The Influence of PET and CT Misalignment due to Respiratory Motion on the Cardiac PET/CT Imaging: a Simulation Study

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A B S T R A C T

Purpose: Potential causes of misalignment between anatomical and functional images in cardiac PET/CT imaging include respiratory and cardiac motion as well as bulk motion. In this study we evaluated the impact of respiratory and cardiac motion between CT and corresponding CT-based attenuation corrected (CTAC) PET images on apparent myocardial uptake.

Methods: PET projection data of the 4D XCAT phantom were analytically generated using an analytic simulator considering the effect of photon attenuation and Poisson noise. The assessment of PET images was performed through qualitative interpretation by an experienced nuclear medicine physician and a volume of interest based quantitative analysis. Moreover, Box and Whisker plots were calculated and bull's eye view analysis performed. PET images were also reoriented along the short, horizontal and vertical long axis views for a better qualitative interpretation.

Results: The simulation study showed that using the attenuation map at end-exhalation of the respiratory phase consistently overestimated the activity concentration in all segments of the myocardial wall as opposed to using the end-inhalation attenuation map image which resulted in underestimation

Conclusion: CT images acquired at end-exhalation could introduce larger errors compared to end-inhalation. These errors decrease significantly when the attenuation map was acquired at mid-inhalation or mid-exhalation phases of the respiratory cycle.

1. Introduction

Imaging of the thorax region using PET for evaluation of myocardial ischemia and viability is a well-established procedure in clinical setting. With the introduction of PET/CT scanners equipped with up to 64 or 128 slice CT scanners, full cardiac assessment is made possible in one imaging session [1]. Various strategies were proposed to reduce the number of CT imaging sessions in cardiac PET/CT to decrease patient dose in multimodality cardiovascular imaging [2, 3]. The different temporal resolutions and breathing patterns between PET and CT data can potentially generate misalignment artifacts leading to inaccuracies in tracer uptake estimate especially in the thorax region [4]. Since the heart is encompassed by the lung and diaphragmatic regions which have different attenuation factors, devising CT protocols with minimal spatial misalignment with PET data is vital for accurate CT-based attenuation correc-

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tion (CTAC) of PET data. Misalignment between CT and PET data due to involuntary respiratory and cardiac motion as well as physical patient motion (global motion) was identified as the major source of artifacts and bias in myocardial wall imaging. As such, much worthwhile research focused on minimizing or correcting for this mismatch [5-6]. This misalignment can potentially be reduced by optimizing CT data acquisition protocols. For example, slow CT scanning improves the alignment between two modalities but bears some drawbacks which prevented its adoption in the clinic [7]. Alessio et al. [8] showed that using cine CT leads to an acceptable alignment between CT and PET images.

The aim of the present study is to quantitatively evaluate the effect of respiratory and cardiac motion on tracer uptake in myocardial PET imaging following CTAC of PET data. Simulation study based on the 4D XCAT phantom were used to assess the influence of complex cardiac and respiratory motion and dedicated CT acquisition protocols on the accuracy of CTAC in myocardial PET imaging.

