed in size since the last conventional imaging does not justify PET.
- PET avidity in a residual mass at the end of planned therapy is not an indication for PET imaging during surveillance.
References


# PEDONC-9: Bone Tumors

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**PEDONC-9.1: General Remarks**

These guidelines include both benign and malignant lesions.

- Unless specified below, individuals who are < 18 years old should be imaged according to this guideline section. Exceptions include:
  - Osteogenic sarcoma individuals of all ages should be imaged according to guidelines in **PEDONC-9.3: Osteogenic Sarcoma (OS)**
  - Ewing sarcoma and Primitive Neuroectodermal Tumor individuals of all ages should be imaged according to guidelines in **PEDONC-9.4: Ewing Sarcoma and Primitive Neuroectodermal Tumors (ESFT)**
  - Chondrosarcoma individuals of all ages should be imaged according to guidelines in **ONC-12.6: Bone Sarcomas-Initial Workup/Staging**
  - Chordoma individuals of all ages should be imaged according to guidelines in **ONC-12.6: Bone Sarcomas-Initial Workup/Staging**
  - Giant cell tumor of bone and enchondroma individuals of all ages should be imaged according to guidelines in **ONC-12.9: Benign Bone Tumors-General Considerations**
  - Other benign bone tumor individuals of all ages should be imaged according to guidelines in **PEDONC-9.2: Benign Bone Tumors-General Considerations**
  - All bone tumors should be evaluated by plain x-ray prior to any advanced imaging
PEDONC-9.2: Benign Bone Tumors

- **Osteochondroma**
  - MRI without contrast or with contrast after evaluation for preoperative planning
  - MRI without contrast and with contrast when there is clinical concern for malignant transformation based on new or worsening pain symptoms or a change on a recent plain x-ray

- **Osteoid osteoma**
  - CT without contrast is often the primary study when osteoid osteoma is suspected
  - Bone scan SPECT (CPT® 78320) for suspected osteoid osteoma.
  - MRI without and with contrast if CT without contrast is not definitive

- **Other benign tumors**
  - Variety of diagnoses, including osteoblastoma, aneurysmal bone cysts, fibrous dysplasia, chondroblastoma and others
  - MRI without and with contrast is the primary modality for advanced imaging of bone tumors to help narrow differential diagnoses and determine whether biopsy is indicated
  - CT (contrast as requested) to visualize specific bony details
  - For preoperative planning
  - MRI without and with contrast for surveillance to evaluate new findings on plain x-ray or new/worsening clinical symptoms not explained by a recent plain x-ray

**Background and Supporting Information**

- Bone tumors occur in both adult and pediatric individuals, but some are more common in one age group than the other
- PET does not reliably distinguish between benign and malignant bone tumors and should not be performed prior to biopsy
- Plain X-ray appearance is diagnostic for many benign bone tumors, and advanced imaging is generally unnecessary except for preoperative planning
- Plain X-ray appearance is diagnostic for osteochondroma for the majority of individuals and advanced imaging is generally unnecessary
- For certain tumors, CT (contrast as requested) provides better visualization of specific bony details, and requests after evaluation by the operating surgeon for preoperative planning should generally be approved
- Surveillance imaging, when indicated, should utilize plain x-ray
- Some benign bone tumor types carry a risk of malignant degeneration over time, but routine advanced imaging surveillance has not been shown to improve outcomes for these individuals
- There are no data to support the use of PET in the evaluation of benign bone tumors, and PET requests should not be approved without biopsy confirmation of a malignancy.
**PEDONC-9.3: Osteogenic Sarcoma (OS)**

**Osteogenic Sarcoma Initial Staging:**

- All bone tumors should be evaluated by plain x-ray prior to any advanced imaging.
- MRI without and with contrast is the preferred primary site imaging.
  - CT (contrast as requested) if there is a contraindication to MRI or if requested after evaluation by the operating surgeon to clarify inconclusive MRI findings for preoperative planning.
  - MRA and/or CTA may rarely be indicated for complicated surgical resections after evaluation by the operating surgeon to clarify inconclusive MRI findings for preoperative planning.
  - Requests for CT, MRA, or CTA should be forwarded for medical director review.
- CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) is superior to PET/CT for the detection of pulmonary metastases and in the initial workup of all suspected malignant bone tumors. It should be completed prior to anesthesia exposure if possible.
- Other staging imaging should be deferred until a histologic diagnosis is made, initially by biopsy.
  - Whole body PET/CT (CPT® 78816) is the preferred study for initial staging of OS after histologic diagnosis is established.
  - Nuclear bone scan may be substituted for PET imaging if PET not available. See **PEDONC-1.3: Modality General Considerations**.
  - If PET/CT is negative at initial diagnosis, bone scan is preferred for asymptomatic surveillance for bony metastases at time points after local control surgery. See **PEDONC-1.3: Modality General Considerations**.
  - CT Abdomen and Pelvis with contrast (CPT® 74177) in the initial metastatic staging of pediatric OS only for evaluation of inconclusive PET findings or primary site is abdomen or pelvis.

**Osteogenic Sarcoma Treatment Response:**

- Restaging 10 to 12 weeks post neoadjuvant chemotherapy prior to local control surgery:
  - MRI without and with contrast of primary site.
  - CT Chest with (CPT® 71260) or without contrast (CPT® 71250).
  - Whole body PET/CT (CPT® 78816) or bone scan. See **PEDONC-1.3: Modality General Considerations**.
- Restaging post local control surgery until the end of planned chemotherapy:
  - MRI without and with contrast of primary site approximately 6 weeks after surgical procedure and at the end of planned chemotherapy.
  - Plain x-rays of the primary site and chest every 2 months.
  - CT Chest (with or without contrast, as requested):
    - Measurable pulmonary metastases: every 6 weeks and at the end of planned chemotherapy.
    - No measurable pulmonary metastases: every 4 months and at the end of planned chemotherapy.
 Bone scan (see PEDONC-1.3: Modality General Considerations) every 4 months and at the end of planned chemotherapy
  - Whole body PET/CT in place of bone scan, if positive for distant bone metastases at initial diagnosis

  ▶ Post local control surgery when metastatic disease has resolved with chemotherapy
  - CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned chemotherapy
  - MRI without and with contrast of primary site every 2 cycles during treatment and at the end of planned chemotherapy
  - Whole body PET/CT (CPT® 78816) or bone scan (see PEDONC-1.3: Modality General Considerations) if previously positive for bony metastases every 2 cycles during treatment and at the end of planned chemotherapy.
  - Imaging may be indicated more frequently around the time of surgical resection of primary or metastatic lesions to assess for resectability
  - PET during active treatment for recurrent pediatric cancer in only rare circumstances when results are likely to result in a treatment change, including a change from active treatment to surveillance. These requests will be forwarded for Medical Director review

**Osteogenic Sarcoma Surveillance Imaging:**

▶ Appendicular bone primary tumor site
  - Plain x-rays of the primary tumor site every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, then annually for 2 years after completion of all therapy
  - MRI for surveillance imaging of appendicular primary sites only for the following:
    - The individual does not have an endoprosthesis that will cause MRI or CT artifact
    - To clarify inconclusive findings on plain x-ray
    - To evaluate significant pain symptoms suggestive of primary site recurrence

▶ Axial bone primary tumor site
  - MRI without and with contrast of the primary tumor site every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, then annually for 2 years after completion of all therapy

▶ Metastatic disease surveillance
  - Individuals with localized OS:
    - CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 3 months for 1 year, then every 4 months for 1 year after completion of all therapy
    - Chest x-ray (CXR) for pulmonary recurrence surveillance after 24 months
    - CT Chest to clarify inconclusive CXR findings
  - Individuals with metastatic or recurrent OS:
    - CT Chest with (CPT® 71260) or without contrast (CPT® 71250) every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, and then annually for 2 years after completion of all therapy
Nuclear bone scan (see PEDONC-1.3: Modality General Considerations) for evaluation of distant bony metastases every 3 months for 1 year, then every 6 months for 2 years, then annually for 2 years after completion of all therapy.

