J of Nuclear Medicine Technology, first published online November 8, 2021 as doi:10.2967/jnmt.121.262943

Determining the minimal required ultra-low dose CT for reliable attenuation correction of ^{18}F-FDG PET-CT: a phantom study

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Abstract

To investigate minimal required sub milli-Sievert (mSv) ultra-low dose CT and corresponding tube current and voltage for reliable attenuation correction and semi- quantitation in ^{18}F-FDG PET-CT in an effort for radiation dose reduction.

Method

We performed a PET-CT investigational study using a NEMA torso phantom containing six spheres (diameter: 10, 13, 17, 22, 28, 37 mm) filled with a fixed concentration of 60 kBq/ml and a background of 15 kBq/ml of ^{18}F-FDG. Two sets of PET images, separated by 2 hours, were acquired for 3 minutes in a single bed position using 3-D mode with and without time-of-flight in a GE D-690 scanner. Several sets of CT images were acquired for attenuation correction with different combinations of tube voltage (80, 100, 120 kVp) and effective mAs (tube current-time product divided by pitch), using the maximum beam collimation (64 x 0.625 mm). The lowest CT acquisition technique available on this scanner is 10 mA, 0.4 s and 1.375 for the tube current, tube rotation time and pitch, respectively. The CT radiation dose was estimated based on the computed tomography dose index volume ($CTDI_{vol}$) measurements performed following the standard methodology and the Imaging Performance Assessment of CT Scanners (ImPACT) calculator. Each of the CT techniques was used for attenuation correction to the same PET acquisition, using ordered-subset expectation maximum (OSEM) algorithm with 24 subsets and 2 iterations. The maximal and average radioactivity (kBq/ml) and standardized uptake values (SUV) of the spheres were measured. The minimal ultra-low dose CT for attenuation correction was determined by reproducible SUV measurements (±10%) compared to our reference CT protocol of 100 kVp and 80 mA for 0.5 s rotation.

Results

The minimal ultra-low dose of CT for reproducible quantification in all spheres (<10% relative

difference) was determined to be 0.3 mSv for a combination of 100 kVp and 10 mA at 0.5 s rotation, 0.984 helical pitch (0.26 mGy measured CTDIvol) . Based on these results we could confidently determine the CT parameters for reliable attenuation correction of PET images while significantly reducing the associated radiation dose.

Conclusion

Our phantom study provided guidance in using ultra-low dose CT for precise attenuation correction and semi-quantification of ^{18}F-FDG PET imaging, which can further reduce CT dose and radiation exposure to patients in clinical PET-CT studies.

Clinical application

Based on the data, we can further reduce the radiation dose to sub-mSv using an ultra-low dose CT protocol for reliable attenuation correction in clinical ^{18}F-FDG PET-CT studies.

INTRODUCTION:

Recent evidence from a retrospective large cohort study of over 178,600 United Kingdom residents with radiation exposure from computed tomography (CT) scans in childhood assessed a relative risk of 3.18 for leukemia with a cumulative dose of >30 mGy, obtainable from as few as 5-10 head CT scans in patients under 15 years of age, and a relative risk of 2.82 for brain cancer with a cumulative dose of 50-74 mGy, obtainable from as few as 2-3 head CT scans, as compared to a cumulative dose of <5 mGy (*1*). In a study of 680,000 Australians exposed to CT scans in childhood and adolescence, Mathews et al reported an incidence rate ratio of 1.24 for all cancers with an observed dose-response relation of 0.16 per additional CT scan using an estimated average effective radiation dose of 4.5 mSv per scan (*2*). Therefore, the risk of cumulative radiation exposure from medical imaging could be substantial, especially for pediatric patients.

