Quantification of PET and CT Data Misalignment Errors in Cardiac PET/CT: Clinical and Phantom Studies

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***Abstract* – PET/CT units with high temporal resolution (particularly with 64-slice CT capability) are increasingly used as in clinical diagnosis and prognosis of cardiovascular disease. Since the CT sub-system in the combined PET/CT unit is used to perform attenuation correction of acquired PET data, misalignments between patient positioning for both scans can cause artifacts in the myocardial PET images potentially resulting in false positive artifacts. The aim of this study is to evaluate the misalignment effect (induced by spurious or physiological patient motion in-between the two modalities) on regional and global uptake values in the myocardial region. In this study, we used both phantom (RSD thorax phantom) and clinical studies (two FDG and one NH_3 rest/stress). Manual shifts between the CT and PET images ranging from 0 to 20 mm in six different directions were applied. Thereafter, attenuation correction was applied to the emission data using the manually shifted CT images in order to model patient motion between PET and CT. The reconstructed PET images using shifted CT images for attenuation correction were compared with the PET images corrected with the hypothetically misalignment free original CT image. The criteria and figures of merit used included VOI and linear regression analysis. The analysis was performed using 500 VOIs located within the myocardial wall in each PET dataset. The VOIs were uniformly distributed across all myocardial wall regions to assess the overall influence of PET and CT misalignment. The absolute percentage relative difference increased in all simulated movements with increasing misalignments for both phantom and clinical studies (up to 30% in some regions for the 20 mm shift). In conclusion, increasing the misalignment between PET and CT studies resulted in increased changes in the tracer uptake value within the myocardium both on a regional and global basis with respect to the reference as revealed by the various figures of merit used. The variation was more significant for right and down movements versus left and up directions.**

Keywords - PET/CT, Cardiac Imaging; Misalignment; Attenuation Correction

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I. Introduction

The advent of combined PET/CT scanners is considered as a major advance in medical imaging technology that lead to improved patient management. PET/CT systems offer significant advantages over separate PET and CT imaging including decreased overall scanning time and increased accuracy in lesions localization in clinical oncology. Nowadays cardiac PET/CT scanners, especially those equipped with dedicated 64-slice CT capability, are widely used for clinical diagnosis of cardiovascular disease, including the use of cardiac CT angiography given its relevance in early detection coronary artery disease (CAD) [1]. Cardiac PET imaging using ^{18}F-FDG is used for evaluation of myocardial viability whereas ^{82}Rb or ^{13}NH3 offer the potential for myocardial perfusion assessment.

One of the main challenges is the possibility of adverse effects on CT-based attenuation correction (CTAC) of PET data owing to the fact that misalignment between CT and PET data resulting from, either physiological (respiratory and cardiac motion) or patient motion, is known to generate motion induced artifacts during CTAC of PET data [2,3].

Since PET/CT scanners utilize the CT component for attenuation correction of PET data and given that the heart is surrounded by organs and tissues such as lungs and diaphragm, with considerable difference in photon attenuation properties, the misalignment between attenuation and emission data is the most important obstacle that reduces the interpretative confidence and quantitative accuracy of myocardial PET studies.

The issue of whether PET and CT misalignment produces medically significant errors on myocardial interpretation in cardiac PET/CT is still under investigation. The quantification of lower shift thresholds between PET and CT data below which the interpretation of myocardial images is risk free has proven to be a difficult task and is still an open question requiring more research and development efforts.

The influence of physiological motion (respiratory and cardiac motion) in addition to patient motion on CTAC has received growing interest in the past few years. Simulation studies of dynamic phantoms emulating respiratory motion reported 25% error on CTAC of PET images [4]. Chin *et al.* [5] reported an error on the order of 6% due to respiratory motion in myocardial PET analysis in a canine study.

The aim of this study was to investigate the impact of different levels of misalignment between CT and PET data using both phantom and clinical studies. A limited number of publications assessed the impact of misalignment between CT and PET data in dedicated cardiac PET/CT scanners with volumetric 64-slice CT [6]. This spurred the research presented in this paper, where a more realistic anthropomorphic RSD (Radiology Support Devices, CA) phantom was utilized for the purpose of accurate quantitative analysis using realistic experiments.

