Direct Measurement of Arterial Input Function in White Matter

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Introduction

Estimating the arterial input function (AIF) is the first step in most DSC and DCE MRI analyses. Ideally, signal intensity would be measured in a large vessel and converted to contrast agent concentration (*C*) using a suitable relationship between *C* and relaxivity. There are, however, a number of difficulties involved with intravascular signal measurements: saturation in the vessel, partial volume effects due to low imaging resolution and dispersion and delay of AIF between the measured vessel and the tissue of interest. These problems are partially resolved by using an AIF derived from a reference tissue, e.g., normal white matter. However, one difficulty in this approach is finding a relaxivity model that accurately describes the relationship between relaxivity and *C*. Since the vasculature and magnetic field perturbation effects are too complicated to be replicated via physical phantoms and *in vivo* calibration measurements are difficult, theoretical models and Monte Carlo simulations are employed to estimate *C* in white matter.

Two theoretical limiting cases have been applied to describe the loss of transverse magnetization: the static dephasing regime (SDR) and the diffusion narrowing regime (DNR). In the latter regime the signal dephasing time is long enough for molecular diffusion to average out phase shifts caused by different magnetic moments (1). Because the distance between vasculature in white matter is greater than proton diffusion lengths in a typical gradient-echo experiment the SDR not the DNR should hold (1,2).

$$r_2^* = \frac{\left[\left(\frac{2}{3}\omega T_E\right)^5 + \frac{2}{3}\left(\omega T_E\right)^2 + 1\right]^{1/5}}{T_E} \qquad \text{Eq. [1]}$$

The SDR is divided into two time regimes, short dephasing times, $\omega T_E << 1$, and long dephasing times, $\omega T_E >> 1$, where $\omega = 4/3\pi\Delta\chi\gamma B_0$ for vessels described by randomly oriented cylinders (3). Kiselev has presented expressions for SDR relaxivity at both long and short dephasing times and an interpolation formula, Eq. [1], between the two (4). In this study we compared AIFs derived from both blood and white matter in 10 patients scanned at 3T. We compared white matter AIFs calculated using the full SDR model, Eq. [1], with those calculated assuming a simple linear relationship between relaxivity and *C*, Eq. [2] (3).

$$r_2^* = \frac{\frac{2}{3}\omega T_E - 1}{T_E} \qquad \text{Eq. [2]}$$

$$S = S_o e^{-r_2^*(C)T_E} \qquad \text{Eq. [3]}$$

Methods

Blood signal measurements were taken from the sagittal sinus and converted to *C* using Eq. [3] where $r_2^*(C) = 1.45C^2 + 4.5C$, which has previously be determined experimentally in bulk blood at 3 T with 30% hematocrit (5). White matter signal measurements were converted to *C* by combining Eqs. [1] and [3] where $\Delta\chi(C) = \chi_o + kC$, χ_o is the natural magnetic susceptibility of blood at 35% oxygenation extraction (0.038 ppm) (6) and *k* is Gd-DTPA susceptibility (0.026 ppm) measured *in vitro* (7). The linear approximation of *C* was obtained using Eq. [2] for relaxivity (3). Blood volume in white matter was assumed to be 2.5% and the white matter AIFs were scaled appropriately to match the blood AIF. Finally, a gamma variate function was fitted to the concentration time curves to approximate the contrast bolus and the area under the gamma variate calculated to give CBV in arbitrary units. CBV values for blood were compared to the full SDR and linear white matter estimates using Bland-Altman plots.

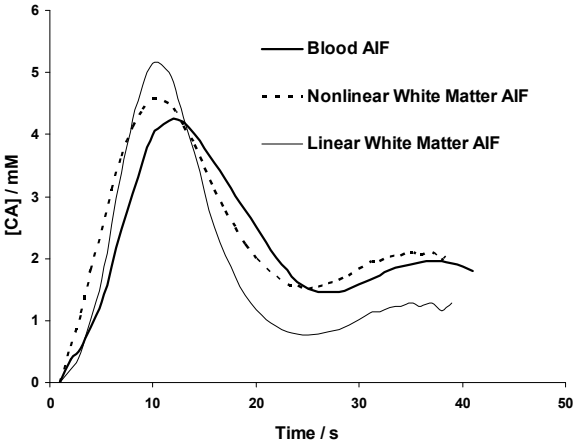

Figure 1. Concentration time curves of blood (thick solid line), white matter calculated using Eq. [1] (dashed line) and Eq. [2] (thin solid line).

Results

Fig. 1 show typical AIFs derived from blood and white matter in one subject. The full SDR model gives a white matter AIF that that is very close in amplitude and shape to the blood AIF. The linear model gives a higher peak and lower tail. Fig. 2 shows Bland-Altman plots of full SDR (a) and linear (b) white matter AIF CBV estimates. The mean CBV differences between blood and white matter measurements were 3% and 16% for the full SDR and linear models respectively.

Discussion

The results demonstrate that Eq. [1], which accounts for both long and short dephasing times of the SDR, accurately describes relaxivity in white matter more accurately than Eq. [2] which only considers the long dephasing time. Considering that no arbitrary scale factors were used, the agreement between the full SDR and blood AIFs is remarkable, giving strong support for the accuracy of the model. Remaining differences between the AIF curves and CBV values can be attributed to dispersion and to possible errors in several assumptions: 1) The hematocrit levels in bulk blood which have been shown to substantially affect relaxivities. 2) Blood volume in white matter which has been reported to range between 2-3%. 3) The variation in magnetic susceptibility of blood between different vasculature types.

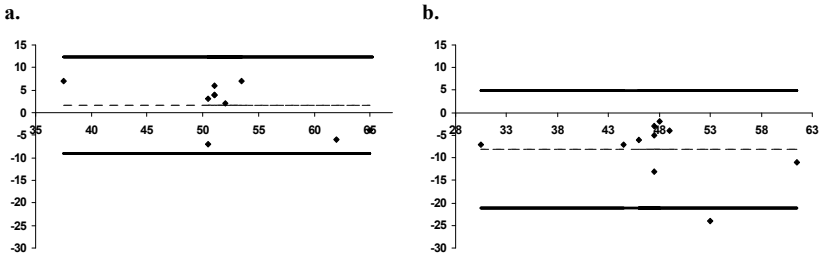

Figure 2. Bland-Altman plots for the correct white matter AIF CBV (a) and erroneous white matter AIF CBV (b) measurements. The y axis represents the difference and the x axis the mean of estimated white matter and blood CBV respectively. The dashed line indicates the mean difference and the solid lines show ± 95% limit agreements (i.e., approximately twice the standard deviation of the difference).

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