We recently published the results of a phantom study indicating the minimal radioactivity concentration for reproducible maximal standardized uptake value (SUVmax) (±10%) quantification to be 1.8 kBq/ml for 10 minutes, 3.7 kBq/ml for 3-5 minutes, 7.9 kBq/ml for 2 minutes, and 17.4 kBq/ml for 1 minute acquisition with reference standards at 10 min acquisition (*3*). In light of increased efforts to achieve submillisievert (sub-mSv) CT studies, iterative reconstruction techniques including adaptive statistical iterative reconstruction (ASIR from GE Healthcare) and model-based iterative reconstruction (MBIR or Veo from others) have been employed to maintain image quality. Not without controversies (*4*,*5*), favorable reports have been published in coronary CT angiography (*4-7*), chest CT (*8*) for pulmonary embolism (*9*), urinary tract stone (*10*), and CT colonography (*11*,*12*). Alternatively, dose reduction by sparse-sampled computed tomography (*13*) was achieved in 10 patients by acquiring images at only 25% of the angular projections with subsequent reconstruction of the image data using an iterative algorithm. The authors reported no significant differences in detection of sub-centimeter lung lesions between images reconstructed from standard dose filtered back projection, sub-mSv filtered back projection, and sub-mSv iterative reconstruction, with equal confidence in reporting using the sub-mSv iterative reconstruction technique. The scans were reported to be 0.25 mSv or only one-tenth of the standard dose.

While these computer algorithms may restore image quality for qualitative assessment, we are concerned in how ultra-low counts in submillisievert CT studies can affect the standard uptake values (SUVs), if they are to be utilized for attenuation correction. The reproducibility of SUVs, a semi-quantitative parameter widely used in clinical positron emission tomography (PET) scans, is essential to assess aggressiveness of disease and response of disease to treatments in comparison studies. Since these algorithms are used during image reconstruction, the precision in SUVs is not expected to improve with the paucity of counts, unless quantitation software is modified. Souvatzoglou et al (*14*) reported only a moderate correlation between the mean values in all segments using low-dose (LDCT), ultra-low-dose (ULDCT) and slow CT (SCT) for attenuation correction in 27 cardiac PET/CT scans with no differences in scoring of qualitative assessment in the 3 groups. Xia et al (*15*) investigated the feasibility of using ultra-low dose CT for attenuation correction to reduce the additional radiation burden in respiratory motion compensation. We pursued basic measurements using a phantom over a wide range of CT attenuation scan settings in search of a minimal radiation dose threshold, below which SUV determination may not be reliable.

Methods and materials:

A hybrid PET-CT General Electric (GE) Discovery 690 (D-690) scanner was used for the experiment (GE Healthcare). GE D690 is equipped with a lutetium-yttrium-orthosilicate (LYSO) detector and a 64-slice CT scanner. GE D-690 scanner has a detection block of 54 (9 x 6) of individual LYSO crystals (dimensions of 4.2 x 6.3 x 25 mm^3), coupled to a single squared photomultiplier tube with 4 anodes. The D-690 consists of 24 rings of detectors (total 13824 LYSO crystals) for an axial field of view (FOV) of 157 mm. The transaxial FOV is 700 mm. The D-690 uses a low energy threshold of 425 keV and a coincidence time window of 4.9 ns. The D-690 operates in 3D mode only. The CT of D-690 is LightSpeed VCT with 912 channels x 64 rows, which allows full 360 degree rotation scans with variable time ranging from 0.35 to 2 sec and reconstructed slice thickness of 0.625 mm, 1.25 mm, 2.5 mm, 5 mm and 10 mm for the maximum fan beam collimation of 40 mm.

We acquired PET-CT images using a National Electrical Manufacturers Association (NEMA) International Electrotechnical Commission (IEC) Body Phantom Set™ (Data Spectrum Corporation, Hillsborough, NC) (Figure 1), containing 6 hollow spheres (diameter: 10, 13, 17, 22, 28, 37 mm) filled with 60 kBq/ml in a background of 15 kBq/ml (a target to background ratio 4:1) at the beginning (Series 1) and the end (Series 2) of a two-hour time interval of the radioactive decay. PET images were acquired for 3 minutes in a single bed position in list mode using ordered-subset expectation maximum (OSEM) algorithm with 24 subsets and 2 iterations with a Gaussian 2-mm filter using an AW workstation (GE Healthcare) equipped with version 4.5 software. Multiple CT images were acquired for attenuation correction using different combinations of tube voltage (80, 100, 120 kVp) and effective tube current-time product mAs, at maximum beam collimation. The available settings to achieve the lowest effective dose were 10 mA, 0.4 s rotation, and a pitch of 1.375. The CT images were reconstructed using conventional filtered back projection. The GE adaptive statistical iterative reconstruction (ASIR) software for CT dose reduction was not available in our PET-CT scanner at the time of this study.