2. Materials and Methods
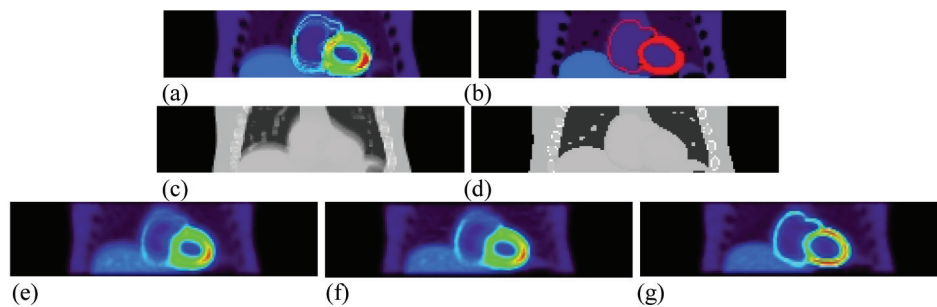
2.1. Simulation Study

The NURBS-based 4D XCAT phantom [9] was used to evaluate the impact of misalignment artifacts due to respiratory and cardiac motion. A dataset with normal respiratory and cardiac cycles was utilized corresponding to 5 and 1 sec durations, respectively. Two 3D 256×256×81 voxelized binary files representing activity and attenuation maps in the XCAT phantom at various respiratory and cardiac phases were used as input to the simulation process. The activity maps of individual organs were assigned according to Buther et al. [10]. The simulated datasets were divided into 4 respiratory phases including end-exhalation, mid-inhalation, end-inhalation and mid-exhalation and 4 cardiac cycles: (1) end diastole (ED); (2) 62% contraction of left ventricle; (3) 17% relaxation of left ventricle; (4) 58% relaxation of left ventricle. In addition to 20-phase gating, averaging over respiratory and cardiac cycles was also considered. To ascertain the effect of misalignment produced by respiratory motion on the quantification of PET images, the impact of scanning at different respiratory phases along with the end-diastole (ED) cardiac cycle were considered during attenuation correction of PET emission data. Since many centers do not use breath hold CT image for attenuation correction of PET images, attenuation corrected PET emission data with corresponding attenuation maps averaged over all respiratory and cardiac cycles were considered as a reference due to CT anatomy data aligned with corresponding emission data. For each respiratory and cardiac phase, PET projection data were analytically generated using the projection utility of the STIR software package [11] considering the effect of photon attenuation and

Table 1. Absolute percentage difference of tracer uptake in various myocardial segments of the XCAT phantom between PET images corrected for attenuation using an attenuation map averaged over respiratory and cardiac cycles as a reference vs. PET images corrected for attenuation using attenuation maps derived from various respiratory and cardiac phases.

Myocardial wall	Absolute percentage difference in tracer uptake			
	Respiratory phase at full exhalation Cardiac phase in ED	Respiratory phase at mid inhalation Cardiac phase in ED	Respiratory phase at full inhalation Cardiac phase in ED	Respiratory phase at mid exhalation Cardiac phase in ED
Anteroseptal	8.84	1.68	5.16	1.68
Anterolateral	7.08	3.79	5.02	4.33
Lateroanterior	10.87	3.31	9.55	3.31
Lateroinferior	11.39	1.89	9.59	1.89
Inferolateral	13.66	0.76	8.18	1.40
Inferoseptal	14.44	1.50	8.49	0.71
Septoinferior	13.89	1.45	8.04	1.45
Septoanterior	11.60	2.47	6.71	2.47
Apex	27.94	2.94	16.17	2.94

*ED: end diastole

Figure 1. Coronal view of the XCAT phantom. **(a)-(b)** activity maps obtained by averaging over all cardiac and respiratory cycles and at mid-inhalation respiratory phase and end diastolic cardiac cycle; **(c)-(d)** Attenuation maps obtained corresponding to the above mentioned phases; **(e)-(f)** Images obtained from PET emission data averaged over all cardiac and respiratory cycles corrected for attenuation using the above mentioned attenuation maps; **(g)** PET image obtained using dual cardiac-respiratory gating of the data corrected with matching respiratory and cardiac phase (mid-inhalation, end-diastole).

adding Poisson noise as follow: First, attenuated PET data are produced using the original activity map and corresponding reference attenuation map. Second, the attenuated emission sinogram is corrected for attenuation using the different attenuation generated in different phase of respiratory cycle. Third, the sinogram resulting from the previous step is reconstructed using STIR's Ordered Subset Maximum A Posteriori One-Step-Late (OSMAPOSL) reconstruction algorithm to provide the corrected PET image. The analytical simulation strategy used in this study was already validated in our previous work [12, 13].

