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# Standardization of Administered Activities in Pediatric Nuclear Medicine Part 2: A Report of the First Nuclear Medicine Global Initiative Project

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**ABSTRACT**

The Nuclear Medicine Global Initiative (NMGI) was formed in 2012 and consists of 13 international organizations with direct involvement in nuclear medicine. The underlying objectives of the NMGI were to promote human health by advancing the field of nuclear medicine and molecular imaging, encourage global collaboration in education, and harmonize procedure guidelines and other policies that ultimately lead to improvements in quality and safety in the field throughout the world. For its first project, the NMGI decided to consider the issues involved in the standardization of administered activities in pediatric nuclear medicine. It was decided to divide the final report of this project into two parts. Part 1 was published in the spring of 2015. This manuscript presents Part 2 of the final report. It discusses current standards for administered activities in children and adolescents that have been developed by various professional organizations. An evaluation of the current practice of pediatric nuclear medicine specifically with regard to administered activities as determined by an international survey of 313 nuclear medicine clinics and centers from 29 countries is presented. Lastly, this report provides recommendations for a path forward toward global standardization of the administration of radiopharmaceuticals in children.

Keywords: Pediatrics, administered activity, dosimetry

## INTRODUCTION

In the summer of 2012, a number of international organizations directly involved in the practice and science of nuclear medicine decided to engage in a project of common interest for the betterment of the field worldwide. The underlying objectives were to promote human health by advancing the field of nuclear medicine and molecular imaging, encourage global collaboration in education, and harmonize procedure guidelines and other policies that ultimately lead to improvements in quality and safety in the field throughout the world. This endeavor was named the Nuclear Medicine Global Initiative (NMGI) and includes societies from various countries as well as several multinational organizations in the field of nuclear medicine (Table 1).

The group decided that the first NMGI project would be to consider the issues involved in the standardization of administered activities in pediatric nuclear medicine. Part 1 of this report described the reasons for the choice of project (*1*). It also provides a review of the value of pediatric nuclear medicine, current understanding of the carcinogenic risk of radiation as it pertains to the administration of radiopharmaceuticals in children, and the application of dosimetric models in children. Gaps in current knowledge on these topics were also discussed. A listing of pertinent educational and reference resources, available in print and online, was provided and described.

This Part 2 report describes the findings and conclusion of the first NMGI project. It also provides an in depth description of the current standards for administered activities in children and adolescents that have been developed by various organizations. An evaluation of the current practice of pediatric nuclear medicine, specifically with regard to administered activities as determined by an international survey of nuclear medicine clinics and centers, is also included. Lastly, the report recommends a path forward toward global standardization of the administration of radiopharmaceuticals in children.

## CURRENT STANDARDS FOR PEDIATRIC ADMINISTERED ACTIVITIES

Optimization of pediatric administered activity is a complex process of risk versus benefit that is further complicated by the clinical requirements of the examination being performed, variation in physiological uptake of the radiopharmaceutical, patient attenuation and patient positioning, the counting statistics of static versus dynamic imaging, whether pediatric sedation is used and its influence on imaging time, the spatial resolution and sensitivity of the imaging system, reconstruction and filtering algorithms, and the risk associated with the radiation dose (*2-7*). The development of an objective measure of the performance of an imaging procedure for any given administered activity is challenging. Thus, the nuclear medicine community may rely on tools such as surveys that use the collective experience of the community to help develop guidelines and standardize administered activities. However, some such surveys have shown large variations in practice, resulting in a necessary focus on dedicated pediatric facilities for consistent findings (*8*); even then, disparities have been found (*9*), and Treves et al. used such findings to initiate development of the 2010 North American Consensus Guidelines (*10,11*).

A review of the literature and discussions within the NMGI confirmed there were 4 main guidelines on pediatric administered activity currently in use: the 2010 North American Consensus Guidelines (*10,11*), the European Association of Nuclear Medicine (EANM) dosage card (*12-14*), the Japanese Society of Nuclear Medicine (JSNM) guidelines (*15*), and the Administration of Radioactive Substances Advisory Committee (ARSAC, UK) “Notes for Guidance on the Clinical Administration of Radiopharmaceuticals and Use of Sealed Radioactive Sources” (revised 2014) (*16*). The ARSAC notes will not be discussed because the scaling factor from adult administered activity to pediatric administered activity used in the ARSAC document is based on an older version of the EANM guidelines. A comparison of the ARSAC pediatric administered activity schedule with a more recent EANM dosage card has already been presented by Rixham and Roberts (*17*). The North American group and the EANM recently published “harmonized” guidelines (*18,19*).

**EANM Dosage Card (2007 and 2014)**

The EANM guidelines started with a report by Piepsz et al., who presented a radiopharmaceutical schedule for an adult-to-pediatric scaling factor that was based on body surface area calculated from patient weight based on the practice from 4 institutions (*20*). These scaling factors were subsequently studied by Jacobs *et al*., who investigated whether the factors gave weight-independent effective doses or weight-independent count rates (*21*). They concentrated their analysis on the effective dose variation with weight and performed a cluster analysis and found 3 significant clusters, called A, B, and C, that represented the weight variation. Cluster A corresponded to renal imaging agents, cluster C to thyroid imaging using radioiodine, and cluster B to the majority of the other radiopharmaceuticals.

This clustering approach was used by Lassmann et al. to develop the EANM pediatric dosage card, with each radiopharmaceutical in one of the 3 classes (Clusters A, B or C). Each radiopharmaceutical had a corresponding minimum activity and baseline activity that was scaled by body weight to give the administered activity (*12*). Unlike the previous approach of a scaling factor applied to an adult activity, Lassmann et al. presented minimum activities and baseline activities that were developed by the Paediatric and Dosimetry Committee of the EANM for good practice. These baseline values meant that the administered activities were not directly related to adult reference levels. They advised, however, that the calculated activities should be capped if the scaling by weight resulted in an activity that exceeded national diagnostic reference levels for a radiopharmaceutical.

The 2007 EANM dosage card subsequently underwent minor corrections (*14*) and was extended with additional notes for $^{18}$F-fluorine and $^{18}$F fluoro-2-deoxy-D-glucose ($^{18}$F-FDG) (*13*). This was recently updated to the 2014 EANM dosage card to harmonize with the North American Consensus Guidelines (*18*).

**North American Consensus Guidelines (2010 and 2014)**

A 2007 survey of 13 specialized pediatric hospitals showed significant variations in the administered activity for pediatric patients (*9*). This finding led to a partnership between the Image Gently campaign, SNMMI, Society for Pediatric Radiology, and American College of Radiology. Several joint workshops resulted in the development of the 2010 North American Consensus Guidelines for 11 commonly used radiopharmaceuticals (*10,11*). These guidelines use adult reference activities that are scaled by body weight (except for gastric emptying and cystography), minimum administered activities (except for cystography), and maximum administered activities for MAG3, $^{123}$I-MIBG, cystography, and gastric emptying. For a number of the procedures, the guidelines advise that the EANM 2007 dosage card may be used instead of the recommended parameters. An important difference between the EANM dosage card and the

North American Consensus Guidelines is that the latter advocates the use of a linear weight adjustment of the administered activity, whereas the EANM scaling by body weight is nonlinear for all classes. The basis for the linear weighting is that when the administered activity for single-photon emitting radiopharmaceuticals is adjusted based on patient weight the count density varies little from infancy to adolescence (i.e., a range of patient weights and ages). The guideline uses this relationship combined with weight-based scaling from an adult reference activity.  Use of the 2010 North American Consensus Guidelines results in slightly lower administered activity for infants and small children compared with the 2007 EANM dosage card except for DMSA scans and Na-$^{18}$F scans, in which the doses are much lower compared with the 2007 EANM dosage card (see Figure 1) (*22*).  As noted above, these guidelines were recently updated to the 2014 North American Guidelines to harmonize with the EANM dosage card (*18*). These harmonized guidelines do not exactly agree in all instances as the respective guidelines continue to use different dosage calculation approaches as described above.

