Original article

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Coronary calcium score scan-based attenuation correction in cardiovascular PET imaging

Pardis Ghafarian[a,e], Seyed Mahmoud Reza Aghamiri[a], Mohammad Reza Ay[b,c,d], Babak Fallahi[d], Arman Rahmim[h], Thomas H. Schindler[f], Osman Ratib[e] and Habib Zaidi[e,g]

Objective Cardiac positron emission tomography (PET)/CT imaging is a noninvasive procedure allowing the assessment of coronary artery disease (CAD). CT-based attenuation correction of PET data is essential for accurate quantitative analysis in PET/CT imaging. Coronary artery calcium scoring CT (CaScCT) is used as a noninvasive tool for the diagnosis of atherosclerosis in patients with medium risk for CAD. In addition to the CaScCT examination, current cardiac rest/stress NH_3 or ^{18}F-fluorodeoxyglucose viability PET/CT protocols incorporate a correlated low-dose CT scan for attenuation correction purposes (ACCT). As a result, the patient receives a non-negligible radiation dose. The aim of this study is to evaluate the possibility of using CaScCT images for AC of myocardial rest/stress/viability PET data with the aim of reducing patient dose.

Methods Since in cardiac PET/CT protocols, the CaScCT examination is usually reconstructed using a small field-of-view, the CaScCT data were reconstructed again with extended field-of-view (ExCaScCT) and used for AC of the corresponding PET data. The feasibility study was performed using 10 patients including four NH_3 perfusion and six ^{18}F-fluorodeoxyglucose viability examinations acquired on the Biograph TP 64 PET/CT scanner. The assessment of PET images corrected using both ACCT and ExCaScCT images was carried out through qualitative assessment performed by an expert nuclear medicine specialist in addition to the regression analysis and the Bland–Altman plots, and 20-segment myocardial bull's eye view analysis.

Results Despite the good agreement between PET images corrected using ACCT and ExCaScCT images as expressed by the correlation coefficient and slope of the regression line in viability (0.949 ± 0.041 and 0.994 ± 0.124) and stress perfusion examinations (0.944 ± 0.008 and 0.968 ± 0.055), the rest perfusion examinations had weak correlation (0.454 ± 0.203 and 0.757 ± 0.193). This is attributed to the fact that the CaScCT scan is performed immediately after the stress/viability ACCT in our protocol that leads to a small misalignment between the CaScCT and stress/viability ACCT images, whereas there is a large misalignment between the CaScCT and rest ACCT images. The bull's eye view analysis showed that the difference between the uptake values was larger in the inferior wall because of diaphragm motion.

Conclusion Our preliminary results seem to suggest that the calcium score study could be used for attenuation correction of cardiac PET images, thus allowing the elimination of ACCT in viability and stress perfusion studies and as such reduce patient dose. *Nucl Med Commun* 31:780–787 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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[a]Department of Radiation Medicine, Shahid Beheshti University, [b]Research Center for Science and Technology in Medicine, [c]Department of Medical Physics and Biomedical Engineering, [d]Research Institute for Nuclear Medicine, Tehran University of Medical Sciences, Tehran, Iran, [e]Geneva University Hospital, Division of Nuclear Medicine, [f]Cardiovascular Center, Nuclear Cardiology, [g]Geneva Neuroscience Center, Geneva University, Geneva, Switzerland and [h]Department of Radiology, Johns Hopkins University, Baltimore, Maryland, USA

Correspondence to Dr Habib Zaidi, PhD, Division of Nuclear Medicine, Geneva University Hospital, CH-1211 Geneva 4, Switzerland
Tel: +41 22 372 7258; fax: +41 22 372 7169;
e-mail: habib.zaidi@hcuge.ch

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Introduction

Coronary artery disease (CAD) is one of the most important syndromes causing death around the globe. Positron emission tomography (PET) imaging is one of the well-established tools for the evaluation of myocardial perfusion and viability, ischemic and blood flow quantification in patients with CAD [1,2]. As the heart is surrounded by large organs of different densities such as the lung, diaphragm and liver [3], patient-specific non-uniform attenuation correction (AC) of emission data is essential for the correct interpretation of cardiac PET images [4]. With the advent of hybrid PET/CT scanners, CT images are currently used for AC of the corresponding PET data [5]. PET/CT systems offer significant advantages over stand-alone PET including decreased overall scanning time and improved localization of vessels or territories in cardiac imaging. Dedicated cardiac PET/CT scanners equipped with a 64-slice CT capability are widely used for the assessment of cardiac disease, where clinical protocols usually include CT angiography and calcium score examinations. Cardiac PET imaging using ^{18}F-fluorodeoxyglucose (FDG) is used for the evaluation of myocardial viability whereas either ^{82}Rb or ^{13}N-ammonia (NH_3) is used for myocardial perfusion assessment. However, there are some limitations in the use of CT-based attenuation correction (CTAC) including misalignment between the emission and transmission images because of cardiac motion [6,7], differences in temporal resolution between PET and CT [8,9] and the propagation of CT artefacts into PET images during the AC process [10–12].

