On the Theoretical Basis of Perfusion Measurements by Dynamic Susceptibility Contrast MRI

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Introduction

Magnetic resonance imaging of the first passage of a bolus of a blood pool contrast agent is a developing method for assessment of the regional perfusion [1,2]. This method implies a comparison of the contrast agent (CA) concentration time courses in both a volume of interest (VOI) and in a reference voxel in a feeding artery. In practice the CA concentration is measured indirectly via the associated increase in the transverse relaxation rate. It is assumed that the underlying dependence is linear and has the same form in both the VOI and the reference voxel. In order to examine these assumptions a complete simulation of the measurements has been undertaken. This includes the bolus passage, the related changes in the MR signal and the data processing performed according to Refs [1,2]. The simulation is noise free in order to analyse the inherent properties of the method.

Methods

The starting point of the simulation are the time course of the CA concentration in the reference artery $c_f(t)$ and the residue function $R(t)$ which describes the microcirculation. The signal change in the reference voxel is calculated using the linear effect of the CA on the relaxation rate with the relaxivity which is supposed to be known from in-vitro measurements such as [3]. The blood CA concentration in the VOI is calculated as a convolution $R(t)\ast c_v(t)$. The increase in the relaxation rate of the intravascular protons is calculated using the same relaxivity as in the reference artery. The extravascular protons experience an enhanced relaxation too. This is caused by an increase in the microscopic inhomogeneities of the magnetic field due to the susceptibility effect of the CA. The extravascular signal is calculated by means of the theory [4-6] that has been originally aimed to the quantification of the BOLD effect. This theory has been further developed in order to describe the relaxation effect of the arterioles, capillaries and venules during the bolus passage. A comparison with the Monte Carlo simulation [7] has shown a very good agreement. The total MR signal is obtained as a sum of the intra and the extravascular contributions to the total signal.

The simulated data are processed as described in [1]. This gives values of the blood flow, blood volume and the residue function which are referenced to as “apparent” in order to contrast their true counterparts. A comparison of the apparent and the actually used quantities leads to the conclusion formulated below. This study is focused on the spin-echo measurement techniques which are mainly used in practice due to their subjective sensitivity to the microvessels. All numerical results are presented for realistic microcirculation data and the NMR parameters chosen as close as possible to those of the experimental studies [8,9].

Results

The simulation has shown that none of the two assumptions described in Introduction is valid. The relation between the increase in the relaxation rate and the CA concentration in the VOI differs from that in the reference artery and is nonlinear.

It follows from the mathematical nature of the deconvolution that the apparent blood flow $f_{app}$ is determined by the linear response of the relaxation rate on small changes in the CA concentration. This yields an analytical dependence between $f_{app}$ and the true blood flow $f$:

$$f_{app} = \frac{1}{\gamma} \left[ w_b + w_p \frac{k}{\nu} \left( v_i R_{2c} + v_e R_{2v} \right) \right] f$$

Here $\zeta$ is the blood volume fraction in tissue, $w_b$ and $w_p$ are the weights of the intravascular blood and the parenchyma in the total signal, $k$ and $\nu$ are the increases in the blood susceptibility and the relaxation rate per one mM of the CA, $\gamma$ is the natural magnetic susceptibility of venous blood, $R_{2c}$ and $R_{2v}$ are the contributions to the relaxation rate in parenchyma from the deoxygenated blood in veins and capillaries respectively, $v_i$ and $v_e$ are the exponents in the dependence of $R_{2c}$ and $R_{2v}$ on $\gamma$. All quantities which depend on the CA concentration $c$ are taken at $c=0$. For the moderate fields such as $1\% \nu_i = \nu_e = 2$. For high fields $\nu_i = 2/3$. Numerical evaluation of the above formula gives $f_{app} = 1.8f$.

The shape of the apparent residue function $R_{app}(t)$ is strongly affected by the nonlinearity in the dependence of the parenchymal signal on the blood CA concentration. In particular $R_{app}(t)$ can increase in spite of the requirements imposed by the physiological meaning of the true function. An example is shown in figure 1. The odd behaviour of $R_{app}(t)$ has been cross validated with an analytical calculation for low CA concentrations.

The relation between the apparent and the true blood volume depends on the signal response for all CA concentrations. An example of the simulation results is shown in figure 2. A deviation from a constant is dominated by the nonlinearity in the venous contribution to the relaxation rate in parenchyma.

Discussion

The inherent feature of the $T_2$ contrast perfusion measurements is the contribution of the extravascular protons to the variations of the total signal. The parenchymal protons are dephased via the susceptibility effect of the blood pool contrast agent. This gives rise to a significant correction to the measured blood flow and to a nonlinear relation between the profile of the passing bolus and the resulted changes in the MR signal.

A validation of the perfusion measurements performed in comparison with PET [8,9] has shown a good agreement while the present theory predicts about 80% overestimate of the blood flow and an even higher error for the blood volume. This can be considered as a reasonable agreement taking into account several uncertainties in the experimental and physiological parameters, unclear effect of the filtering of or fitting to the noisy experimental data and the restriction of the monotonous decrease of the residue function. Another way to validate the theory would be to test the numerous parameter dependencies that follow from the obtained equation.

To sum up the dynamic susceptibility contrast MRI has not reached yet the goal of the absolute perfusion quantification. Good news is that the method is sensitive to the same parameters of the microvasculature which are in the focus of studies based on the BOLD effect. Thus the $T_2$ perfusion measurements can bridge between these approaches.

References