NORTH AMERICAN CONSENSUS GUIDELINES FOR ADMINISTERED RADIOPHARMACEUTICAL ACTIVITIES IN CHILDREN AND ADOLESCENTS

Introduction

A survey conducted at 13 premier pediatric hospitals in North America [1] indicated that administered radiopharmaceutical activities in children varied quite widely. The survey showed that among the institutions surveyed, the administered activity per kilogram and the maximum administered activity in children older than one year varied on average by a factor of 3 and in one case by a factor of 10. Of concern is that the minimum administered activity varied on average, by a factor of 10 and as much as a factor of 20 for one procedure! The greatest variability in administered dose occurred in the smallest, youngest and most vulnerable patients. Please note that the survey only included leading pediatric institutions in North America. Since there are no standards or guidelines available, one would assume that the variability among other institutions would be even greater.

Based on this information and the desire to limit radiation exposure to children and adolescents from diagnostic nuclear medicine procedures to the lowest levels consistent with quality imaging, colleagues in the field of pediatric nuclear medicine established a Workgroup and conducted several workshops focusing on achieving consensus on radiopharmaceutical administered activities in pediatric patients. The Workgroup consisted of pediatric nuclear medicine physicians, technologists and physicists in North America, representing the Society of Nuclear Medicine (SNM) through the Pediatric Imaging Council, and also the Society for Pediatric Radiology and the American College of Radiology (ACR). These efforts have had the encouragement of the Alliance for Radiation Safety in Pediatric Imaging, which sponsors the Image Gently Campaign. It should be noted that both the SNM and SNM Technologist Section are supporting members of the Alliance (http://www.pedrad.org/associations/5364/ig/).

Initial planning took place at the Society for Pediatric Radiology Annual Meeting, Carlsbad, CA, in April, 2009. The Pediatric Dose Reduction Workgroup was established co-chaired by Dr. Treves, Gelfand and Parisi. Initially there were 13 participants from children’s hospitals and university hospitals, with the group eventually numbering 21 participants. Consensus sessions took place at the SNM Annual Meeting, Toronto, ONT, in June, 2009, Society for Pediatric Radiology Annual Meeting. Boston, MA, in April 2010 and at the SNM Annual Meeting, Salt Lake City, UT, in June 2010. Attendance at consensus sessions was 20 to 40 persons (Appendix 1). In addition, a Symposium on Pediatric Radiopharmaceutical Dosimetry was held at the Annual Meeting of the SNM in Toronto on June 14, 2009 in conjunction with the 3rd International Symposium on Radionuclide Therapy and Radiopharmaceutical Dosimetry (ISRTRD) (approximately 65 attendees, attached program in Appendix 2). At the same SNM meeting, there was also a categorical seminar dedicated to Dose Reduction in Pediatric Nuclear Medicine.

As a result of these consensus workshops, the Workgroup has achieved consensus on
pediatric administered radiopharmaceutical doses for 11 commonly used radiopharmaceuticals, in terms of (1) administered activity/kg and (2) minimum administered radiopharmaceutical doses for the smallest patients (Please see the attached consensus guidelines, “dose consensus guidelines MBq first 08 15 10 ver3.doc”)

Several questions needed to be answered in order to arrive at a consensus. Pediatric administered activities are generally computed using formulae that reduce adult administered activity in the form:

\[
\text{Pediatric administered activity} = (\text{dose formula}) \cdot (\text{adult reference activity})
\]

Formulae have included:

(a) patient weight (kg)/70
(b) patient body surface area (m2)/1.73 m2
(c) Webster’s formula
(d) “PRD chart”

Many hospitals used formulae b, c and d that result in much larger administered activities per kg in infants and small children than in adolescents. For example, using body surface area, Webster’s formula or the “PRD chart” all resulted in administered activities/kg in a one year old that were two times higher than the administered activities/kg in an adolescent. Administered activities/kg were also increased in 5 and 10 year old children, particularly when Webster’s formula was used. Advocates of formulae b, c and d 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 formula (a), based on weight only, counts per unit area varied little from infancy through adolescence for two commonly radiopharmaceuticals in children, \(^{123}\text{I-}	ext{MIBG}\) and \(^{99m}\text{Tc-}	ext{medronate}\) [2].

A second area of concern was the adult reference activity. For \(^{99m}\text{Tc-MDP}\), typical adult administered activities are 740-925 MBq (20-25 mCi). For \(^{18}\text{F-FDG}\), a typical adult administered activity is 555 MBq (15 mCi). Most children’s hospitals and pediatric nuclear medicine specialists at university hospitals had already reduced the reference activity for these two radiopharmaceuticals to 555 and 370 MBq (15 and 10 mCi), respectively. These reduced reference activities have been incorporated into the consensus guidelines.