The cardiac coronary calcium scan CT (CaScCT) is a noninvasive method that evaluates the presence, location and extent of calcified plaque in the coronary arteries [13]. With the introduction of multislice CT, there is an increasing interest to use CaScCT for the prognosis of patients with medium risk for CAD [13–16]. High coronary artery calcium scores act as a marker indicating an elevated risk for cardiovascular disease [17,18]. In addition, the association of anatomical information from CaScCT with functional information provided by PET on hybrid PET/CT systems contributes a valuable tool to the clinicians for the interpretation, diagnosis and prognosis of cardiovascular disease. A complete assessment on a dedicated PET/CT scanner includes CT angiography, CaScCT and one or two low-dose CT scans for AC of PET data in viability or perfusion examinations [4,19,20]. The need for three or four CT examinations in a single session increases patient dose [2,21], and as such dose reduction remains an important and challenging issue.

The aim of this study is to evaluate the feasibility of using CaScCT images for the purpose of AC in myocardial viability and perfusion PET imaging with the aim of reducing patient dose by removing one or more low-dose CT examinations. To the best of our knowledge, the feasibility of using CaScCT for AC of cardiac SPECT data was only recently reported [22]. Another more recent contribution was independently reported on the same application for cardiac perfusion PET imaging [23]. It is worth emphasizing that in Buckhard *et al.* [23], the investigators manually aligned low-dose CT scans and CaScCT before performing CTAC, whereas we relied on the relevance of hardware-based alignment excluding the need for additional alignment as performed in routine clinical practice.

Materials and methods

PET/CT scanner

PET/CT imaging was performed using the Biograph TP 64 scanner (Siemens Medical Solutions, Erlangen, Germany) offering advanced cardiovascular imaging capabilities including volumetric CT to visualize the anatomy of the heart's blood vessels. The PET sub-system consists of 39 rings with a total of 24 336 lutetium oxyorthosilicate crystals of dimensions $4 \times 4 \times 25\,mm^3$. The PET scanner operates in a fully three-dimensional mode and has an axial field-of-view (FOV) of 162 mm. The CT sub-system consists of a 40-rows ceramic detector with 1344 channels per row and adaptive collimation. The CT scanner uses the z-sharp technique to acquire 64 slices per rotation.

Study population

Ten patients including four NH_3 perfusion examinations and six ^{18}F-FDG viability examinations were used in this feasibility study. Their mean age was 66.5 ± 8 years (range 56–82 years) with a mean body mass index of $29.4 \pm 4.6\,kg/m^2$ (range $24.1–37.8\,kg/m^2$). All patients underwent routine PET/CT examinations in our department. For ^{18}F-FDG studies, the protocol consists of a low-dose CT scan (ACCT) for CTAC [120 kVp, 74 effective mAs (CareDose), 24×1.2 collimation, 0.45 : 1 pitch, 1 s rotation time] with regular shallow breathing followed by a CaScCT scan (120 kVp, 190 effective mAs, 24×1.2 collimation, 0.2 : 1 pitch, 0.33 s rotation time) acquired in breath hold at end-inspiration. PET data were then acquired for 10 min in a list-mode format. For NH_3 studies, after injection of a pharmacological stress test (dipyridamole), a low-dose CT scan (120 kVp, 74 effective mAs, 24×1.2 collimation, 0.45 : 1 pitch, 1 s rotation time) was performed with regular breathing instructions followed by the CaScCT scan (120 kVp, 190 effective mAs, 24×1.2 collimation, 0.2 : 1 pitch, 0.33 s rotation time) with breath hold at end-inspiration. PET emission data (stress examination) were then acquired for 6 min in a list-mode format. Thereafter, a second injection of ^{13}N-ammonia was performed (rest examination), followed by a low-dose CT using the same parameters described above for the stress study. The level of calcium present in this population was relatively low.

