Diagnostic nuclear medicine in pediatric oncology-what we should know before scanning?

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SUMMARY

Cancer is second only to trauma as a cause of death in children, accounting for approximately 10% of all childhood deaths. The application of radioisotopes in the treatment of malignant diseases in children consists of detecting and estimating the degree of tumour spread by application of tumour-specific and non-specific radiopharmaceuticals, as well as the treatment of some malignant diseases. Paramount to any successful nuclear medicine examination is the establishment of acquisition protocols that allow high quality images to be obtained while ALARA principles are followed. Pediatric-specific issues should be anticipated and addressed in the planning of the studies to maximize the utility of the technique in this challenging group of patients, so the goal of this article is to summarize general prerequisites for the application of nuclear medicine diagnostic procedures in pediatric oncology patients.

Key words: *Medical Oncology; Pediatrics; Neoplasms; Diagnostic Imaging; Positron-Emission Tomography and Computed Tomography; Tomography, Emission-Computed, Single-Photon; Nuclear Medicine; Radiation Dosage*

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Wider application of pediatric nuclear medicine as a specific and particularly delicate field of nuclear medicine started in the 70s (1). The methods made it possible to obtain diagnostic information which was not easily, if at all, obtainable by means of other diagnostic procedures (1).

Breakthroughs in the development of selective radiopharmaceuticals labeled with short-lived isotopes and the improvements in instrumentation led to a massive application of nuclear medicine methods in pediatrics, due to the reasonable low exposure to radiation and significantly improved chances of obtaining reliable and fast diagnoses. The past two decades have seen a remarkable increase of medical imaging (2-4). Worldwide estimates for 2000–2007 indicate that 3.6 billion medical procedures with ionizing radiation are performed annually, with approximately 1% of these procedures performed on children (2, 4). Worldwide, the average annual per-capita effective dose of medicine (about 0.6 mSv of the total 3.0 mSv received from all sources) has approximately doubled in the past 10–15 years. That is why awareness of the frequency and radiation dose in radiologic and nuclear medicine procedures should be an integral part of ordering examinations, especially in children.

Illnesses in children differ from those in adults mostly in their clinical presentation, course and outcome. Some illnesses characteristic of adulthood do not appear in childhood at all, some present themselves with uncharacteristic clinical features and the course of illness, while others manifest themselves in children almost identically as in adults.

Apart from requiring the applications of basic nuclear medicine methods, pediatric oncological patients require additional attention, since the illnesses, as well as the therapy are often accompanied by pain and vomiting, which can compromise the procedure. Furthermore, the psychological approach to sick children and their parents is crucial, especially when the course of the disease is uncertain.

Paramount to any successful nuclear medicine examination is the establishment of acquisition protocols that allow high quality images to be obtained following ALARA principles. Moreover, successful examination can be defined as the one which achieves a high-quality study and where both the child and the parent feel that their emotional needs have been considered (5).

Only high quality nuclear medicine functional images can provide valuable clinical information for the management of pediatric patients with malignancies. Pediatric-specific issues should be anticipated and addressed in the planning of the studies in order to maximize the utility of the technique in this challenging group of patients. Therefore, the goal of this article is to summarize general prerequisites for the application of nuclear medicine diagnostic procedures in pediatric oncology patients.

DEFINING THE INDICATIONS

In order to conduct nuclear medicine procedures in children, it is necessary to have a cooperation between a specialist in the given field of child pathology and a nuclear medicine physician. After getting acquainted with the clinical features of the child's illness, and taking into consideration the analyses performed previously, it is necessary to define whether a particular nuclear medicine procedure yields a response to the diagnostic task. The procedure is then modified in accordance with the child's clinical features. Alternatively, the method is dropped if the physicians estimate that the imaging of choice would not solve the diagnostic problem. In some cases, it is necessary for the nuclear medicine physician to perform appropriate check-ups (for osteomyelitis, trauma, nodes on the neck, abdominal masses, tumours).

A detailed explanation of the procedure (including proper hydration, scanning duration, and expectance from the procedure itself) should be given to the patient and their parents in the written form during the appointment preceding procedure. In addition, a technologist or nuclear medicine physician should talk with the patient and parents during the appointment for the purpose of reducing their anxiety and fear of the procedure (6).

THE CHOICE OF RADIPHARMACEUTICALS AND DOSE CORRECTION

Most nuclear medicine diagnostic procedures designed for children utilise the same radiopharmaceuticals applied in adults, with the modified and reduced amount of radiation administered. In the first few months following birth, which is a period characterised by insufficient maturation of the

organs, special care should be taken when choosing radiopharmaceuticals with renal elimination.

