Estimation of perfusion and other vascular parameters from first part of bolus passage

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Introduction: A number of vascular parameters can be extracted from dynamic MRI during administration of a contrast agent. The estimation problem is often formulated using the theory of linear, time-invariant systems. In this framework, vascular parameters can be derived from the impulse response function (IRF), which express all characteristics of a linear system. The estimation of the IRF involves deconvolution and is very noise-sensitive for finite bolus durations. Often, however, only few, specific vascular parameters are wanted. We present a relatively simple method targeted at extracting perfusion, vascular delay and the initial rate at which contrast agent leaves a voxel. These parameters are all derived from the first part of a bolus passage. The analysis constitutes a generalization of the Mullani and Gould first-pass method described in [1] for which outflow was a limitation.

Theory: The arterial concentration $C_a(t)$ of an intravenous contrast agent is related to the perfusion F and the tissue concentration $C_t(t)$ by the convolution integral in Eq. 1 where R(t) is the normalized IRF that describes the gradual washout of a bolus of infinitely short duration.

$$(1):\ C_t(t) = F\int_0^t C_a(\tau)\cdot R(t-\tau)\,d\tau \qquad (2):\ R(t-\tau) = 1/n!\sum_{n=0}^{\infty} k_n(t-\tau)^n$$

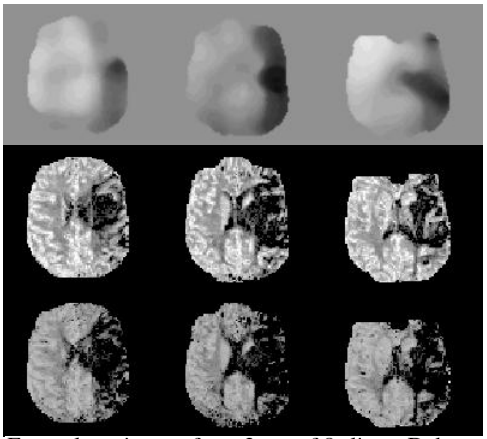
Equation 2 is a Taylor expansion of the impulse response valid for positive arguments. As long as a negligible amount of contrast agent has left a given voxel, only the zero-order term is significant. The first order term describes initial outflow. Higher-order terms come into play later. Here we focus on the first two terms and rewrite Eq. 1:

$$(3):\ C_t(t) = F(\int_0^t C_a(\tau)\,d\tau + k_1\int_0^t C_a(\tau)(t-\tau)\,d\tau) = Fg_0(t) + kg_1(t) \text{ where } k = F\cdot k_1 \text{ and } g_0, g_1 \text{ are moments of } C_a$$

Equation (3) describes how the tissue concentration initially increases in proportion to the accumulated contrast g_0 as determined by the perfusion. The negative slope k_1 of the impulse response, being the rate at which contrast agent initially leaves a voxel after arrival, determines the initial deviation from proportionality. Hence both F and k can be derived from the initial part of the concentration curves by simple regression. The delay between the actual and measured arterial supply can be estimated by minimizing the fit error χ^2 that has a distinct minimum for the true delay if the fitted data contains both baseline measurements and data acquired after a significant amount of contrast agent has left the voxel, e.g. 10 seconds after bolus arrival. Due to the linearity of the method, spatial smoothing can be used to determine delays regionally. Since only the period around bolus arrival is used for the analysis, apodized sinc-interpolation is useful for shifting the time series by fractional time-steps.

Methods: A Siemens Vision 1.5 Tesla whole-body scanner was used to acquire T2*-weighted echo-planar imaging data (TE/TR=66/1500ms, FOV 230mm, 128x128 matrix, 5 mm thickness) during injection of a bolus of intravascular contrast agent (Gd-DTPA, 0.1 mmol/kg). Data were aligned to compensate for motion during the measurement. ΔR2* curves were calculated and a linear relation to concentration was assumed. Delay estimation was based on data smoothed with a square 29mm spatial kernel. The resulting delay maps were used to estimate F and k_1 voxelwise in original spatial resolution. Comparisons were made to perfusion estimated by a commonly used SVD method [2] for normal volunteers, where the effect of delay is limited with respect to F.

Results: Maps of delay, perfusion and negative slope of the IRF at time zero are shown for a 68 year old stroke patient (a. cerebri media infarction) examined in the acute phase 8 hours after onset of symptoms. The delays reflect vascular effects and the acquisition order of slices. For normal volunteers, high linear correlations were observed between SVD and first-pass perfusion estimates but the ratio is not 1 precisely and an offset may occur. Both effects are small. For healthy subjects, the SVD perfusion maps are similar to those calculated from the initial part of the bolus only, but the former appear considerably more noisy.



Example estimates from 3 out of 8 slices: Delays, perfusion and rate at which contrast agent initially leaves voxel.

Discussion: The method offers a simple, direct approach to estimation of vascular parameters. Except for the delay estimation, the method is linear, which facilitates analysis. It may seem a waste that only the first few points of the bolus passage are used to estimate the perfusion. That is common to all analysis methods, however, as the later concentration measures are influenced by later parts of the IRF also, and therefore mostly contribute to the estimation of those. By a targeted approach, the sensitivity to noise in irrelevant parts of data is limited. The method is in principle insensitive to saturation of the signal by contrast agent, which is a common problem. Weighted fitting in the time domain can be used to ignore periods of saturation.

[1] NA Mullani and KL Gould, J Nucl Med 24: 577-581, 1983

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