Optimization of scanning time of ^{18}F-FDG whole body PET/CT imaging in obese patients using quadratic dose protocol

Marianie Musarudin, PhD[1], Nurul Hanisah Badrul Fikli, BSc[1], Nur Farahiyah Zulkaffli, MMedPhys[1], Ab Rashid Jusoh, MMed Sci[1], Mohamad Aminudin Said, MSc Phys[2]

[1]School of Health Sciences, Universiti Sains Malaysia, Malaysia, [2]Nuclear Medicine Department, Institut Kanser Negara, Ministry of Health Malaysia, Malaysia

ABSTRACT

Introduction: ^{18}F-FDG imaging of overweight and obese patients is often challenging due to higher scattering and attenuation. Degradation of positron emission tomography (PET) image quality as the body weight increases is best overcome by using the quadratic dose protocol. Previously the implementation of this protocol on a Bismuth Germanium Oxide (BGO) scintillation crystal-based PET/CT system at Institut Kanser Negara (IKN), Malaysia practices using the linear dose protocol (T_{min}=2.5 minutes). Hence, this study aims to optimize the T_{min} of the quadratic dose protocol for ^{18}F-FDG PET/CT.

Materials and Methods: This study was conducted based on the guideline published by the European Association of Nuclear Medicine (EANM) version 2.0 FDG-PET/CT and conducted in two phases. Firstly, 100 whole-body scan ^{18}F-FDG PET/CT images were selected for the average coefficient of variation (COV) analysis in the liver region. Second, a NEMA 2012/IEC2008 phantom was used to obtain the relationship between the $COV_{phantom}$ and the scanning time. Finally, the images acquired using the two T_{min} were quantitatively compared using contrast recovery coefficient (Q_H), signal to noise ratio (SNR), and visibility (V_H). Independent t-test between each image quality parameter performed with p-value <0.05 considered significant.

Results: The average COV of the liver was 17.7%. Currently, this value was clinically accepted to produce appropriate image quality at IKN. Interpolation at COV=17.7% gave a T_{min} value of 2.9 minutes. Comparisons show that the two T_{min} yielded equivalent PET/CT image quality (p-value of Q_H=0.774, SNR=0.780 and V_H=0.915).

Conclusion: The optimal T_{min} defined in this study was 2.9 minutes, 27.6% shorter than the T_{min} previously defined based on COV=15%. Despite the higher average COV, the shorter T_{min} beneficial in the lower total ^{18}F-FDG activity administered, reduce the internal dose to the patient while producing equivalent image quality.

KEYWORDS:
Minimal scan time, optimization, quadratic dose, ^{18}F-FDG, PET/CT

INTRODUCTION

Degradation of positron emission tomography (PET) image quality is associated with the increment of the body weights of patients. This is due to the high scattering and attenuation events.[1,2] Several methods were suggested to overcome such problems, for instance, longer scanning time,[1,3,4] time-of-flight (TOF),[5] increasing Fluorodeoxyglucose (^{18}F-FDG) dose[6] and depth of interaction (DOI) method.[7,8] For the ^{18}F-FDG dose, three dose protocols are currently practice in many PET imaging centres. The protocols are linear, constant, and quadratic dose protocols. The disadvantage of the linear and constant dose protocols was that the image quality degraded as the body mass increased. In a previous research, a comparison of the linear dose protocol and the quadratic dose protocol in obese patients turned out that the quadratic dose protocol produced constant image quality in obese patients.[6]

Currently, Institut Kanser Negara Malaysia (IKN) is implementing a linear dosing protocol for the whole-body scan (WBS) ^{18}F-FDG imaging. Based on the previous findings presented by other researchers, the implementation of this dosing protocol caused poor image quality for overweight and obese patients.[6] Hence, an attempt in implementing quadratic dose protocol at IKN institution using NEMA 2012/IEC 2008 phantom was previously performed.[9] However, implementation of the respective protocol based on the recommendation by the European Association of Nuclear Medicine (EANM) resulted in a longer scanning time compared to the current linear dose protocol practices in our institution.[9] 3.8 minutes minimal scan time (T_{min}) was previously obtained in our study compared to the current clinical practice of 2.5 minutes scanning time. In accordance with that, optimization of the quadratic dose protocol for the WBS ^{18}F-FDG was the main aim of this study. The optimization was performed based on the evaluation of the coefficient of variation (COV) value measured on the WBS ^{18}F-FDG images. The COV value is considered appropriate for the optimal image quality because it is currently accepted by the physicians at the IKN. This study provides information valuable for optimal WBS ^{18}F-FDG imaging that is likely allows optimal image quality for overweight and obese patients.

