Journal of Nuclear Medicine, published on July 23, 2015 as doi:10.2967/jnumed.115.156141

Dose Optimization of the Administered Activity in Pediatric Bone Scintigraphy: Validation of the North American Consensus Guidelines

(Pediatric Bone Scan Dose Optimization)

Karen L. Ayres, MD; Stephanie E. Spottswood, MD; Dominique Delbeke, MD PhD;

Ronald Price, PhD; Pamela K. Hodges, BS CNMT; Li Wang, MS MSE; William H. Martin, MD

Vanderbilt Children's Hospital/ Vanderbilt University Hospital

Department of Radiology and Radiologic Sciences

Karen Ayres, MD, R4 Resident at Vanderbilt

1161 21st Avenue South

Medical Center North, Suite CCC-1121

Nashville, TN 37232-2675

(615) 322-3780 (office)

(615) 322-3764 (fax)

karen.ayres@vanderbilt.edu

Word Count: 2616

Abstract

The 2010 North American Consensus Guidelines (NACG) for pediatric administered doses and the European Association of Nuclear Medicine (EANM) dosage card recommend lower administered activities than those given at our institution. We compared the quality of the lower-activity images to the higher-activity images to determine if the reduction in counts affects overall image quality.

Keywords: dose reduction, pediatric bone scintigraphy

Methods:

Twenty patients presenting to our pediatric radiology department for bone scintigraphy were evaluated. Mean weight was 20 kg. Patients were referred for oncologic (n=5), infectious/inflammatory (n=5), and pain (n=5) evaluation. Dynamic anterior and posterior images were acquired for 5 minutes for each patient. Data were subsampled to represent different administered activities corresponding to the activities recommended by the NACG and EANM dosage card. Images were evaluated for diagnostic quality and acceptability for daily clinical use.

Results:

There was no statistically significant difference in the diagnostic quality of the images from any of the three protocols. Pathologic uptake was correctly identified independent of the administered activity , although there was one false-positive on an EANM image. When subjectively evaluating images as acceptable for daily clinical use, there was a slight preference for the higher activity images over the NACG (p=0.04).

Conclusion:

The recommended administered activities of the NACG produce images of diagnostic quality, while reducing patient radiation exposure.

Keywords: North American Consensus Guidelines, dose reduction, pediatric bone scintigraphy.

Introduction

Radiation dose reduction is a major goal within the imaging community. The rate of use of ionizing radiation was quantified in a study analyzing the use of diagnostic ionizing radiation studies in over 350,000 children, selected based on continuous enrollment in United Healthcare between 2005 and 2007 in five major markets including Dallas, Texas, and Orlando, Florida. Forty-three percent of these children were exposed to radiation from at least one diagnostic imaging procedure performed over the three year observation period.(*1*) Twenty-five percent of the children had at least two imaging procedures during that time period, and 16% had at least three. Bone scintigraphy was the most commonly performed nuclear medicine procedure. This is important to recognize because children are at greater risk of radiation side effects such as latent malignancy due to their rapid development and their relatively long life expectancy. Based on atomic bomb survivor data, the likelihood of solid tumor malignancy after exposure to ionizing radiation was 1.0-1.8 times higher in a ten-year-old child than a young adult, and the risk of leukemia was approximately double. (*2*) As many children have multiple imaging procedures, cumulative exposure must also be considered.

In 2010, experts in nuclear medicine collaborated to produce the North American Consensus Guidelines (NACG).(*3*) The NACG were updated in 2014 with no change to the recommended bone scintigraphy administered activities.(*4*) These guidelines provide recommendations for standardized administered activities for many common nuclear medicine studies performed in children including bone scintigraphy, renography, and ^{18}F-FDG PET/CT. When compared to administered activities in many imaging institutions, including our own, the NACG recommended activity for bone scintigraphy was much lower for all patient weights. The aim of the present study is to evaluate the quality of bone scintigraphy images utilizing the administered activities recommended in the NACG, as compared to the ones administered at our institution based on body surface area. The NACG were also compared to the 2008 EANM dosage card (equivalent to the since-released 2014 EANM dosage card).

