Developing and Implementing an Imaging Optimization Study in Pediatric Nuclear Medicine: Experience and Recommendations from an IAEA-Coordinated Research Project

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The International Atomic Energy Agency instituted a coordinated research project on the evaluation and optimization of pediatric imaging, addressing the lack of consistency in this field. The purpose was to develop and test an optimization schema for the practices of pediatric radiology and nuclear medicine. **Methods:** A 5-step optimization schema was developed. Once a protocol optimization is identified, the steps are as follows: identification of the imaging situation; collection of administered-activity data and evaluation of the diagnostic image quality at baseline; comparison of baseline administered activity data with published standards or other benchmarks; identification of intervention, if necessary; and implementation of intervention and evaluation. **Results:** Within the coordinated research project, two sites considered optimization projects regarding nuclear medicine. In this work, renal imaging using ^{99m}Tc-dimercapto-succinic acid (DMSA) projects are presented as examples. Site 1 acquired its standard 300-s static ^{99m}Tc-DMSA studies as 5-frame dynamic studies in 29 children. Frames were added to simulate different levels of administered activity. Image quality was subjectively judged on a 3-point Likert scale. A 30% reduction in administered activity with increased imaging duration (350 s) across all age groups was shown to be acceptable. This reduction was implemented and evaluated in 31 subsequent children, yielding administered activities significantly lower than baseline (mean relative differences of 30%, 37%, and 38% for children aged 0–5, 5–10, and 10–15 y, respectively). Site 2 performed a phantom study to determine the impact of lowering administered activity on image noise, finding that administered activities could be significantly lowered if longer imaging times were used. This led to a 50%–70% reduction from baseline with no loss in image quality. **Conclusion:** A dose optimization approach was applied successfully for several procedures commonly performed in pediatric nuclear medicine. Results are reported for renal cortical imaging using ^{99m}Tc-DMSA, leading to significant reductions in administered activity (and thus radiation dose). This optimization schema can be successfully implemented by nuclear medicine clinics seeking to improve their approach to imaging children.

Key Words: pediatric imaging; optimization study; dose reduction

The clinical utility of nuclear medicine imaging in children has been clearly established for many applications, including neurology, urology, orthopedics, gastroenterology, endocrinology, and oncology (1–8). However, children are a critical group of patients for exposure to ionizing radiation because of their increased radiosensitivity and longer life expectancy. For a particular examination, there can be wide variations in image quality and administered activities among different nuclear medicine departments, depending not only on the protocol being followed but also on the experience of the personnel and the suitability of the equipment. Dose optimization in nuclear medicine imaging not only is motivated by the need for continuous improvement in the quality of practices but also is a legal requirement (9,10) that should be achieved through a multidisciplinary approach. In 2015, the International Atomic Energy Agency established a coordinated research project (CRP) (11) with the purpose of enhancing the potential of participating institutes to improve the efficiency of existing modalities for pediatric medical imaging. The CRP included both diagnostic radiology and nuclear medicine practices and aimed at developing and implementing optimization strategies in pediatric imaging. Institutes participating in the CRP were from 10 different International Atomic Energy Agency member states (Austria, Brazil, Chile, Cuba, Egypt, Germany, Ghana, Indonesia, United Kingdom, and United States). The Department of Nuclear Medicine, Isotopes Center, Havana, Cuba, and the Medscan Nuclear Medicine and PET/CT Center, Concepcion, Chile, specifically contributed to the nuclear medicine part of the project. One of these sites will be referred to as Site 1 and the other Site 2.

The optimization methodology developed under this CRP was applied to children but can be equally adopted for any other

population. Optimizing a diagnostic nuclear medicine procedure does not necessarily translate into a reduction of administered activity but, more correctly, to the administration of the most appropriate activity. The ultimate objective of medical imaging is to draw appropriate diagnostic information from the images produced. Thus, any optimization process necessarily needs to consider the resulting clinical image quality.

This paper focuses on the work done for nuclear medicine procedures and can be used as an educational tool providing practical guidance on developing an optimization study and its successful implementation, with illustrations from the work presented and the lessons learned.