Calcium score-based attenuation correction

The routine cardiac PET/CT protocol involves a small FOV reconstruction (200 mm) of the CaScCT scan. To use CaScCT for AC, the raw CT data were re-reconstructed with an extended FOV (700 mm) option. This reconstructed image is referred to as ExCaScCT. The three-dimensional PET list-mode data were first rebinned to two-dimensional sinograms and subsequently corrected for detector sensitivity, dead time and scatter. Subsequently, the emission data of all the patients (both viability and perfusion examinations) were corrected for attenuation using both ACCT and ExCaScCT. PET images were reconstructed using the attenuation weighted, ordered subset expectation maximization iterative reconstruction algorithm. The default parameters used for the reconstruction of clinical studies were eight subsets, six iterations, 5 mm Gaussian smoothing and a 256×256 image matrix. Furthermore, the misalignment between ACCT and ExCaScCT was quantified using the commercial coregistration package provided in the HERMES multimodality fusion software (Hermes Medical Solutions, Stockholm, Sweden). An in-house developed software implemented in MATLAB (The MathWorks Inc., Natick, Massachusetts, USA) was used for the generation of attenuation maps from both ACCT and ExCaScCT images.

Assessment strategy

A volume of interest (VOI)-based quantitative analysis was performed on the myocardial wall of PET images for the assessment of the influence of ACCT and ExCaScCT on the recovery of activity during the AC process. Nearly 200 VOIs were drawn in the myocardial wall in each PET image and a linear regression correlation and Bland–Altman plots were generated between the PET data corrected for attenuation with ACCT and ExCaScCT. The correlation coefficient (R^2) and the slope (S) of the regression line were determined. Moreover, perfusion and viability PET images were evaluated using a 20-segment model of bull's eye view for the left myocardium ventricle. Each region of the bull's eye view was normalized to the maximum value, and relative percentage counts (0–100) in each segment were converted to five-point scores, namely 0 = normal counts, 1 = mild reduction in counts, 2 = moderate reduction in counts, 3 = severe reduction in counts and 4 = absent counts [24]. For further quantitative assessment, the summed stress score (SSS) and summed rest score were used for the evaluation of perfusion scores for the stress and rest images of perfusion examinations. We defined a new parameter entitled the summed metabolism score (SMS) for the evaluation of viability examinations defined as the total score in all segments in the bull's eye view model.

We calculated the mean absolute percentage difference of tracer uptake in all segments in the myocardial wall as related to the bull's eye view analysis. Linear correlation and Bland–Altman plots were calculated to assess the agreement between the two AC techniques (ACCT and ExCaScCT).

Statistical analysis

Agreement between ACCT and ExCaScCT in the AC PET images was expressed by linear regression analysis (Pearson's correlation coefficient and slope of the regression line) and Bland–Altman analysis using a 95% confidence interval reported as mean $\pm$ 1.96 $\times$ SEM. Comparison of uptake values in PET as related to the bull's eye view was evaluated using the two-sided paired t-test. P values less than 0.05 was considered statistically significant. Statistical analysis was performed using the SPSS software (SPSS Inc., Chicago, Illinois, USA, version 16).

Results

Table 1 summarizes the misalignment between ACCT and ExCaScCT images as evaluated by rigid-body registration using the HERMES multimodality fusion software. The larger misalignment between the ACCT and ExCaScCT in the NH_3 rest examinations is because of the fact that rest ACCT is acquired after the stress examination whereas the CaScCT scan is acquired right after stress ACCT thus ensuring minimal misalignment. As our aim is to replace ACCT by ExCaScCT for use in AC of PET data, an understanding of the level of misalignment between these two CT images makes sense for the purpose of this study. A low misalignment between these images guarantees reproducible and similar results when ACCT is replaced with ExCaScCT during the CTAC procedure.

Table 1 Evaluation of misalignment between ACCT and ExCaScCT images for all patients in this study

Examination	x (cm)	y (cm)	z (cm)	xy (°)	xz (°)	yz (°)
1V	0.827	−0.004	0.978	0.035	0.012	−0.138
2V	0.034	0.024	−0.586	−0.07	0.134	0.428
3V	0.182	−0.156	0.684	−0.006	0.079	−0.159
4V	0.542	0.031	0.002	−0.222	0.313	−0.272
5V	0.104	−0.165	6.369	0.034	−0.184	0.604
6V	−0.036	0.088	0.261	0.075	0.116	0.400
7S	−0.002	0.125	0.018	0.161	0.012	−0.041
7R	1.634	0.172	0.191	0.643	0.154	0.095
8S	0.143	−0.008	0.782	−0.104	0.002	0.442
8R	−0.249	−0.082	1.006	0.023	0.163	0.691
9S	−0.255	0.007	1.396	0.022	−0.002	0.45
9R	−0.086	0.107	1.004	−0.122	−0.003	−0.055
10S	0.367	0.253	0.719	0.417	0.197	0.741
10R	0.687	0.310	0.677	0.559	0.622	0.152