The radioactivity of the spheres with both maximal and average standardized uptake values (SUVmax and SUVave) were measured by applying volume of interests (VOI) of spheres with a threshold 41% of maximal value in serial PET images using a GE Advanced Workstation. We co-registered CT images and adjusted the size of VOI accordingly to make sure all VOIs were placed correctly. The SUV computation was derived from the radioactivity concentration (kBq/ml) divided by total administered radioactivity within the phantom (kBq) and normalized to the total weight of the phantom. The variability of the SUV measurements in each sphere from the attenuation corrected PET images using CT images with various combination of tube current and voltage was calculated against the value in each sphere obtained using our standard clinical acquisition setting (100 kVp, 80 mA, 0.5 s rotation and 0.984 helical pitch) as the reference. A deviation of SUV (±10%) in comparison with reference standard is considered acceptable in accordance to the test-retest variability of 20% for ^{18}F-FDG PET studies. Radiation dose estimation for CT scans was based on the computed tomography dose index ($CTDI_{vol}$) measured using the standard methodology (*16*) and the Imaging Performance Assessment of CT Scanners (ImPACT) CT Patient Dosimetry Calculator, version 1.0.4 (*17*). The ImPACT CT dosimetry calculator is a computer software package that calculates organ and effective doses from CT examinations and makes use of the National Radiological Protection Board (NRPB) Monte Carlo published dose data sets (*18*). The Monte Carlo dose data provide normalized organ dose data for irradiation of a mathematical anthropomorphic phantom with a range of CT scanners, which are all normalized to an isocenter air dose in the absence of any phantom. Since the particular output of the CT scanner in our PET/CT system is not included in the NRPB database, we selected from the database the model of our scanner (GE LightSpeed VCT) and manually input (the software provides this option) the measured $CTDI_{vol}$ values for each individual CT attenuation scan to properly scale the normalized organ doses.

Results:

We performed visual assessments first for all the PET and CT images of the phantom and spheres (Figure 1). We were able to identify the spheres clearly, including the smallest at 10 mm, in all the attenuation-corrected PET images with various CT settings, even at the lowest dose technique after 2 hours of radioactive decay. The detectability of PET was not significantly impacted by low dose CT setting (Figure 1) or low radioactivity of ^{18}F-FDG. However, we were not able to clearly delineate the spheres in CT images at the lower doses (Figure 1 bottom three rows).

We also measured both SUVmax and SUVave within the spheres of the phantom from the attenuation-corrected PET images using the CT images with various combinations of kVp and mAs (Figure 1). We found overall good consistency in SUVmax and SUVave measurements from attenuation-corrected PET images over a range of effective mAs (10-600 mA, 0.4-0.5 s rotation and 0.984 pitch) at 120 kVp (Figures 2A and 3A) and 100 kVp (Figures 2B and 3B). We also found good consistency in SUVmax and SUVave (±10%) measurements over the range of 30-160 mA with 0.5 s and 0.984 pitch at 80 kVp, below which we found a notable reduction (>10%) of SUVmax and SUVave at 10-20 mA, 0.5 s, 0.984 pitch and 10 mA, 0.4 s, 1.375 pitch at 80 kVp (last three sets of measurement points on Figures 2C and 3C). We repeated the PET and CT acquisition of the phantom after 2 hours of radioactive decay and found good reproducibility (data not shown).

We concluded that the minimum required radiation dose of the helical CT attenuation scan (0.984 pitch) for precise quantification in all spheres (±10%) was determined by the combination of 100 kVp, 10 mA, 0.5 s, 0.984 pitch with a consequent 0.26 mGy measured $CTDI_{vol}$ and 0.3 mSv estimated effective dose (Table 1).

Discussion

Our phantom study explored lower limits within the sub-millisievert realm of ultra-low dose CT used for attenuation correction required for reproducible semi-quantification in ^{18}F-FDG PET imaging. We confirmed that the SUV measurements from the attenuation- corrected PET were very consistent, even at very low dose settings of the CT. Therefore, we may confidently further reduce the current CT dose in the routine clinical PET-CT studies without compromising the SUV measurements. One important clinical application is to reduce the CT technique in pediatric patients, as they are most susceptible for potential harm from unnecessary radiation exposure, although young and all adults can benefit from reduction in accumulated radiation dose.

