A tale of two phases: Can the worst of scans become the best of scans with motion correction?

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Received Apr 30, 2018; accepted Apr 30, 2018
doi:10.1007/s12350-018-1305-9

See related article, pp. 1918–1929

Regular readers to this journal will be aware of the important role that myocardial blood flow (MBF), using dynamically acquired positron emission tomography (PET), plays in the management of patients with suspected coronary artery disease (CAD). It is an established diagnostic technique,[1] demonstrating increased prognostic value[2] and risk stratification.[3] Introduction into routine clinical practice relies upon the underlying data being accurate, robust, and repeatable. This requires rigorous assessment of the impact of various technical factors which manifest along the imaging pathway: from the preparation of the patient and acquisition of the data to application of appropriate compartmental and tissue permeability models.

An excellent review on the technical factors affecting MBF calculation was given by Moody et al[4] and very recently, the ASNC and SNMMI have published a joint statement giving guidance on the routine use of dynamic PET for calculation of MBF.[5] These papers are a valuable resource to assist in standardizing the technique and also identifying and avoiding potential pitfalls. While users can mitigate many technical factors, one that will arguably always be present in one degree or another is patient motion; the impact of which on MBF calculation has been investigated by several authors.[6,7] These studies demonstrate the need for universal access to robust motion correction methods for routine use, in much the same way that myocardial perfusion SPECT has had for many years to adjust raw projection data prior to reconstruction.

The errors arising from patient motion can be categorized in two ways: incorrect time-activity curve data due to inappropriate positioning of volumes of interest on the PET voxel data and attenuation correction errors due to frame-by-frame PET-CT mis-registration. The type and cause of patient motion is generally either periodic physiological sources such as respiratory motion, or more random effects such as in response to the effects of vasodilator stress agents,[8,9] or actual physical movements of the patient. Respiratory motion effects and to some extent physical movements of the patient may be automatically corrected by data-driven techniques[10] however this is likely to be particularly challenging in the case of dynamic PET using short-lived tracers. Alternative automated correction techniques may use external markers or monitoring.[6,11] Current commercial implementations of motion compensation focus on periodic respiratory motion and usually involve reconstructing data during the quiet breathing phase. Such data is summed over all breathing cycles during the acquisition, hence is not applicable to more random patient motion that has no regular temporal pattern. Despite this, Naum et al demonstrated that up to 80% of frames can be affected by some degree of motion during exercise stress using external markers, and that correcting the PET data for the changes in marker position can adequately compensate for these movements.[11] In our experience however we find that patient motion rarely conforms to an affine translation of the patient and, more generally, cardiac motion manifests as a non-trivial motion vector containing morphological changes along with rotational and translational shifts; hence frame-by-frame reconstruction and attenuation correction would be considered vital in any motion correction regime.

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J Nucl Cardiol 2019;26:1930–3.
1071-3581/$34.00

In this issue, Lee et al[12] join the growing number of publications focussed particularly on patient motion and its impact on the accuracy of MBF quantification. While motion correction of dynamic PET data is certainly not a novel concept, even in cardiac PET,[13] what Lee et al uniquely demonstrate is that the magnitude of motion varies significantly within the distinct physiological phases of tracer kinetics, i.e., the immediate vascular bloodpool phase and the later tissue uptake phase. Their study employs commercially available software that allows the user to manually apply a motion shift. The frame-by-frame motion correction approach employed by the software in the study is performed post-reconstruction and is independent to the PET scanner. We shall discuss potential of implications of this latter factor later in this editorial.

Their study has a well thought-out approach with clear aims and outcomes. It is performed on a large cohort of patients thus providing data of good statistical quality. The authors demonstrate (Figure 4 in the study) that motion in the early phases has a far more marked impact on the calculation of MBF and, as with other studies, demonstrate that the effect is greater in stress images compared with resting images. In addition to assessing motion in the different temporal phases, the authors apply interesting methods to isolate the impact of motion in particular directions. In Figure 5 of the study, they elegantly demonstrate that the RCA territory is most susceptible to motion artifacts due to superior-inferior motion, with up to 60% changes to MBF occurring in stress imaging. We believe this may originate from changes in the patients breathing patterns during pharmacological stressing, with different patterns and magnitudes seen for different stress pharmaceuticals and infusion durations.[8,9] While the authors' conclusions suggest that motion in early frames is most important, we believe that whether motion occurs in early or late phases of the scan may simply be relative. If the reference segmentation is derived from late images, it is quite feasible to interpret that motion is in the early phase, and therefore an analysis of the differential motion (frame-to-frame) would perhaps be more insightful. It is also possible that this biphasic description would be stress agent dependent as the definition of the left ventricle could be based on frames coincident with the relaxation from stress agent induced side-effects within the patient. Nonetheless, what Lee et al have helped to demonstrate is that the pattern and assessment of motion throughout a dynamic cardiac perfusion PET study is both multifactorial and in essence non-trivial.

