Nonlinear partial volume effects in DCE-MRI

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Introduction: Conversion of observed signal change to contrast concentration is generally performed as a preliminary step in the analysis of concentration-time curves measured in dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI). The presence of nonlinearity (dependent on the details of the pulse sequence parameters used in data acquisition) is a well-known concern, particularly in the first-pass of the bolus in arterial blood where peak concentrations can easily be 5-20mM. Depending on the specific tissue type being imaged and the presence of vessels within an individual voxel, blood volume fraction (v_b) can range from a few to one hundred percent. Here we discuss the interplay between the nonlinearity of the signal-concentration relationship and the partial volume effect in the context of pharmacokinetic (PK) modeling, demonstrate that significant biases occur in all PK parameters over a wide range of v_b, and discuss means of correcting for these nonlinear partial volume effects.

Methods: Synthetic tissue concentration-time curves were generated for each $K^{trans} \in \{0.05,0.1,0.2,0.3,0.4,0.5,0.75,1.0\}$, and $v_e \in \{0.1,0.2,0.3,0.4,0.5\}$ for v_b values ranging from 0.0 to 1.0. The population-averaged arterial input function (AIF) from ref. 1 was used, and tissue concentration was computed from the extended Tofts-Kety compartment model:

$$C_t(t) = K^{trans} C_p(t) \otimes e^{-k_{ep} t} + v_b C_b(t) \quad (1)$$

using FFT convolution. Pre-contrast $T_{1,0}$ values of 1000 ms and 1440 ms for tissue and blood, respectively, were assumed and *in vivo* values for contrast relaxivities were set to $r_1 = 4 \times 10^{-3}\, mM^{-1}s^{-1}$ and $r_2 = 5 \times 10^{-3}\, mM^{-1}s^{-1}$. The standard expression for steady state signal in a spoiled gradient echo pulse sequence was then used to compute the signal for tissue and blood separately and the total signal was determined by the volume fraction weighted sum of the contribution from these two compartments. Simulated acquisition parameters were chosen to be typical for DCE-MRI data with a 3D SPGR sequence: TR=3 ms, TE=1 ms, flip angle = 20 degrees. The resulting signal data were fit using two different approaches : [1] signal was converted back to estimated concentration by solving the nonlinear concentration-signal equation as described in ref. 2, with the resulting concentration-time curves then fit to Eq. (1) using a linearized regression model, and [2] relative signal enhancement, defined as in ref. 2, was fit directly using nonlinear regression with a model for measured signal that incorporated Eq. (1) into the concentration-dependent relaxivity within the fast exchange limit. Simulation results were then tested in data from eight malignant brain tumor patients studied under an IRB-approved protocol. Patient data was acquired with: TR=2.73-3.45 ms, TE=0.88-1.38 ms, and flip angle = 15-25 degrees. Acquisition time was 3.0-6.0 seconds per frame. The AIF was measured in the middle cerebral artery or sagittal sinus. Concentration-time curves for a single slice of data through the lesion in each of the eight patients were fit using methods [1] and [2] and PK parameter values determined.

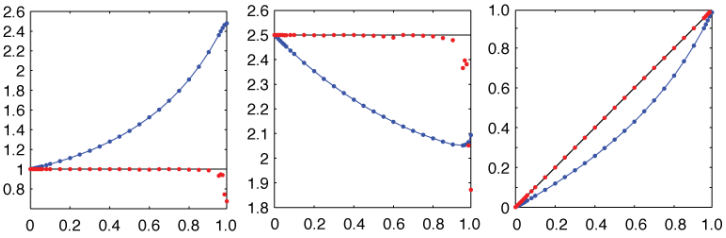

Figure 1. K^{trans} (left), k_{ep} (middle), and v_b (right) estimated as a function of v_b (x-axis) with method [1] (blue) and method [2] (red), with true values (black).

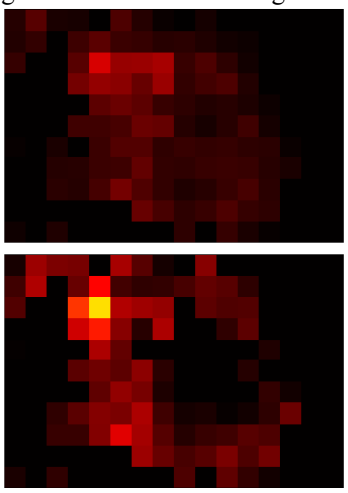

Figure 2. v_b in a tumor computed from concentration (method [1], upper panel) and from signal (method [2], lower panel).

Results: Figure 1 shows simulation results for PK values characteristic of tumor. Blue points are fits to concentration data (method [1]), and red points are fits to signal data (method [2]). True parameter values are indicated by black lines. Images of v_b in a patient with pleomorphic xanthoastrocytoma are shown for both methods in Figure 2 over a range of 0 (black) to .2 (white).

Discussion: Interplay between nonlinearity in the measured signal/concentration relationship and partial volume effects is a potentially significant source of systematic bias in PK parameter estimates when signal data is converted to concentration prior to model fitting. Biases in K^{trans} and k_{ep} may be either positive or negative, depending on the values of other PK parameters, and can be large (>+/-100%) for large blood volume fraction, while v_b tends to be systematically underestimated by 20-50%. Use of a signal model directly incorporating the effect of contrast eliminates these potentially large biases and allows accurate estimation of PK parameters from measured DCE-MRI data.

References

1. GJM Parker *et al., Magn. Reson. Med.* 2006 **56** 993-1000.
2. MC Schabel *et al., Phys. Med. Biol.* 2008 **53** 2345-2373.