Quantifying Gd-Albumin Concentration Profiles in the Rat Brain after CED

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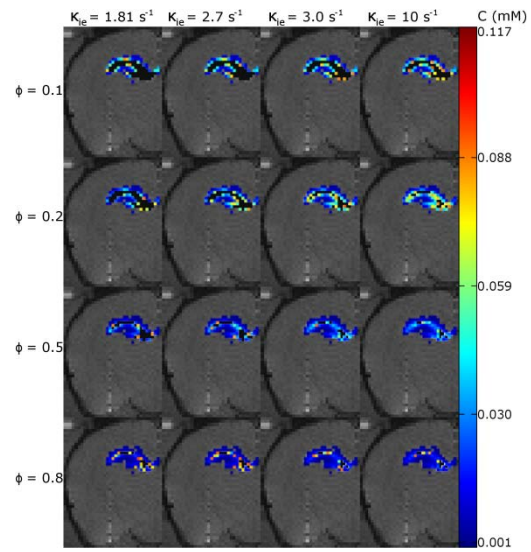
Introduction

Convection enhanced delivery (CED) is the direct infusion of an agent into the extracellular space of tissues and has emerged as a promising local delivery method. As a surrogate for other agents, gadolinium-labeled albumin (Gd-albumin) was infused into the rat hippocampus to determine the influence of tissue architecture on infusate distribution [1]. Although spatial distributions are important, estimating CA concentration profiles may provide a better evaluation of CED as concentration is more closely related to efficacy of delivery. CA relaxivity can be used, in conjunction with in situ relaxation times, to estimate CA concentration. However, in compartmentalized media, such as central nervous system tissue, relaxation with CA present in one or more compartments is not mono-exponential and may best be modeled with a system of Bloch-McConnell equations [2] that take into account exchange rates (κ), water volume fractions (ϕ) and contrast-agent relaxivity in each compartment. In this study, we assess the implementation of a two-site exchange (2SX) model, where the intracellular and extracellular spaces represent the two compartments, for measuring concentration of CA delivered by CED.

Experimental

A 2SX model of spin echo signal was derived and fit to dynamic contrast-enhanced MRI (DCE-MRI) data collected during infusion of Gd-albumin (MW ~87 kDa, ~35 Gd-DTPA molecules per albumin; R. Brasch Laboratory, University of California, San Francisco, CA) into the rat hippocampus. The 2SX model was developed with the following assumptions: 1) steady-state water exchange between compartments, 2) native relaxation rates in both compartments are equal and 3) only spins in the extracellular and intracellular spaces contribute to MR signal. The 2SX model was fit to DCE-MRI data for a range of intracellular to extracellular water exchange rates (κ_{ie}) and uniform ϕ.



Results and Discussion

Concentration profiles of Gd-albumin in the hippocampus were estimated for a single slice (see figure) for different κ_{ie} (increasing across) and different uniform ϕ (increasing down). Black voxels indicate regions where the 2SX model under predicts MR signal and, therefore, cannot estimate CA concentration. Previous studies have measured κ_{ie} = 1.81 s^{-1} [3] and ϕ = 0.2 [4]; however, the 2SX model under predicts signal in 29.5% of voxels with this combination of input parameters. The majority under-predicted voxels occur near the hippocampal fissure, a fluid-filled space within the hippocampus, indicating the need for a spatially-varying input ϕ to capture heterogenous tissue structure within the hippocampus.

Conclusions

Although a 2SX model appears to accurately reflect CA-supplemented relaxation in this media, a better understanding of model input parameters is needed to generate reliable estimations of *in vivo* concentrations.

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