This article was accepted: 25 July 2021
Corresponding Author: Marianie Musarudin
Email: marianie@usm.my

MATERIALS AND METHODS

Study design

This was a retrospective study. The inclusion criteria included the patients who underwent WBS ^{18}F-FDG PET/CT from July to August 2019 at IKN. The exclusion criteria set was patients with cancer in the liver area. In this study, the background value was calculated in the liver due to the homogeneous tissue distribution in this area.[10] Nevertheless, for the cases of cancerous liver, the presence of cancer cells in the liver causes the uptake of the ^{18}F-FDG in the respective region to be higher and thus invalid for the normal background analysis. The WBS images of the patients were collected from the report retrieved from the picture archiving and communication system (PACS system) at IKN. All images were acquired using a PET Discovery ST scanner equipped 8 slice CT- scanner, 36 detector rings PET scanner. The detector of this scanner is a Bismuth Germanium Oxide (BGO) scintillation crystal.

Definition of optimal T_{min} for quadratic dose protocol WBS ^{18}F-FDG

This study was conducted in two phases. In the first phase, 100 WBS ^{18}F-FDG images were used for the analysis of the COV of the patient, $COV_{patient}$. To describe the prevalence of obese patients who underwent ^{18}F-FDG PET/CT, with a tolerable error of ±5% in the patients' population of ^{18}F-FDG PET/CT from the Nuclear Medicine Department, IKN with 170 patients, the sample size calculation was based on the results obtained by National Health and Morbidity Survey (NHMS) 2019, the current prevalence of obesity among Malaysian adults was 19.7%.[11] The statistically acceptable sample size was estimated to be 100 with a 10% dropout consideration. COV=15% is currently recommended by the EANM guideline as a reference value. However, this is somehow arbitrary.[12] Since we are considering the accepted image analysis and diagnosis of our institution population, the average value of the $COV_{patient}$ was used to derive the T_{min}. Other than that, at IKN, the prescribed activity to the patient is 5 MBq/kg while EANM outlines a different formulation.[13] Therefore, some modification in the definition of T_{min} is necessary to fit with the current protocol practices in our institution. During the calculation, the most uniform region in the image, which is the liver was considered for the analysis.[10] Three rectangular shapes volume of interest (VOIs), covering the maximum area of the liver were drawn on the axial, coronal, and sagittal view of the liver region by using the PMOD software Version 3.7 (Figure 1). The COV was determined by the ratio between the SD with the mean value of the VOIs (Equation 1).[14] The SD was representing as the standard deviation of the VOIs while the mean represented the mean of the pixel value.

$$COV = \frac{SD}{Mean} \times 100 \qquad [1]$$

Based on the EANM recommendation, the T_{min} of the quadratic dose protocol should be defined by interpolation of the COV against the scanning time curve at COV=15%.[15] However, in this study, the definition was performed based on the average COV measured on the reconstructed images of patients at our institution. Hence, in the second phase of the experiment, we defined the relationship between the $COV_{phantom}$ and the scanning time to define the T_{min}. For this purpose, NEMA 2012/IEC 2008 image quality phantom was repeatedly scanned using six scanning times, 1, 3, 5, 7, 10, and 15 minutes. The background compartment of the phantom was considered for the COV calculation due to its homogenous character. Following that, five 30 x 30 x 30 mm VOIs were drawn at the background area as shown in Figure 1(b).

EANM guidelines version 1.0 for FDG-PET tumour imaging adhered to the PET/CT image reconstruction.[16] The image reconstruction corrected for the geometrical response, detector efficiency, system dead time, random coincidences, scatter, and attenuation. The images were reconstructed using the 3D-OSEM (ordered subset expectation maximization) algorithm in the iterative method. Two iterations and 21 subsets with the standard Gaussian post-filters with a 6.0 mm full-width half-maximum (FWHM) were used. Analysis was performed using PMOD software Version 3.7.