Table 1 show the administered activities and effective dose equivalents for children of different weights when following the three different administered activities protocols, highlighting the variability most notably in the smallest children. Data was derived from the International Commission on Radiological Protection Publication 106. (*5*)

Methods

Institutional Review Board approval for the project was granted as a Quality Assurance project, and the need for written informed consent was waived. Twenty pediatric patients referred to our nuclear medicine department for bone scintigraphy were prospectively studied. Clinical indications included malignancy, infection/ fever of unknown origin, and pain. Patients ranged from 2 months to 16 years old, with the exception of one patient who was 20 years old but within pediatric weight for dosing (50.5 kg). Patient demographics are presented in Table 2.

Patients were administered our standard institutional activities of ^{99m}Tc-methylene diphosphonate (MDP) based on a body surface area based nomogram. (*6*) For all patient weights, our institutional activities were greater than the suggested activities based on the NACG and EANM dosage card. Dynamic anterior and posterior images of the chest were acquired for 5 minutes in 30-second frames using a low energy, high resolution parallel-hole collimator with an energy window of 140 keV +/- 10%. The imaging time at our institution is five minutes as this provides between 500,000 and 1,000,000 counts, which falls within the recommendation of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) (*7*), and most patients can lie reasonably still for five minutes. Images acquired over longer than five minutes are subject to increased motion artifact. Images were acquired approximately 2.5 hours following the administration of the radiopharmaceutical, which is standard and also in line with the SNMMI guidelines.

The data were then subsampled to produce images simulating lower activities by summing a number of frames proportionate to the decreased activity. For example, when the NACG administered activity for a patient was 50% of the institutional administered activity, then 50% of the counts (5 of the 10 frames, representing 2.5 minutes of imaging time) were utilized to generate the NACG image. Percentages were rounded to the nearest ten percent. These reconfigured images were equivalent to images that would have been acquired over 5 minutes using the lower administered activities as per the different imaging protocols. Institutional, EANM, and NACG images were generated for each patient, as well as an arbitrary 1-minute image, for a total of 80 images.

The images were evaluated independently by two experienced nuclear medicine physicians, including a pediatric nuclear medicine specialist, using the following subjective grading scale: 1=poor, 2=fair, 3=good, 4=excellent. Images were presented one at a time, and the readers were blinded to which imaging schedule was used to generate each image. Readers were asked to describe any pathologic uptake. Four of the 20 patients had pathology in the chest, using the contemporaneous diagnostic bone scintigraphy as the gold standard for presence of visible pathology.

At a second separate setting, two experienced nuclear medicine physicians independently evaluated the images for acceptability for daily clinical practice in an unblinded fashion. High- and low-dose images were compared side-by-side, with the readers unblinded to which image represented the NACG, EANM, institutional, and 1-minute images. While evaluating all four images for a given patient, readers were asked which of the images were subjectively acceptable for daily clinical use.

The statistical likelihood of producing a diagnostic quality image was compared among the different administered activity strategies utilizing Pearson's chi-squared test. The Pearson test was also applied to the designation of acceptable or not for daily clinical use. There were not enough patients with pathological findings within the included field of view to apply statistical analysis to this evaluation.

Results

In our first analysis, the statistical likelihood of producing a diagnostic image with each of the 4 imaging strategies was evaluated. "Diagnostic" was defined as a 2, 3, or 4 on the 1-4 scale. Separate analysis of the likelihood of producing a "2" versus a "3" or "4" was performed, and the results were similar. One hundred percent of the highest-activity images, based on our institution's nomogram, were diagnostic. Ninety-two percent of the NACG and 92% of EANM images were diagnostic. These values were not significantly different (p-values of 1 and 0.08

when comparing NACG images to our institution's images and the EANM images, respectively). Sixty percent of the 1-minutes images were diagnostic, which was significantly lower than the other imaging protocols (p-value <0.001 as compared to NACG). These results are graphically summarized in Figure 1.

