Influence of X Ray Computed Tomography (CT) Exposure and Reconstruction Parameters on Positron Emission Tomography (PET) Quantitation

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Original research

Keywords: Positron-emission tomography, Tomography, X-Ray Computed, Positron Emission Tomography Computed Tomography

DOI: https://doi.org/10.21203/rs.3.rs-35526/v1

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Abstract

**Background:** The CT of PET CT provides diagnostic information, anatomic localisation and attenuation correction (AC). When only AC is required very low dose CT is desirable. CT Iterative reconstruction (IR) improves image quality with lower exposures however there is little data on very low dose IR CT for AC of PET. This work aims to assess the impact of CT exposure and reconstruction algorithm on PET voxel values.

**Method:** An anthropomorphic torso phantom was filled with physiologically typical [18]F concentrations in heart, liver and background compartments. A 17mm diameter “tumour” was included in the right lung. PET was acquired followed by 24 CT acquisitions with varying CT exposures (15-50mAs, 80 – 120kVp, pitch 0.671 - 0.828). Each CT was reconstructed twice using filtered back projection (FBP) or IR and these used for AC of PET. Regions of interest (ROIs) were drawn in liver, soft tissue and over “tumour” on each test reconstruction (TR) and compared with the reference reconstruction (RR), (50mAs, 120kVp, pitch 0.828, IR). Comparison of voxel values in each TR compared to the RR was undertaken using a paired t-test and by calculating which and what proportion of voxels in each TR differed by a quantitatively significant difference (QSD) from the corresponding RR voxel.

**Results:** TRs reconstructed using lower dose CTs underestimated mean and maximum ROI activity relative to the RR; greater with IR than FBP. Once CT dose index (CTDI) increased to 1 mGy the differences were less than QSD. On voxel analysis all TRs were significantly different to the RR (p <0.0001). TRs reconstructed at the lowest CT exposure with IR had 6% of voxels that differed by greater than the QSD. Differences were reduced with increasing CTDI and FBP reconstruction. Voxels which exceeded the QSD were spatially localised to regions of high activity, at interfaces between different attenuation and in areas of CT beam hardening.

**Conclusions:** Very low dose CT exposures are feasible for accurate PET AC. Scanner specific validation should be employed prior very low dose CT AC for PET reconstruction.

Background

Positron emission tomography (PET) is a routine imaging modality with wide clinical applications especially in oncology particularly with 2-fluoro-2-deoxyglucose (FDG). Currently, clinical PET scanners are combined with x-ray computed tomography (CT) scanners. The combined PET CT scanners have proved to be a revolution with the exquisite molecular imaging providing by PET being complemented by the CT which provides anatomic diagnostic information, anatomic localisation and an attenuation correction (AC) map [1, 2]. However, the CT component of PET CT examinations may not necessarily be required for all of these purposes in all examinations and X-ray exposure should be optimised for the indication(s) for which the CT component is being performed - higher exposures are required for diagnosis and much lower exposures may be used for generation of AC maps. While much lower
radiation exposures are needed to generate CT based AC maps, it is essential that the AC maps must remain accurate to enable accurate PET reconstruction and quantitation.

Traditionally, CT has been reconstructed with filtered back projection (FBP) techniques. More recently iterative reconstruction (IR) algorithms have been used for CT reconstruction which are reported to result in better noise reduction, improved image quality and lower radiation dose in a variety of situations (including CT coronary angiography, abdominal and thoracic imaging) [3]. The ability of IR to reduce radiation exposures while maintaining image quality for diagnostic CT raises the question about whether IR would also enable further reductions in the required exposures for generation of AC maps for PET reconstruction. While the reductions in CT exposure may be small for routine clinical situations, there are specific situations where minimising exposures from CT performed for AC would be especially beneficial when frequent serial PET scans are being performed such as for biodistribution and dosimetric studies for development of novel positron emitting radiopharmaceuticals or for respiratory or cardiac gated studies. In these circumstances even small reductions in radiation exposure may be cumulatively significant.

Therefore the aim of this work is two-fold - firstly to determine the CT acquisition parameters needed for generation of AC maps and secondly to determine if IR enables further reductions in radiation exposures while maintaining the accuracy of AC for PET reconstruction.