**Japanese Society of Nuclear Medicine (JSNM) Guidelines (2014)**

Parts 1 and 2 of the JSNM consensus guidelines for pediatric nuclear medicine have been translated into English (*15*). These guidelines were developed by the JSNM Optimization Committee for Pediatric Nuclear Medicine and were based on a survey of 14 Japanese institutions (*23*). The guidelines are based on the EANM class, baseline activity, and minimum activity, with weight-based multipliers for each class of radiopharmaceutical. However, the JSNM modified the EANM dosage card to develop a JSNM dosage card for 24 radiopharmaceuticals (*15*). The JSNM dosage card is significantly different from the EANM dosage card for DMSA, MAG3, MAA, and MIBI with the JSNM recommending slightly higher activities. There are also some significant differences from the North American Consensus Guidelines for MAG3, MDP in older children, DMSA, $^{123}$I MIBG, and $^{18}$F.

**Comparison of the Guidelines and a Move towards Harmonization**

There are 2 common components of the main guidelines for pediatric administered activity. For the majority of the radiopharmaceuticals, each guideline uses a minimum activity developed on the basis that an activity below this minimum may lead to a substandard examination. All 3 guidelines adjust the administered activity according to patient weight. Although the use of weight-based activity adjustment has been debated, it has remained a popular approach (*2*,*20*,*24*,*25*). The North American Consensus Guidelines recommend linear scaling by weight because this results in a small variation in counts per unit area from infancy to adolescence. However, preservation of counts may result in a significant increase in effective dose to some children. The alternative method that preserves effective dose rather than counts may be considered although this could lead to substandard imaging in some cases due to low counts (*21*). All 3 guidelines recommend minimum activities, with significant differences for some of the radiopharmaceuticals. In general, the minimum activity is based on experience rather than science. There is particular concern that positron emission tomography/computed tomography (PET/CT) minimum activities may be too high and that it may be possible to reduce the radiation dose to our smallest patients (*26*,*27*).

As noted above, the EANM dosage card and North American Consensus Guidelines have been harmonized as recently reported (*18*). Figure 1 illustrates some changes to the EANM dosage card for $^{99m}$Tc-DMSA as a result of this harmonization, with the 2014 EANM dosage card and consensus guidelines now producing similar activities. An important aspect of the harmonization is the scaling factors used for weight-based corrections. If the EANM class A renal imaging radiopharmaceuticals are considered separately, then the scaling factors for class B and class C radiopharmaceuticals are approximately linear for children weighing >10 kg (Figure 2). This means that the administered activity for a significant number of children could be modeled as a linear weight-based function, similar to the North American Consensus Guidelines, although with a different offset that could reflect a minimum activity. One of the arguments against adoption of the EANM dosage card is the complexity of applying the method and the chance of an error. However, it can be easily programmed into a spreadsheet or a computer application since the calculation is, in general, fairly straightforward. The EANM and the SNMMI have developed web-based tools and smartphone applications that can be used by nuclear medicine clinics to perform the calculations and determine the recommended administered activity for their pediatric patients (www.snmmi.org/pedactivitytool, http://www.eanm.org/publications/dosage_calculator.php?navId=285 ).

## VARIATIONS IN THE PRACTICE OF PEDIATRIC NUCLEAR MEDICINE

### Previous Surveys

*Survey of North American Pediatric Institutions (2007 and 2013).* A survey of dedicated pediatric institutions in North America was performed in 2007 regarding their approach to determining administered activities in smaller patients for 16 nuclear medicine procedures commonly performed in children (*9*). For each procedure, the institutions were asked if they modified the amount of administered activity by patient size and, if so, by what method. They were also asked about the maximum activity they would administer to a large child (e.g., >70 kg) and the minimum activity they set as a limit for very small patients. If the institution indicated that they modified the administered activity according to the patient's body weight, they were asked to provide the activity per weight (in MBq/kg or mCi/kg).

Thirteen dedicated pediatric institutions responded to the survey. Most of the institutions scaled the administered activity by body mass for smaller patients. In general, there was a reasonably wide variation in the values reported across the institutions. The maximum activity and the activity per kilogram varied on average across procedures by about a factor of 3 and for one procedure varied by a factor of 10. The variability in minimum activity was even greater, varying on average by a factor of 10 and by as much as a factor of 20 in one case. Consider $^{99m}$Tc-DMSA renal scanning as a typical case. One institution indicated that they administered 1.11 MBq/kg, while another used 3.70 MBq/kg. For minimum activity, one institution indicated a limit of 5.55 MBq, while another used 74 MBq. The variability for some of the procedures was considerably worse than this. This level of variability became a topic of discussion among the North American pediatric nuclear medicine community, eventually leading to the development and publication of the North American Consensus Guidelines of administered doses for children and adolescents, which was adopted by the SNMMI, American College of Radiology, and Society for Pediatric Radiology and promoted by the Image Gently campaign (*10,11*).

A follow-up survey of the same 13 pediatric institutions was conducted in 2013. In the intervening 6 years, the results of the initial survey had been published, the North American

Consensus Guidelines had been approved and published, and Image Gently had run a “Go With the Guidelines” public relations campaign that sought to deliver a poster containing a table of the guidelines to every nuclear medicine clinic in North America (*28*). All 13 sites that completed the initial survey completed the follow-up as well. The following pertains to the 8 procedures in the survey that also were included in the North American guidelines. For the maximum activity in larger children, the median value across institutions was reduced for 4 procedures, remained the same for 4 procedures, and was consistent with the North American guidelines in both cases in which a maximum activity was defined. The median of the minimum activity for very small patients was reduced for 3 procedures, remained the same for 5 procedures, and was consistent with the North American guidelines for 5 of the 8 procedures. For those that scaled the administered activity by weight for children, the median was reduced for 7 procedures, remained the same for one procedure, and was consistent with the North American guidelines for 5 of the 8 procedures. All 13 institutions indicated that they were familiar with Image Gently and the North American guidelines. Ten of the 13 institutions stated that they modified their administered activities according to the North American guidelines.

A survey of 194 general hospitals in the United States regarding the practice of pediatric nuclear medicine was recently performed. This survey included hospitals with more than 300 beds and excluded dedicated pediatric, military veterans, orthopedic, and psychiatric hospitals. The survey included questions that categorized the size of the hospital and whether it was a community or teaching hospital. It also asked whether the hospital performed imaging of children and how the administered activity for smaller children was determined for 5 procedures commonly performed in children ($^{99m}$Tc-MDP bone scans, $^{99m}$Tc-MAG renal studies, $^{99m}$Tc-DMSA renal studies, hepatobiliary studies with $^{99m}$Tc-labeled IDA derivatives, and FDG PET). A total of 121 hospitals responded to the survey (62% response rate): 50% were in an urban setting, 51% described themselves as “community, teaching” hospitals, and 80% indicated that they performed nuclear medicine studies in children. Of the institutions that performed nuclear medicine studies in children, 86% performed $^{99m}$Tc-MDP bone scans, 69% performed $^{99m}$Tc-MAG renal studies, 59% performed $^{99m}$Tc-DMSA renal studies, 39% performed hepatobiliary studies with $^{99m}$Tc-labeled IDA derivatives, and 30% performed FDG PET studies. Essentially all of the hospitals indicated that they scaled the administered activity for smaller patients by body weight. In all cases but one (maximum activity for MAG3 renal scans of 222 MBq rather than the guideline value of 148 MBq), the median values across the institutions were consistent with the North American guidelines, although there tended to be a reasonable amount of variability on either side of the median value. In addition, 83% were familiar with the Image Gently campaign, 58% were familiar with the North American guidelines, and 55% modified their administered activities based on the North American guidelines.

