Patient motion effects on the quantification of regional myocardial blood flow with dynamic PET imaging

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Purpose: Patient motion is a common problem during dynamic positron emission tomography (PET) scans for quantification of myocardial blood flow (MBF). The purpose of this study was to quantify the prevalence of body motion in a clinical setting and evaluate with realistic phantoms the effects of motion on blood flow quantification, including CT attenuation correction (CTAC) artifacts that result from PET–CT misalignment.

Methods: A cohort of 236 sequential patients was analyzed for patient motion under resting and peak stress conditions by two independent observers. The presence of motion, affected time-frames, and direction of motion was recorded; discrepancy between observers was resolved by consensus review. Based on these results, patient body motion effects on MBF quantification were characterized using the digital NURBS-based cardiac-torso phantom, with characteristic time activity curves (TACs) assigned to the heart wall (myocardium) and blood regions. Simulated projection data were corrected for attenuation and reconstructed using filtered back-projection. All simulations were performed without noise added, and a single CT image was used for attenuation correction and aligned to the early- or late-frame PET images.

Results: In the patient cohort, mild motion of 0.5 ± 0.1 cm occurred in 24% and moderate motion of 1.0 ± 0.3 cm occurred in 38% of patients. Motion in the superior/inferior direction accounted for 45% of all detected motion, with 30% in the superior direction. Anterior/posterior motion was predominant (29%) in the posterior direction. Left/right motion occurred in 24% of cases, with similar proportions in the left and right directions. Computer simulation studies indicated that errors in MBF can approach 500% for scans with severe patient motion (up to 2 cm). The largest errors occurred when the heart wall was shifted left toward the adjacent lung region, resulting in a severe undercorrection for attenuation of the heart wall. Simulations also indicated that the magnitude of MBF errors resulting from motion in the superior/inferior and anterior/posterior directions was similar (up to 250%). Body motion effects were more detrimental for higher resolution PET imaging (2 vs 10 mm full-width at half-maximum), and for motion occurring during the mid-to-late time-frames. Motion correction of the reconstructed dynamic image series resulted in significant reduction in MBF errors, but did not account for the residual PET–CTAC misalignment artifacts. MBF bias was reduced further using global partial-volume correction, and using dynamic alignment of the PET projection data to the CT scan for accurate attenuation correction during image reconstruction.

Conclusions: Patient body motion can produce MBF estimation errors up to 500%. To reduce these errors, new motion correction algorithms must be effective in identifying motion in the left/right direction, and in the mid-to-late time-frames, since these conditions produce the largest errors in MBF, particularly for high resolution PET imaging. Ideally, motion correction should be done before or during image reconstruction to eliminate PET-CTAC misalignment artifacts. © 2016 American Association of Physicists in Medicine. [http://dx.doi.org/10.1118/1.4943565]

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1. INTRODUCTION

Noninvasive regional myocardial blood flow (MBF) quantification with positron emission tomography (PET) has been shown to have superior diagnostic and prognostic value compared to conventional relative perfusion imaging.\(^1\)-\(^5\) For PET imaging, a radio-labeled molecule of interest, called a tracer, is introduced to the patient, most commonly by intravenous injection. A dynamic sequence of images is acquired starting from the time of injection until biodistribution of the tracer to the perfused tissues is completed over several minutes. Regions of interest (ROI) is typically defined on the reconstructed dynamic images and used to sample the tissue time-activity curves (TACs), corresponding to the time-dependent change of tracer concentration within the organ(s) of interest. TACs measured in the heart muscle (myocardium) and LV cavity (arterial blood) can be further processed using tracer kinetic analysis to noninvasively quantify regional MBF.

Sampling of tissue TACs using ROIs that are stationary across all dynamic time-frames assumes that the patient and organs of interest are not moving with respect to the camera. However, there is evidence that motion of patients and/or settling of the heart within the patient chest cavity during cardiac PET imaging is highly prevalent.\(^6\),\(^7\) Clinically, motion of the patient body is often caused by discomfort in response to pharmacologic stress, coughing, settling, or gradual relaxation of the thoracic muscles of the rib cage. Motion can also be observed from downward translation of the heart within the thorax due to gradual conformance of the soft tissues, following transition from the sitting position during patient preparation to supine position during imaging, sometimes referred to as “heart creep.” Patient or heart motion during a dynamic acquisition results in misalignment between the PET data and the attenuation correction (AC) map used during reconstruction, resulting in imaging artifacts in the misaligned time-frames.\(^8\),\(^9\) In addition, patient motion causes heart misalignment between successive dynamic image frames, leading to distorted TACs due to inconsistent spatial sampling, whereas within-frame motion blurs the image spatially. It has been demonstrated that this motion can reduce the accuracy of MBF quantification.\(^10\)

