Quantitative Dynamic Cardiac ^{82}Rb PET Using Generalized Factor and Compartment Analyses

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We have addressed 2 major challenges of ^{82}Rb cardiac PET, noninvasive estimation of an accurate input function and absolute quantitation of myocardial perfusion, using a generalized form of least-squares factor analysis of dynamic sequences (GFADS) and a novel compartment analysis approach. **Methods:** Left and right ventricular (LV+RV) time–activity curves (TACs) were generated from 10 rest/stress studies, and 30 myocardial TACs were modeled to cover a range of clinical values. Two-dimensional PET Monte Carlo simulations of the LV, RV, myocardium, and other organs were generated separately and combined using the above TACs to form 30 realistic dynamic ^{82}Rb studies. LV and RV TACs were estimated by GFADS and used as input to a 2-compartment kinetic analysis that estimates parametric maps of myocardial tissue extraction (k_1) and egress (k_2), as well as LV+RV contributions (f_v, r_v), by orthogonal voxel grouping. In addition, 13 patients were injected with 2.22 ± 0.19 GBq (60 ± 5 mCi) of ^{82}Rb and imaged dynamically for 6 min at rest and during dipyridamole stress. **Results:** In Monte Carlo simulations, GFADS yielded estimates of the 3 factors and corresponding factor images, with average errors of −4.2% ± 6.3%, 3.5% ± 4.3%, and 2.0% ± 5.5% in the LV, RV, and myocardial factor estimates, respectively. The estimates were significantly more accurate and robust to noise than those obtained using TACs based on manually drawn volumes of interest ($P < 0.01$). The 2-compartment approach yielded accurate k_1, k_2, f_v, and r_v parametric maps; the average error of estimates of k_1 was 6.8% ± 3.6%. In all patient studies, our approach yielded robust estimates of k_1, k_2, f_v, and r_v, which correlated very well with the status of the subject and the catheterization results. **Conclusion:** Quantitative dynamic ^{82}Rb PET using generalized factor analysis of dynamic sequences and compartmental modeling yields estimates of parameters of absolute myocardial perfusion and kinetics with errors of <9%.

Key Words: quantitative ^{82}Rb cardiac PET; factor analysis of dynamic sequences; compartment analysis

J Nucl Med 2005; 46:1264–1271

Cardiac PET with ^{82}Rb allows the assessment of absolute myocardial perfusion, as well as coronary flow reserve (CFR), using a column generator (*1–7*) in clinics that lack a cyclotron or other infrastructural support required to produce radionuclides such as ^{13}N-ammonia. The short half-life of the radiotracer (76 s) makes possible rapid rest/stress paired studies within a very short time (~15 min), allowing rest and stress imaging under virtually identical conditions and decreasing the total time required to scan each patient. In addition to the poor spatial resolution due to the relatively long positron range of the ^{82}Rb positron emitter, the major challenges of parametric ^{82}Rb imaging are estimation of an accurate input function from noisy data without arterial blood sampling and the absolute quantitation of myocardial perfusion. One approach, proposed by Lin et al. (*8,9*), to deal with noise is to filter the reconstructed volume before region-of-interest quantitation using wavelet transforms. Compartmental modeling for ^{82}Rb cardiac PET has also been investigated (*3,8,10*), and 2 models have been proposed by Gould (*10*): a model that reduces the 2 compartments to one unknown, flow, which is calculated from myocardial uptake and arterial input function, and a compartmental model that fits the model equations to observed myocardial and blood time–activity curves (TACs) to estimate the 2 unknowns. The physiologic model of ^{82}Rb kinetics in the myocardium has also been compared with reduced-order models by Coxson et al. (*11*).

In this study, we used a generalized form of the least-squares factor analysis of dynamic sequences (FADS) to obtain a robust estimate of left and right ventricular (LV+RV) input functions automatically, without the need to draw volumes of interest (VOIs), and developed a compartment model based on orthogonal grouping to estimate on a voxel-by-voxel basis, rather than within selected VOIs, extraction of ^{82}Rb in the myocardium. We validated our approach by Monte Carlo simulation studies and demonstrated clinical feasibility by patient studies.