II. Material and methods

A. PET/CT scanner

PET/CT imaging was performed on the Biograph TP 64 scanner (Siemens Medical Solutions, Erlangen, Germany) installed at the Division of Nuclear Medicine, Geneva University Hospital. The Biograph TP 64 is a dedicated PET/CT scanner allowing cardiovascular imaging with the possibility of using volumetric CT used to visualize the anatomy of the heart's blood vessels. The PET module of the system consists of 39 rings with a total of 24,336 lutetium oxyorthosilicate (LSO) crystals of dimensions 4×4×25 mm. The PET scanner has an axial field of view of 162 mm and operates in the fully three-dimensional mode. The CT module of the system consists of a 40-rows ceramic detector with 1344 channels per row and adaptive collimation. The CT scanner uses the z-sharp technique in order to acquire 64 images per rotation.

B. Patient studies

The assessment of errors arising from CT and PET misalignment was performed using three clinical cardiac PET/CT examinations (one NH_3 perfusion and two FDG viability studies). For FDG patients, after a low dose CT scan (120 kVp, 74 effective mAs, 14.3 s duration, 0.45:1 pitch) with regular shallow breathing, the PET data were acquired for 10 min in list-mode format, where patients were injected with 370 MBq FDG. For myocardial perfusion studies, after injection of pharmacological stress drug, a low dose CT scan (120 kVp , 74 effective mAs, 14.3s duration, 0.45:1 pitch) was obtained with regular breathing instructions followed by PET perfusion at stress. Data were acquired in list-mode where the patients were injected with 1 GBq of NH_3, and then a second injection of 1 GBq of NH_3 was started for PET acquisition at rest mode. This was followed by a low dose CT under the same conditions as for the rest study. The patients selected for this study did not present any visual misalignment between CT and PET data.

C. RSD torso phantom study

The phantom study was performed in order to have perfectly aligned PET and CT data in the absence of cardiac or respiratory motion. The RSD phantom is a fully tissue-equivalent anthropomorphic phantom allowing accurate anatomic modeling of the human torso. It is well suited for evaluation of delectability, extent and severity of myocardial infarction in male and female patients. The phantom includes basic thorax, heart, lungs and liver. The anatomic heart model in this phantom is based on vacuum-formed shells. It was designed using high resolution, contrast-enhanced, ultrafast CT data from a normal patient, slightly modified to facilitate its use. The left and right chambers are connected at the atrium region to make a single compartment which can be filled and flushed independently. The volume of the heart chambers is 284 ml, while the volume of the myocardial wall is 238 ml.

In order to model typical FDG distribution in the normal human thorax one hour after administration of 370 MBq of FDG, the individual organs in the phantom were filled with ^{18}F as follows: thorax cavity (43.46 MBq), myocardial wall (5.712 MBq), left lung (1.221 MBq), right lung (1.739 MBq) and liver (12.446 MBq). Thereafter, the RSD phantom was scanned using the same protocol used for patient studies.

D. Attenuation correction and image reconstruction

To model the misalignment between CT and PET data for both phantom and clinical studies, the CT images were manually shifted using the *fusion registration* utility implemented within the *Syngo* software (Siemens Medical Solutions) in six different directions (left, right, backward, forward, up and down) from 0 to 20 mm in steps of 5 mm. The accuracy of manual misalignment was validated by experimental measurements of a ^{68}Ge cylindrical source normally used for daily quality control of the PET scanner. This was achieved by applying different physical shifts between CT and PET data. After manual shifting of CT images, the resampled CT were transferred to the main consol for attenuation correction of PET data.

The 3D PET listmode data were first rebinned to 2-D sinograms and subsequently corrected for detector sensitivity, dead time, scatter and attenuation. PET images were then reconstructed by means of the attenuation weighted, ordered subset expectation maximization (OSEM) iterative reconstruction algorithm. The default parameters used for reconstruction of both phantom and clinical studies were 8 subsets, 6 iterations, 5 mm Gaussian smoothing and a 256×256 image matrix. In total, 25 datasets were reconstructed for each PET acquisition including one PET/CT combination without misalignment and 24 PET attenuation corrected using shifted CT images.

