ORIGINAL ARTICLE

Comparing Radiation Dose Between Contrast-Enhanced and Non-Contrast-Enhanced CTAC Acquisition in ^{18}F-FDG-PET/CT Examination

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ABSTRACT

Introduction: Hybrid Positron Emission Tomography with Computed Tomography (PET/CT) imaging is well established in the oncology setting. However, in the current cancer diagnostic imaging approach in Malaysia patients need separate CT and PET/CT examinations for morphologic and physiologic cancer staging, respectively, as PET/CT is unable to produce images with optimum diagnostic quality. Therefore, introducing contrast media into CT attenuation correction (CTAC) acquisition to increase image quality have raised concerns on heightened radiation exposure. This study aimed to verify the amount of external radiation exposure irradiated to the patient converging to the scanning protocol implemented in whole-body (WB) ^{18}F-FDG-PET/CT examination. **Methods:** A retrospective study was conducted to determine the radiation dose delivered during CTAC acquisition of ^{18}F-FDG-PET/CT examination at three hospitals providing PET/CT imaging services in Penang State. The implemented scanning protocols and parameters, and the effective dose received by the patient were analysed based on dose length product (DLP) and CTDIvol reported by the scanner. **Results:** CTAC of WB ^{18}F-FDG-PET/CT imaging was executed as either non-contrast (NC-CTAC) or contrast-enhanced (CE-CTAC). CE-CTAC produced a 250% higher radiation dose compared to NC-CTAC. The scanning parameter differences that significantly contributed to increased radiation dose were the tube current and pitch value. **Conclusion:** CE-CTAC delivered a higher radiation dose than NC-CTAC acquisition in WB ^{18}F-FDG PET/CT imaging due to different mAs and pitch as scanning parameters.
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Keywords: PET/CT imaging, CT attenuation correction (CTAC), Radiation dose, Hybrid imaging

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INTRODUCTION

The utilisation of hybrid whole-body (WB) PET/CT, which integrates Positron Emission Tomography (PET) into Computed Tomography (CT) imaging, is a modality of choice in oncology. A PET/CT imaging provides an outstanding reduction of total examination time and enhanced image quality (1). This hybrid imaging shows a significant role in the assessment of the cancer stage and therapy responses in cancer patients (2). However, the patient radiation dose is increased substantially from combined PET and CT, particularly in a contrast-enhanced CTAC (CE-CTAC) protocol (2). CT attenuation correction (CTAC) acquisition is performed to increase low-contrast tissue differences and improve images' diagnostic value for more accurate staging and therapy planning (2-4).

An effective dose is the mean absorbed dose received by the patient from standardised whole-body irradiation. However, it was reported that combined imaging of PET/CT has increased the effective dose whereby the patient received an effective dose of approximately 8.5 mSv to 13.45 mSv from the external exposure, which is X-radiation from CT scanning, as well as 5.7 to 7.0 mSv of internal exposure from Gamma radiation dose received from injected radiotracer (5-9). There are several protocols that can be opted to complete image acquisitions of whole-body Fluorine-^{18}

Fluorodeoxyglucose (WB ^{18}F-FDG) PET/CT imaging. Apart from low-dose non-contrast CTAC (NC-CTAC), the introduction of contrast media into CTAC acquisition has been rising in clinical practice. Several literatures stated that CE-CTAC PET/CT is proposed for cancers involving the gastrointestinal tract, head and neck, lymph nodes, pancreas, ovaries, and for those with resectable multiple tumours (2, 3, 10-13). A study conducted in Malaysia also concluded that CE-CTAC PET/CT imaging increased the reliability of radiotracer uptakes measurement in the liver and subsequently increase the accuracy of the study (14).

Different image acquisition protocol yields different cumulative radiation dose received by a patient. However, limited studies had been addressing the issue of radiation dose derived from external exposure especially involving the CE-CTAC of PET/CT imaging. Therefore, this study was conducted to compare the effective dose delivered to the patient in CE-CTAC versus NC-CTAC acquisition during WB ^{18}F-FDG PET/CT imaging. Since radiation dose is influenced by scanning parameters, this study also aimed to compare different scanning parameters employed during WB ^{18}F-FDG PET/CT imaging and their correlation with the effective doses. The findings could be used as an initial strategy in altering the current scanning parameters to obtain an excellent diagnostic quality of PET/CT images without compromising the dose received by patients.

