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Developing and implementing an imaging optimization study in pediatric nuclear medicine: Experience and recommendations from an IAEA Coordinated Research Project

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ABSTRACT

Rationale: The International Atomic Energy Agency (IAEA) instituted a Coordinated Research Project (CRP) 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: 1) identification of the imaging situation, 2) collection of administered activity data and evaluation of the diagnostic image quality at baseline, 3) comparison of baseline administered activity data to published standards or other benchmarks, 4) identification of intervention, if necessary, 5) implementation of intervention and evaluation. **Results:** Within the CRP, two institutes considered optimization projects regarding nuclear medicine. In this work, renal imaging using ^{99m}Tc-DMSA projects are presented as examples. Site 1 acquired their 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 difference of 30% (age group 0-5 y), 37% (5-10 y) and 38% (10-15 y)). Site 2 performed a phantom study to determine the impact of lowering administered activity on image noise, indicating 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. **Conclusions:** 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.

INTRODUCTION

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 of 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 is not only motivated by the need for a continuous improvement of the quality of practices, but is also a legal requirement (*9,10*) which should be achieved through a multidisciplinary approach. In 2015, the International Atomic Energy Agency (IAEA) 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 IAEA Member States (Austria, Brazil, Chile, Cuba, Egypt, Germany, Ghana, Indonesia, United Kingdom and United States). The Department of Nuclear Medicine, Isotopes Center (CENTIS), Havana, Cuba and 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 and can be equally adopted to 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 the appropriate diagnostic information drawn from the images produced. Thus, any optimization process necessarily needs to consider the resulting clinical image quality.

This paper focusses 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 learnt.

MATERIALS AND METHODS

Institutes from ten 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 pre-optimization 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 following the intervention is finally performed for comparison with the baseline situation and verification of a positive result.

Step 1: 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 three age ranges: 0-5, 5-10 and 10-15 years. The institutes involved in the project identified static renal scintigraphy (^{99m}Tc-DMSA), dynamic renal scintigraphy (^{99m}Tc-MAG3) and bone scintigraphy (^{99m}Tc-MDP) as the three most frequent procedures in children. Figure 2 shows the distribution of pediatric studies at Site 1 during 2018 and at Site 2 during 2017.

Step 2.a: 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 months. The data collected included patient age, height, weight, and gender. 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.

Step 2.b: Evaluation of the diagnostic image quality at baseline

Image quality was assessed both qualitatively through an Image Quality Factor (IQF) representing a 3-point Likert scale, and quantitatively using phantom measurements. The IQF adopted for the purposes of the CRP ranged from IQ1 to IQ3:

- IQ1: Unacceptable image quality (could not diagnose, would request a rescan)
- IQ2: Borderline acceptable image quality (can diagnose but do not welcome images of this quality)
- IQ3: 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 of a multidisciplinary approach to dose optimization. Such subjective assessment depends greatly on both, the evaluator and the clinical question, so this may not directly be 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 (and thus different administered activity) levels have on image quality can be determined and compared.

Step 3: 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, recommendations of 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.

Step 4: Identification of interventions for improvement

Based on these assessments, a procedure can be identified as suboptimal and it can thus be determined that an intervention is necessary. However, it should not always be assumed that an intervention is needed. In some cases, the current practice may continue to be acceptable, or the value of a reasonable intervention be marginal not warranting an intervention at this 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.

Step 5: Implementation and evaluation of the intervention

Once determined that an intervention is 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 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 one month or for 30 cases).

Once the evaluation period is complete, the resulting patient data needs 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 to the proposed value and the previously prescribed level. These activity levels can also be compared to 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 shall be adopted.

Working groups from Cuba and Chile implemented this methodology for several nuclear medicine procedures commonly performed in children. The institutional medical committee approved this study in 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 implemented with slightly different approaches. For both centers only one dual-head gamma camera equipped with low energy high resolution collimators was involved in the study. The systems used were Spirit DH-V (Mediso, Hungary) and Sophy DST-XLi (SMV, France) for Cuba and Chile, respectively.

