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Evaluation of Effective Dose and Cancer Risk Associated with Low Dose Protocols in Whole-Body Dual-Modality ^{18}F-FDG PET/CT Examinations

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Abstract

Objective: This study aimed to retrospectively calculate patient effective dose from whole body PET/CT scanning with the low-dose protocol on the PHILIPS GEMINI TF PET/CT scanner and to evaluate the LAR of cancer for male and female patients using the BEIR VII report model.

Methods: The radiation dose associated with a CT was calculated according to the CT dose-length product. The PET effective dose was estimated based on the assumption of the injected ^{18}F-FDG activity using ICRP publication 80. The estimated doses were also modified by the weight of each patient. The total effective dose was computed by the summation of the CT and the PET component. LAR of cancer was calculated using the approach described in the BEIR VII report.

Results: The mean of CT dose-length product was 311.75±24.79 mGy.cm, and its individual by depended on the scan length of the patient. The CT contribution to the total effective dose was 5.62±0.44 mSv with the CT protocol setting at 120 kVp and tube current-exposure time of 50 mAs. For the PET component, the mean administered activity of ^{18}F-FDG was 205.61±17.63 MBq. Correspondingly, the total effective dose was found to be 4.83±1.03 mSv when scaling with patient weight. Hence, the mean total effective dose of dual-modality PET/CT was 10.45±1.02 mSv. Additionally, the total effective dose was also reported, according to the age and gender of the patient. The total effective dose was estimated as follows: children male: 10.90±1.09 mSv and children female: 10.91±3.30 mSv, adult male: 10.19±0.97 mSv and 10.62±1.02 mSv for adult female, respectively. In addition, LAR of cancer incidence was 0.13% and 0.05% for children and adult, respectively. The incidence of cancer risks increased when age of patient at exposure decreased.

Conclusion: The effective dose from the PHILIPS GEMINI TF PET/CT studies with low dose protocols was found to be lower than that previously reported in the literature. With the same result of LAR of cancer incidence, the risk was low in our studies and was not the major consideration in PET/CT follow-up imaging.

Key words: PET/CT; patient dose; FDG; dose-length product; LAR

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Introduction

Positron emission tomography (PET), now almost 45 years after its initial development in 1970, has become an established nuclear medicine imaging modality that has proved especially useful in clinical oncology[1]. However, PET alone is limited by its lack of anatomical localization and attenuation correction of the PET data. Therefore, the dual-modality imaging in the form of PET and Computed Tomography (CT) is provided for co-registered functional and anatomical data in a single image study, which is provided for the correction of the PET data alone[2-4]. The 2-deoxy-2-[fluorine-18]fluoro-D-glucose (^{18}F-FDG) is most widely used in clinical oncology with PET/CT scanner. The most important aspect is the ability to accurately localize increased FDG activity to specific normal or abnormal anatomic locations, which may be difficult or even impossible with PET alone[5]. The imaging of ^{18}F-FDG from this dual-modality system has been widely accepted in routine nuclear medicine imaging, especially in clinical oncology. However it is also associated with an increase in the radiation dose received by the patient. A whole body of ^{18}F-FDG PET/CT examinations are generally accompanied by substantial radiation dose to the patients that may enhance the cancer risk[6].

We have started routine service of PET/CT imaging in Ramathibodi Hospital since 2011. The number of malignancy patients for whole-body ^{18}F-FDG PET/CT examinations was increased about 60.52% from June 2011 to December 2014. Therefore, we aimed to *(a)* retrospectively calculate patient effective dose from whole body ^{18}F-FDG PET/CT scanning with the low-dose protocol, and to *(b)* evaluate the lifetime attributable risk (LAR) of cancer for male and female patients using the Biological Effects of Ionizing Radiation (BEIR VII report) model.