MATERIALS AND METHODS

Institutes from 10 different countries participated in the CRP. The optimization schema described below was developed, and each institute agreed to implement it for either diagnostic radiology or nuclear medicine. In this paper, the version developed for nuclear medicine is described, which is very similar to the schema implemented for diagnostic radiology.

The steps followed for the optimization process are outlined in Figure 1. An initial preoptimization data collection of the local situation is followed by a comparison of these data with guidelines and existing activity reference levels to identify deviations and areas for improvement. Potential interventions identified through a multidisciplinary approach need to be translated into practice in the next step, and their efficacy verified. A new data collection after the intervention is finally performed for comparison with the baseline situation and verification of a positive result.

Identification of the Imaging Situation

The first step was to identify the procedures requiring consideration, based on the frequency for pediatric patients and potential radiation dose. Data on the number of procedures performed on children were collected in 3 age ranges: 0–5, 5–10, and 10–15 y. The institutes involved in the project identified static renal scintigraphy (^{99m}Tc-dimercaptosuccinic acid [DMSA]), dynamic renal scintigraphy (^{99m}Tc-mercaptoacetyltriglycine [MAG3]), and bone scintigraphy (^{99m}Tc-methylene diphosphonate [MDP]) as the 3 most frequent procedures in children. Figure 2 shows the distribution of pediatric studies at site 1 during 2018 and at site 2 during 2017.
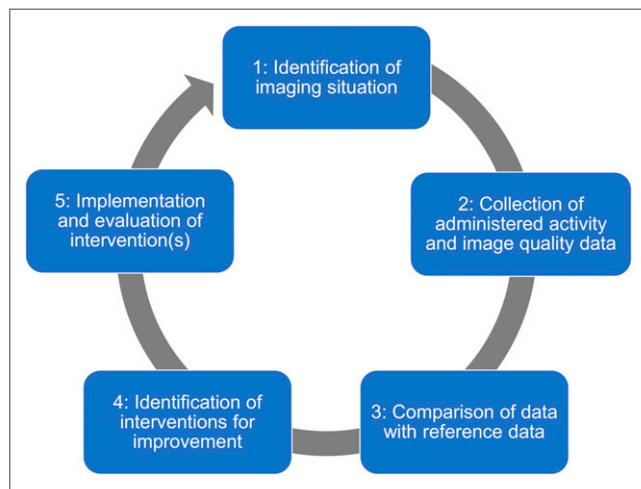

FIGURE 1. General scheme describing the optimization strategy.

Collection of Administered Activity Data at Baseline

A baseline was established by collecting administered activity data for children undergoing the procedures identified above over 9 mo. The data collected included patient age, height, weight, and sex. Activity values were collected for the syringe prepared for administration, as well as residual activity in the syringe after administration. The time of these two measurements and the time of administration were also collected to allow the calculation of the decay-corrected administered activity.

Evaluation of Diagnostic Image Quality at Baseline

Image quality was assessed both qualitatively through an image quality factor representing a 3-point Likert scale and quantitatively using phantom measurements. The image quality factor adopted for the purposes of the CRP ranged from IQ1 to IQ3: IQ1 is unacceptable image quality (could not diagnose, would request a rescan), IQ2 is borderline-acceptable image quality (can diagnose but would not welcome images of this quality), and IQ3 is acceptable image quality (can diagnose and would welcome images of this quality)

Nuclear medicine physicians' involvement was vital at this step of the methodology, highlighting the need for a multidisciplinary approach to dose optimization. Because such subjective assessments depend greatly on both the evaluator and the clinical question, they may not be directly comparable between centers.

Alternatively, physical phantoms simulating the clinical condition can be used to generate images at various noise levels with objective measurements (i.e., contrast, noise, and signal-to-noise ratio) to assess image quality. In this manner, the effect that different count levels (and thus different administered activity levels) has on image quality can be determined and compared.

### Comparison of Data with Reference Data

Baseline administered activities should be compared with well-established references from scientific societies or international organizations. In this study, the recommended administered radiopharmaceutical activities for pediatric patients proposed in the North American Consensus Guidelines (NACG) (*12*) and the European Association of Nuclear Medicine (EANM) pediatric dosage card (*13*) were used for this purpose. This step of the process determines whether an intervention is necessary and, if so, what intervention should be considered.