Four of the 20 patients had pathologic findings based on the interpretations of the contemporaneous diagnostic bone scintigraphy images. All pathology was correctly identified by readers on the institutional, NACG, and EANM images. One EANM image was falsely interpreted as having pathology, and one 1-minute image with pathology was read as equivocal. Due to the low number of patients with pathology, statistical analysis was not performed on this data, but in summation, there were no false-negatives and only one false-positive in the institutional, NACG, and EANM images. When considering the lowest-activity 1-minute images, there was one additional false-negative.

In our second analysis, 100% of our institution's high-dose images were considered adequate for daily clinical work. This was true of 90% of the NACG images and 78% of the EANM images (Figure 2). Twelve percent of the 1-minute images met this criterion. This translated to a slightly statistically significant preference for our institution's images over the NACG images, with a p-value of 0.04. The children for whom the higher activity images were preferred weighed 4.4 kg and 13.9 kg. Representative images for these two patients are presented as Figure 3. Sub-analysis of children over 20 kg showed no significant difference between high- and low-activity images. The NACG acceptability was not significantly different from the EANM acceptability (p-value 0.13). The NACG images were statistically more acceptable than the 1-minute images with a p-value of <0.001.

Discussion

It is important to use the lowest amount of radiation possible when imaging patients of all ages, but especially children, for reasons discussed in the introduction. However, too low a dose can lead to misinterpretations, or, ironically, higher dose if the study has to be repeated. Here, we have presented data that supports the lower activities recommended by the North American Consensus Guidelines. Images representing lower administered activities remained of diagnostic quality, with no statistically significant difference between the NACG images and our institutional images produced using as much as three times the radiation exposure. There was a slightly significant preference for the higher activity images as compared to the NACG images in the unblinded analysis, based on images of 2 of the 20 patients who weighed 4.4 kg and 13.9 kg. Despite this slight preference for the images representing higher counts, pathology was correctly identified on all images regardless of counts. There were no false-negative exams with any of the diagnostic protocols, and only one false-positive, with the caveat that the number of patients with pathology within the field of view was low. Taken together, these data support the use of the NACG imaging for pediatric bone scintigraphy. For smaller children, particularly those weighting less than 20 kg, the NACG guidelines are acceptable, but on-going quality assurance should be performed on these patients as they are imaged to ensure that images are of adequate quality. Images should be evaluated closely prior to release of the patient from the imaging suite to evaluate if additional imaging should be performed. Increasing imaging time for the smaller children is a consideration, but must be balanced with the potential for increased motion artifact.

The strengths of this study are the inclusion of a significant number of patients under 20 kg and the variety of indications for imaging. The major limitation is the small number of patients with pathological findings. Although there were no false-negatives, the number of patients with pathological findings was low. Future research with a greater number of cases with pathology could further investigate if there is a statistically significant chance of missing disease on lower-activity images. Also, we investigated delayed static imaging only. Our data does not include three-phase studies or studies with SPECT imaging, although these are performed much less frequently in pediatrics as compared to adult imaging.

Conclusions: These data validate the use of NACG administered activities for bone scintigraphy. The NACG meet the goal of pediatric dose reduction while maintaining diagnostic quality. For children under 20 kg, the images were less pleasing but still considered diagnostic, and with close quality assurance these smallest children can also be imaged effectively with the lower administered activities.

Acknowledgements: In addition to the input from all the listed authors, I extend gratitude to Dr. Michael Stabin who provided the information from ICRP106 that allowed me to calculate effective doses for ^{99m}Tc-MDP.

References:

1. Dorfman AL, Fazel R, Einstein AJ, et al. Use of medical imaging procedures with ionizing radiation in children: a population-based study. Arch Pediatr Adolesc Med. 2011;165:458-64.

