COMPARTMENT-SPECIFIC WATER APPARENT-DIFFUSION COEFFICIENTS IN MAMMALIAN BRAIN

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Abstract

Diffusion-weighted MRI is sensitive to diffusion of an NMR detectable nucleus, typically water protons, and is routinely used clinically to detect tissue injury. To reflect the many *in vivo* sources of non-Brownian water motion (i.e., restriction of motion due to encounters with biological membranes or macromolecular structures), the diffusion coefficient is known as an apparent diffusion coefficient (ADC).

ADC values for water in brain decrease by nearly 50% at the site of acute stroke. Several mechanisms have been suggested to explain this ADC decrease, though the true mechanism remains unknown. Many hypotheses invoke a two-compartment (intracellular and extracellular) model in which the intracellular water ADC is assumed to be much less than that of extracellular water. Indirect measurements of water ADC values in these two compartments do not support these hypothesis, suggesting that the ADC values are similar. It is desirable to make direct, *in vivo* measurements of compartmental water ADC values, but such measurements are complicated by exchange between the two compartments. Exchange must be taken into account for accurate compartment-specific measurements.

All NMR observables (R_1, ADC, etc.) are time and population averages and, therefore, are affected by exchange between intracellular and extracellular compartments. Previous experiments on rat brain modulated the *in vivo* R_1 using an exogenous small molecule that remains in the extracellular compartment. The agent washes slowly out of the brain, which changes extracellular R_1 as a function of time, and uniquely identifies the extracellular compartment. This dynamic R_1 change enables water exchange rate estimation using Bayesian probability theory and Markov chain Monte Carlo integration with the Bloch-McConnell two-site exchange equations. We have extended this methodology to also encode ADC values into the data acquisition and analysis. This modification, along with knowledge of exchange parameters, uniquely labels the extracellular ADC. This method will allow evaluation of compartment-specific water ADC values in normal tissue and after tissue injury, such as stroke.