Tracking of patient body motion has been evaluated primarily using external fiducial markers with optical or radioactive tracking systems, automated cross correlation analysis in the late uptake frames, and manual alignment.\(^11\)-\(^13\) External markers may neglect nonrigid motion including heart creep, and thus these results may be suboptimal. In addition, late frame motion correction (MC) does not correct for motion in the early time-frames, and manual corrections are subject to operator bias. Motion tracking systems have been reported for brain (by aligning non-AC PET frames to a non-AC reference frame with known alignment), cardiac (by CT segmentation and alignment with the PET frame), or respiratory motion correction (using respiratory gating in conjunction with 4D CT imaging); potentially some of these methods could be used for patient body motion correction.\(^14\)-\(^16\)

This work evaluates the prevalence of patient body motion in a typical clinical population undergoing \(^82\)Rb PET rest and stress perfusion imaging. The results from the clinical prevalence study are then used to determine the spatial and temporal motion parameters (direction, sign, magnitude, and time of motion shift) for a comprehensive computer simulation phantom study. In addition to these motion “acquisition” parameters, several image reconstruction parameters [spatial resolution, PET-CT attenuation correction (CTAC) misalignment] and analysis parameters (LV polar-map regions, and partial-volume and motion corrections) were also evaluated according to variations in current clinical practice. Computer-generated phantom studies are beneficial because the simulated (ground truth) physiology is known and the confounding errors can be measured absolutely. In addition, the study evaluates sources of MBF error in the absence of cardiac and respiratory motion, to quantify the effect on MBF due to patient body motion alone. To the best of our knowledge, a comprehensive 3D modeling study using an NCAT phantom has not been conducted to evaluate the effects of patient body motion on MBF quantification using \(^82\)Rb PET imaging.

2. METHODS

2.A. Clinical prevalence cohort

A total of 236 patients were referred to our clinic for \(^82\)Rb PET rest-stress myocardial perfusion imaging (MPI) from August to November 2010. All patients gave written informed consent as part of the Rubidium-ARMI (NCT01128023) research protocol approved by the University of Ottawa Human Research Ethics Board. The imaging protocol consisted of a low-dose (0.2 mSv) normal-end-expiration CT attenuation scan acquired under resting conditions, followed by a 30-s constant-activity-rate “square-wave” infusion of 10 MBq/kg of \(^82\)Rb (RubyFill\(^\text{TM}\), Jubilant DraxImage, Kirkland, QC) started together with an 8-min PET acquisition in list-mode using a Discovery 690 PET-VCT scanner (GE Healthcare, Waukesha, WI). Cardiac stress was induced using dipyridamole (0.14 mg kg\(^{-1}\) min\(^{-1}\)) infusion for 5 min to increase myocardial blood flow, and a second \(^82\)Rb PET scan initiated 3 min later. Finally, a second low-dose CT attenuation scan was acquired for attenuation correction of the stress PET data. Images were reconstructed using filtered back-projection with an 8 mm Hann window of the Ramp filter, resulting in 128×128×47 voxels of size 3.125×3.125×3.270 mm, and approximately 10 mm isotropic spatial resolution. Corrections for isotope decay, photon attenuation and scatter, random and prompt-gamma coincidences, detector efficiency, and deadtime were all applied to reconstruct quantitative images of the time-dependent regional activity concentration (Bq/cm\(^3\)), according to our standard clinical practice. The 8-min dynamic image sequence used 9×10, 3×30, 1×60, and 2×120 s time-frames. CT and \(^82\)Rb PET image registration was verified manually (and adjusted if needed using the vendor ACQC program) for the heart using a static PET image of tracer uptake (2–8 min).