*Survey of Korean Institutions (2013).* A survey of administered radioactivity for 13 nuclear medicine procedures commonly performed in pediatric patients was conducted at the university-affiliated hospitals in South Korea in 2013. The institutions were asked 1) if they modified the amount of administered radioactivity in pediatric patients and, if so, the selected method and/or calculation equation, 2) about the maximum and minimum activity for large and very small patients respectively, for each procedure, and 3) if there were any special considerations for children younger than 1 year of age. Sixteen institutions responded to the survey. There was a wide variation in the scaling methods based on body weight (body weight × equation constant for each procedures) or age (adult dose × [age + 1]/[age + 7]), and some of the institutions used several guidelines, including the EANM dosage card, Gilday's chart, the Korean Society of Nuclear Medicine manual, and so on. The maximum and minimum activity varied considerably (Table 2). Special considerations for children younger than 1 year of age included the following: 1) minimizing the administered radioactivity and increasing the acquisition time, 2) sedation during the procedure to prevent failure due to motion, 3) more careful attention to aseptic preparation of radiopharmaceuticals because of the lower immunity of infants, and 4) addition of more saline to dilute radiopharmaceuticals, which could minimize the amount of remaining radioactivity in the syringe.

**NMGI International Survey**

Based on a review of the current standards for pediatric administered activities, the survey results described in the preceding text, and discussion within the NMGI working group, it was clear that there were significant variations in the administered activities used in the current practice of pediatric nuclear medicine imaging. Although there has been significant work toward standardization of administered activities by groups such as the SNMMI, EANM, and JSNM as previously discussed, opportunities remain for further improvement and harmonization of the standards worldwide. An international survey on pediatric administered activities was developed to determine whether the 3 main standards were being followed correctly and in their entirety, whether facilities selected between the standards to meet their local requirements or interest, whether other guidelines existed, and whether facilities were developing local practice guidelines. Furthermore, the survey asked about the most frequent imaging procedures being performed to determine whether the most frequent procedures varied between developed and developing countries. These questions were addressed using the collective strength of the NMGI to coordinate international participation in the survey and ensure penetration of the survey into a number of countries to collect a representative sample of worldwide pediatric nuclear medicine imaging practice.

*Description of the Survey and Its Implementation*. The format of the survey was based on one designed to determine if sites were following the 2010 North American Consensus Guidelines. However, the survey was modified to capture data regarding the top 5 pediatric imaging procedures performed by a facility (choosing from a list of 12 procedures, with the option for "other" entries), the guideline that was being followed (if any), and either the typical patient administered activity or the method of adjusting the administered activity for individual patients. Unless a facility is a dedicated pediatric imaging facility, it can be difficult to achieve sufficient numbers of pediatric patients to cover a range of procedures. For this reason, the survey asked for details of administered activity based on the usual operating protocols rather than a collection of details for actual patients. The survey included questions about the gamma camera used for imaging, whether single photon emission computed tomography (SPECT) imaging was mostly performed, and whether SPECT/CT imaging was sometimes performed. It inquired about administered activities for a hypothetical 5-year-old boy (20 kg and 110 cm tall) and a 10-year-old girl (30 kg and 140 cm tall). The latter questions were a quality control check on whether the facility was following a guideline if they stated they were doing so. For facilities performing PET or PET/CT imaging, the survey asked questions about administered activity for whole body pediatric FDG imaging and details on CT acquisition for PET.

The survey was web based for simplification and to ease data consolidation. SurveyMonkey® (SurveyMonkey.com) was used for data collection, and the survey was available in English only as preferred by all NMGI participating organizations. Because it was an international survey, the questions had to be carefully worded to reduce confusion and frustration for participants whose first language is not English.

Participation in the survey was by invitation from the NMGI societies and organizations. Each society managed the participation of their members or the people they were representing.

*NMGI Survey Results*. The survey was open for approximately 1 month (July 21, 2014 until August 19, 2014). There were 335 responses received but after eliminating testing, partial and duplicative entries the final number of responders was 313. The results to be reported are from these 313 responders although it is possible that inaccuracies remain in these entries. For example, there are instances of outliers where it is possible that the entry was a typographic error or the responder did not clearly understand the question being asked. However, even in these cases, it was not possible to discern that the entire entry from the site was not accurate. It was decided that entries would be retained if they were considered to be mostly reasonable even if one value entered appeared to be in error. Since such outliers could tend to skew the data, the median and inter-quartile ranges (25th to the 75th percentile) are reported rather than the mean and standard deviation.

The 313 entries were received from 29 different countries (Table 3). The method of distribution differed from country to country. In some cases, all members of the pertinent national nuclear medicine society were included whereas only a select number of hospitals were contacted in other cases. As a result, the 5 countries with the most entries were Japan (98 of the 313), Australia (46), China (33), Italy (21) and the US (19). Based on this distribution, the responders were organized into 7 regions: Asia (not including Japan) (40 or 12.8% of responding sites), Australia/New Zealand (58, 18.5%), EANM (i.e., member nations of the EANM) (77, 24.6%), Japan (98, 31.3%), Latin America (6, 1.9%), North America (27, 8.6%) and South Africa (7, 2.2%). This variability in response among countries and regions may limit the accuracy and ability to generalize the survey results. However, we still believe that these data provide insight into the global practice of pediatric nuclear medicine. Ninety-three percent of the responders indicated that their practice included general nuclear medicine (with or without

PET/CT or PET) whereas 7% indicated that their practice included PET/CT or PET only without general nuclear medicine. Figure 3 shows 2 histograms of the number of studies performed on pediatric patients at each site. The median and mean numbers of procedures in pediatric patients were 100 and 306, respectively, indicating a very skewed distribution. Most sites did a small number of such studies and a few sites did many more. With respect to PET, 48% of the sites did not perform PET in children, 51% performed PET with a hybrid PET/CT scanner. Only 1% performed PET with a "PET only" scanner with no CT.

Sites were asked to list the 5 general nuclear medicine procedures that they most commonly performed in children ranked from their most to least common not including FDG PET (Table 4). The 3 most common procedures were bone scans using $^{99m}$Tc, radionuclide renogram using $^{99m}$Tc and renal scarring and differential function imaging using $^{99m}$Tc DMSA. These preferences varied regionally (Table 5) although the radionuclide renogram was one of the three most common procedures in for all regions and bone scanning was for 6 of the 7 regions.

