Assessment of Blood-Brain Water Transfer by Arterial Spin Labeling Based T2 Measurements

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In Arterial Spin Labeling (ASL) experiments, only labeled blood water which enters the imaging slab through the vasculature contributes significantly to the perfusion weighted image. Thus ASL provides an exquisite framework to investigate the dynamics of water transfer from vascular to extravascular space in the brain. However, ASL studies of water transfer based on differences in T1 relaxation between the vasculature and the brain have been difficult, mainly because of the substantial signal decay during the long inflow duration [1]. In this work, we measured water transfer via T2 relaxation by evaluating the ASL signal decay at various echo times TE and inflow times TI to derive an apparent T2 at each time point for each voxel. From the time curve of this apparent T2, we derived the dynamics of water exchange from the vasculature to the brain using a two-compartment model.

Theory:

In the model one compartment represented the arterial vasculature (including vessels and capillary bed within a voxel) and the other extracavascular space, i.e. brain tissue. It is further assumed that labeled water is instantaneously at equilibrium and uniformly distributed in each compartment following exchange so that each compartment can be represented by a mean T2 value, namely $T2_a$ (arterial) and $T2_t$ (tissue). For a delta bolus of labeled water arriving in the voxel at time t=0 the transfer from arterial to tissue compartment can be described as function $B(t)$ with boundary conditions $B(t=0)=1$ (vasculature) and $B(t\to\infty)=-1$ (tissue). For a long bolus, B is convolved by the delivery function of inflowing blood which for pulsed ASL is $c(t)=e^{-t/T1_a}$. Hence:

$$B'(ti,TE)=\int_0^{ti} c(ti-t')\cdot B(t')dt'$$

For initial evaluation, we modeled B as a sigmoid function $B(t)\propto\frac{1}{1-e^{(t-m)/b}}$ which is scaled to $B(0)=1$ and $B(t\to\infty)=-1$ (Fig.1). The mean transfer time of labeled water from vascular to extravascular space is derived at the inflection point t=m from the shape of the sigmoid curve. Note m will also depend on the size and dynamics of the arterial compartment in each voxel. The actual exchange rate is proportional to the time constant b. We also assumed that the apparent T2 during the transfer can be approximated by a monoexponential decay and transfers are smooth and a stationary process, and thus proportional to *B*.

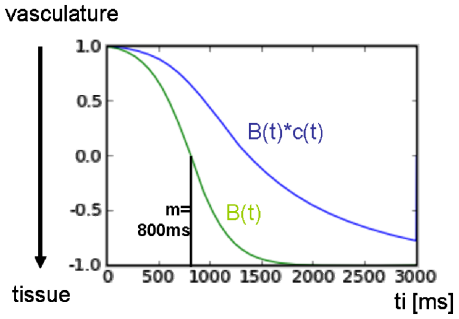

Fig.1: The modeled transfer function B(t) with b=200 ms, m=800 ms (green). Water molecules arrive at the voxel at t=0. b is considered proportional to the transfer rate. In blue B'(t), the same curve after convolution with the inflow function.

Methods:

Datasets have been acquired from five healthy volunteers (23-27 years, 2 male, 3 female) on a 4T scanner (Bruker/Siemens). We used a pulsed ASL sequence with 3D GRASE readout scheme [2]. The labeling delay TI was varied from 500 to 2500ms in increments of 500 to 250ms. Five to ten different TEs were acquired with a step size of 28 ms. Spatial resolution was 4x4x4 mm^3 covering the whole brain with 26 slices. Total scan times varied between 30 and 45 minutes depending on the protocol.

Results:

Temporal changes of the apparent T2 of the ASL signal as a function of blood inflow were resolved (Fig.2). A monoexponential fit of the ASL signal as a function of TE yielded apparent T2 values for inflowing arterial blood and for brain tissue consistent with literature values (at 4.7T: $T2_{plasma}$=220 ms, $T2_{tissue}$ = 50 ms [3]). With theT2 values for arterial blood and brain fixed to 200 and 50 ms, transfer rates for water were derived by fitting the numerical convolution to the data, with the exchange function modeled as sigmoidal. The resulting parameters depended strongly on the selected region. Residual Arterial blood may have contributed in many regions to the perfusion signal, leading to an offset with large m (mean time in the voxel to reach capillary bed). Parameter b was found to be less than 200 ms in most regions. The results imply that the assumption of fast exchange, although if valid in the capillary bed, may not be valid for ASL experiments since in many regions arterial signal contributes to the signal.

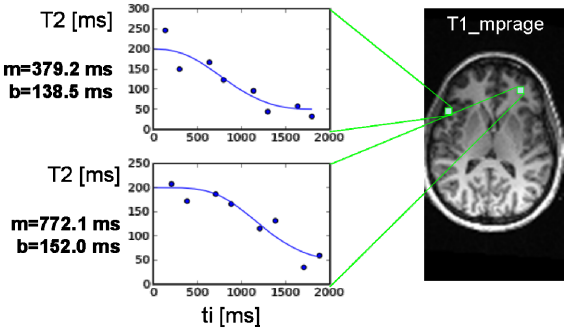

Fig.2: The plotted T2 values have been obtained by exponential fits over TE. Blood arrives at the voxel at ti=0, the arrival time of blood has been estimated by fitting a T1 based single compartment model over inflow times TI. Plots show examples of fits of B'(t) scaled to B'(0)=200ms and B'(inf)=50ms, the T2 values for blood and tissue. The fit yielded b (~transfer rate) and m (mean transfer time in the voxel).

Conclusion:

A method has been presented to measure T2 of the ASL signal and temporal changes of T2 of inflowing blood. An application in assessment of blood water exchange from the measurements has been shown. Though several issues in measuring the exchange rate of blood remain, a framework has been developed for determining transfer rates of blood in the brain at high temporal resolution.

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References:

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