SUPPLEMENTAL MATERIAL

Supplemental Methods

Generation of rest and stress perfusion images

A model-based method was used to generate separate rest and stress standard perfusion images from the two-injection rest/stress single-scan acquisitions (scan B). First, we computed parametric maps of the rest and stress MGH2 kinetic parameters using our rapid computation method[1]. Then, the parametric maps, along with the input function measured during the resting phase of the acquisition, were used to solve the mathematical equations describing the standard one-compartment stationary kinetic model for each voxel of the image matrix. This procedure predicts the measured concentration history resulting from each injection, as though the rest and stress data were acquired separately. Note that the contribution of $^{13}NH_3$ blood from the right and left ventricles to the PET signal (f_{LV} and f_{RV}) was eliminated by removing of the corresponding terms in the one-compartment model equation. The resulting sequence of rest and stress dynamic images were then summed to obtain the final model-based perfusion images. The different steps followed to generate these model-based rest and stress perfusion images are described in Supplemental Figure 3.

The computed perfusion images were then imported into the clinical software corridor4DM (INVIA Medical Imaging Solutions, Ann Arbor MI) and compared with the separate rest and stress perfusion images obtained from scan 1 and scan 3. Summed rest score (SRS) and summed stress score (SSS)[2] were compared for each study.

Supplemental Results

Rest and stress perfusion images

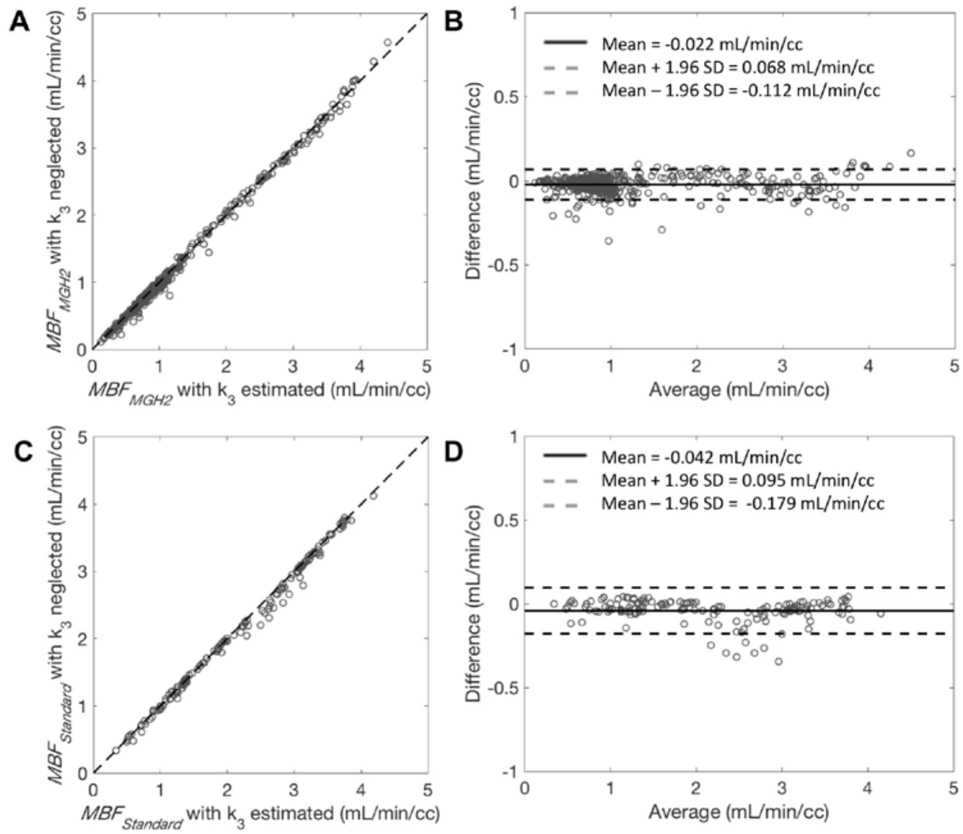
Supplemental Figures 4 and 5 show examples of rest and stress perfusion images generated using our model-based method from scan B, as well as the rest and stress perfusion images (from scan A and C, respectively) acquired separately for comparison. Supplemental Figure 4 shows representative images obtained for a control pig whereas the images presented in Supplemental Figure 5 correspond to a pig scanned with a LAD injury. The model-based perfusion images and polar maps were qualitatively similar to those obtained with separate rest and stress PET acquisition. However, one noticeable difference was the increased heart-to-blood contrast compared to the conventional perfusion images. This attractive feature is specific to our method in which the rest and stress parametric images of the spill-over fractions from right and left ventricles are used to eliminate the blood contribution to the PET signal as described in the methods. This effect resulted in slightly higher summed rest score (SRS) and summed stress score (SSS) than those obtained with the conventional method (Supplemental Table 1) but lead to a comparable classification (normal VS abnormal) by the two methods. Of note, the animal for which the infarct procedure had to be stopped (method section 2.2) presented only a very mild defect in the apex and was classified as normal by the SRS and SSS (study 1 in Supplemental Table 1).

