# Quantification of systematic error in standard formula for computing transverse relaxation rates in DSC–MRI. Implications for blood volume and flow calculations

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**INTRODUCTION:** In dynamic susceptibility contrast (DSC) MRI experiments, the increase in the tissue transverse relaxation rate ($\Delta R_2$) due to the passage of a bolus of intravascular paramagnetic contrast agent (CA) is routinely calculated using eqn. (3) below, neglecting signal enhancement effects due to $T_1$ weighting. In this abstract, the condition for signal enhancement is analysed and an expression for the *enhancement angle*, $\alpha_e$, is given. Next, an expression for the systematic error associated with the use of (3) is obtained; it is shown that such errors can be substantial at low CA concentrations and large flip angles. Finally, the accuracy of blood volume and flow computations is discussed with respect to pulse sequence parameters and the accuracy of the CA concentration in tissue and at the arterial reference site.

**THEORY:** Eqn. (1) gives the magnitude MR signal for a (possibly steady-state spoiled) gradient echo (GE) experiment [4], where $G$ is the detection gain, $\alpha$ is the flip angle, and $R_1$ and $R_2$ are the longitudinal and transverse tissue relaxation rates, respectively. Eqn. (1) depicts signal weighting dependent on $\alpha$, $T_1$ and $T_2$. For GE pulse sequences in the static dephasing regime at long times, the increase $\Delta R_2$ is closely approximated by eqn. (2) [1], where $r_2$ is the transverse tissue relaxivity and $C_t$ is the tissue tracer concentration. Inserting eqn. (2) and the analogous relation for $\Delta R_1$ in (1) results in the concentration dependent MR intensity (Fig. 1). In DSC–MRI, $T_1$ weighting is usually neglected and $\Delta R_2$ calculated using (3), where $I_0 = I(C_t = 0)$ is the baseline intensity.

$$I = G \sin\alpha \frac{1-\exp(-T_R R_1)}{1-\cos\alpha\exp(-T_R R_1)} \exp\left(-T_E R_2\right) \quad (1)$$

$$\Delta R_2 = r_2 C_t \quad (2)$$

$$\Delta R_2 = -T_E^{-1} \ln\left(\frac{I}{I_0}\right) \quad (3)$$

$$|m + 1 - 1/\mathrm{E}_{10}| \leq (m - 1 + \mathrm{E}_{10}) > 0 \quad \text{[see eqn. (5)]} \quad (4)$$

**RESULTS:** ***A. Signal enhancement condition & enhancement angle.*** Signal enhancement depends both on the imaging parameters and the tissue relaxivities. Provided that the enhancement condition (4) holds, sequences using flip angles greater than the *enhancement angle*, $\alpha_e$, cf. (5), will give signal enhancement for a certain range of tracer concentrations, $0 < C \leq C_{max}$ (Fig. 1). For heavily $T_1$-weighted sequences, $m >> \mathrm{E}_{10} \sim 1$, resulting in a small $\alpha_e$ and thus in signal enhancement for a wide range of flip angles. For heavily $T_2$-weighted sequences, $1/\mathrm{E}_{10} = \exp(T_R/T_1) >> m$, and the enhancement condition (4) is not met. ***B. Systematic error of $\Delta R_2$ calculated using* (3).** The absolute error $\varepsilon_{sys}$, eqn. (6), is defined to equal the relaxation rate calculated using (3) minus the true relaxation rate. $\varepsilon_{sys}$ contains two terms. The first one is independent of the CA concentration; it is negative for $0 < \alpha \leq 90°$. The second term is positive for all $\alpha$ and $C_t$. From (2), the relative errors of $\Delta R_2$ and $C$ are the same.

$$\alpha_e = \cos^{-1}\left(\frac{m + 1 - E_{10}^{-1}}{m - 1 + E_{10}}\right), \text{ where: } \begin{matrix} m = (r_1/r_2)(T_R/T_E) \\ E_{10} = \exp(-T_R/T_{10}) \end{matrix} \quad (5)$$

$$\varepsilon_{sys} = T_E^{-1}\left(\ln\frac{1-E_{10}}{1-E_{10}\cos\alpha} + \ln\frac{1-E_{10}\cos\alpha\exp(-T_R r_1 C_t)}{1-E_{10}\exp(-T_R r_1 C_t)}\right) \quad (6)$$

$$e_\zeta = \left[\int \varepsilon_t \Big/ \int C_t - \int \varepsilon_{AIF} \Big/ \int C_{AIF}\right] \Big/ \left[1 + \int \varepsilon_{AIF} \Big/ \int C_{AIF}\right] \quad (7)$$

$$e_f = \left[\varepsilon_t / C_t - \int \varepsilon_{AIF}\Re \Big/ \int C_{AIF}\Re\right] \Big/ \left[1 + \int \varepsilon_{AIF}\Re \Big/ \int C_{AIF}\Re\right] \quad (8)$$

***C. Error in blood volume and flow calculations.*** The expressions for relative blood volume ($\zeta$) and flow ($f$) according to indicator-dilution theory may be found in [5]. The relative systematic error of $\zeta$ and $f$ in terms of the absolute tissue and arterial reference concentration errors ($\varepsilon_t$, $\varepsilon_{\mathrm{AIF}}$) is given by (7) and (8), respectively; in (8), the integrals are time convolutions with kernel the residue function $\Re(t)$ [5]. If the relative errors of $C_t$ and $C_{\mathrm{AIF}}$, denoted by $e_t$ and $e_{\mathrm{AIF}}$, are constant, (7) and (8) both simplify to eqn. (9).