2.2. Assessment Strategy

The attenuation corrected PET images were assessed using both qualitative interpretation and quantitative analysis. 500 volumes of interest (VOIs) were delineated on each PET image using the AMIDE image processing software on myocardial segments of the left ventricle [14]. Moreover, Box and Whisker plots and semi-quantitative analysis of uptake values based on 17-segment bull's eye view model (each segment normalized to the maximum value) were performed. An absolute percentage difference in tracer uptake in all segments in the myocardial wall was also assessed. PET images were also aligned along the short axis and horizontal/vertical long axis views for a clinical interpretation by an experienced nuclear medicine physician.

3. Results

Figures 1(a-b) show the activity maps obtained from the XCAT phantom averaged over all cardiac and respiratory cycles and the study corresponding to mid-

inhalation respiratory phase and end diastolic cardiac phase. The corresponding attenuation maps are shown in Figures 1(c-d). Figures 1(e-f) illustrate PET images corrected for attenuation using the above referenced attenuation maps. It was observed that the emission data obtained from dual cardiac-respiratory gated data corrected with matching respiratory and cardiac phase depicts better sharpness in the myocardial wall (Figure 1(g)). Figure 2 shows the Box and Whisker plots of the relative difference in tracer uptake in 5 segments of the myocardial wall. The anterior and lateral wall produces the strongest effects resulting from respiratory and cardiac motions. The end-inhalation phase resulted in an underestimation of uptake value in all myocardial segments compared to the end-exhalation phase. Figures 3 (a-b) shows the influence of the attenuation map generated at different respiratory and cardiac phases on changes in myocardial uptake on the corresponding PET images.

The impact of relative motion is apparent on myocardial uptake value. An underestimation of the uptake value can be observed in the anterior and lateral regions at end-inhalation (Figure 3(b)) whereas an overestimation is observed in the same regions at end-exhalation (Figure 3(a)). Furthermore, a slight overestimation of activity is also depicted in the anterolateral segment of PET images corrected with mid-exhalation and mid-inhalation respiratory phases (data not shown) but no obvious significant difference is seen between PET images corrected using CT images acquired at mid-exhalation and mid-inhalation phases owing to small changes in the phantom anatomy.
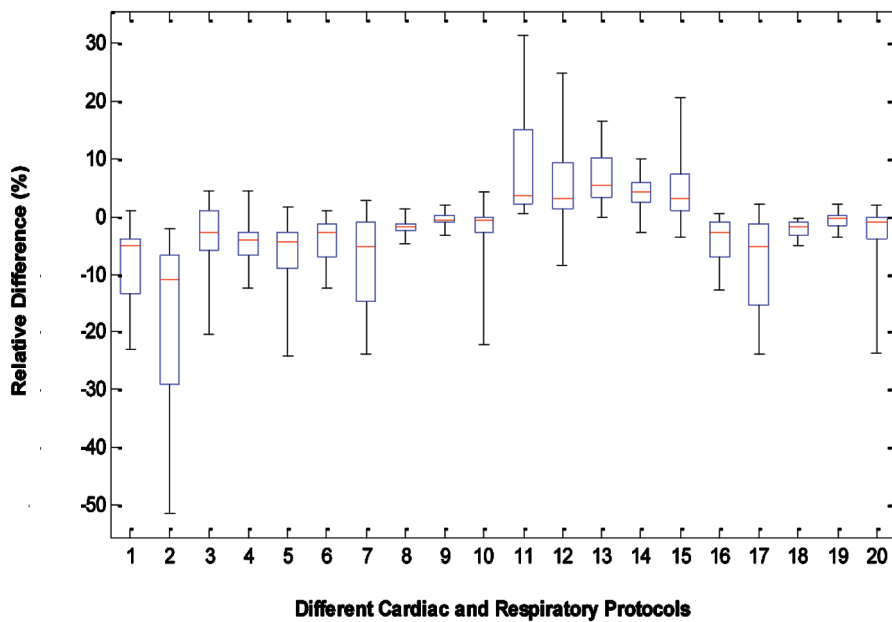
Figure 2. Box and Whisker plots showing (1-5) the relative difference between tracer uptake in five myocardial segments (anterior, lateral, inferior, septal and apex, respectively) between PET images corrected for attenuation using an attenuation map averaged over respiratory and cardiac cycles (serving as reference) and PET images corrected for attenuation using an attenuation map at (1-5) end-exhalation, (6-10) mid-inhalation, (11-15) end-inhalation, and (16-20) mid-exhalation. End diastolic cycle was used in all cases.