2. Pierce DA, Shimizu Y, Preston DL, Vaeth M, Mabuchi K. Studies of the mortality of atomic bomb survivors. Report 12, Part I. Cancer: 1950–1990. Radiat Res. 1996;146:1–27.

3. Gelfand MJ, Parisi MT, Treves ST. Pediatric radiopharmaceutical administered doses: 2010 North American Consensus Guidelines. J Nucl Med. 2011;52:318-322.

4. Lassmann M, Treves ST, EANM SNMMI Paediatric Dosage Harmonization Working Group. Paediatric radiopharmaceutical administration: harmonization of the 2007 EANM paediatric dosage card (version 1.5.2008) and the 2010 North American consensus guidelines. Eur J Nucl Med Mol Imging. 2014;41:1036-1041.

5. International Commission on Radiological Protection. Radiation dose to patients from radiopharmaceuticals: A third addendum to ICRP publication 53, ICRP publication 106. Ann ICRP. 2008;38:1-197.

6. Piepsz A (Chairman), Hahn K, Roca I, Ciofetta G, et al. A radiopharmaceuticals schedule for imaging in paediatrics. Eur J Nuc Med 1990;17:127-129.

7. Donohoe KJ, Brown ML, Collier BD, et al. Society of Nuclear Medicine procedure guideline for bone scintigraphy, version 3.0, approved June 20, 2003.

Figure 1: Percent Diagnostic by Imaging Protocol (blinded analysis)

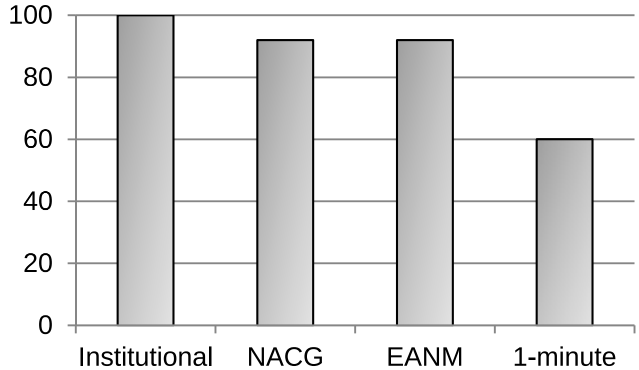

Figure 2: Percent acceptable for daily clinical use (unblinded analysis)

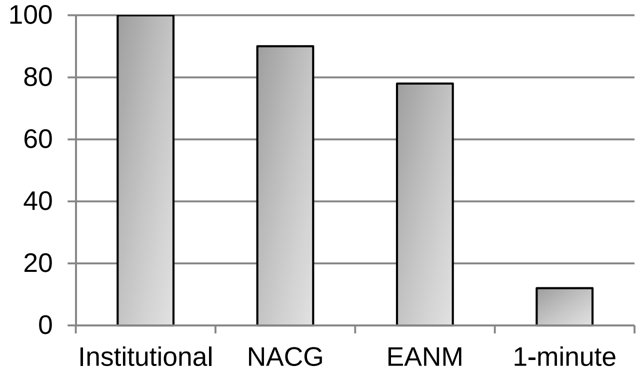

Figure 3: Institutional and NACG images for two patients for which the institutional image was deemed acceptable for daily use but the NACG image was not in unblinded analysis. A/B, 13.9 kg patient with abnormal scan. A) Institutional image, B) NACG image. Abnormal uptake in the abdominal mass and multiple bone metastases is evident on both sets of images. C/D. 4.4 kg patient with negative scan. C) Institutional image, D) NACG image.