Identification of Interventions for Improvement

On the basis of these assessments, a procedure can be identified as suboptimal, and an intervention can thus be determined to be necessary. However, the need for an intervention should not always be assumed. In some cases, the current practice may continue to be acceptable, or the value of a reasonable intervention may be marginal and not warranted at a particular time. However, when an intervention is deemed necessary, a proposed target optimization level is specified. This target could be defined as a set fraction of the current level or a set level relative to the published standard. In some instances, a different level may be specified for each patient size descriptor considered (i.e., patient weight, age, or other measure). However, in many cases, setting a single target level for children of all sizes may be considered appropriate and simpler to implement.

Implementation and Evaluation of the Intervention

Once an intervention is determined to be necessary and a target level is proposed, the clinical procedure is thereby amended. It may be preferable to implement the intervention gradually. All nuclear medicine personnel (physicians, technologists, medical physicists, radiopharmacists, and possibly others) must be informed that the procedure will be revised in a certain way on a certain date. All patients imaged using this protocol on or after the proposed start date will receive the modified administered activity. If it is determined that the intervention introduced a complication that was not foreseen, the clinic may decide to return to
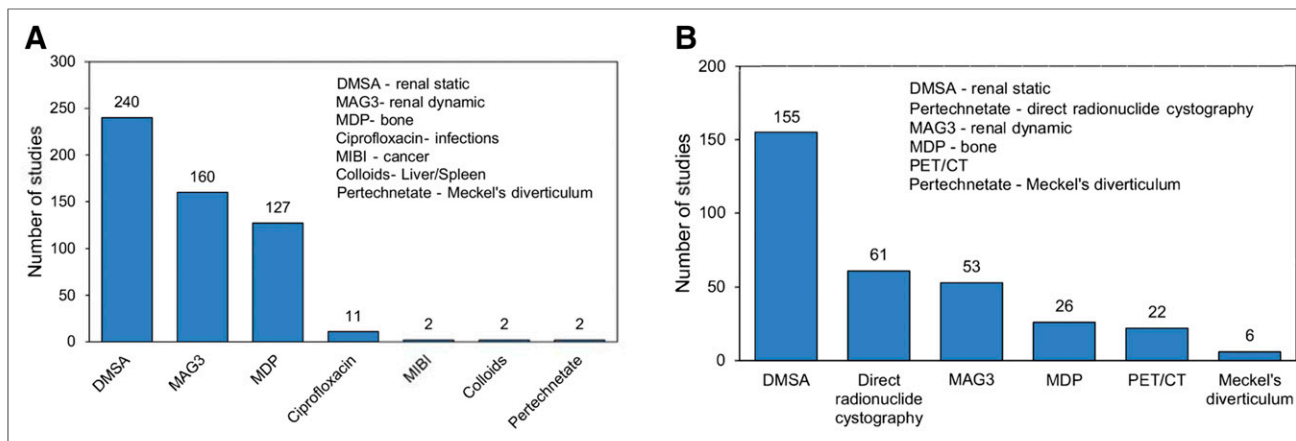
FIGURE 2. Distribution of pediatric studies at site 1 (2018) (A) and site 2 (2017) (B). MIBI = methoxyisobutylisonitrile.

the former administered activity level at any time. Otherwise, the new level should be maintained for a specified evaluation period measured either in time or number of cases (e.g., for 1 mo or for 30 cases).

Once the evaluation period is complete, the resulting patient data need to be evaluated to determine whether the proposed target levels were achieved and whether the image quality remained acceptable. For each patient, the actual administered activity should be compared with the proposed value and the previously prescribed level. These activity levels can also be compared with those prescribed by published standards. Any concerns from the clinical staff that the intervention resulted in marginal or less than adequate image quality also must be considered. If, after this evaluation, it is determined that the target level was reached without a notable reduction in clinical image quality, the new administered activity levels are adopted.

Working groups from sites 1 and 2 implemented this methodology for several nuclear medicine procedures commonly performed on children. The institutional medical committee approved this study at both sites, and the requirement to obtain informed consent was waived. Renal scintigraphy with ^{99m}Tc-DMSA is presented here as an example since it was optimized by both groups, with the methodology being implemented using slightly different approaches. For both centers, only one dual-head γ-camera equipped with low-energy high-resolution collimators was involved in the study. The systems used were Spirit DH-V (Mediso) and Sophy DST-XLi (SMV) for sites 1 and 2, respectively.