A third concern was appropriate adjustment of administered activities for positron emitting radiopharmaceuticals. Because of the differences in the tissue attenuation of photons by the patients and the physics of detection by the PET scanner, the consensus incorporated recent work by Sammer et al (with a theoretic basis in the work by Accorsi et al) [3,4]. This work suggests that administered activity for \(^{18}\text{F-FDG}\) may be further reduced in infants and smaller children.

A final question was maximum administered activity. 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 approximately equal to 70 times the recommended weight-based administered activity per kg. Examples are 370 MBq (10 mCi) for $^{123}$I-MIBG and $^{18}$F-FDG and 555 MBq (15 mCi) for $^{99m}$Tc-medronate. In order to suggest an upper limit, but also provide flexibility for the care of large adolescent patients, the following language that 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 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.”

The consensus guidelines differ significantly from the European Association for Nuclear Medicine (EANM) Pediatric Dose Card [5] in the several important respects:

(a) The administered activities in the consensus guidelines are slightly lower for infants and small children.
(b) Administered activities for $^{99m}$Tc-DMSA and $^{18}$F-fluoride are considerably lower in the consensus guidelines.
(c) 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/kg.
(d) The consensus guidelines more closely represent clinical practice in North America pediatric centers.

The following assumptions were used in constructing the consensus guidelines:

(a) Planar whole body and SPECT imaging studies were performed on a dual detector gamma camera equipped with a high resolution collimator.
(b) The determination of the administered activity for the pediatric patient is based on body weight alone except for nuclear cystogram and the gastric emptying studies.

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.

The Workgroup feels that it is important to promote the distribution of this information to the larger nuclear medicine community and that the SNM is a key vehicle for this. Subsequently, with SNM Board of Directors endorsement, the consensus guidelines may also be disseminated through the Image Gently program and incorporated into joint SNM/ACR Procedure Guidelines. Concurrent endorsement by the Society for Pediatric Radiology has been requested and will also facilitate dissemination of the consensus guidelines.
References


Appendix 1

Pediatric Nuclear Medicine Workgroup

Co-Chairs:

S. Ted Treves
Michael J. Gelfand MD
Marguerite T. Parisi M.D

SNM members

+ Adam Alessio DSc Seattle CH / U Washington
+ Larry Binkovitz MD Mayo Clinic
+ Nanci Burchell CNMT Kansas City Children’s Mercy
  Royal Davis CNMT Boston CH
+ Frederic Fahey DSc Boston CH
+ Michael Gelfand MD Cincinnati CH
+ Daniel Levin MD U Manitoba (Winnipeg)
  Ruth Lim MD Massachusetts Gen Hosp
  Jerry Mandell MD Phoenix CH
+ Massoud Majd MD DC Children’s
+ Helen Nadel MD BC Children’s
+ Meg Parisi MD Seattle CH
  Marla Sammer MD Seattle CH
+ Susan Sharp MD Cincinnati CH
+ Barry Shulkin MD St. Jude Children’s Res Hosp (Memphis)
+ Stephanie Spottswood MD Vanderbilt U (Nashville)
+ Ted Treves MD Boston CH
  Dan Young MD Birmingham CH
  Brad Wyly MD Eggleston CH (Atlanta)

ACR representatives

Jay Harolds MD U Oklahoma (Okla City)
Darlene Metter MD U Texas San Antonio

with encouragement from the Alliance for Radiation Safety in Pediatric Imaging (Image Gently®)

Marilyn Goske MD Cincinnati CH

+ original workgroup member
Appendix 2

Symposium on Pediatric Radiopharmaceutical Dosimetry
SNM’s 56th Annual Meeting in Toronto June 14, 2008
Organizer: S. Ted Treves, MD

Pediatric Radiopharmaceutical Dosimetry
S. Ted Treves, MD
Challenges in Radiopharmaceutical Dose Estimates
Michael G. Stabin, PhD
Pediatric and Customizable Phantom-Based Dosimetry
Wesley E. Bolch, PhD
Software Approaches Towards Radiation Dose Reduction
Alexander Hans Vija, PhD
Instrumentation Approaches Towards Radiation Dose Reductions
Alexander Hans Vija, PhD
European Experience in Pediatric Dosimetry
Michael Lassmann, PhD

Physics and Methodology Approaches to Dose Reduction
Georges N. El Fakhri, PhD

PET/CT Dosimetry
Frederic H. Fahey, D.Sc.