MATERIALS AND METHODS

Generalized Factor Analysis of Dynamic Sequences (GFADS)

Background. FADS is a powerful technique for the analysis of dynamic sequences; its major drawback is that unique solutions are

Received Sep. 2, 2004; revision accepted Apr. 5, 2005.

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Representative Results:

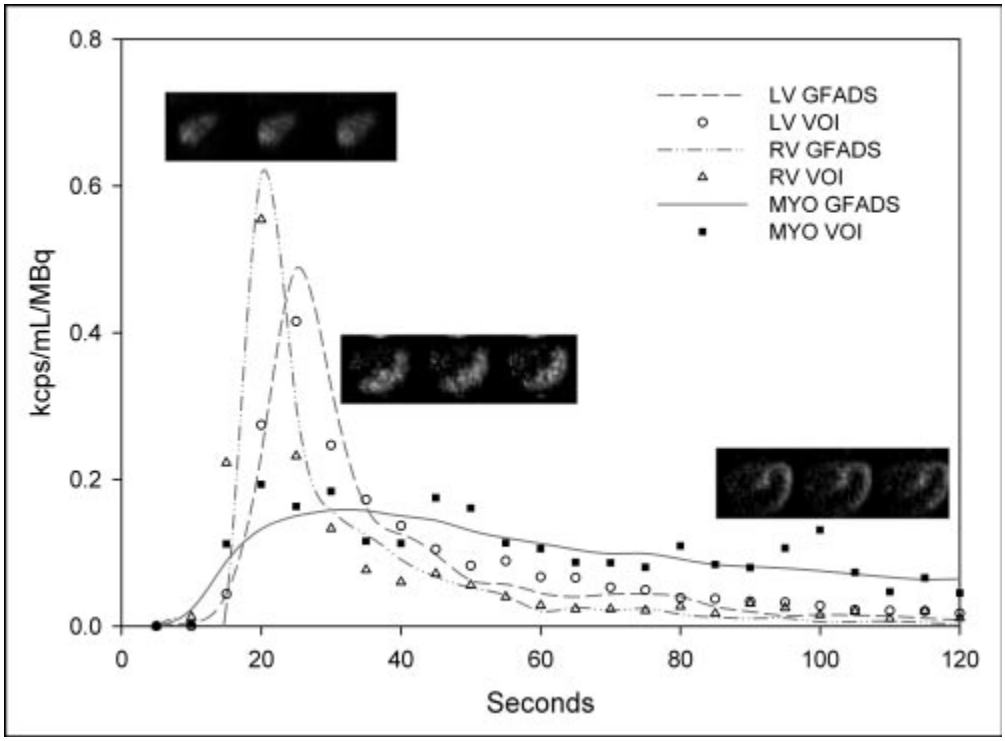

FIGURE 3. Estimated factors and factor images (3 transverse slices) with GFADS for a typical dynamic ^{82}Rb PET study in 93-y-old female with known CAD but with normal myocardial perfusion (SSS = 0). Radioactive decay was not compensated. LV, RV, and myocardium (MYO) were well separated using our uniqueness constraint.

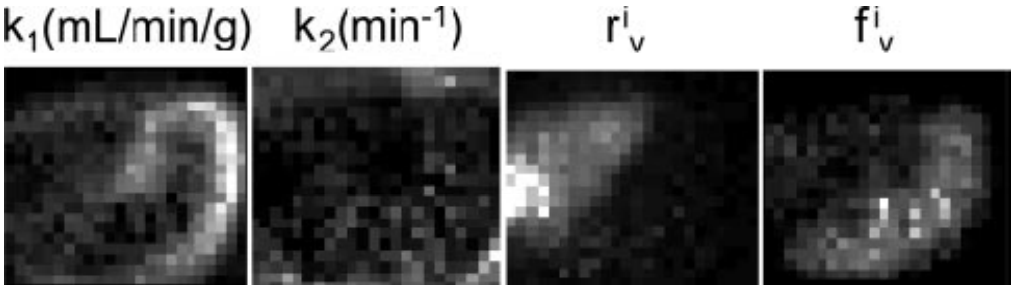

FIGURE 4. Parametric maps of myocardial tissue extraction (k_1) and egress (k_2) as well as RV and LV contributions (f_v^i , r_v^i) from the patient dynamic study shown in Figure 3. Note absence of aberrant points due to orthogonal grouping.