E. Assessment strategy

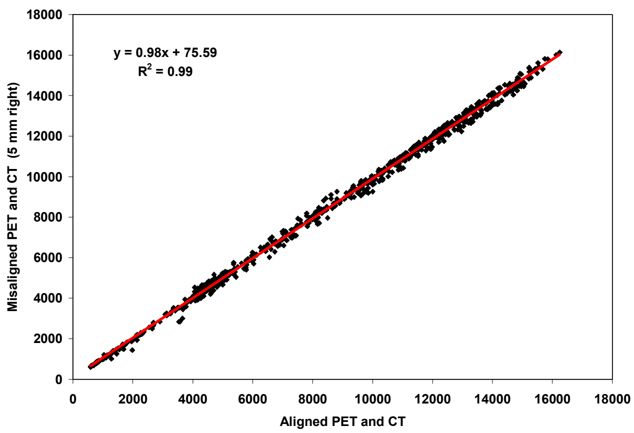
The reconstructed PET images using shifted CT images for attenuation correction were assessed through comparison with the PET images that were corrected with the original CT image without any misalignment (used as gold standard for assessment). The criteria and figures of merit used include VOI analysis used to obtain correlation plots, correlation coefficients, and relative difference. All analysis was carried out by drawing 500 VOIs in the myocardial wall in each PET dataset. The VOIs were uniformly distributed in all regions of the myocardial wall in order to calculate the overall influence of PET and CT misalignment in myocardial wall analysis.

III. Results

Figure 1 shows correlation plots for the RSD phantom between the mean VOIs activity concentration (500 VOIs) in PET images corrected with aligned CT used as gold standard and PET images corrected with shifted CT, when the CT images are shifted in the right direction from 5 to 20 mm. It should be noted that there are 24 different correlation plots in total for each dataset (patient data are not shown). It was observed that the slope of the regression line and the correlation coefficient decreases when increasing the misalignment between CT and PET data.

Table I. shows the calculated correlation coefficients for 24 different misalignment patterns as applied to each dataset. It should be noted that the correlation coefficient quantifies the similarity of PET data corrected with shifted CT images and PET data corrected with perfectly aligned CT.

Fig. 2 shows the Box and Whisker plots of the percentage relative difference between PET data attenuation corrected with aligned CT and PET data corrected with shifted CT images for 24 different misalignment patterns applied to the RSD phantom and patient 2 datasets. The red line shows the median value, whereas the blue box shows the median value of the first and third quartile of relative differences in 500 VOIs. The bars show the minimum and maximum percentage relative differences in each shift pattern.



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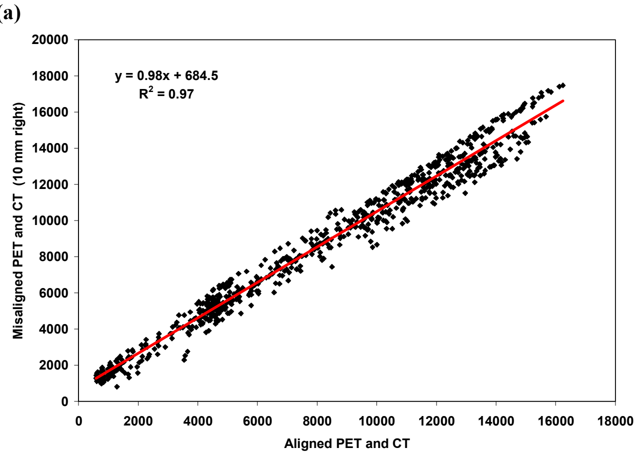