Reconstructed dynamic images were displayed using the FlowQuan\(^\text{t}\) software (uOHI, Ottawa, ON) in cine-mode by sweeping back-forth between time-frames using transaxial,
sagittal, and coronal views centered on the heart. Body motion in the dynamic series was evaluated visually by two independent observers and compared. In cases with any disagreement between observers, a consensus review was performed to establish the time of motion shift, direction, and severity of motion for each scan. Observers recorded the presence/absence of heart motion, affected time-frames, and perceived direction of motion in 3D. In scans where motion was estimated to be 1–2 pixels (3–7 mm), the severity was classified as mild, and in scans with motion greater than 2 pixels (>7 mm), severity was classified as moderate. A small fraction (3%) of scans with low image quality were not assessed (NA) in which the presence or absence of motion could not be reliably discerned. Due to rapid tracer distribution in the early time-frames, motion was only assessed after the first-pass transit of tracer through the heart (typically >90 s depending on the individual scan) where motion could be perceived with confidence. Both rest and stress images were assessed for all patients, thus the total number of scans reviewed was 472.

### 2.B. Computer phantom simulations

Anatomical images were derived using the NURBS-based cardiac-torso (NCAT) phantom as illustrated in Fig. 1.\(^{18,19}\) The NCAT program allows the user to assign activity to all major organs; additionally, it includes a detailed anatomic model of the heart containing the following eight regions: left atrium wall, left ventricle wall, left atrium blood-pool, left ventricle blood-pool, right atrium wall, right ventricle wall, right atrium blood-pool, and right ventricle blood-pool. The phantom used cubic voxels of 3.125 mm and had a transverse sampling grid of 128×128 pixels in 63 slices, thus the simulated phantom dimensions were 40×40×19.7 cm.

Characteristic TACs were assigned to the heart wall (myocardium) and blood regions using data from a previous \(^{82}\)Rb dosimetry study in human patients.\(^{20}\) TACs were also assigned to the following adjacent organs: lungs, liver, kidneys, spleen, stomach wall, and gallbladder. Cardiac and respiratory motions were not simulated to avoid bias from the associated blurring of the myocardial images, so that patient body motion effects were characterized alone.

The tissue attenuation factors were calculated by ray-tracing through the CT attenuation coefficient map and scaled to the known values at 511 keV. The PET images derived from the NCAT phantom were forward projected using the MATLAB\(^{®}\) 2D radon transform (128 angles) to simulate attenuated emission data. The simulated projection data were then corrected for attenuation and reconstructed using filtered back-projection, and then smoothed using a 10 mm full-width at half-maximum (FWHM) 3D Gaussian filter, to simulate the effects of positron range and the intrinsic resolution of the Discovery 690/VCT scanner, as well as the postreconstruction filtering used in clinical practice, herein referred to as the low resolution data set. In addition, a data set with a spatial resolution of 2 mm FWHM was generated, to study the effect of scanner resolution on motion artifacts, herein referred to as the high resolution data set. All simulations were performed with no noise added to avoid the potential effects of noise-bias in the estimation of myocardial blood flow. Images were reconstructed using MATLAB\(^{®}\) 2D filtered back-projection.

The workflow for generating all the motion and correction combinations is illustrated in Fig. 2. A single dataset without any PET motion (nor CTAC artifacts) was generated as the reference-standard [Fig. 2: no motion, Fig. 1(B)] to which PET motion-shifted images were compared. Motion-shifted images were created initially with no motion correction.
Computer simulations used to produce the patient motion and correction test cases. Attenuation of the projection data is denoted by “÷” and attenuation correction by “×.”

(Fig. 2: PET motion and CTAC misalignment, Table I: none), demonstrating both CTAC misalignment and PET dynamic frame misalignment artifacts to replicate uncorrected motion cases, as observed in clinical scans. In addition, data sets with motion correction of the CTAC misalignment artifacts (Fig. 2: CTAC misalignment, Table I: CTAC-alignment) were created, demonstrating PET dynamic motion artifacts, but no CTAC misalignments, to emphasize the effect of patient motion in the PET data by itself. Finally, datasets were generated with PET dynamic motion correction (Fig. 2: PET motion, Table I: PET-dynamic), having no residual motion in the PET data, but with CTAC misalignment artifacts remaining to replicate the effect of postreconstruction motion correction and to emphasize the effect of CTAC misalignment by itself.