**Methods:**

**Phantom.**

The Data Spectrum anthropomorphic torso phantom was filled with physiologically typical [18]F FDG concentrations as was a 17 mm diameter spherical lesion in the left lung (the phantom was filled such that background had a mean standard uptake value (SUV) of 1.0, the heart mean SUV of 4.0, liver mean SUV of 2.5 and “tumour” mean SUV of 4.0. To simulate the impact of attenuation from a patient’s arms, lamb shanks were placed on either side of the phantom. An emission PET scan was performed on a Philips Ingenuity TF 128 PET scanner (Philips Medical Systems, Cleveland) (2.5 minutes per bed position for 3 bed positions) followed by consecutive CT acquisitions at 15, 30, 40 and 50mAs, 80, 100 and 120 kVp and pitch of 0.671 or 0.828, yielding a total of 24 CT acquisitions. Each of the CT acquisitions was then reconstructed with either FBP or IR (iDose level 3, Philips Medical System). This then yielded a total of 48 CT datasets which were then used to generate AC maps for reconstruction of the single PET acquisition. The reference PET dataset was reconstructed using the CT AC map derived from the CT acquisition acquired at 50 mAs, 120 kVp, pitch 0.671 and reconstructed with IR. PET reconstruction was performed using Philips Astonish TF, a list mode fully 3D iterative ordered subset expectation maximization algorithm with "Blob" basis function (3 iterations, 3 subsets, kernel width = 18.1cm, relaxation parameter = 1). PET data are corrected for decay, random coincidences (using the delayed window method), scatter (using the single scatter simulation approximation method) and point spread function effects. This was defined as the reference reconstruction (RR) as it is the current
institutional standard clinical protocol for an average patient, is recommended by the manufacturer and has been validated as quantitatively accurate based on previous phantom studies. All other PET datasets reconstructed using the other combinations of CT acquisition and reconstruction parameters for AC (and using the same PET reconstruction algorithm as above) are termed test reconstructions (TRs). The CT dose index (CTDI) for each CT acquisition was recorded.

Data analysis:

Region of interest analysis

Two-dimensional circular regions of interest (ROIs) were drawn on the soft tissue, liver, lung lesion and on soft tissue where there was evidence of significant beam hardening artefact and the mean, maximum and standard deviation (SD) of SUV determined for each of these regions. Values were compared to the values obtained from the reference PET construction and compared with CTDI.

Voxel analysis

Voxel based analysis was undertaken in R [4-6]. The RR and TR PET datasets were imported into R [7]. Initially voxel data was compared between the TRs and the RR using a paired t-test.

Each voxel in each TR was compared with the matching voxel in the RR and the difference between determined. To assess if the observed differences are potentially quantitatively and diagnostically significant, a quantitatively significant difference (QSD) was defined as one standard deviation of the mean of the ROI drawn over the liver (as used for the ROI analysis described above). For each TR the proportion of all voxels that differed by greater than the QSD from the corresponding voxel in the RR was calculated.

In order to determine if the voxels that differed by QSD were randomly or non-randomly distributed, a volumetric mask was created containing only those voxels in the test PET dataset that were significantly different from the matching voxel in the reference PET dataset. This volumetric mask was then overlaid on the reference PET dataset and representative orthogonal slices displayed [7].

Results:

Acquisitions and CTDI

The 24 different combinations of CT acquisition parameters together with CTDI for each are shown in Table 1.
Table 1
CT acquisition parameter combinations used (reference CT reconstruction shown in bold)

| Current (mAs) | Voltage (kVp) | Pitch | CTDI (mGy) |
|--------------|---------------|-------|------------|
| 15           | 80            | 0.671 | 0.3        |
| 15           | 80            | 0.828 | 0.3        |
| 15           | 100           | 0.671 | 0.5        |
| 15           | 100           | 0.828 | 0.5        |
| 15           | 120           | 0.671 | 0.6        |
| 15           | 120           | 0.828 | 0.6        |
| 25           | 80            | 0.671 | 0.8        |
| 25           | 80            | 0.828 | 0.8        |
| 25           | 100           | 0.671 | 0.9        |
| 25           | 100           | 0.828 | 0.9        |
| 25           | 120           | 0.671 | 1          |
| 25           | 120           | 0.828 | 1          |
| 40           | 80            | 0.671 | 1          |
| 40           | 80            | 0.828 | 1          |
| 40           | 100           | 0.671 | 1.6        |
| 40           | 100           | 0.828 | 1.6        |
| 40           | 120           | 0.671 | 1.6        |
| 40           | 120           | 0.828 | 1.6        |
| 50           | 80            | 0.671 | 2          |
| 50           | 80            | 0.828 | 2          |
| 50           | 100           | 0.671 | 2.6        |
| 50           | 100           | 0.828 | 2.6        |
| 50           | 120           | 0.671 | 3.3        |
| **50**       | **120**       | **0.828** | **3.3**    |