RESULTS

Site 1

Since the 3 most common procedures at site 1 were ^{99m}Tc-DMSA renal cortical scans, ^{99m}Tc-MAG3 renograms, and ^{99m}Tc-MDP bone scans (Fig. 2A), the optimization process was focused on these. The results for renal cortical imaging using ^{99m}Tc-DMSA are presented here as an example. The baseline administered activities for ^{99m}Tc-DMSA were calculated as a fraction of the activity for a 70-kg adult (185 MBq), based on body surface area as recommended in *Operational Guidance on Hospital Radiopharmacy* (*14*). The baseline situation was assessed by reviewing data for 29 patients (aged 6 mo to 18 y), noting age, weight, height, and sex for each. The activity at the time of administration was calculated as the difference between the decay-corrected activities assayed in the preinjection syringe and the residual activity after administration. These baseline levels were significantly higher than those recommended by the NACG (*12*) and the EANM pediatric dosage card (Fig. 3) (*13*). Three age groups, 0–5, 5–10, and

10–15 y, were considered. The administered activities were, on average, 149% (0–5 y), 103% (5–10 y), and 57% (10–15 y) higher than the NACG-recommended values. As a result, it is expected that similar increments apply to the equivalent dose received by the critical organs (kidneys) and to the effective dose.

The adopted optimization strategy was to acquire a dynamic scan (five 1-min frames) rather than static 5-min scan to simulate different levels of administered activity for 45 patients (15 in each age group). Summing these 5 frames provided an image identical to the baseline protocol using a 5-min static acquisition. Summing 2, 3, or 4 frames of the dynamic study simulated the patient receiving an administered activity of 40%, 60%, or 80% of the baseline activity, respectively. In total, 180 images (4 images each for the 45 patients) were randomly presented to the nuclear medicine physicians in charge of the diagnostic evaluation. The physicians' diagnostic response and IQ index for 40%, 60%, and 80% of the baseline activity were compared with 100% (baseline) activity. The images simulating the 40% activity level were judged adequate for quantification, albeit very noisy, which in some cases led to interobserver variations in clinical interpretation. Images simulating the 60% activity level showed no appreciable difference between patients 0–5 y old and patients 5–10 y old, whereas images simulating the 80% activity level were considered to be of the same diagnostic image quality as the baseline activity for all age groups.

For this reason, an initial target reduction level corresponding to 70% of the baseline administered activity was set for children of all ages and was considered an acceptable compromise by the clinicians. A single reduction level across all age groups was decided to be more easily implemented operationally. The same weighting factors as those used during the preoptimization phase and recommended by the International Atomic Energy Agency in 2008 (*14*) were used, but with a recommended activity of 129.5 MBq instead of 185 MBq for a 70-kg adult. However, the scan duration was increased from 300 to 350 s as part of a conservative approach to warrant adequate image quality for patients older than 10 y. It was also agreed to apply filtering techniques to reduce noise in images with borderline count statistics (Tera-Tomo 2D Planar Image Enhancement module, Interview XP 3.00.053.0000; Mediso Medical Imaging Systems).

