

# Comparison of effective radiation doses from X-ray, CT, and PET/CT in pediatric patients with neuroblastoma using a dose monitoring program

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## PURPOSE

We aimed to evaluate the use of a dose monitoring program for calculating and comparing the diagnostic radiation doses in pediatric patients with neuroblastoma.

## METHODS

We retrospectively reviewed diagnostic and therapeutic imaging studies performed on pediatric patients with neuroblastoma from 2003 to 2014. We calculated the mean effective dose per exam for X-ray, conventional computed tomography (CT), and CT of positron emission tomography/computed tomography (PET/CT) from the data collected using a dose monitoring program (DoseTrack group) since October 2012. Using the data, we estimated the cumulative dose per person and the relative dose from each modality in all patients (Total group). The effective dose from PET was manually calculated for all patients.

## RESULTS

We included 63 patients with a mean age of  $3.2\pm 3.5$  years; 28 had a history of radiation therapy, with a mean irradiated dose of  $31.9\pm 23.2$  Gy. The mean effective dose per exam was  $0.04\pm 0.19$  mSv for X-ray,  $1.09\pm 1.11$  mSv for CT, and  $8.35\pm 7.45$  mSv for CT of PET/CT in 31 patients of the Dose-Track group. The mean estimated cumulative dose per patient in the Total group was  $3.43\pm 2.86$  mSv from X-ray (8.5%),  $7.66\pm 6.09$  mSv from CT (19.1%),  $18.35\pm 13.52$  mSv from CT of PET/CT (45.7%), and  $10.71\pm 10.05$  mSv from PET (26.7%).

## CONCLUSION

CT of PET/CT contributed nearly half of the total cumulative dose in pediatric patients with neuroblastoma. The radiation dose from X-ray was not negligible because of the large number of X-ray images. A dose monitoring program can be useful for calculating radiation doses in patients with cancer.

Radiation exposure in children may cause more serious consequences than in adults. The risk of radiation-induced cancer mortality is significantly higher per unit dose in children than in adults because this risk increases inversely with age (1). There are several established reasons for this phenomenon. First, children are innately more vulnerable to develop secondary malignancies. For example, an infant has more than 10 times the risk of cancer induction with the same radiation dose compared with an adult (2). The risk of developing secondary fatal malignancies in children around the age of 10 years is approximately 15% per Sievert (Sv), which is four times higher than that for adults in their forties (2). Second, children have a longer lifespan to develop malignancies after exposure, and most solid cancers have a latency of at least a decade (3). In addition, gonadal irradiation causes more genetic damage in children than in adults (4).

Radiotherapy is the main risk factor for the development of solid second malignant neoplasms within the irradiated body region (5, 6). However, the increasing use of diagnostic imaging studies with ionizing radiation in pediatric practice also raises the issue of radiation hazards (7). The radiation dose from diagnostic computed tomography (CT) is positively correlated with cancer induction in children (8). Moreover, compared with adult CT, pediatric CT may sharply increase the estimated risk of cancer mortality (9). In addition, the use of serial positron emission tomography/computed tomography (PET/CT) in children with malignancies has also raised concerns regarding the harmful effects of a considerable amount of radiation.

Neuroblastoma is the most common extracranial solid cancer in childhood (10). The cumulative radiation dose from frequent imaging studies using ionizing radiation may lead to

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serious problems in pediatric patients with cancer. As the survival rates of pediatric patients with solid tumors have dramatically increased over the last several decades (11), the long-term consequences of radiation exposure from serial imaging studies in these patients have become more important. In addition, PET/CT has emerged as an important diagnostic tool for neuroblastoma (12, 13). Conventional imaging protocols for neuroblastoma include not only CT but also PET/CT before and after treatment, on follow-up, or for evaluation of recurrence (14). Therefore, precise calculation and monitoring of the radiation dose from imaging studies that use ionizing radiation in each neuroblastoma patient are important. However, it is difficult to manually calculate the radiation dose from each modality in each patient.

Recently developed dose monitoring software collects dose information from each patient, either directly from the modality or through the radiology information system, picture archiving and communication system (PACS), or electronic medical records. Using dose monitoring programs, it is possible to calculate, report, and monitor radiation doses, including the effective dose, more easily than before (15). However, few studies have evaluated these programs in clinical practice.

This study aimed to evaluate the utility of a dose monitoring program for calculating and monitoring the effective radiation dose from diagnostic imaging studies, including X-ray, conventional CT, and CT of PET/CT, in pediatric patients with neuroblastoma and

to compare the radiation dose from each modality.

