Incorporation of a Vascular Term into a Reference Region Model for the Analysis of DCE-MRI Data

A. Z. Faranesh[1], and T. E. Yankeelov[2]

[1]Radiology, Stanford University, Stanford, California, United States, [2]Radiology and Radiological Sciences, Vanderbilt University, Nashville, Tennessee, United States

Introduction: Dynamic contrast-enhanced MRI (DCE-MRI) can be used to characterize tumor physiology by tracking the movement of contrast between the vascular and extravascular spaces [1]. Models have recently been developed that allow for the analysis of DCE-MRI data without having to characterize the time course of the contrast agent concentration in the plasma—the so-called arterial input function (AIF) [2,3]. These "reference region" methods do not yet account for the plasma volume contribution, though several investigators have pointed out its significance in tumor studies [4,5]. In this work we explicitly incorporate a vascular term into the formalism and analyze, through simulations, its effect on the extracted pharmacokinetic parameters.

Methods: Simulations were run to calculate the transfer constant (K^{trans}) and extravascular-extracellular volume (v_e) using a reference region model [3] to examine the effects of the plasma volume fraction (v_p). From the concentration time course in the reference region (C_{RR}), plasma concentration (C_p) may be calculated using Eq. 1 (excluding v_p) or Eq. 2 (including v_p).

$$C_p(t) = \left(1/K^{trans,RR}\right)\frac{d}{dt}C_{RR}(t) + \left(1/v_{e,RR}\right)C_{RR}(t) \quad (1)$$

$$C_p(t) = \frac{1}{v_{p,RR}}\int_0^t \frac{dC_{RR}}{dt}(u)\,e^{-K^{trans,RR}\left(\frac{1}{v_{p,RR}}+\frac{1}{v_{e,RR}}\right)(t-u)}\,du + \frac{K^{trans,RR}}{v_{p,RR}\,v_{e,RR}}\int_0^t C_{RR}(u)\,e^{-K^{trans}\left(\frac{1}{v_{p,RR}}+\frac{1}{v_{e,RR}}\right)(t-u)}\,du \quad (2)$$

A plasma curve was generated using parameters previously described [6], with a time step of 1 sec. In the reference region, tissue curves were generated using K^{trans} = 0.08 min^{-1}, v_e=0.1, and v_p=0.02. In the tissue of interest, K^{trans} = 0.25 min^{-1}, v_e=0.4, and v_p=0.01 – 0.1. Noise was added to the tissue curves so that the SNR (relative to the peak reference region concentration) varied from 10 to 100, and they were sampled at an interval of 15 sec. The plasma signal was calculated using Eq. 1 or Eq. 2. This plasma signal was then used to calculate kinetic parameters in the tissue of interest, either excluding or including the vascular signal. A series of 1000 Monte Carlo runs were performed, and the mean and percent root mean square error (RMSE) in the kinetic parameters was calculated.

Results: The mean value of K^{trans} vs. v_p is shown in Fig. 1a (SNR=60). The actual value of K^{trans} (0.25) is shown by the dashed red line. If v_p was excluded from both regions ($nv_{p,rr}$-nv_p), K^{trans} was underestimated for $v_p < 0.06$ and overestimated for $v_p > 0.06$. If v_p was excluded from the reference region and included in the tissue of interest ($nv_{p,rr}$-v_p), K^{trans} increased with v_p, but was less than the true value. If v_p was included in the reference region and excluded from the tissue of interest ($v_{p,rr}$-nv_p), K^{trans} was overestimated by an amount that increased linearly with v_p. If v_p was included in both regions ($v_{p,rr}$-v_p), K^{trans} was slightly underestimated. Fig. 1b plots RMSE vs. v_p (SNR=60). For the $nv_{p,rr}$-nv_p case, the RMSE decreased almost to zero and then increased with increasing values of v_p. For the $nv_{p,rr}$-v_p case, the RMSE decreased linearly with v_p. For the $v_{p,rr}$-nv_p case the error increased linearly with v_p. The error remained relatively stable for the $v_{p,rr}$-v_p case. The SNR sensitivity of the K^{trans} RMSE is shown in Fig. 1c (v_p=0.06). If v_p was excluded from both regions, then the error in K^{trans} decreased with increasing SNR, from 15% to 3%. For all other cases, the errors were relatively stable for SNR > 20, and were 17% ($nv_{p,rr}$-v_p), 62% ($v_{p,rr}$-nv_p), and 15% ($v_{p,rr}$-v_p). The trends for v_e were similar to K^{trans} in both the effects of increasing v_p and SNR (data not shown).