Regional data are plotted (Figures 4-7) for the 2 hypothetical pediatric patients (5 year old boy weighing 20 kg and 110 cm tall; 10 year old girl weighing 30 kg and 140 cm tall) are plotted for the 3 most common procedures, i.e. $^{99m}$Tc bone scan, $^{99m}$Tc renogram and $^{99m}$Tc DMSA as well as for $^{18}$F FDG torso PET. Also shown on these figures are the administered activities that would have been recommended by the North American consensus guidelines (labeled SNMMI), the EANM pediatric dosage card and the Japanese consensus guidelines for these hypothetical patients. For $^{99m}$Tc bone scans, the EANM and JSNM recommendations coincide and, thereby, the line is the same for both in Figure 4. For the $^{99m}$Tc renogram, the North American guidelines recommend separate value for studies performed with and without the renal flow component. In Figure 5, these are show as two lines of different colors. For FDG, the North American guidelines recommend a range of activities which is shown by a shaded area (Figure 7). Table 6 lists the median and the intra-quartile range for all cases displayed in Figures 4-7. In addition, for the 3 regions that have current guidelines for administered activities in children, the percentage of sites that are exactly in compliance or are within 20% of the recommended value from their respective guidelines are reported. These are reported in Table 7.

In general, the 3 regions that have current guidelines for administered activities in children are consistent with their own guidelines. In practically all of these cases, the mode (or most common response) coincides with the value or range of values recommended by their respective guidelines. However, there is also a wide variation about the modal and median values. There were major outliers on some of the figures most likely due to typographical errors. In all cases, South Africa shows less variation than the other regions; perhaps since this region consist of a single nation. In addition, South Africa tends to be in compliance with the EANM Dosage card. For $^{99m}$Tc bone scans (Figure 4), all regions demonstrate a similar variation with the exception of South Africa. For the $^{99m}$Tc renogram (Figure 5) in the 5 year old, the mode of the North American region corresponds to the recommended administered activity for studies with the flow component. Australia/New Zealand and EANM tend to demonstrate higher variation than the other regions for this procedure. For DMSA (Figure 6), Latin America, North America and South Africa show less variation than the other regions. Lastly, Asia and EANM show the largest variation for FDG (Figure 7).

Of the 313 sites, 129 answered questions regarding the acquisition of CT in the context of PET/CT. Seventy-two percent of the sites indicated that they utilized automatic exposure control for the CT acquisitions. However, 9% of the responders did not know if they use this feature and so the percentage of those that do may be higher than 72%. About one third of responders acquire the CT component of PET/CT in children as a diagnostic scan with contrast. One third of the responders have a GE PET/CT system, another one third utilizes a Siemens system and 20% have Philips. Less than 3% specified a different vendor (Toshiba or Shimadsu) and 11% did not specify the vendor.

## DISCUSSION AND RECOMMENDATIONS

Pediatric nuclear medicine should be specifically considered, and attention toward image optimization must be stressed for every imaging procedure and every patient. One of the first reports related to pediatric nuclear medicine dates back to 1961 and was a letter published after a meeting of 75 chairs of pediatric departments in North America were invited to visit the Division of Biology and Medicine of the Atomic Energy Commission and the Medical Department at the Brookhaven National Laboratory (*29*). Some sentences in that report could have been written in 2015: “The knowledge that their use [radioactive isotopes] in children may be associated with both real and unpredictable hazards has led to hesitation and confusion on the part of the pediatrician. On the one hand he is tempted to make use of a new tool which may lead to earlier diagnosis, shorten hospitalization, and point the way to clear-cut approaches to therapy. On the other hand he is restrained by concern about the possible late effects which may follow exposure of a young growing organism to radiation." It is interesting to note that, despite the fact that a nuclear medicine physician and a medical physicist were not mentioned, the basic concepts were already present. Thousands of papers were subsequently published on this topic, particularly related to dose administration in relation to image quality and patient benefit. We know that published data and scientific guidelines are abundant but not always harmonized, and the NMGI has highlighted the efforts that should be addressed and the level of priority.

Based on this initiative, following observations and conclusions were made:

- The value of pediatric nuclear medicine is clearly recognized. However, care must be taken to assure that these studies are applied appropriately in those patients who can best benefit.
- Much information is available both in print and online regarding the appropriate application of nuclear medicine in children as well as our current understanding of radiation dosimetry in these patients. Nuclear medicine professions who image children should take advantage of these materials in order to be better informed and thus better serve our pediatric patients.
- There remain gaps in our knowledge of the biokinetics and radiation dosimetry associated with the application of nuclear medicine in children. There is also limited information regarding the potential risk of adverse health effects from ionizing radiation in children at the dose levels most pertinent to nuclear medicine. More complete understanding of these issues would allow for better optimization of pediatric nuclear medicine.
- There remains a wide variability in the practice of pediatric nuclear medicine across the globe. Clinical sites in those regions that have developed guidelines for administered activities in children tend to be consistent with those guidelines although some wide variations still exist.

As a result of these observations, the following recommendations are put forth:

- Countries and regions that do not currently have pediatric guidelines for administered activities should either develop their own or officially adopt currently existing guidelines.
- Those regions that currently have guidelines should expand these to all nuclear medicine procedures practiced in children and should continue to strive for harmonization among these guidelines.
- Administered activity for paediatric patients should be incorporated into audit processes for Nuclear Medicine sites, whether by local / country based programs, or other audit methods (e.g. IAEA QUANUM program).
- Paediatric dose recommendations should be incorporated in formal training curriculum, and recertification programs, for all Nuclear Medicine professionals.
- All organizations involved in nuclear medicine should disseminate the findings and recommendations of this endeavor to their members and constituents. The appropriate use of pediatric nuclear medicine and the adherence to guidelines for administered activities for children and adolescents should be very actively promoted to a wide audience

This initiative can pave the way not only toward further studies on dose optimization in pediatric nuclear medicine, but also toward better awareness of the problems and opportunities in the medical community.

## CONCLUSION

The NMGI has demonstrated that a global effort recognized in every country can be successfully conducted by a community of scientists who aim to provide the best possible treatment for their patients. We will strive to continue this initiative with even more enthusiasm and commitment.

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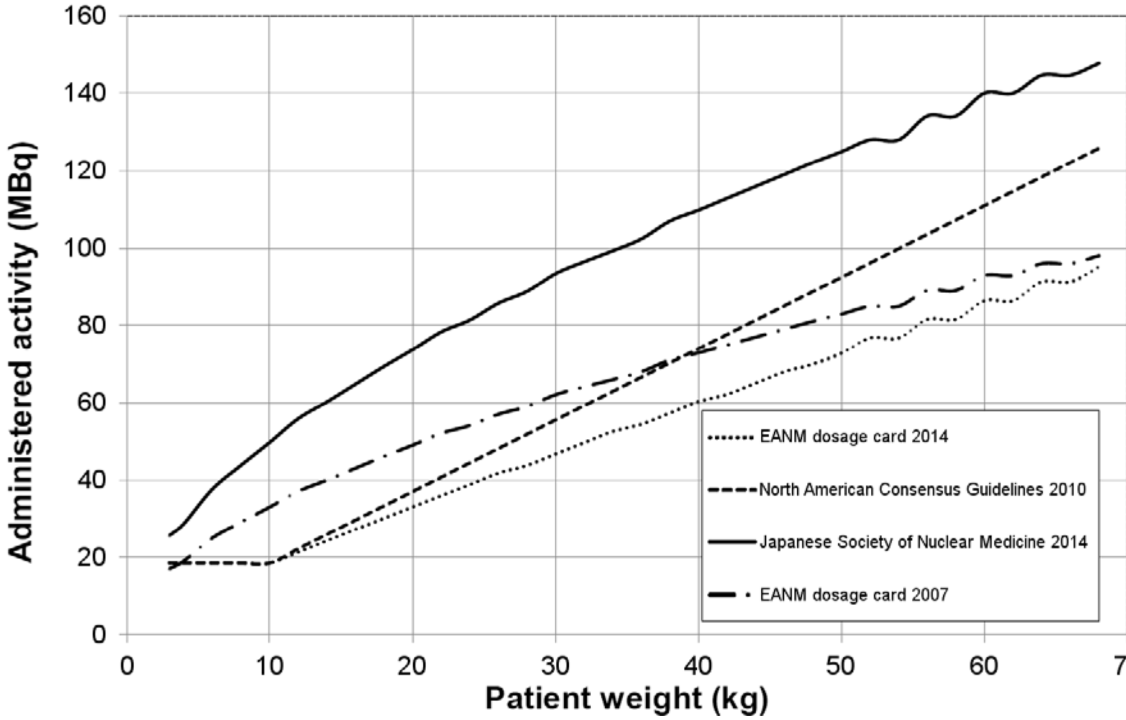