PET/CT in the following circumstances:
- Conventional imaging reveals findings that are inconclusive or suspicious for recurrence, and PET avidity will determine whether biopsy or continued observation is appropriate
- Rare circumstances where obvious clinical symptoms show strong evidence suggesting recurrence, and PET would replace conventional imaging modalities
- Restaging after biopsy-confirmed recurrence
- These requests will be forwarded for Medical Director review

**Background and Supporting Information**
- Bone tumors occur in both adult and pediatric individuals, but some are more common in one age group than the other
- PET does not reliably distinguish between benign and malignant bone tumors and should not be performed prior to biopsy
- CT Abdomen and Pelvis with contrast (CPT® 74177) is not routinely indicated in the initial metastatic staging of pediatric OS
- Distant bony metastases cause a significant change in treatment approach
- PET has superior sensitivity to bone scan (95% vs. 76%) but equivalent overall diagnostic accuracy (98% vs. 96%) for detection of bony metastases in pediatric OS
- Most OS individuals undergo restaging after 10 to 12 weeks of neoadjuvant chemotherapy prior to local control surgery to confirm the absence of progressive disease prior to the extended break necessary for postoperative healing
- Individuals with metastatic disease do not routinely undergo local control surgery unless metastatic disease has resolved with chemotherapy
- MRI is not routinely indicated for surveillance imaging of appendicular primary sites
- PET is generally not indicated during active treatment for recurrent pediatric cancer
- PET/CT has no established role for asymptomatic surveillance of OS
**PEDONC-9.4: Ewing Sarcoma and Primitive Neuroectodermal Tumors (ESFT)**

**ESFT Initial Staging:**
- All bone tumors should be evaluated by plain x-ray prior to any advanced imaging.
- Soft tissue masses, without bony involvement, that are ill-defined or non-discrete should be evaluated by limited ultrasound prior to any advanced imaging.
- MRI without and with contrast is the preferred primary site imaging.
  - CT (contrast as requested) if there is a contraindication to MRI or if requested after evaluation by the operating surgeon to clarify inconclusive MRI findings for preoperative planning.
  - MRI Chest without and with contrast for chest wall primary tumors, in addition to the CT Chest for pulmonary metastasis detection.
  - MRA and/or CTA may rarely be indicated for complicated surgical resections, after evaluation by the operating surgeon to clarify inconclusive MRI findings for preoperative planning.
  - Requests for CT, MRA, or CTA should be forwarded for medical director review.
- CT Chest with (CPT® 71260) or without contrast (CPT® 71250) in the initial workup of all suspected malignant bone tumors and completed prior to anesthesia exposure if possible.
- Other staging imaging should be deferred until a histologic diagnosis is made, initially by biopsy.
  - Bone and bone marrow metastases can occur in ESFT, and cause a significant change in treatment approach. PET/CT can replace bone scan and bone marrow biopsy in ESFT individuals in the initial staging of all ESFT individuals after histologic diagnosis is established.
    - Whole body PET/CT (CPT® 78816) is the preferred study for initial staging of ESFT.
  - Bone scan (see: PEDONC-1.3: Modality General Considerations) may be substituted for PET imaging if PET not available.
  - If PET/CT is negative for bony metastases at initial diagnosis, bone scan (see PEDONC-1.3: Modality General Considerations) is preferred for asymptomatic surveillance at all-time points after completion of therapy.
  - CT Abdomen and Pelvis with contrast (CPT® 74177) only in the following situations:
    - Evaluation of inconclusive PET findings.
    - Primary site involving the abdomen or pelvis.
**ESFT Treatment Response:**

- **Restaging after neoadjuvant chemotherapy prior to local control surgery:**
  - MRI without and with contrast of primary site
  - CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250)
  - Whole body PET/CT (CPT® 78816) or bone scan. (see **PEDONC-1.3: Modality General Considerations**)

- **Restaging following local control surgery until the end of planned chemotherapy:**
  - MRI without and with contrast of primary site 3 months after surgical procedure and at the end of planned chemotherapy
  - Plain X-rays of the primary site and chest immediately after local control then every 3 months
  - CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250):
    - Measurable pulmonary metastases: every 6 weeks and at the end of planned chemotherapy
    - No measurable pulmonary metastases: every 3 months and at the end of planned chemotherapy
  - Whole body PET/CT (CPT® 78816) or bone scan (see **PEDONC-1.3: Modality General Considerations**) at the end of planned chemotherapy

- **Post local control surgery when metastatic disease has resolved with chemotherapy**
  - CT Chest with (CPT® 71260) or without contrast (CPT® 71250) every 2 cycles during treatment and at the end of planned chemotherapy
  - MRI without and with contrast of primary site every 2 cycles during treatment and at the end of planned chemotherapy
  - If previously positive for bony metastases, whole body PET/CT (CPT® 78816) or bone scan (see **PEDONC-1.3: Modality General Considerations**) every 2 cycles during treatment and at the end of planned chemotherapy.
  - Imaging may be indicated more frequently around the time of surgical resection of primary or metastatic lesions to assess for resectability.

- **PET in rare circumstances when results are likely to result in a treatment change, including a change from active treatment to surveillance. These requests will be forwarded for Medical Director review.**
**ESFT Surveillance Imaging:**

- **Appendicular bone primary tumor site:**
  - Plain X-rays of the primary tumor site every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, and then annually for 2 years after completion of all therapy
    - MRI for surveillance imaging of these primary sites after completion of chemotherapy:
      - The individual does not have an endoprosthesis that cause MRI or CT artifact
      - To clarify inconclusive findings on plain X-ray
      - To evaluate significant pain symptoms suggestive of primary site recurrence

- **Axial bone or any soft tissue primary site:**
  - CT with contrast or MRI without and with contrast of the primary tumor site every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, and then annually for 2 years after completion of all therapy

- **Metastatic disease surveillance:**
  - **Individuals with localized ESFT:**
    - CT Chest with contrast (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 3 months for 1 year then every 4 months for 1 year after completion of all therapy
    - Chest x-ray (CXR) for pulmonary recurrence surveillance after 24 months, and CT Chest to clarify inconclusive CXR findings
  - **Individuals with metastatic or recurrent ESFT:**
    - CT Chest with (CPT® 71260) or without contrast (CPT® 71250) every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, then annually for 2 years after completion of all therapy
  - Nuclear bone scan (see PEDONC-1.3: Modality General Considerations) for evaluation of distant bony metastases every 3 months for 1 year, then every 4 months for 1 year, then every 6 months for 1 year, then annually for an additional 2 years after completion of all therapy.
  - **PET/CT only** in the following circumstances:
    - Conventional imaging reveals findings that are inconclusive or suspicious for recurrence, and PET avidity will determine whether biopsy or continued observation is appropriate
    - Rare circumstances where obvious clinical symptoms show strong evidence suggesting recurrence and PET would replace conventional imaging modalities
    - Restaging after biopsy-confirmed recurrence
    - These requests will be forwarded for Medical Director review
**Background and Supporting Information**