The adequacy of CT-based attenuation correction for pediatric PET was conducted using several phantoms previously (*19*). The study suggested that adequate attenuation correction can be obtained with very-low-dose CT (80 kVp, 5 mAs, 1.5:1 pitch) for pediatric patients, and such correction can lead to a 100-fold dose reduction relative to diagnostic CT (*19*). Our current study also demonstrated the adequacy of CT-based attenuation correction with low dose CT at the setting of 80 kVp, 15 mAs (30 mA with 0.5 s), 0.984 pitch, but we did notice >10% reduction in SUV measurements at lower dose CT settings, and noticeable degradation of the image quality impacting the anatomical localization. The introduction of new iterative reconstruction algorithms in CT might allow further reduction in the CT radiation dose settings while maintaining the image quality for anatomical localization. However, detailed quantitative image quality investigations using appropriate phantoms are needed to validate its feasibility. Weight-based, low-dose pediatric whole-body PET/CT protocols were proposed by the group at Seattle Children's Hospital (*20*). They used weight-based adjusted ^{18}F-FDG dose for PET and age-based categorical for CT settings. The customized low dose protocols could potentially reduce 20-

50% of radiation dose from CT alone, while maintaining the diagnostic quality (*20*).

At the time this study was conducted, the standard CT settings in the GE D690 at Yale-New Haven Hospital were 80 mA, 0.5 s rotation time, 0.984 pitch and 100 kVp for standard adult with body weight of 70 kg and 80 kVp for the pediatric protocol., 2.7 mSv and 1.4 mSv estimated effective doses, respectively. The CT images were reconstructed with the conventional filtered back projection algorithm, providing satisfactory imaging quality for anatomical localization.

Based on the results of this study, we could confidently reduce the radiation dose to sub-mSv using an ultra-low dose CT protocol for reliable attenuation correction and anatomical localization in clinical ^{18}F-FDG PET-CT studies.

Limitation and future direction

Please note we focused only on the impact of PET SUV measures from ultra-low dose CT in current study. No image quality analysis was performed because this was beyond the purpose of this study. However, the impact of the radiation dose reduction on the image quality should be assessed if both reliable attenuation correction and accurate anatomical information extraction are expected from CT images of a PET-CT study. The new iterative reconstruction algorithms available in CT should be further investigated to improve the image quality of the ultra-low dose CT images to provide acceptable anatomical information in PET-CT studies.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS:

Question: To investigate minimal required sub mSv ultra-low dose CT and corresponding tube current and voltage for reliable attenuation correction and semi- quantitation in ^{18}F-FDG PET-CT in an effort for radiation dose reduction.

Pertinent Findings: The minimal ultra-low dose of CT for reproducible quantification in all spheres (<10% relative difference) was determined to be 0.3 mSv for a combination of 100 kVp and 10 mA at 0.5 s rotation, 0.984 helical pitch (0.26 mGy measured CTDIvol). Our phantom study provided guidance in using ultra-low dose CT for precise attenuation correction and semi-quantification of ^{18}F-FDG PET imaging.

Implications for Patient Care: Based on the data, we can further reduce the radiation dose to sub-mSv using an ultra-low dose CT protocol for reliable attenuation correction in clinical ^{18}F-FDG PET-CT studies.

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Table 1: Estimated CT doses (mGy) and effective doses (mSv) from various combinations of kVp and mA.

kVp	**mA**	**CTDIvol (mGy)**	**mSv**
120	600	19.61	32.4
120	300	10.18	16.2
120	80	2.63	4.3
120	40	1.32	2.2
120	30	0.99	1.6
120	20	0.66	1.1
120	10	0.33	0.5
100	600	15.25	20.6
100	300	7.68	10.3
100	80	2.06	2.7
100	40	1.03	1.4
100	30	0.77	1.0
100	20	0.55	0.7
100	10	0.26	0.3
80	160	1.73	2.7
80	80	0.87	1.4
80	30	0.43	0.5
80	20	0.22	0.3
80	10	0.11	0.2
80	10*	0.08	0.1

All 120 kVp CT scans use 0.4s rotation time and pitch of 0.984. All 100 and 80 kVp CT scans use 0.5s rotation time and pitch of 0.984, except for 0.4 s rotation time and pitch of 1.375 where noted by (*).

Figure 1: PET-CT images of the phantom. The representative images of PET (AC), CT , and PET-CT for the phantom and spheres at various CT settings. The CT setting of the top two rows are reference to the regular adult imaging protocol and pediatric imaging protocol respectively at YNHH. In the bottom three rows, the delineation of the spheres was not clear on CT images at the lower radiation dose settings.

