Improved correlation to quantitative DCE-MRI pharmacokinetic parameters using a modified initial area under the uptake curve (mIAUC) approach

H-L. M. Cheng[1,2]

[1]Research Institute & Diagnostic Imaging, The Hospital for Sick Children, Toronto, Ontario, Canada, [2]Medical Biophysics, University of Toronto, Toronto, Ontario, Canada

INTRODUCTION

In dynamic contrast-enhanced (DCE)-MRI of cancer and various vascular pathologies, non-model parameters such as the initial area under the uptake curve (IAUC) [1] have demonstrated better reproducibility and correlation with tumor stage and therapy response than model-based [2] pharmacokinetic parameters [3,4]. This robustness stems largely from obviating key modeling requirements that are significant sources of error, such as sampling the arterial input function (AIF) or fitting noisy data. However, non-model parameters are limited by a lack of clear biological association. In fact, the IAUC is known to be intractably correlated with K^{trans}, v_e, and v_p and cannot be used as a surrogate of any pharmacokinetic parameter over the large range of physiological conditions present in normal and diseased tissue [5]. In this study, we propose modified IAUC (mIAUC) metrics that demonstrate improved association with underlying physiology while retaining the advantages of non-model methods.

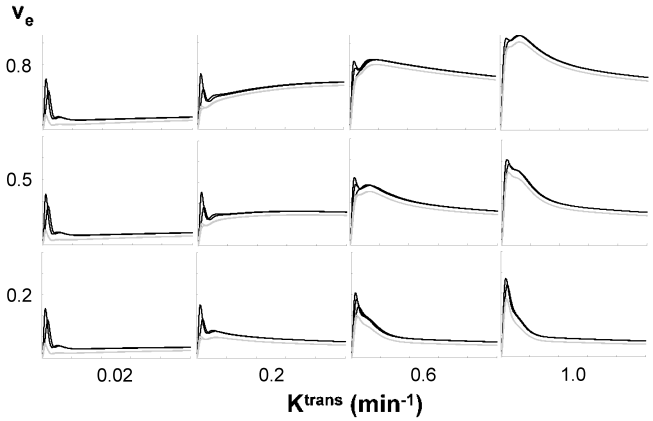

Fig. 1. Simulated tissue curves for low blood volume (vp=0.02, gray) and high blood volume (vp=0.08, black).

METHODS

Simulated tissue uptake curves were generated using the AATH model [6] and an AIF having an initial bolus and biexponential equilibrium phase [7]. Parameter values spanned a large physiological range: flow=0-1 mL g^{-1} min^{-1}, extraction fraction=0-1, interstitial volume v_e=0-1, plasma volume v_p=0.01-0.1. The AIF bolus was also varied to simulate variable contrast injection duration. Sample tissue curves are shown in Fig.1. The proposed mIAUC parameters $IAUC_{ve}$ and $IAUC_{Ktrans}$ are correlates of v_e and K^{trans}, respectively, and are given by:

$$IAUC_{ve} = IAUC_{Tstart-Tend}/(Tend - Tstart) \qquad IAUC_{Ktrans} = \left\{ \left[\frac{(IAUC_{60}/IAUC_{REF60})^{1.15}}{IAUC_{60\text{-}180}/2} \right] \times (IAUC_{180\text{-}300}/2)^{0.49} - 0.9\frac{IAUC_{20}}{IAUC_{REF20}} \right\}^{1.9} \quad \textbf{Eq.[1]}$$

These are formulated on fundamental uptake characteristics. The parameter $IAUC_{ve}$ aims to reflect tissue concentration in the parenchymal phase due to its strong association with v_e. Subscripts represent the integration time interval, with *Tstart* chosen beyond the vascular phase when contrast distribution is relatively stable. The parameter $IAUC_{Ktrans}$ aims to describe the "curvature" of the vascular phase that is seen in Fig.1 to increase with higher K^{trans}. Integration time intervals and correction factors were determined for optimized correlation between $IAUC_{Ktrans}$ and K^{trans}. To maintain robust $IAUC_{Ktrans}$ measurements in the presence of a sizeable plasma volume v_p, a non-linear order-statistic pre-processing filter [8] was applied on the tissue uptake curve to remove narrow initial peaks arising not from high K^{trans} but from high v_p. Normalization against reference tissue (e.g. muscle) is also performed to remove the influence of variable contrast injection protocols.

