Positron emission tomography (PET) has emerged as a functional diagnostic modality and is now routinely used in oncology for detecting and grading tumors, monitoring the response to therapy, distinguishing between residual tumors and post treatment scarring. Conventional imaging relies on morphological changes, whereas, PET being a functional imaging modality detects the disease process in its early phase as metabolic abnormalities generally precede anatomical changes. PET, however, is limited in its ability to provide information on the exact localization of lesions because of the absence of precise anatomic landmarks. PET used in conjunction with computerized tomography (CT) (PET-CT) is more useful as it provides anatomical details and the abnormal uptake on PET can be localized with highest accuracy. Much work has been done regarding PET/PET-CT in the adults but there is paucity in the same in pediatric group. A child must receive special attention when embarking on what is uncertain and often a frightening procedure. While performing PET in pediatric patients, emphasis is given to patient consent, intravenous access, bladder catheterization, and sedation. Based on existing literature and our own experience, we understand that PET-CT can play a very important role in initial staging, restaging, and evaluation of treatment response in lymphoma, neuroendocrine tumors and bone, and soft tissues sarcoma.

KEY WORDS: Fluorodeoxyglucose, pediatric malignancies, positron emission tomography, positron emission tomography-computerized tomography

PATIENT PREPARATION AND ACQUISITION

Patients are kept fasting for at least 4 hr prior to the F-18 FDG study. Hydration is maintained orally, and in small children by intravenous administration of ringer lactate/normal saline. Smaller children are sedated using 0.1 mg/kg midazolam to avoid motion artifacts. Prior to the administration of F-18 FDG, the serum glucose level is measured, which should be below 140 mg/dl. F-18 FDG is administered intravenously with patients in a resting state, in a quiet room {Dose: 5.3 MBq/kg (0.144 mCi)}. Images are acquired 45-60-minute post F-18 FDG administration. In the PET-CT system, the transmission scan is performed first followed by PET acquisition. Data obtained from the CT acquisition is used for low noise attenuation correction of PET emission data and for fusion of attenuation corrected PET images with the corresponding CT images. After completion of PET acquisition, the reconstructed attenuation-corrected PET images, CT images and fused images of matching pairs of PET and CT images are available for review in axial, coronal, and sagittal planes and in three dimensional cine mode.
CLINICAL INDICATIONS

The role of PET is well established in the management of colorectal cancer, breast cancer, lymphoma, melanoma, and lung cancer in adults.[1] However, its role in pediatric malignancies is still limited. Common malignancies that have been studied with PET/PET-CT in children include neuroendocrine tumors, lymphomas, brain tumors, and soft tissue sarcomas.

NEUROENDOCRINE TUMORS

Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms originating from endocrine cells, which are characterized by the presence of secretory granules and have the ability to produce biogenic amines and polypeptide hormones. Based on these characteristics, specific PET radiopharmaceuticals have been developed that reflect the different metabolic pathways of NETs. These include radiopharmaceuticals for glucose metabolism (F-18 fluorodeoxyglucose), uptake of hormone precursors (C-11-5-hydroxytryptophan, C-11- or F-18 dihydroxyphenylalanine, F-18 fluorodopamine), expression of receptors (Ga-68 labeled somatostatin analogs), as well as the synthesis, storage, and release of hormones (C-11 hydroxyephedrine).[2]

NEUROBLASTOMAS

Neuroblastomas (NB) are tumors derived from the neural crest of the sympathetic-adrenal system and are the most commonest extra cranial solid tumor in children, accounting for 8% to 10% of all childhood cancers.[3] The early detection of metastatic neuroblastoma by sufficiently specific and sensitive scanning may reveal otherwise unsuspected and still resectable tumors, facilitating staging and prognosis. At present, MIBG imaging is a well-established procedure, and it is used in the initial staging and restaging, monitoring the response to therapy, and in the early diagnosis of recurrence.[4] It can depict primary and residual/recurrent NB as well as metastatic lesions with an overall accuracy of about 90%. It is also accurate in post therapy prognostication.[5-7]

There is limited data on FDG-PET imaging in neuroblastoma. Shulkin and coworkers in their study reported FDG uptake in neuroblastoma primary tumors and metastases. They compared FDG-PET with MIBG and concluded that the majority of NB are metabolically active and can be detected by FDG-PET imaging but that MIBG was overall superior to FDG-PET imaging.[8-10] Kushner et al., evaluated serial FDG-PET studies in patients with NB and concluded that FDG-PET was accurate in the assessment of treatment response and was better for liver lesions, where there is a significant uptake on MIBG scans.[11] In another study, the same author, suggested that FDG-PET can depict NB lesions and also those that fail to accumulate MIBG.[12] Therefore, in patients with NB, FDG-PET should be performed only if MIBG scintigraphy gives negative results.