MATERIALS AND METHODS

A retrospective study was performed at three private hospitals in Penang, Malaysia, from the month of January to December 2013. All patients' imaging data analysed in this study were performed on the same model of PET/CT scanner (GE Discovery STE by GE Healthcare). The UiTM ethics committee approved the retrospective study (reference: 600-FSK(PT.5/2)).

Patients

A total of 602 patients who were referred for WB ^{18}F-FDG PET/CT were enrolled in this study. Patients with additional scan acquisition such as delayed scan and therapy simulation planning were excluded since the protocol settings differed and reported doses were higher than WB protocols.

CTAC acquisitions protocol

The implemented scanning protocol was localiser, CTAC acquisitions for NC-CTAC or CE-CTAC followed by PET acquisition. The protocol selection of either NC-CTAC or CE-CTAC to be performed as anatomical co-registration CTAC acquisition is based on the availability of the latest radiological diagnostic staging examination. The WB ^{18}F-FDG PET/CT examination was done with a radiotracer ^{18}F-FDG dose of 10 to 15 mCi depending on the patient's body weight.

After radiotracer administration, patients were transferred to the individual waiting area for about an hour. 1000 ml of oral contrast agent was given for the patient to drink while waiting. The scan was commenced after one hour of radiotracer administration. The amount of intravenous contrast agent to be administrated depends on the patient body weight, calculated as 1.5 ml/kg.

For NC-CTAC, the scanning parameters implemented were 120kVp, auto-modulated tube current with effective mAs of 101 to 110, slice thickness 3.75mm, scan interval 3.27mm, pitch 1.75:1, beam collimation 10.0mm and rotation speed 0.8sec/rot. On the other hand, the scanning parameters implemented for CE-CTAC were 120kVp, manual tube current with effective mAs of 301 to 310, slice thickness 3.75mm, scan interval 3.27mm, pitch 1.375:1, beam collimation 10.0mm and spec rotation 0.8sec/rot.

The scan length for CTAC was set to adapt the PET emission bed covered from vertex to mid-tight. Therefore, the data of the scan length of CTAC acquisition is categorised into 3 groups: ±910 mm for 7 frames PET emission acquisition, while ±1040 mm and 1170 mm is utilized to cater to 8 and 9 frames PET emission acquisition, respectively. A study by Brix et al. found the effective dose is correlated with the CT volume dose index (CTDIvol, in mGy) based on the anthropomorphic study and established the coefficient factor for the estimation. Therefore, CTDIvol and dose length product (DLP, in mGy.cm) values provided by the CT units were recorded after every exposure and were applied indirectly to evaluate the radiation dose received by the patient (5, 8, 15).

Dosimetric measurement using reported $CTDI_{vol}$

Data collection and analysis involved the quantitative data. The effective dose for whole-body (EDT) from external radiation exposure was calculated based on reported CTDIvol using the following equation:

$$ED_T = T_{CT}^{E} . CTDI_{vol} \quad \text{(Eq. 1)}$$

where the constant of coefficient of $T_{CT}^{E} = 1.47 \pm 0.02$ mSv / mGy (6).

Dosimetric measurement using reported DLP

Apart from quantifying effective dose using CTDIvol, DLP is another CT dose descriptor. The effective dose delivered from CTAC acquisition was calculated using the reported DLP by the equation:

EDT (mSv) =
DLP (mGy. Cm) x 0.018 (mSv / mGy. Cm) (Eq. 2)

The conversion factor of effective dose per unit DLP was 0.018 mSv/mGy.cm (14, 15).

Statistical analysis

Statistical analysis was performed using Statistical

Package for the Social Sciences (SPSS) version 17.0. Kolmogorov-Smirnov test and Levene's test were used to determine the conformity of numeric data to a normal distribution and homogeneity of variance, respectively. $P < 0.05$ was considered statistically significant for numeric data. Next, an independent sample T-test was performed to compare the mean dose received by patients from NC-CTAC and CE-CTAC samples groups. Analysis of variance (ANOVA) was done on non-contrast CTAC among the centres under study to determine the significance of variation in the effective dose. Pearson product-moment correlation test was used to analyse the correlation between the scanning parameters and the effective dose.

