

Enhancing Cardiac PET by Motion Correction Techniques

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Abstract

Purpose of Review Cardiac positron emission tomography (PET) images often contain errors due to cardiac, respiratory, and patient motion during relatively long image acquisition. Advanced motion compensation techniques may improve PET spatial resolution, eliminate potential artifacts, and ultimately improve the research and clinical capabilities of PET. **Recent Findings** Combined cardiac and respiratory gating has only recently been implemented in clinical PET systems. Considering that the gated image bins contain much lower counts than the original PET data, they need to be summed after correcting for motion, forming motion-corrected, high-

count image volume. Furthermore, automated image registration techniques can be used to correct for motion between CT attenuation scan and PET acquisition.

Summary While motion correction methods are not yet widely used in clinical practice, approaches including dual-gated non-rigid motion correction and the incorporation of motion correction information into the reconstruction process have the potential to markedly improve cardiac PET imaging.

Keywords Cardiac PET imaging · Gated PET · Coronary imaging · PET motion correction

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Introduction

Cardiac positron emission tomography (PET) imaging is a useful non-invasive tool in the diagnosis and risk stratification of patients with suspected coronary artery disease (CAD). Cardiac PET is widely utilized in clinical practice, and measures of myocardial blood flow and perfusion provide an assessment of ischemic burden which can in turn guide the clinician towards management decisions including the need for revascularization. In future clinical practice, coronary PET imaging may provide valuable information about plaque vulnerability and the presence and extent of high-risk disease activity. By providing absolute quantification of tracer distribution, cardiac PET can provide detailed information about physiological as well as molecular and biological processes. With the increasing availability of hybrid PET/CT and PET/MR imaging systems, anatomical information can be obtained alongside the biological data from PET, thereby allowing more precise localization of PET signal.

Due to the relatively long PET acquisition times (5–30 min), resulting images are blurred by cardiac, respiratory, and gross patient motion. Motion artifacts may degrade image

quality and lead to inaccurate interpretation, which could in turn lead to misdiagnosis. To deal with the errors caused by motion, one solution is to use PET data gating; the entire raw dataset is divided in subsets, or bins, representing a particular cardiac or respiratory phase. This method provides image datasets with reduced motion, at the expense of lowering count statistics, since the total raw counts are spread over the multiple bins. To overcome the PET statistical count drop, the different cardiac and/or respiratory phase bins can be summed together after correcting for respiratory or cardiac motion between the bins. Although these techniques are not yet used in clinical routine, they have great potential to improve the quality of PET in cardiovascular imaging. In this review, we will discuss the novel motion correction techniques which may be applied to gated cardiac PET data. We will also discuss the potential problems and solutions related to patient motion between the CT scan and PET scan.

Motion Degrades PET Image Quality

Cardiac, respiratory, and patient motion can degrade PET images and lead to a loss of spatial resolution. This is particularly problematic when imaging the small-caliber, tortuous coronary arteries and may ultimately hinder the clinical utility of high-resolution PET for this novel application [1]. Natural tidal breathing causes the heart to move more than 1 cm during each respiratory cycle, predominantly in the cranio-caudal direction [2]. In a recent study of 11 patients undergoing respiratory-gated PET [3], an average of 8 mm of motion occurred during the PET acquisition as a consequence of respiration. Cardiac motion also degrades the PET signal. It has been reported that each cardiac cycle leads to a mean myocardial motion of 12–13 mm [4]. Furthermore, average coronary artery motion has been found to be 8–26 mm, the right coronary artery (RCA) presenting the most noticeable motion [5]. In addition to cardiac and respiratory motion, gross patient motion during image acquisition can be of further detriment to image quality. For example, in cardiac studies of ^{18}F -flurpiridaz involving data acquisition over 10 min, patient motion of up to 5 mm was described [6]. It may be assumed that studies requiring data acquisition over a longer period, such as up to 30 min required for coronary imaging, may result in a higher degree of gross patient motion. Therefore, accurate detection and correction of such motion is of key importance in minimizing diagnostic errors and maximizing the clinical utility of cardiac PET [7].

In order to appreciate the difficulties arising from motion, it is important to compare the respiratory, cardiac, and patient motion amplitude with the resolution of PET. The latter may reach 4 mm for static objects [8], but in a clinical setting, maximal resolution is more likely to reach 6–8 mm [9]. However, the recent development of novel high-resolution

reconstruction techniques, which take advantage of resolution recovery compensation, could enable PET to reach a static resolution of 2 mm [10]. Indeed, these new techniques have been applied to cardiac PET, demonstrating improvements [11]. Thus, when such new reconstruction techniques are utilized, the effect of physiological and patient motion is likely to have a greater influence on clinical image quality than the physical resolution of the PET scanner.

