Optimizing DSC-MRI Acquisition Parameters to Minimize Extravascular T_1 and T_2* Effects Due To Contrast Agent Leakage: A Simulation Study

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Introduction: Dynamic susceptibility contrast (DSC) MRI methods for assessing tumors are confounded by the extravasation of Gadolinium (Gd) agents into the extravascular extracellular space (EES) resulting in simultaneous changes in the EES T_1 and T_2^* that can confound susceptibility-induced signal decreases and yield unreliable cerebral blood volume (CBV) and flow (CBF) measurements (1). To the best of our knowledge, a methodological study of these T_1 and T_2^* EES relaxation interactions has not been reported. This is of note since the parameter estimates extracted from a DSC analysis could be significantly affected by both pulse sequence acquisition parameters as well as native tissue characteristics. In this contribution we perform a series of simulations in which we systematically vary relevant MRI pulse sequence and physiological parameters and assess the errors returned in CBF and CBV.

Methods: The gradient-echo signal after contrast injection can be written as shown in Eq. 1, where TR is the repetition time, TE is the echo time, T_1 and T_2^* are the pre-contrast relaxation times, α is the flip angle, r_1 is the contrast agent (CA) T_1 relaxivity, v_p and v_e are the plasma and EES volume fractions, $C_p(t)$ and $C_e(t)$ are the concentrations of CA in the plasma and EES, and k_p and k_{EES} are the plasma and EES susceptibility calibration factors. The use of this new factor, k_{EES}, is needed since extravasated CA will create field distortions that are dissimilar to those produced by CA compartmentalized within the vasculature. Generally the simulations consisted of: (1) Selection of relevant input physiological and pulse sequence parameters, (2) creation of the arterial input function (AIF), blood plasma and EES concentration time curves for a DSC-MRI study, (3) generation of DSC-MRI signals and ΔR_2^* ($=1/T_2^*(t) - T_{20}^*$, where T_{20}^* is the pre-contrast T_2^* value) time curves with and without leakage effects, (4) computation of CBV and CBF using the ΔR_2^* time curves and (5) determination of percent difference between the extracted CBV and CBF with and without leakage effects. Simulations have been completed for a wide variety of parameters and initial conditions but for compactness we will focus the results on these commonly utilized sequence parameters: α/TE = 1) 15/20 w/out CA preload (PL), 2) 30/50 w/out PL, 3) 60/50 w/PL and the dual echo approach w/out PL.

$$S_{post}(t) = \frac{S_o(1 - e^{-TR\cdot r_1\cdot v_e\cdot C_e(t)}e^{-TR/T_1})e^{-TE/T_2^*}e^{-TE\cdot k_{EES}\cdot v_e\cdot C_e(t)}e^{-TE\cdot k_p\cdot v_p\cdot C_p(t)}\cdot\sin(\alpha)}{1 - e^{-TR\cdot r_1\cdot v_e\cdot C_e(t)}e^{-TR/T_1}\cdot\cos(\alpha)} \quad [1]$$

Figure 1

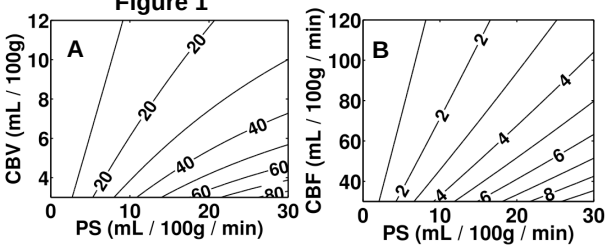


Figure 2

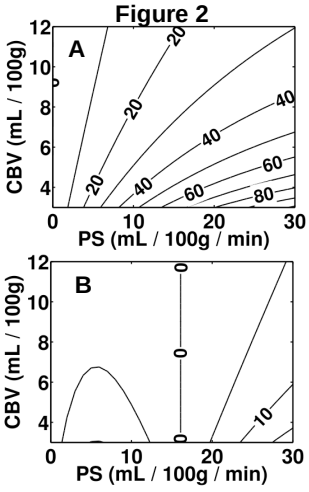
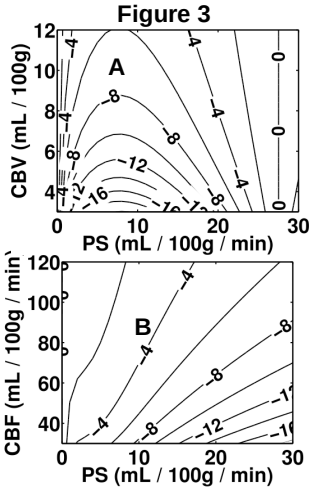
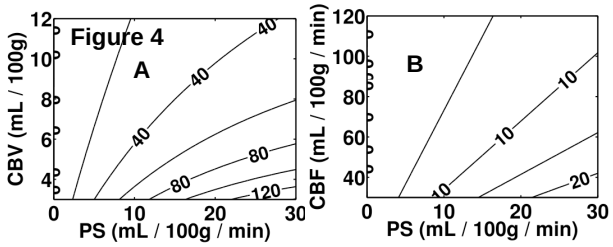


Figure 3



Results: Figure 1 shows the percent different between the CBV (A) and CBF (B) computed from ΔR_2^* time curves with and without leakage effects computed for a pulse sequence using a α/TE =15/20, no CA preload and a pre-contrast T_1 of 1.5 sec. For all pre-contrast T_1 values this approach greatly overestimated the true CBV but provided highly reliable CBF estimates. Figure 2 shows similar plots (CBV only) for the pulse sequence using a α/TE =30/50, no CA preload and 1.0 (A) and 2.0 (B) secs pre-contrast T_1s. For the 2 sec pre-contrast T_1 and *PS* values of approximately 17 ml / 100g / min the ΔR_2^* time courses exhibited little or no leakage effects because the pulse sequence's sensitivity to EES T_1 and T_2^*-induced changes were such that these effects were balanced and simply canceled. For PS values lower than 17 ml / 100g / min the T_1 effects dominated the calculated ΔR_2^* time courses and resulted in an underestimation of the calculated *CBV* whereas above this PS value the T_2^* effects were greater and resulted in an overestimation of the *CBV.* Such balance points were found for many combinations of pulse sequence and physiological parameters. Figure 3 shows CBV (A) and CBF (B) results for the pulse sequence using a α/TE =60/50, CA preload and a 1.5 sec pre-contrast T_1. Disregarding the extreme values of input parameters this approach could reasonably provide *CBV* measurements to within 20% of the actual value and 15% for *CBF*. The success of this approach relies on its inherent balanced sensitivity to T_1 and T_2^* leakage effects. The dual approach (Fig. 4) greatly overestimated the CBV (A) and slightly overestimated the CBF (B) for all values of PS and pre-contrast T_1.

Figure 4



Discussion: The observation that the EES T_1 and T_2^* leakage effects compete with one another and depend greatly on pre-contrast T_1 has important implications for the reliability of CBV and CBF estimates, post-processing based leakage correction methods (or lack thereof) and the attempts to estimate permeability (or K^{trans}) using DSC-MRI studies. In these simulations, pulse sequences that had a balanced sensitivity to EES T_1 and T_2* leakage effects (e.g α/TE 60/50) yielded the most reasonable estimates of CBF and CBV even without post-processing correction methods.

References: 1. Donahue, MRM 43:845-853; 2004.