RESULTS

A total of 602 patients' data was reviewed in the research including 295 males and 307 females. The patient distribution among the three hospitals under study denoted as H1, H2 and H3 were 38%, 36% and 25%, respectively. The age of the study sample ranged from 18 to 89 years old. The mean age of female samples was 54 in H1 and 49 in H2 and H3 while the mean age of male samples was 56, 51 and 49 in H1, H2 and H3, respectively.

Upon analysing the acquisition protocols, CTAC in WB ^{18}F-FDG PET/CT examination was executed in two different approaches based on the request from the oncologist. In H1, the WB PET/CT examination was done as either NC-CTAC or CE-CTAC WB ^{18}F-FDG PET/CT. The decision on which protocol to be implanted is depended on the availability of the latest diagnostic CT images. Should the patient have done a diagnostic CT examination within 3 months, NC-CTAC is done as an integral part of WB ^{18}F-FDG PET/CT and CE-CTAC is the protocol to be implemented if the patient does not have the latest diagnostic CT staging scan. Among 231 samples from H1, 54% performed CE-CTAC while 46% performed NC-CTAC WB ^{18}F-FDG PET/CT examination. On the other hand, H2 and H3 only performed low-dose NC-CTAC as an integral part of the WB ^{18}F-FDG PET/CT as administration of contrast during CTAC in WB PET/CT is not a common practice in Malaysia.

Analysis of effective dose based on the type of examination

Findings has shown there were statistically significant differences in effective dose between NC-CTAC and CE-CTAC in WB ^{18}F-FDG PET/CT imaging, as shown in Table I. Effective dose calculated from CTDIvol using Equation 1 and DLP using Equation 2 showed that, when comparing the effective dose based on these two types of CTAC acquisitions, CTDIvol dose descriptor showed that the radiation dose received by the patient from NC-CTAC was about 12mSv. However, when CE-CTAC is implemented as an integral part of attenuation correction acquisition in WB PET/CT examination, the patient received a 250% higher radiation dose (42.18 ± 4.94 mSv versus 11.63 ± 1.20 mSv). Besides, taking calculation into DLP is another dose descriptor, statistically significant differences in effective dose (DLP) are notified, in which CE-CTAC delivered 130% higher radiation dose as compared with NC-CTAC (32.48 ± 4.87 mSv versus 13.71 ± 1.22 mSv).

Table I: Mean effective dose calculated from $CTDI_{vol}$ and DLP.

Effective dose	Type of Examination		*p*-value
	Non-contrast PET/CT	Contrast-enhanced PET/CT	
Calculated from $CTDI_{vol}$	11.63 ± 1.20	42.18 ± 4.94	< 0.001
Calculated from DLP	13.71 ± 1.22	32.48 ± 4.87	< 0.001

Analysis of inter-hospital effective dose from non-contrast CTAC acquisition

The present study has shown that no statistically significant differences were found in the effective dose (CTDIvol and DLP) received by the patients who went through the NC-CTAC protocol between the three centres (Table II).

Table II: Mean effective dose ($CTDI_{vol}$ and DLP) for 3 centres

	Hospitals		
	H1	H2	H3
N	106	219	152
Mean Effective dose $CTDI_{vol}$ (mSv)	11.73 ± 1.26	11.60 ± 1.18	11.63 ± 1.19
Mean Effective dose DLP (mSv)	13.70 ± 0.85	13.60 ± 0.57	13.88 ± 1.91

Analysis of scanning parameters

Study has shown that no statistically significant differences were found in scan length (mm) between the NC-CTAC and CE-CTAC (Table III). All hospitals under study utilized the same method in which seven to nine PET frames were required to cater to whole-body imaging of coverage from vertex to mid-thigh. This had demanded about 900 to 1200 mm scan length for both NC-CTAC and CE-CTAC to enable fusion with PET emission scan.