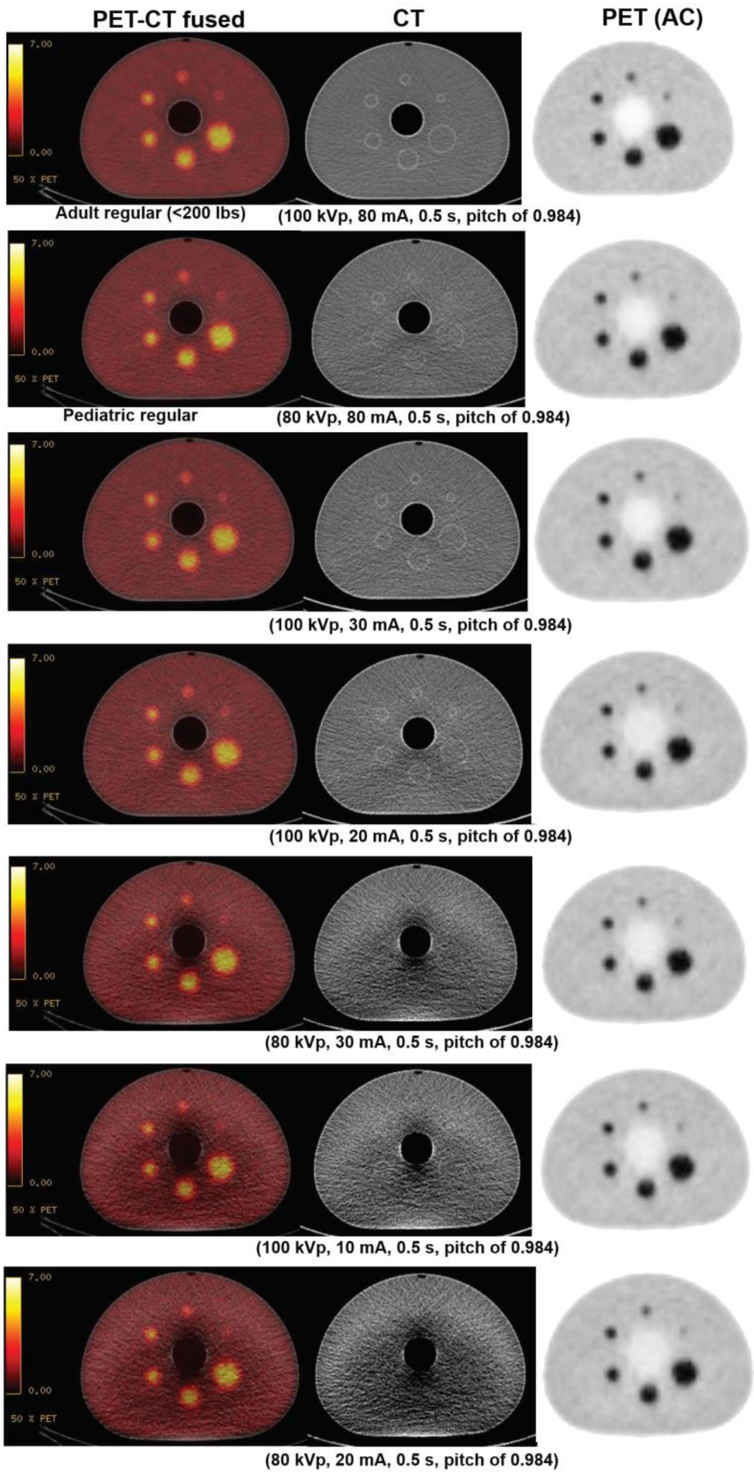


Figure 2: Impact on SUVmax from attenuation correction with various CT settings (a) 120 kVp (b) 100 kVp (c) 80 kVp. The attenuation-corrected SUVmax measures are overall consistent for all the spheres with CT settings of (a) 120 kVp and 10-600 mA (b) 100 kVp and 10-600 mA (c) 80 kVp and 30-160 mA. The attenuation-corrected SUVmax measures are slightly decreased (>10%) for some spheres with CT settings of (c) 80 kVp and 10-20 mA.

