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REVIEW

PET/CT in paediatric oncology: indications and pitfalls

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Introduction

PET/CT has become an important imaging modality in the non-invasive evaluation and monitoring of children with known or suspected malignant diseases. Recently, multiple reports on feasibility and practical aspects, review articles and some original studies addressing PET/CT in paediatric oncology have been published. Although publications on the additional value of combined PET/CT compared to both stand-alone modalities are still limited in paediatrics, it can already be anticipated that the combination of morphological and functional information obtained by integrated PET/CT will improve the accuracy of staging and will change patient management in a significant number of paediatric patients. This review focuses on practical aspects and potential pitfalls in performing and reporting whole-body PET/CT in children and on clinical indications in paediatric oncology.

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Specific prerequisites for PET/CT acquisition in children

Patient preparation

In order to keep the anxiety of the child and the parents to a minimum, the whole procedure should be explained in advance [1]. Children should fast for 4–6 h before the study. A fasting time longer than that should be avoided as a really hungry child is usually not very compliant. The prohibition of soft drinks and sweets should be addressed explicitly. In nurslings, FDG injection should be timed before the next breast or milk feed. Special preparation such as sedation should be organized in conjunction with the referring physician. Sedation is usually not necessary above the age of 3½ years [2].

Uptake in brown fat is seen in 15–20% of PET scans in children and adolescents. Keeping the child warm before and during the uptake phase can reduce brown fat uptake; the preparing room should be warm enough and an additional blanket is recommended. Premedication with moderate doses of propanolol, fentanyl or diazepam seem to partly block the uptake of FDG in brown adipose fat tissue and is recommended by several groups (for protocols see [1]). Furthermore, the child should avoid exercise, talking or chewing before or after FDG injection. Before the start of the scan the child should be encouraged to void and a nappy should be changed.

Adaptation of PET protocols

Especially for children, radiation doses need to be kept as low as reasonably achievable (ALARA principle) [3]. Therefore,

it is the responsibility of the nuclear medicine physician or radiologist to optimize the imaging protocols for young patients [4, 5]. For PET imaging, the administered radioactivity should be adjusted for body weight according to the latest version of the EANM paediatric dosage card [6–10]. In children, 3D acquisition mode is recommended as activity can be reduced to nearly one-half compared to the 2D mode.

Principles of PET/CT protocols

In principle, there are two different ways of using the CT component in PET/CT [2, 11]. On the one hand, a CT scan with low radiation exposure can be performed for the purpose of attenuation correction of the PET data (so called low-dose CT). This low dose enables anatomical orientation, which is a major advantage in comparison to PET performed as a single modality. On the other hand, a CT scan obtained as part of PET/CT can meet the quality level of a diagnostic CT scan [11–13]. In this setting, CT has to be performed with adequate tube current-time product and tube voltage, usually following intravenous administration of iodinated contrast medium and, if performing a CT of the abdomen/pelvis, with oral contrast medium. Furthermore, the CT protocol can be adapted to the clinical question with a mixture of both, e.g. combining a contrast-enhanced normal-dose CT of the neck and chest with a low-dose CT of the abdomen and pelvis.

Adaptation of CT protocols

Optimization of CT protocols for contrast-enhanced normal-dose CT and low-dose CT in children includes weight- and axial-diameter-adapted CT parameters as well as age-adapted amounts of contrast agents in case of contrast-enhanced CT [5, 14–20]. The use of on-line dose modulation systems, which have been provided by the CT manufacturers, is recommended (e.g. CARE Dose®, Siemens Medical Solutions; Dose Wise™, Philips Medical Systems; Smart mA, GE Medical Systems). Radiation doses must be taken into consideration when an additional normal-dose CT scan is requested by the paediatrician [17, 18]. Therefore, a well-defined clinical indication after tapping the full potential of concurrent imaging modalities without radiation exposure is mandatory. Sufficient diagnostic information may yet be derived from US (e.g. peripheral lymph node status, neck, salivary and thyroid glands) and/or MRI (e.g. brain, neck, abdominal and pelvic organs, heart, peripheral arteries). On the contrary, contrast-enhanced chest CT gives superior diagnostic information on lung parenchyma, especially with regard to pulmonary metastases, mediastinal and hilar lymph node status, and mediastinal vascular and cardiac morphology in comparison to US and MRI.

Recently, clinically significant incidental findings from the dose-reduced unenhanced CT portion have been reported [21]. Therefore, it is urgently recommended to evaluate the low-dose CT scans carefully and to report all pathological findings.

