2016 Update of the North American Consensus Guidelines for Pediatric Administered Radiopharmaceutical Activities

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Pediatric nuclear medicine provides important clinical information in the care of children. Although nuclear medicine techniques have been in use in adults for more than half a century, with well-established standards for radiopharmaceutical administered activities, this has not been the case for the pediatric population. As pediatric nuclear medicine grew in use practitioners faced with imaging children used a number of methods to select administered activities. For the most part, pediatric administered activities were influenced by varying combinations of tradition, existing dosage schedules, age of available equipment, practitioner preference, and direct extrapolation from adult administered activities An informal survey in 2009 showed that only 4 of 22 radiopharmaceutical package inserts provided recommended pediatric administered doses (*1*). Instead, package inserts included the "orphan statement": "Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides."

Radionuclide imaging in children was initially limited to those patients with proven oncologic disorders, mainly for diagnosis of extent of disease and to evaluate for metastases. This limited use was the result of radiation exposure concerns with older radiopharmaceuticals with long half-lives and relatively high emission energies, low photon flux, β particle emissions, and unfavorable imaging characteristics. In addition, imaging equipment required long acquisition times and produced images with poor spatial resolution. With the development of short-lived radiopharmaceuticals and much lower radiation exposures, as well as the introduction of modern equipment, pediatric nuclear medicine expanded to include evaluation of physiology, benign disorders, and nononcologic diseases. With this expansion and the introduction of novel tracers, identification and dissemination of appropriate administered doses took on new importance.

Early methods of calculating doses included the Clark rule, the Young rule, the area method, and the Webster rule. However, these methods provided a very wide range of recommendations. No consensus among practitioners provided dose standards. A 2008 survey of 13 North American pediatric nuclear medicine clinics revealed a wide range of administered radiopharmaceutical activities in children. The survey examined 16 of the most common radiopharmaceuticals used in children. In patients older than 1 year, administered dose variability ranged from a factor of 3 to a factor of 10. However, in children younger than 1 year, this variability ranged by a factor of 10 and, in 1 case, by a factor of 20 (*2*).

After the publication of this survey, the Image Gently Alliance, the SNMMI, and the Society for Pediatric Radiology endorsed the formation of an expert group to develop consensus guidelines on pediatric radiopharmaceutical administered doses. The inherent aim was to reduce the large variability of administered doses, which in turn could have the effect of reducing overall pediatric radiation exposures. This group produced the 2010 North American Consensus Guidelines for Pediatric Radiopharmaceutical Administered Doses (*3,4*). Both similarities and differences between the European and the North American guidelines were evident (*5*); these were harmonized in 2014 (*6–8*).

The original North American guidelines included recommendations for 12 radiopharmaceutical applications. Following expert consensus workshops at SNMMI Annual Meetings, additional radiopharmaceuticals were included: ^{99m}Tc-HMPAO and ^{99m}Tc-Ceretec for brain imaging, ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin for myocardial perfusion imaging, ^{123}I-NaI for thyroid imaging, ^{99m}Tc-red blood cells for blood pool imaging, ^{99m}Tc-white blood cells for infection imaging, and ^{68}Ga-DOTATOC and ^{68}Ga-DOTATATE for neuroendocrine tumor imaging. A table with these additions and updates is now available (Table 1, facing page) and is available in a poster format from SNMMI and the Image Gently Alliance.

Publication and dissemination of this information has had a positive effect in the practice of pediatric nuclear medicine. Recent surveys have indicated that a large fraction of those familiar with the guidelines have altered their practice in pediatric nuclear medicine to become more compliant (*9,10*). Therefore, it is apparent that further dissemination of the guidelines is needed. The development of these guidelines for pediatric administered radiopharmaceuticals has filled a long-standing need. It is important to consider that these guidelines should continue to be refined by more experience and new scientific work and that new procedures should be added to the guidelines as they become more routinely available in children. There is a need for more data on radiopharmaceutical biodistribution and biokinetics in children—data that at present are quite scarce or nonexistent. Sophisticated phantom modeling for children

TABLE 1
2016 Update: North American Consensus Guidelines for Pediatric Administered Radiopharmaceutical Activities[1]

