Pediatric Radiopharmaceutical Administered Doses: 2010 North American Consensus Guidelines

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Dose reduction has been a work in progress in pediatric imaging for nearly a decade. A 1996 report indicated that the long-term risk of carcinogenesis due to ionizing radiation in atomic bomb survivors was higher than had been previously estimated. For solid tumors, representing about 75% of excess cancer mortality, the likelihood of a radiation-induced malignancy after exposure to ionizing radiation was about 1.0–1.8 times higher in a 10-y-old child than in a young adult. For leukemia, representing the remaining 25% of excess cancer mortality, the likelihood of a radiation-induced malignancy after exposure to ionizing radiation was about twice as high for a 10-y-old child as for a young adult (*1*).

The new risk estimates led to dose-reduction efforts in pediatric imaging that initially focused on CT. Because of the increased use of CT and the relatively high effective radiation dose per study, CT had emerged as a major source of medical radiation received by children in the United States. A careful look at CT image quality and CT exposure parameters indicated that significant reductions in absorbed radiation dose per study were possible without compromising the diagnostic information or image quality of pediatric CT scans (*2–6*). The ALARA concept, As Low As Reasonably Achievable, was extended to pediatric diagnostic imaging and may be restated as imaging at the lowest absorbed radiation dose that is consistent with quality imaging.

The need for reduced CT exposure was then publicized—in the public domain, in the pediatric radiology community, and throughout general radiology. The introduction of reduced-exposure parameters was assessed in a follow-up survey (*7–9*). Equipment manufacturers made improvements in CT technology that facilitated the reduction of radiation exposures in children. In addition, at this time new dose-reduction efforts are under way in pediatric interventional radiology and fluoroscopy (*10*).

A survey conducted in 2008 revealed a wide variation of pediatric radiopharmaceutical administered doses among 13 leading pediatric hospitals in North America (*11*). Among the institutions surveyed, the administered activity per kilogram and the maximum administered activity in children older than 1 y varied on average by a factor of 3 and, in 1 case, by a factor of 10. Minimum administered activity varied, on the average, by a factor of 10 and as much as a factor of 20 for 1 procedure. The greatest variability in administered dose occurred in the smallest, youngest, and most at-risk patients. Because the survey included only leading pediatric institutions in North America, concern was raised that the variability among other institutions would be even greater. The survey highlighted the need for a consensus on pediatric radiopharmaceutical administered doses for nuclear medicine imaging in children. The ALARA concept may be extended to pediatric nuclear medicine and restated as the use of the lowest administered activities in children that are consistent with high-quality imaging.

The response to this need for dose reduction and uniformity was the formation of a Pediatric Nuclear Medicine Dose Reduction Workgroup, consisting of pediatric nuclear medicine physicians, technologists, and physicists in North America, representing the Society of Nuclear Medicine through the Pediatric Imaging Council, the Society for Pediatric Radiology, and the American College of Radiology (Appendix). The workgroup conducted consensus workshops at annual meetings of the Society of Nuclear Medicine and the Society for Pediatric Radiology. Dose reduction was also featured in categoric courses presented at the 2009 and 2010 Society of Nuclear Medicine annual meetings. Likewise, dose reduction and image optimization in conventional and hybrid imaging were prominently featured in the Pediatric Nuclear Medicine Special Focus Session entitled "New Challenges" at the 52nd Annual Meeting of the Society for Pediatric Radiology in 2009. A symposium on pediatric radiopharmaceutical dosimetry was also held at the Society of Nuclear Medicine 2009 annual meeting.

As a result of these consensus workshops, the Workgroup has achieved consensus on pediatric administered radiopharmaceutical doses for 9 commonly used radiopharmaceuticals, in terms of administered activity per kilogram

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and minimum administered radiopharmaceutical dose for the smallest patients. For 2 additional radiopharmaceuticals, a dose range was specified. Table 1 contains the North American Consensus Guidelines for these radiopharmaceuticals.

The following important questions had to be answered for the Workgroup to arrive at a consensus.

- What is the method by which pediatric administered activities should be calculated?

Pediatric administered activities are generally computed using formulas that reduce adult administered activity in the form:

$$\text{Pediatric administered activity} = (\text{dose formula}) \times (\text{adult reference activity}).$$

Dose formulas have included:

(a) patient weight (kg)/70
(b) patient body surface area (m^2)/1.73 m^2
(c) Webster's formula (*12*)
(d) The European Association of Nuclear Medicine (EANM) Paediatric Dose Card (*13*)

Many hospitals have used patient BSA and Webster's formulas, which result in much larger administered activities per kilogram in infants and small children than in adolescents (Tables 2 and 3). For example, using BSA, Webster's formula resulted in calculated administered activities per kilogram in a 1-y-old that were 2 times higher than the administered activities per kilogram in an adolescent. Administered activities per kilogram were also increased in 5- and 10-y-old children, particularly when Webster's formula was used. Advocates of the patient BSA and Webster's formulas stated that more counts were needed to obtain good-quality images in infants and small children. Data were then acquired that indicated that, when the radiopharmaceutical was administered according to the first formula, based on weight only, counts per unit area varied little from infancy through adolescence for 2 common radiopharmaceuticals used in children, ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) and ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) (*14*).