Supplemental Tables

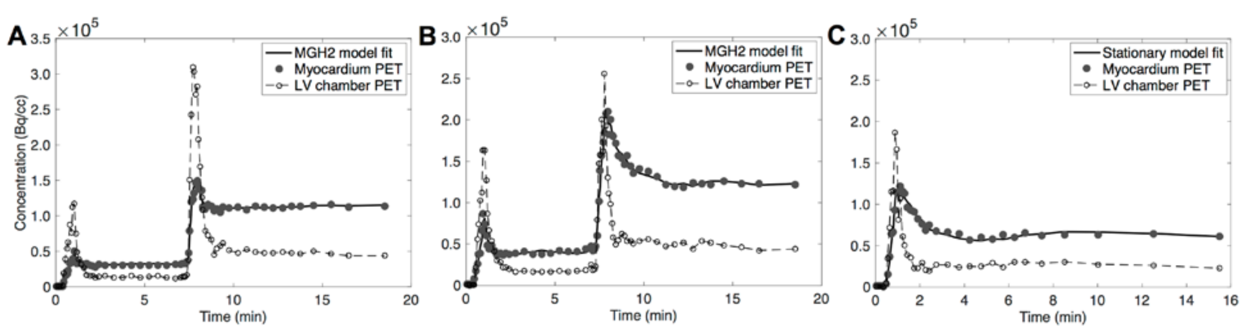
Supplemental Table 1. SRS and SSS scores for the MGH2 and standard methods.

Study	Rest standard (Rest A)	Rest MGH2 (Scan B.1)	Stress standard (Stress C.1)	Stress MGH2 (Stress B.2)
1	1	1	1	1
2	0	2	0	0
3	1	3	1	1
4	1	1	1	1
5	6	7	6	7
6	6	7	5	6
7	1	2	1	1
8	0	1	0	1
9	8	9	8	8