Table 1 summarizes the influence of using different attenuation maps on tracer uptake in the myocardial region. It can be clearly seen that using attenuation maps at the end of the breathing cycles can produce severe over/ underestimations of PET tracer uptake in all myocardial segments. In particular, significant artificial uptake can be observed in the apex region when attenuation correction is performed using attenuation maps acquired at the end-exhalation and end-inhalation respiratory phases.

4. Discussion

A major pitfall in PET/CT imaging is the mismatch between PET and CT data owing to respiratory and cardiac motion as well as bulk motion of the patient [15]. As such, attenuation corrected PET images with misaligned CT can project lung tissues onto the myocardial wall [15] or liver dome and a part of the diaphragm onto the thorax region, leading to clinical
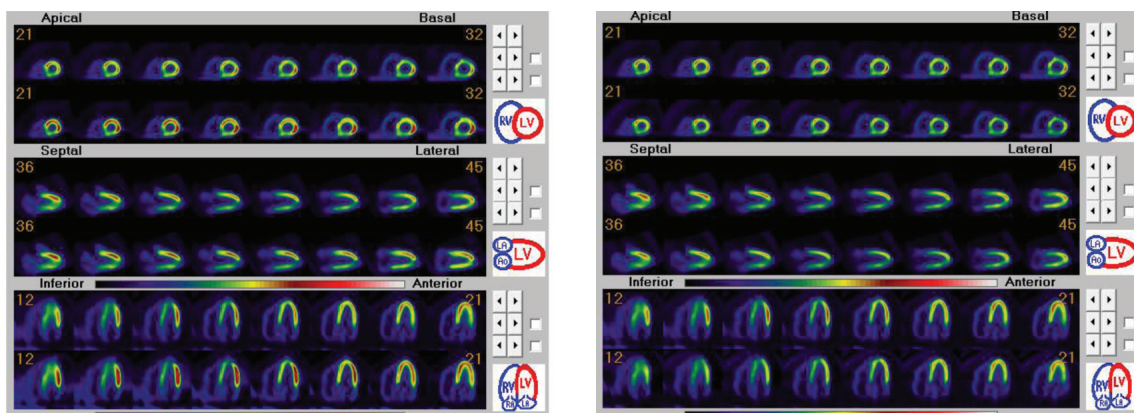
Figure 3. Representation of typical short, vertical and horizontal long axis of attenuation corrected PET images of the XCAT phantom using the following attenuation maps: (top row) averaged over respiratory and cardiac cycles serving as reference vs. (bottom row); (a) end-exhalation at the end diastolic cardiac cycle; (b) end-inhalation at the end diastolic cardiac cycle.