Table III: Mean Scan Length and mAs applied on the whole-body ^{18}F-FDG PET/CT

	Type of Examination		*p*-value
	Non-contrast PET/CT	Contrast-enhanced PET/CT	
N	477	125	
Scan Length (mm)	991.3924 ± 71.87	987.2359 ± 82.51	0.608
Effective mAs	155.48 ± 2.87	305.43 ± 2.86	< 0.001

Apart from that, the examination was done through a fixed tube potential of 120 kVp. The tube current (mA) used was automated tube current modulation (ATCM) for NC-CTAC while CE-CTAC in H1 employed manual mA and was set patient-by-patient basis based on the scan length and attenuation measurement from the scout

scan. As tabulated in Table III, the study's finding shows that mAs used for NC-CTAC were significantly different from CE-CTAC (with a mean of 155.48 ± 2.87 versus 305.43 ± 2.86). The relationship between the mAs and the effective dose calculated from CTDIvol and DLP was investigated using Pearson product-moment correlation coefficient. As illustrated in Fig. 1 and 2, there was a strong, positive correlation between the mAs and the effective dose calculated from CTDIvol ($r = .98$, $p < 0.01$) and DLP ($r = .95$, $p < 0.01$). It is shown that higher mAs result in a higher effective dose.

Apart from the scan length and tube current, the pitch value was another scan parameter that differs between NC-CTAC and CE-CTAC. In the present study, NC-CTAC and CE-CTAC employed pitch of 1.750 and 1.375, respectively. The differences in the amount of radiation dose produced by both implemented pitches

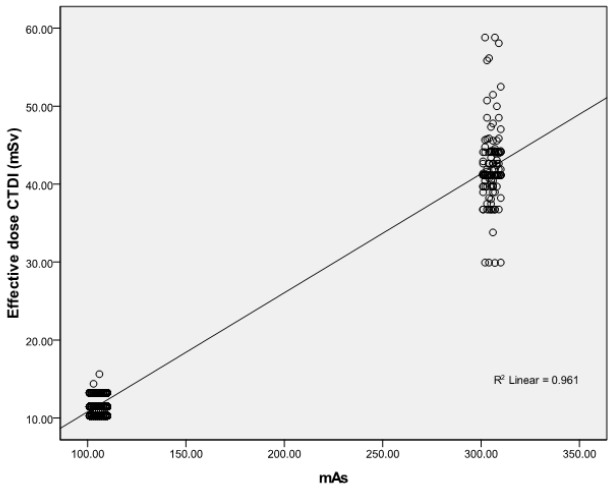

Figure 1: Scatterplot graph of effective dose derived from $CTDI_{vol}$ versus mAs. The graph shown a strong linear positive correlation between the effective dose and the mAs with a coefficient of determination of 0.961.

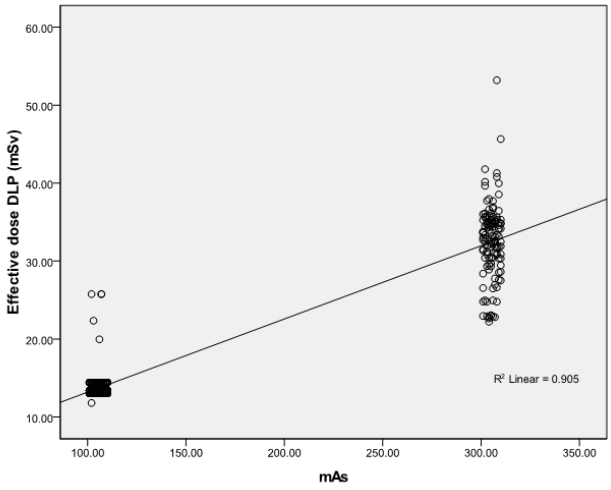

Figure 12: Scatterplot graph of effective dose derived from DLP versus mAs. The graph shown a strong linear positive correlation between the effective dose and the mAs with a coefficient of determination of 0.905.

were statistically significant. As illustrated in fig. 3 and 4, correlation analysis has shown that there is a strong linear negative relationship between selected pitch and the effective dose calculated from CTDIvol ($r = -.98$, $p < 0.01$) and DLP ($r = -.95$, $p < 0.01$). It proved that lowering the pitch value results in a higher effective dose delivered to the patient.