After introduction of the optimization intervention, data for 31 pediatric patients were collected for the following evaluation. The acquired images were considered by the clinicians to be of sufficient image quality and adequate for a sound diagnosis in all cases. Although the administered activities were still above the
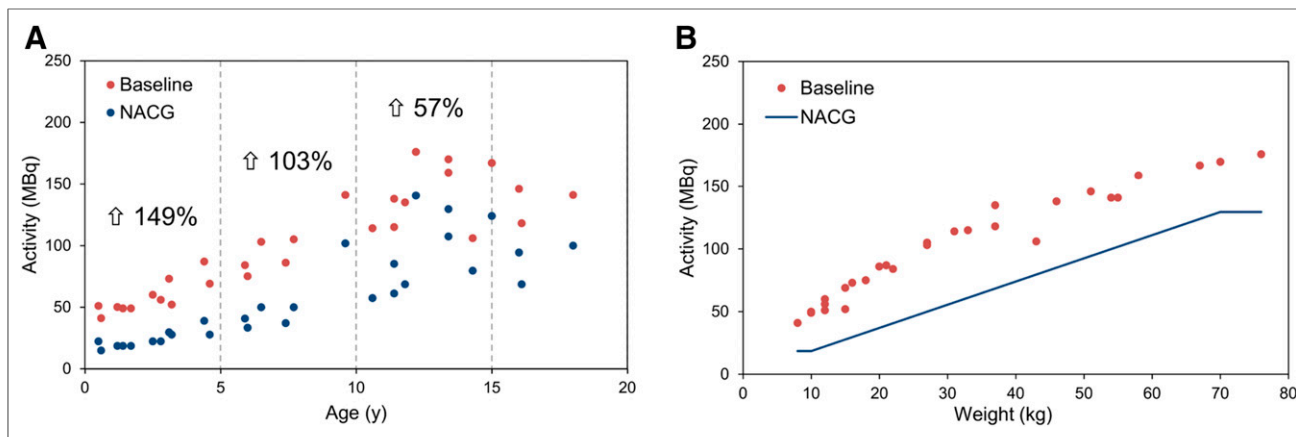
FIGURE 3. (A) Activities administered for ^{99m}Tc-DMSA renal cortical scans at baseline and NACG-recommended activities for same patients. Average relative difference compared with NACG-recommended values is reported for each age group. (B) Same data reported as function of weight.

NACG recommendations for all patients, these activities were significantly lower than the baseline values. The mean relative differences from the NACG recommendations decreased to 75%, 38%, and 10% for children 0–5, 5–10, and 10–15 y old, respectively (Fig. 4A). The considerable reduction in administered activities allowed, especially for larger children, better compliance with international recommendations (Fig. 4B).

The approach followed in this department represents a graded optimization and was agreed upon—and considered to be acceptable by—the clinicians. This approach could potentially be followed by further interventions after an adjustment period. For example, the results shown in Figure 4 suggest that a greater reduction in administered activity might be possible for smaller patients. Regarding the other procedures considered, the optimization process for ^{99m}Tc-MDP bone scans and ^{99m}Tc-MAG3 renal studies resulted in an average reduction in administered activity by 22% and 27%, respectively.

Site 2

Site 2 sought to optimize its pediatric nuclear medicine practice regarding 4 procedures: renal cortical imaging using ^{99m}Tc-DMSA,

renal functional imaging using ^{99m}Tc-MAG3, bone imaging using ^{99m}Tc-MDP, and PET/CT imaging using ^{18}F-FDG. The choice of the 3 planar procedures was based on a review of the number of pediatric nuclear medicine studies performed in the previous year (Fig. 2B). During that time, about 50% of the pediatric examinations performed were ^{99m}Tc-DMSA studies. The second most common procedure was direct radionuclide cystography looking for urinary reflux. Since this procedure is less amenable to the optimization approach and the resulting radiation dose is already quite low (15), the next two most common procedures were considered: ^{99m}Tc-MAG3 renal imaging and ^{99m}Tc-MDP bone imaging. As with site 1, this paper describes the approach for optimizing ^{99m}Tc-DMSA planar imaging in children as an example. In total, 155 patients were examined using ^{99m}Tc-DMSA in 2017, and the breakdown by age group was 100, 24, and 31 for children 0–5, 5–10, and 10–15 y old, respectively.