Figure 1. Comparison of the $^{99m}$Tc DMSA pediatric administered activity guidelines from the 2014 EANM dosage card, the 2014 JSNM guidelines, the 2007 EANM dosage card, and the 2010 North American Consensus Guidelines. This is an example of the large difference between the 3 guidelines for some of the radiopharmaceuticals, although there is better agreement between the 2014 EANM dosage card and the 2010 North American Consensus Guidelines for smaller children compared with the 2007 EANM dosage card.

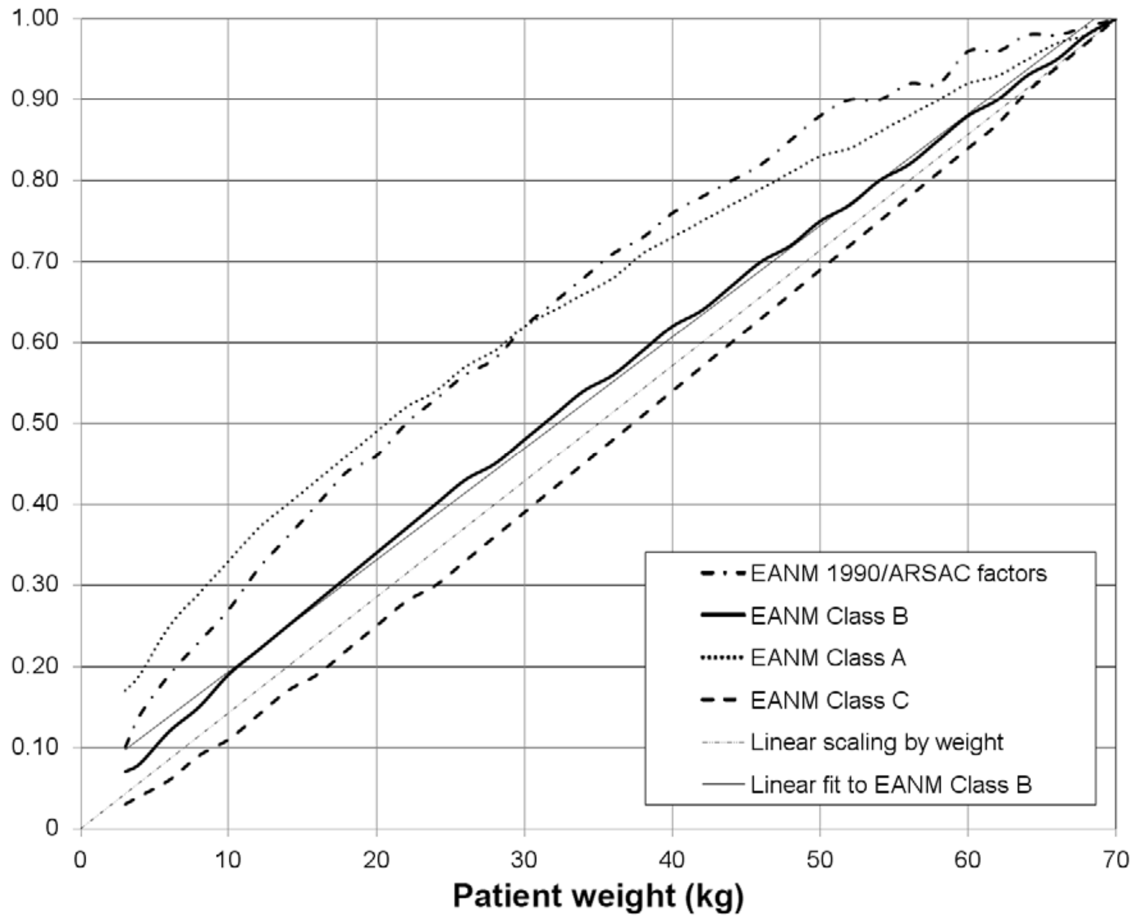


Figure 2. The 2007 EANM dosage card scaling factors as derived from Jacobs et al (21) compared with the EANM 1990/ARSAC scaling factors and a linear weighting factor. The EANM class B and class C are remarkably linear except for small patients, as illustrated by the linear trend line fitted to class B. The renal imaging scaling factors of class A are nonlinear.

