Steady State Effects on Cerebral Blood Flow Measurements using Dynamic Contrast-Enhanced Perfusion MRI: A Simulation Study

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INTRODUCTION: MR perfusion measurements based on dynamic contrast enhanced (DCE) T_1 weighted imaging can accurately quantify cerebral blood flow (CBF) (1) simultaneously with cerebral blood volume and blood brain barrier permeability (2,3). DCE perfusion techniques generally use a spoiled gradient echo imaging sequence, often with a saturation prepulse. Due to the short imaging time needed for bolus-tracking, this imaging sequence can result in steady state effects. In particular during the bolus passage, where T_1 changes rapidly, the history of the longitudinal magnetization can lead to a non-trivial behaviour of the MR signal. To quantify perfusion, the concentration of contrast agent must be estimated from changes in the MR signal. The use of a signal equation for this purpose may result in faulty estimates of contrast concentration which will in turn lead to a biased perfusion estimate. Here we study how steady state effects bias DCE perfusion estimates using simulations of the Bloch equation.

METHODS: An arterial input function (AIF) was modeled as a gamma-variate, $C_a(t) = C_0 \cdot t^r \cdot \exp(-t/b)$, where t is time. We chose values r = 3 and b= 1.5 (4), and C_0 = 0.5 mM, resulting in an AIF peak height of 2.2 mM close to what is typically observed. The tissue concentration was modeled as $C_t(t) = \mathrm{CBF} \cdot C_a(t) \otimes R(t)$ with a mono-exponential residual impulse function $R(t) = \exp(-t/\mathrm{MTT})$, where MTT is the mean transit time. We used grey matter values MTT = 4 s and CBF = 60 ml/100g/min. All contrast agent concentrations $C(t)$ were converted to R_1 changes using $\Delta R_1(t) = r_1 \cdot C(t)$, with relaxivity r_1 = 4 $\mathrm{mM^{-1}s^{-1}}$. We examined the effect of the R_1 changes on the MR signal from a spoiled gradient echo imaging sequence with an initial saturation prepulse β and an α pulse before each k-space line. The z magnetization M_z was simulated using the Bloch equations, assuming that all transverse magnetization is spoiled. The magnetization right before RF pulse $n+1$, is then

$$M_z(n+1) = M_z(n) \cdot \cos(\theta) \cdot \exp(-\tau/T_1) + M_0[1-\exp(-\tau/T_1)]$$

where θ = α or β, and τ = TR or TD, depending on whether RF pulse n was an α pulse or the saturation prepulse. TR is the repetition time and TD the delay following the saturation prepulse. Both centric and linear k-space encoding was considered. The total number of α pulses was 33, TR = 4 ms and TD = 120 ms (as in (1)). Baseline R_1 for tissue and for blood were set to 1.2 Hz and 0.8 Hz, respectively, and the corresponding M_0 values were 0.5 and 1.0 in dimensionless units. The simulated MR signal was obtained as $M_z(k=0) \cdot \sin(\alpha)$. The resulting signal curves were converted back to R_1 curves using the signal equation for a saturation recovery (5) and then to concentration of contrast agent. The concentration curves were baseline corrected and the initial inswinging removed, as is usual practice. The thus generated concentration curves $C_{a,est}(t)$ and $C_{t,est}(t)$ were now deconvolved to yield estimated CBF and MTT values. Finally, we computed the percent deviation of the estimated CBF from the prescribed value.

RESULTS: Fig. 1a) and b) show the estimated arterial (red) and tissue (black) concentration time courses (symbols), for values of α and β as given in the legend. The model curves are shown as lines for reference. In Fig. 1a) where the prepulse flip angle is smaller than 90º, both C_a and C_t are overestimated. In Fig. 1b) where the prepulse is larger than 90º, both C_a and C_t are underestimated, albeit C_a less severely than C_t. The CBF estimation error as a function of the prepulse angle β is shown in Fig. 1c), for various values of α and for both centric (filled circles) and linear (open circles) k-space encoding. Note that for an exact 90º prepulse the contrast agent concentration time course and hence the CBF is always correctly estimated, because no M_z magnetization is transferred. Finally Fig. 1d) and e) show the CBF bias as a function of saturation delay. In case of centric phase encoding (filled circles), the CBF bias increases as TD is lowered. For linear phase encoding (open circles), the CBF bias shows little sensitivity to TD.