Radiation Risk
S. James Adelstein, MD, PhD

Brainstorming Session: Issues Regarding Consensus and Standardization
Michael J. Gelfand, MD; S. Ted Treves, MD
### TABLE 1: North American Consensus Guidelines for Administered Radiopharmaceutical Activities in Children and Adolescents

Please also see notes at the end of table 1 (*)

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Recommended Administered Activity (based on weight only)</th>
<th>Minimum Administered Activity</th>
<th>Maximum Administered Activity</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{123}$I-MIBG</td>
<td>5.2 MBq/kg ($0.14 \text{ mCi/kg}$)</td>
<td>37 MBq ($1.0 \text{ mCi}$)</td>
<td>370 MBq ($10.0 \text{ mCi}$)</td>
<td>The EANM Dosage Card 2007 version¹ administered activity may be used in patients over 10 kg.</td>
</tr>
<tr>
<td>$^{99m}$Tc-MDP</td>
<td>9.3 MBq/kg ($0.25 \text{ mCi/kg}$)</td>
<td>37 MBq ($1.0 \text{ mCi}$)</td>
<td></td>
<td>The EANM Dosage Card 2007 version¹ administered activity may also be used.</td>
</tr>
<tr>
<td>$^{18}$F-FDG</td>
<td>body 3.7-5.2 MBq/kg ($0.10-0.14 \text{ mCi/kg}$)</td>
<td>37 MBq ($1.0 \text{ mCi}$)</td>
<td></td>
<td>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 2007 version¹ administered activity may also be used.</td>
</tr>
<tr>
<td>$^{99m}$Tc-DMSA</td>
<td>1.85 MBq/kg ($0.05 \text{ mCi/kg}$)</td>
<td>18.5 MBq ($0.5 \text{ mCi}$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isotopic Form</td>
<td>Activity (MBq/kg)</td>
<td>Activity (mCi/kg)</td>
<td>Administered Activity (MBq)</td>
<td>Administered Activity (mCi)</td>
</tr>
<tr>
<td>--------------</td>
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</tr>
<tr>
<td>$^{99m}$Tc-MAG3</td>
<td>without flow study</td>
<td>3.7 MBq</td>
<td>37 MBq</td>
<td>148 MBq</td>
</tr>
<tr>
<td></td>
<td>with flow study</td>
<td>5.55 MBq</td>
<td>37 MBq</td>
<td>148 MBq</td>
</tr>
<tr>
<td>$^{99m}$Tc-IDA</td>
<td>1.85 MBq</td>
<td>18.5 MBq</td>
<td>9.25 MBq</td>
<td>0.5 mCi</td>
</tr>
<tr>
<td>$^{99m}$Tc-MAA</td>
<td>if Tc-99m used for ventilation</td>
<td>2.59 MBq</td>
<td>14.8 MBq</td>
<td>0.4 mCi</td>
</tr>
<tr>
<td></td>
<td>no Tc-99m ventilation study</td>
<td>1.11 MBq</td>
<td>9.25 MBq</td>
<td>0.25 mCi</td>
</tr>
<tr>
<td>$^{99m}$Tc-pertechnetate (Meckel diverticulum imaging)</td>
<td>1.85 MBq</td>
<td>9.25 MBq</td>
<td>9.25 MBq</td>
<td>0.25 mCi</td>
</tr>
<tr>
<td>$^{18}$F-sodium fluoride</td>
<td>2.22 MBq</td>
<td>18.5 MBq</td>
<td>18.5 MBq</td>
<td></td>
</tr>
</tbody>
</table>

8
<table>
<thead>
<tr>
<th></th>
<th>(0.06 mCi/kg)</th>
<th>(0.5 mCi)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc (for cystography)</td>
<td>No weight-based dose</td>
<td>No more than 37 MBq ($1.0 mCi$) for each bladder filling cycle</td>
<td>$^{99m}$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 techniques for $^{99m}$Tc, many of which will work well with lower administered activities.</td>
</tr>
<tr>
<td>$^{99m}$Tc-sulfur colloid (for oral liquid gastric emptying)</td>
<td>No weight-based dose</td>
<td>9.25 MBq ($0.25 mCi$)</td>
<td>37 MBq ($1.0 mCi$)</td>
</tr>
<tr>
<td>$^{99m}$Tc-sulfur colloid (for solid gastric emptying)</td>
<td>No weight-based dose</td>
<td>9.25 MBq ($0.25 mCi$)</td>
<td>18.5 MBq ($0.5 mCi$)</td>
</tr>
</tbody>
</table>

(*) This information is intended as a guideline only. Local practice may vary depending on patient population, choice of collimator, and the 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 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 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 permit them to do so. Higher administered activities may be required in selected patients.

No recommended dose is given for $^{67}$Ga-citrate. Intravenous $^{67}$Ga-citrate should be used very infrequently and only in low doses.