Methods

1. Patients

A total of 532 cases of patients (229 males, 303 females) imaged with PHILIPS GEMINI TF PET/CT scanner at Ramathibodi Hospital was reviewed. All patients received both verbal and written information about the study. After a six-hour fasting period, the patient was injected with 185 MBq of ^{18}F-FDG. Height and weight were recorded. Meanwhile, the research project was approved by the Institutional Review Board of Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

2. Whole body imaging

The whole body PET/CT scan was performed one hour after intravenous injection of ^{18}F-FDG using non-contrast CT for attenuation at the same level with imaging acquired at 2 min per bed position. The patient was scanned from the level of vertex to upper thighs with arms above the head. The PET/CT scanner (PHILIPS GEMINI TF) with Time-of-Flight (TOF) technology and the three dimensions (3D) acquisition mode and iterative reconstruction method was prepared in this study. The scanner has four rings of LYSO block detectors giving 18 cm axial field of view, 90 cm patient aperture, and is integrated with a 64 detector CT scanner. All patients were performed with CT scanner according to 120 kVp with 50 mAs per slice, 0.829 for pitch and 0.75 sec for rotation time, respectively. Images were reconstructed

at a slice thickness of 4 mm at 4-mm interval for interpretation.

3. Dose calculations

The effective dose from the CT component (ED_{CT}) of the examination was calculated corresponding dose-length product (DLP) values and conversion factor (k):

$$ED_{CT}\ (mSv) = k\ (mSv/mGy.cm) \times DLP\ (mGy.cm) \quad .....Eq.1$$

DLP was determined by multiplying the volume computed tomography dose index (CTDIvol) value by the scan length in the units of centimeters. The CTDIvol value is reported in the units of mGy. Once the CTDIvol values had been measured on a particular CT scanner by the manufacturer, they were stored in a table and could be computed from the technique factors used to scan the patient[7-9]. For the k conversion factor, we used the value of 0.018 mSv/mGy.cm, which is the conversion factor suggested for the whole body PET/CT scan[4].

The effective dose from the PET component (ED_{PT}) of the examination was calculated corresponding to the administrated activity of ^{18}F-FDG. The means of dose coefficients of FDG were provided by the International Commission On Radiological Protection (ICRP) in its Publication 80[10] for a variety of organs and tissues of the adult hermaphrodite MIRD phantom. ICRP has reported the dose coefficients according to the weight range category of patients; 0.019 mSv/MBq for a 70 kg adult, 0.025 mSv/MBq for a 57 kg adult, and 0.036 mSv/MBq for a 33 kg child, respectively. The weight range category was applied as necessary to patients who fell into the nearest of category such as larger than 65 kg, 45-65 kg, and less than 45 kg[4,11]. However, the effective dose that was calculated from the standard ICRP model may not be true for the individual patient and may be overestimated. The effective doses, which were also modified by the weight-scaled of each patient (ED_{PT}), were applied to this study[4].

.....Eq.2

Finally, The total effective dose (EDTOTAL) associated with dual-modality PET/CT scanner was computed by the summation of the CT and the PET component.

$$ED_{TOTAL}\ (mSv) = ED_{CT} + ED_{PT} \quad .....Eq.3$$

4. Risk assessment using the BEIR VII report

The lifetime attributable risk (LAR) for the patient undergoing whole body dual-modality PET/CT examinations was estimated by using the BEIR VII report[12,13]. The whole body LAR of cancer was calculated according to the data available in table 12D-1 for all types of cancer. This table shows lifetime risk estimates of cancer incidence and mortality resulting from a single dose of 100 mSv at several specific ages. Estimates are shown for all types of cancer, leukemia, solid cancer, and cancer of several specific sites. For example, a 20-year-old male received a dose of 8.5 mSv to the whole body from a PET/CT scan. Table 12D-1 shows the estimated lifetime risk of being diagnosed with all cancer types for a male exposed to 100 mSv at age 20 as 977 per 100,000. The estimate for a male exposed at 8.5 mSv was obtained as (8.5 / 100) × 977 = 83 per 100,000 (about 1 in 1,200).

Results

Clinical information of our patients (229 males, 303 females) with ^{18}F-FDG PET/CT examinations was retrospectively reviewed. The mean of age, weight and height was 58.66±14.23 (range, 13-90) years, 60.88±11.55 (range, 34-103) kilograms, and 160.51±8.70 (range, 141-186) centimeters, respectively.

