# Kinetic models and blood signal modeling for dynamic cardiac MRI Perfusion Studies

E. DiBella[1,2], N. Pack[1,2], C. J. McGann[3]

[1]UCAIR, Radiology, University of Utah, Salt Lake City, UT, United States, [2]Bioengineering, University of Utah, Salt Lake City, UT, United States, [3]Cardiology, University of Utah, Salt Lake City, UT, United States

*Introduction:*

Quantitative or semi-quantitative analysis of dynamic contrast MRI data is performed to determine absolute blood flow values or as a more robust means of determining ischemia than visual assessment, since such analyses can be more sensitive to disease and less affected by artifacts. Some of the most common analysis methods are maximum upslope, the Fermi function and the two compartment model. These models are most often used without regard to signal from the blood in the tissue or from spillover of blood signal in the left ventricular blood pool. While blood signal has been modeled in resting myocardial perfusion studies [1], and right ventricular and left ventricular spillover has been corrected as a separate step [2], there has not been a systematic comparison of models with and without blood signal modeling. Here we studied five different "models" for estimating myocardial perfusion. The model with the most parameters was based on a two compartment model and can be written as:

$$S_t(t) = (1-p)K^{trans} \exp^{-(K^{trans}/v_e)t} \otimes S_b(t-t_0) + V_b S_b(t-t_0) + pS_b(t)$$

where $S_t(t)$ is the signal difference from the tissue of interest, $S_b$ is the signal difference from a region chosen in the left ventricular blood pool, $V_b$ is the (fractional) amount of blood signal from vasculature in the tissue, $t_0$ is a delay term, and $p$ is the fraction of signal from the left ventricular blood pool that appears in the tissue region of interest (the $(1-p)$ term assumes an equal amount of tissue signal spills out of the tissue). This model was fit for 5 parameters per region of interest ($K^{trans}$, $v_e$, $t_0$, $V_b$, and $p$). Note that $V_b$ and $p$ are differentiated by the fact that the signal included from $p$ must be simultaneous with the arterial input function. The second model had no blood terms; $V_b$ and $p$ were set to 0. The third model was equivalent to the first except $p=0$ and the time delay was global in that a single $t_0$ for all of the regions in the same slice was estimated. The fourth model used a Fermi function (4 parameters per region). The fifth "model" used the maximum upslope method, normalized to the upslope of the input function.

*Methods*:

Three volunteers were imaged with dynamic contrast MRI, 0.022-0.025 mmol/kg Gd-DTPA (6 cc/sec injection rate), at adenosine stress and at rest. The low doses were used to obtain a nearly linear relation to gadolinium concentration in the input function. Three short axis slices and 1-2 long axis slices (not analyzed) were obtained every heartbeat. A saturation recovery turboFLASH sequence was used on a 3T Siemens Trio (TR/TE 2/1 msec, TI~100 msec, flip=12°, linear phase encode order, 8mm slices). 70 time frames were acquired for each slice. The dynamic image frames upsampled to ~0.9 mm pixels were registered manually. Endocardial and epicardial contours were then traced on each of the slices in a selected time frame. Each slice was divided equally into 6 tissue regions. The regions were normalized to have the same pre-contrast value to account for the coil sensitivity pattern and signal difference curves were calculated. The curves were fit with the five different models described above. The parameters were bounded to physiological ranges. The fit error (chi-square value) and the coefficient of variation of the perfusion measurement for each of the 6 contrast injections were computed and averaged.

*Results:*

Fig. 1 shows that the model with the most parameters fit the data the best, as expected. The upslope method is not included in Fig. 1 since it uses only a small portion of the data. Somewhat surprisingly, the same model, the one with spillover and $V_b$ terms, gave the lowest coefficient of variation of perfusion (Fig. 2); this result implies that the blood modeling parameters are physiologically significant. The aggregate flow reserve results were fairly similar between most of the models (Fig. 3), with upslopes giving the lowest reserve and the Fermi function the highest (and most similar to those reported from other modalities).

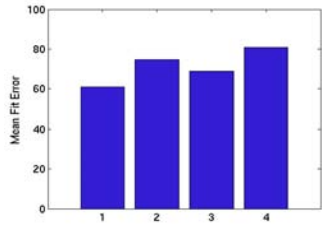


Figure 1: Mean fit error for the four convolution-based models. As described above, model #1 is a compartment model with all terms, #2 is the same but $V_b=0$ and $p=0$, #3 is the same as #1 but only a single delay term and $p=0$, #4=Fermi. No fit error is given for the upslope method (model #5).

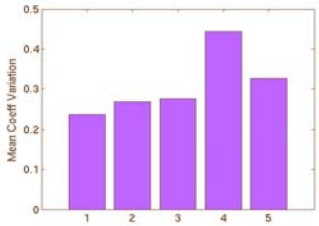


Figure 2: Mean coefficient of variation for the 5 models. The model numbers are the same as listed in the caption of Fig. 1. This is averaged over the rest and stress flows in the 6*3*3=54 regions and does not use the flow reserve data, though the trends are similar to the flow reserve error bars in Fig. 3.

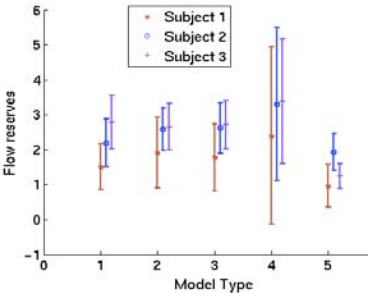


Figure 3: Perfusion reserve from each of the 3 subjects with different models. The model types are described above in the text and in the caption of Fig. 1.

*Discussion and Conclusions:*

In cardiac perfusion imaging, most published works ignore blood in the signal; spillover and blood in the capillaries ($V_b$) are not modeled. Good results have been reported without modeling blood signals, but it is known that some of the signal does arise from the vasculature within the tissue and that spillover is present depending on acquisition resolution and on the definition of the endocardial border by a user. While the results in Figs. 1-2 clearly indicate Model #1 is the method of choice, results on a regional basis can show dramatic differences between the modeling approaches. Model #1, with the most parameters, tends to trade-off between time delay and the blood terms, making the solution less unique. Evidently in these datasets, this is outweighed by data that are fit consistently. As well, the flow reserves for most of the models are lower than expected for normal subjects although the literature reports a range of flow reserve values from MRI and one might expect lower values due to decreasing extraction fraction of gadolinium at high flows [1]. These results show enough promise to warrant testing the novel 5 parameter model in more subjects and subjects with known disease to determine the model's sensitivity and specificity.

*References*

1. Larsson, Rosenbaum, and Fritz-Hansen, "Quantification of the effect of water exchange in dynamic contrast MRI perfusion measurements in the brain and heart", *MRM 46:272-281, 2001.*

2. Koestler, Ritter et al. "Correction for partial volume errors in MR heart perfusion imaging", *MRM 51:848-852, 2004.*