- Bone tumors occur in both adult and pediatric individuals, but some are more common in one age group than the other.
- PET does not reliably distinguish between benign and malignant bone tumors and should not be performed prior to biopsy.
- ESFT can also occur in the soft tissues, soft tissue masses without bony involvement that are ill-defined or non-discrete should be evaluated by limited ultrasound prior to any advanced imaging.
- CT Chest with (CPT® 71260) or without contrast (CPT® 71250) is superior to PET/CT for the detection of pulmonary metastases, and is indicated in the initial workup of all suspected malignant bone tumors and should be completed prior to anesthesia exposure if possible.
- Other staging imaging should be deferred until a histologic diagnosis is made, initially by biopsy, as definitive resection is performed after neoadjuvant chemotherapy.
- Bone and bone marrow metastases can occur in ESFT and cause a significant change in treatment approach.
- CT Abdomen and Pelvis with contrast (CPT® 74177) is not routinely indicated in the initial metastatic staging of pediatric ESFT.
- All ESFT individuals undergo restaging after ~12 weeks of neoadjuvant chemotherapy prior to local control surgery to confirm the absence of progressive disease prior to the extended break necessary for postoperative healing.
- Individuals with metastatic disease do not routinely undergo local control surgery unless metastatic disease has resolved with chemotherapy.
- PET is generally not indicated during active treatment for recurrent pediatric cancer.
- MRI is not routinely indicated for surveillance imaging of these primary sites after completion of chemotherapy.
**References**


**PEDONC-10: Pediatric Germ Cell Tumors**

**Pediatric GCT Initial Staging:**
- US as initial imaging for ovarian, testicular, and abdominal extragonadal GCT
  - CT Chest with contrast for mediastinal primary tumors
  - Advanced imaging only for ovarian masses that are < 10 cm in size, have minimal or no visible solid component on ultrasound, and have normal tumor markers when ultrasound is insufficient for immediate preoperative planning
  - CT Abdomen/Pelvis with contrast (CPT® 74177) for initial staging prior to histologic confirmation of a primary mass suspected to be GCT
  - MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) to clarify inconclusive CT findings or with a known contraindication to CT contrast
- CT Chest with contrast (CPT® 71260) in the initial workup of all pediatric GCT and should be completed prior to anesthesia exposure if possible
- MRI Brain without and with contrast (CPT® 70553) for symptoms suggesting CNS metastases
  - Nuclear Bone scan (see **PEDONC-1.3: Modality General Considerations**) for initial evaluation of bony metastases with systemic symptoms or bone pain

**Pediatric GCT Treatment Response:**
- For individuals receiving adjuvant chemotherapy:
  - CT Chest/Abdomen/Pelvis (CPT® 71260 and CPT® 74177) with contrast can be approved every 2 cycles (~every 6 weeks) for disease not completely resected at initial diagnosis
  - CT imaging may be indicated more frequently to assess for surgical resectability in individuals who have received more than 4 cycles of chemotherapy
- For individuals at the end of planned chemotherapy or following neoadjuvant chemotherapy:
  - CT Chest/Abdomen/Pelvis with contrast (CPT® 71260 and CPT® 74177) for initially unresectable tumors.
  - Imaging of any metastatic sites at the end of planned therapy with the same modality used during initial staging
  - CT study (short interval) for suspicious lesions seen on conventional imaging if the relapse risk is determined to be low by the treating physician and biopsy would cause unnecessary morbidity for the individual
Pediatric GCT Surveillance Imaging:

- CT Chest/Abdomen/Pelvis with contrast (CPT® 71260 and CPT® 74177) for any clinically significant rise in tumor markers or symptoms suggesting recurrent disease
- CT Abdomen/Pelvis with contrast (CPT® 74177) every 3 months for 1 year, then every 6 months for 1 year after completion of all therapy
- For stage I treated with surgery only:
  - Chest xray every 3 months for 1 year then every 6 months for 1 year after completion of all therapy
  - CT Chest is only to evaluate abnormal CXR findings
- For stage II-IV:
  - CT Chest with contrast (CPT® 71260) every 3 months for 1 year, then every 6 months for 1 year after completion of all therapy
  - Surveillance after 24 months should use CXR
- Individuals with brain or bone metastases should have surveillance imaging on the same schedule as the primary site imaging with the same modality used during initial staging

Background and Supporting Information

- Malignant pediatric germ cell tumors commonly include one of four histologic subtypes (yolk sac tumor, choriocarcinoma, embryonal carcinoma, or mixed histology), but the overall treatment strategies are similar for all malignant germ cell tumors. Tumors can occur in testicular, ovarian or extragonadal primary locations
- This section applies to primary germ cell tumors occurring outside the central nervous system in children who are ≤ 15 years at the time of initial diagnosis. For individuals who are > 15 years at diagnosis, overall prognosis is inferior and these individuals should be imaged according to adult guidelines in: ONC-20: Testicular and Nonepithelial Ovarian (Germ Cell) Cancer
- Sex cord stromal tumors (granulosa cell, theca, Sertoli, and Leydig tumors) are rare in pediatrics and should be imaged according to adult guidelines. See ONC-20: Testicular, Ovarian and Extragonadal (Germ Cell) Tumors
- For CNS Germ Cell Tumors, see PEDONC-4.7: CNS Germinomas and Non-Germinomatous Germ Cell Tumors (NGGCT)
- Ovarian, testicular, and abdominal extragonadal GCT should have ultrasound and tumor markers (AFP, β-hCG) as initial evaluation
- Ovarian masses that are < 10 cm in size, have minimal or no visible solid component on ultrasound, and have normal tumor markers are almost universally benign teratomas or functional cysts and advanced imaging is not necessary unless ultrasound is insufficient for immediate preoperative planning.
- The degree of abdominal exploration and node sampling necessary for adequate staging is determined in part by imaging findings and is required for preoperative planning.
Testicular primary tumors can defer abdominal imaging until after histologic confirmation at the discretion of the operating surgeon.

There has been no published evidence to date supporting the routine use of PET/CT in the evaluation of pediatric GCT. Additionally, PET has been found to have similar efficacy to CT imaging in initial staging of adults with non-seminomatous GCT (the majority of pediatric GCT are non-seminomatous)

Individuals with localized GCT not receiving post surgical adjuvant therapy should be imaged using surveillance guidelines after surgery is completed

Individuals receiving adjuvant chemotherapy are usually treated with 4 to 6 cycles of combination chemotherapy. The primary method of response assessment is by tumor marker decrease

PET as a marker of treatment response has been shown not to be predictive of outcomes in GCT and is not indicated. Suspicious lesions seen on conventional imaging should be biopsied to confirm active disease

The primary method of surveillance in pediatric GCT is frequent assessment of serum tumor markers.
References

# PEDONC-11: Pediatric Liver Tumors

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PEDONC-11.1: General Remarks

- Primary hepatic germ cell tumors should follow imaging guidelines in: PEDONC-10: Pediatric Germ Cell Tumors
- Primary hepatic sarcomas should follow imaging guidelines in: PEDONC-8.3: Non-Rhabdomyosarcoma Soft Tissue Sarcomas (NRSTS)
- Imaging requests relating to liver transplant surgery and surveillance should follow guidelines in: AB-42: Transplant
- The primary method of surveillance in hepatoblastoma is frequent assessment of serum tumor markers (primarily AFP)
PEDONC-11.2: Hepatoblastoma

Hepatoblastoma Initial Staging:

- Ultrasound imaging for most suspected liver tumors as initial evaluation
- Ultrasound may be approved even after MRI or CT imaging in order to allow evaluation for tumor thrombus
- Once a primary liver mass is discovered, definitive imaging prior to histologic diagnosis may involve any of the following:
  - CT Abdomen/Pelvis with contrast (CPT® 74177)
  - MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) is preferred for evaluating tumor margins and vascular anatomy
  - MRI and CT imaging for some tumors during initial evaluation
  - MRA Abdomen (CPT® 74185) or CTA Abdomen (CPT® 74175) to evaluate vascular invasion
- CT Chest with (CPT® 71260) or without contrast (CPT® 71250) in the initial workup of all pediatric liver tumors and should be completed prior to anesthesia exposure if possible
  - Bone scan (see PEDONC-1.3: Modality General Considerations) for initial evaluation of bony metastases only with systemic symptoms or bone pain.
- MRI Brain without and with contrast (CPT® 70553) only for symptoms suggesting CNS metastases
- PET/CT only in very rare circumstances for preoperative planning when MRI and CT scans are insufficient for surgical decision making. These requests will be forwarded for Medical Director Review.
Hepatoblastoma Treatment Response:
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) every 2 cycles and at the end of planned therapy for individuals with incomplete resection at initial diagnosis
- CT Abdomen/Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) every 2 cycles and at the end of planned therapy for individuals with incomplete resection at initial diagnosis
  - While the majority of individuals will require abdomen and pelvis imaging at all time points, the pelvis imaging may be omitted at the discretion of the ordering physician
- MRA Abdomen (CPT® 74185) or CTA Abdomen (CPT® 74175) to evaluate vascular invasion
- Imaging of any metastatic sites with the same modality used during initial staging
- Imaging more frequently to assess for surgical resectability in individuals who have received more than 4 cycles of chemotherapy
- Abdominal ultrasound if tumor thrombus was detected at initial diagnosis. If no tumor thrombus was present, continued ultrasound evaluations are only indicated with a specific reason documented in the clinical records
- PET/CT should only be considered in very rare circumstances for preoperative planning when MRI and CT scans are insufficient for surgical decision making. These requests will be forwarded for Medical Director review

Hepatoblastoma Surveillance Imaging:
- For surveillance in individuals with an AFP of > 100 ng/mL
  - CT Chest and Abdomen with contrast (CPT® 71260 and CPT® 74160) for any clinically significant rise in tumor markers or symptoms suggesting recurrent disease
- For individuals with AFP ≤ 100 ng/mL at diagnosis or recurrence, the following imaging is appropriate:
  - CT Abdomen with contrast (CPT® 74160) every 3 months for 2 years, then every 4 months for 2 years after completion of all therapy
  - Chest x-ray or CT Chest with contrast (CPT® 71260) every 3 months for 2 years, then every 4 months for 2 years after completion of all therapy
  - Individuals with brain or bone metastases should have surveillance imaging on the same schedule as the primary site imaging with the same modality used during initial staging
Background and Supporting Information

- Pediatric liver tumors primarily include hepatoblastoma and hepatocellular carcinoma, but hepatic germ cell tumors and primary hepatic sarcomas occur with some frequency. Tumor markers are useful for initial evaluation as well as treatment response, particularly in hepatoblastoma.

- Most suspected liver tumors will have ultrasound and tumor markers (AFP, β-hCG, CEA) as initial evaluation.

- There has been no published evidence to date supporting the routine use of PET/CT imaging in the evaluation of pediatric hepatoblastoma during initial imaging, treatment response, or surveillance. PET/CT should not be approved in lieu of biopsy of suspicious lesions.

- Individuals with localized hepatoblastoma of pure fetal histology are often cured with surgery alone and do not receive adjuvant therapy. These individuals should be imaged using surveillance guidelines after surgery is complete.

- Individuals receiving adjuvant chemotherapy are usually treated with 2 to 8 cycles of combination chemotherapy. Tumor marker decrease is important in response assessment but does not eliminate the need for advanced imaging in individuals with unresected hepatoblastoma.

- The primary method of surveillance in hepatoblastoma is frequent assessment of serum tumor markers (primarily AFP).

- No specific imaging for surveillance in individuals with an AFP of > 100 ng/mL at diagnosis or recurrence.
**PEDONC-11.3: Pediatric Hepatocellular Carcinoma**

**Pediatric HCC Initial Staging:**

- Ultrasound for most suspected liver tumors as initial evaluation
- Ultrasound may be approved even after MRI or CT imaging in order to allow evaluation for tumor thrombus
- Once a primary liver mass is discovered, definitive imaging prior to histologic diagnosis including any of the following:
  - CT Abdomen/Pelvis with contrast (CPT® 74177)
  - MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197)
  - Some tumors may require both MRI and CT during initial evaluation
  - MRA (CPT® 74185) or CTA (CPT® 74175) Abdomen to evaluate vascular invasion
- CT Chest with (CPT® 71260) or CT Chest without contrast (CPT® 71250) in the initial workup of all pediatric liver tumors and should be completed prior to anesthesia exposure if possible
- MRI Brain without and with contrast (CPT® 70553) only for symptoms suggesting CNS metastases
  - Nuclear bone scan (see **PEDONC-1.3: Modality General Considerations**) for initial evaluation of bony metastases only in individuals with systemic symptoms or bone pain
- PET/CT should only be considered in very rare circumstances for preoperative planning when MRI and CT are insufficient for surgical decision making. These requests require Medical Director review
**Pediatric HCC Treatment Response:**

- For individuals with disease not completely resected at initial diagnosis, the following every 2 cycles (~6 weeks) and at the end of planned therapy:
  - CT Chest with (CPT® 71260) or without contrast (CPT® 71250)
  - CT Abdomen and Pelvis with contrast (CPT® 74177) or MRI Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197)
    - While the majority of individuals will require abdomen and pelvis imaging at all time points, the pelvis imaging may be omitted at the discretion of the ordering physician
    - MRA (CPT® 74185) or CTA (CPT® 74175) Abdomen to evaluate vascular invasion.
- Imaging of any metastatic sites with the same modality used during initial staging
- Abdominal ultrasound if tumor thrombus was detected at initial diagnosis If no tumor thrombus was present, continued ultrasound evaluations are only indicated with a specific reason documented in the clinical records
- PET/CT in very rare circumstances for preoperative planning when MRI and CT scans are insufficient for surgical decision making. These requests will be forwarded for Medical Director review

**Pediatric HCC Surveillance Imaging:**

- CT Abdomen with contrast (CPT® 74160) every 3 months for 1 year, then every 6 months for 1 year, then annually for 3 years after completion of all therapy
- Chest x-ray or CT Chest with contrast (CPT® 71260) every 3 months for 1 year, then every 6 months for 1 year, then annually for 3 years months after completion of all therapy

**Background and Supporting Information**

- Individuals with brain or bone metastases should have surveillance imaging on the same schedule as the primary site imaging with the same modality used during initial staging
- Most suspected liver tumors will have ultrasound and tumor markers (AFP, β-hCG, CEA) as initial evaluation.
- PET/CT should not be approved in lieu of biopsy of suspicious lesions
- The majority of hepatocellular carcinoma individuals are treated with surgery alone and do not receive adjuvant therapy. These individuals should be imaged using surveillance guidelines after surgery is completed
- PET/CT has no documented role in the surveillance evaluation of pediatric hepatocellular carcinoma.
References


PEDONC-12: Retinoblastoma

PEDONC-12.1: General Remarks 145
PEDONC-12.2: Retinoblastoma Imaging 146
PEDONC-12.1: General Remarks

- Retinoblastoma is primarily a disease of the infant and young child, and presents with leukocoria (loss of red reflex)
- Detailed evaluation by a physician with significant training and/or experience in retinoblastoma (most commonly a pediatric ophthalmologist or pediatric oncologist) prior to considering advanced imaging
- Retinoblastoma can be unilateral, bilateral, or trilateral (involving the pineal gland)
  Extraocular spread of retinoblastoma is rare and generally confined to the brain
**PEDONC-12.2: Retinoblastoma Imaging**

**Retinoblastoma Initial Staging:**
- MRI Orbits (CPT® 70543) and Brain (CPT® 70553) without and with contrast in the initial workup
  - Brain imaging may be omitted or deferred at the discretion of the treating ophthalmologist or oncologist
- Spinal MRI without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) if there is evidence of CNS metastasis on:
  - Ophthalmologic exam
  - MRI Brain
  - Lumbar CSF cytology
- CT of Chest (CPT® 71260) and MRI of Abdomen and Pelvis without and with contrast (CPT® 74183 and CPT® 72197) with clinical symptoms to suggest metastatic disease
- Orbital CT (contrast as requested) and orbital ultrasound if ordered by the treating ophthalmologist for a specified indication
  - Nuclear bone scan (see **PEDONC-1.3: Modality General Considerations**) is the preferred imaging modality for systemic bone pain suggestive of boy metastases