Before optimization, the baseline dosing schema for 1-, 5-, and 10-y-old patients was based on an internal standard leading to respective values of 100, 125, and 155 MBq, corresponding to respective activities 550%, 378%, and 310% higher than those recommended by EANM for the corresponding patient ages. To evaluate the potential impact of dose optimization on image
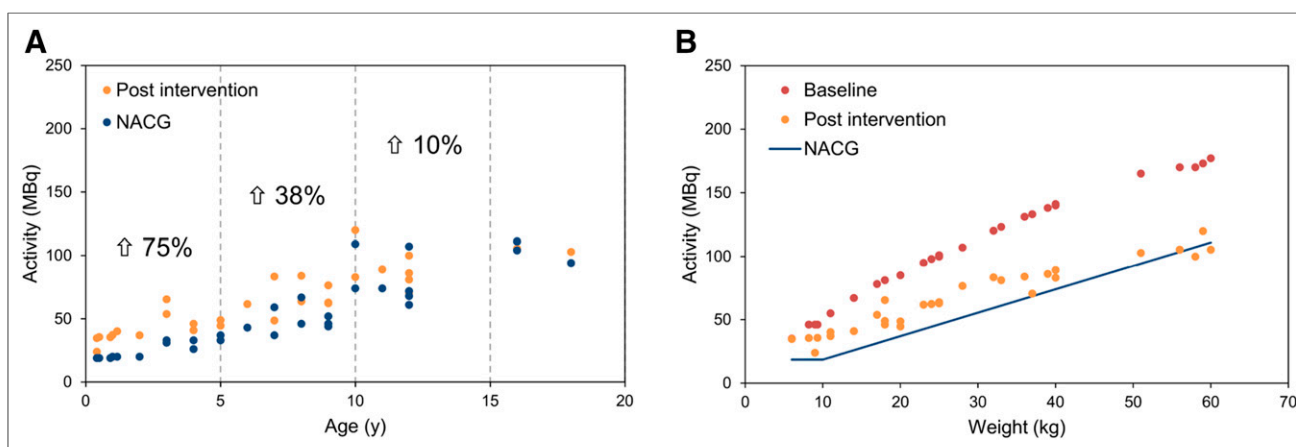
FIGURE 4. Activities administered to pediatric patients for ^{99m}Tc-DMSA renal cortical scans after introduction of optimization intervention. (A) Comparison, as function of age, with NACG-recommended activities for same patients. Average relative difference compared with NACG-recommended values is reported for each age group. (B) Comparison, as function of weight, with activities that would have been administered at baseline and NACG-recommended values for same patients.

quality, a phantom experiment was performed. Cylindric polyethylene vials of 24.2, 44.3, and 66.3 mL were used to simulate the kidneys of a 1-, 5-, and 10-y-old child, respectively (16,17). For each age, 2 cylinders were filled with water mixed with basically equal activity of ^{99m}Tc-NaTcO$_4$ and placed within a water-filled cylindric tomographic phantom (21.6-cm inner diameter, 18.6-cm inner height) to simulate renal imaging. The amount of activity placed in each simulated kidney assumed that 40% of the administered activity distributes to the renal cortex at 4 h after injection (18), given that the acquisition start time in clinical practice is 3 h after administration. Since the clinical ^{99m}Tc-DMSA scans were acquired for 300 s, the noise level for that acquisition time was considered a baseline value. The noise level is given by

$$N = \frac{100\%}{\sqrt{\frac{\text{total counts}}{\text{number of pixels}}}},$$

where "total counts" and "number of pixels" have to be considered in the whole image. The clinical baseline of 300 kilocounts per image is considered acceptable according to international guidelines (2) and corresponds to a noise level, N, of 23%. A noise level of 25% was also considered.

In Figure 5, the baseline administered activity levels for 3 ages is compared with the simulated value for noise levels of 23% and 25%, as well as with the level recommended by the EANM and a level 50% higher than that recommended.

For the 10-y-old, the level 50% higher than the EANM recommendation is consistent with noise levels of 23% and 25%, respectively. A reduction of administered activity leading to noise levels of 23% and 25% yielded activity levels comparable to the median values for Europe and Latin America from the international survey of the Nuclear Medicine Global Initiative (19). Using this level for the 10-y-old, we determined that 300 kilocounts could still be acquired in about 5 min. However, reaching the same level for the 5-y-old and the 1-y-old would take longer, approximately 8 and 16 min, respectively.

The proposed target was an administered activity ranging from the EANM-recommended value and the same value increased by 50%. The highest value of this range corresponded to reductions of 72%, 60%, and 52% for the 1-, 5-, and 10-y-old children, respectively. This is likely to be only the first of a series of optimization steps; further reduction may be realized in the future.
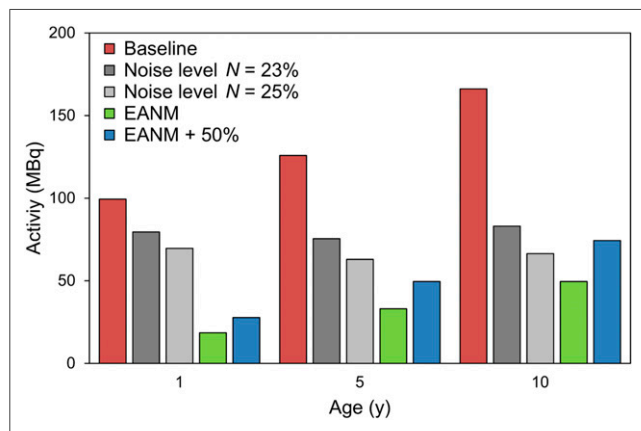
FIGURE 5. Baseline administered activity level for 3 example ages, simulated activity value corresponding to noise level of 23% and 25%, activity recommended by EANM, and same value increased by 50%.