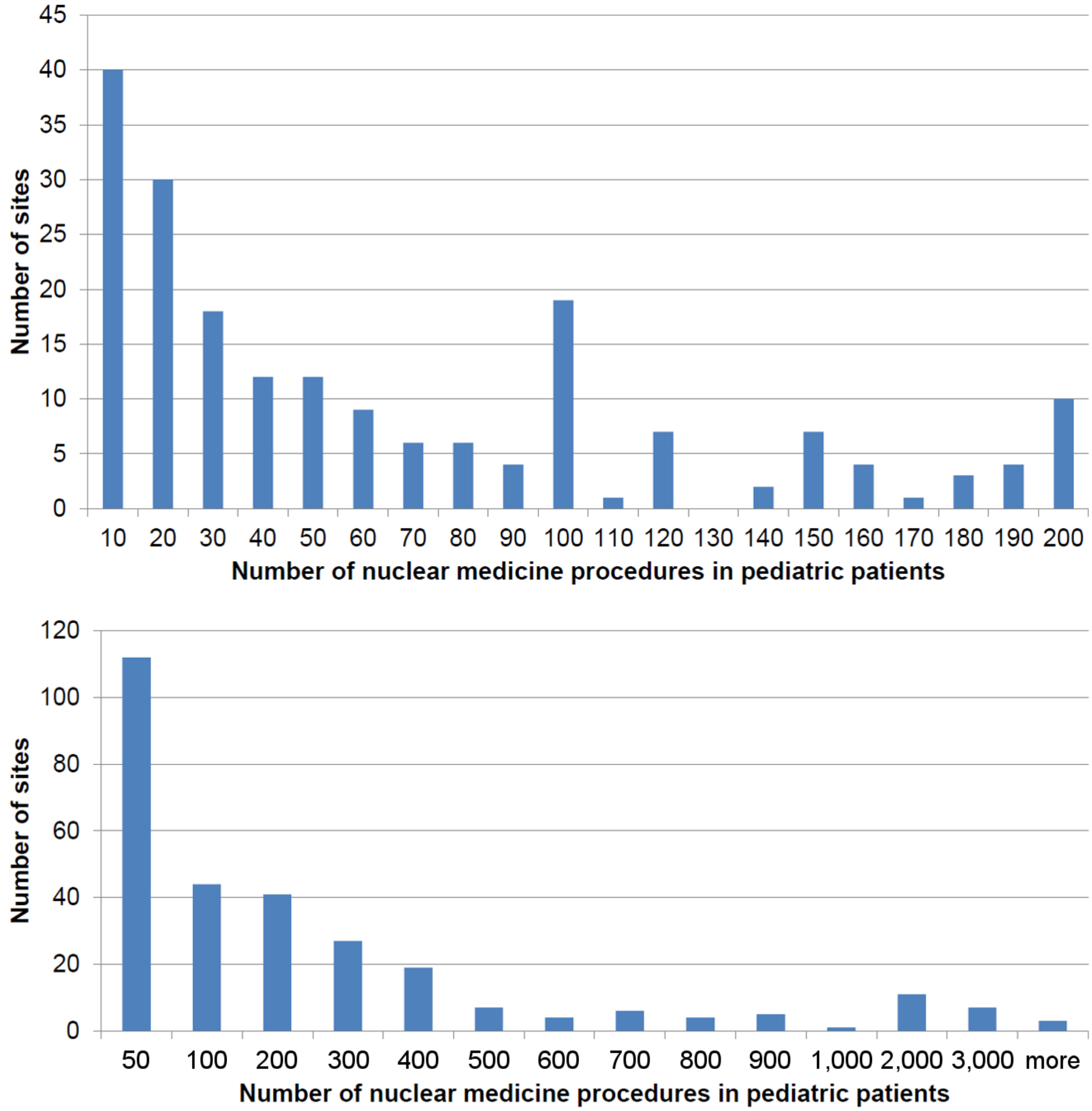


Figure 3. Number of nuclear medicine procedures in pediatric patients per year as a function of site. A. This figure plots the number of procedures in pediatric patients for all sites. B. This figure expands the plot for sites performing less than 200 studies per year.

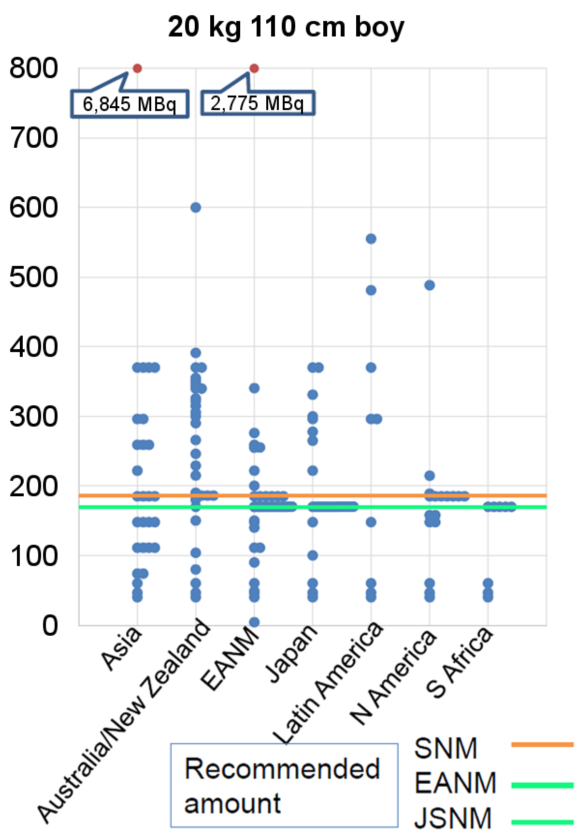


Figure 4. Administered activities for $^{99m}$Tc bone scans for 2 hypothetical patients (5 year old 20 kg boy and a 10 year old 30 kg girl) as a function of region. The recommended levels for the SNMMI, EANM and JSNM are shown. Note that in the instance of $^{99m}$Tc bone scans, the EANM and JSNM recommendations coincide. This figure demonstrates wide variation within and across regions. For those regions with pediatric standards (EANM, Japan and North America), the most common response was consistent with the recommended amount but wide variation was still demonstrated.

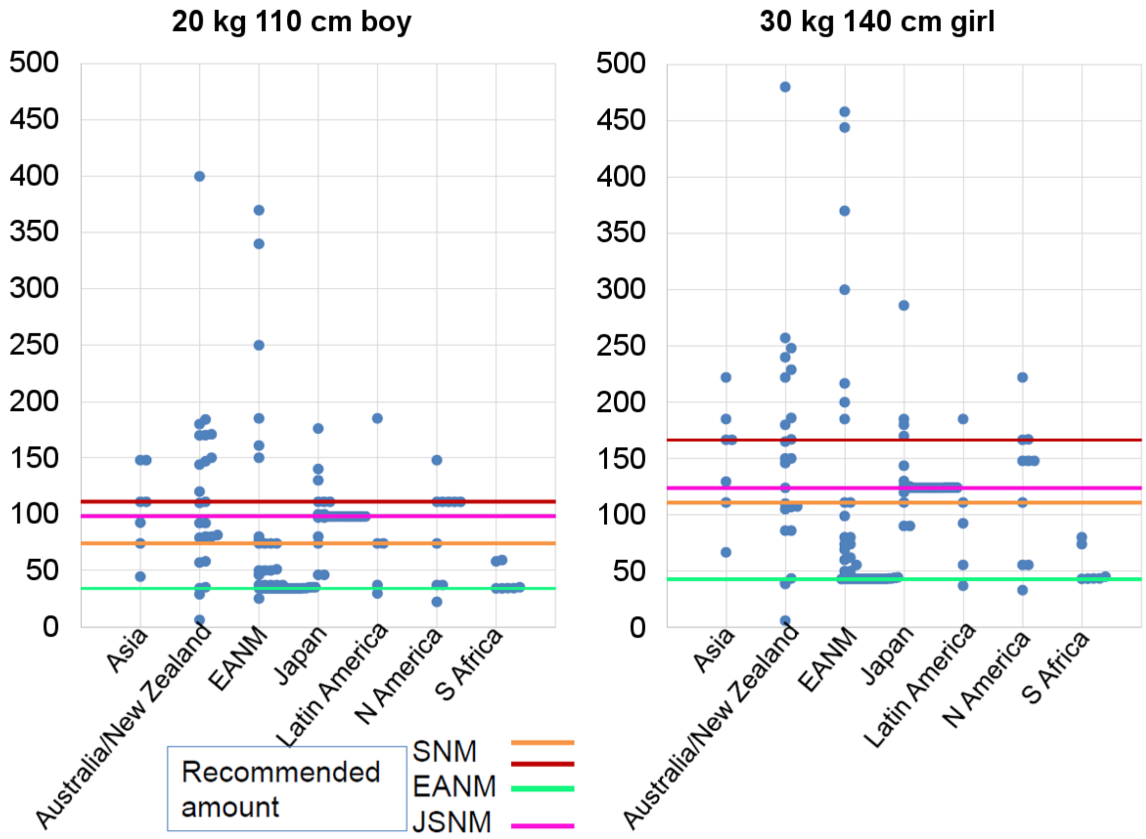


Figure 5. Administered activities for $^{99m}$Tc renograms for 2 hypothetical patients (5 year old 20 kg boy and a 10 year old 30 kg girl) as a function of region. The recommended levels for the SNMMI, EANM and JSNM are shown. Note that the SNMMI lists 2 values, one for studies with a flow component and another without the flow component, both of which are shown. More sites were consistent with the value with the flow component.

