Determination of Myocardial Blood Flow by Model-Independent Deconvolution

Signal intensity (SI) averages were measured for 16 myocardial sectors for each image of a dynamic series covering the first pass and recirculation of the injected contrast agent, using the AHA segmentation model. The resulting signal intensity curves and the associated times at which each image was acquired are used for determination of regional blood flow. Figure 1, reproduced here from the main body of the manuscript, provides an example of signal intensity changes in the inferior-septal segment, for rest and hyperemia. A region of interest (ROI) in the center of the left ventricle was used to sample signal intensity changes for the arterial input of contrast.
Figure 1 (reproduced from main body of manuscript): Quantitative myocardial perfusion at rest and during adenosine vasodilatation in the same patient as in figure 1. Top figure demonstrates the signal intensity (SI) curves (arbitrary units = a.u.) during the first pass of a contrast agent bolus in the hypertrophied basal myocardial segment (marked as *) and the bottom figure represents the SI curves in the blood pool used as the arterial input function.

The assumption of a linear relationship between signal intensity changes, and contrast agent concentration changes, is central for the analysis and estimation of blood flow from signal intensity curves. For this reason a T1-weighted sequence is used, with short echo-times to minimize the sensitivity to magnetic susceptibility and motion. Signal saturation is most likely to be observed in the left ventricular blood pool, because the contrast bolus is more compact in the LV blood pool than during transit through a tissue region of interest. With a contrast dosage of 0.25 mmol/kg, we estimate peak contrast concentrations in the LV blood pool to be on the order of 1.8 mmol/L with normal LV function. For Gadodiamide, a concentration of 1.8 mmol/L corresponds to a peak relaxation rate constant of approximately 7 s⁻¹. Furthermore, it is important to minimize the effects of blood inflow in the ventricular cavity, i.e. the signal enhancement through inflow should be reduced by using a slice imaged during diastole to determine the arterial input function. Figure 2 shows the relation between signal and relaxation rate measured...
in phantoms with a saturation recovery prepared gradient echo sequence as used in this study, and also illustrates how inflow could alter this relationship.

**Figure 2**: The circles show the relation between signal intensity, measured with a saturation-recovery prepared turbo FLASH sequence, and the relaxation rate in saline-filled phantoms doped with Gd-DTPA contrast agent. The R1 relaxation rate constant of the phantoms was determined with a spin-echo sequence. The evolution of the longitudinal magnetization of flowing blood, imaged with a non-slice-selective saturation recovery prepared turbo FLASH acquisition, was simulated using the approach of Peeters et al.,\(^2\) and assuming a linear phase encoding order. The blue solid line shows the simulation result for stationary fluid, while for the green curve a velocity of \(v=10\) cm/s was assumed with otherwise identical parameters. The slice thickness was equal to 8 mm in the simulations. The dotted line represents a linear extrapolation from the region of low R1 values, and corresponds to the assumption of strict linear proportionality between signal intensity and signal, which was used for the analysis of the perfusion studies.

The central volume principle states that the tracer residue in a tissue region can be thought of as resulting from the convolution of the measured arterial input with the tissue residue impulse response. The tissue impulse response represents the tracer residue curve one would observe for a hypothetical arterial input equivalent to a very brief impulse. The tissue impulse response has some useful properties for blood flow estimation: The area under the tissue impulse response curve equals the effective distribution volume during the first pass, and the amplitude or height of the impulse response equals the blood flow in and out of the tissue ROI.\(^3,4\) The tissue impulse response, \(R(t)\), cannot be measured directly, and the measured tissue residue curve, \(q(t)\), equals the convolution integral for the arterial input function, \(i(t)\), and the tissue impulse response, \(R(t)\):\(^4\)
\[ q(t) = \int_0^t i(\tau) \cdot R(t - \tau) \cdot d\tau \quad (1) \]

To solution of this relationship for the tissue impulse response, \( R(t) \), is equivalent to the process of differentiation, and division, both of which are much more sensitive to noise in the data, than integration. The numerical solution therefore needs to be stabilized by imposing some side constraints.

