Parameter Influence in Dynamic-Contrast-Enhanced MRI Analyses

X. Li¹, W. D. Rooney¹, and C. S. Springer, Jr.¹
¹Advanced Imaging Research Center, Oregon Health & Science University, Portland, Oregon, United States

Introduction: Extremely informative (Dynamic-Contrast-Enhanced) DCE-MRI has been adopted widely for clinical applications. Pharmacokinetic modeling of these data is becoming increasingly popular. Here, simulations based on Gradient Recalled Echo (GRE) data acquisition and a three site water exchange model (1) for pharmacokinetic interpretation are used to investigate parameter influence (2) in DCE-MRI analyses. It is shown that the speed of contrast reagent (CR) extravasation plays the most important role in determining the nature and degree of parameter influence, while the MRI pulse sequence parameter values also have an effect.

Method: The matrix form of the three-site-two-exchange (3S2X) equations (1) was used for all simulations. GRE sequence parameters employed were: TR/FA: 5 ms/15°. The pre-contrast T1 value for each site was set equal to 1.6 s. This way, parameter sensitivity can be better addressed without distractions from pre-CR T1 differences, which can be obtained prior to DCE. Average compartmental water lifetime (τ) values were fixed at 0.3 s. When desired, constraint to the 3S2X fast-exchange-limit (FXL) condition is achieved by setting each τ to 0.001 s. With pre-CR T1 values all equal, both exchange systems are truly in their FXL conditions before CR arrival, even with 0.3 s τ values.

Results: Six Ktrans (volume CR transfer constant) magnitudes (10^{-6} – 10^{-3} min^{-1}) were used to define different CR extravasation rate regimes. The arterial input function (AIF) was derived from averaging five individually measured AIFs from human femoral arteries. For numerical use, this AIF (plasma [CR] time-course, Fig. 1a, circles) was then fitted with a linear function for the uptake phase and a biexponential function for the washout phase (Fig. 1a, solid curve). Parameter influence is evaluated by monitoring the DCE-MRI signal intensity change caused by a 20% change in a specific parameter (2) while holding all others constant. Fig. 1b shows a 3S2X example for Ktrans = 0.04 min^{-1}. The solid curve defines the reference DCE-MRI time-course. The four other time-courses result from 20% changes in each of: Ktrans, τ (average intracellular water lifetime), vb (blood volume fraction), and ve (extravascular extracellular volume fraction). The reference values of vb and ve are 0.02 and 0.12, respectively.

Parameter influence (“strength”) is defined by comparing the square root of the difference between the reference time-course and that introduced by a 20% change in a specific parameter (a univariate approach for local sensitivity estimates). The relative differences, normalized within each individual Ktrans regime, (10^{-6} – 10^{-3} min^{-1}), are summarized in Figure 2 for both FXL-constrained (FXL-c) and 3S2X analyses. Panels a, b, c summarize relative FXL-c parameter influence changes for DCE acquisition windows of 5, 10, and 15 min, respectively. Panels d, e, f show the corresponding results from the 3S2X analyses. It is clear that the most influential parameter is different in different Ktrans regimes. ve sensitivity generally decreases with decreasing Ktrans, while vb becomes the most influential parameter when Ktrans is smaller than 10^{-3}. Ktrans is the most influential parameter when CR extravasation has Ktrans on the order of 0.01 - 0.1 min^{-1}, most relevant to cancer applications. For DCE-MRI analysis without consideration of disproportionate compartmental signal T2 quenching (3, 4), the water lifetime parameters become noticeably sensitive only at large Ktrans for τ, and very small Ktrans for τ (average capillary water lifetime). In fact, τ becomes the 2nd most influential parameter when Ktrans is less than 10^{-1} min^{-1} (not shown). With almost no extravasation, Ktrans sensitivity approaches zero for these acquisition windows.

Discussion: Parameter influence analyses provides significant insight for DCE data modeling. The CR extravasation rate regime is the most important consideration for data modeling. DCE-MRI sequence parameters will also affect parameter influence. When disproportionate compartmental quenching is evident (3,4) [it is likely always present to some extent], water exchange parameters can become much more influential - even with these GRE sequences which are conventionally considered to be exchange-insensitive.

Grant Support: NIH: RO1-NS40801, RO1-EB00422, NIH EB 007258.