Image Gating

To overcome the effects of cardiac and respiratory motion, PET gating methods are used during acquisition. Gating consists of dividing the raw PET signal into subsets or bins. It is typically performed either as phase gating (binning signal into identical percentage locations within a cycle) or as amplitude gating (binning signal into identical displacement locations). Phase gating is widely accepted to be sufficient for cardiac gating, considering that displacement of the heart wall is fairly consistent from beat to beat. Amplitude gating has been found to be more appropriate for respiratory gating, particularly for patients with highly variable respiratory patterns [12, 13]. Respiratory gating can be achieved by use of external devices such as elastic respiratory belts with sensors to monitor changes in pressure throughout the respiratory cycle [14] or alternatively by a video camera that follows chest wall movement [15]. Respiratory-gating systems send trigger signals at the beginning of a respiratory phase and/or displacement level in order to organize data into specific bins. Cardiac gating is usually performed using the patient's electrocardiogram (ECG) tracing to organize data into phases of the cardiac cycle.

In the context of cardiac PET imaging, the need for gating time cardiac and respiratory motion simultaneously (so called dual-gating) presents a greater challenge. The use of external devices for respiratory gating may lead to increased patient discomfort as well as greater complexity of cardiac imaging protocols. Moreover, stress imaging and use of isotopes with a short half-life such as ^{82}Rb make a dual-gating technique even more difficult to set up. To overcome these challenges, use of signals obtained from standard ECG electrodes during cardiac PET [3], bio-impedance approaches, and techniques based on accelerometers [16] allowing simultaneous acquisition of both respiratory- and cardiac-gating signals have recently been suggested. These techniques have the potential to minimize logistical barriers in the adoption of dual-gating for cardiac PET in the clinical setting.

Data-driven (or self-gated) techniques have further been considered. As an alternative to using an external device, these techniques utilize the raw list-mode PET data to compute respiratory-gating signals retrospectively [17–19]. One software approach involves following the respiratory motion

of the myocardium from the PET data alone, by means of image-processing techniques; the centroid of the myocardial activity is tracked without external respiration measurements. This method has been evaluated in cardiac imaging and has demonstrated comparable results with techniques using external respiratory monitoring [17]. However, such software techniques rely upon a PET tracer signal in the organs of interest and therefore, in coronary PET imaging, where only a small activity is observed in the myocardium, these techniques may be more difficult to apply.

Attenuation Correction Issues from Motion

Prior to image reconstruction, PET data are corrected for numerous degrading effects such as scatter events, random events, and detector efficiency. The largest correction is for photon attenuation that can lead to 10- to 150-fold reductions/errors in detected signal depending on patient morphology [20]. In PET/CT systems, attenuation correction is performed with an attenuation map derived from the CT acquisition. Considering that PET imaging is acquired over multiple respiratory cycles and CT imaging is acquired at essentially only one location in the respiratory cycle, misalignment of these temporally different scans is common and often occurs in the diagnostic region of interest (along anterior and lateral free wall of myocardium adjacent to the left lung), leading to moderate to severe artifacts in 40% of cardiac PET-helical CT acquisitions [21], as illustrated in Fig. 1. These misalignment artifacts are well appreciated in cardiac PET/CT [22, 23], representing one of the leading challenges in performing accurate cardiac PET imaging in the presence of respiratory motion [24].

Ideally, PET images would be formed from phase-matched attenuation maps [25, 26]. In PET/CT, phase-matched CTs can be generated from gated 4D CT acquired in cine mode using “step-and-shoot” techniques or using low-pitch helical mode [15, 27–29]. Considering the complexity of generating phase-matched CT images, free-breathing CT, end-expiration CT, or the average of cine CT images [30, 31] are preferably used in clinical practice. Along with these clinically available

techniques, there has been a multitude of proposed future solutions for this problem such as image-based and data-domain registration of PET and CT data [15, 32–34]. Vendors software solutions for attenuation maps registration are becoming available for routine clinical use [34].