A total of 532 patients were imaged with PET/CT scanner after the administered activity of ^{18}F-FDG (205.61±17.63 MBq) for one hour. The mean DLP from CT component was 311.75±24.79 mGy.cm. The CT contribution to the mean effective dose (ED_{CT}) was 5.62±0.44 mSv with the CT protocol setting of 120 kVp and tube current-exposure time 50 mAs. For the PET component, the mean effective dose (ED_{PT}) was found to be 4.83±1.03 mSv when scaling with patient weight. Hence, the mean of total mean effective dose (ED_{TOTAL}) per patient of dual-modality ^{18}F-FDG PET/CT was 10.45±1.02 mSv. Table 1 summarizes the mean ED for the total cohort of 532 patients, according to the age and gender.

The LAR for the patient undergoing whole body dual-modality ^{18}F-FDG PET/CT examinations was estimated by using the BEIR VII report. The risk of cancer incidence of our patients was 0.125% (about 1 in 799) and 0.129% (about 1 in 775) for children male and female and 0.046% (about in 2195) and 0.054% (about 1 in 1883) for adult male and female, respectively. Figure 1 shows the LAR for cancer risk estimation using the ED_{TOTAL}, which was estimated according to age and gender.

Discussions

The main clinical application of ^{18}F-FDG PET/CT imaging is in the diagnosis of oncology patients, including staging work-up and follow-up treatment. The ED_{TOTAL} from PET/CT examinations depend on the administrated activity of ^{18}F-FDG and the CT protocol used[4,14,15]. This means that the ED_{TOTAL} was associated with the sum of the PET (ED_{PT}) and CT (ED_{CT}) effective dose values.

The administrated activity of ^{18}F-FDG in the patient has caused internal exposure (ED_{PT}). In our study, the mean administered activity of ^{18}F-FDG was 205.61±17.63

Table 1 Summary of the mean ED for the total cohort of 532 patients according to the age and gender.

	Adults		Children	
	Male	Female	Male	Female
Age (yrs)	60.75±12.18	58.85±13.18	15.91±1.19	15.00±3.87
Body weight (kgs)	67.34±11.09	56.49±9.62	54.98±9.57	49.00±7.00
Body height (cms)	167.50±6.26	155.21±6.01	168.18±10.01	158.00±12.57
Administered activity (MBq)	206.56±17.70	205.05±17.53	203.34±20.30	196.03±14.00
DLP (mGy.cm)	325.67±24.43	302.37±19.05	296.39±39.78	288.84±17.00
ED_{CT} (mSv)	5.86±0.44	5.44±0.34	5.53±0.42	5.20±2.88
ED_{PT} (mSv)	4.33±0.94	5.18±0.96	5.19±0.60	5.70±2.39
ED_{TOTAL} (mSv)	10.19±0.97	10.62±1.02	10.90±1.09	10.91±3.30

MBq. Our result was lower than that in the study of Yunus NA et. al; it was 375±63.45 MBq[15]. With the TOF technology and the 3D acquisition mode of PET/CT scanner of our study, the administrated activity of 18F-FDG may be decreased. It should be compromised between image quality and radiation safety. In addition, Etrad C, et. al. showed that the average ^{18}F-FDG specific activity was 20 % lower for PET units equipped with the TOF technology with 49 PET/CT scanner surveyed in France[16]. However, the administrated activity of ^{18}F-FDG depended on patient weight. The ^{18}F-FDG injection dosage in children, especially in infants and small children, must be considerate. The European Association of Nuclear Medicine (EANM) set 14 MBq for 3D acquisition as the minimum recommended administration activity, and the North American consensus guidelines set 37 MBq as the minimum recommended administration activity of ^{18}F-FDG for pediatric patients[17,18]. The weight range of our patients was found to be 34 to 103 kilograms, and the desired activity of 185 MBq (Mean; 205.61 and SD; 17.63 MBq) was injected in all patients. This activity was sufficient for image quality with whole body imaging leading to lower ED_{PT} in our patients. However, The ED_{PT} was calculated with mass scaling of the individual patient, and the effective dose calculated from the standard ICRP model may not be true for the individual patient and may be overestimated. The ED_{PT} was found to be 4.83±1.03 mSv when scaling with patient weight. The estimated ED_{PT} of ^{18}F-FDG was approximately 2.35 $\times 10^{-2}$ mSv/MBq.