RESULTS

Site 1

Since the three most common procedures at Site 1 were ^{99m}Tc-DMSA renal cortical scans, ^{99m}Tc-MAG3 renograms and ^{99m}Tc-MDP bone scans (Figure 2A), it was decided to focus the optimization process on these. As an example, the results for renal cortical imaging using ^{99m}Tc-DMSA will be presented. 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 the Operational Guidance on Hospital Radiopharmacy (*14*). The baseline situation was assessed by reviewing data for 29 patients (age 6 months to 18 years) noting age, weight, height and gender for each. The activity at time of administration was calculated as the difference of the decay-corrected activities assayed in the pre-injection 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 (*13*) (Figure 3). Three age groups, 0-5, 5-10 and 10-15 years, were considered. The administered activities were on average 149% (0-5 years), 103% (5-10 years) and 57% (10-15 years) 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 (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. A total of 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 the 40, 60 and 80% of the baseline activity images were compared with the 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 for the 0-5 and 5-10 year old patients, while 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 pre-optimization phase and recommended by the IAEA in 2008 (*14*) were used, but with a recommended activity for a 70 kg adult of 129.5 instead of 185 MBq. However, the scan duration was increased from 300 to 350-s, as part of a conservative approach to warrant an adequate image quality for patients older than 10 years. It was also agreed to apply noise reduction filtering techniques (Tera-Tomo 2D Planar Image Enhancement module, Interview XP 3.00.053.0000, Mediso Medical Imaging Systems, Hungary) to images with borderline count statistics.

After the 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 NACG recommendations for all patients, these activities were significantly lower compared to the baseline values. The mean relative differences from the NACG recommendations decreased to 75% (0-5 years), 38% (5-10 years) and 10% (10-15 years) (Figure 4A). The considerable reduction in administered activities allowed, especially for larger children, a better compliance with international recommendations (Figure 4B).

The approach followed in this department represents a graded optimization approach, agreed with, and considered to be acceptable by the clinicians. As previously mentioned, this could potentially be followed by further interventions after an adjustment period. For example, the results shown in Figure 4 suggest that there might be a potential for greater reduction in activity administration 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 of the administered activity of 22% and 27%, respectively.

Site 2

Site 2 sought to optimize their 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 (Figure 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 described and the resulting radiation dose is already quite low (*15*), the next two most common procedures were considered which were ^{99m}Tc-MAG3 renal 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. 155 ^{99m}Tc-DMSA patients were examined in 2017, and the breakdown by age group was 100 (0-5 years), 24 (5-10 years) and 31 (10-15 years).

Prior to optimization, the baseline dosing schema was based on an internal standard leading to values for 1, 5 and 10-year old patients of 100, 125 and 155 MBq, corresponding to activities 550, 378 and 310% higher than those recommended by EANM for the corresponding patient ages, respectively. To evaluate the potential impact of dose optimization on image quality, a phantom experiment was performed. Cylindrical polyethylene vials of 3 sizes (24.2, 44.3 and 66.3 mL) were used to simulate the kidneys of a 1, 5 and 10-year old child, respectively (*16,17*). For each age, two cylinders were filled with water mixed with basically equal activity of ^{99m}Tc-$NaTcO_4$ and placed within a water-filled cylindrical tomographic phantom (21.6 cm inner diameter, 18.6 inner height) to simulate renal imaging. The amount of activity placed in each simulated kidney was determined assuming that 40% of the administered activity distributes to the renal cortex at 4 h post injection (*18*), given that the acquisition start time in clinical practice was 3h after administration. Since the clinical ^{99m}Tc-DMSA scans were acquired for 300 s, the noise level for that acquisition time was considered as a baseline value. The noise level is given by

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

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

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

For the 10-year old, the level 50% higher than the EANM 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-year old, it was determined that 300 kcounts could still be acquired in about 5 minutes. However, reaching the same level for the 5 and 1-year old would take longer, approximately 8 and 16 minutes, 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-year old child, respectively. This is likely to be the first of a series of optimization steps, and thus further reduction may be realized in the future.