- What adult reference activities are used?

For ^{99m}Tc-MDP, typical adult administered activities are 740 or 925 MBq (20 or 25 mCi). For ^{18}F-FDG, a typical adult administered activity is 555 MBq (15 mCi). Recommended adult administered activities in the Society of Nuclear Medicine procedure guidelines are 740–1,110 MBq (20–30 mCi) for ^{99m}Tc-MDP and 370–740 MBq (10–20 mCi) for ^{18}F-FDG (*14,15*). In contrast, the implied reference administered activities in the 2007 EANM Dose Card for a 70-kg patient are 490 MBq (13 mCi) for a ^{99m}Tc-MDP bone scan, 363 MBq (9 mCi) for ^{18}F-FDG when a 2-dimensional PET scanner is used, and 196 MBq (5.3 mCi) for ^{18}F-FDG when a 3-dimensional scanner is used.

When we surveyed the Workgroup members at children's and academic general hospitals, we found that pediatric nuclear medicine specialists at these hospitals had already reduced the reference activities for ^{99m}Tc-MDP and ^{18}F-FDG to 555 MBq (15 mCi) and 370 MBq (10 mCi), respectively. These reduced reference activities have been incorporated into the consensus recommendations.

- What is the appropriate adjustment of the administered activities of positron-emitting radiopharmaceuticals?

Because of the differences in tissue attenuation of photons and the physics of PET scanner detection, the consensus guidelines incorporate recommendations from recent studies by Sammer et al. (with a theoretic basis in the work by Accorsi et al.) (*12,15,16*). These studies suggest that administered activity for ^{18}F-FDG may be further reduced in infants and smaller children.

- What is the maximum administered activity for each radiopharmaceutical?

In pediatric nuclear medicine practice, many adolescent patients weigh more than 70 kg and a few exceed 100 kg. Most pediatric nuclear medicine practitioners in the Workgroup used a fixed maximum administered activity that was approximately 70 times the recommended weight-based administered activity. Examples are 370 MBq (10 mCi) for ^{123}I-MIBG and ^{18}F-FDG and 555 MBq (15 mCi) for ^{99m}Tc-MDP. To suggest an upper limit, but also provide flexibility for the care of large adolescent patients, the following language has been appended to the consensus guidelines: "For patients who weigh more than 70 kg, it is recommended that the maximum administered activity not exceed the product of the patient's weight (kg) and the recommended weight-based administered activity. Some practitioners may choose to set a fixed maximum administered activity equal to 70 times the recommended weight-based administered activity, for example, approximately 370 MBq (10 mCi) for ^{18}F-FDG body imaging." The North American Guidelines for pediatric administered radiopharmaceutical doses were approved by the Society of Nuclear Medicine and the Society for Pediatric Radiology Boards of Directors on September 15, 2010, and October 7, 2010, respectively.

The pediatric administered radiopharmaceutical doses in the North American Consensus Guidelines differ from the EANM Paediatric Dose Card in several important respects. The administered activities in the consensus recommendations are slightly lower for infants and small children (*14*). Recommended administered activities for ^{99m}Tc-

TABLE 1
North American Consensus Guidelines for Administered Radiopharmaceutical Activities in Children and Adolescents*

