Parametric Aspects of First Pass DCE MRI Myocardial Studies

X. Li[1], C. Springer[1], M. Jerosch-Herold[1]

[1]Advanced Imaging Research Center, Oregon Health & Science University, Portland, Oregon, United States

Abstract: Values for parameters measuring a pseudo first-order rate constant for contrast reagent (CR) extravasation, K^{trans}, and the blood volume fraction, v_b, can be determined from the pharmacokinetic analysis of first-pass Dynamic-Contrast-Enhanced (DCE) MRI myocardial data. These vary between the resting and hyperemic conditions.

Introduction: The DCE MRI approach is widely used for determination of myocardial perfusion. A typical "first-pass" data acquisition lasts fewer than one hundred heart beats [1]. A new, comprehensive three-site-exchange [3SX] DCE MRI model [2] makes it possible to estimate pharmacological parameters, as well as physiological parameters in addition to flow. Results presented here suggest that the 3SX model can reliably differentiate between resting and hyperemic cardiac conditions. For such a short DCE data acquisition, involving a very low contrast reagent (CR) dose and potentially high flow rate and blood fraction during hyperemia**,** it is important to evaluate the contributions of equilibrium transcytolemmal and (particularly) transendothelial water exchange effects.

Methods: MRI studies were performed on eleven volunteers [ages 48 – 80y, mean = 62y (SD 9y), 4F/7M**]** with a 1.5 Tesla clinical MRI scanner (Siemens Medical Systems, Iselin, NJ). After obtaining written informed consent for this IRB-approved study, the participant was positioned supine on the MRI table, and an i.v. needle was inserted into an antecubital vein for injection of MR contrast and infusion of adenosine. A flexible 4-element phased array coil was secured on the participant's chest at the level of the heart. During the MRI examination, the blood pressure was monitored oscillometrically in the MRI scanner with a cuff that was inflated by remote control approximately every five minutes at baseline, and every minute during iv. adenosine. The heart rate was monitored with a continuous three-lead, MRI-compatible electrocardiographic recording. T_1-weighted gradient echo imaging of two-to-three slices having the short axis orientation, with a non-slice-selective saturation recovery magnetization preparation, was used to image the first-pass of an injected CR bolus through the heart. The MR pulse sequence parameters were: TR/TE/TI/flip angle = 2.2 ms / 1.2 ms / 90 ms / 18°, 256 read-out points and 60% phase encoding resolution, with linear ordering of phase encodings, a receiver bandwidth of 610 Hz/pixel, slice thickness of 8 mm, and a field of view of 280-380 mm by ~300 mm. A bolus dose (0.04 mmol per kg of body weight) of CR (Magnevist, Berlex, Wayne, NJ) was administered through an antecubital vein, starting at the 3rd or 4th heart beat, at a rate of 7 mL/s using a power injector, followed by a saline flush of 15 mL at the same injection rate. A first DCE-MRI scan was performed during rest, followed by a second scan about 15 minutes later during maximal vasodilation by iv. adenosine (0.14 mg/kg/min for 3 minutes before start of the DCE-MRI scan). The adenosine infusion was turned off after acquisition of the first 10-15 images.

Image Analysis: Region-of-interest (ROI) signal intensity curves were generated with the MASS cardiac MRI image analysis software (Laboratory for Clinical and Experimental Image Processing, Leiden University, The Netherlands), by manually segmenting the images along the endocardial and epicardial borders. The myocardium was subdivided into eight transmural sectors of equal circumferential extent along the myocardial centerline. The mean signal intensity in each myocardial sector was calculated for each of a series of images to obtain the regional signal intensity time-dependence. The mean ROI signal intensity before left ventricle contrast enhancement was subtracted as a baseline correction of each signal curve. The corrected curves were scaled to compensate for spatial inhomogeneities in the sensitivity profile of the receive-only phased-array RF coil. An ROI within the left ventricle was used to derive the arterial input function (AIF).

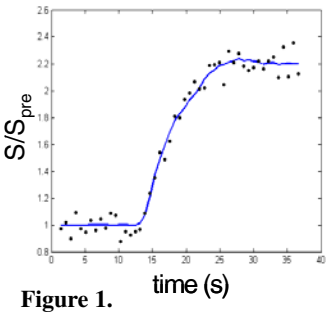

Figure 1.