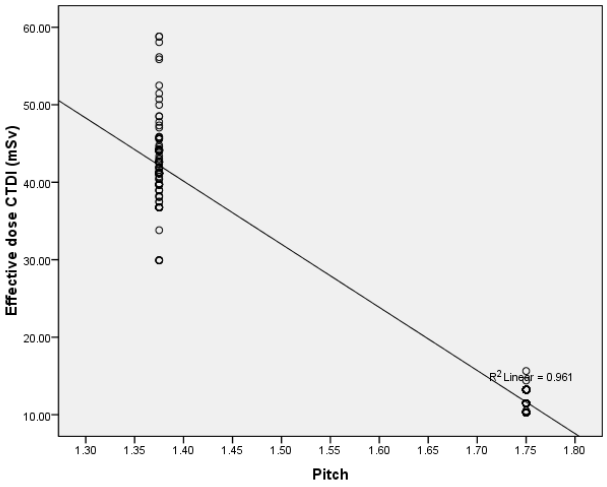

Figure 3: Scatterplot graph of effective dose derived from $CTDI_{vol}$ versus pitch value. The graph shown a strong linear negative correlation between the effective dose and the pitch with a coefficient of determination of 0.961.

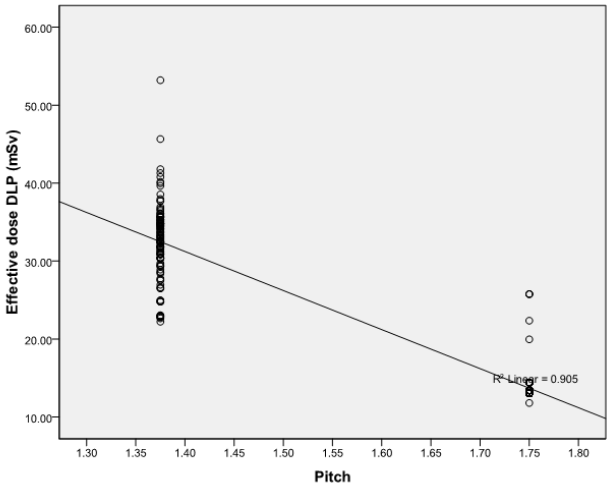

Figure 4: Scatterplot graph of effective dose derived from DLP versus pitch value. The graph shown a strong negative correlation between the pitch and the effective dose with a coefficient of determination of 0.905.

DISCUSSION

Due to its significant contribution to oncology imaging, hybrid PET/CT imaging favours effective patient management and plays a significant role in staging and assessing adjuvant and non-adjuvant therapies response in cancer patients (1,2). The patient distribution among the three hospitals under study denoted as H1, H2 and H3 were 38%, 36% and 25%, respectively. H1 recorded the highest number of patients because it is an oncology specialist centre where cancer staging is usually

assessed with WB PET/CT examination. This imaging modality is the preferred imaging diagnostic tool due to its anatomical and functional imaging ability in a single examination (10, 17). H2 on the other hand focused on medical tourism activities where a lot of patients from neighbouring countries such as Indonesia and Thailand came to seek oncology treatment.

Apart from that, the oncologist in H1 justified the type of examination to be performed based on the patient's medical management history. In H1, CT attenuation correction (CTAC) acquisition in WB ^{18}F-FDG PET/CT examinations was performed either with non-contrast (NC-CTAC) or high-quality diagnostic contrast-enhanced (CE-CTAC). Which protocol is used depends on the indication of the patient and the availability of a recent diagnostic CT scan examination. CE-CTAC of WB ^{18}F-FDG PET/CT was not justified in the patient who recently had done the diagnostic CT scan within three months. This diagnostic imaging chain pathway is corresponding to the study by Bockisch et al. in which it is stated that if the clinical oncology workup had recently done the contrast-enhanced diagnostic CT on a conventional CT system, it is tolerable to obtain only a low-dose CT or NC-CTAC as the integral acquisition of WB ^{18}F-FDG PET/CT examination (17, 18). The justification should be made on a case-by-case basis on which protocol should be implemented for CTAC acquisition of WB ^{18}F-FDG PET/CT examination to deflect double or over-exposure of patients (18).

