# PET and PET/CT in Pediatric Gastrointestinal Tract Oncology

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**KEYWORDS**

- Pediatric oncology • Childhood malignancy
- PET • Gastrointestinal lymphoma
- Hepatoblastoma • Hyperinsulinism

Childhood cancers represent about 1% of all new cancer cases[1] and are the second highest cause of death (12.8%) in children in the United States.[2] Pediatric malignancies differ from adult neoplasms in both distribution and prognosis. Lymphohematopoietic cancers are the most common during childhood, as approximately 40% of all cancers. Nervous system cancers account for approximately 30%, and embryonal tumors and sarcomas account for approximately 20% of childhood cancers.[2] Childhood gastrointestinal malignancies include extranodal lymphoma of gastrointestinal tract; hepatic tumors; pancreatic tumors; and other rare neoplasms, such as gastrointestinal adenocarcinoma, biliary cancers, and gastric cancers. Metastases to gastrointestinal tract, although rare, may occur from neuroblastoma, Wilms' tumor, osteogenic sarcoma, and desmoplastic small round cell tumor.[3–5] Unlike incidence patterns in adults, there is a relatively wide age range in the pediatric age group, with two peaks, the first in early childhood and the second in adolescence.[6] The 5-year disease-free survival and cure in most childhood cancer is about 80%. This high survival rate reflects progress in the understanding of tumor biology and incremental improvements in diagnosis and therapy.[7,8]

Imaging of tumor metabolism using positron emission tomography (PET) has been wildly successful.[9–16] Such functional imaging can be used together with anatomic imaging to diagnose, characterize, or monitor tumors before and after therapeutic treatment.[17,18] Furthermore, the introduction of combined PET with CT has been an advancement in diagnostic imaging allowing synergistic interpretation and precise anatomic localization of the metabolic information. In pediatric population, the scan time is critical and the use of CT for attenuation correction has shortened the scan time.[19] The role of PET imaging in pediatric malignancies is still evolving with limited literature.[19,20]

This article reviews PET imaging in pediatric gastrointestinal oncology with a special focus on gastrointestinal lymphoma, liver malignancies, and pancreatic tumors.

## PATIENT PREPARATION

Undertaking examination on children can be challenging. Child preparation for PET imaging includes a sheet wrapped around the body, sand bags and holding devices for immobilization, reliable intravenous access, and bladder

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PET Clin 3 (2008) 227–238
doi:10.1016/j.cpet.2008.10.004

catheterization to avoid discomfort and possible contamination.[21,22] Sedation may be used according to the guidelines of the Society of Nuclear Medicine, the American Academy of Pediatrics, and the American Society of Anesthesiology.[23,24] Sedation may potentially affect tracer biodistribution but it is not known to affect tumor metabolism. Parents may accompany their child.[25]

## RADIATION DOSIMETRY

The recommended dose of fluorodeoxyglucose (FDG) for children ranges from 0.15 to 0.30 (5–10 MBq) mCi/kg with a total dose of 1 mCi (37 MBq) and not more than 20 mCi (750 MBq).[26] Ruotsalainen and colleagues[27] reported the absorbed radiation dose in a series of 21 infants. Bladder wall is the target organ. Absorbed dose per unit in variable organs of infants is higher than that reported in adults. The total body absorbed dose is lower in infants, however, compared with adults.[25,27] Using PET-CT, the radiation doses of the CT part using 80 mA and 140 kV is 3 to 5 mSv. The effective doses from diagnostic CT procedures are estimated to be of 1 to 10 mSv. The dose from a diagnostic CT procedure may vary depending on the type of CT procedure, patient size, CT system, and operating technique.[28–30]

## PHYSIOLOGIC AND VARIANT FLUORODEOXYGLUCOSE DISTRIBUTION IN CHILDREN

Thymus and bone growth centers may show increased FDG uptake and is specific for children.[31,32] Increased FDG uptake has been encountered in the brain (mainly the subcortical gray matter)[27]; salivary glands; myocardium; renal pelves; ureters; and bladder. There is mild uptake of liver, spleen, and bone marrow. Occasionally, FDG uptake may also be noted in the thyroid gland and vocal cords.[33–35] Following chemotherapy, diffuse increased FDG uptake has been noted in bone marrow, in spleen, and occasionally in the thymus.[36–38] Increased FDG activity in the breast of a teenage girl or in the testicle of a teenage boy is frequent and should be regarded as normal variant. In addition, brown fat activity in pediatric population is frequently more prevalent and more intense.

## GASTROINTESTINAL LYMPHOMA

Non-Hodgkin's lymphoma accounts for about 60% of all lymphomas and 10% of childhood malignancies.[39] Primary extranodal lymphoma represents 25% of the non-Hodgkin's lymphoma incidence in the United States. Approximately 50% of extranodal lymophoma occur in the gastrointestinal tract.[40,41] In the pediatric group, small and large intestines are the most common locations of involvement (**Fig. 1**). Every extranodal site has special clinical characteristics and management.[42] Hodgkin's disease, a malignant process of the lymphoreticular system, constitutes 6% of childhood cancers.[39] Approximately 30% of children with Hodgkin's disease have the propensity of extranodal spread including liver and spleen.[43] Studies show that most extranodal lymphomas arise from lymphoid cells of lineage different from those of the lymph nodes and spleen.[44,45] The alternative lymphoid system is known as mucosa-associated lymphoid tissue. Mucosa-associated lymphoid tissue lymphocytes have specific receptors that allow homing to extranodal tissues.[46] The homing capacity of mucosa-associated lymphoid tissue lymphocytes can explain some of the extranodal spread pattern.[47] Immunophenotype of mucosa-associated lymphoid tissue lymphomas helps distinguish them from other neoplastic proliferations of small lymphoid cells. Mucosa-associated lymphoid tissue lymphocytes are positive for clonal surface Ig and pan B-cell antigens (CD22, CD20, and CD19), but negative for both CD5 and for CD10.[48,49] The prognosis of childhood lymphoma has improved with survival rate of about 90%.[39]

FDG-PET and PET-CT proved to be useful for detection, staging, restaging, monitoring therapy response, and evaluation of recurrence in patients with lymphoma.[9,50–54] The routine application of PET imaging in pediatric oncology, however, has not been fully established.[55]

CT remains the most commonly used modality in management of patients with lymphomas.[56–58] CT interpretation depends on the size and shape of lesions, however, which takes time to be detectable. Furthermore, CT may not differentiate between fibrosis-necrosis and residual disease after therapy.[59–61] For many years, gallium scintigraphy has been the functional imaging modality for high-grade non-Hodgkin's lymphoma at the time of diagnosis and in evaluation of response to treatment that may solve some CT challenging cases.[33,62] Gallium, however, has some drawbacks. It has low sensitivity and specificity for infradiaphragmatic disease because of physiologic uptake of gallium in the abdomen. Because of low resolution, it is difficult to evaluate intermediate and low-grade lymphomas. Moreover, a long time interval between injection and scanning (3 days) is required to clear the background activity.[33]

PET imaging has features that make it preferable to gallium scintigraphy: a shorter interval between