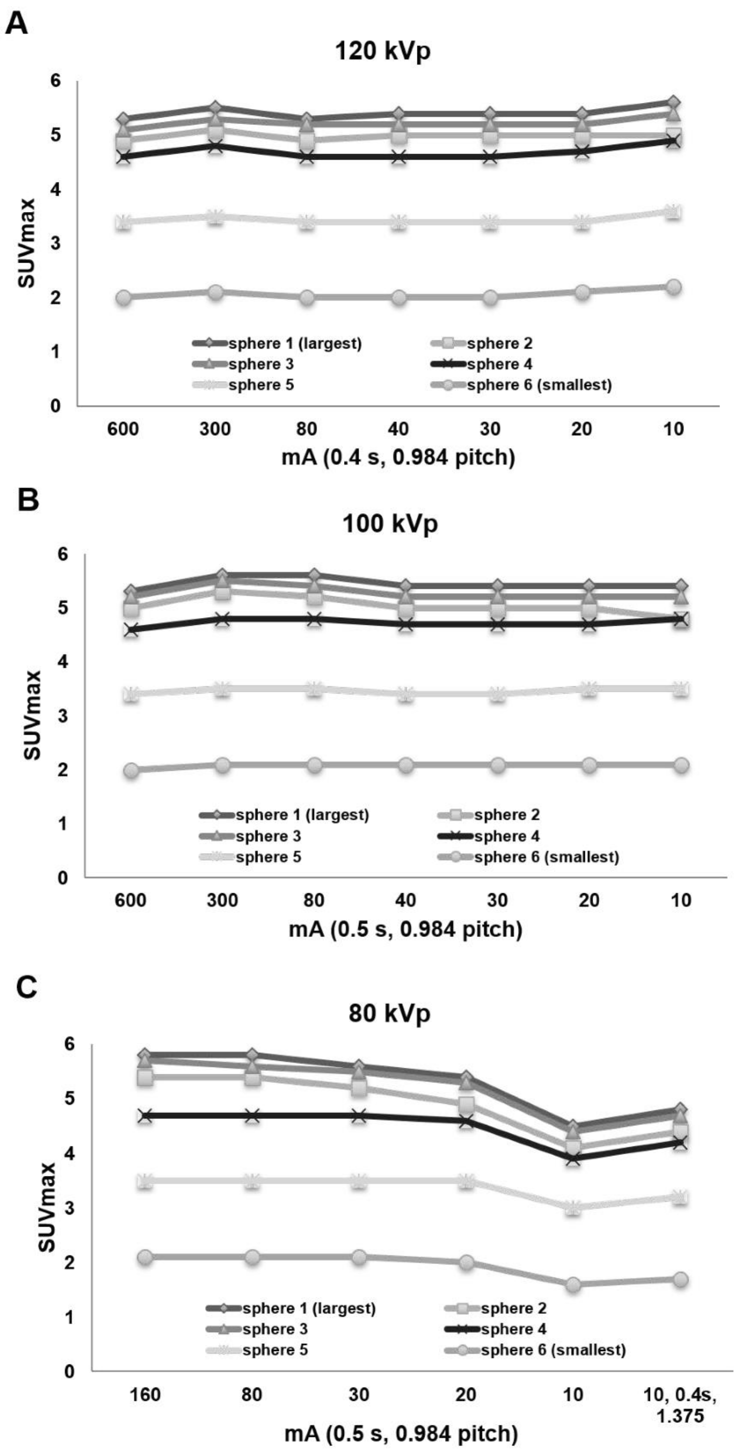
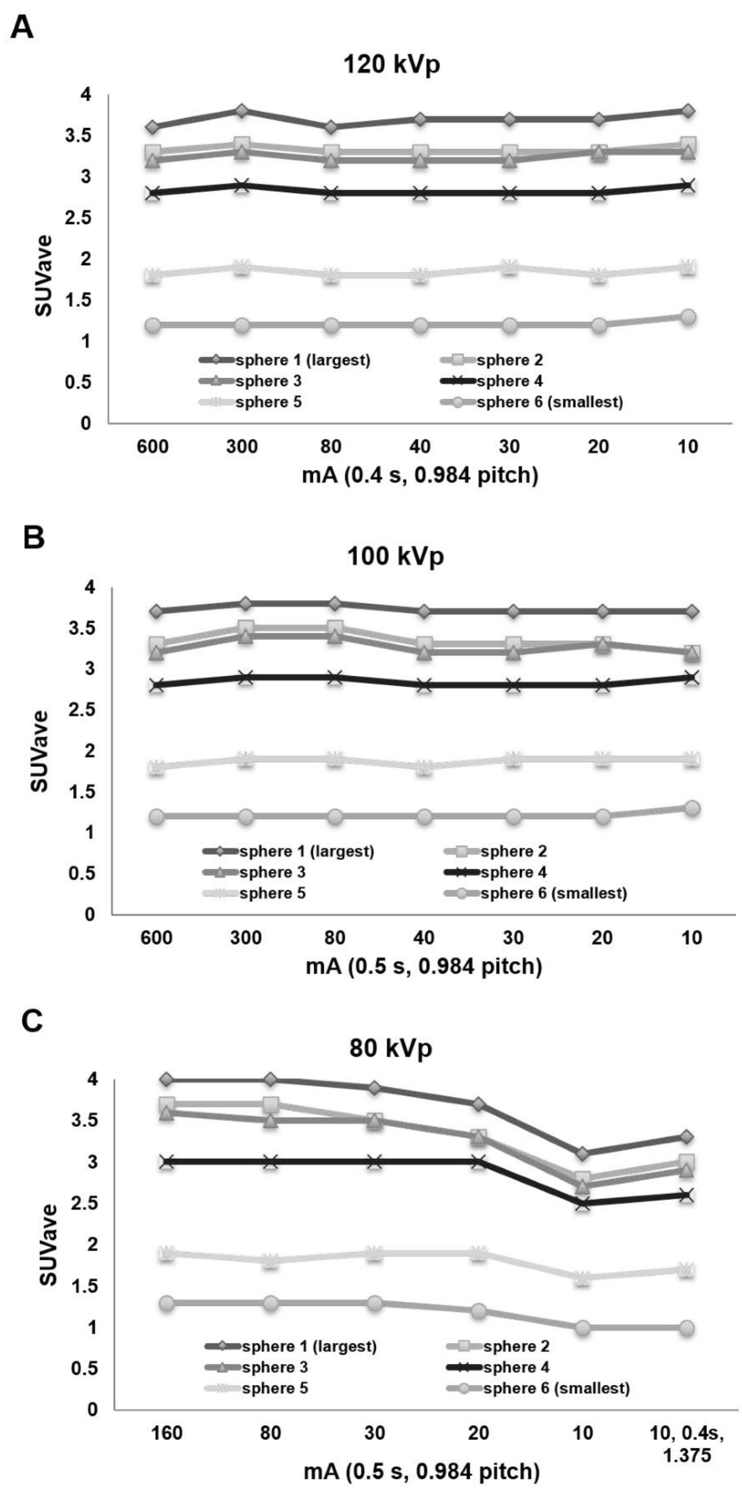
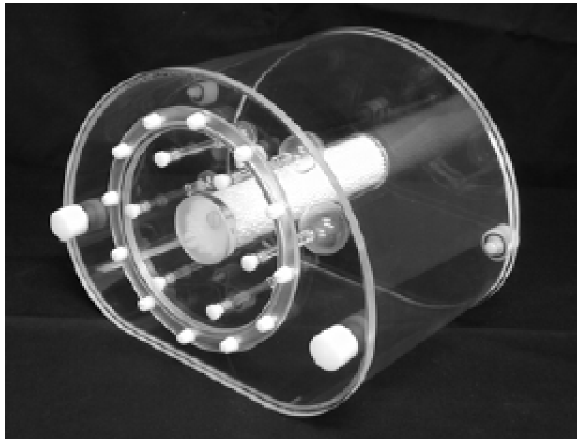