The new mIAUC metrics are compared with conventional IAUC and Tofts' model parameters on 5000 tissue curves with randomly assigned K^{trans}, v_e, v_p and variable bolus injection durations. A temporal resolution of 1.5 s and total imaging time of 10 minutes were used. Noise was added to both tissue and AIF curves, using a signal-to-noise level of 20 in pre-contrast tissue.

RESULTS

$IAUC_{Ktrans}$ and $IAUC_{ve}$ are more strongly correlated with K^{trans} and v_e compared to conventional IAUC parameters. Correlation is maintained in the presence of large plasma volumes and variable contrast injection rates. Integration intervals for $IAUC_{ve}$ are preferably taken from later times (> 5 min). The new metrics are highly correlated with true K^{trans} and v_e (ρ=0.97 and 0.95), outperformed only when Tofts' model was used in conjunction with a rapidly measured AIF (ρ=0.98 and 0.98) (Fig.2).

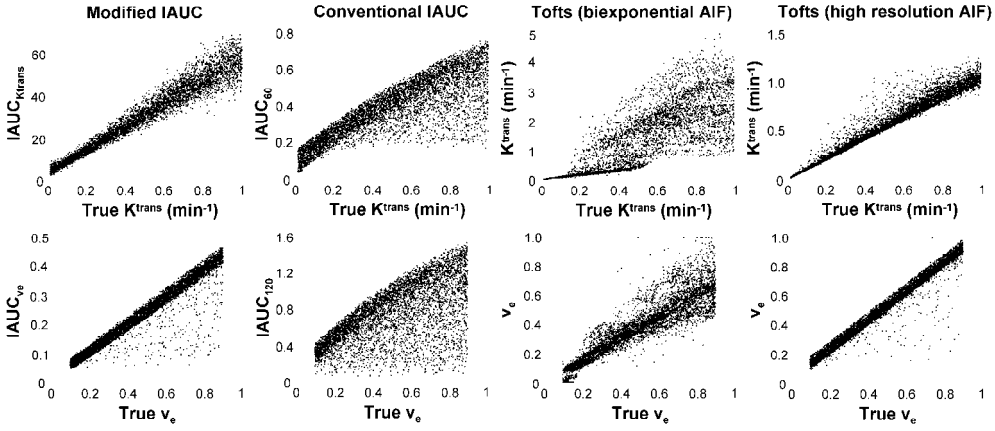

Fig. 2. Performance of the proposed mIAUC method under noisy conditions compared with conventional IAUC and Tofts' model parameters.

CONCLUSIONS

A modified IAUC method is introduced that maintains advantages of non-model DCE-MRI (e.g. no AIF measurement or curve-fitting) while providing stronger correlation with physiology compared to conventional IAUC or pharmacokinetic modeling with an inadequately sampled AIF.

REFERENCES: [1] Evelhoch JL. JMRI 1999; 10:254. [2] Tofts PS. JMRI 1997; 7:91. [3] Robinson SP, et al. Br J Cancer 2003; 88:1592. [4] Liu G, et al. J Clin Oncol 2005; 23:5464. [5] Walker-Samuel S, et al. Phys Med Biol 2006; 51:3593. [6] St Lawrence KS, et al. J Cereb Blood Flow Metab 1998; 18:1365. [7] Cheng HL. JMRI 2008; 28:736. [8] Arce GR, et al. IEEE Trans Image process 1996; 5:827.