Other radiotracers like C-11-hydroxyephedrine (HED) have shown promising results in NB.[13,14] Franzius and coworkers compared HED with I-123-MIBG and detected more lesions with HED than MIBG. The overall sensitivity for HED was 99%, whereas I-123-MIBG was 93%. Other agents still in experimental phase include F-18 fluoro-3-iodobenzylguanidine, F-18 fluorodopamine (F-18FDA), and F-18 dihydroxyphenylalanine (F-18 DOPA).[15]

PHAECHROMOCYTOMA

Pheochromocytomas are catecholamine-secreting NETs arising from chromaffin cells of the adrenal medulla. Paragangliomas are chromaffin cell tumors arising in the sympathetic and parasympathetic paraganglia. Anatomical imaging with CT or MRI are initial investigations of choice and a have high sensitivity (93-100%). I-123 MIBG is the functional agent of choice, with a specificity of 95% to 100% and sensitivity upto 90%.[16] FDG-PET has limited sensitivity for solitary benign or malignant pheochromocytomas (approx 70%); however, it has a role in detection of metastases when MIBG scintigraphy is negative.[17,18] Newer agents like C-11-HED have shown better results in patients with pheochromocytoma with a sensitivity of 90% for both primary and metastatic deposits.[19] F-18 DOPA and F-18 FDA have also shown diagnostic sensitivity superior to FDG and specificity similar to radioiodinated MIBG.[20] In a study by Ilias et al., F-18 FDA localized in the primary tumor and metastatic sites in all patients with pheochromocytoma, showing a large number of lesions not depicted with I-131 MIBG.[21]

LYMPHOMAS

Lymphoma is a common malignancy in children and accounts for 6% of childhood cancers. Accurate staging of Hodgkin disease (HD) and non Hodgkin lymphoma (NHL) is essential to achieve a high cure rate. PET can play an important role in the initial staging, monitoring the response to therapy, and differentiating fibrosis from residual/recurrent disease.[22] Rini et al., compared F18-FDG-PET and Gallium-67 whole-body and SPECT in children and young adults in initial staging of HD and concluded that PET is superior to Ga-67 whole-body and SPECT.[23] PET is more accurate than conventional staging methods for pretreatment staging in pediatric
lymphomas with accuracy of 96.7% and 85.2%, respectively.\textsuperscript{[24]} PET-CT/PET is associated with change in staging in approximately 33-50% of pediatric patients with HD and NHL.\textsuperscript{[12]} FDG-PET/PET-CT is also useful for monitoring the response to therapy and detecting the disease relapse in follow-up of pediatric lymphomas. PET has high negative predictive value as compared to CT for monitoring the response to therapy and disease recurrence, ranging from 90-100%, but has low positive predictive value ranging from 18.2-94%.\textsuperscript{[20]} The low positive predictive value is due to the increased uptake in numerous non-oncologic processes such as infections, brown fat, post treatment thymic hyperplasia, transforming germinal centers, and effects of therapy on normal tissues, which can mimic recurrent or residual tumor.\textsuperscript{[26]}

**HEPATOBLASTOMA**

Hepatoblastoma is the most common primary liver tumor in children, accounting for 79% of pediatric liver malignancies in children younger than 15 years, with most cases reported before the age of 5 years.\textsuperscript{[27]} Localization of primary and recurrent disease is necessary for appropriate clinical decision-making and treatment. F-18 FDG PET/PET-CT has no role in the initial diagnosis of hepatoblastoma. Few studies have evaluated the role in staging or restaging and assessing the response to therapy.\textsuperscript{[28]} PET is helpful in detecting early recurrence and for assessing response to therapy in patients with negative AFP levels.\textsuperscript{[27,28]} However, caution must be taken in interpretation of positive results, as false positive results do occur due to inflammatory processes like necrotizing granuloma and also due to regenerative liver tissue.\textsuperscript{[30]} These tumors being rare, many more prospective multicenter studies are necessary to determine the true clinical utility of FDG-PET imaging in the management of children with primary hepatic malignancies.