Due to the lack of a true gold standard, assessing the efficacy of motion correction techniques remains a challenge. Currently, we believe the most reliable assessment to be visual inspection of the dynamic data and overlying regions by experienced users to verify that the placement of voxel data within the regions is appropriate, which is the approach taken by Lee et al. Recently an alternative statistical-based approach has been suggested using a Bayesian framework to assess improvements in confidence measurements for MBF calculations.[14] The method shows promise but more research in this area is required.

With a focus on standardization of MBF calculation, it has been demonstrated that different software packages give good agreement if using the same kinetic model.[15] However, there is no consistent strategy for addressing patient motion in various commercial packages. In our institution, we have experience of both Corridor4DM from Invia as used in the work by Lee et al and *Syngo*.PET MBF from Siemens Healthineers. Comparing just these two packages demonstrates the stark differences in motion correction techniques. Corridor4DM employs a manual frame-by-frame adjustment approach while *Syngo*.PET MBF tracks the motion of the left ventricle. Both techniques have pros and cons. Manual adjustment requires more user input and may be susceptible to operator variability—something that was not evaluated by Lee et al. Automated techniques should be more reproducible but can be problematic in the early frames where activity is concentrated in the bloodpool and accurate myocardial segmentation is not possible. This can lead to errors in both the blood input function (BIF) but also substantial spill-over of bloodpool activity. Interestingly, the authors propose a method by which analysis of this spill-over can be used to register the early, challenging frames. An example shown in Figure 1 from our institution using *Syngo*.PET MBF illustrates how the bloodpool spill-over results in an artificially increased MBF in the RCA territory. Following frame-by-frame motion correction of the dynamic data, the polar map of the MBF is far more uniform. The figure also demonstrates incorrect placement of the BIF volume of interest in the case without motion correction. This causes a reduction in the area under the BIF curve that consequently produces a global over-estimation of the MBF which is a compounding error on top of the regional RCA territory error. To fully demonstrate this, the MBF values before motion correction were 2.86, 3.55, 4.16 and 3.36 $mL \cdot g^{-1} \cdot min^{-1}$ for LAD, LCx, RCA and global regions respectively. By comparison, the MBF values after motion correction were 2.45, 2.71, 2.30 and 2.48 $mL \cdot g^{-1} \cdot min^{-1}$ for the same regions respectively. These observations are consistent with those described by Lee et al. The importance of correct time-activity curves cannot be emphasized enough. As demonstrated by the above example and Vasquez et al, the placement