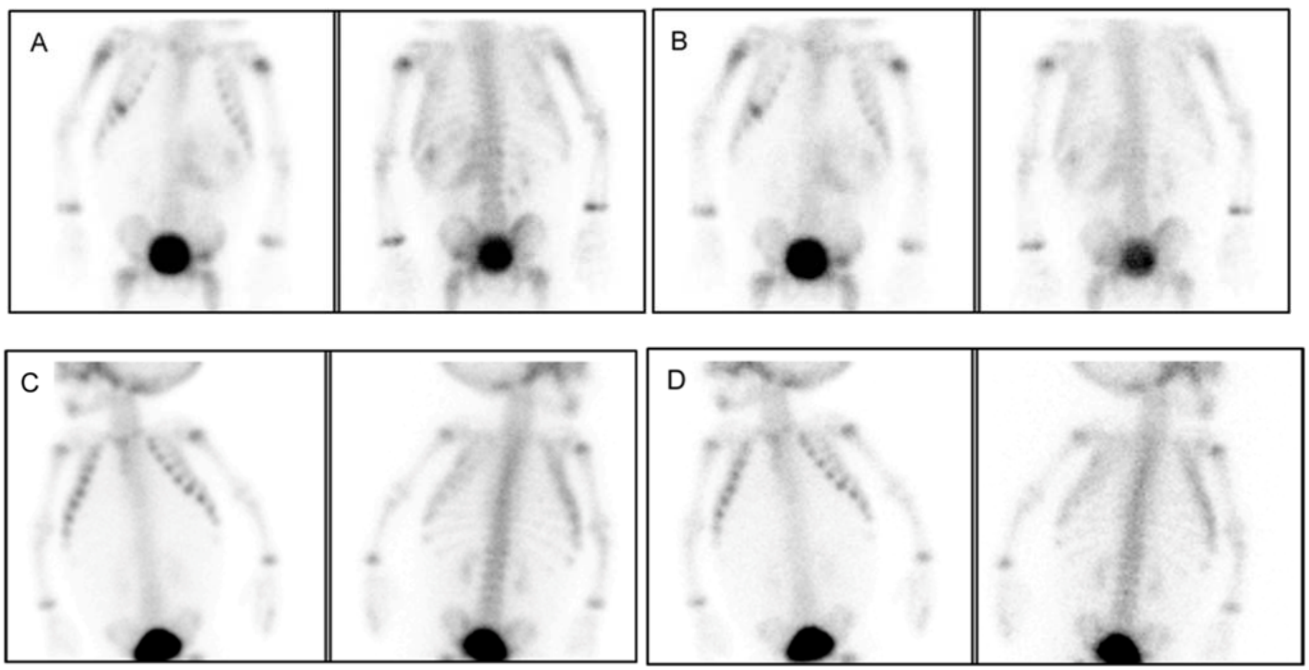

Table 1: Administered activities and effective doses for the three dosing schedules. Note that EANM activities include patient weights of 6 kg and 68 kg rather than 5 kg and 70 kg, based on the design of the EANM dosage card.

Institutional			
Weight (kg)	MBq	mSv	
5	148	7.8	
10	207	5.6	
20	370	5.1	
30	444	5.0	
40	570	5.5	
50	666	5.4	
60	696	4.7	
70	740	4.2	
North American Consensus Guidelines (NACG)			
Weight (kg)	MBq	mSv	Effective Dose Reduction v. Institutional
5	46	2.5	-68%
10	93	2.5	-55%
20	185	2.6	-49%
30	278	3.1	-38%
40	270	3.6	-35%
50	463	3.8	-30%
60	555	3.7	-21%
70	648	3.7	-12%
European Association of Nuclear Medicine (EANM) Dosage Card			
Weight (kg)	MBq	mSv	Effective Dose Reduction v. Institutional
6	60	3.2	-59%
10	95	2.6	-54%
20	170	2.4	-53%
30	240	2.7	-46%
40	310	3.0	-45%
50	375	3.0	-44%
60	445	3.0	-36%
68	490*	2.8	-33%

Table 2: Patient demographics and indications for imaging

Gender	10 female, 10 male
Age	
Range	2 months to 16 years, and one 20-year-
Mean	7.1 years
Median	4.5 years
Weight	
Range	4.4 kg – 61.4 kg
Mean	28.3 kg
Median	19.8 kg
Indication	
Oncologic	10
Infectious/inflammatory	5
Back pain	5