The process for calculating the impulse response was described previously, and summarized here briefly, with examples from the present study. The integral in equation [1] can be approximated by a sum over discrete time points \( t=[t_1...t_n] \), that we assume equally spaced, with the sampling interval, \( \Delta t \), defining the temporal resolution.\(^5\-\(^7\) The myocardial impulse response was represented as sum of B-splines, a generalization of the Bézier curve, which imposes some degree of smoothness:

\[ R(t_i) = \sum_{j=1}^{p} B_j^{(k)}(t_i) \cdot \alpha_j \quad (2) \]

In the above sum \( B_j^{(k)} \), represents a B-spline of order \( k \), for the knot sequence \( \tau_1 \leq \tau_2 \ldots \leq \tau_{p+k} \), where \( p+k \) is the number of knots\(^8\), and the \( \alpha_j \) are weighting factors for the spline components. The problem of determining all \( R(t_i) \) values of the impulse response is reduced to the determining the amplitudes, \( \alpha_j \), of the \( p \) spline components. The number of spline components (\( p \)) was set to 12, based on previous simulations, and \( p<<n \), where \( n \) is the number of time points in \( R(t_i) \).

Regularization was used to assure that solving for the \( \alpha_j \) coefficients does not suffer from numerical instability.\(^5\-\(^7\) Regularization means that side-constraints are applied so that the addition of small amounts of noise to the measured data, would only result in relatively small changes in the impulse response, as one would expect for linear, “well-behaved” system. The weight given to the side constraint has to be chosen to balance the discrepancy between measured data and the calculated tissue residue curve, against the requirement of a reasonably smooth shape of the impulse response. A first order difference operator (L), applied to the B-spline coefficients, can be used for this purpose as a side constraint to reduce oscillations in the amplitudes of the B-spline coefficients.
along the ordinate axis, versus the goodness of fit measure, along the abscissa, for different weightings of the smoothness side constraint.\textsuperscript{9} The horizontal part of the L-curve indicates the range of $\lambda$-values where the side-constraint causes the solution to be sufficiently smooth such that the value of the smoothness constraint changes little with the regularization parameter $\lambda$. The vertical part of the L-curve corresponds to solutions that give rise to small residuals, but the smoothness of the solution, varies dramatically with the regularization parameter. The optimal $\lambda$-value ($\lambda_{\text{opt}}$) corresponds to the location of the L-curve with the greatest curvature, i.e. the “corner” of the L-curve, i.e. before the impulse response starts to show large oscillations in amplitude if $\lambda$ is further reduced.\textsuperscript{9-11} The impulse response, $R(t)$, is calculated from equation 2 as a sum of B-splines with the coefficients ($\alpha_i$) that are obtained with $\lambda=\lambda_{\text{opt}}$. Finally the predicted tissue response, is obtained through equation 1. Figure 3 shows the L curves that result from the tissue curves and the arterial inputs, corresponding to baseline and hyperemic states respectively, and shown in Figure 1.

The Gd-DTPA contrast agent can traverse the capillary barrier. As a result the impulse response shows an initial, relatively rapid decay, for the contrast that quickly transits through the capillary without escaping into the interstitial space. After this initial decay the impulse response falls off at a much slower rate that is not appreciable over the time period covered by the first pass measurements, partly reflux of contrast from the interstitial space into the vascular space only becomes detectable when the concentration of Gd-DTPA in the blood pool declines appreciably.

Other approaches, based on modeling of the transit and capillary exchange in the microcirculation have been used to estimate myocardial blood flow.\textsuperscript{12, 13} An advantage of the model-independent approach used in this study is the absence of model parameters, only a few of which can be optimized by fitting to the measured data, with others kept fixed at carefully chosen “default” settings. Therefore a largely model-independent approach has increasingly been used for analysis of myocardial perfusion with MRI.\textsuperscript{14-16}
Figure 3: Left: The value of the smoothness side constraint for the impulse response is evaluated for a range of the regularization parameter $\lambda$, and plotted against the sum of the residuals (magnitude) evaluated for the same values of $\lambda$, with the corresponding impulse response. The shape has an L-shaped knee and the corresponding value of $\lambda$ represents an optimal choice for the regularization parameter. Right: The impulse response, shown here for rest (top) and hyperemia (bottom), was represented as a sum of B-splines. This B-spline representation was chosen to improve the numerical stability of the deconvolution process. The tissue impulse response curves shown here correspond to the optimal choices of the regularization parameter. The blood flow is estimated from the amplitude of the impulse response.
Cited Literature