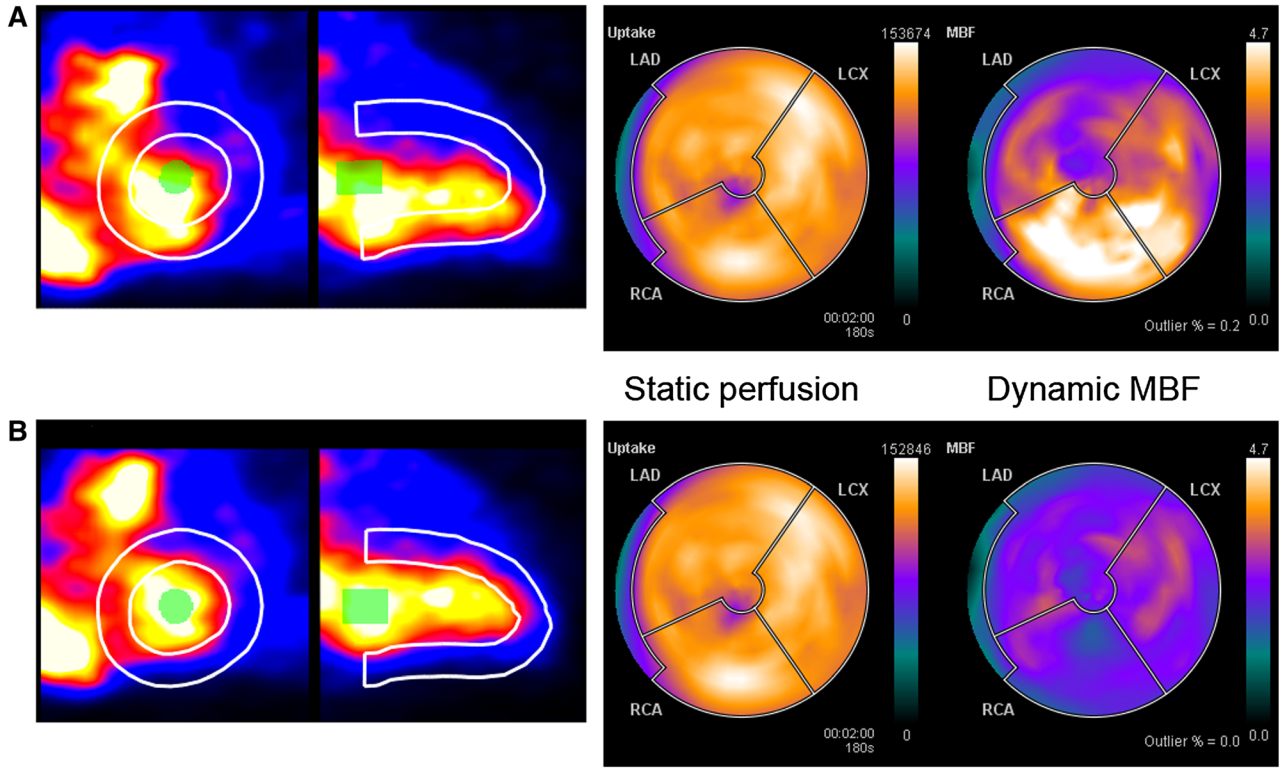

Figure 1. Example stress MBF case with substantial motion in the early frames before (**A**) and after (**B**) frame-by-frame motion correction. Data shown were processed by Siemens *Syngo*.PET MBF software. The pairs of polar plots show the static perfusion, obtained from summing the last 2 minutes of data, and the MBF determined from the dynamic data. Note that the color scale limits for the MBF polar plots with and without motion correction are set equal. The green volume of interest in the left-hand images is used to measure the bloodpool activity to produce the blood input function.

of the region used to derive the BIF has a significant impact on the calculated MBF.[16]

An important consideration with any motion correction scheme is the balance between adequately sampling the temporal variation in position while maintaining enough count statistics to reliably infer spatial information. The authors of the current study use fine time-sampling over the initial phase, where the spatial change from frame to frame is higher, followed by coarser sampling in the second tissue phase where the count statistics are lower. While this methodology has been shown to provide optimal sampling for MBF calculation,[17] and would reduce inter-frame motion, it remains to be demonstrated that this would accurately capture intra-frame motion in the tissue phase. By analyzing cardiac displacement throughout the entire image process (pre and post infusion) Vleeming et al[9] have demonstrated that, while the greatest rate of change in motion occurs around the time of the stress agent and tracer infusion, significant motion does indeed occur in the later frames and hence one could postulate that adequate compensation for motion may require optimisation independent to achieving accurate MBF calculations.

A limitation that the authors point out is that their motion correction is only performed on data after image reconstruction. Their technique does not account for frame-by-frame mis-registration caused by patient motion between the PET data and the attenuation map, derived from the CT image. The effect of systematic mis-registration between PET data and the attenuation map has been shown to have substantial impact on MBF calculation.[18] However, there has yet to be a demonstration of the impact on MBF calculation of subtle frame-by-frame mis-matches between the PET and attenuation map. The ability to feed back manual frame-by-frame motion adjustments into the PET reconstruction is something that we can only expect from vendors of PET hardware if such technology would become available as a commercial product. While this approach would seem to be the gold standard technique, it is not without limitation. For example, one must first reconstruct the dynamic data to define required frame-by-frame shifts and then repeat the reconstruction with the

motion shifts applied, hence doubling the reconstruction task that is required. Something that may be a limitation for centers performing high throughput. One may hypothesize that as time-of-flight (TOF) performance improves with new detector technology, this may become less important as TOF data have been shown to be more robust in situations where there is inconsistency between the PET data and attenuation map.[19] Alternatively, the so-called ''joint reconstruction'' approaches to perform attenuation correction based solely on the PET data may provide more consistent attenuation correction in the presence of patient motion.[20]

CONCLUSIONS

What Lee et al and the body of literature quoted previously reach consensus upon is the importance of motion correction in dynamically acquired myocardial perfusion PET in order to provide accurate and meaningful myocardial blood flow data. Patient motion is an issue that needs to be addressed. We share the opinion expressed by the authors and urge manufacturers to assist users by developing means of effective motion correction to provide consistently reliable MBF data. Ideally corrections should have minimal user involvement to improve consistency. Further work is required to fully optimize motion correction techniques. In particular, the evaluation of optimal framing to strike the balance of detecting and correcting motion adequately while still enabling reliable calculation of MBF. We hope that future technological advances may lead to image reconstruction that is more robust in the presence of patient motion.

Disclosure

The authors' department received reimbursement for a recent collaborative project on motion correction in cardiac PET from Siemens Healthineers. The project was completed before the editorial was written.

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