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Short Communication

Dose Optimisation of ^{18}F-Flurodeoxyglucose for Whole Body PET Oncology Examination in CDNI of UPM

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ABSTRACT

A shift to administration of optimal dose of ^{18}F-FDG between 4 and 5 MBq/kg from the current practice of higher doses potentially yields a reasonable-to-excellent PET image. For this purpose, whole-body MIP images of 32 patients (23 men, 9 women, age 51.9 ± 13.7 years), administered with ^{18}F-FDG (activity 5.3 ± 0.5 MBq/kg, 45 minutes uptake time) for whole-body PET/CT examinations, were evaluated. Image quality was assessed visually by two radiologists using a three-point scoring scale: poor, reasonable and excellent. The interobserver agreement revealed a kappa value higher than 0.7. Therefore, the utilisation of ^{18}F-FDG dose between 4 and 5MBq/kg is considered an optimum dose for whole-body PET/CT examination.

Keywords: ^{18}F-FDG, PET/CT, PET image quality, optimum dose, administered dose/body weight (kg), MIP

INTRODUCTION

The Centre for Diagnostic Nuclear Imaging (CDNI) of Universiti Putra Malaysia (UPM) is equipped with a Siemens® Biograph 64 True-V Positron Emission Tomography (PET)/Computed Tomography (CT) scanner (Germany) operating on a 64-multislice CT detector system. This Siemens® Biograph 64 system has the latest technology of lutetium oxyorthosilicate (LSO) for its camera detector. LSO offers greater sensitivity and improves dead time and counting rate performance, which allow it to handle even very high activity levels as compared to traditional bismuth germanate (BGO) detector (Nagasaki *et al*., 2011; Everaert *et al*., 2003; Nutt, 2002).

However, the recommended doses of ^{18}F-FDG are inconsistent among countries due to facility setup, protocol and patient

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factors. Although the current practice in CDNI employs the administration of ^{18}F-FDG dose between 6 and 8 MBq/kg,the author reiterates that, with a greater sensitivity of LSO camera detector equipped in PET/CT system at CDNI, an optimal dose of ^{18}F-FDG between 4 and 5 MBq/kg administered to the patient is sufficient to achieve a reasonable-to-excellent image quality without compromising the medical diagnostic aspect. Interestingly, dose optimisation of ^{18}F-FDG has been proven to significantly reduce the total effective dose received by patients undergoing PET/CT examination and also technologists during the dose preparation.

MATERIALS AND METHODS

Patient Preparation and Administration of ^{18}F-FDG

A total of 32 patients were recruited in this study. Prior toundergoing the PET/CT whole-body examination,patients were required to fast for at least 6 hours before the scheduled appointment time. Upon admission at the centre, the patients' body weight and height were taken (average of 61.7 ± 6.2 kg, BMI averaged, 22.7 ± 1.2 kg/m^2) and blood glucose level (average, 5.10 ± 0.9 mmol/L) was recorded in their respective examination forms. Nonetheless, patients with hyper or hypoglycaemia conditions were excluded from the study to eliminate any possible bias on the uptake of ^{18}F-FDG. The patients were then briefed by a radiologist on the complete procedure and also possible adverse effects prior to giving and signing an informed consent.

^{18}F-FDG dose ranging from 4 MBq to 5 MBq/kg (average of 5.3 ± 0.5 MBq/kg), which had been prepared in the hot laboratory, was intravenously administered to the patients. The dose prepared was lower than the usual practice as to prove that a lower dose of ^{18}F-FDG was sufficient to yield a reasonable-to-excellent image quality. The total dose given was calculated in accordance to the patients' body weight. Then, the patients were asked to lie down on a bed in a dimly lit room for approximately 45 minutes to minimise brain and muscle stimulations during the ^{18}F-FDG uptake.

Image Acquisition

Quality Assurance and Quality Control of PET/CT Scanner

Routine quality control procedures were performed by a radiographer on the PET/CT scanner in accordance to IAEA Human Health Series No. 1, Quality Assurance for PET and PET/CT Systems prior to the examination. This was to ensure that the system was operated within the tolerance level without affecting the image quality of PET/CT, patients' dose of CT, accuracy of CT-based attenuation corrections and accuracy of CT and PET co-registration (IAEA 2009).

