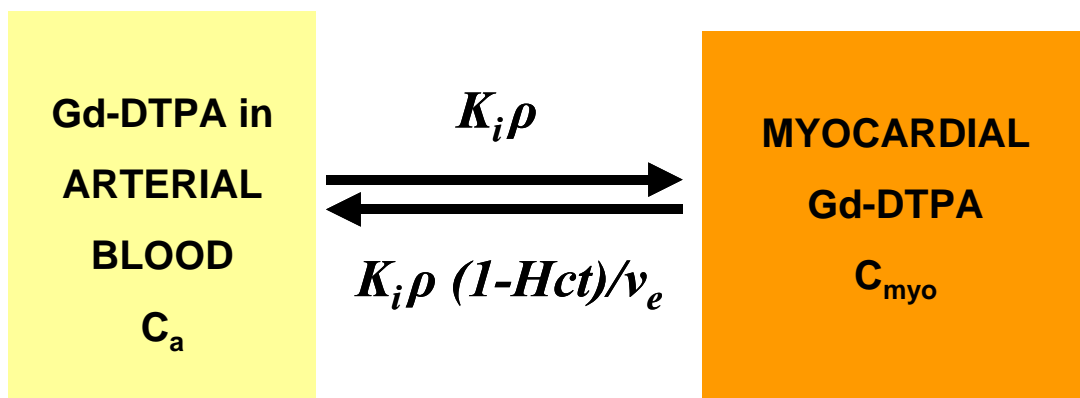
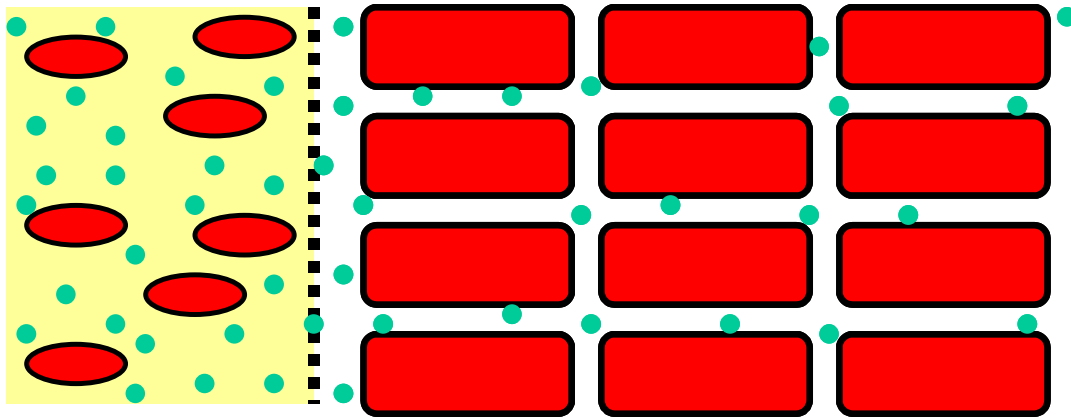


Quantification of myocardial perfusion using Gd-DTPA and SAT-turboFLASH MRI

This document reviews the model equations required for quantification of dynamic regional MRI data recorded from myocardium and aorta using SAT-turboFLASH sequences after Gd-DTPA injection [1]. The model is applied in program fit_dtpa, which can be downloaded from <http://pet.utu.fi/staff/vesoik/programs/>

Compartment model for Gd-DTPA in myocardium

Gd-DTPA does not enter the erythrocytes or myocytes, but does penetrate the capillary wall in the heart muscle.



This model can be described with the following differential equation, which can be solved using convolution [1, eq. 1], or e.g. second order Adams-Moulton method, as is done in our application.

$$\frac{dC_{myo}(t)}{dt} = K_i \rho C_a(t) - \frac{K_i \rho (1-Hct)}{v_e} C_{myo}(t) \quad (1)$$

In this equation, C_{myo} is the concentration of Gd-DTPA in the total tissue volume, and C_a is the concentration in arterial blood. In our application the tissue density, $\rho=1 \text{ g/mL}$ [1], is not considered. v_e is the extravascular extracellular volume fraction. Influx constant, K_i , is related to the perfusion, F (a true parameter of interest), and extraction, E , with the following equation:

$$F = \frac{K_i}{E} \quad (2)$$

Extraction is not known, but a value for it is required for the estimation of the Gd-DTPA concentration in the vascular space, which is approximated by the venous whole blood concentration, C_b [1, eq. 2]. By default, our application uses value $E=0.5$.

$$C_b(t) = (1-E)C_a(t) + E \frac{1-Hct}{v_e} C_{myo}(t) \quad (3)$$

Signal equation for SAT-turboFLASH sequence

Signal (SI) can be calculated from equation (4), which is represented as such from the equation (6) in the article of Larsson et al. (2001):

$$SI = \Omega M_0 \sin(\alpha) \left[\left(1 - e^{-TR_1}\right) \left(\cos(\alpha) e^{-TRR_1}\right)^{n-1} + \left(1 - e^{-TRR_1}\right) \frac{1 - \left(\cos(\alpha) e^{-TRR_1}\right)^{n-1}}{1 - \cos(\alpha) e^{-TRR_1}} \right] \quad (4)$$

ΩM_0 represents the calibration coefficient, α is the flip angle (default 8°), n is the number of phase encoding steps (default 48), TI is the time from the center of the 180° RF pulse to the first α pulse (default 0.055 s), and TR is the repetition time (default 0.0020 s). R_1 is the intrinsic relaxation rate.