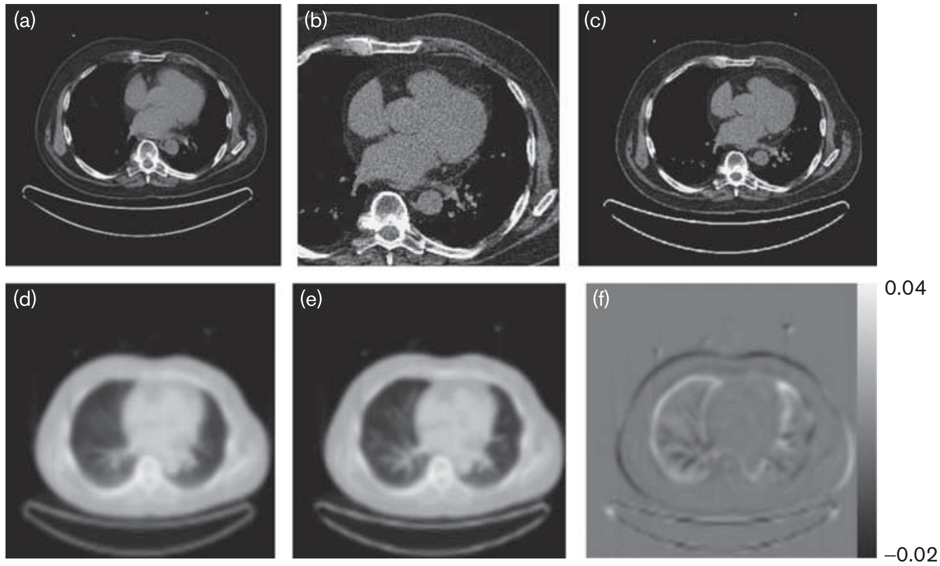
X, Y, Z translation in the *x, y, z* direction.
XY, XZ, YZ rotation in the *xy, xz, yz* planes.
ACCT, attenuation correction computed tomography; ExCaScCT, extended coronary artery calcium scoring CT; R, rest mode in perfusion examination; S, stress mode in perfusion examination; V, viability examination.

Figure 1 shows a typical transaxial slice from ACCT, CaScCT, ExCaScCT and the generated attenuation maps (μmaps) reconstructed using the calculated AC factors extracted from the scanner database. The difference between the two generated μmaps is also shown. The matching of myocardial outline indicated an acceptable alignment between the two methods. Figure 2 shows a typical short axis, vertical and horizontal long axis slices and a polar map for one of the viability examinations corrected for attenuation using both ACCT and ExCaScCT. A good correlation is obvious between PET images corrected with both the CT images in all segments of the myocardial wall.

Figure 3 shows the correlation plot between PET data corrected for attenuation using ACCT and ExCaScCT for one viability examination and one perfusion (rest and stress) examination. It should be noted that 200 VOIs were used for the calculation of the correlation plot in each PET image. VOIs of varying size were drawn in different areas of the myocardium to cover the entire myocardial area.

The correlation coefficients and slopes resulting from the regression analysis of the VOIs for all the patients are presented in Fig. 4. There is an excellent correlation between the mean uptake value in the myocardial wall when using ACCT and ExCaScCT for AC of the viability

Fig. 1



A typical transaxial slice showing CT images corresponding to (a) attenuation correction computed tomography (ACCT) (b) coronary artery calcium scoring CT, (c) extended coronary artery calcium scoring CT (ExCaScCT), and generated attenuation maps (μmaps) illustrating (d) ACCT, (e) ExCaScCT (f) difference image between ACCT and ExCaScCT. The scale is also shown for the latter.

and stress perfusion studies, whereas there is a weak correlation in the rest perfusion study because of the large misalignment between rest ACCT and ExCaScCT.

The mean absolute percentage difference of tracer uptake in all myocardial segments for both viability and perfusion examinations (excluding the rest perfusion examination) are summarized in Table 2. Given that a difference exceeding 10% between the two different methods could be clinically significant for the clinical interpretation of PET images [19], it seems that there is a small discrepancy between PET images corrected using both the AC techniques in each myocardial region.

