Reproducibility and Accuracy of Quantitative Myocardial Blood Flow Assessment with $^{82}$Rb PET: Comparison with $^{13}$N-Ammonia PET

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$^{82}$Rb cardiac PET allows the assessment of myocardial perfusion with a column generator in clinics that lack a cyclotron. There is evidence that the quantitation of myocardial blood flow (MBF) and coronary flow reserve (CFR) with dynamic $^{82}$Rb PET is feasible. The objectives of this study were to determine the accuracy and reproducibility of MBF estimates from dynamic $^{82}$Rb PET by using our methodology for generalized factor analysis (generalized factor analysis of dynamic sequences [GFADS]) and compartment analysis. Methods: Reproducibility was evaluated in 22 subjects undergoing dynamic rest and dipyridamole stress $^{82}$Rb PET studies at a 2-wk interval. The inter- and intraobserver variability of MBF quantitation with dynamic $^{82}$Rb PET was assessed with 4 repeated estimations by each of 4 observers. Accuracy was evaluated in 20 subjects undergoing dynamic rest and dipyridamole stress PET studies with $^{82}$Rb and $^{13}$N-ammonia, respectively. The left ventricular and right ventricular blood pool and left ventricular tissue time–activity curves were estimated by GFADS. MBF was estimated by fitting the blood pool and tissue time–activity curves to a 2-compartment kinetic model for $^{82}$Rb and to a 3-compartment model for $^{13}$N-ammonia. CFR was estimated as the ratio of peak MBF to baseline MBF. Results: The reproducibility of the MBF estimates in repeated $^{82}$Rb studies was very good at rest and during peak stress ($r^2 = 0.935$), as was the reproducibility of the CFR estimates ($r^2 = 0.841$). The slope of the correlation line was very close to one for the estimation of MBF (0.986) and CFR (0.960) in repeated $^{82}$Rb studies. The intraobserver variability of MBF was less than 3% for the estimation of MBF at rest and during peak stress as well as for the estimation of CFR. The interobserver variability of MBF was 0.950 at rest and 0.975 during peak stress. The correlation between the MBF estimates obtained at rest and those obtained during peak stress in $^{82}$Rb and $^{13}$N-ammonia studies was very good ($r^2 = 0.857$). Bland–Altman plots comparing CFR estimated with $^{82}$Rb and CFR estimated with $^{13}$N-ammonia revealed an underestimation of CFR with $^{82}$Rb compared with $^{13}$N-ammonia; the underestimation was within ±1.96 SD. Conclusion: MBF quantitation with GFADS and dynamic $^{82}$Rb PET demonstrated excellent reproducibility as well as intra- and interobserver reliability. The accuracy of the absolute quantitation of MBF with factor and compartment analyses and dynamic $^{82}$Rb PET was very good, compared with that achieved with $^{13}$N-ammonia, for MBF of up to 2.5 mL/g/min.

Key Words: myocardial blood flow; PET; $^{82}$Rb; $^{13}$N-ammonia

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PET measures of myocardial blood flow (MBF) (in mL/min/g) and coronary vasodilator reserve are very sensitive for evaluating microvascular function in vivo (1–3). Although the quantitation of MBF with $^{13}$N-ammonia and $^{15}$O-water as PET flow tracers has been validated, these tracers are seldom used clinically because they are cyclotron products with short physical half-lives (10 and 2 min, respectively) and therefore require an on-site cyclotron. In contrast, $^{82}$Rb can be produced with a column generator; consequently, it is the agent most commonly used for assessing myocardial perfusion in patients with known or suspected coronary artery disease (CAD) (4–10). Although this approach has been shown to be highly accurate for the detection of obstructive CAD (11,12), it underestimated the extent of underlying CAD, especially in patients with multivessel disease. This limitation could be overcome by adding the quantification of MBF to routine visual or semiquantitative assessments of myocardial perfusion.

We and others have shown that the absolute quantitation of MBF and coronary flow reserve (CFR) with dynamic $^{82}$Rb PET is feasible in humans (7–10,13,14). However, little is known about the accuracy and reproducibility of this approach to estimating MBF. Accordingly, we sought to determine the reproducibility of MBF estimates with $^{82}$Rb PET as well as the intra- and interobserver reliability of these quantitative measures. In addition, we determined the accuracy of the quantitative $^{82}$Rb PET approach by
Representative Results:

FIGURE 1. Typical factors and corresponding factor images associated with $^{82}$Rb (A) and $^{13}$N-ammonia (B) dynamic studies in same subject. AU = arbitrary units; MYO = whole myocardium.

FIGURE 2. Transverse, coronal, and sagittal slices (left) as well as short-axis, long-vertical-axis, and horizontal-axis images (top right) of $^{82}$Rb (A) and $^{13}$N-ammonia (B) stress studies in same subject. Polar maps of relative perfusion and absolute hyperemic MBF are also shown; white corresponds to highest values in color scale (bottom right).
FIGURE 5. Reproducibility of rest MBF and stress MBF estimated with $^{82}$Rb at 2 visits. (A) Correlation plot of 2 MBF measurements. (B) Bland–Altman plot of 2 MBF measurements.
FIGURE 6. Comparison of rest MBF and stress MBF estimated with $^{82}$Rb and $^{13}$N-ammonia. (A) Correlation plot of $^{82}$Rb and $^{13}$N-ammonia MBF measurements. (B) Bland–Altman plot of $^{82}$Rb and $^{13}$N-ammonia MBF measurements. Bland–Altman plot illustrates slight overestimation of MBF at rest and underestimation during peak stress with $^{82}$Rb compared with $^{13}$N-ammonia.