Equations for intrinsic relaxation rates

In Larsson et al (2001) the equations for intrinsic relaxation rates of myocardium, R_{1myo} , and blood, R_{1b} , (eq. 3) are given as below:

$$R_{1myo}(t) = R_{10myo} + r_1 \frac{1}{1-v_b} C_{myo}(t) \quad (5a)$$

$$R_{1b}(t) = R_{10b} + r_1 C_b(t) \quad (5b)$$

Relaxation rates without contrast agent, R_{10myo} and R_{10b} , default to 1.0 s^{-1} and 0.67 s^{-1} . r_1 is the longitudinal relaxivity, assumed to be the same for tissue and blood (default 4.3).

Conversion of aortic SI data to arterial blood curve

Prior to any other computations, the model input, C_a , is calculated from the MRI signal (SI) curve derived from aortic region. This consists of the following steps:

1. Determine the baseline

Signal curve *baseline* is determined as an average of signal values measured before contrast agent infusion. If the first measurement value is $>5\%$ higher than the *baseline*, *baseline* is computed again without the first value.

2a. If this is the first study, determine calibration coefficient

Calibration coefficient ΩM_0 is calculated from the equation (4), where *baseline* is used as SI and R_{10b} is used as R_I .

2b. Alternatively, if there is background from a previous study, determine R_{10b}

Relaxation rate R_{10b} with background contrast agent is calculated as R_I from the equation (4), where *baseline* is used as SI and calibration coefficient ΩM_0 is assumed to be the same as it was in the previous study.

3. Compute R_I curve

$R_{Ib}(t)$ is solved as R_I at each measurement point by placing measured signal $SI(t)$ and the calibration coefficient determined in previous step into Eq. (4).

4. Compute curve of arterial blood concentration

Equation (5b) for blood compartment is applied to compute the arterial blood concentrations, $C_a(t)$, from the $R_{Ib}(t)$ curve [1, eq. 3]:

$$C_a(t) = \frac{R_{Ib}(t) - R_{10b}}{r_1} \quad (6)$$

Simulation of myocardial signal

For nonlinear estimation of model parameters, the curve of myocardial MRI signal needs to be simulated with any given set of parameters K_i , v_e and v_b . This is accomplished in the following steps:

1. Determine the baseline

Signal curve *baseline* is determined as an average of signal values measured from myocardial region before contrast agent infusion. If the first measurement value is $>5\%$ higher than the *baseline*, *baseline* is computed again without the first value.

2a. If this is the first study, determine calibration coefficient

The relaxation rate R_{10} without contrast agent is calculated as a volume weighted average of R_{10b} and R_{10myo} , Eq. (7), and is thereafter used as R_1 , together with the *baseline* as SI , in the equation (4) to calculate the calibration coefficient ΩM_0 .

$$R_{10} = v_b R_{10b} + (1 - v_b) R_{10myo} \quad (7)$$

2b. Alternatively, if there is background from a previous study, determine R_{10myo}

The relaxation rate R_{10} without contrast agent is calculated from eq. (4) where *baseline* is used as SI , and calibration coefficient ΩM_0 is assumed to be the same as it was in the previous study for the same myocardial region. Thereafter, myocardial relaxation rate R_{10myo} is calculated from the equation (7).

3. Simulate the myocardial and blood concentration curves

Concentrations $C_{myo}(t)$ and $C_b(t)$ are simulated using equations (1) and (3).

4. Compute the R_1 curve

$R_{1myo}(t)$ and $R_{1b}(t)$ are computed using equations 5a and 5b and the simulated concentrations in tissue and in (venous) blood. Assuming fast water exchange between the vascular and extravascular space [1, equation 4], the simulated relaxation rate curve is calculated as:

$$R_1(t) = v_b R_{1b}(t) + (1 - v_b) R_{1myo}(t) \quad (8)$$

5. Compute the simulated signal curve

Simulated MRI signal curve, $SI^{sim}(t)$, is then computed using Eq. (4), and the relaxation rate curve and calibration coefficient from the previous steps.

Estimation of model parameters

Model parameters K_i , v_e , v_b , and ΔT (Gd-DTPA appearance time difference in plasma and tissue) are estimated applying a nonlinear least squares method, using Powell-Brent optimization algorithm. The steps in the nonlinear parameter estimation procedure (“fitting”) are:

1. *Set (guess) initial values for the model parameters, p*
2. *Compute simulated signal curve $SI^{sim}(t)$ using $C_a(t)$ and parameter values*

Time difference (ΔT) is used to shift the simulated curve forward in time.

3. *Compute the sum of squares*

The cost function, $Q(p)$, sum of squared differences between the observed values and simulated values (n time points) is calculated for the current set of model parameters as:

$$Q(p) = \sum_{i=1}^n (SI(t_i) - SI^{sim}(t_i))^2 \quad (9)$$

4. *Check for convergence*

If the cost function (sum of squared differences) is smaller than a given limit value, or if the cost function is not decreasing, the minimization routine stops, and the best set of parameters found so far is assumed to be the correct set model parameters. Otherwise Powell-Brent algorithm continues from step 2.

References

1. Larsson HBW, Rosenbaum S, Fritz-Hansen T. Quantification of the effect of water exchange in dynamic contrast MRI perfusion measurements in the brain and heart. *Magn. Reson. Med.* 2001;46:272-281.