Figure 5a shows the linear regression plot between the SSS (perfusion) and SMS (viability) calculated from the bull's eye view analysis of PET images corrected for attenuation using both ACCT and ExCaScCT for all the patients included in this study (stress perfusion and viability examinations excluding rest perfusion because of the large misalignment between rest ACCT and ExCaScCT). An excellent correlation was also found for SSS and SMS between the PET images corrected for attenuation using ACCT and ExCaScCT ($R^2 = 0.967$, $P = 0.825$). The Bland–Altman plot shown in Fig. 5b showed that the measured uptake values for the majority of patients (viability and stress perfusion) are within the 95% confidence interval.

Discussion

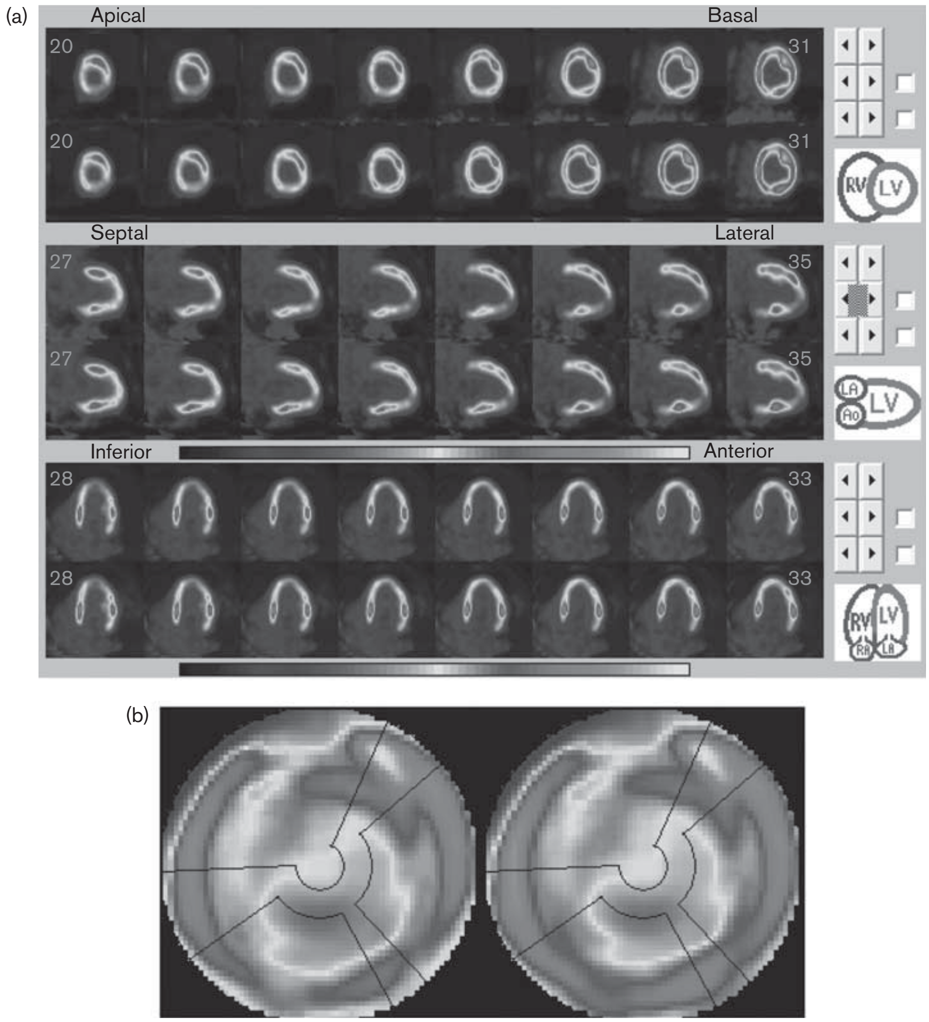
The combination of molecular and anatomical imaging achieved by PET/CT scanners, particularly those with a 64-slice (and above) CT capability dedicated for coronary angiography is a powerful tool for the diagnosis and prognosis of cardiac disease. Nowadays, calcium scoring is more widely adopted and is considered as the marker of choice for the prediction of extension of heart disease in medium risk CAD patients.