Coronary PET Imaging

The increase in PET resolution has allowed the study of small structures of interest. Indeed, coronary plaque imaging has become feasible, and it has been demonstrated for several tracers despite the small caliber and tortuous nature of coronary vessels and small volumes of coronary plaques. In coronary plaque imaging, PET activity originating from the arterial wall needs to be quantified with respect to standard uptake value (SUV) and target-to-background ratio (TBR). The development of PET/CT scanners with high-end 64-slice or higher CT has permitted the localization of small coronary plaque lesions using accurate superposition with high-resolution CT angiography [7, 35–37].

Coronary PET imaging and tracer quantification are extremely sensitive to motion of the arteries, which can lead to loss of an already limited image resolution and significantly reduce SUV or TBR measures. In the case of coronary PET using ^{18}F -FDG, an additional limitation is posed by uptake of the tracer by the metabolically active myocardium, which may obscure plaque activity due to arterial/myocardial motion [38]. Interfering cardiac motion may be one of the key reasons why studies investigating the role of ^{18}F -FDG in measuring coronary plaque inflammation have been less promising than in the study of the larger, stationary carotid vessels [35, 36, 39]. To overcome blurring of the PET signal as a consequence of cardiac motion during imaging of the coronary arteries, one approach has been to utilize only one cardiac bin (the diastolic phase), therefore using only 25% of the counts from the entire PET acquisition [7]. In a recent study using ^{18}F -sodium fluoride, this method enabled improved localization of coronary plaques but at the cost of an increase in noise and reduction in measured counts (standardized uptake value). However, this method only partially compensates for cardiac motion and

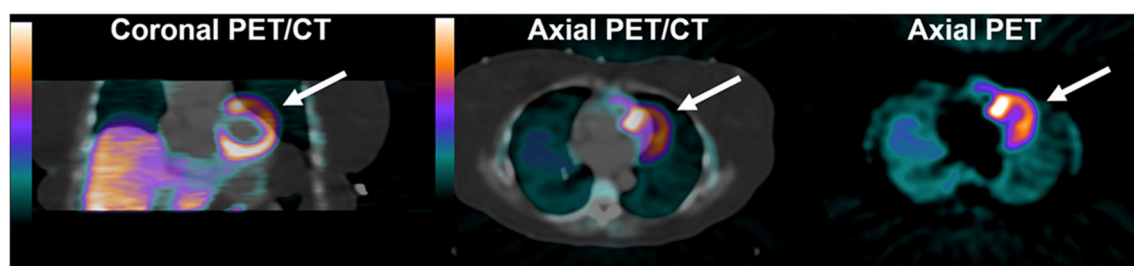


Fig. 1 Example of cardiac PET/CT perfusion exam with PET and CT misalignment. The CT acquisition was performed at a location in the respiratory pattern with more inspiration than the average location

during PET imaging. This leads to misalignment along the lateral free wall and an artifactual perfusion defect at that location

does not account for respiratory or gross patient motion. Nonetheless, eliminating more of the PET data to account for respiratory motion would lead to a further increase in noise and loss of count statistics, reducing the accuracy of the results.

Motion Correction Techniques

Segmentation-Based Methods

One solution to preserve count statistics in cardiac PET imaging is to correct for motion between the individual cardiac and/or respiratory bins. If the gated images provide a clear definition of the myocardium, cardiac motion may be estimated straightforwardly by detecting the myocardium and tracking its contours. “Motion-frozen” cardiac motion correction approaches have previously been proposed, aimed at increasing imaging resolution in cardiac SPECT and PET [4, 40]. First, the motion vectors are determined by tracking the movement of the left ventricle segmentations in the gated data. Then, non-linear registration techniques are applied to transform the gated images according to these motion vectors. This motion correction method showed improvements compared to classical reconstruction techniques regarding myocardial wall thickness and contrast-to-noise ratio [40] and diagnostic outcome [41].

Registration-Based Methods

In coronary PET imaging, the structures of interest do not allow direct warping from the left ventricular segmentation results because there may be no clear uptake in the myocardium. In a recent ^{18}F -NaF coronary imaging study [42], a motion correction method was employed to enhance image quality and improve uptake estimates. PET data from 17 patients was reconstructed using 10 cardiac phases (bins). Subsequently, all the bins were registered locally to the end-diastolic bin, using a non-linear motion correction method [43] guided by the coronary arteries extracted from the same patient CT angiography. The motion-corrected images were then created by summing of all registered bins. These images were compared with the reference standard of using only the end-diastolic image of PET data with 25% of the counts as used in previous studies or ungated images [7]. The motion-corrected data created from 10 bins resulted in a significantly higher TBR (+11%) and a greatly reduced noise (−50% due to the use of counts from all the cardiac gates), as seen in Fig. 2.