misinterpretation. One approach to reduce the effect of misalignment due to different temporal resolutions between transmission and emission data is to optimize respiratory patterns of the attenuation map in order to achieve high quality images in the thorax region. In agreement with the observations made by Chin et al, [16] the overestimation of tracer uptake in PET images was present in all segments of the myocardial wall when the attenuation map at end-exhalation is used in comparison to end-inhalation. Similar to the findings of Fitzpatrick and Wells [17], our results demonstrated a slight overestimation of tracer uptake on attenuation corrected PET images using attenuation maps obtained at mid-inhalation and mid-exhalation. Greatest misalignment artifacts were observed in the anterior and lateral myocardial wall segments that are in line with our previous study [18]. This can be attributed to the fact that the anterior and lateral wall segments have the largest contact with lung tissue relative to other segments of the myocardial wall (inferior and septal) and the large differences between attenuation factors of myocardial wall and lung tissues. Even though exhalation spans nearly 2/3 of the respiratory cycle, PET images corrected using attenuation maps at end-inhalation exhibited less errors in the myocardial wall relative to those corrected using attenuation maps at end-exhalation. This is consistent with the findings of Cook at al [19]. This is because, at end-exhalation, the heart region in PET images is incorrectly replaced by liver regions, whereas at end-inhalation, it is replaced by lung tissue. The latter produces a larger difference in attenuation factors [19]. The main findings of the simulation study are that PET images corrected using attenuation maps obtained at mid-exhalation and mid-inhalation provided images that are highly comparable to those corrected using CT images averaged over the entire respiratory cycle, in comparison to attenuation maps obtained at extreme phases of the respiratory cycle.

5. Conclusions

We analyzed the effect of cardiac and respiratory motion in CT-based attenuation corrected PET images in the myocardial wall using the XCAT phantom. Simulation studies revealed that the smallest misalignment artifact appears when the attenuation maps are generated at mid-exhalation or mid-inhalation. Even though under these circumstances, non-negligible errors can be observed in the anterolateral wall. Our results demonstrate that an overestimation of tracer uptake was observed at end-exhalation, mid-inhalation and mid-exhalation compared to end-inhalation. Using CT im-

ages at extreme phases of the respiratory cycle do not produce attenuation maps suitable for attenuation correction of corresponding PET data. The anterior and lateral segments of the myocardium were also susceptible to errors in these cases. In conclusion, it seems that in clinical situations the magnitude of the errors will be more severe at end-exhalation compared to end-inhalation phase. However, more clinical evaluation with large patient population is suggested.

Acknowledgment

References

[1]. M. Hacker, "Cardiac PET-CT and CT Angiography," Curr Cardiovasc Imaging Rep, vol.6, no.2, p. 191-196,2013.

[2]. P. Ghafarian, S.M. Aghamiri, M.R. Ay, B. Fallahi, A. Rahmim, T.H. Schindler, O. Ratib and H. Zaidi, "Coronary calcium score scan-based attenuation correction in cardiovascular PET imaging," Nucl Med Commun, vol. 31, no. 9, p. 780-7, 2010.

[3]. H. Zaidi, R. Nkoulou, S. Bond, A. Baskin, T. Schindler, O. Ratib and J. Declerck, "Computed Tomography calcium score scan for attenuation correction of N-13 ammonia cardiac positron emission tomography: Effect of respiratory phase and registration method," Int J Cardiovasc Imaging, vol. 29, no. 6, p. 1351-60, 2013.

[4]. R. Nakazato, D. Dey, E. Alex₋nderson, A. Meave, M. Jiménez, E. Romero, R. J₋come, M. Pe☐a, D.S. Berman and P.J. Slomka, "Automatic alignment of myocardial perfusion PET and 64-slice coronary CT angiography on hybrid PET/CT," J Nucl Cardiol, vol. 19, no. 3, p. 482-91, 2012.

[5]. P. Ghafarian, M.R. Ay, A. Fard-Esfahani, A. Rahmim and H. Zaidi " Quantification of PET and CT misalignment errors due to bulk motion in cardiac PET/CT imaging: Phantom and clinical studies, " Frontiers in Biomedical Technologies, vol. 1, no. 3, p. 159-167,2014.

[6]. R.G. Wells, T.D. Ruddy, R.A. DeKemp, J.N. DaSilva and R.S. Beanlands, "Single-phase CT aligned to gated PET for respiratory motion correction in cardiac PET/CT," J Nucl Med, vol. 51, no.8, p. 1182-90, 2010.

[7]. J.A. Nye, F. Esteves and J.R. Votaw, "Minimizing artifacts resulting from respiratory and cardiac motion by optimization of the transmission scan in cardiac PET/CT," Med Phys, vol. 34, no. 6, p. 1901-6, 2007.