The simulated motion and correction parameters are summarized in Table I. Body motion was simulated by a discrete shift of the PET data between time-frames at 30, 60, 120, and 240 s, in one of the six directions (±X right/left, ±Y posterior/anterior, and ±Z superior/inferior) with magnitudes of ±0.9375 (herein called ±1 cm) and 1.8750 cm (herein called ±2 cm), and nonlinear motion sometimes present in clinical cases was not simulated. A single CT image was used for attenuation correction and aligned to the early (first frame) or late (last frame) PET images. In clinical practice, CT images are typically aligned to the late PET frames, thus motion during the dynamic PET scan leads to CTAC artifacts in the early PET frames due to CTAC misalignment. Nevertheless, we also simulated alignment in the early (blood-pool) time-frames and corresponding motion misalignment in the late time-frames. Ideal motion correction was evaluated by excluding PET motion and/or CTAC misalignment from the PET simulations.

Quantification of regional MBF was accomplished using our in-house validated software program (FlowQuant®, Ottawa, ON). Uptake images were generated by averaging the last 6 min of the dynamic image data (2–8 min), reducing image noise (for clinical scans), and achieving high myocardium-to-blood-pool contrast. Uptake images were then used to estimate the size, orientation, and location of the myocardium using a fully automated process. Regions of interest with fixed epicardial and endocardial extent were generated and used to sample the dynamic image sequence to derive myocardial TACs, as previously described. The median of three blood-pool region TACs [LV cavity (C), base (B), and left atrium (A)] was used as the arterial blood input function for tracer kinetic modeling at all time-frames. Using the blood (input) and myocardium (output) TAC functions, the parameters of a 1-tissue-compartment kinetic model with globally derived average distribution volume were estimated. The program produces values of regional and global MBF in units of mL/min/g using regional and global partial-volume corrections (PVCs) as

![Diagram](image-url)

**Fig. 2.** Computer simulations used to produce the patient motion and correction test cases. Attenuation of the projection data is denoted by “÷” and attenuation correction by “×.”

| Stage | Parameter | Description |
|-------|-----------|-------------|
| Acquisition | Motion direction | X (left/right), Y (anterior/posterior), Z (superior/inferior) |
| | Motion sign | Positive (left/anterior/sup), negative (right/posterior/inferior) |
| | Motion magnitude | 1, 2 cm |
| | Motion time (of shift) | 30, 60, 120, 240 s |
| Reconstruction | Spatial resolution | High, low (2, 10 mm FWHM) |
| | CTAC alignment | Early, late PET reference frames |
| Analysis | Polar-map segment | Anterior, posterior, lateral, septal, apex |
| | Partial-volume correction | Regional, global |
| | Motion correction | None, PET-dynamic, CTAC-alignment |

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previously described.\textsuperscript{17,21} Briefly, the regional PVC estimates a separate recovery coefficient for every polar-map sector, as the complement of the total blood volume fraction (1 – TBV), shown in Fig. 4. The global PVC applies a patient-specific average recovery coefficient estimated as 1 – TBV\textsubscript{mean}.

The regional MBF data (polar-maps) were then analyzed using a standard 5-segment model consisting of the following anatomic regions: anterior, posterior, septal, lateral, and apex. Data reported from the 5-segment model represent the average MBF value in each segment. MBF errors were determined by calculating the absolute relative difference (in %) of each segment in the 5-segment model of a motion case from the baseline case without motion. There were 5760 total data points over nine simulated parameters generated from this study as shown in Table I.

2.C. Statistical analysis

The magnitudes of motion observed in the clinical cohort are reported as mean ± standard deviation (95% confidence interval). The proportion of measured magnitudes and directions of motion are presented as percentages.

For the computer simulation studies, multivariate analysis of MBF errors was carried out using analysis of variance (ANOVA) of the individual simulation parameters, as well as 2- and 3-parameter interactions (with detailed results shown in the supplementary material).\textsuperscript{28} Motion effects highlighting important interactions were chosen from among the most highly significant 2- and 3-parameter interactions. The median interaction effects were illustrated as box plots, with outliers defined as >1.5 times the interquartile range above the median values. Post hoc pairwise comparison of median values was performed using the Wilcoxon rank-sum test at the 95% confidence level.

All statistical analyses were performed using MATLAB\textsuperscript{®} (Mathworks, Natick, MA). P-values < 0.05 were considered statistically significant.

3. RESULTS

3.A. Clinical prevalence cohort

The average patient age was 64 ± 11 yr (range 33–89); 51% of the patients were male.