Other algorithmic solutions were explored recently in the context of ^{18}F -NaF coronary imaging [44], aiming at comparing demons [45] versus level-set [43] non-linear registration techniques for registration of the coronary artery PET images. This study showed that the demons

method produces smoother and more realistic motion fields, while keeping the improvements in terms of TBR and noise reduction, as compared to the use of only one bin of PET data [7].

Cardiac motion correction was also applied to ^{18}F -NaF PET imaging of the aortic valve in patients with aortic stenosis in order to improve the reproducibility of quantitative tracer uptake in the aortic valve [46]. For this purpose, 15 patients with aortic stenosis underwent two combined ^{18}F -NaF (125 MBq) PET and CT angiography scans within 2 months. A motion correction algorithm [47] was then applied to align PET images from four cardiac gates in both PET studies, leading to improved reproducibility (measured as the SUV difference) between the two repeated studies, as compared to ungated and one bin data. Thus, motion correction may lead to enhanced value of ^{18}F -NaF aortic valve PET in risk stratification and guiding clinical management of patients with aortic stenosis.

Motion Correction Within Reconstruction

Each of the registration methods described previously are applied after PET reconstruction. Ultimately, a motion correction method which is directly incorporated into image reconstruction is desirable [48] as this has been shown to produce less noise and bias in the images than conventional post-reconstruction correction methods [49, 50]. Furthermore, the potential misregistration of attenuation maps with the PET data can only be corrected for during the reconstruction. Some preliminary studies have demonstrated that a motion correction step can indeed be integrated directly into the reconstruction process. In the work by Hong et al. [51, 52], a mass preservation optical flow method [53] was applied to cardiac-gated PET images after reconstruction. Then, the resulting motion vectors were integrated back into the reconstruction process. The resulting images presented a superior signal-to-noise ratio, without sacrificing spatial resolution. Respiratory non-rigid motion correction has also been investigated to be integrated in a list mode-based reconstruction on phantom data [54]. Further studies should evaluate the benefits of such a reconstruction-based motion correction over techniques applying post-processing motion correction.

Dual-Gated Motion Correction

In cardiac PET, dual cardiac and respiratory gating presents significant challenges in maintaining image quality due to the fact that count statistics in individual bins are much lower than original ungated or static images. A consequence of utilizing only a limited number of bins to compensate for motion is the increase in noise observed in each frame containing only counts from certain phases of the cardiac and respiratory cycle. Indeed, the noise observed in each bin is greater than that observed in the image acquired from the entire cardiac

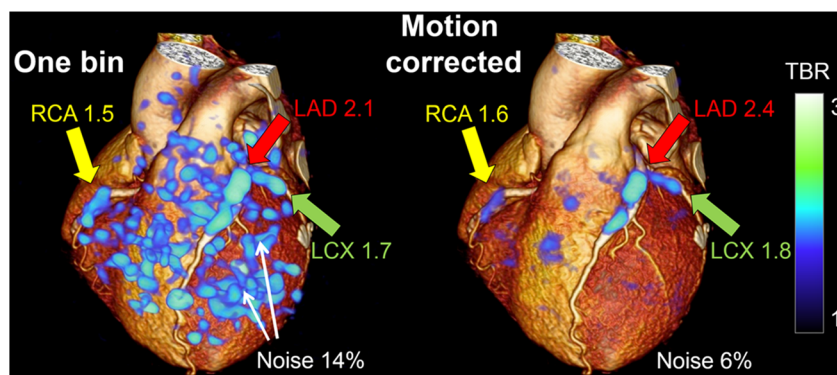


Fig. 2 Three-dimensional rendering of one-bin image (25% of PET counts) as in the study of Joshi et al. [7] (*left*) and motion-corrected image (*right*) superimposed on rendered CCTA volume. Increased uptake is seen in right coronary artery (RCA), left anterior descending (LAD), and left circumflex (LCX) coronary arteries in high-noise, one-

bin image and remains clear in motion-corrected image (This research was originally published in JNM. Rubeaux et al. Motion correction of ^{18}F -NaF PET for imaging coronary atherosclerotic plaques. *J Nucl Med* 2016; **57**(1): 54–9. © by the Society of Nuclear Medicine and Molecular Imaging, Inc.) [42•]

and respiratory cycle. Thus, the compromise between gating and image noise must be carefully considered [55]. However, dual cardiac and respiratory gating has demonstrated to favor improved spatial resolution and discrimination of the myocardial walls when compared to an ungated acquisition [3].