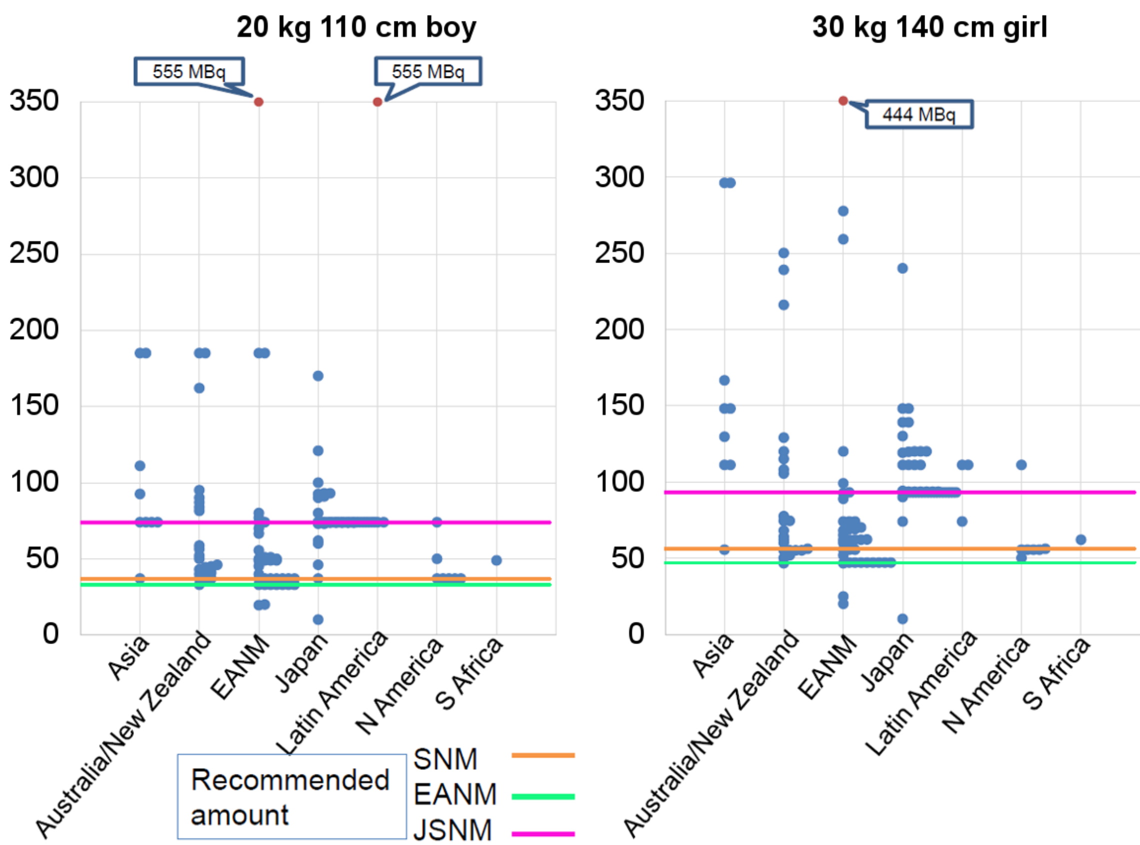


Figure 6. Administered activities for imaging of the renal cortex using $^{99m}$Tc DMSA for 2 hypothetical patients (5 year old 20 kg boy and a 10 year old 30 kg girl) as a function of region. The recommended levels for the SNMMI, EANM and JSNM are shown. This figure demonstrates wide variation within and across regions. For those regions with pediatric standards (EANM, Japan and North America), the most common response was consistent with the recommended amount but wide variation was still demonstrated.

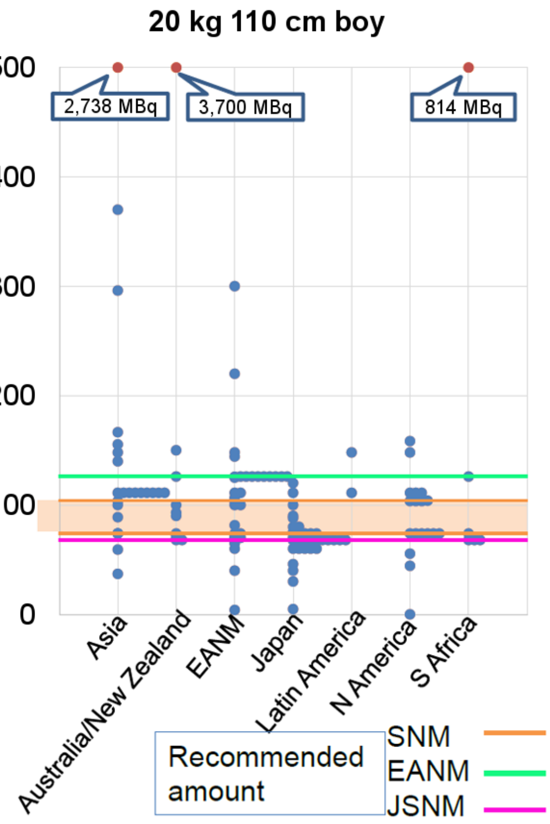


Figure 7. Administered activities for $^{18}$F FDG PET scans of the torso for 2 hypothetical patients (5 year old 20 kg boy and a 10 year old 30 kg girl) as a function of region. The recommended levels for the SNMMI, EANM and JSNM are shown. Note that the SNMMI recommends a range of administered activities.

**Table 1.** NMGI Participants

| | |
|---|---|
| Asia and Oceania Federation of Nuclear Medicine and Biology | Henry Hee-Seung Bom |
| Australian and New Zealand Society of Nuclear Medicine | Darin O'Keeffe, Andrew Scott |
| Canadian Association of Nuclear Medicine | Norman Laurin |
| Chinese Society of Nuclear Medicine | Shaoli Song, Gang Huang |
| European Association of Nuclear Medicine | Arturo Chiti, Michael Lassmann |
| International Atomic Energy Agency | Rodolfo Nuñez-Miller |
| Japanese Society of Nuclear Medicine | Mayuki Uchiyama |
| Korean Society of Nuclear Medicine | Yun Young Choi |
| Latin American Association of Societies of Nuclear Medicine and Biology | Fernando Mut |
| Society of Nuclear Medicine India | Prasanta Pradhan |
| Society of Nuclear Medicine and Molecular Imaging | Frederic Fahey |
| South African Society of Nuclear Medicine | Nischal Soni |
| World Federation of Nuclear Medicine and Biology | Luis Vargas |

**Table 2.** Median Value of Minimum and Maximum Administered Doses in Korean Children (15 University Hospitals)

| Radiopharmaceutical | Minimum (range) (MBq)/number of respondents | Maximum (range) (MBq)/number of respondents |
|---|---|---|
| $^{99m}$Tc-DMSA | 29.6 (14.8-74.0)/14 | 129.5 (92.5-370.0)/12 |
| $^{99m}$Tc-MAG3 | 37.0 (14.8-111.0)/14 | 185.0 (74.0-555.0)/12 |
| $^{99m}$Tc-MDP | 74.0 (22.2-185.0)/13 | 555.0 (370.0-1480)/12 |
| $^{99m}$Tc-DISIDA | 37.0 (18.5-74.0)/11 | 185.0 (111.0-370.0)/10 |
| $^{123}$I-MIBG | 37.0 (18.5-81.4)/7 | 185.0 (74.0-333.0)/7 |
| $^{99m}$Tc (Meckel's diverticulum) | 42.6 (9.3-74.0)/12 | 222.0 (74.0-555.0)/12 |
| $^{99m}$Tc (thyroid) | 37.0 (10.0-74.0)/13 | 138.8 (79.9-370.0)/12 |
| $^{123}$I (thyroid) | 11.1 (3.0-111.0)/6 | 74.0 (20.0-185.0)/7 |
| $^{99m}$Tc-HMPAO or ECD | 99.9 (37.0-222.0)/14 | 647.5 (18.5-1665)/12 |
| $^{99m}$Tc-MIBI | 95.5 (37.0-185.0)/6 | 740.0 (259.0-1110.0)/8 |
| $^{99m}$Tc denatured RBC | 28.5 (18.5-79.9)/12 | 277.5 (40.0-925.0)/10 |
| $^{67}$Ga (tumor) | 11.1 (10.0-37.0)/5 | 79.9 (74.0-296.0)/5 |
| $^{18}$F-FDG | 74.0 (37.0-185.0)/13 | 370.0 (185.0-555.0)/10 |