After implementation of these new levels, the assayed administered activities of 20 patients were compared with both the recommended values and the values for the 18 patients before the implementation, that is, the baseline (Figs. 6A and 6B vs. age and weight). Figure 6C shows the relative difference in administered activities between baseline and postimplementation patients, compared with the EANM-recommended values. Image quality was evaluated—and the adequate amount of administered activity was assessed—by nuclear medicine physicians with the support of medical physicists and technologists involved in the optimization process.

Although the target range allowed for administered activities 50% higher than values suggested by the EANM, the actual levels of administered activity tended to be closer to the recommended
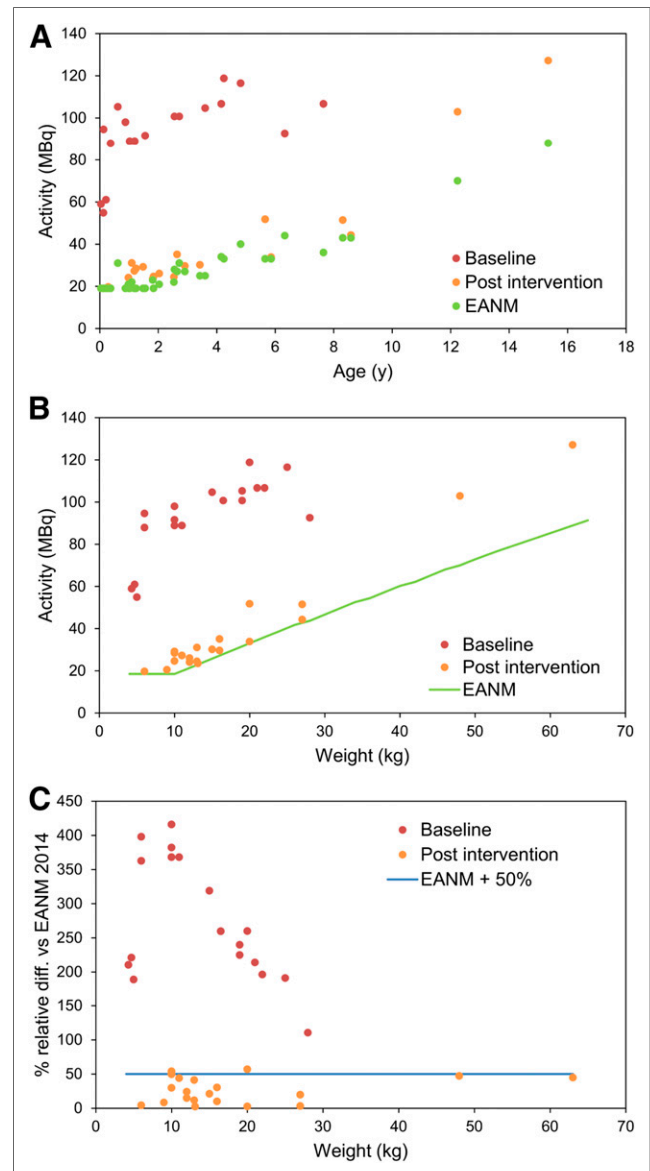
FIGURE 6. (A and B) Activities administered to pediatric patients for ^{99m}Tc-DMSA renal cortical scans at baseline, after introduction of optimization intervention, and EANM-recommended activities for same patients as function of age (A) and weight (B). (C) Relative difference in administered activities at baseline and after introduction of optimization intervention compared with EANM-recommended values.