**SARCOMAS**

In musculoskeletal cancers, osteosarcoma (OS) and the Ewing sarcoma family of tumors (ESFT) are the most common childhood primary bone cancers. Several authors have evaluated the role of FDG-PET in the initial diagnosis of osteosarcoma but with limited success. Aoki et al.\textsuperscript{[31]} evaluated the FDG-PET in differentiating primary benign tumors from giant cell tumors, osteosarcoma, and chondrosarcomas. The authors reported that FDG-PET may have limitation in distinguishing accurately malignant from benign or differentiating between the malignant tumors. However, FDG-PET is useful in detection of metastases to lung and bones (Figure 2). In these patients, a sensitivity, specificity, and accuracy of 50%, 98%, and 97%, respectively has been noted for detection of metastasis by FDG-PET. For spiral CT, these values were 75%, 100%, and 94%, respectively.\textsuperscript{[32]} There is a definite role of FDG-PET in assessing the response to neoadjuvant chemotherapy in patients with osteosarcoma. In a study by Nair et al.,\textsuperscript{[33]} FDG-PET was able to predict tumor necrosis accurately by visual assessment and by tumor to background ratio (TBR) on scans after chemotherapy and before surgery.

Franzius et al.\textsuperscript{[34]} compared FDG-PET and conventional imaging in patients with primary bone tumors for detection of recurrence. The sensitivity, specificity, and accuracy were 96%, 81%, and 90%, respectively, for PET, and 100%, 56%, and 82%, respectively, for conventional imaging modalities. The authors suggested that FDG-PET is a good adjunct to MRI in differentiating viable

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image1.png}
\caption{Non-Hodgkins lymphoma for staging: Axial section of CT shows multiple left cervical lymph nodes (A). Intense FDG uptake was seen in PET (B) and PET-CT (C) in cervical lymph nodes seen on CT}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image2.png}
\caption{Post operated case of osteosarcoma of lower end of right femur. Whole body CT image does not show any abnormality in bones and soft tissue (A). PET-CT (B) image also shows normal scan. CT scan of the same patient in lung window shows bilateral pulmonary nodules (C). FDG uptake was seen on PET-CT image in the lung parenchymal nodule suggestive of pulmonary metastases (D)}
\end{figure}
tumor from post therapeutic changes in patients with sarcomas and thereby assessing response to therapy.

Ewing sarcomas are small, round cell tumors of the musculoskeletal system. They are the second most common group of bone sarcomas in children, after osteosarcoma. FDG-PET has been found to be helpful in the detection, grading, and management of the Ewing’s sarcoma family of tumors. Hawkins et al. evaluated 33 pediatric patients with OS and ESFT using FDG-PET. Standardized uptake values (SUV) before and after chemotherapy were analyzed and correlated with chemotherapy response. All ESFT patients and 28% of OS patients had a favorable histologic response to chemotherapy, which correlated well with SUV values.

Alveolar rhabdomyosarcoma accounts for 20% to 30% of childhood rhabdomyosarcoma and has a worse prognosis than embryonal rhabdomyosarcoma as metastatic disease is more common in the former [Figure 3]. Hematogenous spread to the lung is the most frequent route of spread. Arush et al. assessed the use of PET in the detection of regional and metastatic nodes in alveolar rhabdomyosarcoma of extremities.

**BRAIN TUMORS**

PET/PET-CT can be used in differentiating post treatment sequel (both post surgical and post radiation changes) from active tumor and in the localization of persisting tumor amenable to radiosurgical treatment. F-18 FDG has limitation in brain tumor imaging due to high physiological uptake of FDG in the normal brain tissue. FDG-PET may be helpful in differentiating between anaplastic astrocytoma and glioblastomas among high-grade tumors. This differentiation is based on the metabolic status of the tumor as compared to normal brain parenchyma. Studies have shown utility of PET with C-11 Methionine in diagnosis and evaluation of the treatment efficacy in childhood brain tumors. The assessment of tumor metabolic activity using PET with C-11 Methionine can provide prompt evaluation of treatment efficacy and control of recurrence.