Estimation of ^{18}F-FDG dose activity administered

Interpolation of the $COV_{phantom}$ against the scanning time at the $COV_{patient}$ gave the T_{min} value for this imaging protocol. Substitution of this T_{min} value into Equation 2 resulted in patient-specific activity ^{18}F-FDG for the specific body weight of a patient. The respective equation is described in Equation 2, where A is the product of ^{18}F-FDG activity to be administered (in MBq), *t* is (in seconds) the scanning time per bed position based on the clinical setting, w_{ref} is the reference body weight, A_{ref} is the reference FDG activity.[15] For the comparison, we considered both COV=15% and COV=17.7% in the calculation.

$$A.t = \frac{w^2}{W_{ref}^2} . A_{ref} . T_{min} \qquad [2]$$

The COV=17.7% used in this study was derived based on the average COV measured on the liver region of the patient reconstructed images at our department. These images were currently resulted in accepted image quality for diagnosis by the physician at IKN. Hence, adoption of this value in the T_{min} definition will result in optimal scanning time for our imaging protocol. In addition, the different COV values defined in our institution contributed by the 5 MBq/kg prescribed activity protocol practiced in IKN.

Based on the recommendation by EANM Research Ltd. (EARL), w_{ref} = 75 kg and A_{ref} = 300 MBq [16], thus can be simplified to Equation 3.

$$A = 0.053.w^2 . \frac{T_{min}}{t} \qquad [3]$$

Verification of optimal T_{min} image quality

To verify the image quality obtained by using the T_{min} defined in this study, a NEMA 2012/IEC2008 phantom was repeated scanned using the respective T_{mins} and EANM recommended T_{min}. Based on a previous study, the COV=15% suggested T_{min}=3.8 minutes for the WBS PET/CT imaging.[9] This 15% COV which was recommended by EANM was regarded as the reference and standard value in this study.[15,16] Meanwhile, in the current study, COV=17.7% which was considered as the minimum and clinically acceptable COV suggested T_{min}=2.9 minutes. Quantification of the images obtained using the two T_{mins} was performed to quantitatively compared the two. The images were quantified using the following parameters:

i. Contrast recovery coefficient (Q_H)

$$Q_H \frac{\frac{M_S}{M_B}-1}{R-1} \times 100 \quad [4]$$

Where M_S and M_B were the mean count of the sphere and background respectively, and R was the tumor background ratio.[7]

ii. Signal to noise ratio (SNR)

$$SNR= \frac{T_S-T_B}{SD_B} \quad [5]$$

Where T_S was the total number of counts in spheres while T_B was the total number of counts in the background. SD_B was the standard deviation in the background.[17]

iii. Visibility (V_H)

$$V_H= \frac{M_S - M_B}{SD_B} \times \sqrt{N_{voxel}} \quad [6]$$

Where the M_S and M_B were the mean number of counts in spheres and background while N_{voxels} was the number of voxels in the spheres.[18]

Statistical Package for the Social Sciences version 26 (SPSS Inc., Chicago, IL, USA) was used to perform data analysis. Parametric analysis, independent t-test was applied to determine differences between each image quality variable and T_{min}. A p-value of <0.05 was considered statistically significant.

RESULTS

Figure 2 shows the $COV_{patient}$ measured at the liver of the patient on the reconstructed images. For the 100 samples analyzed, the $COV_{patient}$ ranged from 14% to 34%. Out of 100, only eight samples were recorded with COV>24%. 92% (92 samples from 100) of the samples were reported with COV in the ranges of 14% to 22%. The average COV was 17.7% (Σ COVpatient / 100 samples).

In Figure 3(a), the data for $COV_{phantom}$ against the scanning time was presented. The data were fitted with a power-law function, and the relationship between the two was presented by COV= 28.884 $t^{-0.457}$. At COV equal to 17.7%, the calculated T_{min} was 2.9 minutes. A similar value should be obtained if T_{min} = 17.7% is substituted into the fitted power-law function.