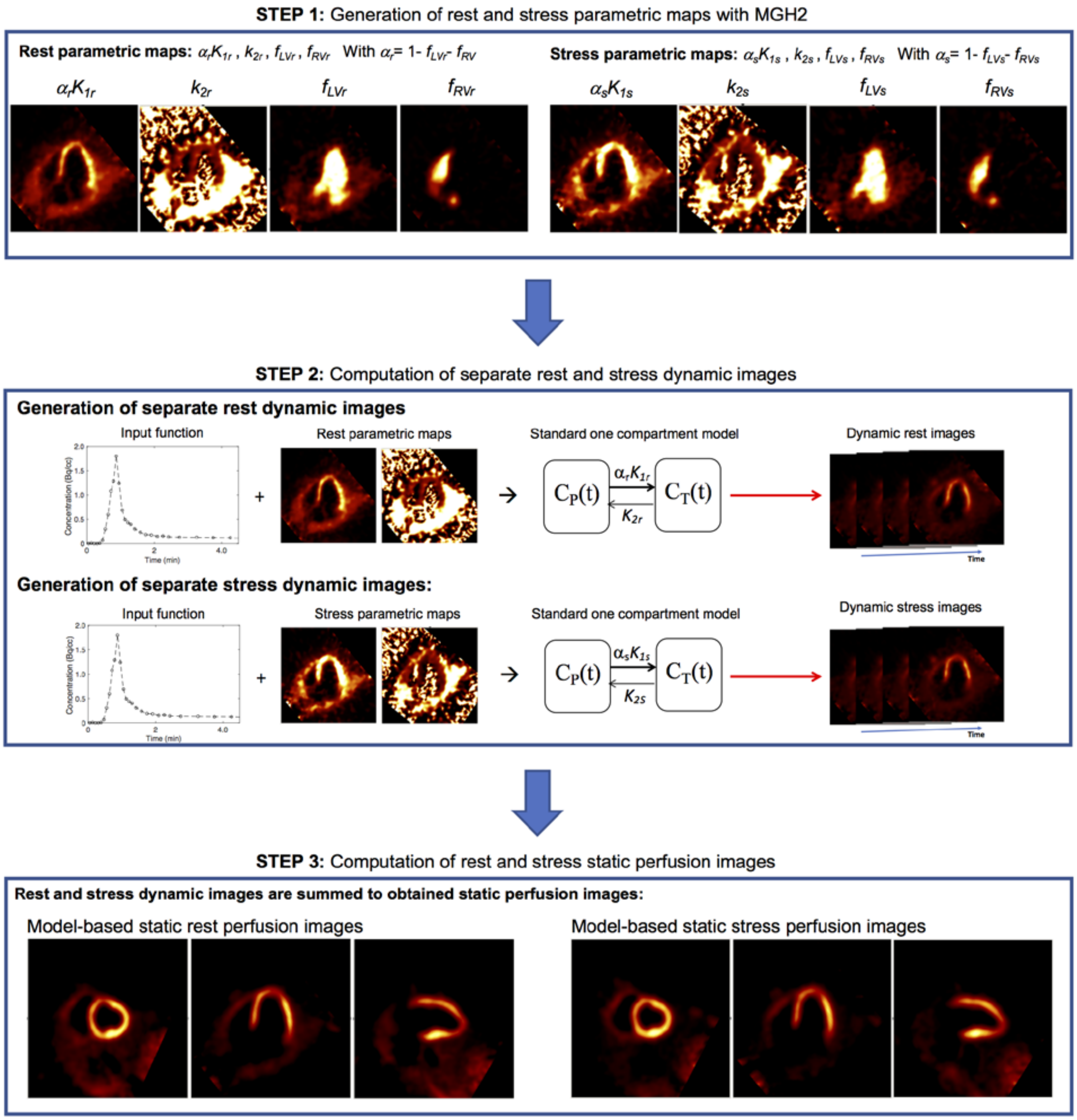
Supplemental Figures



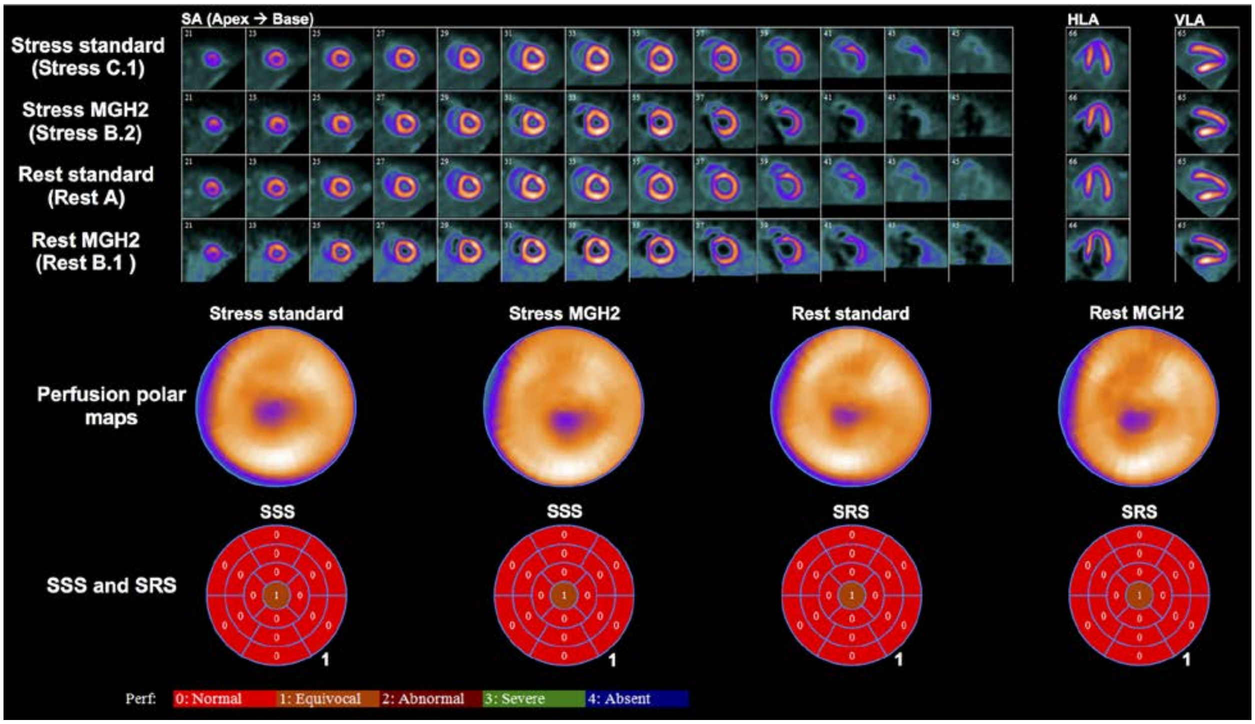
Supplemental Fig. 1



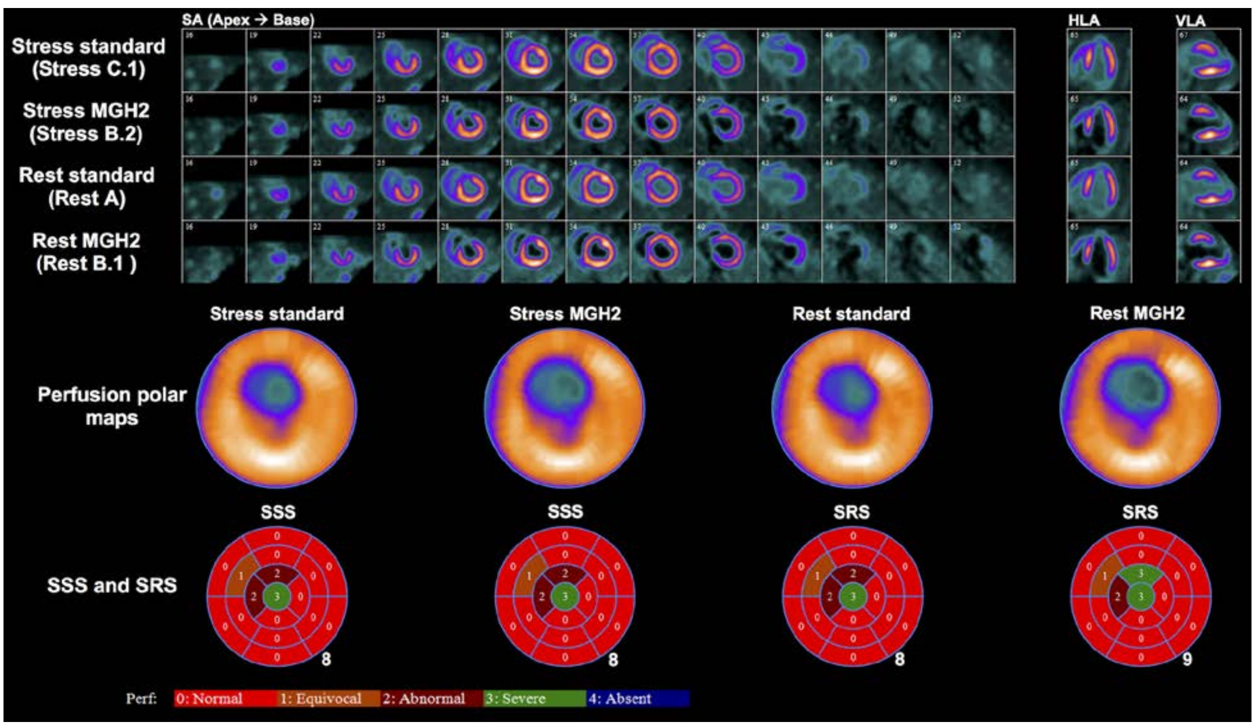
Supplemental Fig. 2



Supplemental Fig. 3



Supplemental Fig. 4



Supplemental Fig. 5

Figure Legends

Supplemental Fig. 1: A. Scatter plot for the 17 segments of all studies (scan 1 and 2 grouped) comparing the MGH2 flow estimates while neglecting k_3 and using only 12 min of PET measurements against those obtained while including k_3 and using the full 20 minutes duration of data for model fitting. **B.** Corresponding Bland-Altman plot to data shown in A. **C.** Scatter plot for the 17 segments of all studies (scan 3 only) comparing the flow estimates obtained with the standard method while neglecting k_3 and using only 4.5 min of PET measurements against those obtained while including k_3 and using the full duration of data for model fitting. **D.** Corresponding Bland-Altman plot to data shown in C. In **A and C**, dashed lines represent lines of identity. **In B and D**, bold line is the mean difference between flow estimates (obtained with and without including k_3) and dashed lines are mean difference ± 1.96 standard deviations.