**Retinoblastoma Treatment Response:**
- MRI Orbits (CPT® 70543) and/or Brain (CPT® 70553) every 2 cycles (~ every 6 weeks) and at the end of planned therapy
- For individuals with metastatic disease, imaging of known positive areas using the same modality at initial staging every 2 cycles (~ 6 to 8 weeks) and at the end of planned therapy

**Retinoblastoma Surveillance:**
- Surveillance using advanced imaging for unilateral retinoblastoma after enucleation or exenteration only for evaluation of specific clinical concerns
- MRI Orbits (CPT® 70543) and Brain (CPT® 70553) for individuals undergoing ocular salvage treatment approaches every 6 months for 2 years following completion of therapy
- MRI Brain without and with contrast (CPT® 70553) every 6 months for 5 years from the time of diagnosis with retinoblastoma
Background and Supporting Information

- CT should generally be avoided in retinoblastoma individuals under one year of age or with family history of retinoblastoma due to substantially increased risks for secondary malignancy.
- PET has no documented role in the evaluation of retinoblastoma.
- The primary method of surveillance in retinoblastoma is examination under anesthesia (EUA). Although some older children can be sufficiently evaluated by exam without anesthesia (EWA).
- Surveillance using advanced imaging is generally not indicated for unilateral retinoblastoma after enucleation or exenteration, but can be approved for evaluation of specific clinical concerns.
- Individuals with bilateral retinoblastoma or germline mutation in RB1 are at increased risk for subsequent pineoblastoma.
- Routine MRI follow up for pineal disease is not currently supported by evidence in unilateral retinoblastoma individuals without germline RB1 mutations.
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PEDONC-13.1: General Remarks

- Pediatric nasopharyngeal carcinoma (NPC) is rare in comparison to adult NPC but is responsible for up to 50% of nasopharyngeal cancers in children and has higher rates of aggressive type III EBV-associated histology than adult NPC.

- Standard upfront treatment in pediatric NPC consists of 3 to 4 cycles of neoadjuvant chemotherapy followed by definitive chemoradiotherapy. Rare individuals with lower stage disease may be treated with radiotherapy alone.
PEDONC-13.2: Pediatric NPC Imaging

Pediatric NPC Initial Staging:

- MRI Brain without and with contrast (CPT® 70553) and MRI Neck without and with contrast (CPT® 70543) CT Head without and with contrast (CPT® 70470), CT Maxillofacial without and with contrast (CPT® 70488) and/or CT Neck with contrast (CPT® 70491) for individuals with documented contraindication to MRI imaging (avoidance of sedation should not be the sole reason)
- CT Chest with contrast (CPT® 71260) in initial staging
- Whole body PET/CT (CPT® 78816) after histologic confirmation of NPC to evaluate for distant bony metastases
  - Bone scan when PET/CT is unavailable (see PEDONC-1.3: Modality General Considerations)

Pediatric NPC Treatment Response:

- MRI Brain without and with contrast (CPT® 70553) and MRI Neck without and with contrast (CPT® 70543) for response assessment at the following time points:
  - Following completion of neoadjuvant chemotherapy
  - Following completion of chemoradiotherapy
- CT Chest with contrast (CPT® 71260) and whole body PET/CT (CPT® 78816) or bone scan (See PEDONC-1.3: Modality General Considerations) at the following time points:
  - Following completion of neoadjuvant chemotherapy, only if positive at initial diagnosis
  - Following completion of chemoradiotherapy
- PET during active treatment for recurrent pediatric cancer in rare circumstances when results are likely to result in a treatment change, including a change from active treatment to surveillance. These requests will be forwarded for Medical Director review

Pediatric NPC Surveillance:

- MRI Brain without and with contrast (CPT® 70553) and MRI Neck without and with contrast (CPT® 70543) every 3 months for 1 year, then every 6 months for 2 years after completion of all planned therapy
- CT Chest with contrast (CPT® 71260) every 3 months for 1 year, then every 6 months for 2 years after completion of all planned therapy
  - Whole body PET/CT (CPT® 78816) or bone scan (see PEDONC-1.3: Modality General Considerations) only in the following situations:
    - Clarification of specified inconclusive findings seen on conventional imaging (should not replace biopsy)
    - Restaging to identify sites of disease when EBV PCR levels are abnormally high and conventional imaging is negative
    - Restaging after histologically confirmed recurrence of NPC
  - These requests will be forwarded for Medical Director review
**Background and Supporting Information**

- Quantitative EBV DNA PCR measured at initial diagnosis can serve as an effective tumor marker if elevated at initial diagnosis.
- Skull base invasion is common in pediatric NPC and has a dramatic impact on prognosis, and is more easily recognized on MRI imaging.
- PET is generally not indicated during active treatment for recurrent pediatric cancer.
  - Whole body PET/CT (CPT® 78816) or bone scan (see **PEDONC-1.3: Modality General Considerations**) are not indicated for routine surveillance in asymptomatic individuals.
References


# PEDONC-14: Pediatric Adrenocortical Carcinoma (ACC)

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PEDONC-14.1: General Remarks

Pediatric Adrenocortical Carcinoma (ACC) is rare, with fewer than 25 cases diagnosed each year. Most individuals are diagnosed because of virilizing symptoms or detection on screening imaging recommended for specified cancer predisposition syndromes.

See: PEDONC-2: Screening Imaging in Cancer Predisposition Syndromes
**PEDONC-14.2: Pediatric ACC Imaging**

**Pediatric ACC Initial Staging:**
- CT Abdomen without and with contrast (CPT® 74170) or MRI Abdomen without and with contrast (CPT® 74183) in the initial staging
- CT Chest with contrast (CPT® 71260) in initial staging
  - Nuclear bone scan (see **PEDONC-1.3: Modality General Considerations**) to evaluate for bony metastases at initial diagnosis.

**Pediatric ACC Treatment Response:**
- Individuals with ACC treated with surgery alone and not receiving adjuvant therapy should be imaged using surveillance guidelines after surgery
- CT Abdomen without and with contrast (CPT® 74170) or MRI Abdomen without and with contrast (CPT® 74183) for individuals treated with chemotherapy for response assessment every 2 cycles (~ 6 weeks) during chemotherapy and following completion of all planned chemotherapy
- CT Chest with contrast (CPT® 71260) every 2 cycles (~ 6 weeks) during chemotherapy and following completion of all planned chemotherapy
  - Nuclear bone scan (see **PEDONC-1.3: Modality General Considerations**) every 2 cycles (~ 6 weeks) during chemotherapy only if positive for distant metastases at initial diagnosis and following completion of chemotherapy
- CT Abdomen without and with contrast (CPT® 74170) or MRI Abdomen without and with contrast (CPT® 74183) for individuals treated with radiotherapy for response assessment at the completion of radiotherapy

**Pediatric ACC Surveillance**
- CT Abdomen without and with contrast (CPT® 74170) or MRI Abdomen without and with contrast (CPT® 74183) every 3 months for 2 years, then every 6 months for 3 years after completion of all planned therapy
- CT Chest with contrast (CPT® 71260) for individuals with metastatic ACC every 3 months for 2 years, then every 6 months for 3 years after completion of all planned therapy
- Nuclear bone scan (See **PEDONC-1.3: Modality General Considerations**) in all individuals with suspected bone recurrence

**Background and Supporting Information**
- The majority of ACC individuals are treated with surgery alone and do not receive adjuvant therapy
- Surveillance CT Chest is not indicated for individuals with localized disease at diagnosis
References
**PEDONC-15: Pediatric Melanoma and Other Skin Cancers**

- Pediatric melanoma staging is assigned using the American Joint Committee on Cancer (AJCC) staging for adult melanoma.
- Non-melanoma skin cancers are extremely rare in pediatric individuals and established age-specific guidelines for management of these tumors do not exist.
- Imaging guidelines and treatment approaches are consistent with those used for adults with melanoma and other skin cancers, and these individuals should follow the imaging guidelines in section **ONC-5: Melanomas and Other Skin Cancers**.
References


**PEDONC-16: Pediatric Salivary Gland Tumors**

The majority of pediatric salivary gland tumors arise in the parotid gland. Approximately 10 to 15% of tumors arise in the submandibular, sublingual, or minor salivary glands.