To calculate the ED_{CT}, the value of DLP was required. The DLP was determined by multiplying the CTDIvol with the scan length in the units of centimeters. All patients were performed with low dose CT protocol according to 120 kVp with 50 mAs per slice, 0.829 for pitch and 0.75 sec for rotation time, which were associated with CTDIvol of 2.9 mGy. The mean DLP was found to be 311.75±24.79 mGy.cm corresponding to the scan length of whole body PET/CT imaging (vertex to upper tights) which was 107.58±8.38 cm (range 96.0-129.6 cm).

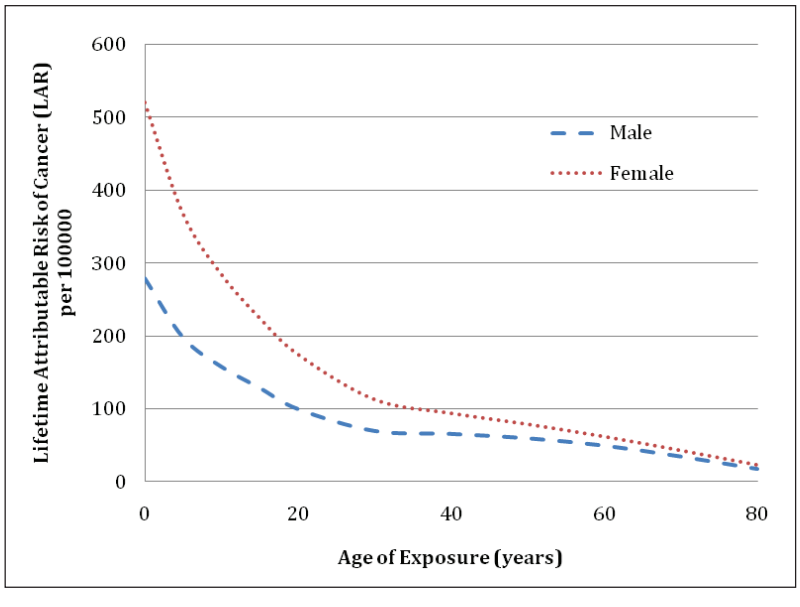

Figure 1 The LAR for cancer risk estimation using the ED_{TOTAL}, which was estimated according to age and gender

When our CT protocol was performed, the ED_{CT} was found to be 5.62±0.44 mSv (range 5.20-6.77 mSv). In contrast, when a diagnostic-quality CT scan (a standard kVp of 140, 190 mA, and a pitch of 1.25) was used for a PET/CT examination, the ED_{CT} was 22 mSv[14].

The ED_{TOTAL} for the whole body ^{18}F-FDG PET/CT examinations was 10.45±1.02 mSv and ranged from 7.87 to 13.26 mSv. Our study revealed that there was a correlation with patient weight, administered activity of ^{18}F-FDG and scan length. Comparing to the previous study, this ranges from 14.0 to 21.5 mSv[2,15,19,20].

To calculate the LAR for the patient undergoing whole body ^{18}F-FDG PET/CT examinations, Table in BEIR VII report was applied to this study. The risk of cancer incidence was 0.125% (about 1 in 799) and 0.129% (about 1 in 775) for children male and female and 0.046% (about in 2195) and 0.054% (about 1 in 1883) for adult male and female, respectively. Figure 1 shows that the excess lifetime risks for cancer incidence and mortality from whole body ^{18}F-FDG PET/CT examinations was quite small, but tended to be higher in women than in men of the same age and also higher when the patient was exposed to radiation at the younger age, especially before 30 years of age. Our result was similar to the publications of Huang B, et al. and Brig G, et al.[3,21]. However, the accuracy of estimating the radiation risk for low-level ionizing radiation with ^{18}F-FDG PET/CT examinations is still a difficult problem to solve, and this requires a number of patients.

Conclusions

The effective dose from the PHILIPS GEMINI TF PET/CT studies with low dose protocols was found to be lower than that in the previously reported literature. With the same result of LAR of cancer incidence, the risk was low in our studies and was not a major consideration in PET/CT follow-up imaging. However, radiation dose to the patients have to compromise between the image quality and radiation safety according to the ALARA concepts.