## Methods

### Patients and examinations

The Institutional Review Board of Severance hospital approved this retrospective study and required neither patient approval nor informed consent for reviewing the patients' images and medical records. We searched the electronic medical record in our institution from January 2008 to October 2014 to collect information from pediatric patients with pathologically diagnosed neuroblastoma since records from 2008 were available for retrieval in the electronic system. We reviewed the medical records of these children for age at the time of diagnosis, gender, organ of tumor origin, and body weight on the day of PET or PET/CT. In addition, we reviewed the history of radiation therapy, with irradiated dose and duration.

Furthermore, we reviewed the diagnostic imaging studies performed on these children to collect the acquisition number of each imaging modality from 2003 to December 2014 because PACS (Centricity; GE Healthcare) was adopted at our hospital in 2003. We included diagnostic imaging studies with ionizing radiation, such as X-ray, conventional CT, PET, and PET/CT, and those without ionizing radiation, such as ultrasonography and magnetic resonance imaging (MRI). We did not evaluate the radiation dose from other nuclear medicine imaging studies except PET or PET/CT because of the different methodologies used to calculate the radiation dose in these studies and the limited clinical information regarding the old data. We calculated the total duration of exams for each patient.

### Dose calculation and analysis

We used a commercially available dose monitoring program (DoseTrack; version 1.0, 2012, GE Healthcare) to calculate the effective dose from X-ray, conventional CT, and CT of PET/CT in each patient. The program monitors radiation doses from all imaging modalities using ionizing radiation. For X-ray exams, it directly uses the data from the equipment or uses average dose data by equipment or by study. For conventional CT or CT of PET/CT exams, it collects dose information from the Digital Imaging and Communications in Medicine. The effective dose was calculated as the sum of the organ doses using tissue weighting

factors from the National Radiological Protection Board-R262 for X-ray and the International Commission on Radiological Protection (ICRP) 102 for conventional CT and CT of PET/CT. The radiation dose from PET was calculated by multiplying the fluorodeoxyglucose activity by the dose coefficient. The fluorodeoxyglucose activity was assumed to be 5 MBq per body weight in kg (16), and we used the tissue weighting factors from ICRP 103.

Radiation dose data from this program was available from October 2012 in our hospital. For patients with exams performed after October 2012, the radiation dose was calculated using the DoseTrack program (DoseTrack group). We collected the effective dose data by modality per patient using the program and calculated the mean effective dose per X-ray, conventional CT, and CT of PET/CT examination. For studies performed before October 2012, the effective dose was estimated by applying the mean dose per exam calculated by the data from the DoseTrack group. We calculated the mean cumulative radiation dose per person and the relative doses from X-ray, conventional CT, and CT of PET/CT in all patients (Total group).

### Statistical analysis

We used descriptive statistics for age, duration and number of imaging studies, and doses from diagnostic imaging studies or radiotherapy. Statistical analysis was performed using SPSS Statistics (version 20.0, IBM Corp.) to evaluate data normality and calculate mean values with standard deviations. Relative doses between X-ray, CT, CT of PET/CT, and PET were summarized using simple proportions.

## Results

The study included 63 patients (39 males and 24 females) from January 2008 to October 2014. The mean age at the time of diagnosis was  $3.2 \pm 3.5$  years. The organs of tumor origin were as follows: adrenal gland ( $n=44$ ), mediastinum ( $n=10$ ), retroperitoneum ( $n=7$ ), brain ( $n=1$ ), and maxillary sinus ( $n=1$ ). Twenty-eight patients had a history of therapeutic irradiation. The mean dose of radiation therapy was  $31.9 \pm 23.2$  Gy, with a range of 4.5–97.2 Gy.

The mean duration of imaging studies conducted was  $872.1 \pm 790.0$  days, from 2003 to 2014. The total number of examinations included 5,359 X-ray, 413 conventional

### Main points

- PET and PET/CT contributed to more than 70% of the total diagnostic radiation doses in pediatric neuroblastoma patients.
- The average cumulative dose per patient from CT of PET/CT was 18.35 mSv, which accounted for 46% of the total dose and was greater than twice of the average cumulative dose of 7.66 mSv from conventional CT.
- Patient irradiation should be considered when selecting the imaging modality and interval, as the relative dose from X-ray accounted for up to 9% of the total dose due to the large number of exams.
- A dose monitoring program can be helpful for calculation of radiation dose and may contribute to dose reduction through patient-oriented selection of imaging modality and optimization of dose protocol in pediatric oncology patients.

CT, 98 PET, 82 PET/CT, 337 ultrasonography, and 303 MRI studies. The mean number of examinations performed per patient was  $85.1 \pm 68.8$  X-ray,  $7.0 \pm 5.5$  CT,  $2.7 \pm 2.4$  PET, and  $2.2 \pm 1.6$  PET/CT. Thirty-one patients underwent exams after October 2012 and were categorized as the DoseTrack group.