CTAC substantially reduces the total scanning time and yields much lower statistical noise in the generated attenuation maps [20]. However, full heart assessment using cardiac PET/CT imaging including angiography, coronary calcium score, viability and/or perfusion is considered a high-dose examination. This study considered the possibility of using the coronary calcium score CT scan for CTAC of cardiac PET data with the aim of reducing patient dose in a full heart assessment using a dedicated 64-slice PET/CT scanner. Moreover, the misalignment between ACCT and ExCaScCT was investigated using the qualitative visual assessment performed by an experienced nuclear medicine physician and quantitative analysis.

In Fig. 3c, there is a considerable number of data points lying below and separated from the line of regression because of the larger magnitude of misalignment between PET and CaScCT images, which results in a lower correlation between the data points. These data points belong to the ROIs located close to the border of the myocardial wall where the lung tissue will overlie with the myocardial wall because of the different respiratory patterns and as such result in lower activity recovery in comparison with PET data corrected using ACCT.

Figure 4 shows a good correlation between the corrected PET images using ACCT and ExCaScCT in the viability and stress perfusion examinations, whereas a weak

Fig. 2



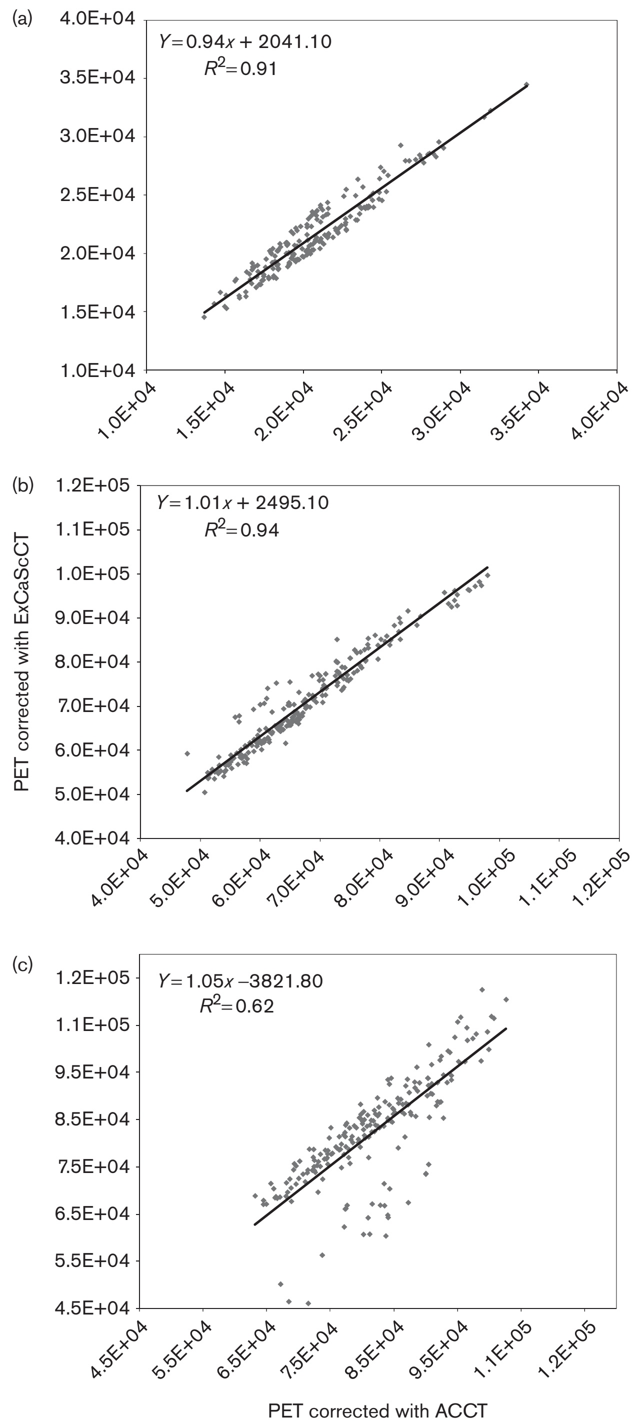
(a) Representation of typical short, vertical and horizontal long axis viability positron emission tomography images. Top row shows images corrected for attenuation using attenuation correction computed tomography whereas the bottom row shows images corrected using extended coronary artery calcium scoring CT. (b) Bull's eye view of one of the viability examinations corrected for attenuation using both attenuation correction computed tomography (left) and extended coronary artery calcium scoring CT (right).

correlation was observed in the rest perfusion examination. As discussed earlier, this is mainly because of the fact that in our protocol, CaScCT and stress ACCT were acquired right before the stress PET emission scan, whereas the rest ACCT was acquired 20 min later before the rest emission scan and as such there is a large misalignment between CaScCT and rest ACCT. Earlier studies have shown that a combination of many factors such as patient motion, respiratory and cardiac motion, and pharmacological stress could cause significant misalignment between the CT and PET images [20,25]. These errors may create an erroneous AC factor and cause lower uptake values in some segments, thus leading to a false–positive diagnosis of the myocardial wall.