Radiopharmaceutical	Notes	Administered activity	Minimum administered activity	Maximum administered activity
^{123}I-MIBG	[A]	5.2 MBq/kg (0.14 mCi/kg)	37 MBq (1.0 mCi)	370 MBq (10.0 mCi)
^{99m}Tc-MDP	[A]	9.3 MBq/kg (0.25 mCi/kg)	37 MBq (1.0 mCi)	
^{18}F-FDG	[A, B]	Body: 3.7-5.2 MBq/kg (0.10–0.14mCi/kg)	26 MBq (0.7 mCi)	
		Brain: 3.7 MBq/kg (0.10 mCi/kg)	14 MBq (0.37 mCi)	
^{99m}Tc-DMSA	[A]	1.85 MBq/kg (0.05 mCi/kg)	18.5 MBq (0.5 mCi)	100 MBq (2.7 mCi)
^{99m}Tc-MAG3	[A, C]	Without flow study: 3.7 MBq/kg (0.10 mCi/kg)	37 MBq (1.0 mCi)	148 MBq (4.0 mCi)
	[A]	With flow study: 5.55 MBq/kg (0.15 mCi/kg)		
^{99m}Tc-IDA	[A, D]	1.85 MBq/kg (0.05 mCi/kg)	18.5 MBq (0.5 mCi)	
^{99m}Tc-MAA	[A]	If ^{99m}Tc used for ventilation: 2.59 MBq/kg (0.07 mCi/kg)		
	[A]	No ^{99m}Tc ventilation study: 1.11 MBq/kg (0.03 mCi/kg)	14.8 MBq (0.4 mCi)	
^{99m}Tc-pertechnetate (Meckel diverticulum imaging)	[A]	1.85 MBq/kg (0.05 mCi/kg)	9.25 MBq (0.25 mCi)	
^{18}F-sodium fluoride	[A]	2.22 MBq/kg (0.06 mCi/kg)	14 MBq (0.38 mCi)	
^{99m}Tc (for cystography)	[E]	No weight-based dose	No more than 37 MBq (1.0 mCi) for each bladder filling cycle	No more than 37 MBq (1.0 mCi) for each bladder filling cycle
^{99m}Tc-sulfur colloid (for oral liquid gastric emptying)	[F]	No weight-based dose	9.25 MBq (0.25 mCi)	37 MBq (1.0 mCi)
^{99m}Tc-sulfur colloid (for solid gastric emptying)	[F]	No weight-based dose	9.25 MBq (0.25 mCi)	18.5 MBq (0.5 mCi)
^{99m}Tc-HMPAO (Ceretec)/^{99m}Tc-ECD (Neurolite) for brain perfusion		11.1 MBq/kg (0.3 mCi/kg)	185 MBq (5 mCi)	740 MBq (20 mCi)
^{99m}Tc-sestamibi (Cardiolite)/^{99m}Tc-tetrofosmin (Myoview) for myocardial perfusion (single scan or first of 2 scans, same day)		5.55 MBq/kg (0.15 mCi/kg)	74 MBq (2 mCi)	370 MBq (10 mCi)

TABLE 1 (Continued)

Radiopharmaceutical	Notes	Administered activity	Minimum administered activity	Maximum administered activity
^{99m}Tc-sestamibi (Cardiolite)/^{99m}Tc-tetrofosmin (Myoview) for myocardial perfusion (second of 2 scans, same day)		16.7 MBq/kg (0.45 mCi/kg)	222 MBq (6 mCi)	1,110 MBq (30 mCi)
Na^{123}I for thyroid imaging		0.28 MBq/kg (0.0075 mCi)	1 MBq (0.027 mCi)	11 MBq (0.3 mCi)
^{99m}Tc-pertechnetate for thyroid imaging		1.1 MBq/kg (0.03 mCi/kg)	7 MBq (0.19 mCi)	93 MBq (2.5 mCi)
^{99m}Tc-RBC for blood pool imaging		11.8 MBq/kg (0.32 mCi/kg)	74 MBq (2 mCi)	740 MBq (20 mCi)
^{99m}Tc-WBC for infection imaging		7.4 MBq/kg (0.2 mCi/kg)	74 MBq (2 mCi)	555 MBq (15 mCi)
^{68}GA-DOTATOC or ^{68}Ga-DOTATATE (*18*)	[G]	2.7 MBq/kg (0.074 mCi/kg)	14 MBq (0.38 mCi)	185 MBq (5 mCi)