Region of interest analysis.
The region of interest analysis demonstrated that both mean SUV for liver and soft tissue were underestimated at low CT exposure parameters. However, when CT was reconstructed using FBP irrespective of the CT exposure parameters the mean SUV of ROIs in liver and soft tissue were within one standard deviation of the mean SUV of the RR. However, IR of the CT resulted in much greater underestimation of the mean SUV for liver and soft tissue which at low CT exposures was greater than one standard deviation of the mean SUV of the RR. For the lung lesion the maximum SUV was assessed as the maximum SUV is the most used quantitative parameter for lesional analysis in clinical practice and to avoid partial volume effects. This demonstrated a similar trend with only a slight underestimation of lesional maximum SUV on CT reconstructed with FBP at low CT exposure parameters but a greater underestimation of lesional maximum SUV on CT reconstructed with IR at low CT exposure parameters (Figure 1).

When compared with delivered radiation, there is concordant pattern with greater underestimation of SUV at low CTDI when the CT is reconstructed with IR than with FBP. At CTDIs greater than approximately 1 mGy the estimated SUV is similar regardless of reconstruction method (Figure 1).

**Voxel analysis**

On individual voxel analysis using a paired t-test, all TR's differed significantly from the RR (p < 0.0001).

Representative graphs of the difference between the SUV of each voxel in the TR compared to the RR relative to the voxel SUV in the RR are shown in Figure 2. These demonstrate three findings. Firstly that the greatest differences in voxel values are at the lowest CT exposures. Secondly, the differences are a systematic underestimation of voxel SUV in the test PET datasets (i.e. RR – TR is greater than 0), especially in voxels with higher SUV. Lastly, the difference is much greater with IR than with FBP.

The fraction of all voxels that differed by greater than the QSD for each TR is shown in Figure 3. This demonstrates that with small increases in exposure and the use of FBP there is a rapid reduction in the number of voxels in the TR that exceed QSD. It also highlights that beam voltages of 80kVp are insufficient to generate quantitatively accurate CT AC maps despite increasing beam current.

Spatial assessment of voxel differences is shown in Figure 4. This demonstrates that those voxels where there is a QSD between TR and RR are spatially localised especially in areas of high activity, where there are changes in CT density (e.g. air to soft tissue interfaces), and in regions of prominent CT artefacts (such as associated with CT beam hardening in line with the spine and adjacent “limbs”).

**Discussion**

PET is a widely adopted molecular imaging modality, being highly sensitive, inherently quantitative and able to image a wide range of molecular processes. It has important established clinical and research applications. In oncology, particularly using 2-fluoro-2-deoxyglucose (FDG) it has proven application for
diagnosis, staging, treatment response and detection of relapse which results in significant changes in disease staging, treatment modality and intent [8, 9]. In addition to FDG there are now a wide range of other PET radiopharmaceuticals in clinical and research use. Quantitation in PET is of particular importance as there is increasing evidence that quantitative parameters predict outcome [10] and is essential for biodistribution and dosimetry calculations for both clinical and research applications [11, 12].

