A Four Site Linear Exchange Model for DCE-MRI

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Introduction: The significance of the inclusion or exclusion of water exchange effects between various tissue and vascular water compartments remains a subject of active interest and debate. In order to systematically investigate the potential impact of exchange on *in vivo* DCE-MRI data acquired in human brain tumors, we implemented a four-site linear exchange (4SLX) model that includes separate compartments corresponding to intracellular, extracellular extravascular, blood plasma, and erythrocyte spaces. This 4SLX model, building on earlier work [1,2], allows flexible inclusion of arbitrary models describing the distribution of contrast agents within the various compartments [3], enabling us to realistically model both water exchange and contrast pharmacokinetics in various parameter regimes. The impact of inclusion of water exchange on parameter estimates was investigated by comparing model regressions with and without exchange. We also systematically investigated the relative effect of assuming fast, intermediate, and no exchange conditions for each pair of compartments.

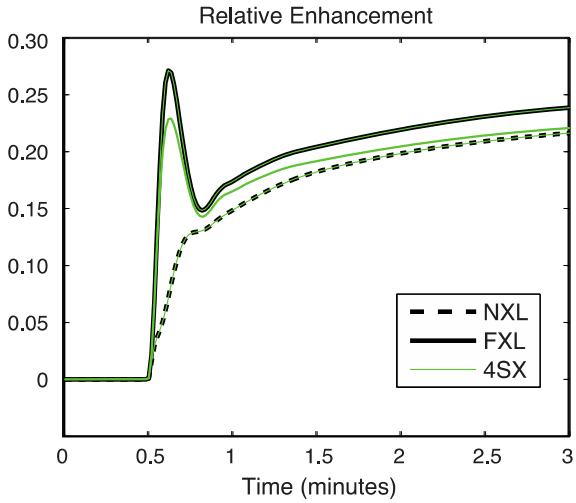

Figure 1. Modeled relative signal enhancement in tissue for FXL, NXL, and intermediate exchange regimes.

Methods: DCE data were acquired on a 3T Siemens scanner under an IRB-approved protocol with a 3D-SPGR sequence. Acquisition parameters were: TR=2.86ms, TE=0.96ms, alpha = 20 deg., voxel size 2x2x2 mm, 3.47s per frame. The AIF was determined using blind estimation as described in [4]. Nonlinear regression was used to estimate pharmacokinetic model parameters. Data were fit with a two-compartment exchange (2CX) model and with the 4SLX model for each imaging voxel. Initial guesses for the 2CX parameters were the same, and water exchange parameters in the 4SLX model were initially set to the fast exchange limit. Model parameters were averaged over all voxels for which 2CX flow estimates were significant at the 95% level.

Results: When exchange parameters were allowed to vary freely in the 4SLX model, we found median flow (F) was 0.13 vs. 0.11 (2CX). Extraction (E) was 0.14 vs. 0.17 (2CX). EES volume (ve) was 0.085 vs. 0.088 (2CX). Capillary transit time (tc) was 8.5s vs. 10.5s (2CX). Blood volume (vb) was 2.2% vs. 2.1% (2CX). All differences were found to be significant at the 95% level using the 2-sided Kolmogorov-Smirnov test. We found tumor median water lifetimes of 1230ms for intracellular-EES exchange, 440ms for EES-plasma exchange, and 90ms for plasma-erythrocyte exchange. Figure 1 plots simulated signal enhancement curves in the fast exchange limit (FXL), no exchange limit (NXL), and intermediate exchange regimes for these median parameters. Black curves were computed directly from the SPGR signal model in the FXL and NXL, while green curves were computed from the full 4SLX model in the appropriate limits. Figure 2 shows

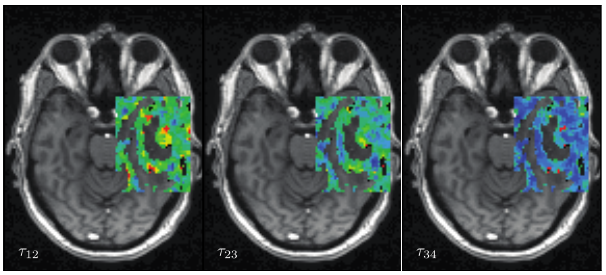

Figure 2. 4LSX parameter maps for intracellular-EES exchange lifetime (left), EES-plasma lifetime (middle), and plasma-erythrocyte lifetime (right).

Discussion: We demonstrate that it is possible to include the effects of water exchange within the context of the 2CX model. While voxelwise estimates of exchange parameters varied widely in this exchange-insensitive data, our tumor-averaged estimates are consistent with values previously reported in tumors. Inclusion of these water exchange parameters resulted in modest, but statistically significant changes in other pharmacokinetic parameters, with blood flow increasing by 18%, extraction decreasing by 18%, ve decreasing by 3%, tc decreasing by 19%, and vb increasing by 5%. In situations where exchange insensitivity cannot be easily achieved (at high field, due to SAR limitations on achievable flip angle), simulations suggest that neglect of water exchange can become a major contributor to uncertainty in pharmacokinetic model parameters.

References

1. R Ouwerkerk *et al., J. Magn. Reson.* 2001 **148** 425-435.
2. X Li *et al., Magn. Reson. Med.* 2005 **54** 2127-2139.
3. SP Sourbron *et al., Magn. Reson. Med.* 2011 **66** 735-745.
4. MC Schabel *et al., Phys. Med. Biol.* 2010 **55** 4807-4823.