References

1. Graffeth LK. Use of PET-CT scanning in cancer patients- technical and practical considerations. BUMC Proceedings. 2005;18(4):321-30.
2. Mahmud MH, Nordin AJ, Saad FFA, Azman AZF. Estimation of patient radiation dose from whole body ^{18}F-FDG PET/CT examination in cancer imaging: a preliminary study. Journal of Physics: Conference Series. 2014;546:012008.
3. Huang B, Law MW, Khong P. Whole-body PET/CT Scanning: Estimation of Radiation Dose and Cancer Risk. Radiology. 2009;251(1):166-74.
4. Willowson KP, Bailey EA, Bailey DL. A retrospective evaluation of radiation dose associated with lo dose FDG protocols in whole-body PET/CT. Australas Phys Eng Sci Med. 2012;35:49-53.
5. Kapoor V, McCook BM, Torok FS. An Introduction to PET/CT imaging. Radiographics. 2004;24(2):523-43.
6. Kaushik A, Jaimini A, Tripathi M, D'Souza M, Sharma R, Mishra AK, et al. Estimation of patient dose in ^{18}F-FDG and 18F-FDOPA PET/CT examinations. J Cancer Res Ther. 2013;9(3):477-83.
7. Christner JA, Kofler JM, McCollough CH. Estimating effective dose for CT using dose-length product compared with using organ doses: consequences of adopting International Commission on Radiological Protection publication 103 or dual-energy scanning. AJR Am J Roentgenol. 2010;194(4):881-9.
8. Guttikonda R, Herts BR, Dong F, Baker ME, Fenner KB, Pohlman B. Estimated radiation exposure and cancer risk from CT and PET/CT scans in patients with lymphoma. Eur J Radiol. 2014; 83(6):1011-5.
9. Tonkopi E, Ross AA, MacDonald A. JOURNAL CLUB: CT dose optimization for whole-body PET/CT examinations. AJR Am J

Roentgenol. 2013;201(2):257-63.

10. ICRP. Radiation dose to patients from radiopharmaceuticals. Publication 80. New York: International Commission on Radiological Protection; 1998.
11. Brix G, Lechel U, Glatting G, Ziegler SI, Munzing W, Muller SP, et al. Radiation exposure of patients undergoing whole-body dual-modality ^{18}F-FDG PET:CT examination. The Journal of Nucler Medicine. 2005;46(4):608-13.
12. Wen JC, Sai V, Straatsma BR, McCannel TA. Radiation-related cancer risk associated with surveillance imaging for metastasis from Choroidal melanoma. JAMA OPHTHALMOL. 2013; 131(1):56-61.
13. Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation NRC. Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII-Phase 2. Washington, DC.: National Academies Press; 2006.
14. Park E. Radiation Dosimetry in ^{18}F-FDG PET/CT. In: Kim EE, Lee M-C, Inoue T, Wong W-H, editors. Clinical PET and PET/CT: Springer New York; 2013. p. 121-7.
15. Yunus NA, Abdullah MHRO, Said MA. Estimation of effective dose received by patients undergoing whole-body PET/CT examination. IEEE Colloquium on Humanities, Science and Engineering. 2014:419-22.
16. Etard C, Celier D, Roch P, Aubert B. National survey of patient doses from whole-body FDG PET-CT examinations in France in 2011. Radiat Prot Dosimetry. 2012;152(4):334-8.
17. Lassmann M, Biassoni L, Monsieurs M, Franzius C, Dosimetry E, Paediatrics C. The new EANM paediatric dosage card: additional notes with respect to F-18. European journal of nuclear medicine and molecular imaging. 2008;35(9):1666-8.
18. Treves ST, Parisi MT, Gelfand MJ. Pediatric Radiopharmaceutical doses:New Guidelines. Radiology. 2011;26(2):347-9.
19. Sonoda LI, Sanghera B, Wong WL. Investigation of dose minimisation protocol for ^{18}F-FDG PET-CT in the management of lymphoma postchemotherapy followup. Scientific World Journal. 2012;2012:208135.
20. Considerations Regarding Radiation Exposure in Performing FDG-PET-CT [Internet]. 2012. Available from: http://www.imagewisely.org.
21. Brix G, Nekolla EA, Nosske D, Griebel J. Risks and safety aspects related to PET/MR examinations. European journal of nuclear medicine and molecular imaging. 2009;36 Suppl 1:S131-8.