Supplemental Fig. 2: Model fits corresponding to data shown in Figure 2 but using the full duration of PET measurements and including k_3 as a model parameter **A:** Rest-rest scan (scan 1); **B:** Rest-stress scan (scan 2); **C:** Stress alone scan (scan 3).

Supplemental Fig. 3: Diagram portraying the different steps for the generation of the model-based rest and stress perfusion images. In Step 1 parametric images of the model parameters are estimated from the simultaneous rest/stress data. In Step 2 the measured input function and the model parameters from Step 1 are substituted in the model equations for a single flow compartment. This has the effect of separating the contributions from rest and stress. The model equations predict accurately the measured PET concentration history for each voxel, allowing time-integration of these curves (voxel-by-voxel) to estimate the perfusion image in Step 3.

Supplemental Fig. 4: Top panel: Perfusion images of a control pig displayed with the clinical software corridor4DM. First and third rows (‘Stress standard’ and ‘Rest standard’) show the stress and rest perfusion images acquired separately with scan 3 and scan 1 respectively. Second and fourth rows (‘Stress MGH2’ and ‘Rest MGH2’) show the model-based stress and rest perfusion images generated from scan 2. Bottom panel: Perfusion polar maps as well as SSS and SRS scores corresponding to the perfusion images shown on the top panel.