**Table 3**. Distribution of the survey entries by country

| Country | Sites |
|---|---|
| Albania | 1 |
| Australia | 46 |
| Belgium | 7 |
| Canada | 8 |
| Chile | 1 |
| China | 33 |
| Croatia | 1 |
| Czech Republic | 7 |
| Denmark | 2 |
| Germany | 4 |
| Hungary | 6 |
| Israel | 11 |
| Italy | 21 |
| Japan | 98 |
| Malta | 1 |
| Mexico | 3 |
| Netherlands | 7 |
| New Zealand | 12 |
| Portugal | 4 |
| Serbia | 2 |
| South Africa | 7 |
| South Korea | 5 |
| Spain | 1 |
| Sri Lanka | 1 |
| Thailand | 1 |
| Turkey | 2 |
| United States | 19 |
| Uruguay | 1 |
| Venezuela | 1 |
| | |
| Total | 313 |

**Table 4**. The 5 general nuclear medicine procedures most commonly performed in children at the reported sites.

| Procedure | N | |
|---|---|---|
| Bone Scan (e.g. Tc-99m MDP) | 159 | 21.2% |
| Renogram (e.g. Tc-99m MAG3) | 148 | 19.7% |
| Renal Scarring/Differential Function (e.g. Tc-99m DMSA) | 137 | 18.2% |
| Neuroendocrine Tumor Imaging (123I-MIBG) | 46 | 6.1% |
| Thyroid Scan | 40 | 5.3% |
| Meckel's Diverticulum (e.g. Tc-99m O4) | 38 | 5.1% |
| Cerebral Perfusion Scintigraphy | 34 | 4.5% |
| Hepatobiliary | 28 | 3.7% |
| Tumor Imaging (Ga-67) | 24 | 3.2% |
| Gastro-esophogeal Reflux (e.g. Tc-99m Sulfur Colloid) | 20 | 2.7% |

**Table 5**. Regional variation in the 5 procedures most commonly performed in pediatric patients. Values in parentheses are percentages.

| Region | 1st Most Common | 2nd Most Common | 3rd Most Common | 4th Most Common | 5th Most Common |
|---|---|---|---|---|---|
| Asia | Bone (31) | Thyroid (13) | Renogram (11) | DMSA (11) | Hepato (11) |
| Australia/NZ | Bone (29) | Renogram (23) | DMSA (20) | Thyroid (7) | Meckel's (6) |
| EANM | Renogram(27) | Bone (22) | DMSA (22) | MIBG (8) | Meckels/RNC(6) |
| Japan | DMSA (21) | Renogram(15) | Brain SPECT (13) | Bone (12) | Ga-67 (9) |
| Latin America | Bone (30) | Renogram(25) | DMSA (15) | Six studies tied with 5% | |
| No America | Bone (27) | Renogram(19) | MIBG (15) | DMSA (11) | Thyroid (7) |
| So Africa | Renogram(29) | Bone (21) | Gastro reflux (17) | | |

**Table 6**. Administered activities (MBq) for 2 hypothetical patients (5 year old boy 20 kg and 10 year old girl 30 kg) for a $^{99m}$Tc bone scan, $^{99m}$Tc renogram scan, $^{99m}$Tc DMSA scan and $^{18}$F FDG torso PET scan. The median value (and 25$^{th}$ and 75$^{th}$ percentile) values are reported for each region.

| Procedure | Asia | Australia New Zealand | EANM | Japan | Latin America | No America | So Africa |
|---|---|---|---|---|---|---|---|
| $^{99m}$Tc Bone Scan 5YO 20 kg | 185 (139, 268) | 285 (186, 344) | 170 (170, 185) | 170 (170, 265) | 333 (296, 453) | 185 (171, 186) | 170 (170, 170) |
| $^{99m}$Tc Bone Scan 10YO 30 kg | 278 (222, 389) | 395 (279, 460) | 240 (240, 278) | 240 (240, 359) | 407 (287, 444) | 278 (255, 278) | 240 (240, 240) |
| $^{99m}$Tc Renogram 5YO 20 kg | 111 (83, 130) | 101 (74, 155) | 37 (34, 74) | 98 (98, 99) | 74 (37, 74) | 111 (46, 111) | 34 (34, 47) |
| $^{99m}$Tc Renogram 10YO 30 kg | 167 (120, 178) | 146 (86, 186) | 45 (43, 80) | 124 (124, 125) | 93 (56, 111) | 148 (69, 162) | 44 (43, 60) |
| $^{99m}$Tc DMSA Renal Scan 5YO 20 kg | 74 (74, 111) | 50 (41, 86) | 49 (37, 51) | 74 (74, 74) | 74 (74, 74) | 37 (37, 44) | 49 (49, 49) |
| $^{99m}$Tc DMSA Renal Scan 10YO 30 kg | 148 (111, 167) | 68 (55, 112) | 62 (47, 74) | 93 (93, 111) | 111 (93, 111) | 56 (56, 56) | 62 (62, 62) |
| $^{18}$F FDG PET Scan 5YO 20 kg | 111 (94, 125) | 82 (71, 98) | 111 (73, 126) | 68 (68, 74) | 130 (120, 139) | 89 (74, 109) | 68 (68, 74) |
| $^{18}$F FDG PET Scan 10YO 30 kg | 167 (149, 215) | 118 (106, 146) | 167 (111, 178) | 96 (96, 111) | 231 (199, 264) | 144 (111, 164) | 96 (96, 107) |

**Table 7**. Pediatric Guideline Compliance. For the 3 regions that have established (Japan, EANM and North America), the fraction of sites that were exactly compliant with the pertinent guideline as well as the fraction that was within 20% of the guideline is reported.

| **Procedure** | **JSNM** | **JSNM 20%** | **EANM** | **EANM 20%** | **SNMMI** | **SNMMI 20%** |
|---|---|---|---|---|---|---|
| $^{99m}$Tc bone scan 5YO 20 kg | 60.0% | 64.0% | 43.2% | 70.3% | 46.7% | 93.3% |
| $^{99m}$Tc bone scan 10YO 30 kg | 56.0% | 64.0% | 36.8% | 68.4% | 46.7% | 93.3% |
| | | | | | | |
| $^{99m}$Tc renogram 5YO 20 kg* | 54.8% | 80.6% | 39.5% | 81.4% | 50.0% | 50.0% |
| $^{99m}$Tc renogram 10YO 30 kg* | 61.3% | 77.4% | 40.5% | 57.1% | 30.0% | 50.0% |
| | | | | | | |
| $^{99m}$Tc DMSA renal scan 5YO 20 kg* | 64.4% | 75.6% | 18.4% | 39.5% | 71.4% | 71.4% |
| $^{99m}$Tc DMSA renal scan 10YO 30 kg* | 57.8% | 71.1% | 24.3% | 35.1% | 71.4% | 85.7% |
| | | | | | | |
| $^{18}$F FDG torso PET scan 5YO 20 kg | 39.5% | 76.3% | 30.3% | 51.5% | 58.8% | 82.4% |
| $^{18}$F FDG torso PET scan 10YO 30 kg | 39.5% | 71.1% | 27.3% | 57.6% | 47.1% | 70.6% |