Table demonstrates the acquisition numbers and estimated effective dose from each modality. In the DoseTrack group, the mean duration of exams was  $353.6 \pm 260.0$  days. Exams with ionizing radiation in this group included 1,090 X-ray, 81 CT, and 17 PET/CT. The mean radiation dose per exam for this group was  $0.04 \pm 0.19$  mSv for X-ray,  $1.09 \pm 1.11$  mSv for conventional CT, and  $8.35 \pm 7.45$  mSv for CT of PET/CT. In the Total group, the mean cumulative radiation dose per person was  $3.43 \pm 2.86$  mSv from X-ray,  $7.66 \pm 6.09$  mSv from conventional CT,  $18.35 \pm 13.52$  mSv from CT of PET/CT, and  $10.71 \pm 10.05$  mSv from PET. The mean radiation dose per exam was  $3.44 \pm 1.25$  mSv for PET. The relative radiation dose from each modality was 8.5% for X-ray, 19.1% for conventional CT, 45.7% for CT of PET/CT, and 26.7% for PET.

## Discussion

This is the largest study with the longest period of evaluation of radiation dose in pediatric patients with cancer. We calculated, estimated, and analyzed the effective radiation dose in 63 pediatric patients with neuroblastoma over the last 12 years using a dose monitoring program. The average cumulative dose per patient from CT of PET/CT was 18.35 mSv, accounting for 46% of the total dose and was two-fold greater than the average cumulative dose of 7.66 mSv from conventional CT.

Whole body imaging is unavoidable in patients with metastatic cancer. However, the whole-body scanning of PET/CT has substantial radiation exposure. The reported radiation dose from standard PET/CT with diagnostic contrast-enhanced CT and CT topography was 21 mSv for a 55 kg 15-year-old, 18 mSv for a 20 kg five-year-old, and 15 mSv for a 10 kg one-year-old child (17). Moreover, the cumulative radiation dose from PET/CT per patient has been reported to be up to 399 mSv (18). However, the dose from PET alone contributed to less than a quarter of the total dose from PET/CT (3). A retrospective review of 78 pediatric patients with cancer also demonstrated that the average effective doses from CT, PET, and PET/CT were 20.3 mSv, 4.6 mSv,

and 24.8 mSv, respectively (18). In this study, the average effective dose from PET was 3.44 mSv, comparable with previous results. However, the estimated cumulative radiation dose from PET per person was 10.71 mSv, accounting for one-fourth of the total dose.

In our study, the average estimated effective dose from CT of PET/CT was 18.35 mSv, which is similar to levels reported in previous studies. In addition, the proportion of the effective dose from CT of PET/CT to the effective dose of the total exams was considerable, accounting for approximately 46%. We can reduce the radiation dose from PET/CT by replacing this study with PET/MRI.

PET/MRI is an emerging modality that can serve as a good alternative to PET/CT with less radiation exposure for pediatric patients with cancer. Because PET/MRI does not use the radiation of CT, as opposed to PET/CT, it produces the equivalent of only a fifth of the effective dose of PET/CT (3). Therefore, tracking exact doses from different modalities in each patient using a dose monitoring program and individualized selection of the most appropriate imaging study may help reduce the radiation dose in the management of children with malignancies.

The relative radiation dose from X-ray examination was about 9% in our study, although a single X-ray exam produced only 0.04 mSv, which was 27 times lower than the dose from a CT exam. Short-term X-ray follow-up may be required in cases of neutropenic fever or patients with cancer in the intensive care unit. However, the comparable relative doses of X-ray and CT in these patients suggest that the cumulative radiation dose from X-ray should not be ignored. Greater consideration of patient irradiation is needed when selecting the imaging modality and interval, including X-ray, in children with malignancies.

The basic principles of radiation protection are justification and optimization. Clinicians and radiologists may justify imaging studies on patients using ionizing radiation under risk-benefit analysis. Optimization indicates adjusting the radiation dose to be as low as reasonably achievable (ALARA). A diagnostic reference level indicates a nationwide standard dose level with the purpose of discouraging practice with unjustified values and promoting adoption of optimal doses (19). Justified use of examinations would reduce not only radiation exposure

but also the patient's discomfort, time, and money. Dose monitoring programs may be used to reduce radiation exposure by selecting an alternative modality with a lower dose. We can also adjust the dose protocols for studies of the same modality, which may produce comparable imaging quality with lower doses. Furthermore, the technology may be applied to establish dose reference levels or to develop guidelines for use of imaging studies from diagnosis to follow-up in a scenario of specific disease, even though radiation dose is not the only guideline for the decision of which imaging studies to perform.

