Perfusion and water exchange effects on T1-based measurements of blood volume

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Introduction: Quantification of blood volume (BV) is achieved by modeling of the signal intensity and time curves following bolus injection or by application of a two-compartmental model under conditions of fast exchange following injection of an intravascular contrast agent. Using the latter technique, Bauer et al demonstrated bias from perfusion under physiological conditions because arterial blood is non-exchanging[1]. However, given intravascular (τ_i) and extravascular (τ_e) water lifetimes of approximately 100 and 800ms respectively[2], the system should be in intermediate exchange. With the aim of optimizing methodology for BV quantification, this abstract describes a numerical solution to for T_1-based measurements of BV accounting for both perfusion and intermediate water exchange. The solution was validated by comparison to analytical solutions for fast exchange blood volume quantification with and without perfusion, and for relaxation under conditions of intermediate exchange without perfusion.

Methods: Tissue was modeled as a system of four compartments (arterial blood, intravascular blood, extravascular water, and venous blood), with water exchange between intravascular and extravascular spaces and perfusion at a constant rate between the arterial, intravascular, and venous spaces. The numerical solution for T_1 relaxation of this system was constructed from the Bloch equations, with only the intravascular and extravascular compartments contributing to the measured signal. The model also accounted for RF chopping such that an initial inversion pulse was toggled off for every even-numbered iteration of the signal-time evolution. Addition of odd- and even-numbered iterations results in a monoexponentially-decaying T1-weighted signal time course, facilitating quantification using a weighted least-squares regression of the logarithmically-transformed signal intensities and inversion times. Blood volume was then quantified from intravascular T_1 ($T_{1,i}$) and tissue T_1 ($T_{1,t}$) using a model of fast exchange between two compartments:

$$BV(\%) = (1/T_{1,t,pc} - 1/T_{1,t,endog}) / (1/T_{1,t,pc} - 1/T_{1,i,endog}) \quad (1)$$

where the subscript 'pc' denotes post-contrast injection and 'endog' denotes endogeneous[3].

The simulation was validated via comparison to known analytical solutions. Eq. 1 is directly applicable to the numerical predictions under conditions of true fast exchange (τ_i and τ_e of 1 and 8ms). Inclusion of perfusion results in a linear dependence of BV on $T_{1,i}$ when the inversion pulse is non-selective, where the y-intercept is the true BV, and an independence of BV on $T_{1,i}$ when the inversion pulse is slice-selective[1]. Given removal of the additive T_1 contribution by RF chopping, the fidelity of modeling under conditions of intermediate exchange was evaluated using the analytical solution for a two-compartmental model of T_2 relaxation[4]. Reasonable physiological parameters for myocardial measurements were assumed (τ_i of 100ms, BV = 11.2%, τ_e = (1-BV)* τ_i /BV = 792ms, basal and maximal perfusion lifetimes or τ_p of 3000 and 750ms, $T_{1,i,endog}$ = 1000ms, $T_{1,t,endog}$ = 1200ms). $T_{1,t,pc}$ between 100 and 900 ms were evaluated for each τ_p, τ_i, and inversion.

Results: The simulation predictions mapped identically to analytical solutions under conditions of fast and intermediate exchange (Fig a). Under fast exchange conditions, perfusion resulted in a sigmoidal dependence of BV on $T_{1,t,pc}$ following global inversion and an independence of BV on $T_{1,t,pc}$ following slice-selective inversion (Fig. b). With intermediate exchange and perfusion, sigmoidal dependencies of BV on $T_{1,t,pc}$ were observed. With basal flow, the y-intercept of the more linear portion of the BV and $T_{1,t,pc}$ curve was more than 20% less than the true BV following global inversion, while the plateau of the BV and $T_{1,t,pc}$ curve was more than 10% less than the true BV following slice-selective inversion (Fig c). Differences from truth were elevated under conditions of peak flow. Solutions were found to be independent of RF chopping. From numerical modeling, the precision in BV at a given $T_{1,t,pc}$ is predicted to be approximately twice the precision in T1 (%).

Conclusions: Numerical modeling predicts considerable bias in T1-based quantification of BV during the steady-state of an intravascular contrast agent, because of failure of the fast exchange assumption. This prediction is counter to the experimental results of Bauer et al, which motivates future model validation in porcine myocardium utilizing intravascular agents (ie. Gadomer, Schering AG). Given model validation, one may anticipate greater robustness when a model of intermediate exchange is fitted to signal intensities at multiple inversion times. However, one may anticipate perfusion bias in compartmental T1 analysis, plus failure of the assumption of monoexponentiality and requisite knowledge of τ_e and τ_e.

References: 1) Bauer et al, MRM, 1996 ; 2) Bjornerud et al, MRM, 2003; ; 3) ; 4)

Figure: (left) Overlapping of numerical and analytical solutions under conditions of fast (FE) and intermediate (IE) exchange without perfusion; (mid) numerical solution under conditions of fast exchange with global (GI) and slice-selective (SI) inversion with basal (BF) and peak (PF) flow; and (right) numerical solution with physiological parameters for exchange with basal and peak flow. For all cases, the true BV was 11.2%.