In a recent study [56•], motion correction was applied to dual-gated Flurpiridaz F18 cardiac PET data. The dual-gating data consisted of eight cardiac and four respiratory bins, as shown in Fig. 3. Therefore, a single-image bin contained less than 5% of the counts as compared to the ungated image. The dual-motion correction method was then applied in two consecutive steps. First, the cardiac-gated images were non-

linearly registered to the end-diastolic gate by motion tracking of the detected left ventricle endocardial and epicardial borders using the segmentation-based method described previously [40]. Then, to compensate for respiratory motion, the four cardiac end-diastolic, motion-corrected bins (one for each respiratory gate) were registered to the end-inspiration bin using a rigid transformation [6]. This dual-motion correction method resulted in a final motion-free, end-diastole/end-inspiration static image with better contrast-to-noise ratio and decreased wall thickness compared to ungated data, as illustrated in Fig. 4. This final motion-corrected image includes all counts from the full cardiac and respiratory cycles.

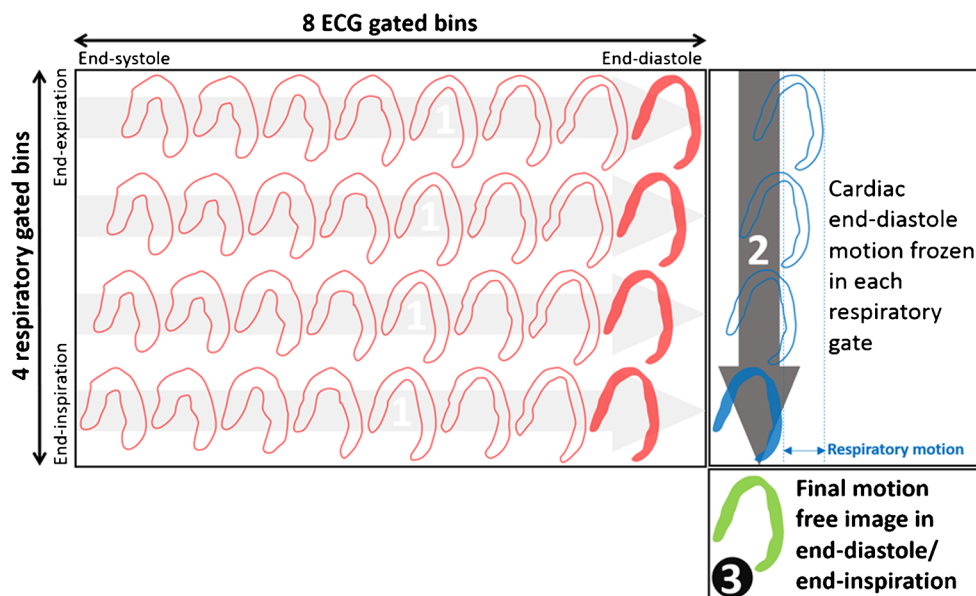


Fig. 3 Illustration of dual-respiratory/cardiac motion correction (MC) technique. 1. Cardiac-MC processing separately in each respiratory phase (contoured red bins) to end-diastolic phase (solid red bins). 2. Respiratory-MF processing of cardiac end-diastolic bins (contoured blue bins) to end-inspiration bin (solid blue bin). 3. Final motion-free

image in end-diastole/end-inspiration (solid green bin). ECG: electrocardiography (This research was originally published in JNM. Slomka et al. Dual-gated motion-frozen cardiac PET with Flurpiridaz F18. *J Nucl Med*. 2015;**56**(12):1876–81. © by the Society of Nuclear Medicine and Molecular Imaging, Inc.) [56•]