Results: Figure 1 shows the data (filled circles) from one ROI of one subject, in the resting state. It also shows a fitted (blue) curve from the 3SX model with K^{trans} = 0.24 min^{-1}, and v_b =0.034. The curve is textured because of the numerical integration of the experimental AIF.

The sensitivities of model parameters to the DCE data were tested with other calculations. **Figure 2** shows contour plots of the natural logarithm of the reduced chi square statistic, $\chi^2 = \Sigma[S_{data}(t) - S_{model}(t)]^2$, for the data from one myocardial segment of the same subject as in Fig. 1, in the resting state. For each panel, the only two parameters varied were those labeled on the axes, while others were fixed at reasonable values. The parameters tested were: K^{trans}, v_b, τ_b (reciprocal of the unidirectional rate constant for water extravasation), v_e (extracellular, extravascular space [EES] volume fraction), and τ_i (mean lifetime of intracellular water molecules). These could be called "chi-by-eye" contours. The χ^2 value decreases as the contour color shifts in the blue direction. On all data segments tested, only the K^{trans}, v_b pair shows consistently the well-defined, funnel-type contour desired.

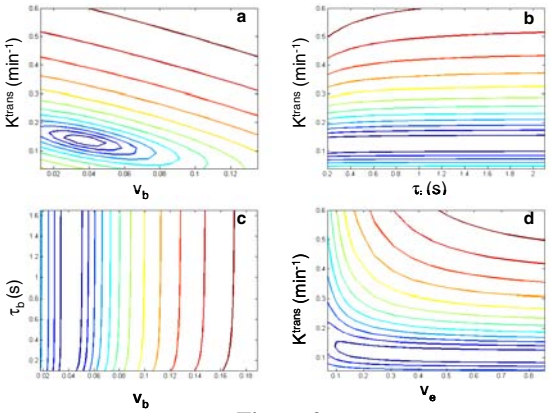

Figure 2.

We conducted two-parameter (K^{trans} and v_b) fittings of the ROI data from all eleven subjects, in the resting and hyperemic conditions. A summary is shown in **Figure 3**. Those parameter values held constant included: τ_b = 0.4 s, τ_i = 0.7 s, and an EES of 20%. Each colored line connects the resting and hyperemic conditions of a given subject, with the same color error bar representing one standard deviation for all eight ROI segments within that subject. Though inter-subject variation is large, the difference between rest and hyperemia is highly consistent.

Discussion: The DCE MRI data acquisition window will largely determine the nature of the data modeling. Mapping out parametric space is a good and reliable starting point in understanding the pharmacokinetics of a biological system that allows limited data sampling. With only first-pass DCE data (covering only one or two minutes after CR injection), the blood CR concentration will remain high during the entire DCE data acquisition. This will in turn dominate the DCE MRI modeling, and make information directly related to CR and blood pool, namely K^{trans} and v_b, readily available.

The effects of equilibrium transendothelial water exchange, though, remain very important, even if its kinetics cannot be easily determined with the short data acquisition used. Though the τ_b value is quite indeterminate over the range surveyed in Fig. 2c, χ^2 surely rises out of its minimum before reaching τ_b = 0 [the fast-exchange-limit; an assumption implicit in the standard model (2)] and $\tau_b = \infty$ [the slow-exchange-limit]. Thus, the exchange cannot be totally ignored.

Likewise, though the τ_i value is indeterminate over the range surveyed in Fig. 2d, it would be surprising if the χ^2 minimum really persisted to a τ_i value of 11 s, which has been reported (3), or to τ_i = 0.

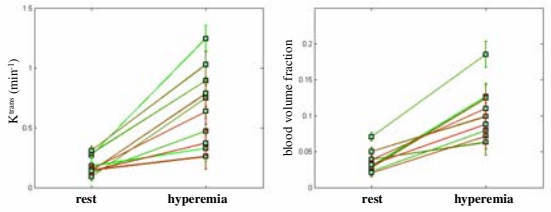

Figure 3.

Grant Support: NIH: RO1-NS40801, RO1-EB00422 , RO1-HL65394

References: 1. Atkinson, Burstein, Edelman, *Radiology* **174**:757-762 (1990). **2.** Li, Rooney, Springer, (a) *Proc. Int. Soc. Magn. Reson. Med.* **12**:145 (2004), (b) *Magn. Reson. Med.* **54**: 1351-1359 (2005). 3. Nordhøy, Anthonsen, Bruvold, Brurok, Skarra, Krane, Jynge, *Magn. Reson. Med.* **52**:506-514 (2004).