Roughly 75% of pediatric salivary gland tumors are benign, most commonly pleomorphic adenoma.

The most common malignant tumors occurring in the salivary glands are mucoepidermoid carcinoma, adenoid cystic carcinoma, acinic cell carcinoma, undifferentiated carcinoma, and rarely adenocarcinoma.

American Joint Committee on Cancer (AJCC) staging is used for pediatric as well as adult salivary gland tumors.

Imaging guidelines for malignant pediatric salivary gland tumors are consistent with those used for adults with salivary gland tumors, and these individuals should follow the imaging guidelines in section **ONC-4: Salivary Gland Cancers**.
**References**


PEDONC-17: Pediatric Breast Masses

- Ultrasound (CPT® 76641 and CPT® 76642) is the primary modality used for evaluation of pediatric breast masses.
- MRI has very limited utility in evaluation of pediatric breast masses prior to biopsy, but may be indicated in rare cases for surgical planning when ultrasound is non-diagnostic.
- All advanced imaging requests for pediatric breast masses should be forwarded for Medical Director review.

Background and Supporting Information

- Less than 1% of pediatric breast lesions are malignant, and advanced imaging is generally not recommended without histological confirmation of malignancy.
- Mammography has limited utility in pediatric breast mass evaluation due to the high mammographic breast density in this age group, and the risk of the radiation exposure outweighs the benefit of this modality.
- BI-RADS classification may overstate the risk of malignancy or need for biopsy in pediatric individuals.
References


PEDONC-18: Histiocytic Disorders

PEDONC-18.1: General Remarks 165
PEDONC-18.2: Langerhans Cell Histiocytosis (LCH) 166
PEDONC-18.3: Hemophagocytic Lymphohistiocytosis (HLH) 169
PEDONC-18.4: Non-Langerhans Cell Histiocytoses 170
PEDONC-18.1: General Remarks

- The majority of histiocytic disorders occurring in the pediatric population are either Langerhans Cell Histiocytosis (LCH) or Hemophagocytic Lymphohistiocytosis (HLH)
- The Non-Langerhans cell histiocytoses encompass a variety of diseases, and have limited imaging considerations except as specified later in this section
**PEDONC-18.2: Langerhans Cell Histiocytosis (LCH)**

**LCH Initial imaging studies:**

- Chest x-ray (CXR)
- Abdominal ultrasound (CPT® 76700)
- Skeletal survey
- MRI Brain without and with contrast (CPT® 70553) for any of the following:
  - Headaches or visual or neurologic disturbances
  - Polyuria/polydipsia or other endocrine abnormalities
  - Skull or craniofacial (including jaw) bone involvement
  - Otorrhea or hearing loss (CT Temporal Bone may be substituted if requested)
  - Other signs or symptoms suggesting intracranial involvement, including neurodegeneration syndrome
- CT Chest with (CPT® 71260) or without contrast (CPT® 71250) for any of the following:
  - Abnormal CXR
  - Symptoms of pulmonary involvement and normal CXR
- MRI Abdomen without and with contrast (CPT® 74183) for any of the following:
  - Elevated liver function tests (usually > 5X upper limit of normal)
  - Abnormalities seen on Abdominal ultrasound
    - CT Abdomen with contrast (CPT® 74160) can be substituted if requested by ordering physician to avoid general anesthesia
- MRI Spine without and with contrast (Cervical-CPT® 72156, Thoracic-CPT® 72157, Lumbar-CPT® 72158) for any of the following:
  - Vertebral lesions seen on skeletal survey
  - Clinical symptoms (including back pain) suggesting spinal involvement and negative skeletal survey
- Whole body PET/CT (CPT® 78816) for any of the following:
  - Multifocal bone involvement seen on skeletal survey
  - Bone pain and negative skeletal survey
  - Other clinical symptoms suggesting multisite disease
- Whole body Tc-99m bone scan (CPT® 78306) can be approved in lieu of PET for the same indications if PET is unavailable
LCH Treatment Response:

- Both PET/CT and CT with contrast and MRI without and with contrast only for simultaneous treatment response evaluation with specific documentation showing that both are necessary.
- CT and/or MRI and/or PET-CT (if modality showed disease at initial diagnosis):
  - After 6 weeks of treatment and after 12 weeks of treatment for those with persistent measurable disease.
- Following the initial phase, treatment response evaluation every 3 months while receiving active treatment:
  - Shorter interval imaging for documented signs or symptoms concerning for disease progression.
- At the end of planned therapy:
  - Chest x-ray (CXR).
  - Abdominal ultrasound (CPT®76700).
  - Skeletal survey.
  - Repeat of all additional imaging studies positive at initial workup (except PET).
- PET during active treatment for recurrent pediatric cancer only in rare circumstances when results are likely to result in a treatment change, including a change from active treatment to surveillance. These requests will be forwarded for Medical Director review.

LCH Surveillance Imaging:

- Surveillance imaging is determined by areas of disease involvement:
  - Bone involvement:
    - Plain x-ray of involved bony areas at 6 weeks, then at 3 and 6 months after completion of therapy.
    - Additional films are not necessary only when symptoms suggest new or recurrent disease.
    - PET to evaluate individuals with recurrent disease.
    - Skull or craniofacial (including jaw) bone involvement should be imaged according to CNS involvement section below.
  - Pulmonary involvement:
    - CXR every 6 months after completion of therapy.
    - CT Chest with (CPT® 71260) or without contrast (CPT® 71250) For new abnormalities on CXR or new pulmonary symptoms with a negative CXR.
  - CNS involvement:
    - MRI Brain without and with contrast (CPT® 70553) at 6 weeks, 3 months, and 6 months after completion of all therapy for previously documented measurable intracranial lesions.
    - If negative at 6 months, continued surveillance at 1, 2, 4, 7, and 10 years after completion of all planned therapy.
If residual measurable intracranial lesions are present at 6 months, imaging every 3 months until negative or unchanged on two consecutive studies, at which time the schedule in the previous bullet should begin:

- MRI Brain without and with contrast (CPT® 70553) for documented hypothalamic-pituitary dysfunction at 1, 2, 4, 7, and 10 years after completion of all planned therapy
- MRI at any time for worsening neurologic symptoms
- Intraspinal lesions should be imaged according to the same guidelines as brain imaging using MRI without and with contrast of all involved spine levels