After the implementation of these new levels, the assayed administered activities of 20 patients were compared to both the recommended values and to that for the 18 patients prior to the implementation, i.e. the baseline (Figures 6.A and 6.B vs age and weight). Figure 6.C shows the relative difference of the administered activities for baseline and post-implementation patients compared to the EANM recommended values. Evaluation of image quality and assessment of the adequate amount of administered activity were performed 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 EANM, the actual levels of administered activity tended to be closer to the recommended levels. Since the image count of 300 kcounts and noise level of 23% were retained, there was no reduction in image quality. For the other procedures considered, the optimization process for ^{99m}Tc-MDP bone scans and ^{99m}Tc-MAG3 renal studies, resulted in average reductions of the administered activity of 20% and 64%, respectively.

DISCUSSION

Projects at two medical centers using the optimization schema described in this report for renal cortical planar imaging using ^{99m}Tc-DMSA are presented here as examples. This examination had the highest impact in dose reduction to the population of pediatric patients due to the number of procedures performed yearly and the achieved reduction in administered activities, while maintaining adequate diagnostic quality. Target reductions of administered activities were 30% for Site 1 and 52 to 73% for Site 2. For the 5-year old, the target administered activity values 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 where the administered activities were considerably higher initially at Site 2 compared to Site 1. The age of the equipment between the two institutes also varied.

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

Patient demographics, prevalence of clinical conditions regarding the renal cortex, and referral patterns are most likely different in the regions where the two institutes are located. The expectations of the clinical staff regarding the image quality necessary for the 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 be best realized.

The optimization process must be performed by a multidisciplinary working group, with the nuclear medicine physician bearing the responsibility for the evaluation of image quality and assessment of the adequate amount of administered activity. Basic quantitative metrics (such as contrast and image noise) can complement the evaluation of the image quality during the selection of activity levels providing diagnostic information. In both sites, subjective grading of clinical quality by expert observers was used and the optimal level of administered activity was determined that ensured adequate image quality. At Site 2 a phantom evaluation relying on an objective noise index value was also utilized.

Although the two projects led to substantial reduction in the administered activity (Table 1), both also proposed a longer scan duration. Longer imaging times can be problematic when imaging small children leading potentially to more patient motion. For ^{99m}Tc-DMSA imaging, most of the patients tend to be under 5 years old. If imaging time is much longer than 5 minutes, 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 providing clinically adequate imaging with less total counts, some clinics may opt for a faster scan time in small children rather than lower administered activity.

CONCLUSION

As part of an IAEA CRP, an optimization schema was developed specific for pediatric radiology and nuclear medicine. This approach was applied successfully at 2 clinical sites (one in Cuba and one in Chile) for several procedures commonly performed in pediatric nuclear medicine. As examples, the optimization of the same procedure (renal cortical imaging using ^{99m}Tc-DMSA) at the two sites are presented that led to significant reductions in administered activity (and thereby radiation absorbed dose) of between 30 and 70%. Therefore, this optimization schema can be successfully implemented at practically any nuclear medicine clinic seeking to improve their approach to imaging children.

KEY POINTS

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

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

IMPLICATIONS FOR PATIENT CARE: A dose reduction for pediatric patients can be achieved through the optimization methodology developed.

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TABLE 1

Comparison of administered activities (MBq) for 3 example ages (1, 5, and 10 years old) for the ^{99m}Tc-DMSA projects at Sites 1 and 2 for baseline (BL) and after optimization (Opt) to the recommended values for the EANM Pediatric Dosage Card (EANM) and the North American Consensus Guidelines (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

FIGURE 1. General scheme describing the optimization strategy.