Respiratory motion can cause artefacts in corrected PET images and this effect is more critical for cardiac imaging [26]. Our results indicate that the variation of uptake value is more significant at the inferior wall compared with the other walls (Table 2) because of the respiratory motion. This is in agreement with Livieratos *et al.* [27] who reported that cardiac excursion during respiration had the most variation in the cranio-caudal direction compared with the transverse and horizontal directions. In line with the observations made by Chin *et al.* [28], regional uptake values in PET images corrected using both the AC techniques (ACCT and ExCaScCT) decrease at the inferolateral wall. In agreement with the results of Le Meunier *et al.* [29], the regional difference activity showed a greater decrease in the anterolateral region compared with the septal region.

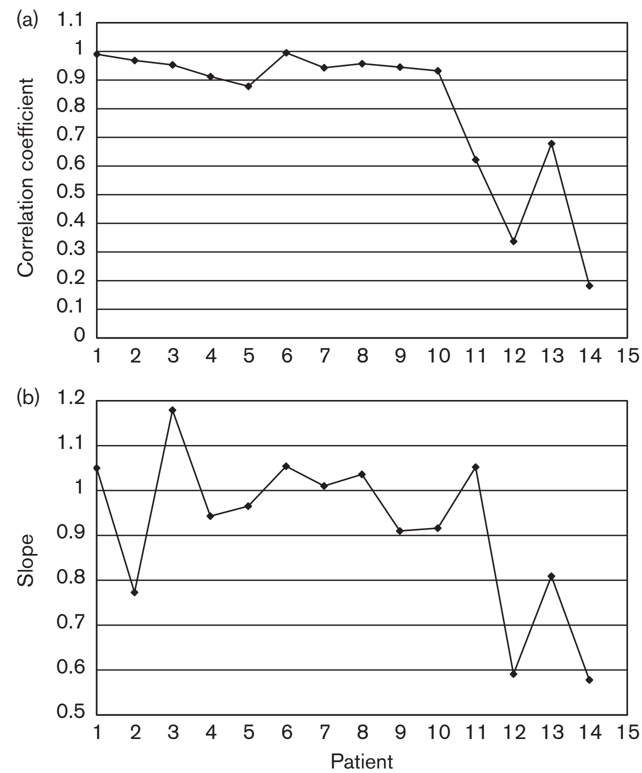
No significant differences were observed between PET images corrected using both the AC techniques (viability and stress perfusion examinations) when comparing the

Fig. 3



Correlation plots between the positron emission tomography (PET) images corrected for attenuation using attenuation correction computed tomography (ACCT) and extended coronary artery calcium scoring CT (ExCaScCT). (a) Viability examination, (b) stress perfusion examination and (c) rest perfusion examination ($n = 200$, $P < 0.0001$).