Liver involvement
- Surveillance Ultrasound Abdomen (CPT® 76700) every 6 months

**Background and Supporting Information**

- LCH includes a heterogeneous group of disorders formerly known by other names including histiocytosis X, eosinophilic granuloma, Letterer-Siwe Disease, Hand-Schuller-Christian Disease, and diffuse reticuloendotheliosis
- Most common sites of involvement are skin, bones, liver, lung, and pituitary, though other sites are possible
- PET should not be used to replace skeletal survey during initial imaging in LCH
- Individuals with localized or single site disease treated only with local therapies or observed should be imaged according to surveillance guidelines
- Individuals receiving systemic therapy will usually undergo treatment for ~12 months. Treatment response is assessed using any modalities showing disease at initial diagnosis after ~6 weeks of treatment
- Once PET/CT shows no remaining FDG-avid lesions, additional PET imaging is not indicated
- PET is generally not indicated during active treatment for recurrent pediatric cancer
- Bone involvement
  - Skull or craniofacial (including jaw) bone involvement at diagnosis are at higher risk for CNS recurrence
- CNS involvement
  - CNS LCH has a particularly high rate of refractory and recurrent disease, and requires longer imaging surveillance
- Liver involvement
  - Persistent liver involvement is rare, and imaging after completion of LCH therapy will be highly individualized depending on degree of liver dysfunction and plans for supportive therapy or liver transplant
PEDONC-18.3: Hemophagocytic Lymphohistiocytosis (HLH)

- Advanced imaging requests for HLH should be forwarded for medical director review.
- Common studies that may be indicated in the initial evaluation of HLH include:
  - Ultrasound Abdomen (CPT® 76700)
  - CT Abdomen and/or Pelvis (contrast as requested)
  - MRI Abdomen (CPT® 74183) and/or Pelvis (CPT® 72197) without and with contrast
  - CXR
  - CT Chest with contrast (CPT® 71260)
  - MRI Brain without and with contrast (CPT® 70553)

- Whole body PET/CT (CPT® 78816) for the purpose of identifying a site for tissue diagnosis of a primary source of infection or malignancy if conventional imaging has been completed and is unrevealing.
  - If a malignancy is identified as the inciting factor for HLH, additional imaging decisions for that malignancy should be based on the appropriate diagnosis-specific guidelines.

**Background and Supporting Information**
- There are no standard imaging studies required for the diagnosis and initial evaluation of HLH. Advanced imaging studies may be necessary to assess organ dysfunction as HLH commonly affects the liver, spleen, and bone marrow, and less commonly the kidneys, lungs, and brain.
- It is not required to perform ultrasound or plain film in a stepwise fashion if CT or MRI is planned as individuals with HLH can deteriorate rapidly.
- There is no established standard role for PET in the diagnosis or treatment response evaluation of HLH.
  - Secondary HLH is very difficult to treat if the primary cause is not concurrently treated.
**PEDONC-18.4: Non-Langerhans Cell Histiocytoses**

- **Juvenile Xanthogranuloma (JXG):**
  - Skin and/cervical nodules: CT with contrast of involved nodal areas
  - Systemic JXG with multiorgan involvement:
    - MRI Brain (CPT® 70553) and/or Orbits (CPT® 70543) without and with contrast
    - CT Neck (CPT® 70491), Chest (CPT® 71260), and/or Abdomen (CPT® 74160) with contrast

- **Rosai-Dorfman Disease (RDD):**
  - MRI Brain (CPT® 70553) and/or Orbits (CPT® 70543) without and with contrast
  - Nuclear bone scan (see **PEDONC-1.3: Modality General Considerations**)
  - CT Neck (CPT® 70491), Chest (CPT® 71260) and/or Abdomen/Pelvis (CPT® 74177) with contrast
  - Whole body PET/CT (CPT® 78816) if PET/CT will provide critical information for major treatment decision making that cannot be obtained using conventional imaging or biopsy. These requests will be forwarded for Medical Director review.
  - CT with contrast for evaluation of new or worsening clinical symptoms suggesting recurrent disease

- **Erdheim-Chester Disease (ECD):**
  - ECD Initial imaging studies:
    - MRI Brain (CPT® 70553) and/or Orbits (CPT® 70543) without and with contrast
    - Nuclear bone scan (see **PEDONC-1.3: Modality General Considerations**)
    - Whole body PET/CT (CPT® 78816)
    - CT Neck (CPT® 70491), Chest (CPT® 71260) and/or Abdomen/Pelvis (CPT® 74177) with contrast
    - CTA Chest or MRA Chest (CPT® 72175 or CPT® 71555) or Abdomen (CPT® 74175 or CPT® 74185) to evaluate vascular tree involvement
    - Cardiac MRI without and with contrast (CPT® 75561)
  - ECD Treatment Response:
    - Treatment response imaging every 3 months during active treatment using any modalities showing disease at initial diagnosis, including PET/CT
    - Once PET/CT shows no remaining FDG-avid lesions, additional PET imaging is only indicated when conventional imaging studies are inconclusive and acute treatment decisions will be made based on PET results. These requests will be forwarded for Medical Director review.
ECD Surveillance Imaging:
- CT and/or MRI and/or PET-CT and/or Nuclear bone scan and/or Whole Body PET/CT and/or CTA and/or MRA and/or Cardiac MRI (if modality showed disease at initial diagnosis) every 3 months for the first year after completion of treatment and then every 6 months
- PET/CT if conventional imaging is inconclusive for suspected recurrence. These requests will be forwarded for Medical Director review.

**Background and Supporting Information**

- Non-Langerhans Cell histiocytoses includes diagnoses such as juvenile xanthogranuloma (JXG), sinus histiocytosis with lymphadenopathy (Rosai-Dorfman disease, RDD), and Erdheim-Chester disease (ECD)

- In general, these are localized cutaneous or nodal disease without need for regular advanced imaging, but important exceptions are listed in this section

- Juvenile Xanthogranuloma (JXG):
  - Generally involves only skin or cervical nodes, and involutes spontaneously
  - There is no established role for PET in the diagnosis or treatment of JXG

- Rosai-Dorfman Disease (RDD):
  - Characterized by bulky adenopathy (usually cervical) with frequent systemic involvement
  - There is no established role for PET in the diagnosis or treatment of RDD
  - Because of the paucity of evidence for PET, PET/CT should not be used to replace tissue confirmation for any clinical scenario in RDD
  - There is no established role for routine surveillance imaging of asymptomatic individuals after treatment for RDD

- Erdheim-Chester Disease (ECD):
  - An aggressive histiocytic disorder with overall poor prognosis that is characterized by long bone involvement with frequent spread to multiple organs
  - Most individuals will receive systemic therapy
  - Once PET/CT shows no remaining FDG-avid lesions, additional PET imaging is not indicated unless conventional imaging studies are inconclusive and acute treatment decisions will be made based on PET results. These requests will be forwarded for Medical Director review
  - PET/CT is not supported for routine surveillance of ECD
References


PEDONC-19: Long Term Pediatric Cancer Survivors

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PEDONC-19.1: General Remarks

- This section applies to individuals who have passed the end of the surveillance imaging period for their specific cancer, or 5 years after completion of therapy, whichever occurs first.

- As these are long term survivors, many individuals falling under this guideline section will have reached adult age. However, these guidelines relate specifically to late effects of childhood cancer treatment and should be applied to all long term childhood cancer survivors regardless of current age.