Fundamental to high-quality, highly sensitive and quantitative PET imaging is accurate AC. Initially, AC for PET was performed with sealed line sources [13], however approximately 20 years ago Beyer and colleagues described development of the first combined PET CT scanner, using the CT component for generation of attenuation maps for PET reconstruction [1]. Combined PET CT is now widely accepted as superior to PET alone [2] and is now standard of care for PET imaging. In addition to providing AC, the CT component of the PET CT study may be used for anatomic localisation or diagnosis. Current practice guidelines recommend selecting CT acquisition parameters depending on the intended use, with recommendations for reduced voltage and/or current when the CT is used for AC only and with higher exposures required when CT is also used for diagnosis [14]. In most clinical and research purposes, in addition to AC, the CT component of a PET/CT study will also be used for anatomic localisation or diagnosis. However, in select circumstances the CT component may only be required for AC, particularly when multiple repeated attenuation correction CTs are required over a short period of time. One example of this is for gated studies where an AC CT is required for each phase of the gated study. Another situation where CT may only be performed for AC is early phase human biodistribution and dosimetry studies where PET/CT scans are performed repeatedly in the same subject over a short timeframe, typically hours [12, 15]. In this setting, accurate AC maps are required for accurate quantitation, however in the short interval between scans no anatomic change would be expected and thus the CT component would serve no other purpose. In these settings, the repeated acquisition of CT may contribute more to the overall patient radiation exposure than the injected radiopharmaceutical, and thus it is essential that radiation exposure from the CT component be minimised according to the ALARA principal. This study was undertaken to establish the minimum CT exposures and optimise reconstruction parameters for accurate biodistribution and dosimetric assessment in preparation for a first in human study of a novel PET radiopharmaceutical for imaging cell death [16].

There is limited data regarding optimisation of the CT component of the PET CT acquisition. Recently, Bertolino and colleagues undertook a systematic review of CT protocols performed within a PET CT scan. Their rationale for undertaking this was the observation that unlike the PET acquisition, there is a lack of robust scientific literature regarding the optimisation of CT protocols used in PET CT. They concluded that dose is heavily dependent on the protocol intent (AC, anatomic localisation or diagnosis). They did not conclude on specific parameters for CT acquisition within a PET CT rather suggested periodic quality control considering technological advances [17]. There is very little data regarding dose optimisation of CT performed for AC. Faye and colleagues used five different anthropomorphic phantoms (newborn to medium adult) to assess the impact of acquisition parameters on CT image noise and adequacy of PET AC. They reported that significant dose reductions could be achieved, reporting that in paediatric patients
adequate AC could be obtained with very low dose and with only an increase in tube voltages required to prevent under correction in adults. There are several differences between this previous study and this study. Firstly, Faye and colleagues assessed the adequacy of AC for PET quantitation qualitatively by visual inspection of the images – no quantitative analysis was performed on the reconstructed PET images (although this was undertaken on the CT AC map). Secondly, the study was performed on a PET CT scanner without capability for IR of CT [18].

Brady and Shulkin undertook a phantom and retrospective patient study to assess ultralow dose CT protocols reconstructed using adaptive statistical iterative reconstruction (ASIR) on PET and CT image quality and quantitation. With this protocol they reported no change in SUV, background uniformity or spatial resolution of PET with up to 90% dose reduction and that there was an average deviation of only 2% for all cylindrical/spherical target lesions. In contrast to the current study, regions of interest were not considered outside of the target lesion (beyond background uniformity) and the scanner was from a different manufacturer with a different IR algorithm [19].

The paucity of published literature, and the absence of any specific data related to equipment at this institution or the specific application of quantitative imaging for first in human biodistribution, radiation dosimetry calculation and imaging, was the impetus for undertaking this study. With the intent of doing whole-body biodistribution studies, accurate quantitation at all sites (not just lesional sites) is essential and hence the region of interest analysis assessed both lesional and non-lesional regions. Voxel analysis of the reconstructed PET datasets were similarly undertaken to provide the broadest insight into subtle quantitative changes throughout the study.

However, determining what level of change is significant is more challenging and is dependent on many factors including technical, biologic and physical [20]. In this study which selected a change equivalent to 1 SD of SUV measured in the ROI within the liver as significant, which equates to a change in SUV of 0.09 or ~4% of the mean SUV of the liver. It is acknowledged that this is a small change and in isolation would not be regarded as significant. However, to enable accurate comparison between studies whether performed for clinical indications (such as for assessment of treatment response following commencement of therapy) or for biodistribution and dosimetry calculations, Boellard described a wide range of factors which can affect PET quantification and stresses the importance of standardisation to minimise variability and improve accuracy of quantification. In particular, Boellard identified reconstruction parameters has a potential source of variability of up to 30% [20]. In defining the PERCIST 1.0 criteria, Wahl and colleagues use the SD of uptake within the liver in the formula for calculations both before and following treatment, and in addition state that been liver SUV should generally be within 0.3 from study to study and much of this variability will be accounted for by biologic factors. Hence, an SUV change of 0.09 is approximately 30% of the expected interstudy reproducibility of mean liver uptake [21].

