Incorporating the Effect of Capillary Transit Time in DCE-MRI Pharmacokinetic Analysis

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INTRODUCTION

Quantitative dynamic contrast-enhanced (DCE) MRI has shown value for characterizing microcirculation physiology, or changes therein, associated with various diseases and conditions, including cancer, ischemia, and inflammation [1]. Estimation of parameters related to flow, endothelial permeability, blood volume, and the interstitial volume is influenced by physiological unknowns, such as the arrival and transit times of the bolus. While the bolus arrival delay has been shown to introduce significant error into parameter estimates [2,3], the effects of capillary transit times have not been addressed in DCE-MRI. In this work, we investigate the error incurred in pharmacokinetic parameters due to finite transmit times and show that a modification to the common Tofts model [4] can significantly improve parameter accuracy.

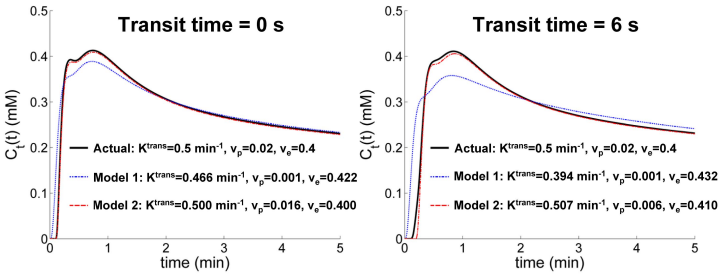

Fig. 1. Proposed model (red, Eq.[2]) is robust to bolus delay and transit time. Conventional model (blue) is Tofts [4]. Tissue curves are shown for a 6 s delay.

THEORY

The tissue concentration time-course can be calculated from the AATH model [5] to include bolus delay T_d and mean transit time T_c. It can be shown that invoking the mean value theorem to simplify the vascular term results in the following equation:

$$C_t(t) = v_p C_p(t - T_d - \theta T_c) + EF_p \int_0^{t-(T_d+T_c)} C_p(\tau) \exp\left(\frac{-EF_p}{v_e}(t - \tau - (T_d + T_c))\right) d\tau \quad [1]$$

where $0 \le \theta \le 1$. By substituting $t_o = T_d + T_c$ and $K^{trans} = EF_p$, Eq.[1] can be approximated as:

$$C_t(t) = v_p C_p(t - t_o) + K^{trans} \int_0^{t-t_o} C_p(\tau) \exp\left(\frac{-K^{trans}}{v_e}(t - \tau - t_o)\right) d\tau \quad [2]$$

where K^{trans}, v_p, v_e are the transfer constant, plasma volume, and interstitial space, respectively.

METHODS

To generate tissue uptake curves, an arterial input (AIF) similar in form to that measured experimentally in a patient cohort [6] was simulated. The AATH model was then used to simulate tissue time-courses for a range of parameter values: K^{trans}=0.01-1 min^{-1}, v_p=0.01-0.2, v_e=0.1-0.4, T_d=0-30s, T_c=0-12s. The tissue curves were then fitted to both Tofts [4] and the proposed model (Eq.[2]). Fitting was performed both for (1) high temporal resolution, where the AIF and tissue curves were sampled every 1 s, and (2) low temporal resolution (5-30 s), where the AIF was fitted to a biexponential function prior to model fitting. Median values of each parameter estimate were obtained over all combinations.

RESULTS

Fig.1 shows that the proposed model (Eq.[2]) can maintain parameter accuracy in the presence of both delay and transit time, whereas accuracy suffers using conventional model. Accuracy is maintained for K^{trans} and v_e over a large range when Eq.[2] is applied to high temporal resolution data (Fig.2A). Plasma volume v_p is underestimated with increasing transit times. Slower sampling introduces additional underestimation in K^{trans}, which is reduced to approximately 20% for longer T_c (Fig.2B).

CONCLUSIONS

A modification to Tofts model is shown to improve the accuracy of pharmacokinetic parameters in the presence of finite transit times T_c. Only one additional parameter is required, and both K^{trans} and v_e can be estimated accurately. Reliability is reduced for v_p and also under slower sampling, since T_c influences mainly the vascular phase of tissue uptake, which is the portion most critical to v_p estimation and most susceptible to under-sampling.

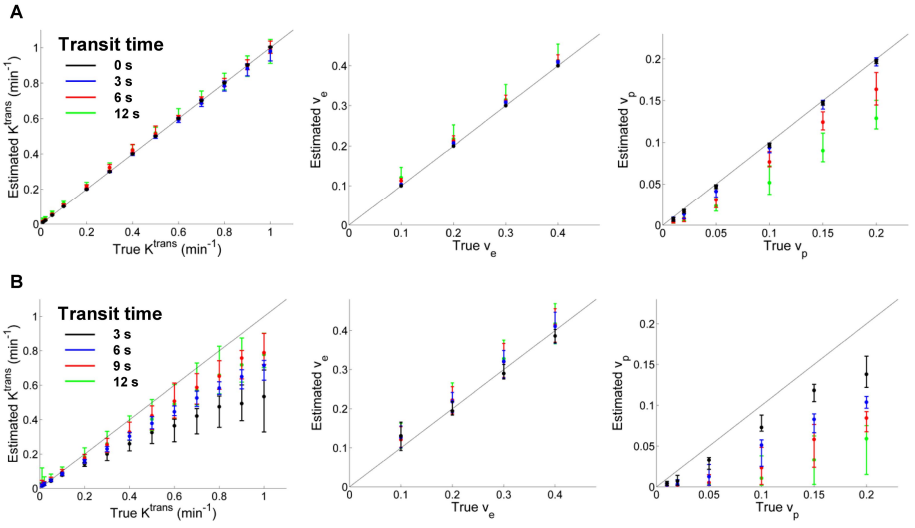

Fig. 2. The influence of capillary transit time on parameter estimates K^{trans}, v_e, and v_p. Two scenarios are shown: (A) high temporal resolution data (1 s), (B) low temporal resolution data (10 s), with AIF fitted to a biexponential function. Data is plotted as median values (dots) and interquartile range (error bars).

REFERENCES: [1] Padhani AR. JMRI 2002; 16:407. [2] Cheong LH, et al. Phys Med Biol 2003; 48:N83. [3] Kershaw LE, et al. MRM 2006; 56:986. [4] Tofts PS. JMRI 1997; 7:91. [5] St Lawrence KS, et al. J Cereb Blood Flow Metab 1998; 18:1365. [6] Parker GJ, et al. MRM 2006; 56:993.