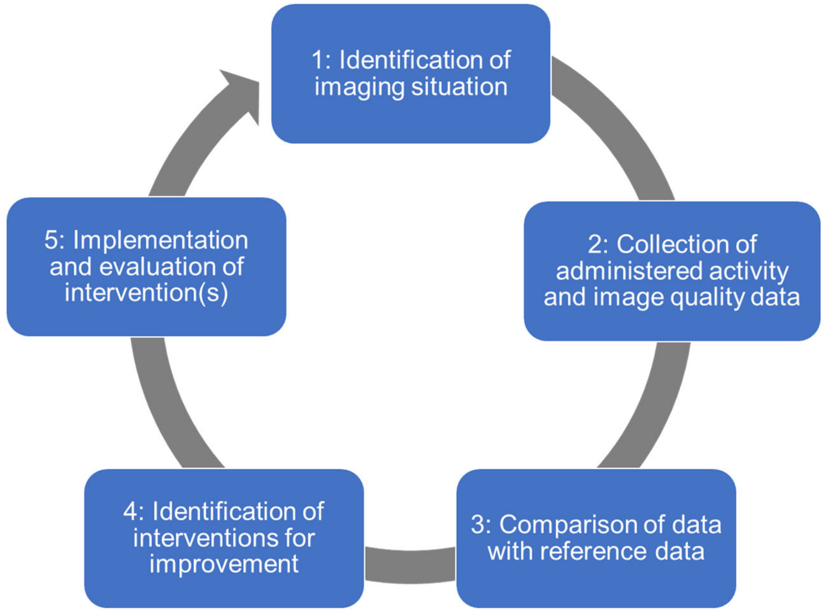

FIGURE 2. Distribution of pediatric studies A) at Site 1 (2018) and B) at Site 2 (2017).

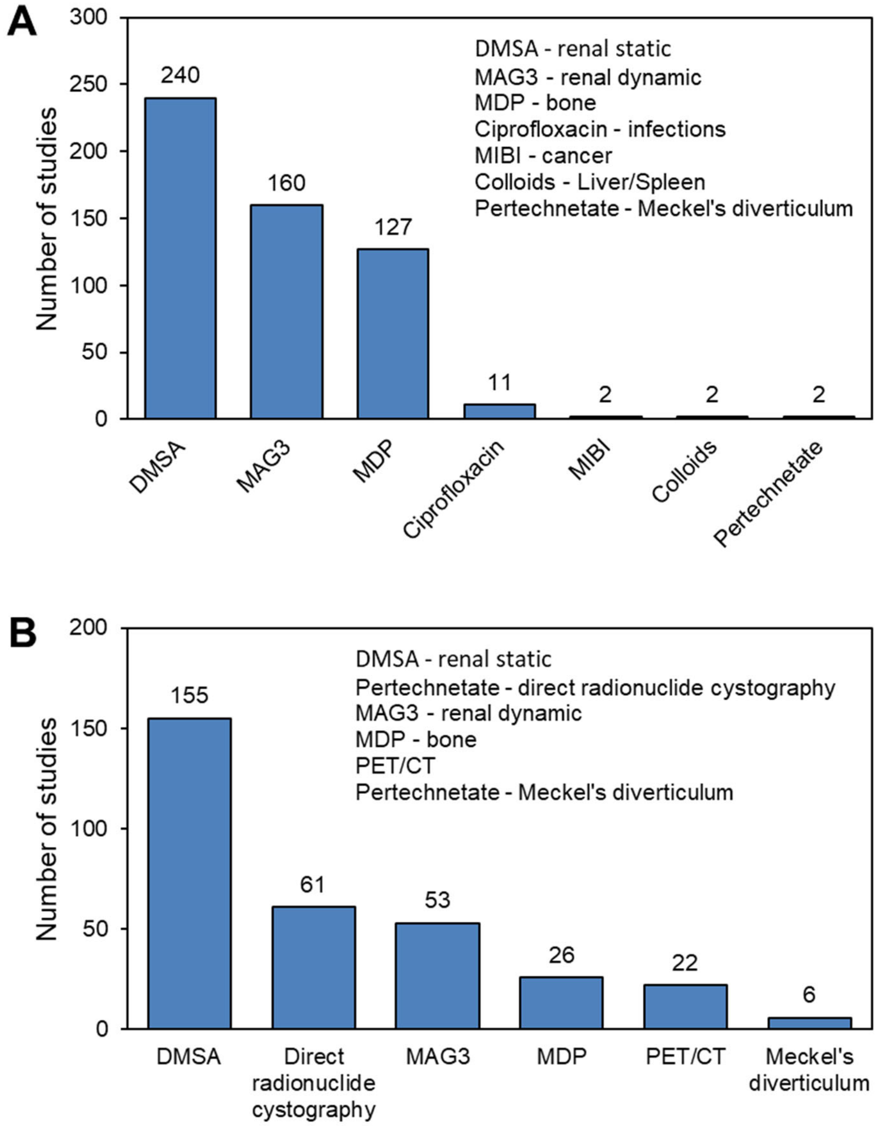

FIGURE 3. A) Activities administered for ^{99m}Tc-DMSA renal cortical scans at baseline and NACG recommended activities for the same patients. The average relative difference compared to NACG recommended values is reported for each age group. B) Same data reported as a function of weight.