Fig. 4

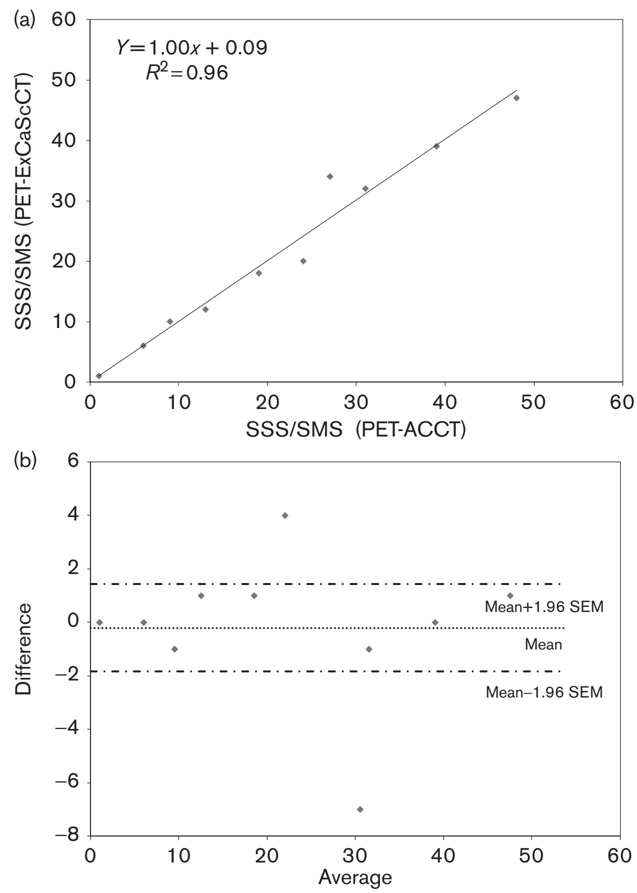


(a) Plots of correlation coefficients (R^2) and (b) slopes resulting from the regression analysis of volume of interests located in the myocardial wall of the attenuation corrected positron emission tomography images using both attenuation correction computed tomography and extended coronary artery calcium scoring CT; the slopes of the regression lines and the correlation coefficients. (Patients; 1–6: viability examination, 7–10: stress perfusion scan, 11–14: rest perfusion scan).

score value in 20 segments of the myocardial model (Fig. 5). More recently, Burkhard *et al.* [23] showed that the CaScCT scan can be used for AC of both the rest and stress perfusion examinations through a manual alignment of ACCT and CaScCT images, whereas we assessed the feasibility of using CaScCT for CTAC without any additional alignment before CTAC as a more convenient procedure in routine clinical protocols.

It is well established that misalignment may lead to some bias when it comes to quantitative analysis. However, correction of misalignment is a challenging and time-consuming process and manual registration is not always the best approach. It should be emphasized that the aim of this study is to evaluate the feasibility of using CaScCT images for the purpose of AC in myocardial viability and perfusion PET imaging (the study by Burkhard *et al.* was limited to myocardial perfusion) with the aim of reducing patient dose in cases when we can rely on hardware-based alignment as performed in routine clinical practice, thus excluding the need for additional software-based registration. Owing to the large misalignment between CaScCT and rest PET images, deformable registration is required in those cases, as the rigid-body manual registration as performed by Burkhard *et al.* [23]

Fig. 5



(a) Linear regression analysis and (b) Bland–Altman plot comparing scoring uptake values [summed stress score (SSS) for stress perfusion and summed metabolism score (SMS) for viability examinations] of positron emission tomography (PET) images in the 20-segment model of bull's eye view corrected using attenuation correction computed tomography (ACCT) versus extended coronary artery calcium scoring CT (ExCaScCT) for all patients included in this study (viability and stress perfusion examinations, the rest data were excluded). SEM is the standard error of the mean defined as $SD/\sqrt{n}$).

Table 2 Variation of uptake values in myocardial wall through bull's eye view in PET images for all patients corrected with ACCT and ExCaScCT

Myocardial wall	Mean absolute percentage difference in uptake value (% ± SD)
Anteroseptal	2.52 ± 2.1
Anterolateral	2.57 ± 1.9
Lateroanterior	2.26 ± 2.0
Lateroinferior	3.02 ± 2.5
Inferolateral	5.68 ± 4.0
Inferoseptal	6.58 ± 4.5
Septoinferior	4.02 ± 3.9
Septoanterior	3.81 ± 3.6
Apex	1.92 ± 1.1

ACCT, attenuation correction computed tomography; ExCaScCT, extended coronary artery calcium scoring CT.

has limited value. This is being investigated now using the deformable registration approach suggested by Bond *et al.* [30] and will be reported in future studies. One of the main achievements of this study is the possibility of using CaScCT for both perfusion and viability PET studies when an optimized acquisition protocol that does not require software-based alignment of CaScCT and PET images is available.

In our protocol, the patient-absorbed dose delivered by ACCT and CaScCT were 6 and 12.81 mGy, respectively. This study shows the possibility of using the CaScCT scan for AC thus eliminating the ACCT scan in both viability and stress perfusion examinations. This modified protocol can reduce the patient dose by at least 6 mGy. Our future efforts will be directed towards expanding the number of patient examinations using a large pool of clinical data sets. Although the present analysis did not show significant differences between PET images corrected for attenuation using ACCT and ExCaScCT in viability and stress perfusion examinations, whether or not this approach can be adopted clinically remains to be explored.

Conclusion

The preliminary results of this study showed that ExCaScCT can be a used for CTAC of PET images. This feasibility study suggested the potential to eliminate the ACCT scan in viability and stress perfusion studies for the described protocol, thus allowing a substantial reduction of patient dose.

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