Referring to Figure 3(a), the power-law fitting parameters were a=28.884 and b=-0.457. Hence, by using the fitted equation y= 28.884$x^{-0.457}$ the calculated value of the T_{min} equal to 2.9 minutes. Meanwhile, at COV=15% as recommended by EANM, the T_{min} was 4.19 minutes.

Figure 3(b) shows the empirical 18F-FDG activities that were estimated to be administered to the patient based on the specific body weight of the patients. The data presented here were compared for COV=15% and COV=17.7% protocols. For the ranges of body weights assumed, a consistent increment of 23% 18F-FDG activity was noted between COV=17.7% and COV=15% protocol. COV=15% consistently gave higher 18F-FDG activity compares to the COV=17.7%.

Figure 4 shows the analysis of the quality for the resulting images that were performed using T_{min} derived at COV=17.7% and COV=15%, resulted from T_{min}=2.9 minutes in the current study and T_{min}=3.8 minutes as reported in a previous study.[9] For the three parameters analyzed, a small percentage difference was observed between the two T_{min}s. A maximum deviation of 7.3% was reported in the Q_H of smaller spheres (5.65 ml and less). Meanwhile, the deviation was in the range of 0.6% and 2.7% for spheres 27.02 ml and 11.56 ml (Figure 4(a)). For SNR and V_H, the same pattern of results was shown in Figure 4(b) and Figure 4(c) where the percentage difference in the range of 0.2% to 5.5% was recorded. For the three image quality, independent t-test analysis indicates that all the three parameters did not significantly differ between the two T_{min} (p-value of QH=0.774, SNR=0.780 and VH=0.915) (Table I).

DISCUSSION

Degradation of PET image quality is one of the issues with the increment of the body weight of the patients, due to higher scattering and attenuation.[1,2] One of the best methods proved to produce a consistent image quality for overweight patients was the quadratic dose protocol. Nevertheless, implementation of the quadratic dose protocol suggested a longer scanning time compares to the current 2.5 minutes practices in IKN for the linear dose protocol. This finding has been published, whereby 3.8 minutes scanning time was proposed for the quadratic dose protocol.[9] However, in this study, the definition of T_{min} at COV=15% resulted in T_{min}=4.19 minutes. The difference between this T_{min} (4.19 minutes) and the T_{min} presented in the previous study (3.8 minutes) most probably due to the experimental error. In this study, we have improved the accuracy of the quantified data by repeating the measurement and data analysis three times.

Table I: Association between the T_{min} and image quality parameters

	T_{min} (minutes)	N	Mean (SD)	Std. Error Mean	F	p-value
QH	2.9	6	0.562 (0.174)	0.710	0.087	0.774
	3.8	6	0.570 (0.163)	0.664		
SNR	2.9	6	33.665 (10.302)	4.206	0.082	0.780
	3.8	6	33.583 (9.673)	3.949		
VH	2.9	6	522.083 (460.435)	187.972	0.915	0.915
	3.8	6	514.317 (443.876)	181.212		

Note: Data for T_{min}=2.9 minutes and T_{min}=3.8 minutes were expressed as mean ± SD; No significant difference between T_{min} and image quality parameters was determined by independent t-test at 0.05 level of significance.