Conclusions: The importance of the plasma term in calculating K^{trans} and v_e from the reference region model were analyzed. If the v_p term was included in both regions, this resulted in an RMSE of 10-15% for the range of v_p and SNR studied. If the v_p is not known in the reference region, then it should also be excluded from the tissue of interest calculations. The largest errors resulted if the vascular term was included in the reference region and excluded from the tissue of interest. These findings are consistent with previous AIF driven DCE-MRI analyses in which the effects of a vascular term were investigated [7]. Planned studies will apply these methods *in vivo* to directly compare a reference region model incorporating the vascular term to that of a standard AIF analysis.

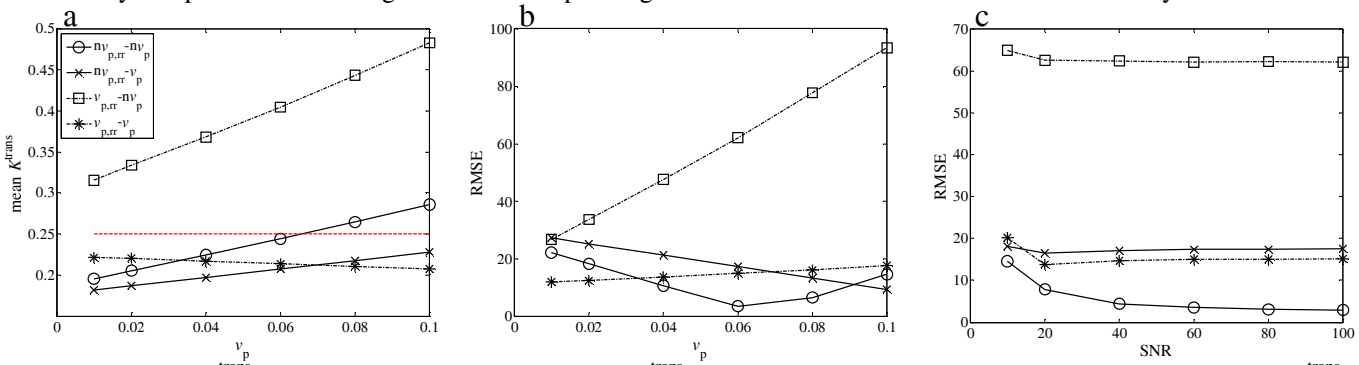

Figure 1: (a) Mean K^{trans} vs. v_p (SNR=60). True value of K^{trans} (0.25) is shown by the red dashed line. (b) Error in K^{trans} vs. v_p (SNR=60). (c) Error in K^{trans} vs. SNR (v_p=0.06).

References: [1] Tofts PS, et al. J.Magn Reson.Imaging. 1999; 10:223-232. [2] Kovar DA, et al. J Magn Reson Imaging. 1998; 8:1126-1134. [3] Yankeelov TE, et al. Magn Reson Imaging. 2005; 23:512-529. [4] Harrer JU, et al. J Magn Reson Imaging. 2004; 20:748-757. [5] Henderson E, et al. J Magn Reson Imaging. 2000; 12:991-1003. [6] Parker GJM, et al. Magn Reson Med. 2006; 56:993-1000. [7] Buckley DL. Magn Reson Med. 2002; 47:601-606.