In addition, estimating secondary cancer risk with effective dose requires careful consideration. First, effective dose has basic uncertainties when used for the estimation of individual risk by radiation. Effective dose is a whole body equivalent of partial body irradiations. The classic method to calculate effective dose with organ dose and tissue weighting factor uses an oversimplified human phantom, highly variable sets of coefficients, and outdated scanners (20). Martin (21) reported that estimating effective dose using organ dose in a reference patient resulted in variations of up to 40%. ICRP has suggested that effective dose can be used to compare doses between different diagnostic procedures and to compare similar technologies and procedures at different institutions (22). However, uncertainties exist when comparing doses between studies of different body parts, because heterogeneous energy deposition within tissues results in innate error in deriving organ doses (23). Second, the estimated cancer risks of dose levels below 100 mSv are based on extrapolation from epidemiologic data of greater doses. Therefore, the cancer risks for low effective doses in the diagnostic range may have been over- or underestimated (24). Third, as the risk of cancer induction is stochastic, there is no threshold dose in developing radiation-induced cancers; all exposures bear a certain level of risk. As each radiation exposure is statistically independent from prior exposures, the cumulative dose should be interpreted not as accumulated injury but as added probability; a previous history of irradiation, which is irrelevant to the risk of further exposure, should not discourage the necessary medical use of ionizing radiation in the future (25, 26).

While radiotherapy is an important treatment option, it delivers a significantly higher dose of radiation than diagnostic studies

**Table.** Radiation dose in diagnostic imaging modalities in pediatric patients with neuroblastoma

	Conventional X-ray	CT of CT	PET/CT	PET
<b>DoseTrack group (n=31)</b>				
Total number of exams	1090	81	17	
Estimated total effective dose (mSv)	90.44	107.13	138.79	
Mean effective dose per exam (mSv)	0.04±0.19	1.09±1.11	8.35±7.45	
<b>Pre-DoseTrack group (n=32)</b>				
Total number of exams	4269	332	65	
Adopted mean effective dose per exam (mSv)	0.04±0.19	1.09±1.11	8.35±7.45	
Estimated total effective dose (mSv)	170.76	361.88	542.75	
<b>Total group (n=63)</b>				
Total number of exams	5359	413	82	180
Estimated total effective dose (mSv)	214.36	450.17	684.70	620.54
Estimated cumulative dose per person (mSv)	3.43±2.86	7.66±6.09	18.35±13.52	10.71±10.05
Relative dose (%)	8.5	19.1	45.7	26.7

and has a known risk of solid second malignant neoplasms within the irradiated body region (5). Radiation therapy increases the risk of subsequent cancer by more than four fold in pediatric patients with neuroblastoma (27). There was a dose-dependent increase in the risk of radiation-induced thyroid cancer below the dose level of 30 Gy in children with malignancies, which also applies to the patients in this study (28). Therefore, we emphasize the reduction of radiation doses in radiotherapy and in diagnostic studies. Recently, proton beam therapy has been suggested to lower the risk of developing secondary malignancy by reducing the radiation dose in patients with neuroblastoma (6).

There are several limitations in our study. First, data from the dose monitoring program was available for a limited period. There may be a discrepancy between the estimated dose of the total group and the actual effective dose because we did not consider changes in study protocols or equipment models during the last 12 years at our institution. There may also be differences between exam rooms or examiners. Second, radiation exposure from fluoroscopy, interventional procedures, and nuclear medicine modalities other than PET or PET/CT was not evaluated in the dose analysis. It was not easy to calculate the radiation dose from all modalities manually, because our study included a long period during which dose monitoring software was unavailable. The third limitation was the retrospective

study design. We could not evaluate the effect of an exact dose calculation in each patient using the dose monitoring program with regard to the selection of imaging modality. Further prospective studies should include all diagnostic imaging modalities and evaluate the effect of a dose monitoring program for radiation dose reduction.

In conclusion, accurate calculation and monitoring of the radiation dose from imaging studies is critical for pediatric patients with cancer. In our study, PET and PET/CT accounted for almost 72% of the total radiation dose in pediatric patients with neuroblastoma. The radiation dose from X-ray was not negligible, due to the large number of studies performed. A dose monitoring program can play a crucial role in the calculation of radiation dose, comparing doses between imaging studies by the same or different modalities, and ultimately, reduction of radiation dose by patient-oriented selection of imaging modalities and optimization of dose protocols in pediatric patients with cancer.

#### Conflict of interest disclosure

The authors declared no conflicts of interest.

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