Figure 3: Impact on SUVave from attenuation correction with various CT settings (a) 120 kVp (b) 100 kVp (c) 80 kVp. The attenuation-corrected SUVave measures are overall consistent for all the spheres with CT settings of (a) 120 kVp and 10-600 mA (b) 100 kVp and 10-600 mA (c) 80 kVp and 30-160 mA. The attenuation-corrected SUVave measures are slightly decreased (>10%) for some spheres with CT settings of (c) 80 kVp and 10-20 mA.

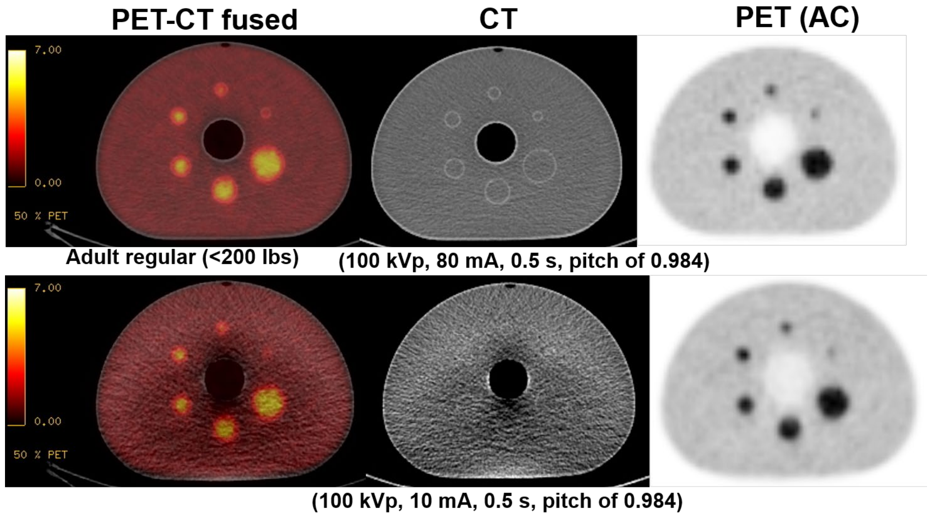


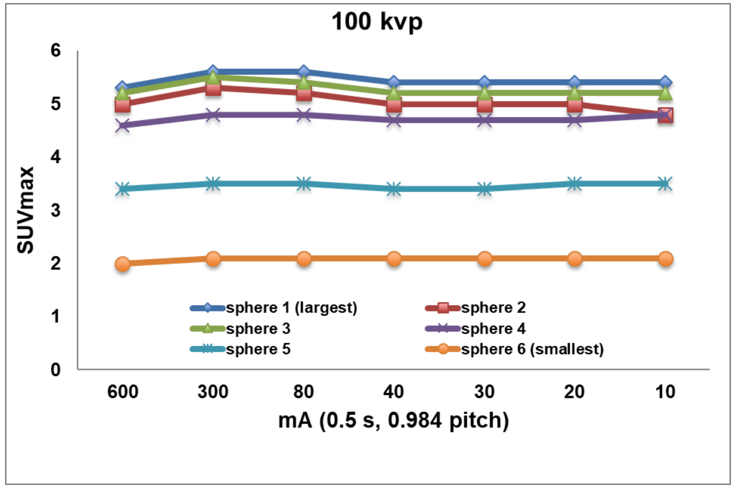
Minimal required CT setting for reliable attenuation correction of ^{18}F-FDG PET-CT

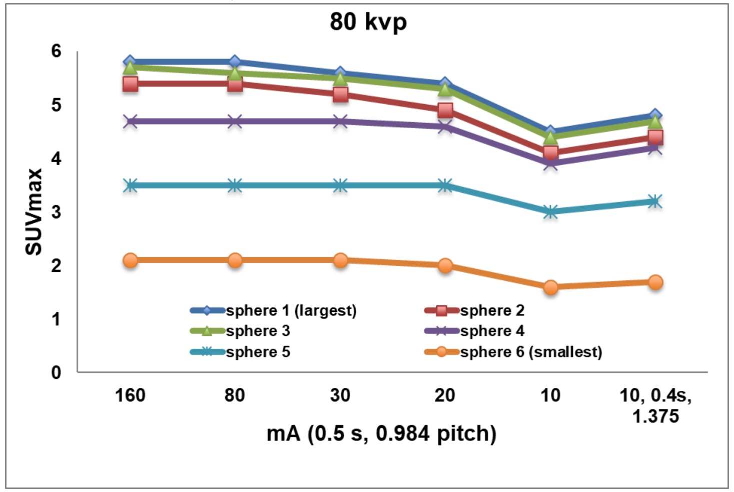


a NEMA IEC Body Phantom Set™

GE Discovery 690 scanner







Estimated CT doses

kVp	mA	CTDIvol (mGy)	mSv
100	600	15.25	20.6
100	300	7.68	10.3
100	**80**	**2.06**	**2.7**
100	40	1.03	1.4
100	30	0.77	1.0
100	20	0.55	0.7
100	**10**	**0.26**	**0.3**