The prevalence of motion is illustrated in Fig. 3(A). Severe motion (>7 mm) occurred with the highest frequency of 38%. In 35% of cases, there was no motion observed, and in 24% of cases, there was some mild motion evident. In 3% of scans the direction and/or magnitude could not be assessed (NA). The mean magnitude of motion reported automatically by FlowQuant\textsuperscript{®} using cross correlation of sequential time-frame images was 0.5 ± 0.1 [0.3–0.7] cm, and 1.0 ± 0.3 [0.7–1.8] cm for mild and severe motion cases respectively, agreeing well with the visual classification of motion magnitude. Both rest and stress scans were analyzed for all patients. No significant differences in the direction or magnitude of motion were observed between rest and stress scans.

Figure 3(B) illustrates the prevalence of motion direction in the combined pool of patients with mild or severe motion. Motion occurred most commonly in the axial direction with 30% of motion in the superior (+Z) direction and 15% in the inferior (−Z) direction. Motion in the Y direction was predominantly posterior (29%). Motion in the X direction accounted for 24% of cases, with relatively similar proportion in the left (+X) and right (−X) directions. Using this information, computer phantom simulations were designed using the worst-case results (moderate motion). Bidirectional shifts of ±0.9375 and ±1.8750 cm were simulated in each of the X, Y, and Z directions, representing the average (1.0) and maximum (1.8) cm values for moderate and severe motions, respectively, as determined in the clinical prevalence study.

The prevalence of motion time (following a detected shift) is shown in Fig. 3(C), demonstrating a relatively constant probability (dashed line median) of motion shift over the entire time-course of the scans. A substantially lower frequency of motion was recorded during the first minute, likely due to the confounding effects of the rapidly changing biodistribution during the tracer first-pass through the heart and lungs immediately following injection. Based on these results, the times for simulated body motion were selected to cover most of the scan length, with added focus on the early times when the tracer activity was changing rapidly at 30, 60, 120, and 240 s, as shown in the example time-activity curves (Fig. 4).

3.B. Computer phantom simulations

Example MBF polar-maps computed for the reference case (without any PET motion) are shown in Fig. 4. Without
motion, the polar-map using regional PVC looks quite similar to that with global PVC, indicating relatively uniform partial-volume effects over different regions of the simulated LV myocardium.

All of the simulated parameters had a statistically significant effect on the MBF error, as shown in Table II.

The reductions in MBF error associated with each simulated parameter are illustrated in Fig. 5. The worst-case combination of parameter values results in a mean MBF error of 240%. The effects of changing a single parameter value from this worst-case combination are shown in rank order from smallest to largest improvement in MBF error. Data are averaged over all segments and positive-negative directions (10 points total). As expected, PET-dynamic motion correction results in the single largest improvement from 240% using the worst-case combination down to 10%, with residual errors due mainly to the effects of CTAC misalignment. Regional partial-volume correction has the least effect, still resulting in ~220% residual error. CTAC alignment with the early (blood-pool) PET images reduces the MBF error by a factor of 2% to ~120%. These results show that patient body motion in the dynamic PET image sequence is a much larger source of error than CTAC misalignment effects, and therefore should be the first priority for accurate correction.

3.C. Parameter interaction effects

Figure 6 shows the most highly significant interaction (CTAC alignment, motion direction and sign) affecting MBF.
error. The largest MBF errors occurred for right (+X) motion when the CTAC was aligned with the late PET frames, and for left (−X) motion when the CTAC was aligned with the early PET frames. This corresponds with the well-established CTAC alignment artifacts observed clinically in the lateral wall, at the interface of low attenuating lung and high attenuating heart tissue. Similar magnitude MBF errors were measured in the septal segments (Fig. 6 polar-map inset), associated with misalignment of the RV blood-pool sampling in early frames. There were significant differences in the effect of X-direction motion vs other directions.

Figure 7 shows the significant interaction of motion direction and motion correction (at 2 cm magnitude) on MBF error. Errors were highest in the cases with no motion correction (none) or with CTAC-alignment correction only, regardless of direction. When PET-dynamic motion correction was performed, errors were significantly decreased (p < 0.05), and residual errors were due solely to CTAC misalignment. MBF errors were significantly higher for motion in the X vs Y,Z directions, with or without CTAC-alignment correction (p < 0.05).