Image interpretation and pitfalls

FDG uptake in thymus is common in children, especially after chemotherapy. The inverted “V” is the characteristic appearance, but sometimes differentiation between physiological thymus and a mass in the anterior mediastinum may be difficult. In children, uptake in lymphoid tissue of Waldeyer`s ring is often very prominent and should not be misinterpreted as pathology, e.g. lymphoma infiltration. Furthermore, symmetrical uptake in the laryngeal muscles is physiological, especially in small children after crying. After chemotherapy or colony stimulation factor (G-CSF), uptake in bone marrow and spleen is commonly increased. Tracer uptake in brown fat is seen in children in up to 20% and can partially be blocked by warmth and premedication (see above). The uptake pattern is most often symmetrical and involves neck, supraclavicular, mediastinal, paraspinal, perirenal, and para-aortic regions. Exact correlation of the PET and CT scans is extremely helpful to demonstrate or exclude additional pathological uptake within this regions. Sometimes the brown fat uptake may be so prominent that interpretation of the study is compromised. Physiological elimination of FDG via kidneys, ureter and bladder may sometimes cause difficulties differentiating urinary activity from pathological findings, e.g. abdominal lymph node metastases. PET/CT image fusion helps to avoid most misinterpretations, but, in case of doubt, another abdominal PET scan after fluid and furosemide is helpful. In girls from the age of about 12 years, physiological high ovarian uptake and endometrial uptake may be seen depending on the phase of the menstrual cycle. Fusing the FDG uptake with the anatomical location of the ovaries by CT helps to differentiate physiological uptake from potential lymph node metastases.

Given the potential causes for misinterpretation in children, images should be reported by physicians with specific expertise in paediatric PET/CT [22].

Clinical indications for PET/CT in paediatric oncology

Most PET studies in paediatric oncology have, up to now, been performed using stand-alone PET scanners; however, studies during the last 3–5 years have increasingly been performed using combined PET/CT scanners. Although only a limited number of studies defining the additional

clinical benefit of combined PET/CT for paediatric patients have been published so far [23], the following recommendation can be given [2, 9, 24–27]:

In *sarcoma* patients, FDG-PET is useful in staging, therapy monitoring, and detection of recurrences [23, 28–34]. However, FDG-PET has been proven to be less sensitive than spiral chest CT in the detection of pulmonary metastases from sarcomas [29, 32, 35]. Furthermore, according to international, multicentre therapy studies in childhood sarcomas (EURAMOS, EURO-EWING, CWS), chest CT is part of the recommended staging program. PET/CT, including contrast-enhanced normal-dose CT, should always be preferred to performing PET and CT in two separate sessions when both modalities are clinically indicated. Thus, PET/CT with contrast-enhanced normal-dose chest CT is to be preferred in sarcoma patients (Ewing tumour, soft-tissue sarcomas and osteosarcomas) [36]. As MRI is the preferred morphological imaging modality for primary bone tumours, PET with low-dose CT is usually sufficient for extra-thoracic regions.

In paediatric *lymphoma* patients, morphological imaging is usually performed using a combination of US, MRI and/or CT of various parts of the body [37, 38]. Most patients receive at least a contrast-enhanced normal-dose chest CT for staging and assessing therapy response. FDG-PET has been demonstrated to change staging and therapeutic management in 32% of paediatric lymphoma patients [24, 37–40]. Therefore, PET/CT with contrast-enhanced normal-dose chest CT is recommended in these patients. In a few individual situations, PET/CT with (additional) diagnostic cervical, abdominal and/or pelvic CT may be indicated. Furthermore, PET/CT with normal-dose CT is required for radiotherapy planning and should be performed in potential radiotherapy positioning [41]. PET/CT including diagnostic CT is obsolete if the clinical question can be answered by another morphologic imaging technique without radiation exposure (e.g. US or MRI). In these cases, the PET scan should be combined with low-dose CT providing anatomical information. As in adults [42], PET/CT is expected to substantially improve lesion staging and monitoring response in paediatric lymphoma patients. Whether PET with low-dose CT instead of diagnostic CT is sufficient in therapy monitoring situations will be the subject of further evaluation. Furthermore, FDG-PET is integrated in an ongoing international multicentric therapy trial for monitoring therapy [41]. Patients with complete morphological response on CT or negative PET scan will not receive radiotherapy in order to reduce the risk of secondary malignancies.

In *neuroblastoma*, PET/CT with low-dose CT using FDG is indicated in MIBG-negative cases. Furthermore, there are specific PET tracers, such as C-11-hydroxyephedrine (HED), for tumours of the sympathetic nervous system that can be used for PET/CT imaging for detection of disease, staging and monitoring therapy. However, there are only few studies using specific PET tracers in neuroblastoma patients [43, 44].

In *other paediatric malignancies,* including germ cell tumours and hepatoblastoma, PET/CT may be helpful in individual cases, but the literature on the use of PET/CT in these entities is limited so far.

Conclusion

PET/CT has already been used in many institutions worldwide and will replace stand-alone PET in the future. In children, it is mandatory to adapt the acquisition protocols of both components, PET and CT, in order to reduce radiation exposition. In paediatric oncology patients, clinical applications of PET/CT include staging, monitoring therapy and therapy planning in lymphomas, soft-tissue and osseous sarcomas, and neuroblastoma. In other entities, PET/CT may be of diagnostic value but the literature is limited. Knowledge of the specific distribution patterns of FDG in children enhances the quality of reports and helps to avoid misinterpretation.

Conflicts of interest The authors have declared that there are no conflicts of interest.

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