Supplemental Fig. 5: Top panel: Perfusion images of a pig with LAD injury displayed with the clinical software corridor4DM. First and third rows (‘Stress standard’ and ‘Rest standard’) show the stress and rest perfusion images acquired separately with scan 3 and scan 1 respectively. Second and fourth rows (‘Stress MGH2’ and ‘Rest MGH2’) show the model-based stress and rest perfusion images generated from scan 2. Bottom panel: Perfusion polar maps as well as SSS and SRS scores corresponding to the perfusion images shown on the top panel.

Supplemental References

1. Guehl NJ, Normandin MD, Wooten DW, Rozen G, Ruskin JN, Shoup TM, Woo, J, Ptaszek LM, El Fakhri G, Alpert NM. Rapid Computation of Single PET scan Rest-Stress Myocardial Blood Flow Parametric Images by Table Look Up. *Med Phys.* 2017;44:4643-51. doi: 10.1002/mp.12398.
2. Hansen CL, Goldstein RA, Akinboboye OO, Berman DS, Botvinick EH, Churchwell KB, Cooke CD, Corbett JR, Cullom SJ, Dahlberg ST, et al. American Society of Nuclear Cardiology. Myocardial perfusion and function: single photon emission computed tomography. *J Nucl Cardiol.* 2007;14:39-60. doi: 10.1016/j.nuclcard.2007.09.023