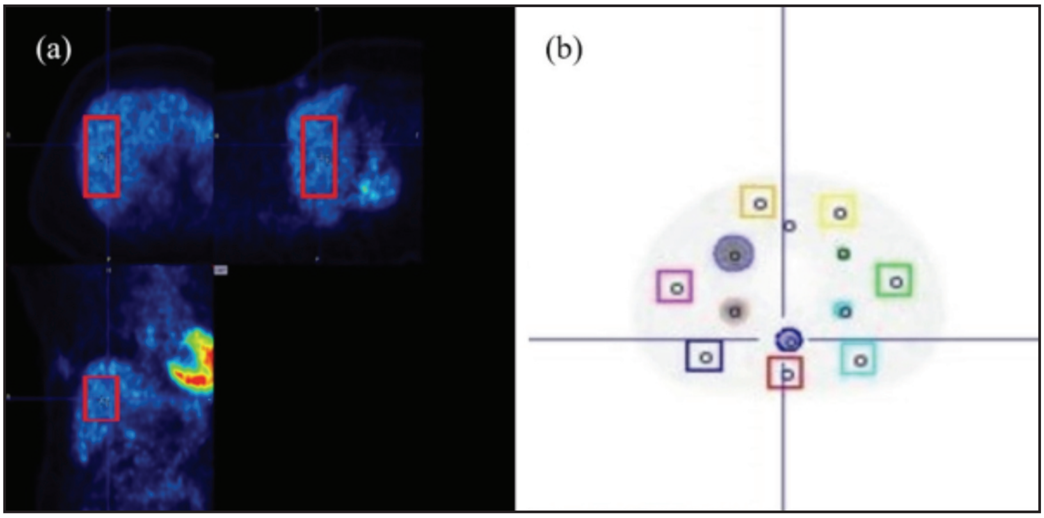

Fig. 1: The VOI defined using PMOD software (a) in the liver of the patient reconstructed image (b) at the background area of the phantom.

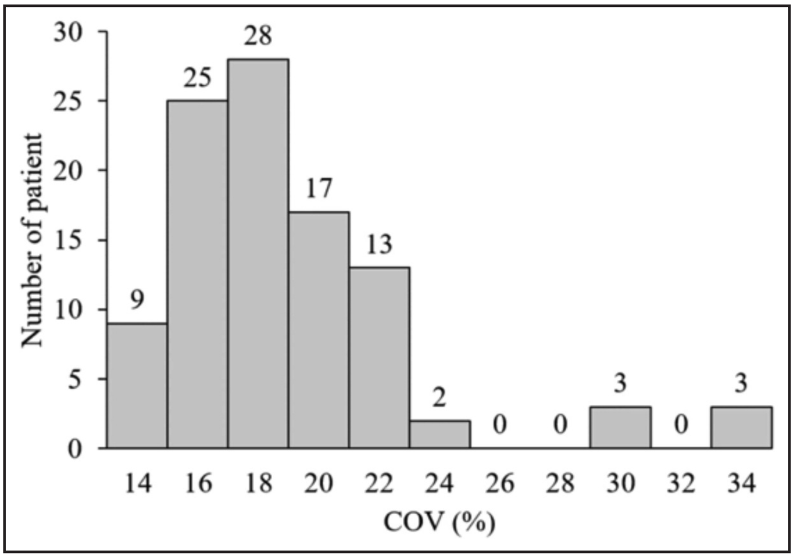

Fig. 2: Histogram of $COV_{patient}$ measured on the WBS ^{18}F-FDG PET/CT images of the patient.