The administered radioactivity in children should be the smallest dose which can yield satisfactory findings. The calculation of the reduced dose is performed by means of adult dose correction, taking into consideration age, body weight or the surface area of the child. The concept of the "minimal administered dose" is applied in infants. This stands for the minimum applied radioactivity which can yield conclusive findings (7).The latest version of the EANM paediatric dosage card for ^{18}F and ^{18}F-FDG suggests a minimum injected activity of FDG of 26 MBq for 2D mode scan acquisitions and 14 MBq for 3D mode scan acquisitions (8). The EANM dosimetry and Paediatric committees further reduced the values of the minimum recommended activity for^{18}F-FDG after considering the reports from two groups, which reported their satisfactory clinical experience with low ^{18}F-FDG activities in very young and lightweight children (9, 10).Society for Pediatric Radiology and American College of Radiology reached a consensus on a scheme that scaled the administered activity by the patient's weight (11).

DOSIMETRY OF RADIOPHARMACEUTICALS

The radiopharmaceutical dose for children differs the adult dose mainly due to the patient size, whereas absorbed fractions differ from those of adults because children's organs are smaller and closer to each other. The basic equation developed by the MIRD Committee is used when calculating the radiation dose for organs of patients of different sizes and ages (12, 13). The organ receiving the highest dose is referred to as the critical organ (Table 1), while sum of individual organ doses based on their weight and the biological radiosensitivity of each organ presents the effective dose (14, 15).

Table 1. Critical organ and effective dose for common pediatric nuclear medicine procedures

	Maximum Administrated Activity (MBq)*	Children age				
		1Yr	5Yrs	10Yrs	15Yrs	Adult
^{99m}Tc-MDP	740					
Bone surface(mGy)		54.5	46.0	45.6	49.2	46.6
ED(mSv)		2.8	2.9	3.9	4.2	4.2
^{99m}Tc-ECD	740					
Bladder wall(mGy)		13.4	23.0	30.5	37.2	37.0
ED(mSv)		4.1	4.6	5.3	5.9	5.7
^{99m}Tc-Sestamibi	740					
Gallbladder(mGy)		32.9	20.9	20.4	27.0	28.9
ED(mSv)		5.4	5.9	6.3	7.2	6.7
^{99m}Tc-MAG3	370					
Bladder wall(mGy)		17.2	19.8	31.3	44.1	42.7
ED(mSv)		1.2	1.3	2.2	2.8	2.7
^{123}I-MIBG	370					
Liver(mGy)		16.6	18.5	22.4	25.6	24.8
ED(mSv)		3.4	3.8	4.5	5.0	4.8
^{18}F-FDG	370					
Bladder wall(mGy)		25.6	35.9	44.4	48.8	50.5
ED(mSv)		5.2	5.9	6.6	7.3	7.4

*The maximum administered activity is that which would be administered to a 70-kg adult. The pediatric administered activity is scaled by the patient's weight (15,16).
ED=effective dose

Table 2. Effective dose of of commonly used radiopharmaceuticals in pediatric oncology patients

Radiopharmaceuticals	Maximum Administrated Activity (MBq)*	Effective dose for different age groups(mSv)				
		1 Yr	5 Yrs	10 Yrs	15 Yrs	Adult
^{18}F-FDG	389	5.2	5.3	6.4	7.6	7.4
^{67}Ga citrate	222	19.9	19.9	20.3	22.7	22.2
^{99m}Tc- HMPAO	740	5.1	5.4	5.8	6.4	6.9
^{99m}Tc- MDP	740	2.8	2.8	3.7	4.1	4.2
^{99m}Tc-MIBI	740	4.7	4.6	5.4	5.8	5.8

*The maximum administered activity is that which would be administered to a 70-kg adult. The pediatric administered activity is scaled by the patient's weight (15,16).

Table 2 presents the effective dose of commonly used radiopharmaceuticals in pediatric oncology patients. Absorbed radiation doses in all the major nuclear medicine imaging procedures, including the doses absorbed in ^{18}F-FDG-PET scans, are similar to each other, but still considerably reduced in comparison to that absorbed from ^{67}Ga citrate (16, 17). The models presented estimate the absorbed radiation by studying critical organs, and effective doses for different radiopharmaceuticals based on adult physiology. Hence, they may not be appropriate for all children due to wide individual differences in anatomy and physiology in comparison to the standard models. Therefore, the radiation dose for a given pediatric patient may vary by as much as 100%–200% from the estimates (18).

Children's parents are given the necessary advice and they often prefer to remain with the child during the nuclear medicine procedure. The exposure rate constants for ^{18}F and ^{99m}Tc are 0.0154 and 0.00195 mR per hour per MBq at 1 meter, respectively (18). Even if the parent stays within 1 meter of the patient during the entire period of uptake and imaging, the exposure of the parent would be no more than 5.5 mR (18). Therefore, parents are safe to stay with their children during the nuclear medicine imaging.

INSTRUMENTATION AND THE USE OF METHODS

Optimal application of nuclear medicine procedures in children requires the use of a gamma camera with a large field of view. In infants, babies and toddlers, an enlarged image of the internal organs is a necessity, so converging and pinhole collimators are used for this age range. The software enlargement (zoom) can also be used for the same purpose. A high resolution parallel collimator is used in older children.