In CT scans performed for diagnosis, IR has been reported to result in improved image quality while reducing CT dose, however unexpectedly, it was observed that at the lower CT exposures IR of the CT resulted in greater underestimation of activity compared to FBP CT reconstruction. This is contradictory
to that observed by Brady and Shulkin [19]. This is likely due to differences in the IR algorithms and subsequent generation of segmented CT AC maps used in that study and in the current study, and highlights the need for periodic quality control audit specific for each scanner as suggested by Bertolini and colleagues [17].

In conclusion, this study demonstrates the impact of CT acquisition parameters and reconstruction algorithms on AC for PET reconstruction and identifies appropriate parameters and algorithms to minimise exposure when CT is performed only for AC of PET studies on the Philips Ingenuity TF scanner. More generally it demonstrates a method for assessment of the impact of CT acquisition parameters and reconstruction algorithms on quantitative accuracy of PET reconstructions that is broadly applicable to all PET CT scanners to enable scanner specific CT dose optimisation.

**Abbreviations**

| Abbreviation | Full Term                     |
|--------------|-------------------------------|
| CT           | X-ray computed tomography    |
| PET          | Positron emission tomography  |
| AC           | Attenuation correction        |
| FBP          | Filtered back projection      |
| IR           | Iterative reconstruction      |
| TR           | Test reconstruction           |
| RR           | Reference reconstruction      |
| QSD          | Quantitatively significant difference |
| ROI          | Region of interest            |
| CTDI         | CT dose index                 |
| SD           | Standard deviation            |

**Declarations**

_Ethics approval and consent to participate:_

Not applicable.

_Consent for publication:_

Not applicable.

_Availability of data and material:_


The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Funding:**

Not applicable.

**Authors’ contributions:**

IH: Study concept, execution, R data analysis and manuscript preparation; CR: data acquisition and region and analysis; TH: study concept and design, data acquisition and analysis; MH: study concept and design, data acquisition and analysis; BM: study concept and design and data analysis.

**Acknowledgements:**

Nil.

**Competing interests:**

The authors declare that they have no competing interests.

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Figures
Figure 1

Mean SUV of liver (a), soft tissue (c), soft tissue in beam hardening region (e) and maximum SUV of the lung lesion (g) for each RR. The values from the RR are indicated by the dotted black line, and 1 standard deviation below the mean of the RR SUV is indicated by the dotted grey line (not applicable for the maximum SUV of the lung lesion). Mean SUV of liver (b), soft tissue (d), soft tissue in beam hardening region (f) and maximum SUV of the lung lesion (h) for each CT test reconstruction relative to CTDI. Shaded areas indicate confidence limits based on locally weighted regression fitting [22].
Figure 2

Graphs of voxel SUV differences between TRs and RR for individual voxels plotted against RR voxel SUV for 3 representative CT acquisition parameter combinations for low (CTDI 0.3 mGy) (A,B), medium (CTDI 1.0 mGy) (C,D) and high (CTDI 3.3 mGy) (E,F) X-ray exposure. CT reconstructed with filtered back projection (A,C,E) and iteratively (B,D,F). The green line is the linear regression fit for difference against reference value, and the blue line is the line of zero difference.
Figure 3

Proportion of voxels in TRs that differed from the RR by greater than QSD.
Figure 4

Representative axial, coronal and sagittal images of the phantom for 3 representative CT acquisition parameter combinations for low (CTDI 0.3 mGy) (A,B), medium (CTDI 1.0 mGy) (C,D) and high (CTDI 3.3 mGy) (E,F) X-ray exposure. CT reconstructed with FBP (A, C, E) and iteratively (B, D, F). The grayscale images are from the TR reconstruction (scale SUV 0 – 4.5). The red overlay are those voxels in the TR that differ by greater than the QSD from the RR.