Figure 8 shows the significant interaction of motion direction and time of motion shift (at 2 cm magnitude) on MBF error. The errors for motion at 60 and 120 s were similar, and significantly higher than motion at 30 and 240 s. These results confirm that the MBF error is again higher for X motion vs Y,Z motion, and that midscan motion (e.g., 1–2 min) is much worse than motion near the start or end of the scan only. The highest overestimation in MBF occurred with motion in the X-direction, at 60 or 120 s after scan start-time.

Figure 9 shows the significant effect of PVC, segment, and direction (for late CTAC alignment as per clinical practice). Regional (A) and global (B) PVC in each segment are shown for motion in the right (+X) direction and +Z-direction (superior) directions. The greatest errors occurred when using late CTAC alignment with motion at 60 or 120 s. For early-frame CTAC alignment, the median values were lower segment by segment (data not shown). In the presence of motion, regional PVC generally produced greater regional MBF errors compared to global PVC, indicating that the global PVC method may be more robust against body motion effects than regional PVC. There were significant differences in the median values between the posterior/anterior and lateral/septal walls and in the anterior and septal segments using regional partial-volume correction. Median MBF error drops significantly for the left (−X) direction for both regional and global partial-volume correction methods. Similar regional effects to the +Z-direction (superior) were observed for the −Z (inferior) direction, with the posterior wall increasing to 158% and the septal wall decreasing to 9% using regional PVC. There is much improved regional uniformity across segments using global vs regional PVC.

### Table II. Multivariate ANOVA analysis of the simulated parameter effects on MBF.

| Parameter                  | Degrees of freedom | F-statistic | p-value |
|----------------------------|--------------------|------------|---------|
| Correction (none/CTAC/PET) | 2                  | 192        | <0.001  |
| CTAC (early/late)          | 1                  | 19         | <0.001  |
| PVC (global/regional)      | 1                  | 71         | <0.001  |
| Resolution (high/low)      | 1                  | 57         | <0.001  |
| Direction (X/Y/Z)          | 2                  | 192        | <0.001  |
| Magnitude (1/2 cm)         | 1                  | 588        | <0.001  |
| Sign (+−)                  | 1                  | 7.9        | 0.005   |
| Time of motion shift       | 3                  | 178        | <0.001  |
| Segment (ant/pos/sep/lat/apex) | 4               | 6.4        | <0.001  |

Fig. 5. Reduction in MBF error associated with each independent simulation parameter compared to the worst-case combination of parameter settings (global PVC, late CTAC alignment, high resolution, X direction, ±2 cm magnitude, 60 120 s time of motion shift, no MC). Error bars are ±SD reflecting changes in the Sign and Segment parameters.
3. DISCUSSION

To our knowledge this study is the most comprehensive investigation of the common effects of patient body motion on MBF measurement using dynamic $^{82}$Rb-PET imaging. This work confirmed that patient motion is highly prevalent in a clinical population of cardiac perfusion exams, as reported earlier in our preliminary study.\(^7\) In 38% of patients with moderate body motion, the observed average shift was 1 cm, but in severe cases it was as high as 1.8 cm. There was no significant difference in the prevalence of motion between rest and stress.

This study confirms that greater MBF errors occur with larger magnitude patient motion, with MBF errors exceeding true MBF values by up to a factor of five. Optimal CTAC alignment correction can result in larger MBF error, due to the fact that misaligned frames have higher activity without CTAC artifacts, and thus affect the kinetic modeling by biasing the misaligned frames more strongly. However, optimal correction of dynamic PET alignment alone results...
in a dramatic reduction of median MBF errors to within 20%–50% of the true value on average, with the residual error resulting from CTAC misalignment in some time-frames. The main finding of this work, therefore, is that motion correction algorithms should prioritize correction of dynamic PET sequence over dynamic CTAC alignment correction. Nevertheless, the optimal long-term goal is to correct for motion effects in both the PET dynamic sequence and corresponding motion-free CTAC alignment.

Perfect motion-correction of the dynamic PET sequence may not be possible. In such cases, it is important to understand what other variables can be controlled to reduce MBF error. For instance, motion in the X direction (left/right) is more detrimental than motion in either the Y (anterior/posterior) or Z (superior/inferior) directions. Fortunately, the prevalence data (Fig. 3) suggest that X motion is least common, accounting for only 24% of cases with motion, compared to 76% in Y or Z directions.