$$e_\xi = \frac{e_t - e_{AIF}}{1 + e_{AIF}} = e_f \quad (9)$$

The following figures depict normalised MR intensity curves and CA concentration error curves for typical CA concentrations and various flip angles:

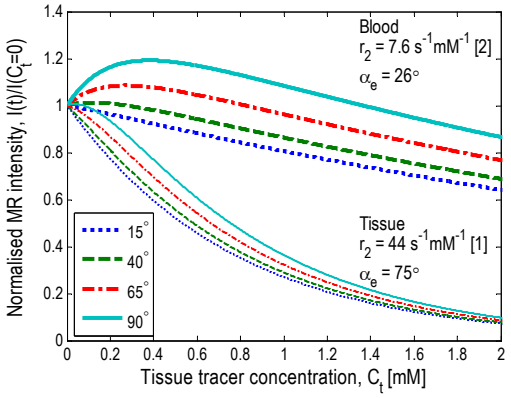


**Fig. 1:** Magnitude signal (1) normalised to baseline vs. typical tissue tracer concentrations in brain tissue for various $r_2$ and $\alpha$; $T_{10}$ = 760 ms, $r_1$ = 4.5 $s^{-1}mM^{-1}$ at 1.5 T [3], $T_R/T_E$ = 1000/30 ms.

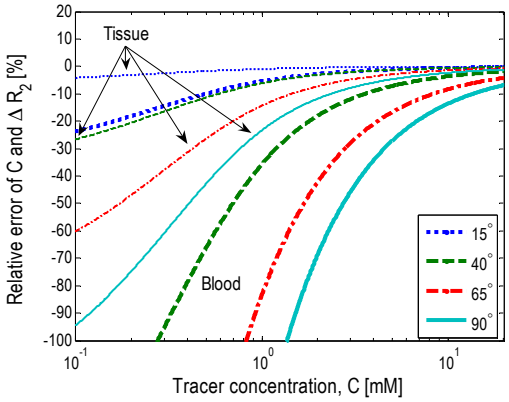


**Fig. 2:** Relative systematic error (6) of a CA concentration calculated by (3). All parameters as in Fig. 1. Thin (thick) lines correspond to tissue (blood) $r_2$, respectively.

**DISCUSSION AND CONCLUSIONS:** ***A.*** The choice of flip angle $\alpha$ in GE experiments influences the amount of signal enhancement caused by a bolus of intravascular tracer (Fig. 1). The use of large flip angles for improved signal-to-noise ratio (SNR) may lead to undesired signal enhancement with possible $\Delta R_2$ ambiguities due to (1) no longer being a one-to-one mapping; this may lead in turn to errors in the calculated tracer concentration. In DSC–MRI, a transient signal enhancement is typically seen on arrival of the CA due to $T_1$ effects. ***B.*** Figs. 1 and 2 show that eqn. (3) is accurate only for sufficiently large tracer concentrations and small flip angles. From eqn. (6), the systematic error of $\Delta R_2$ computed using (3) is negative for all $C$ (Fig. 2). $|\varepsilon_{sys}|$(%) increases with $r_2$, $\alpha$ and decreasing $C$ since all three conditions increase the $T_1$ weighting. For a typical dose of Gd-based CA, the expected CA concentrations in blood and grey/white matter are ~18, 1.1 and 0.45 mM, respectively (cf. ref. [24] in [1]). For the tissue and pulse sequence values shown in Fig. 1, selecting $\alpha \leq 15°$ keeps the relative error $|\varepsilon_{sys}| \leq 5\%$ for these particular concentration values. ***C.*** Fig. 2 shows that for a typical DSC–MRI experiment, the pulse sequence parameters $T_R$, $T_E$ and $\alpha$ may be selected to minimise the relative error of the concentrations calculated using (3). In the example, for $T_R/T_E$ = 1000/30 ms and $\alpha < 15°$ the errors of $C_{\mathrm{AIF}}$ and $C_t$ being approximately constant over the expected concentration range and the relative error of blood volume and flow is given by (9). To conclude, using eqn. (3) in general causes systematic errors in $\Delta R_2$ and the calculated CA concentration. Blood flow and volume errors can be minimised using suitable pulse sequence parameters, in particular sufficiently small flip angles. Alternatively, if flip angles greater than $\alpha_e$ are required to improve the SNR, thus rendering (3) inaccurate, a post-processing algorithm can be used to correct for the systematic error (6).

**REFERENCES: [1]** B.F. Kjølby *et al.*, MRM 56:187–197 (2006). **[2]** M. van Osch *et al.*, MRM 49:1067–1076 (2003). **[3]** A.F. Stalder *et al*, MRM 59:113–123 (2008). **[4]** Z-P. Liang and P.C. Lauterbur, *Principles of Magnetic Resonance Imaging: A Signal Processing Perspective*, Wiley-IEEE Press (1999). **[5]** V.G. Kiselev, MRM 46:1113–1122 (2001). **ACKNOWLEDGEMENTS:** The authors acknowledge financial support from the Spanish Ministry for Science and Innovation (ref. CICYT TEC2006-13966-C03-02) and DGA (CONAID) – CAI (ref. CM 3/09; Aragón, Spain).