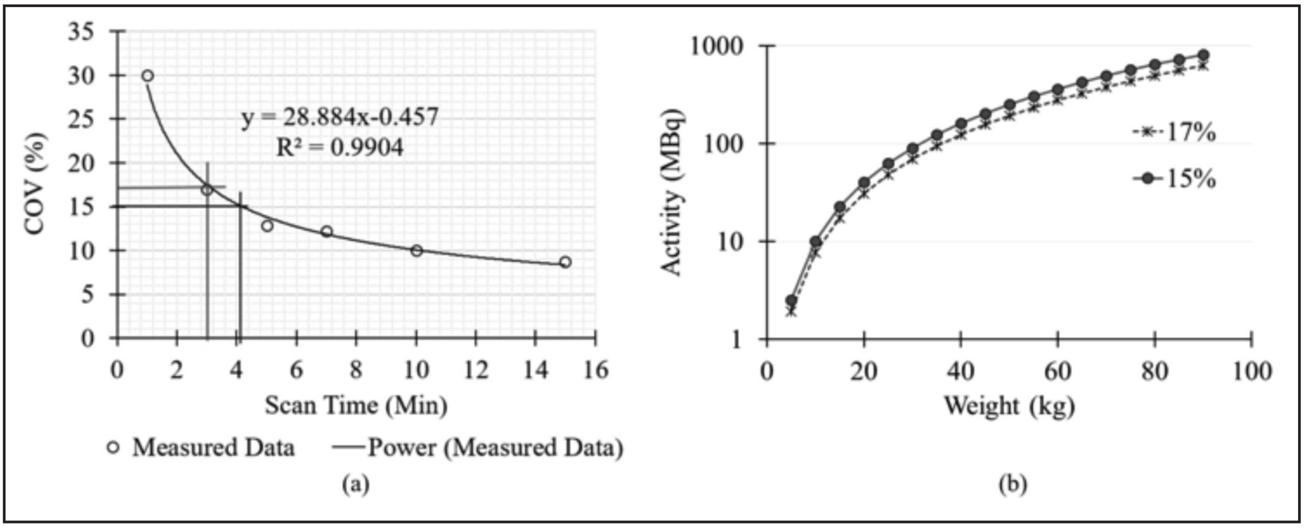

Fig. 3: (a) Comparison between the T_{mins} obtained in this study and recommendation by EANM (2015). (b) Estimated ^{18}F-FDG activity to be administered based on COV=15% and COV=17.7% quadratic dose calculation.

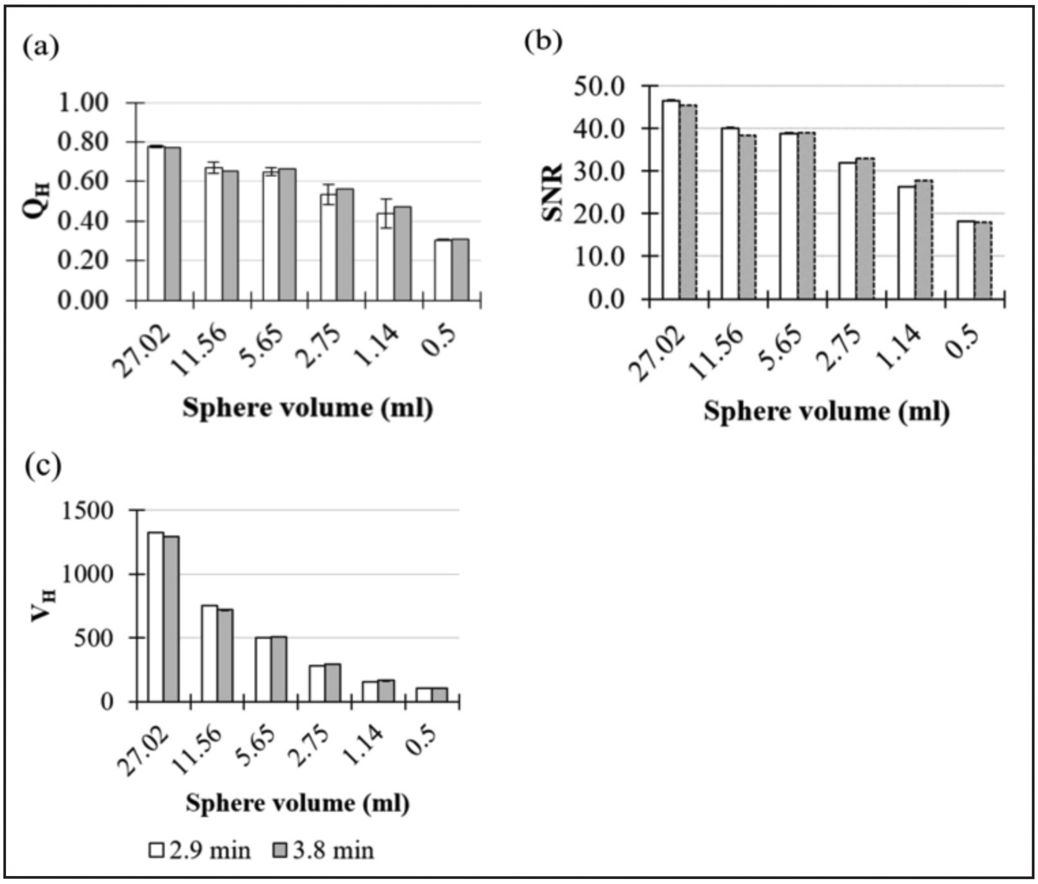

Fig. 4: Quantitative analysis of image quality for T_{min}=2.9 minutes and T_{min}=3.8 minutes. Error bar presented the percentage difference between the two data (a) contrast recovery coefficient (Q_H) (b) signal to noise ratio (SNR) (c) visibility (V_H).