Imaging Protocol

Following the 45-minute uptake time, the patients were brought to the PET/CT suite. The radiographer assisted the patients during the procedure. The patients were positioned with their arms above the head, lying supine on the scanning table throughout the examination. A low dose (150 mAs, 120 kVp) axial CT topogram scan was performed from the base of skull to the mid-thigh region using a modulated 4D care dose system for the purpose of study

planning. An Optivantage™ dual head injector was used to deliver about 80 to 100 ml of contrast (Omnipaque), with the delivery rate set at 2 to 3 ml per second. This was done to encourage renal excretion and enhance the contrast of structures or fluids in the body for the purpose of diagnostic imaging.

Upon completion of the CT image acquisition, the second phase of the study was commenced with PET image acquisition. The PET images were acquired in 3-dimensional (3D) mode on all patients in 5 different bed positions at 2 minutes per bed position. At the end of the examination procedure, all the images were reconstructed using the iterative algorithm technique. CT data fused to PET data was used for attenuation correction of the PET images. Meanwhile, a3D maximum intensity projection (MIP) and 2D multiplanar image in axial, coronal and sagittal were made available for reviewing. Each of the 3D MIP images of the 32 study subjects were then analysed and scored visually using a 3-score system: poor, reasonable and excellent by two nuclear radiologists.

Statistical Analysis

The interobserver of the agreement between two nuclear radiologists was evaluated using kappa measure of agreement (K). Kappa values of >0.8 indicate almost perfect agreement while kappa values of 0.61 to 0.80 indicate substantial agreement (Viera *et al*., 2005).

RESULTS

Patients' body weight was recorded and an average of 61.7 ± 6.2 kg was attained, with average BMI value of 22.7 ± 1.2 kg/m^2 and average blood glucose level of 5.10 ± 0.9 mmol/L.

The visual analysis of MIP PET images for each of the image was given the scores of "excellent", "reasonable" and "poor", as shown in Fig.1.

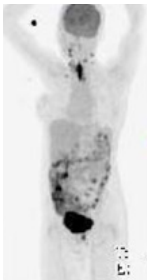
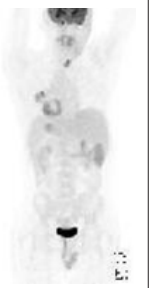
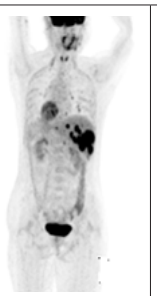
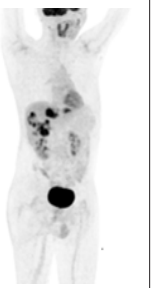
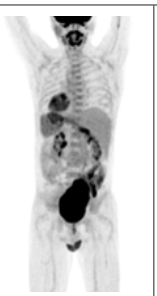
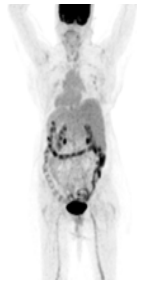
"Poor"		*"Reasonable"*		*"Excellent"*	
					
*(a) F, 54 yr old, **6.35 MBq/kg*	*(b) M, 51 yr old, **7.60 MBq/kg*	*(c) F, 50 yr old, 4.67 MBq/kg*	*(d) M, 47 yr old, 4.59 MBq/kg*	*(e) M, 48 yr old, 4.97 MBq/kg*	*(f) F, 65 yr old, 4.75 MBq/kg)*

Fig.1: Representative MIP whole body PET/CT images quality scoring system

As observed in Figures 1(e) and (f), the MIP images were considered as excellent by nuclear radiologists based on the low background noise to the image sharpness and the intensity of ^{18}F-FDG in the organ of interest: the brain, liver and urinary bladder. In contrast to Figures 1(a) and (b), the region of interest drawn was rather faint. Meanwhile, the MIP images of 1(a) and 1(b) were from the patients who had been administered with ^{18}F-FDG doses at 6 to 8MBq/kg.

The cross tabulation of the visual analysis scores of PET image quality given by two nuclear radiologists in relation to the activity administered per kg of body weight of ^{18}F-FDG is summarised in Table 1.

TABLE 1 : Cross Tabulation on Interobserver Agreement of Visual Analysis Scores of PET Scan Image Quality in Relation to Administered Activity of 18F-FDG (4 to 5 MBq/kg)

Cross tabulation on visual analysis scores of PET image quality

Nuclear Radiologist 1	Image quality	Nuclear Radiologist 2			Total
		Poor	Reasonable	Excellent	
	Poor	2	0	0	2
	Reasonable	1	8	3	12
	Excellent	0	1	17	18
	Total	3	9	20	**32**

The tabulated scores of the PET image quality presented in Table 1 show that out of the 32 images analysed by two nuclear radiologists, 30 images (94%) were classified as reasonable and excellent by Nuclear Radiologist 1 as compared with only 29 images (91%) by Nuclear Radiologist 2. The interobserver agreement between the two nuclear radiologists on the PET image scoring was evaluated in the statistical analysis using the kappa measure of agreement (K). The agreement between the two nuclear radiologists for the complete group of PET image quality was apparently substantial, with a kappa value of 0.709 ($p < 0.05$).