The simulation results also show that motion which occurs during the middle frame of the scan (60–120 s represents midframe in a 15 frame scan) results in far greater MBF errors than motion which occurs at the beginning or near the end of the scan (Fig. 8). However, the effect of motion near the end of the scan is worse than motion near the beginning, likely because the later time-frames are used to define the ROIs for TAC sampling, resulting in more mispositioned time points, along with CTAC misalignment in majority of time-frames. Furthermore, motion in late frames results in blurring of static MPI images and ECG-gated images typically averaged over the last 6–8 min, which are used for clinical interpretation.24 We speculate that the maximum MBF error occurs when the largest number of time-frames is misaligned with each other, which is consistent with our findings that midspace motion results in the largest MBF errors.

In our prevalence study, almost all motion was detected in the late time-frames (data not shown). Late time-frames consist of the majority of the exam time (e.g., 6 min of an 8 min scan) and therefore have a greater likelihood of capturing a motion shift event. In addition, motion is easier to discern in late time-frames when the heart uptake is nearly completed, and the spatial distribution is static compared to the early time-frames. In the absence of effective motion correction techniques, MBF and MPI errors may be best mitigated by cropping PET acquisition data from the time of motion shift, so long as sufficient data remain to reconstruct diagnostic quality images. Our results suggest that early frame motion may be relatively well tolerated by MBF quantification algorithms, resulting in only small MBF errors. Furthermore, early time frame data are not used to reconstruct MPI or ECG-gated uptake images.

Similar errors are observed with early and late CTAC alignments. The main difference between early and late CTAC alignment are that large errors occur when the CTAC is aligned in the early-frames for right (+X) shifts, whereas if the CTAC is aligned in the late frames, large errors are observed for left (−X) shifts (data not shown). Similar converse effects are observed for Y and Z shifts.

Similar effects to superior/inferior (±Z) shifts are observed for anterior/posterior shifts (±Y) except largest errors in MBF come from the anterior (median = 24%), septal (median = 84%), and apex (median = 51%) for anterior (−Y) shifts, and anterior (median = 16%), septal (median = 30%), and apex (median = 22%) for posterior (+Y) shifts when calculated using regional PVC. For global PVC, the median value for
all segments for either anterior or posterior motion drops to 10% on average.

The highest overestimation in MBF occurs with motion in the positive X-direction when CTAC is aligned with the late PET images, using either a regional (Regional) or global (Global) partial-volume correction. Therefore, if the direction of motion can be determined, CTAC alignment and PVC methods can be chosen to minimize the error in MBF. This is important for cases where only approximate corrections for motion can be made. Larger errors in MBF were observed with the high resolution simulations; these results may be more applicable to longer-lived tracers such as $^{13}$N-ammonia where higher spatial resolution imaging is possible. Recent developments in PET-MR and time-of-flight (TOF) PET may offer unique solutions to the problem of patient motion. For instance with MR, tagged myocardial imaging can be used to assess regional motion due to the distortions in the magnetization patterns. Alternatively with TOF PET, both the activity and attenuation images can be reconstructed simultaneously, thus eliminating
CTAC-misalignment artifacts for static imaging.\textsuperscript{26,27} Further work is needed to develop and evaluate the potential of these emerging methods for dynamic PET motion correction.

Limitations of this study are that these are noiseless simulations, only one direction of motion at a time was simulated, the same TAC based on $^{82}$Rb-PET kinetics was applied to the LV and RV blood, and there was no motion simulated within frames. In addition, only one numerical phantom was used with the same internal organ morphology for all simulations, and the simulated motion was rigid and thus did not consider nonlinear effects from patient motion sometimes present in clinical cases.

5. CONCLUSION

This study highlights the importance of dynamic PET motion correction, as well as the relative effects of motion parameters and corrections. Mild-to-moderate patient motion occurs in more than 60% of clinical scans and can have highly detrimental effects on MBF calculations. Motion correction of the reconstructed PET dynamic image sequence reduces MBF bias, but CTAC alignment errors should also be addressed to further reduce MBF error. Motion correction algorithms should be developed with highest priority targeting of mid- and late-time-frame motion, high resolution imaging, and motion in the X-direction, since these cases produce the largest errors in MBF estimation.

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28 See supplementary material at http://dx.doi.org/10.1118/1.4943565 for analysis of variance (ANOVA) for computer simulation parameters tables.