NOTES: 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 >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, expressed as MBq/kg or mCi/kg (for example, ~10 mCi [370 MBq] for ^{18}F-FDG body imaging). The administered activities assume use of a low-energy high-resolution collimator for ^{99m}Tc radiopharmaceuticals and a medium-energy collimator for ^{123}I-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 selected patients. No recommended administered activity is given for intravenous ^{67}Ga-citrate; intravenous ^{67}Ga-citrate should be used very infrequently and only in low doses. [A] The EANM Dosage Card 2014 version 2 administered activity may also be used. [B] The low end of the dose range should be considered for smaller patients. Administered activity may take into account patient mass and time available on the PET scanner. The EANM Dosage Card 2014 version 2 administered activity may also be used. [C] Administered activities assume that image data are reframed at 1 min/image. Administered activity may be reduced if image data are reframed at a longer time per image. [D] A higher administered activity of 1 mCi may be considered for neonatal jaundice. [E] ^{99m}Tc-sulfur colloid, ^{99m}Tc-pertechnetate, ^{99m}Tc-DTPA, or possibly other ^{99m}Tc radiopharmaceuticals may be used. There is a wide variety of acceptable administration and imaging techniques for ^{99m}Tc cystography, many of which will work well with lower administered activities. An example of appropriate lower administered activities is found in the 2014 revision of the EANM Paediatric Dose Card 2. [F] The administered activity may be based on patient weight or on the age of the child. [G] The administered activity is based on the EANM Dosage Card 2014 version 2 dosage for a 60-kg patient, using the minimum and maximum doses from the EANM Dosage Card. There was little experience with this radiopharmaceutical in children in North America at the time of preparation of this dosage table.

based on sex and body size should help produce better estimates of radiation absorbed doses (*11–13*). The application of advanced image processing software both for planar imaging, as well as for SPECT, can help to reduce levels of administered doses while preserving (and in some cases improving) diagnostic image quality (*14–17*).

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In Memoriam: Robert W. Frelick, MD, 1920–2016

Robert W. Frelick, MD, a prominent Delaware physician whose practice focused on oncology and included early work in nuclear medicine, died on September 1. He received his medical degree as a captain in the U.S. Army from Yale University (New Haven, CT) in 1944. He completed his internship at New Haven Hospital (CT), and was then stationed in Germany from 1945 to 1947. On his return, he completed residency programs at Memorial Wilmington (DE) and at Memorial Sloan–Kettering (New York, NY). From 1950 to 1982 he maintained a private practice in Deerhurst, DE, which included routine house calls. During the same period, from 1952 to 1970, he served at the Wilmington Medical Center as the Director of Nuclear Medicine and as a consultant in medical oncology in hospitals in Delaware and New Jersey. From 1982 to 1987, he was at the National Cancer Institute (NCI; Bethesda, MD), where he was program director of the nationwide Association of Community Cancer Centers (ACCC). He represented NCI as a member of the Commission on Cancer of the American College of Surgeons. In 1987 he became Director of Chronic Diseases for the State of Delaware and medical director of the South Jersey Regional Cancer Center. He also served as a surveyor for the American College of Surgeons and traveled the country evaluating cancer programs at community hospitals. He was a lecturer, assistant professor, and honorary clinical professor at the University of Delaware (Wilmington), Temple University (Philadelphia, PA), and Jefferson Medical College (Philadelphia, PA). He published hundreds of articles and commentary in the peer-reviewed literature. Well into his 90s, he continued to provide medical advice and assistance to family and friends, volunteered at the Claymont Clinic (DE), and participated in grand rounds and medical meetings at Christiana Hospital (Newark, DE) and the Helen F. Graham Cancer Center (Newark), which he helped to found.

Dr. Frelick was an active participant in numerous professional groups including the American Medical Association, the Medical Society of Delaware (president, 1980–1981), the American Society of Clinical Oncology, ACCC (president, 1979–1980, and board of trustees, 1974–1982), and the American School Health Association. He served as a volunteer with CARE Medico in Kabul, Afghanistan, in 1978 and later served on the CARE Executive Committee from 1986 to 1991. He was also an active community volunteer.

In reporting on his death, the ACCC noted that "Dr. Frelick worked to expand and improve access to cancer care and clinical trials, not only in his home state of Delaware, but throughout the country." He is survived by his wife of 72 years and 5 children, 9 grandchildren, and 5 great-grandchildren.