DISCUSSION

A shift to an optimum dose by means of lowering the current dose practice from 6-8 MBq/kg to 4-5 MBq/kg could also potentially yield a reasonable-to-excellent PET/CT image. It is known that the uptake time period, patient's blood glucose level, patient motion, patient comfort and inflammation are the biological and physical factors that attribute to the estimation of standardise uptake value (SUV) and image quality (Boellaard *et al*.,2008). In this study, however, the researchers ensured that all the above-mentioned factors were minimised and controlled to reduce any potential statistical bias.

Referring to Fig.1, the "gold standard" of characterising the excellent quality of the PET image is by looking at the sharp contrast between the organs of interest (brain, liver and urinary bladder) and the low level of background noise (Everaert *et al*.,2003). As observed in Figures 1(e) and (f), the intensity of ^{18}F-FDG in structures of organ or interest appeared to be sharp and homogenous.

The interobserver agreement on the PET images from both the nuclear radiologists in the form of kappa value, 0.709 ($p < 0.05$), revealed the interobserver agreement was substantially good. This finding indicates a good level of agreement during the independent assessment on PET image (Viera *et al*.,2005). As the assessment of the PET image quality given the ^{18}F-FDG dose at 4 to 5 MBq/kg revealed a reasonable-to-excellent quality image, it is recommended that a shift from the current practice of 6-8 MBq/kg to 4-5 MBq/kg of ^{18}F-FDG dose be administered to patients.

Moreover, this recommended low dose is also in compliance with the recommendation by the International Commission on Radiological Protection (ICRP) on dose optimisation (Hishar *et al*., 2014; Hishar *et al*., 2013; Everaert *et al*., 2003). Lowering the current practice dose would directly reduce the effective dose (internal exposure) received by the patients. The effective dose for ^{18}F-FDG is calculated via the amount of radioactivity administered and the entrance exposure (IAEA 2008). The effective dose of internal exposure from intravenous administration of an ^{18}F-FDG activity can be estimated from Eint = Γ. A, where Γ is dose coefficient (18F = 19 μSv/MBq) and A is the administered activity (ICRP 1999). With the suggested dose administration of 4 MBq/kg compared to the current dose practice of 8 MBq/kg, the effective dose received by the patients would be reduced by half.

As shown in Fig.1, even at 4 MBq/kg the ^{18}F-FDG dose has yielded a reasonable-to-excellent image; therefore, the current practice of giving more than 4 MBq/kg to patients should be questioned. Even though some might refute that the radiation exposure received by the patient is outweighed by its justified benefit for medical diagnostic purpose, it is still notright to do so when a better and safer solution does exist. In addition, this approach will also help to reduce the radiation burden, not only to the patient but also to the personnel involved during the preparation of ^{18}F-FDG dose.

As for the expenditure aspect, the operational cost will be greatly reduced because CDNI purchases the ^{18}F-FDG dose from the suppliers in the market. This is due to the optimal dose that will be adjusted, which may directly influence the purchase of ^{18}F-FDG compound. With the optimal dose suggested, the author foresees that the operational cost (particularly the expenditure on ^{18}F-FDG purchase) will be reduced by at least 10 to 15 %. The author is also confident that with the dose suggested, together with the efficiency in the management of patients (patient's scheduling and proper scanning plan), there is no doubt that the operational cost of CDNI will be reduced with the added benefit of reduced radiation exposure to the patients and staff.

Limitations of the study

A limitation of this current study is the small number of patients involved as its sample, with only 32 images analysed. The study was intended to be a preliminary study to prove that with an LSO camera detector of greater sensitivity equipped in PET/CT system at CDNI, ^{18}F-FDG dose activity ranging between 4 and 5 MBq/kg is sufficient for a PET/CT whole–body examination. Thus, the extent of the study may be conducted using a larger number of patients in the future.

CONCLUSION

This short communication is to suggest the implementation of ^{18}F-FDG dose between 4 and 5 MBq/kg for standard diagnostic whole-body PET/CT scans. This preliminary study revealed that the recommended lower dose of ^{18}F-FDG activity is able to yield satisfactory image quality, which does not compromise the diagnostic ability of the test and radiation protection benefits nor incur any additional cost.

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