More evidence for adequate test-retest repeatability of myocardial blood flow quantification with ^{82}Rb PET/CT

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Myocardial blood flow (MBF) and reserve (MFR) can be measured with stress myocardial perfusion imaging (MPI) using PET/CT and they permit evaluation of the combined effects of epicardial coronary artery disease (CAD) and coronary microvascular disease (CMD) on myocardial perfusion.^{1,2} Measurement of MBF and MFR adds incremental value to relative MPI and improves diagnosis of multivessel disease (Figure 1)^{3,4} and prognostication with better risk stratification in patients with known or suspected coronary artery disease (CAD).⁵

Any test used for clinical decision-making and patient management needs to be accurate and should have adequate test-retest repeatability to enable management decisions for individual patients. The accuracy and precision of measurement of MBF with ^{82}Rb PET/CT has been well demonstrated.^{6,7} In this issue of the Journal of Nuclear Cardiology, Byrne et al.⁸ report the (1) day-to-day test-retest repeatability of MBF measurements with ^{82}Rb PET/CT in 40 healthy volunteers undergoing 2 rest and adenosine stress studies and (2) the software reproducibility with analysis using three different commercially available software packages, including one with optional motion correction. A single study has reported test-retest repeatability of MBF measurements with ^{82}Rb PET/CT using dipyridamole.⁹

Several others have reported comparisons between different software packages (syngo.MBF (Siemens Medical Solutions, Illinois, USA), Quantitative Gated SPECT (QGS) (Cedars-Sinai Cardiac Suite, Los Angeles, USA) and Corridor4DM (INVIA, Ann Arbor, MI). The unique aspects of this study are (1) the use of adenosine stress and (2) the evaluation of the effect of motion correction. Test-retest repeatability was very good for rest and stress MBF and MFR (20% to 27%) using all three software packages and similar to the previous study using dipyridamole stress (~20%).⁹ However, the mean MBF and MFR values differed between some software packages; similar values for MFR were observed using syngo.MBF and QGS, whereas slightly higher values were obtained with 4DM (with and without motion correction). These results showing different MFR values, depending on the specific software used, are similar to previous reports^{7,10,11} and emphasize the need for software standardization within individual laboratories and between laboratories for multi-center clinical trials.

It is interesting to note there was a slight worsening of test-retest repeatability following the ‘first-generation’ manual motion correction with 4DM in the present study (Figure 2A), similar to the effects we reported recently for MFR quantification with Tc SPECT imaging.¹² Other studies of the effects of manual^{13,14} and automated¹⁵ motion correction with 4DM in patients with clinically indicated scans have demonstrated improved accuracy for measurement of MBF and MFR, particularly in the right coronary artery distribution and suggest that motion correction may be beneficial, perhaps depending on the patient population. Previous studies have also investigated the effects of other methodological factors on the short-term or minute-to-minute repeatability in ^{82}Rb PET MFR measurements (Figure 2B). These factors include the tracer kinetic model used, location of the arterial blood input function

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Figure 1. Extensive multivessel CAD diagnosed in a patient with a previous lateral wall NSTEMI and recurrent angina. (A) Stress imaging showed moderately reduced tracer uptake in the entire lateral wall and basal anterolateral segment with improvement on rest imaging consistent with a moderate-sized region of moderate ischemia primarily in the LCX distribution (% LV ischemia 7.4%, scar 1.5%). (B) Stress MBF and MFR were severely reduced in the LCX and LAD territories. Coronary angiography showed severe 3-vessel CAD, followed by surgical coronary revascularization.

and spillover from adjacent myocardium, adjustment for changes in the resting heart rate $\times$ systolic blood pressure product, and standardization of the tracer infusion profile.^{16,17} Such short-term repeatability studies have proven very useful to help investigate and reduce the methodological sources of variability. Based on the present study results, it seems that more highly automated and reproducible methods for motion correction will be needed to further improve the day-to-day test–

retest repeatability, which includes both methodologic and biologic variability.

The evolving role of cardiovascular imaging in management of patients with cardiovascular disease has been recently highlighted.¹⁸ The patient population is changing with a greater prevalence of risk factors including advanced age, diabetes, obesity and chronic kidney disease, leading to more coronary microvascular dysfunction and diffuse atherosclerosis. Patients are

Figure 2. Repeatability of myocardial flow reserve (MFR) measurements performed within days (A) or minutes (B). Manual motion correction [MC] did not reduce day-to-day variability for Tc SPECT¹³ or Rb PET using FlowQuant or 4DM-PET software.⁸ Conversely, manual MC has been shown to reduce minute-to-minute variability¹⁴ in addition to other factors, including tracer kinetic model (simplified retention model [SRM] vs tissue compartment model [1TCM]), blood spillover corrections [SOC], resting rate pressure product adjustment (RPP), left atrial vs ventricular input function [LAIF], and constant-activity-rate infusion profile [CAIP]^{16,17}.

presenting more frequently with heart failure and less with acute ischemic syndromes. The usual clinical approach of identifying patients with obstructive epicardial CAD lesions suitable for intervention and for risk stratification using relative MPI can be optimized with the addition of measurement of MBF and MFR. Patient risk can be more accurately defined, particularly in high risk groups. Patient care can be more personalized with possible selection of patients for revascularization assisted by regional MFR data.¹⁹ We are fortunate in nuclear cardiology that measurement of MBF and MFR with ^{82}Rb PET/CT has been shown to be accurate with adequate test–retest repeatability and will likely be very useful in the future management of patients with cardiovascular disease.

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