In conjunction with a different type of examination, the present study has shown that the effective dose between NC-CTAC and CE-CTAC in WB ^{18}F-FDG PET/CT was significantly differed, as shown in Table I. The effective dose calculated from CTDIvol using Equation 1 showed that, when comparing the effective dose based on these two types of CTAC acquisitions, the CTDIvol dose descriptor showed that the radiation dose received by the patient from NC-CTAC was about 12mSv. However, when CE-CTAC is implemented as an integral part of AC acquisition in WB PET/CT examination, the patient received a 250% higher radiation dose (42.18 ± 4.94 mSv versus 11.63 ± 1.20 mSv). Besides, taking calculation into DLP is another dose descriptor, a statistically significant difference in effective dose (DLP) was notified, in which CE-CTAC delivered a 130% higher radiation dose as compared with NC-CTAC (32.48 ± 4.87 mSv versus 13.71 ± 1.22 mSv). On the other hand, there were statistically insignificant differences in the effective dose (CTDIvol and DLP) received by the patients who went through the NC-CTAC protocol between the three centres (Table II). It is justified that given the same scanning parameters influencing the radiation dose, as described in the methodology, the radiation is not dependent on the operator if they followed the pre-set protocol.

Substantial differences between CTDIvol and DLP were principally due to DLP that was independent of tissue attenuation coefficient. The reported DLP on the scanner console has not considered the patient weight and body surface area (8, 15, 19). The findings corresponded to a study done by Brix et al. in which diagnostic high-quality CTAC could yield higher patient doses principally due to the inclusion of critical organs such as the thyroid within the scan range (6). However, a bigger sample size study should be done to understand more regarding the radiation dose pattern since integrating high-quality diagnostic contrasted CT as part of CTAC acquisition of PET/CT imaging is new in the clinical setting.

Since scanning parameters influenced the radiation dose, there are few studies regarding the administration of contrast media for the attenuation correction acquisition component of PET/CT. It is worth studying the differences between NC-CTAC and CE-CTAC in terms of scanning protocols and the effect exerted on radiation dose.

Apart from that, the present study has shown that there were statistically no significant differences in scan length (mm) between the NC-CTAC and CE-CTAC, as shown in Table III. The scanning coverage needs to be synchronized with the PET emission frame setting. Modification in the scan length corresponding to the individual patient-by-patient body size may not be achievable at present PET/CT scanner. This limitation was due to the axial CT scan range set-up being solely in integer multiplies of the fixed axial field of view (FOV) of the PET system (6). All hospitals under study utilized the same method in which seven to nine PET frames were required to cater to whole-body imaging of coverage from vertex to mid-thigh. This had demanded about 900 to 1200 mm scan length for both NC-CTAC and CE-CTAC to enable fusion with PET emission scan. Since the scan length is not affected by how CTAC acquisition data is acquired, effective dose calculated from the dose descriptor of CTDIvol and DLP were independent of the scan length. The finding is congruent with the study by Khamwan et al. that found effective dose in WB ^{18}F-FDG PET/CT is more dependent on tube current and patient's body weight rather than the scan length (20).

The fundamental radiation theory is the main parameters determining the radiation dose are the x-ray voltage peak potential (kVp) and tube current-time (mAs) (21). The present study data was established with the examination done with a fixed tube potential of 120 kVp. A study by Huang et al. (9) even implemented 140 kVp as the scan protocol which subsequently delivered a 31.91 mSv effective dose for NC-CTAC, which is higher than the 12 mSv effective dose in the present study. The utilisation of high kVp is essential in CT scans to reduce the beam hardening effect. Even though it is proved that there is a room for adjusting the kVp setting as mentioned by Bernstine et al. (22), it is seldom practised, averting the possibility of producing

x-ray photons with low penetrating power which would result in the photons being absorbed by the tissues and subsequently reducing the numbers of photons flux onto the detectors. The phenomenon is particularly crucial in large-sized patients. Besides, the reduction of kVp increases the noise level on PET signals, leading to image degradation.