TABLE 1
Administered Activities for 3 Example Ages for ^{99m}Tc-DMSA Projects at Sites 1 and 2 at Baseline and After Optimization: Comparison to Recommended Values for EANM Pediatric Dosage Card and NACG

Age (y)	Weight (kg)	EANM	NACG	Site 1 BL	Site 1 Opt	Site 2 BL	Site 2 Opt
1	10	18.5	18.5	50	35	100	28
5	20	33	37	85	60	125	50
10	32	50	59	120	84	155	74

BL = baseline; Opt = after optimization.
Data are megabecquerels.

levels. Since 300-kilocount images and a 23% noise level were retained, there was no reduction in image quality. For the other procedures considered, ^{99m}Tc-MDP bone scans and ^{99m}Tc-MAG3 renal studies, the optimization process resulted in average reductions of 20% and 64%, respectively, in the administered activity.

DISCUSSION

As examples of the optimization schema described in this report, we have presented projects using ^{99m}Tc-DMSA for renal cortical planar imaging at two medical centers. This examination had the highest impact on dose reduction in children because of the large number of procedures performed yearly and the reduction in administered activities that could be achieved while maintaining adequate diagnostic quality. The target reductions of administered activity were 30% for site 1 and 52%–73% for site 2. For the 5-y-old, the target administered activities are 82% and 50% higher than the EANM-recommended value and 62% and 35% higher than the NACG-recommended value for sites 1 and 2, respectively. Thus, there is still room for improvement, and further reductions are expected in the future. The optimization exercises described in this work are most likely the first steps in an iterative optimization process, as illustrated in Figure 1.

Although the general outline as described in the Materials and Methods section was followed in both projects, the implementation approach varied between the two sites. The baseline conditions were substantially different when the administered activities were initially considerably higher at site 2 than at site 1. The age of the equipment between the two institutes also varied.

For both sites, only one γ-camera was available and involved in this study, thus simplifying the optimization process. If multiple scanner types with different collimators are used, the differences in performance of the systems should be considered. A scanner with lower sensitivity, for example, might require a higher injected activity or longer scan time.

Patient demographics, clinical conditions, and referral patterns most likely differ between the regions where the two institutes are located. Clinical staff expectations about the required image quality for a clinical task may also vary greatly between institutes. Lastly, each institute has its own operational considerations that affect how modifications to the clinical practice may best be realized.

The optimization process must be performed by a multidisciplinary working group, with the nuclear medicine physician being responsible for evaluating image quality and assessing the adequacy of the administered activity. Basic quantitative metrics (such as contrast and image noise) can complement evaluation of image quality during selection of activity levels providing diagnostic information. At both sites, subjective grading of clinical quality by expert observers was used, and the administered activity that optimized image quality was determined. At site 2, a phantom evaluation relying on an objective noise index was also used.

Although the two projects led to a substantial reduction in administered activity (Table 1), both also proposed a longer scan duration. Longer imaging times can be problematic when small children are imaged, because of the potential for more patient motion. For ^{99m}Tc-DMSA imaging, most patients tend to be under 5 y old. If the imaging time is much longer than 5 min, the use of sedation and, in some cases, anesthesia may be necessary to successfully complete the study. Therefore, even if the optimization project supports the potential for clinically adequate imaging with fewer total counts, some clinics may opt for a faster scan time in small children rather than lower administered activity.

CONCLUSION

As part of an International Atomic Energy Agency CRP, an optimization schema was developed specifically for pediatric radiology and nuclear medicine. This approach was applied successfully at two clinical sites for several procedures commonly performed in pediatric nuclear medicine. As an example, optimization of renal cortical ^{99m}Tc-DMSA imaging at these two sites led to significant reductions in administered activity (and thereby absorbed radiation dose) of between 30% and 70%. Therefore, this optimization schema can be successfully implemented at practically any nuclear medicine clinic seeking to improve its approach to imaging children.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Can suboptimal diagnostic procedures be identified and optimized, leading to a reduction in administered activity while maintaining an image quality sufficient for a sound diagnosis?

PERTINENT FINDINGS: An optimization strategy that was developed and applied to different pediatric nuclear medicine procedures resulted in significant reductions in administered activity (and thus radiation dose) of between 30% and 70% and no loss of image quality.

IMPLICATIONS FOR PATIENT CARE: Doses to pediatric patients can be reduced through the optimization methodology.

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