This repetition can affirm the integrity of the data. To optimize the T_{min} for the WBS ^{18}F-FDG PET/CT using the quadratic dose protocol, we analyze the average COV of the WBS ^{18}F-FDG PET/CT images currently available in our PACs system. These images which were currently accepted by the physician for the analysis and diagnosis thus assumed to meet the minimal requirement for the image diagnosis. Based on the analysis, T_{min}=2.9 minutes was defined, which is 0.9 minutes or 23.68% ((0.9/3.8)x100) shorter than the T_{min} defined using COV=15%. This definition was made based on the COV=17.7% measured on the WBS ^{18}F-FDG PET/CT images. The difference in the COV values was the reason for the different T_{min} defined. Higher $COV_{patient}$ calculated on the patient images leads to a lower T_{min} as compared to the COV=15% as recommended by the EARL. The advantage of shorter T_{min} was in a shorter total acquisition time. For instance, the current WBS ^{18}F-FDG PET/CT protocol at IKN for a female patient was six bed positions. The total scanning time for the six bed positions for COV=17.7% was 17.4 minutes. Meanwhile, for COV=15%, the total scanning time was 22.8 minutes. The difference between these two COVs was 5.4 minutes. The disadvantages of longer scanning time were higher risk of movements of patients, inconvenience to the patients, artifacts and also unable to increase maximum daily scan of patients.

Based on Equation 2 and Equation 3, the amount of activity that will be administered to the patients was affected not only by the' body weight of the patients but also by the T_{min} value. Increasing the T_{min} will increase the amount of activity to be administered to the patients. The COV=17.7% of the minimal requirement for the image diagnosis in IKN suggested a lower amount of ^{18}F-FDG activity plus a shorter T_{min} as compare to the COV=15% as recommended by EANM. Since IKN is currently practicing higher COV than the recommended value, the activity administered per patient was practically reduced. For example, in Figure 3(b), for the patient with body weight of 60 kg, it is confirmed that COV= 17.7% gives less dose to the patient compared to COV=15% by 83 MBq.

In this study, the concern was not solely on the amount of activity administered to our patients but we are also considered the results of the quality of the images obtained. As stated before, the COV=17.7% practicing in IKN resulted in shorter T_{min} compares to the T_{min} derived at COV=15% as recommended by the EANM. The practicality of this T_{min} was confirmed by quantitative analysis of the images acquired using the derived T_{min}. Regarding the image analysis in this study, the results show a small percentage difference of each parameter for both T_{min}=3.8 minutes and T_{min}=2.9 minutes even in the smallest 0.5 ml sphere. Nevertheless, a slightly larger percentage deviation was recorded for the smaller sphere as compared to the larger sphere.

CONCLUSION

Analysis of the average COV on the WBS [18]F-FDG PET/CT images resulted in a higher average COV as compared to the recommendation by the EANM. An average COV of 17.7% was calculated from the reconstructed WBS [18]F-FDG PET/CT images, compares to the COV=15% recommended by the EANM. Interpolation of the T_{min} at COV=17.7% gave T_{min} =2.9 minutes, shorter than the T_{min} defined using EARL recommendation. This shorter T_{min} advantages in reducing the total scanning time, lowered the [18]F-FDG activity administered to the patients which reduced the internal exposure and radiation dose to the patients, and eventually more comfort to the patienst. No significant changes of Q_H, SNR and V_H were observed in the reconstructed PET/CT images of 2.9 minutes and 3.8 minutes image acquisition (p>0.05, respectively). Equivalent quality of images was confirmed for the two T_{mins}.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the support given by the staff at the Nuclear Medicine Department, Institut Kanser Negara for the data information and also to the USM for supporting this research. This study has been approved by the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia. This study reference NMRR-19-2847-50388(IIR) had been funded by the USM Short Term Grant (304/PPSK/6315167). We would like to thank the Director General of Health Malaysia for his permission to publish this article.