Apart from that, the tube current used was automated tube current modulation (ATCM) for NC-CTAC while CE-CTAC in H1 employed manual mA and was set patient-by-patient basis based on the scan length and attenuation measurement from the scout scan. The rationale for using manual mode for mAs in CE-CTAC performed at H1 was that the image produced by auto-mA mode was of poor quality, particularly in head and neck regions compared with CT scan images produced by conventional CT scanners. The inferior image quality does not satisfy the requirement of the radiologist. The study finding shows that mAs used for NC-CTAC were significantly different from CE-CTAC (with a mean of 155.48 ± 2.87 versus 305.43 ± 2.86), as tabulated in Table V. In this case, even though the amount of tube current applied was determined by the optimisation value of the scanner, the radiation dose produced was significantly higher than in auto-mA mode.

A previous study suggested that an effective way to reduce the radiation dose was to minimise the mAs (23). Besides, there were no basic physics restrictions on how to bring down the radiation dose from a spiral CT scan. However, reducing mAs faced a significant challenge, especially in PET/CT scanners. The challenge includes the requirement of the CT scanner to provide diagnostic CT images with optimum image quality to execute the detection of subtle diseases. A study by Huang et al. (9) implemented up to 300 mA for normal NC-CTAC WB ^{18}F-FDG PET/CT to produce good quality CTAC images, which is higher than the 110 mA in the present study. It is well known that even within the available range of CT techniques, it is possible to produce CT images that will bias the results of CTAC (22). Therefore, it is crucial to ensure that dose reduction methods might not trade off diagnostic capability and image quality.

In addition, Beyer et al. stressed that a diagnostic CT x-ray tube unable to operate at a very low tube current (mA) (24). This is because even a reduction in mA could reduce patient dose. It also caused reduced numbers of photon flux and resulted in detector artefacts due to limitations in the reconstruction algorithm. Bernstine et al. also emphasized the computation of attenuation coefficient in the CT component of PET/CT scanner might not be as excellent as in conventional CT, causing the introduction of a contrast agent to lead to significant artefacts in the attenuation correction data (22). This is because the structure with a strong contrast opacification in the CT scans may be assigned with a high Hounsfield Unit (HU) value and be deemed as bone by the attenuation correction algorithm, because of over reckoning of regional attenuation coefficient.

Apart from the scan length and tube current, the pitch value was another scan parameter that differs between NC-CTAC and CE-CTAC. Pitch defines how data is collected – whether data is overlapped, contiguous or gapped, which subsequently estimates the amount of data interpolation and image quality in the means of the distance the scanner couch travels per tube rotation. The pitch value of more than 1.5 would increase data interpolation, which subsequently reduced image quality due to the slice blooming effect (25-27). In the present study, NC-CTAC and CE-CTAC employed pitch of 1.750 and 1.375, respectively. Higher pitch in non-contrast CTAC was acceptable since the slightly inferior image quality did not undermine the purpose of anatomical localization and attenuation correction. The approach is validating studies that stated if the CT acquisition is meant only for attenuation correction and anatomical description, the diagnostic potential of the CT is not exploited (10, 22).

In addition, Table VI shows the correlations between pitch value and effective doses. The differences in the amount of radiation dose produced by both implemented pitches were statistically significant. Correlation analysis regarding the relationship between selected pitch value and effective dose delivered proved that the effective dose calculated from both CTDIvol and DLP had a strong negative relationship with the pitch value. Decreases in the pitch value resulted in increased image quality at the expense of increases in radiation dose produced. The findings were in good agreement with the fundamental of CT scans (25-28). Nevertheless, the likelihood to reduce the radiation dose through increased pitch value is impractical in CE-CTAC. The rationale was a significant increase in slice sensitivity profile and image unsharpness resulted by pitch higher than 1.5 decreased diagnostic value of CT images produced.

On top of that, apart from all the parameters discussed, the actual dose received by the patient should be higher than the presented value as the present study only calculates the effective dose from external which is produced by the CT component of the PET/CT system.

CONCLUSION

CE-CTAC delivered a higher radiation dose than NC-CTAC acquisition in WB ^{18}F-FDG PET/CT imaging. The scanning parameters that differ between protocols of NC-CTAC and CE-CTAC in the hospitals under study that contribute to high radiation dose were mAs and pitch, while differences in scan length exert no significant effect on the amount of radiation dose. Therefore, there was considerable room to reduce the CT effective dose, primarily when CT is not meant for diagnostic purposes.

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