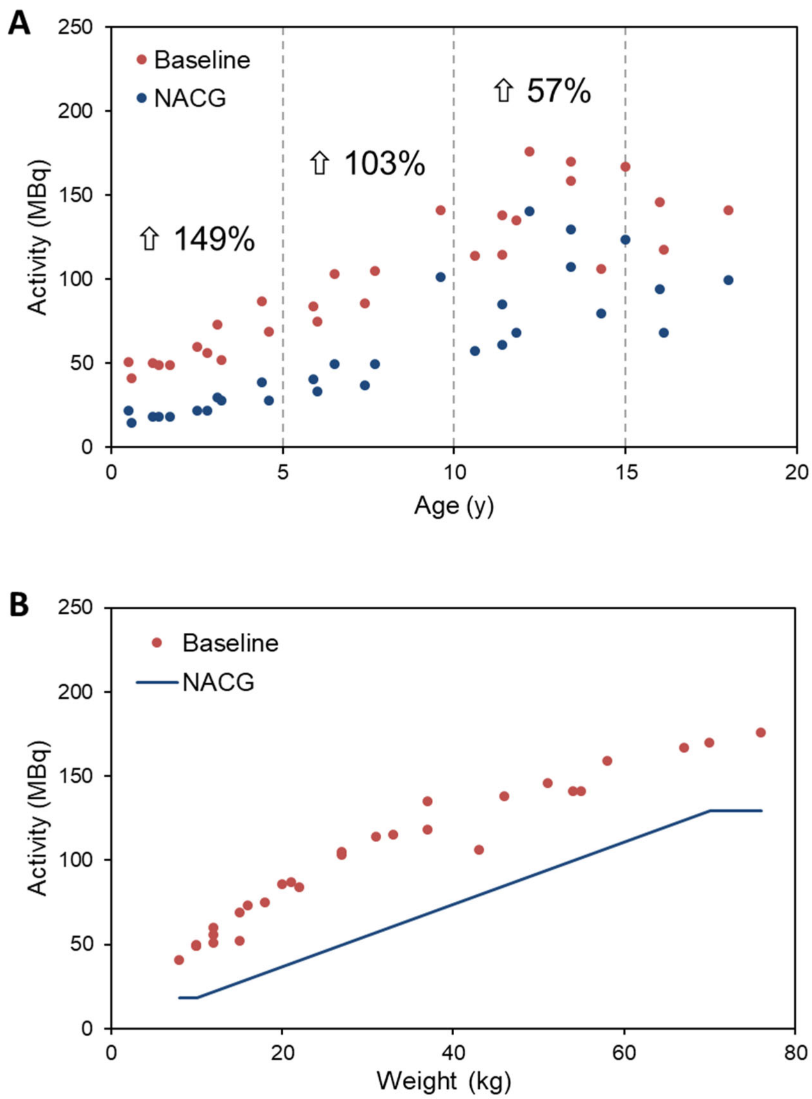

FIGURE 4. Activities administered to pediatric patients for ^{99m}Tc-DMSA renal cortical scans after the introduction of the optimization intervention. A) Comparison, as a function of age, with NACG recommended activities for the same patients. The average relative difference compared to NACG recommended values is reported for each age group. B) Comparison, as a function of weight, with activities that would have been administered at baseline and NACG recommended values for the same patients.