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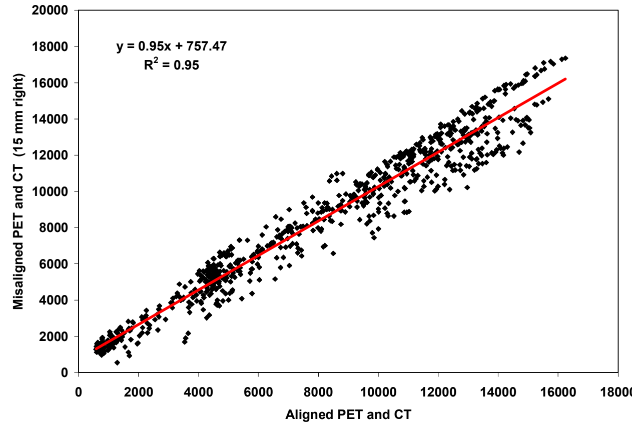

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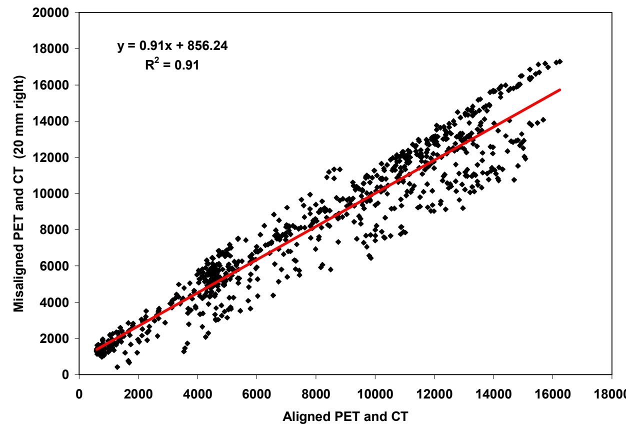


(d)

Figure 1. Linear regression plots for 500 VOIs in the RSD phantom, between aligned and misaligned PET and CT images, with misalignments to the right corresponding to: (a) 5 mm, (b) 10 mm, (c) 15 mm, and (d) 20 mm, respectively.

IV. Discussion

Figures 1-2 and Table I. confirm the evidence that misalignment between PET and CT images, used for attenuation correction of the former, will increase the b. The same behavior was also observed for other datasets (data not shown). The RSD phantom study was designed to accurately quantify misalignments free of cardiac and respiratory motion. The CT images were shifted to the left and to the right to induce artificially the known effect of the lung partially overlapping with the myocardial wall. It should be noted that the trunk part of the RSD thorax phantom was filled with water, shifting up/down and forward/backward had no significant influence on myocardial wall analysis. It is clear that distribution uptake values are altered significantly with increasing misalignments. The Box and Whisker plots show that the variations in the calculated uptake values in all VOIs increase with increasing misalignments between CT and PET data. In the clinical studies, differences between the first and third quartile for misalignments in forward direction is significant in comparison to backward direction owing to cardiac motion. However, given that there was no cardiac motion in the RSD phantom study, this variation was not pronounced in this situation.

TABLE I. SUMMARY OF CORRELATION COEFFICIENTS BETWEEN MEAN VOI ACTIVITY VALUES CALCULATED FROM PET DATA CORRECTED FOR ATTENUATION WITH SHIFTED CT IMAGES AND PET DATA CORRECTED WITH ALIGNED CT.

Shift	RSD Phantom	Patient 1	Patient 2	Patient 3	
				Rest	Stress
5 mm up	0.998	0.996	0.989	0.917	0.944
10 mm up	0.996	0.984	0.950	0.820	0.864
15 mm up	0.992	0.976	0.913	0.700	0.691
20 mm up	0.980	0.964	0.856	0.631	0.598
5 mm down	0.997	0.992	0.958	0.964	0.957
10 mm down	0.994	0.978	0.840	0.815	0.687
15 mm down	0.979	0.949	0.470	0.665	0.437
20 mm down	0.953	0.925	0.223	0.413	0.179
5 mm for[1]	0.997	0.991	0.940	0.929	0.936
10 mm for	0.988	0.961	0.776	0.752	0.785
15 mm for	0.969	0.911	0.577	0.566	0.621
20 mm for	0.939	0.857	0.407	0.428	0.484
5 mm back[2]	0.997	0.993	0.952	0.939	0.934
10 mm back	0.988	0.973	0.835	0.798	0.781
15 mm back	0.977	0.949	0.694	0.642	0.623
20 mm back	0.961	0.914	0.571	0.516	0.495
5 mm left	0.991	0.991	0.991	0.911	0.941
10 mm left	0.984	0.975	0.974	0.745	0.800
15 mm left	0.971	0.950	0.956	0.605	0.658
20 mm left	0.957	0.922	0.940	0.509	0.559
5 mm right	0.997	0.986	0.978	0.881	0.926
10 mm right	0.977	0.947	0.872	0.580	0.687
15 mm right	0.952	0.858	0.618	0.230	0.328
20 mm right	0.910	0.791	0.307	0.100	0.153