- The Children’s Oncology Group has published comprehensive guidelines for the management of long-term childhood cancer survivors, and these are available at: [http://www.survivorshipguidelines.org](http://www.survivorshipguidelines.org)

- A summary of cancer treatment should be available for all individuals in this category and should generally include, at minimum:
  - Type of cancer and stage
  - Dates of diagnosis, recurrence, cancer-related surgeries, beginning and end dates of chemotherapy, radiotherapy, and/or stem cell transplant
  - Protocol number used for treatment and cumulative chemotherapy drug dose exposures
  - Cumulative radiation dose, fraction number, modality, and field exposure

- Annual detailed history and complete physical examination is a critical component of cancer survivorship care and along with laboratory testing serves as the primary method of screening for the majority of late effects.
  - Advanced imaging for asymptomatic screening is not routinely indicated except as specified in this section.
PEDONC-19.2: Cardiotoxicity and Echocardiography

- Screening echocardiography (CPT® 93306, CPT® 93307, or CPT® 93308) for life after exposure to anthracycline chemotherapy or cardiac exposure to radiotherapy
  - Individuals **age < 1 year** at time of first exposure:
    - Echocardiography **every year** for any cardiac radiotherapy exposure or ≥ 200 mg/m² cumulative doxorubicin equivalent exposure
    - Echocardiography **every 2 years** for < 200 mg/m² cumulative doxorubicin equivalent exposure and no cardiac radiotherapy exposure
  - Individuals **ages 1 to 4 years** at time of first exposure:
    - Echocardiography **every year** for any cardiac radiotherapy exposure or ≥ 300 mg/m² cumulative doxorubicin equivalent exposure
    - Echocardiography **every 2 years** for 100 to 300 mg/m² cumulative doxorubicin equivalent exposure and no cardiac radiotherapy exposure
    - Echocardiography **every 5 years** for < 100 mg/m² cumulative doxorubicin equivalent exposure and no cardiac radiotherapy exposure
  - Individuals **age ≥ 5 years** at time of first exposure:
    - Echocardiography **every year** for ≥ 300 mg/m² cumulative doxorubicin equivalent exposure regardless of cardiac radiotherapy exposure
    - Echocardiography **every 2 years** for 200 to 300 mg/m² cumulative doxorubicin equivalent exposure and no cardiac radiotherapy exposure
    - Echocardiography **every 2 years** for < 300 mg/m² cumulative doxorubicin equivalent exposure and cardiac radiotherapy exposure
    - Echocardiography **every 5 years** for < 200 mg/m² cumulative doxorubicin equivalent exposure and no cardiac radiotherapy exposure
  - Individuals of any age with abnormal ventricular function:
    - Echocardiography **every year**

**Background and Supporting Information**

- Exposure to cardiotoxic anthracycline chemotherapy agents is common in pediatric oncology due to the high success rate of this drug class in the treatment of pediatric cancers
- Cardiotoxic anthracycline chemotherapy agents include the following:
  - Doxorubicin
  - Daunorubicin
  - Idarubicin
  - Epirubicin
  - Mitoxantrone
- Cardiac risk is due to the age of the individual at the time of administration and the cumulative drug exposure expressed as doxorubicin equivalent mg/m²
- Stress echocardiography is not indicated as a screening study for anthracyclines cardiotoxicity in the absence of coronary artery disease symptoms. See **CD-1.4: Stress Testing with Imaging – Indications** for imaging guidelines
PEDONC-19.3: Second Malignant Neoplasms (SMN)

SMN—Breast Cancer:
Clinical breast exam every 6 months supplemented with:

- Annual Breast MRI (CPT® 77059) and annual mammogram beginning at age 25 or 8 years after completion of radiotherapy (whichever occurs later) for individuals receiving a cumulative radiation exposure of ≥ 20 Gy in the following fields for any pediatric cancer type except Wilms tumor:
  - Chest (thorax)
  - Whole lung
  - Mediastinal
  - Axilla
  - Mini-mantle, mantle, or extended mantle
  - Total (TLI) or subtotal (SLTI) lymphoid irradiation
  - Total body irradiation (TBI)

- Annual Breast MRI (CPT® 77059) and annual mammogram beginning at age 25 or 8 years after completion of radiotherapy (whichever occurs later) for individuals receiving ≥ 12 Gy of whole lung radiation for treatment of Wilms tumor

SMN—CNS Tumors:

- MRI Brain without and with contrast (CPT®70553) for any individual with a history of brain radiotherapy and new neurologic symptoms, including simple headache

- MRI Cervical (CPT®72156), Thoracic (CPT®72157), and Lumbar Spine (CPT®72158) without and with contrast for any individual with a history of spine radiotherapy and new neurologic symptoms, including change in quality of pain
  - MRI Spine with contrast only (Cervical-CPT®72142, Thoracic-CPT®72147, Lumbar-CPT®72149) if being performed immediately following a contrast-enhanced MRI Brain

- MRI Brain without and with contrast (CPT®70553) annually for individuals with history of brain radiotherapy and persistent neurologic symptoms

- MRI Cervical (CPT®72156), Thoracic (CPT®72157), and Lumbar Spine (CPT®72158) without and with contrast annually for individuals with a history of spine radiotherapy and persistent neurologic symptoms
  - MRI Spine with contrast only (Cervical-CPT® 72142, Thoracic-CPT® 72147, Lumbar-CPT® 72149) if being performed immediately following a contrast-enhanced MRI Brain
SMN—Colorectal Cancer:

- No advanced imaging is currently recommended. See Background and Supporting Information Section for recommended surveillance.

Background and Supporting Information

- SMN—Breast Cancer:
  - Clinical breast exam every 6 months supplemented with advanced imaging.

- SMN—CNS Tumors:
  - These are associated with radiation exposure to the brain and with neurofibromatosis.
  - Routine surveillance of completely asymptomatic individuals with normal neurologic exams is not supported by evidence.

- SMN—Colorectal Cancer:
  - Colonoscopy is recommended every 5 years beginning at age 35 or 10 years after radiation exposure (whichever is later) for individuals with ≥ 30 Gy radiation exposure to the following fields:
    - Thoracic, Lumbar, Sacral, or Whole Spine
    - Extended mantle
    - Hepatic, Renal, Spleen, RUQ or LUQ
    - Paraaortic or Flank/Hemiabdomen
    - Whole Abdomen
    - Inverted Y
    - Pelvic
    - Vaginal
    - Prostate or Bladder
    - Iliac, Inguinal, or Femoral
    - Total (TLI) or subtotal (SLTI) lymphoid irradiation
    - Total body irradiation (TBI)
  - Colonoscopy is also recommended every 5 years beginning at age 35 or 10 years after radiation exposure (whichever is later) for individuals with:
    - Personal history of ulcerative colitis, GI malignancy, adenomatous polyps, or hepatoblastoma
    - Familial polyposis
    - Family history of colorectal cancer or polyps in a first degree (parent or sibling) relative

- While the American Cancer Society recently added computed tomographic colonography (CTC) (AKA “Virtual Colonoscopy”) as an acceptable option for colorectal cancer screening of average-risk adults, the National Comprehensive Cancer Network and United States Preventive Services Task Force concluded that data was too premature to warrant its use in screening. Colonoscopy remains the preferred screening modality for survivors at highest risk of colorectal cancer.
PEDONC-19.4: Osteonecrosis in Long Term Cancer Survivors

- Plain films of symptomatic areas are indicated prior to advanced imaging.
- DEXA or Quantitative CT screening only for those with symptoms to suggest bone density issues.
  - DEXA or Quantitative CT screening is generally not recommended until age 18 unless a specific intervention will be planned based on the imaging results.
- Serial advanced imaging is only indicated in osteonecrosis with specific documentation regarding how the advanced imaging will change current management.
  - MRI without contrast of the affected joint(s) when advanced imaging is necessary for acute management decisions.
- See PEDONC-3.2: Acute Lymphoblastic Leukemia (ALL) for information on imaging osteonecrosis in ALL individuals during active treatment.

Background and Supporting Information

- Osteonecrosis is associated with chemotherapy and radiation exposure during treatment for ALL, NHL, and allogeneic HSCT in pediatrics. Osteonecrosis occurs primarily in hips, knees, and ankles. Osteoradionecrosis of the jaw can occur in individuals receiving radiotherapy to the mandible or maxilla; those receiving ≥ 40 Gy are at highest risk. Although unusual, it can also occur in any bone without symptoms. It is rare in other disease types.
- Routine bone density screening using DEXA or Quantitative CT screening has not been well normalized in the pediatric population.
- Surveillance imaging of asymptomatic individuals to detect osteonecrosis has not been shown to impact outcomes, and it is not standard to alter treatment based on imaging findings alone without symptoms.
  - Follow up MRI of incidentally discovered osteonecrosis findings in asymptomatic individuals has not been shown to impact individual outcomes and is not necessary.
References