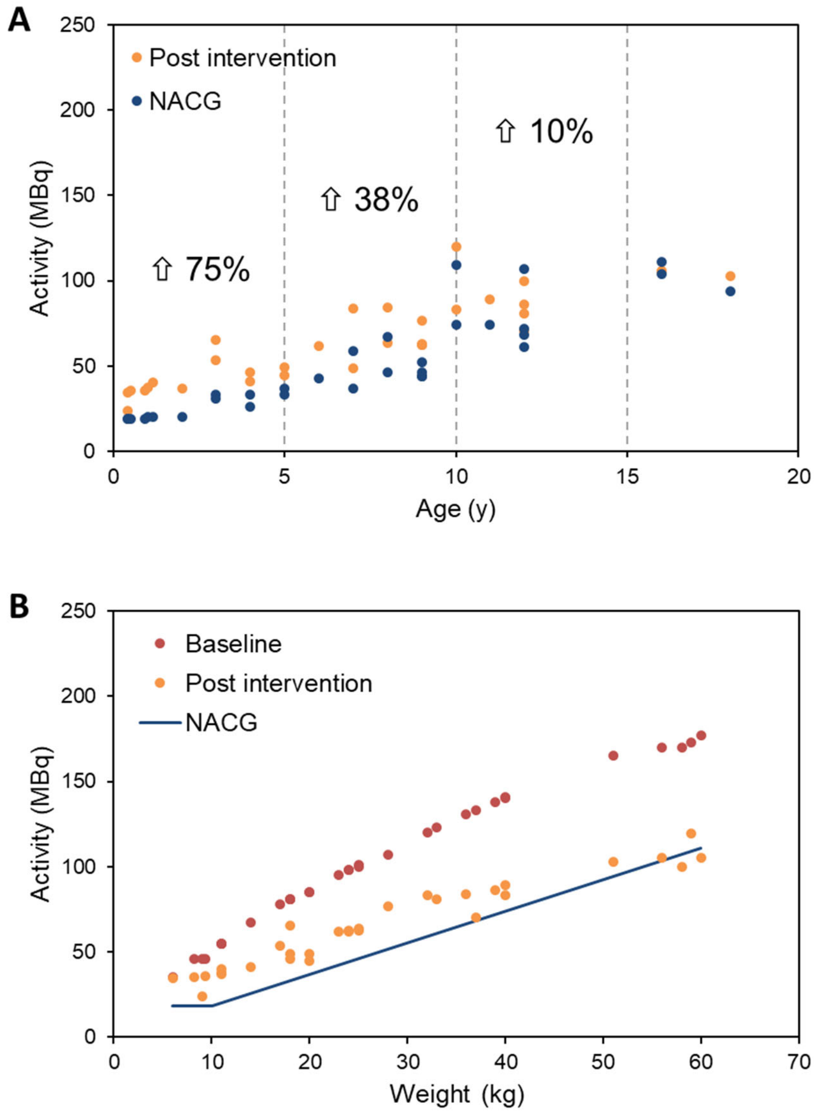

FIGURE 5. Baseline administered activity level for three example ages, simulated activity value corresponding to a noise level of 23% and 25%, activity recommended by EANM and the same value increased by 50%.

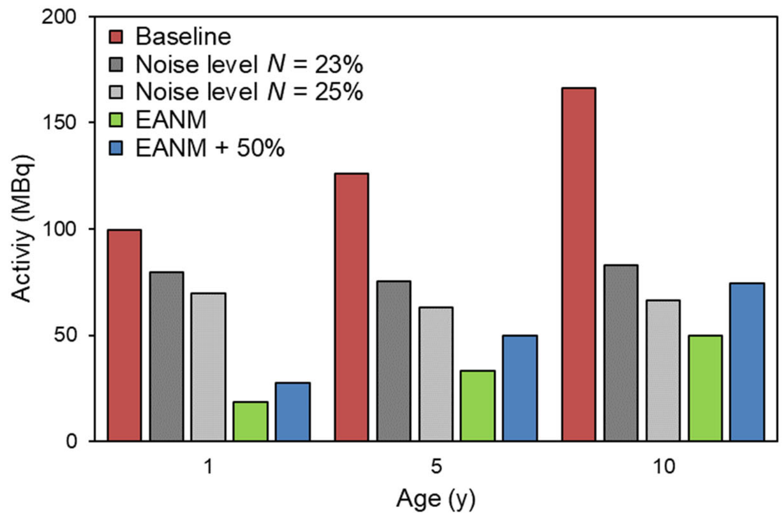

FIGURE 6. Activities administered to pediatric patients for ^{99m}Tc-DMSA renal cortical scans at baseline, after the introduction of the optimization intervention and EANM recommended activities for the same patients as a function of age A) and weight B). C) Relative difference of administered activities at baseline and after introduction of the optimization intervention compared to the EANM recommended values.