Hybrid imaging, including PET/CT and SPECT/CT, has become a standard component of medical imaging (19,20). The combination of the anatomic information from CT and the functional information from PET and SPECT provides clinicians with valuable information. In addition, the CT information can be used for attenuation correction and anatomic localization. The dosimetry associated with CT in PET/CT can be controlled by adjusting various CT acquisition parameters, including the tube voltage (kVp) and the tube current–time product (mAs). CT acquisition parameters should be reduced for pediatric patients by modulation of CT aquistion, including decreasing emission of x-rays through thinner or less attenuating parts (e.g., the lungs) of the body, performing CT over a limited field of view and doing faster CT bed speed (21, 22).

IMMOBILISATION

Immobilisation requires actions which ensure maximum limitation of the child's body movements during the imaging, which results in optimum acquisition, the prevention of artifact creation, high-quality data processing, and reliable findings. Nuclear medicine procedures are mostly painless and comfortable, so the non-pharmacological immobilisation strategy is preferred over the pharmacological one, especially when possible adverse effects of certain sedatives, opiates and neuroleptics are taken into consideration. In older children, immobilisation can effectively be achieved by focusing their attention on toys, computer animations and cartoons, while at the same time using minimal and unobtrusive immobilisation of the child's body. A friendly talk and attitude, as well as motivated staff can most often completely reduce the fear of the procedure by establishing a relationship of trust. The presence of parents or cousins during the procedure further increases the child's trust and in most cases aids the correct procedure application. Imaging is often scheduled for hours at which the child normally goes to bed, which enables the child to sleep through the procedure. Various types of immobilisation mechanisms can also be used to prevent the patients from moving or considerably limit their movement.

PHARMACOLOGICAL IMMOBILIZATION

The application of pharmacological means of immobilization is utilized when it is necessary for the child to lie completely still for a longer period of time (SPECT, SPECT/CT, PET/CT, high-resolution pinhole scintigraphy), and with extremely uncooperative children (psychological retardation, great fear stemming from previous experiences with diagnostic procedures, psychological traumas caused by abuse).

They are mostly administered perorally, but the type of administration is determined by various factors, including age, the duration of the procedure, anesthesiologist's experience, counter indications of specific medication, possibility of antidote administration and availability of life support equipment. The most common medication administered perorally are chlorine hydrate and sodium pentobarbital. Chlorine hydrate in 50-75mg/kg doses is suitable for infants and toddlers weighing up to 15 kg, due to its highly efficient short-term sedation and small chances of causing acute toxicity. Intravenous administration is preferred in older children, and especially in those who are mentally deficient.

Sodium pentobarbital (Nembutal) in 2-6mg/kg doses is often administered due to its short-term effects and low incidence of respiratory depression. Opiates (meperidine and fentanyl), as well as benzodiazepines (diazepam and midazolam) are seldom used. In the recent years, nasal administration of midazolam in 0.2 mg/kg doses has become more common, primarily due to its rapid absorption through nasal mucous, short-term (35-45 min) effect and minimum respiratory depression. Finally, Midazolam syrup (administered in 0.5-0.75 mg/kg doses) is characterised by slower absorption, but parents still most readily choose this type of medicine for their children.

The nuclear medicine physician should consult the anesthesiology department in each institution for specific recommendations on dosages and combinations of sedative drugs and anesthetics (23).

PEDIATRIC ONCOLOGY APPLICATION

Cancer comes right after trauma as a cause of death in children, accounting for approximately 10% of all childhood deaths (24).

The application of radioisotopes in the treatment of malignant diseases in children covers the detection and estimation of the degree of tumour spread by means of applying tumour-specific and non-specific radiopharmaceuticals, as well as the treatment of some malignant diseases. In the recent years, nuclear medicine methods have gained importance in determining the response of the tumour to the applied treatment. The most common radiopharmaceuticals used for planar oncologic scintigraphy include the following: ^{99m}Tc-MDP for bone scan, $^{123/131}$I-MIBG for neuroblastoma patients, and ^{99m}Tc-MIBI for detection of variety of tumors. Single photon emission tomography provides improved spatial resolution of imaging using gamma emitters and, moreover, it can be fused with MR and CT, thus giving anatomic dimension to nuclear medicine imaging. ^{18}F-FDG-PET is increasingly used in pediatric oncology (19,25-29). Diagnostic utility of FDG-PET and its impact on patient management have been supported by many cases of pediatric cancers, especially lymphoma (32%), brain tumors (15%), and sarcomas (13%) (25).

Despite limited experience in this niche of radioisotope application, the data gathered from pediatric oncology centres based on long-term follow ups of children who had been diagnosed and treated for malignant diseases by radioisotopes, increasingly point to the efficiency and safety of this procedure, which comes with no early or late adverse reactions.

Conflict of interest

We declare no conflicts of interest.

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