[8]. A.M. Alessio, S. Kohlmyer, K. Branch, G.Chen, J. Caldwell and P.Kinahan, "Cine CT for attenuation correction in cardiac PET/CT," J Nucl Med, vol. 48, no.5, p.794-801, 2007.

[9]. P. Ghafarian et al, "Is metal artefact reduction mandatory in cardiac PET/CT imaging in the presence of pacemaker and implantable cardioverter defibrillator leads?," Eur J Nucl Med Mol Imaging, vol. 38, no. 2, p. 252-62, 2011.

[10]. M.R. Ay, A. Mehranian, M. Abdoli, P. Ghafarian and H. Zaidi, "Qualitative and quantitative assessment of metal artifacts arising from implantable cardiac pacing devices in oncological PET/CT studies: a phantom study," Mol Imaging Biol, vol. 31, no. 6, p. 1077-87, 2011.

[11]. W.P. Segars, G. Sturgeon, S. Mendonca, J. Grimeset and B. M. W. Tsui, "4D XCAT phantom for multimodality imaging research," Med Phys, vol. 37, no. 9, p. 4902-15, 2010.

[12]. F. Büther, L. Stegger, M. Dawood, F. Range, M. Schⴰfers, R. Fischbach, T. Wichter, O. Schober and K.P. Schⴰfers, "Effective methods to correct contrast agent-induced errors in PET quantification in cardiac PET/CT," J Nucl Med, vol. 48, no. 7, p. 1060-8, 2007.

[13]. K. Thielemans, C. Tsoumpas, S. Mustafovic, T. Beisel, P. Aguiar, N. Dikaios and M.W. Jacobson, "STIR: software for tomographic image reconstruction release 2," Phys Med Biol, vol. 57, no. 4, p. 867-883, 2012.

[14]. A. Akbarzadeh, M.R. Ay, A. Ahmadian, N.R. Alam and H. Zaidi , "MRI-guided attenuation correction in whole-body PET/MR: Assessment of the effect of bone attenuation," Annals of Nuclear Medicine, vol. 27, no. 2, p. 152-162, 2013.

[15]. P. Geramifar, M.S. Zafarghandi, P. Ghafarian, A. Rahmim and M.R. Ay, "Respiratory-Induced Errors in Tumor Quantification and Delineation in CT Attenuation Corrected PET Images: Effects of Tumor Size, Tumor Location and Respiratory Trace - A Simulation Study Using the 4D XCAT Phantom," Molecular Imaging & Biology, vol. 15, no. 6, p. 655-665, 2013.

[16]. A.M. Loening and S.S. Gambhir, "AMIDE: a free software tool for multimodality medical image analysis," Mol Imaging, vol. 2, no. 3, p.131-7, 2003.

[17]. K. Khurshid, R.J. McGough and K. Berger, "Automated cardiac motion compensation in PET/CT for accurate reconstruction of PET myocardial perfusion images, " Phys Med Biol, vol. 53, no. 20, p. 5705-18, 2008.

[18]. B.B. Chin, Y. Nakamoto, D.L. Kraitchman, L. Marshall and R. Wahl, "PET-CT evaluation of 2-deoxy-2-[18F]fluoro-D-glucose myocardial uptake: effect of respiratory motion," Mol Imaging Biol, vol. 5, no. 2, p.57-64, 2003.

[19]. G.M. Fitzpatrick and R.G. Wells, "Simulation study of respiratory-induced errors in cardiac positron emission tomography/computed tomography," Med Phys, vol. 33, no. 8, p. 2888-95, 2006.

[20]. R.A. Cook, G. Carnes, T.Y. Lee and R.G. Wells, "Respiration-averaged CT for attenuation correction in canine cardiac PET/CT," J Nucl Med, vol. 48, no. 5, p. 811-8, 2007.