Non-linear contrast agent relaxivity and the accuracy and sensitivity of DCE MRI measurements

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Introduction: Dynamic Contrast-Enhanced MRI (DCE-MRI) is used to characterize vascular permeability and microcirculation in conditions ranging from brain ischemia to cancer. With the extended Tofts model, tissue contrast concentration, C_t, is given by Eq. [1], where C_p is the plasma concentration, v_p and v_e are the plasma and extravascular extracellular space fractional volumes respectively, and K^{trans} is the volume transfer constant (1). Given C_p the other parameters may be estimated by fitting Eq. [1] to the measured tissue concentration curve. Contrast concentration is normally calculated assuming that the change in relaxation rate is linearly proportional to gadolinium concentration, [Gd], for both T_1 and T_2^*-weighted sequences. However, this is known to be untrue in tissue (2,3). In this study we used computer simulations to compare the effect of non-linearities on the accuracy and sensitivity of DCE MRI estimates of v_p and K^{trans} measured using first-pass, T_1 and T_2^*-weighted protocols.

$$C(t) = v_p C_p + K^{trans} \int_0^t C_p(t') e^{\frac{-K^{trans}}{v_e}(t-t')} dt' \qquad [1]$$

Methods: C_p was simulated using the bolus shape function described by Johnson et al. (4) with parameters found by averaging measurements in five glioma patients. C_t was then calculated using Eq. [1] with a range of v_p (1 – 10%) and K^{trans} (0.01-0.50 min^{-1}). Changes in relaxation rate were then calculated

$$\Delta R = aC_t + bC_t^2 \qquad [2]$$

with values of a and b measured in a yeast phantom (5). Erroneous estimates of concentration, C_t', were then obtained from these signal intensity curves by assuming a linear relationship between ΔR_D and concentration (i.e., assuming b in Eq. [2] is zero).

$$C_t' = \frac{\Delta R}{a} = C_t + \frac{b}{a} C_t^2 \qquad [3]$$

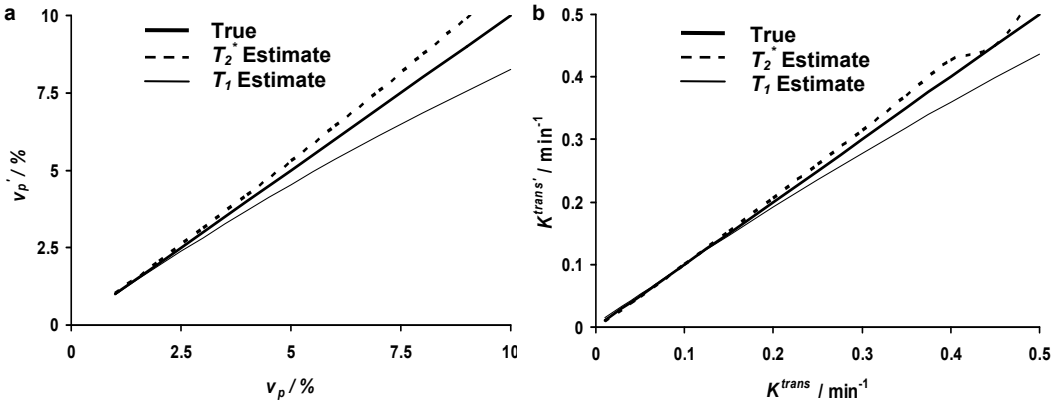
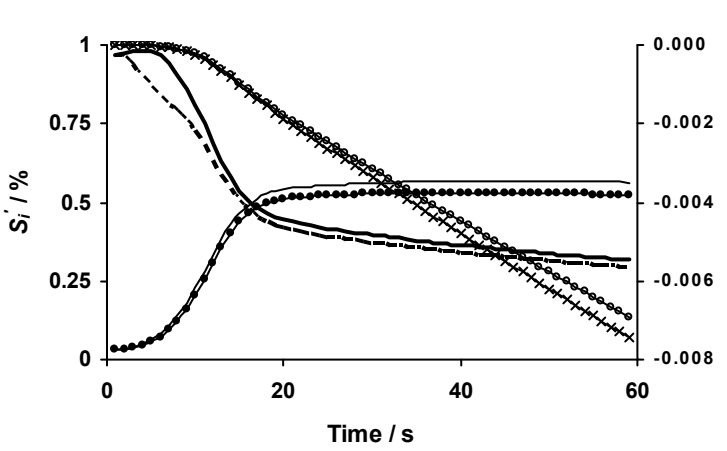


Fig. 1. Percent error in a: v_p and b: K^{trans} using a T_1 and T_2^*-weighted sequence.

Finally, Eq. [1] was fitted to these estimates to obtain the erroneous estimates of of v_p and K^{trans}. Sensitivity, Eqs. [4], was calculated using methods described by Koh et al. and Huang et al. (6,7) where $s_i'(t)$ is the percent change in relaxation rate due to a 1% change in parameter, p_i.

Results: Fig. 1 shows estimates of v_p (Fig. 1a) and K^{trans} (Fig. 1b) over a range of values using T_1 and T_2^*-weighted sequences. As expected, T_2^* estimates (dashed lines) were consistently higher than the true parameter value (thick line) while T_1 estimates (thin line) were lower due to the polarity of the quadratic term, b. Fig. 2 shows a graph of normalized sensitivity functions for v_p, v_e and K^{trans} using typical glioma parameter settings (8). In all three parameters, sensitivity was lower using a T_1-weighted sequences than a T_2^*-weighted sequence.



$$s_i(t) = \frac{\partial \Delta R(t)}{\partial p_i} \qquad [4]$$

$$s_i'(t) = s_i(t) \frac{p_i}{\Delta R(t)}$$

Fig. 2. Normalized sensitivity functions (Eqs. [3]) for v_p, v_e and K^{trans} for typical glioma parameter settings reported by Cheng (8). Secondary axis corresponds to v_e sensitivity.

Discussion and Conclusion: There are several important implications from this study. First, it is difficult to compare parameter estimates made from T_1 and T_2^*-weighted sequences since errors in the two have opposite polarities. Second, errors with T_1 weighted sequences tend to reduce sensitivity (i.e., the difference in estimates is smaller than the true difference). Although T_1 errors cause underestimates in v_p for all parameter values, larger underestimates for highly vascular tumors like meningiomas will reduce measured differences. Errors in T_2^* estimates are not only smaller in absolute terms, but also tend to exaggerate rather than disguise the differences. This is consistent with the higher sensitivity values seen for T_2^* sequences seen in Fig. 2. Note also that v_e sensitivity is very low for both protocols.

References: 1. Tofts PS: J Magn Reson Imaging. 1997 Jan-Feb;7(1):91-101. **2.** Landis CS et al.: Magn Reson Med 2000;44(4):563-574**. 3.** Kiselev VG: Magn Reson Med 2001;46(6):1113-1122. **4.** Johnson G et al.:Magn Reson Med. 2004 May;51(5):961-8. **5.** Patil V et al.: Magn Reson Med. 2009 Oct;62(4):1002-6. **6.** Koh TS et al.: Phys Med Biol 2001;46(5):1519-1538. **7.** Huang SC et al.: J Cereb Blood Flow Metab 1986;6(1):105-119. **8.** Cheng HL: J Magn Reson Imaging 2008;28(3):736-743.

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