DISCLOSURE OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Halpern BS, Dahlbom M, Auerbach MA, Schiepers C, Fueger BJ, Weber WA, et al. Optimizing imaging protocols for overweight and obese patients: a lutetium orthosilicate PET/CT study. J Nucl Med 2005; 46(4): 603-7.
2. El Fakhri G, Santos PA, Badawi RD, Holdsworth CH, Van Den Abbeele AD, Kijewski MF. Impact of acquisition geometry, image processing, and patient size on lesion detection in whole-body [18]F-FDG PET. J Nucl Med 2007; 48(12): 1951-60.
3. Masuda Y, Kondo C, Matsuo Y, Uetani M, Kusakabe K. Comparison of imaging protocols for [18]F-FDG PET/CT in overweight patients: optimizing scan duration versus administered dose. J Nucl Med 2009; 50(6): 844-8.
4. Halpern BS, Dahlbom M, Quon A, Schiepers C, Waldherr C, Silverman DH, et al. Impact of patient weight and emission scan duration on PET/CT image quality and lesion detectability. J Nucl Med 2004; 45(5): 797-801.
5. Lois C, Jakoby BW, Long MJ, Hubner KF, Barker DW, Casey ME, et al. An assessment of the impact of incorporating time-of-flight information into clinical PET/CT imaging. J Nucl Med 2010; 51(2): 237-45.
6. de Groot EH, Post N, Boellaard R, Wagenaar NRL, Willemsen ATM, van Dalen JA. Optimized dose regimen for whole-body FDG-PET imaging. EJNMMI Res 2013; 3(1): 63.
7. Yoshida E, Kitamura K, Nishikido F, Shibuya K, Hasegawa T, Yamaya T, et al. Feasibility study of a highly sensitive LaBr3 PET scanner based on the DOI-dependent extended-energy window. Nucl Instruments Methods Phys Res Sect A Accel Spectrometers, Detect Assoc Equip 2009; 604(1): 363-5.
8. Yoshida E, Kitamura K, Shibuya K, Nishikido F, Hasegawa T, Yamaya T, et al. A DOI-dependent extended energy window method to control balance of scatter and true events. IEEE Trans Nucl Sci 2008; 55(5): 2475-81.
9. Musarudin M, Muhammad Safwan Selvam HS, Said MA. Implementation of quadratic dose protocol for [18]F-FDG whole-body PET imaging using a BGO-based PET/CT scanner, GE Discovery ST. Iran J Nucl Med 2019; 27(2): 73-80.
10. Liu G, Hu Y, Pang L, Yu H, Hu P, Shi H. Variability and reliability of normal liver [18]F-FDG standardized uptake value in relation to placement of volume of interest. Iran J Radiol 2019; 16(2): e84881.
11. Institute for Public Health, National Institutes of Health (NIH), Ministry of Health Malaysia. National Health and Morbidity Survey (NHMS) 2019, Technical Report- Volume I: NCDs - Non-communicable diseases: risk factors and other health problems. 2019.
12. Gnesin S, Kieffer C, Zeimpekis K, Papazyan JP, Guignard R, Prior JO, et al. Phantom-based image quality assessment of clinical [18]F-FDG protocols in digital PET/CT and comparison to conventional PMT-based PET/CT. EJNMMI Phys 2020; 7(1): 1-16.
13. Boellaard R, Delgado-Bolton R, Oyen WJG, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur J Nucl Med Mol Imaging 2015; 42(2): 328-54.
14. Abdi H. Coefficient of variation. Int Encycl Stat Sci 2011; 267.
15. Koopman D, van Osch JAC, Jager PL, Tenbergen CJA, Knollema S, Slump CH, et al. Technical note: how to determine the FDG activity for tumour PET imaging that satisfies European guidelines. EJNMMI Phys 2016; 3(1): 22.
16. Boellaard R, O'Doherty MJ, Weber WA, Mottaghy FM, Lonsdale MN, Stroobants SG, et al. FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: version 1.0. Eur J Nucl Med Mol Imaging 2010; 37(1): 181-200.
17. Ziegler S, Jakoby BW, Braun H, Paulus DH, Quick HH. NEMA image quality phantom measurements and attenuation correction in integrated PET/MR hybrid imaging. EJNMMI Phys 2015; 2(1): 18.
18. Elschot M, Vermolen BJ, Lam MGEH, de Keizer B, van den Bosch MAAJ, de Jong HWAM. Quantitative comparison of PET and Bremsstrahlung SPECT for imaging the in vivo yttrium-90 microsphere distribution after liver radioembolization. PLoS One 2013; 8(2): e55742.