DISCUSSION: We have shown that steady state effects can seriously affect CBF estimates derived from DCE perfusion imaging. The CBF bias is largest for small α flip angles, and decreases to just a few percent for an α flip angle of 30º or above. For these values of α, the CBF bias remains small for all prepulse flip angles from 0º to 180º (Fig. 1c)). This remarkable behaviour probably in part reflects that repeated large α pulses effectively saturate the longitudinal magnetization. In practice of course, an α that is too large will produce image artefacts. Also observe that for e.g. (α,β) = (30º,70º) steady state effects do influence estimates of contrast agent concentration significantly (Fig. 1a)). However arterial and tissue concentrations are affected in a like fashion and therefore the resulting CBF bias is small (1-2%). For smaller α the arterial and tissue concentrations are not affected in a like fashion (Fig. 1b)), and therefore the CBF bias is large. If the saturation delay is decreased the CBF bias increases for centric, but not for linear phase encoding, which again can be ascribed to the action of the α pulses prior to the traversal of the centre of k-space. Based on the results here, we do not expect CBF estimates in the studies (1,2) to be biased by steady state effects.

CONCLUSION: Steady state effects in DCE perfusion MRI will affect CBF estimation if the saturation prepulse is not exact. An α pulse angle of 30º or larger will minimize the CBF bias to a few percent. Additionally the saturation delay must not be much shorter than 100 ms in case of a centric phase encoding.

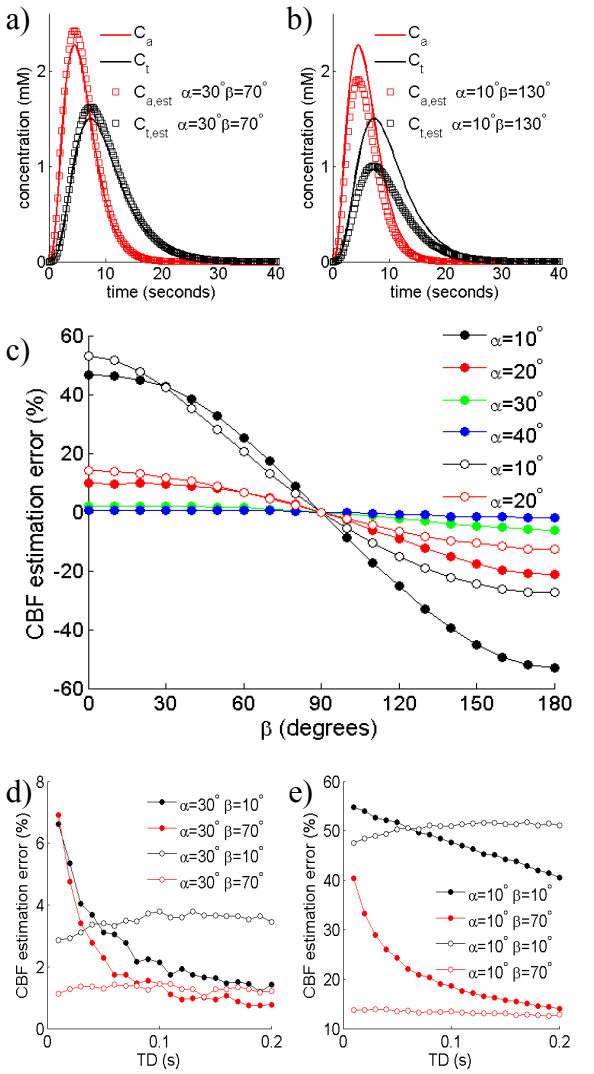

Figure 1. a) and b) Estimated arterial concentration C_a (red squares) and tissue concentration C_t (black squares) for values of the α and β flip angles as given in the legend. Lines are the corresponding true concentrations. Concentration curves have been baseline corrected and initial inswinging has been removed. Tissue curves are multiplied by a factor of 25 for visibility. c) Error of CBF estimation in % as function of saturation prepulse β, for values of the α pulse as given in the legend. Closed circles denote centric, open circles linear phase encoding. d) and e) Error of CBF estimation as function of saturation time delay TD, for values of α and β as given in the legend. Closed circles are for centric, open circles for linear phase encoding.

REFERENCES: (1) Larsson H, et al., JMRI 27:754 (2008); (2) Larsson H, et al., MRM 62:1270 (2009); (3) Sourbron S, et al., MRM 62:205 (2009); (4) Calamante F, et al., MRM 44:466 (2000); (5) Larsson H, et al., MRM 46:272 (2001).