Comparison of a Reference Region Model to Direct AIF Measurement in the Analysis of DCE-MRI Data

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INTRODUCTION There has been recent interest in developing models for analysis of dynamic contrast enhanced MRI (DCE-MRI) data that do not require direct measurement of the arterial input function (AIF); such methods are usually referred to as reference region (RR) models (1,2,3). To the best of our knowledge experimental results obtained from a RR analysis have not been directly compared to direct AIF measurements in the same animal. We have performed such a comparison in a rat tumor model.

THEORY Assuming fast exchange, the Kety theory describes the flow of contrast agent (CA) from the plasma to extravascular space:

$$C_{TOI}(T) = K^{trans}\int_0^T C_p(t)\exp(-(K^{trans}/v_e)\cdot(T-t))dt, \qquad [1]$$

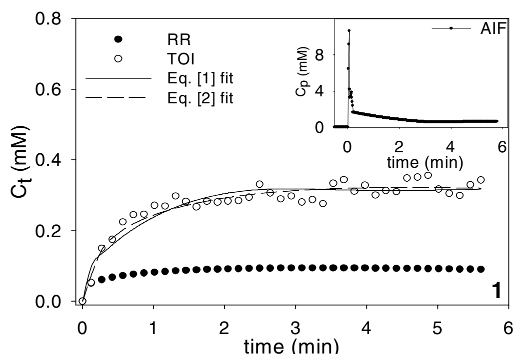
where C_{TOI} and C_p are the concentrations of CA in the tissue of interest (TOI) and blood plasma, respectively, K^{trans} is the CA extravasation rate constant and v_e is the extravascular extracellular volume fraction (4). The RR method establishes a relationship between C_{TOI} and C_{RR} (CA concentration in the RR) allowing the derivation of a model that is independent of C_p. The result is Eq. [2]:

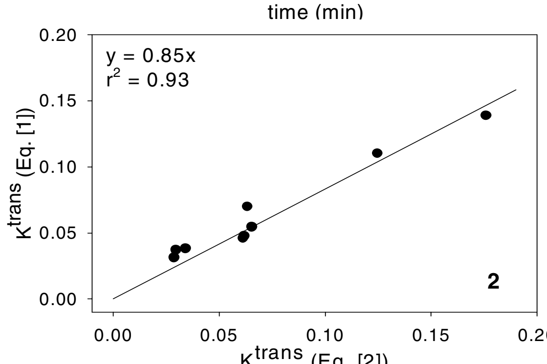
$$C_{TOI}(T) = R\bullet C_{RR}(T) + R\bullet[(K^{trans,RR}/v_{e,RR}) - (K^{trans,TOI}/v_{e,TOI})]\bullet\int_0^T C_{RR}(t)\cdot(\exp(-K^{Trans,TOI}/v_{e,TOI})\cdot(T-t))dt, \qquad [2]$$

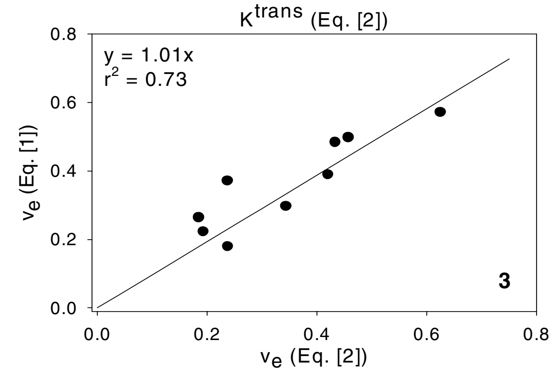
where $K^{trans,RR}$ and $K^{trans,TOI}$ are K^{trans} for the RR and TOI, respectively; $v_{e,RR}$ and $v_{e,TOI}$ are v_e for the RR and TOI, respectively; and $R \equiv K^{trans,TOI}/K^{trans,RR}$.

METHODS Five male Sprague Dawley rats bearing R3230 tumors were imaged on a 1.89T magnet at the Carleton Magnetic Resonance Facility. A gradient echo pulse sequence was designed to provide high temporal resolution for AIF characterization in the aorta (0.9 s) yet adequate temporal resolution for the tumor (~5-15 s, depending on the number of tumor slices) (5). Tissue concentrations-versus-time (measured by the "Bookend Method") and AIF measurements (arterial blood sampling combined with aortic phase imaging) were performed simultaneously for each experiment (5). RR curves were obtained from 21 contiguous voxels within the perivertebral muscle while TOIs were obtained from 9 – 26 contiguous voxels (depending on tumor size) located within the tumor. Each TOI was submitted to Eq. [1] with the measured AIF for a 2-parameter fit (K^{trans}, and v_e) and to Eq. [2] with the measured RR for a 3-parameter fit ($K^{trans,TOI}$, $v_{e,TOI}$, and $K^{trans,RR}$); in this formulation of the RR model, only a value for $v_{e,RR}$ need be assumed and we assumed a value of 0.08 (6 and references therein). Four animals received two injections (the 2nd following five Omniscan half-lives) yielding 9 data sets. Linear regression analysis and a Student's ttest were performed to test for correlation and significant differences between the methods.

RESULTS Figure 1 depicts a TOI (open circles) with the fit obtained from Eq. [1] (solid line) and Eq. [2] (dashed line) as well as the RR (filled circles). The measured AIF is shown in the upper right corner. Figures 2 and 3 depict scatter plots of K^{trans} and v_e obtained from the two methods for all 9 data sets. The r^2 and slope are 0.93, 0.85 for the K^{trans} correlation and 0.73 and 1.01 for the v_e correlation. The student's t-test value for the K^{trans} and v_e correlations were 0.70 (P>0.4) and 0.80 (P>0.4), respectively, indicating no significant difference between values calculated by Eq. [1] or [2]. The mean (absolute) percent difference between the methods was 18.8% for K^{trans} and 19.1% for v_e.







DISCUSSION The data presented here show that, at least when performing ROI analysis, there is a strong and significant correlation between the parameter values extracted by the RR model and those extracted by an AIF driven analysis.

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