The Effects of Parameter Assignment Variation Using a Reference Region Model on Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI)

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INTRODUCTION

In the typical analysis of DCE-MRI data, the contrast agent concentration time course in the blood plasma (C_p) is required. Methods of obtaining an accurate C_p can be difficult and invasive, but models have been developed that allow characterization of a region of interest (ROI) without obtaining C_p [1]. These "reference region" (RR) models calibrate changes in the ROI to those of a reference tissue, $C_{t,RR}$, to extract pharmacokinetic parameters in the ROI. Recently, these models have been modified to include the plasma volume term, which is physiologically more accurate[2]. However, *a priori* knowledge of the RR parameters is required. Here we assess the accuracy of a RR model in determining ROI parameters given an estimated error range for assigned RR parameters with particular interest in how incorporation of the plasma volume term contributes to errors in estimates of ROI parameters.

MATERIALS and METHODS

First, a C_p curve was simulated[3] and applied to construct a reference tissue curve ($C_{t,RR}$) *via* Eq. [1][2]:

$$C_t(t) = K^{trans}\int_0^t C_p(u)e^{-(K^{trans}/v_e)(t-u)}du + v_pC_p(t), \qquad [1]$$

where K^{trans} is the volume transfer constant, v_e is the extravascular extracellular volume fraction, and v_p is the fractional plasma volume[4]. In constructing the RR curve, we varied parameters within the following ranges: 1) K^{trans} from 0.015 to 0.1, 2) v_e from 0.06 to 0.1, and 3) v_p from 0.01 to 0.05[5,6]. The $C_{t,RR}$ curves were used to extract an estimated C_p *via* Eq. [2] [2]:

$$C_p(t) = (1/v_p)\cdot C_t(t) - (K^{trans}/v_p)^2)\cdot\int_0^t C_t(u)\cdot e^{-K^{trans}(1/v_p+1/v_e)(t-u)}du\ , \quad [2]$$

where reference region parameters were fixed at K^{trans} = 0.026 min^{-1}, v_e = 0.086 and v_p = 0.028, as appropriate for skeletal muscle using a 7 kDa CA relevant to further studies[5,6]. In order to investigate how fluctuations in the estimated C_p affect ROI measurements, a $C_{t,ROI}$ was simulated by Eq. 1 with the true C_p and ROI tissue parameters of K^{trans} = 0.25 min^{-1}, v_e = 0.35 and v_p = 0.05. The estimated C_p and $C_{t,RR}$ were then used to estimate parameters in the ROI *via* Eq. [1], and errors in K^{trans}, v_e, and v_p, were assessed.

RESULTS

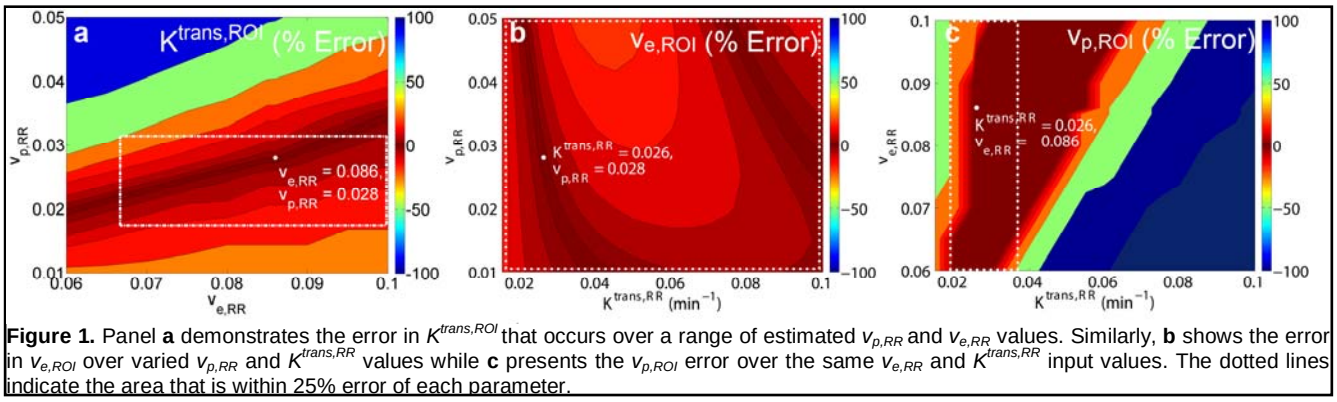

Figure 1. Panel **a** demonstrates the error in $K^{trans,ROI}$ that occurs over a range of estimated $v_{p,RR}$ and $v_{e,RR}$ values. Similarly, **b** shows the error in $v_{e,ROI}$ over varied $v_{p,RR}$ and $K^{trans,RR}$ values while **c** presents the $v_{p,ROI}$ error over the same $v_{e,RR}$ and $K^{trans,RR}$ input values. The dotted lines indicate the area that is within 25% error of each parameter.

In **Figure 1**, panel **a** suggests that variations in $v_{p,,RR}$ from 0.017- 0.032 (-39%- 14% error from true value) and $v_{e,RR}$ from 0.067- 0.1 (-22%- 16%) yield $K^{trans,ROI}$ values with <25% error (dotted line). In panel **b**, error in $v_{e,ROI}$ is <15% for $v_{p,RR}$ of 0.01-0.05 (-64%-79%) and $K^{trans,RR}$ within -62% to +200% (0.01-0.1 min^{-1}). Also, error in $K^{trans,RR}$ estimation beyond 130% can yield a false minimum in $v_{e,ROI}$ error. Panel **c** shows that $v_{e,RR}$ from -30% to 16% (0.06-0.1) and $K^{trans,RR}$ from -26%-35% (0.019-0.035 min^{-1}) produce errors in $v_{p,ROI}$ of <25%.

DISCUSSION

This study assesses how errors in assigned RR parameters translate into errors in extracted ROI parameters when using RR models. Preliminary results indicate parametric variation in RR values can fluctuate over 38% while still predicting ROI parameters within 25% of their true value. Experimental studies are underway to assess this hypothesis by measuring the C_p from the left ventricle (LV) in mice (**Figure 2)** while comparing it to an estimated C_p obtained from paravertebral muscle serving as the RR.

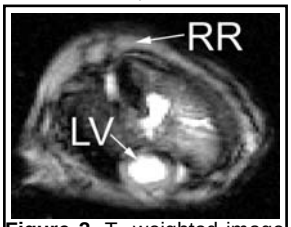

Figure 2. T_1 weighted image of a mouse heart (LV)

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