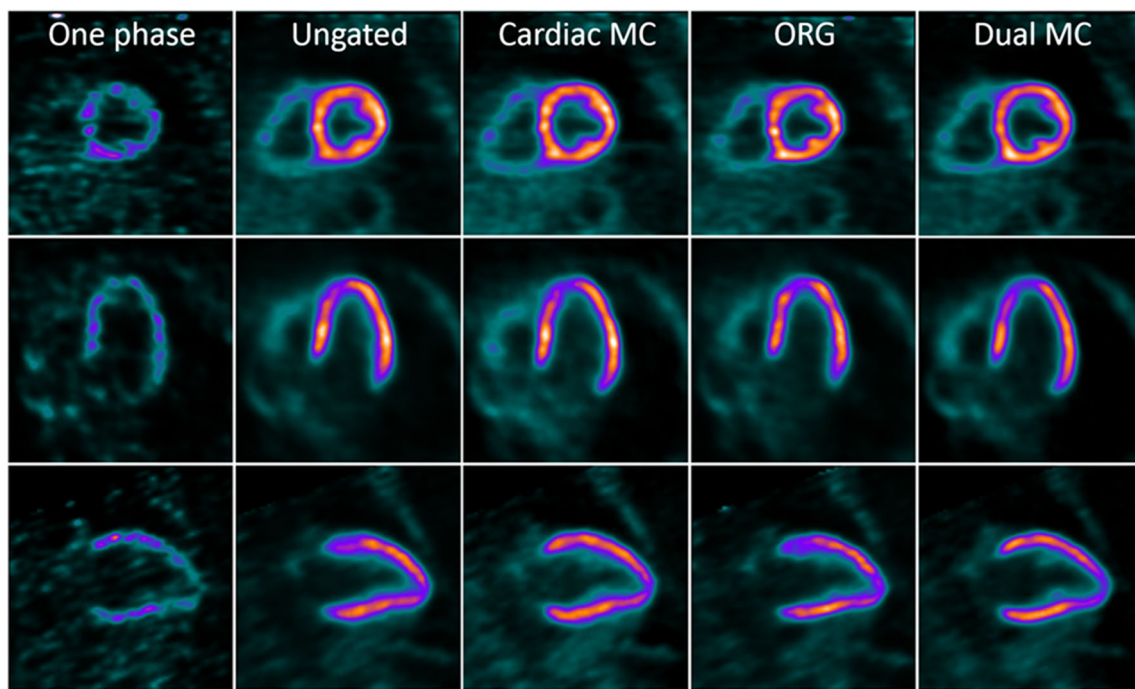


Fig. 4 A 42-year-old female patient with low likelihood of coronary artery disease (weight 86.2 kg [190 lbs]; body mass index 34.7) injected with 284.9 MBq (7.7 mCi) of Flurpiridaz F18 during exercise stress and acquired in dual (cardiac and respiratory) mode. Short-, vertical-, and horizontal-axis views of adenosine stress images. *One phase*: one cardiac gate in end-inspiration; *MC*: motion correction; *dual MC*: dual (cardiac/respiratory) MC; *cardiac MC*: no respiratory gating;

ORG: optimal respiratory gating, a reconstruction technique designed to keep 35% of the PET counts in one optimal respiratory gate in which breathing motion is minimal [57] (This research was originally published in JNM. Slomka et al. Dual-gated motion-frozen cardiac PET with Flurpiridaz F18. *J Nucl Med.* 2015;56(12):1876–81. © by the Society of Nuclear Medicine and Molecular Imaging, Inc.) [56•]

Following the same methodology, other motion correction schemes have been investigated [58] in the context of dual-gated PET imaging on phantom and patient data. This study led to the conclusion that a non-rigid motion correction model gives better results as compared to using only the diastolic image, showing also that relatively straightforward registration schemes, like an affine model, could be employed successfully. Therefore, dual-gated motion correction techniques could be useful in clinical practice. However, no clinical cardiac studies so far have demonstrated the clinical utility of such technique.

Conclusions

Cardiac PET is a useful clinical tool with many current and promising future clinical applications. Recent studies have suggested its potential for coronary imaging, which could represent a major advance in cardiac risk stratification and in the management of patients with coronary artery disease. Despite this, significant challenges are presented by cardiac, respiratory, and gross patient motion, each of which degrades PET image quality and impairs effective image resolution. Ultimately, these challenges hinder the clinical utility of cardiovascular PET imaging. In order for this imaging modality

to fulfill its potential in imaging of small structures, including the coronary arteries, sophisticated techniques are required for the recovery of spatial resolution lost as a consequence of motion. Established techniques including respiratory and cardiac gating have led to improvements but have limitations resulting from a trade-off between reduced motion and increased noise. To overcome this drawback, advanced software registration may be required to correct for motion in dual-gated acquisitions. The most promising techniques include dual-gated non-rigid motion correction methods, as well as the incorporation of motion correction within the reconstruction process. With the development and adoption of these techniques, the potential for evolution of cardiac PET in non-invasive cardiac and coronary imaging is high.

Compliance with Ethical Standards

Conflict of Interest Mathieu Rubeaux and Mhairi Doris declare that they have no conflict of interest.

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