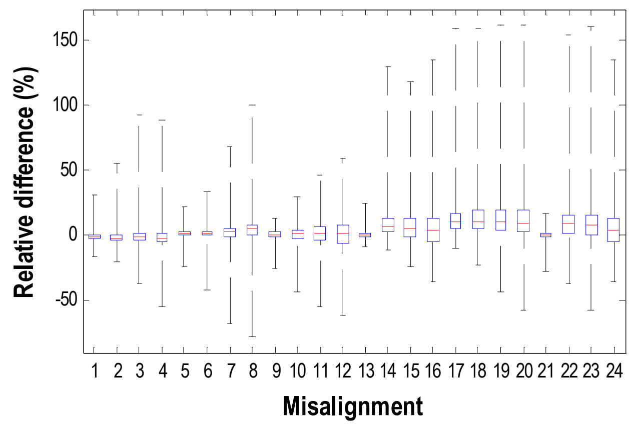
[1]Forward
[2] Backward

It can be concluded that the percentage absolute relative difference for all VOIs increase in all directions with increasing PET and CT misalignment for both the RSD phantom and clinical studies. More detailed and clinically relevant analysis using polar maps for the assessment of the influence of misalignment on myocardial wall uptake is still ongoing. This might help to address the issue of whether PET and CT misalignment produces medically significant errors in cardiac PET/CT examinations.

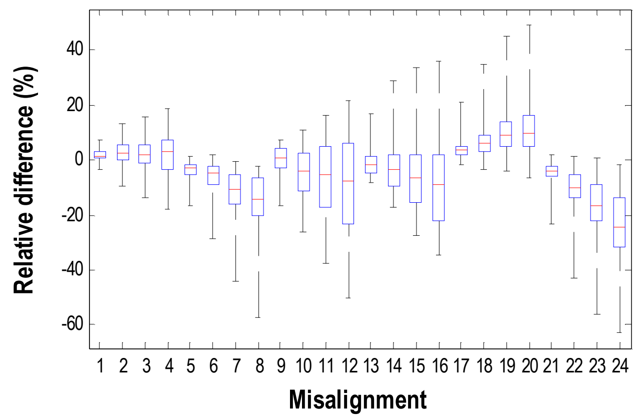
V. CONCLUSION

In conclusion, increasing misalignments between PET and CT images resulted in increasing changes in regional and global uptake values in the myocardial region, with respect to perfectly aligned CT images used as reference (as quantified by various figures of merit). The variation was seen to be more significant for right and down movements versus left and up.

As misalignment between attenuation and emission data occurs frequently in a clinical setting and causes non-uniform uptake values in the myocardial region and erroneous interpretation of PET image, it is important to perform accurate alignment between transmission and emission images before PET image reconstruction. This would potentially involve optimized protocols for minimizing patient motion in-between PET and CT scanning or the development of accurate motion compensation methods to compensate for remaining misalignments.



(a)



(b)

Figure 2. Box and Whisker plots showing the variation of percentage relative difference for: **(a)** the RSD torso phantom; **(b)** a clinical study. (1-4 correspond to 5-20 mm up, 5-8 correspond to 5-20 mm down, 9-12 correspond to 5-20 mm forward, 13-16 correspond to 5-20 mm backward, 17-20 correspond to 5-20 mm left, and 21-24 correspond to 5-20 mm right).

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