Optimizing accuracy and precision with motion correction of PET myocardial blood flow measurements

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INTRODUCTION

The well-validated diagnostic and prognostic value of quantitative estimates of myocardial blood flow (MBF) and flow reserve (MFR) derived from positron emission tomography^{1–5} have generated much enthusiasm for clinical implementation. Quantification of MBF at peak hyperemic stress and MFR can refine referrals for invasive angiography and may potentially improve selection of patients for revascularization.^{6,7} However, in order to apply these population data in a reliable manner to the management of individual patients, optimization of precision and accuracy is required.⁸ Patient motion effects are a major driver of both imprecision and inaccuracy. Work by Otaki et al in the present issue of the *Journal of Nuclear Cardiology* aims to address this issue.⁹

BACKGROUND

Quantification of MBF from PET myocardial perfusion imaging (MPI) is generally accomplished by recording data in list mode starting at the time of injection. These data are reconstructed into dynamic image series which consist of a sequence of snapshot images showing how the radiotracer mixed with the

blood transits through the cardiac chambers (blood pool phase) and distributes into the myocardial tissue (tissue phase). These time series are usually reconstructed with short time frames early as the tracer is in the blood pool phase and with longer frames in the tissue phase to improve count statistics and reduce reconstruction time and storage requirements.¹⁰ Motion can occur within and between these frames in periodic and non-periodic fashion due to respiration and patient movement. An example of motion and its effect on MBF is shown in Figure 1, extracted from Lee et al.¹¹

Several prior studies have demonstrated that motion is a major source of error in the quantification of MBF and MFR,^{11–13} summarized in Table 1. Furthermore, meaningful motion is common (seen in 65% of scans in a sizable clinical sample) and may cause alarmingly large errors as high as 500% in severe cases.¹⁴ More recently, our group analyzed a population of 225 sequential patients who underwent rest-stress Rb-82 PET.¹¹ All studies were motion-corrected by expert physician readers. Results demonstrated a notable regional impact of motion correction in the RCA territory (18.9% average difference), particularly in the blood pool phase, where motion can have major impact on MBF calculations. An illustrative case is provided in Figure 1. This regional finding was further observed by Armstrong et al, with a 23% median change in the RCA territory for cases with severe motion, although it was dominated by a 65% median difference in the apical and mid-anterior segments, which was blamed on tissue-phase motion caused by adenosine.¹⁵

ACCURACY AND PRECISION

Prior studies have clearly shown the necessity for motion correction to obtain accurate MBF and MFR estimates. However, manual strategies may result in

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Figure 1. Example of motion in the blood pool phase inducing error on stress MBF from Lee et al¹¹.

decreased precision as user input generally introduces variability. Otaki et al, in their present study, show that with manual motion correction performed by well-trained operators the test-retest coefficient of variation (CV) for MBF decreases from 16% to 9%. This repeatability study shows that the potential added variability of manual motion correction is offset by the improvement in accuracy which results in matching test-retest MBF estimates. Importantly, they report a low inter-user variability CV of 5% on motion-corrected studies. The excellent results suggest that it is possible to obtain highly repeatable motion correction results within and between operators. The study does however have limitations, as only rest datasets were analyzed whereas

the literature has shown that motion is more prevalent and severe during stress.^{11,13}

What is unknown is whether this level of consistency can be routinely achieved at less experienced, high-volume sites. Inconsistent manual motion correction would not only decrease reproducibility, but could reduce accuracy of estimates, particularly in scans without severe motion. Further real-world studies involving multiple sites would be required to understand the magnitude of this potential challenge. Regardless, it appears certain that skill and training in manual motion correction are additional critical challenges for clinical generalization of quantitative cardiac PET MPI.

Table 1. Recapitulatory table of dynamic motion studies in the literature

Study	N	Tracer	Global percent difference (MBF/MFR)	Regional percent difference (MBF/MFR)
Koshino et al (2012) ¹²	9 ^a	¹⁵ O-Water	7.7%	25.1% ^c
Yu et al (2016) ¹³	7	⁸² Rb	15%/19%	N/A
Lee et al (2018) ¹¹	225	⁸² Rb	4.7%/1.9%	8.0%/6.3% ^d
Otaki et al (2019) ⁹	21 ^b	⁸² Rb	2.9%	2.9% ^e

The percent differences are between motion-corrected values and non-corrected values. When available, stress MBF was used over rest MBF

^aRest only studies with significant motion

^bRest only studies

^cAverage MBF difference from a 9-segment model

^dAverage MBF/MFR difference from 3 vascular regions

^eDifference of the average MBF from 3 vascular regions

Figure 2. Visualization of the improvements made by automatic motion correction on uncorrected MBF outside of the limits of agreement (95% confidence interval) from Lee et al¹⁶.

CHALLENGE AND SOLUTION

If optimal motion correction is essential to achieving maximal accuracy but manual motion correction decreases precision and requires training and experience to avoid unintended increases in errors, what is the solution? We have developed a fully automated motion correction algorithm for dynamic image series based on normalized gradient fields.¹⁶ Figure 2 highlights how the algorithm successfully improves the agreement for

non-corrected studies that fell outside the 95% confidence interval from the physician-corrected reference. The algorithm correlated well with expert readers and rarely requires substantial manual corrections or editing. As a result, correlations between MBF and MFR values obtained by two technologists editing automated motion correction images (CV = 4%) is meaningfully better than uncorrected images (CV = 16%).¹⁷

Regardless of the approach used, the evidence in favor of motion correction is substantial and should now be standard practice for all dynamic PET MPI studies. We applaud Otaki et al for their important contribution and encourage the field to continue work in this area.

Disclosure

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