Radiopharmaceutical	Recommended administered activity (based on weight only)	Minimum administered activity	Maximum administered activity	Comments
^{123}I-MIBG	5.2 MBq/kg (0.14 mCi/kg)	37 MBq (1.0 mCi)	370 MBq (10.0 mCi)	EANM Paediatric Dose Card (2007 version (*13*)) may also be used in patients weighing more than 10 kg.
^{99m}Tc-MDP	9.3 MBq/kg (0.25 mCi/kg)	37 MBq (1.0 mCi)		EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
^{18}F-FDG	Body, 3.7–5.2 MBq/kg (0.10–0.14 mCi/kg) Brain, 3.7 MBq/kg (0.10 mCi/kg)	37 MBq (1.0 mCi)		Low end of dose range should be considered for smaller patients. Administered activity may take into account patient mass and time available on PET scanner. EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
^{99m}Tc-dimercaptosuccinic acid	1.85 MBq/kg (0.05 mCi/kg)	18.5 MBq (0.5 mCi)		
^{99m}Tc-MAG3	Without flow study, 3.7 MBq/kg (0.10 mCi/kg) With flow study, 5.55 MBq/kg (0.15 mCi/kg)	37 MBq (1.0 mCi)	148 MBq (4 mCi)	Administered activities at left assume that image data are reframed at 1 min/image. Administered activity may be reduced if image data are reframed at longer time per image. EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
				EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
^{99m}Tc-iminodiacetic acid	1.85 MBq/kg (0.05 mCi/kg)	18.5 MBq (0.5 mCi)		Higher administered activity of 37 MBq (1 mCi) may be considered for neonatal jaundice. EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
^{99m}Tc-macroaggregated albumin	If ^{99m}Tc used for ventilation, 2.59 mBq/kg (0.07 mCi/kg)	14.8 MBq (0.4 mCi)		EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
	No ^{99m}Tc ventilation study, 1.11 MBq/kg (0.03 mCi/kg)			EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
^{99m}Tc-pertechnetate (Meckel diverticulum imaging)	1.85 MBq/kg (0.05 mCi/kg)	9.25 MBq (0.25 mCi)		EANM Paediatric Dose Card (2007 version (*13*)) may also be used.
^{18}F-sodium fluoride	2.22 MBq/kg (0.06 mCi/kg)	18.5 MBq (0.5 mCi)		
^{99m}Tc (for cystography)	No weight-based dose		No more than 37 MBq (1.0 mCi) for each bladder-filling cycle	^{99m}Tc-sulfur colloid, ^{99m}Tc-pertechnetate, ^{99m}Tc-diethylene triamine pentaacetic acid, or possibly other ^{99m}Tc radiopharmaceuticals may be used. There is wide variety of acceptable administration techniques for ^{99m}Tc, many of which will work well with lower administered activities.
^{99m}Tc-sulfur colloid				
For oral liquid gastric emptying	No weight-based dose	9.25 MBq (0.25 mCi)	37 MBq (1.0 mCi)	Administered activity will depend on age of child, volume to be fed to child, and time per frame used for imaging.
For solid gastric emptying	No weight-based dose	9.25 MBq (0.25 mCi)	18.5 MBq (0.5 mCi)	^{99m}Tc-sulfur colloid is usually used to label egg.

*This information is intended as a guideline only. Local practice may vary depending on patient population, choice of collimator, and specific requirements of clinical protocols.

Administered activity may be adjusted when appropriate by order of the nuclear medicine practitioner. For patients who weigh more than 70 kg, it is recommended that maximum administered activity not exceed product of patient's weight (kg) and recommended weight-based administered activity. Some practitioners may choose to set fixed maximum administered activity equal to 70 times recommended weight-based administered activity, for example, approximately 10 mCi (370 mBq), for ^{18}F body imaging. The administered activities assume use of a low energy high resolution collimator for Tc-99m radiopharmaceuticals and a medium energy collimator for I-123-MIBG. Individual practitioners may use lower administered activities if their equipment or software permits them to do so. Higher administered activities may be required in certain patients. No recommended dose is given for ^{67}Ga-citrate. Intravenous ^{67}Ga-citrate should be used infrequently and only in low doses.

TABLE 2
Pediatric Dose Formulas

Rule	Formula
Body mass (straight weight basis)	(Body mass (kg) × adult dose)/70 kg
BSA	(BSA (m^2) × adult dose)/1.73 m^2
Webster's formula	(Age (y) + 1) × (adult dose)/(age (y) + 7)

Data are adapted from Accorsi et al. (*12*) and Gelfand (*16*).

dimercaptosuccinic acid and ^{18}F-fluoride are considerably lower. Administered activities for orally administered ^{99m}Tc-labeled radiopharmaceuticals and for radionuclide cystography provide a range of administered activities for each type of study rather than an administered activity per kilogram. The consensus recommendations more closely reflect optimal clinical practice in North American pediatric centers.

In the North American Consensus Guidelines, the determination of the administered activity for the pediatric patient is based on body weight, except for radionuclide cystogram and gastric-emptying studies (Table 1).

Appropriate selection of the administered radiopharmaceutical activity depends on the patient population, choice of equipment, specific requirements of the clinical protocols, and the physician's judgment. Therefore, deviation from the administered activities listed in the consensus guidelines should be considered appropriate when clinically indicated. Individual practitioners may use lower administered activity if their equipment or software (*17,18*) permits them to do so. Higher administered activities may be required in certain patients.

When the suggested weight-based administered activities are used, the resulting effective doses are far lower than the current established threshold for radiation-induced carcinogenesis (*19*). A reasonable assumption is to apply the linear no-threshold hypothesis for radiation-induced carcinogenesis when making judgments about the relative radiation-associated risks of different imaging studies. Effective doses from the suggested administered activities in the North American Consensus Guidelines range from 0.0044 mSv (0.044 rem) for ^{99m}Tc-mertiatide (MAG3) in a 1-y-old to 6.7 mSv (0.67 rem) for ^{18}F-FDG in a 10-y-old.

TABLE 3
Administered Activity for Each Dose Formula According to Patient Age Compared with a Dosage Computer on a Straight Weight Basis

Age (y)	BSA	Webster	EANM Paediatric Dose card (2007 version (*13*))
1	194%	200%	136%
5	172%	300%	121%
10	133%	206%	113%
15	116%	140%	107%

Data are from Gelfand et al. (*13*).

APPENDIX

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