Systematic DCE-MRI Parameter Errors Caused by Disproportionate Transverse Relaxation (T2*) Quenching of Tissue Compartmental Water Proton Signals

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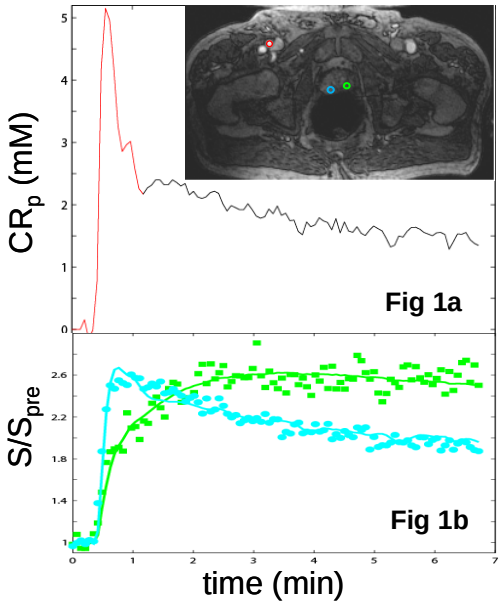
Introduction: Dynamic-contrast-enhanced (DCE)-MRI pharmacokinetic modeling usually ignores potential ^1H_2O signal reduction due to transverse relaxation (T_2^*) effects. Most clinical DCE-MRI applications employ a contrast reagent (CR) dose of 0.1 mmol/kg which could produce a blood plasma CR concentration above 5.0 mM at its peak during the bolus passage. Here, using prostate DCE-MRI data, we investigate a potential T_2^* effect on DCE-MRI model parameter values, by using a water exchange ("shutter-speed") model (1,2) along with a simplified factor to account for putative T_2^* signal quenching.

Method: Prostate ^1H_2O MRI data were acquired with a Siemens TIM Trio (3T) system under an IRB-approved protocol. RF transmitting was through the whole body coil and RF receiving was with a combination of Spin Matrix and flexible Body Matrix RF coils. The DCE-MRI sequence employed a 3D TurboFLASH sequence with a 256*144*16 matrix size and a 360*203 mm^2 field of view, resulting in an in-plane resolution of 1.4 * 1.4 mm^2. Other parameters are: slice thickness: 3 mm; TR/TE/FA: 5.42ms/1.56ms/15º, imaging intersampling interval: 4.16 s. Any T_2^*-induced signal reduction is assumed to be proportional to $[\exp(-(r_2^*[CR] + R_{20})\cdot TE)]$, applying to the ^1H_2O signal from the CR-occupied compartment. For the data here, the most influential CR-containing compartment is the prostate interstitium (1). Thus, r_2^* and [CR] represent the interstitial CR transverse relaxivity and concentration, respectively. [Since susceptibility effects cross compartmental boundaries, surely r_2^* also has a contribution from capillary blood plasma CR.] This T_2^*-reduction factor is then directly applied to the interstitial ^1H_2O signal in the Ernstian MR steady-state DCE-MRI model expression. Parameter uncertainties were determined with sets of Monte Carlo simulations carried out for each ROI-averaged ^1H_2O signal with increasing T_2^* quenching accounted for by choosing an increasing r_2^* value ($mM^{-1}s^{-1}$): 0 (no quenching), 5 (a literature (3) value), 20 (an estimated blood plasma value at 3T), or 40. For each r_2^* and each ROI data set, 200 simulation runs were performed with Gaussian noise ($\mu = 0$, $\sigma = 0.08$) directly added to the normalized ROI data time-course. This resulted in a simulated time-course with a signal-to-noise ratio (SNR) slightly better than that from a single pixel. Random initial guess values were evenly distributed within the parameter space for each simulation fitting.



Results: Figure 1a inset shows a transverse pelvic DCE image slice (anterior up/inferior perspective, ~ 34s post CR injection) of a research subject. Two ROIs are indicated within the prostate gland: one in an area of retrospectively-confirmed prostate cancer, cyan, left; and the other in contralateral normal-appearing prostate tissue, green, right. Figure 1a plots the arterial input function obtained from an ROI in an femoral artery (red). Its magnitude was adjusted using a custom-written numerical approach and an obturator muscle ROI for reference tissue (4). The time-course from the first-pass (red curve) was used to estimate blood volume fraction. Color-matched tissue data time-courses (points) and representative fittings (curves) are seen in Figure 1b.

Figure 2 shows how the K^{trans} (volume fraction CR transfer rate constant product, top) and v_e (extracellular extravascular space, EES, volume fraction, bottom) fitting results would change if increasing interstitial ^1H_2O T_2^* quenching is assumed. With K^{trans} values this large, the algorithm is effectively a two-site (interstitium/cytoplasmae) exchange model (1), and the T_2^*-induced signal reduction is applied to only the EES signal. Assuming the greatest T_2^* reduction ($r_2^* = 40$ $mM^{-1}s^{-1}$) returns K^{trans} and v_e values for the tumor ROI about 35% and 15% greater, respectively, than one would find ignoring this effect. For the normal-appearing tissue, these are 11% and 17% greater, respectively. Conversely, the usual literature analysis includes transverse relaxation neglect (by effectively assuming $r_2^* = 0$) and thus underestimates K^{trans} and v_e to the extent that there is disproportionate relaxation of compartmental ^1H_2O signals.

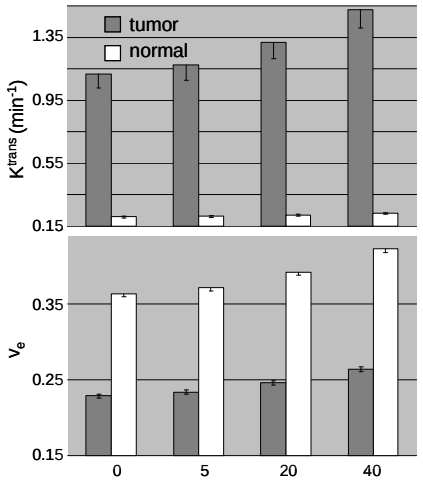


Figure 2

Discussion: The analysis used here is based on an inherently three-site model (1), but multi-step recursive fittings would eventually return a zero (within error) blood volume fraction (v_b) for the tumor tissue. This is not because v_b is actually zero, but only because it is indeterminate due to the very CR-permeable capillary wall. The blood ^1H_2O signal makes a contribution indistinguishable from that of the EES (1). Thus, it is better to use an only two-site model. For consistency, the same two-site model is also used for the normal appearing tissue ROI. The current analysis is conservative in estimating EES signal T_2^*-quenching effects (5). Interestingly, however, the extracted parameters move exactly in the direction seen comparing analyses with the fast-exchange-regime (FXR)-allowed two-site shutter-speed model with the slow-exchange-regime (SXR)-allowed version (1,2,6,7). The former neglects a distinguishable interstitial ^1H_2O signal contribution, which is reduced by exchange and may also be at least partially T_2^*-quenched. For a tumor blood volume estimation using DCE-MRI with extravasating CR, it is prudent to use a lower CR dose (1).

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