Arterial Spin Labeling based T2 measurements of restricted blood-to-tissue water transfer in human brain

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A method is presented to derive quantitative brain maps of water transfer from blood to tissue, based on non-invasive Arterial Spin Labeling (ASL) techniques using additional T2 measurements. A two-compartment perfusion model including T2 and permeability effects is derived based on the General Kinetic Model. Resulting whole-brain maps of transfer time, which is inversely proportional to capillary water permeability, are shown for healthy volunteers acquired on a 3 Tesla system.

Introduction: Recently, the effect of capillary water permeability on ASL has gained considerable interest. [1-4]. An approach to actually measure the permeability or water transfer time spatially resolved is presented in this work and includes measuring T2 of the ASL signal. The developed two-compartment model is based on the General Kinetic Model including permeability and transverse relaxation, which leads to a two-dimensional curve function depending on inflow time TI and echo time TE (fig. 1). In the imaging voxel, a constant probability is assumed for a water molecule in the capillary bed to cross the blood-brain-barrier and enter the parenchyma. This process is described by the transfer time $T_{bl\rightarrow ex}$. With known relative capillary compartment size V_C, the relation with permeability or the permeability surface area product PS is $T_{bl\rightarrow ex} = V_C/PS$.

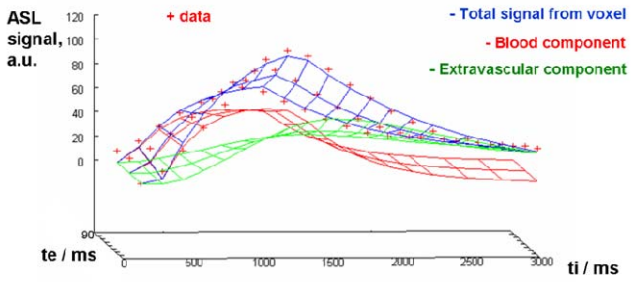

Fig. 1: Data and fit from a gray matter voxel. Parameters and fitting errors are f=104±3 ml/100g/min, τ=346±11 ms, BL=800±4 ms, $T1_{bl}$=1500 ms (fixed), $T1_{ex}$=1300±546 ms, $T2_{bl}$=200±68 ms, $T2_{ex}$=80±15 ms and $T_{bl\rightarrow ex}$=476±85 ms.

Methods: Pulsed ASL measurements [5,6] at different TI and TE were acquired (measurement time 25 min, 26 partitions, 128x56 matrix, 4mm isotropic resolution) on a a clinical MR scanner (Trio, Siemens, Erlangen, Germany; 3 Tesla). TI ranged from 150 to 3000 ms with 150 ms step size, measured TE were 16.5, 49.4 and 82.3 ms. Five healthy volunteers between 23 and 38 years were included. The study was in compliance with local ethics standards, written consent was given. A voxel-wise model fit has been done on the difference images (example plot fig. 1). Resulting maps show water transfer time (fig.2) and other physiological parameters like perfusion and arterial transit time. V_C=0.02 was used for PS calculation.

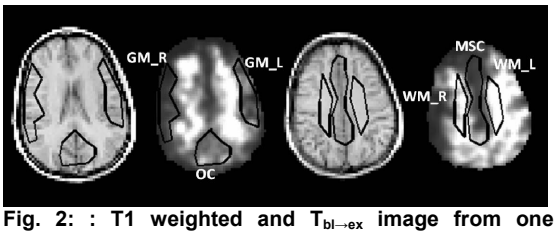

Fig. 2: : T1 weighted and $T_{bl\rightarrow ex}$ image from one subject, showing selected ROIs

Results: Stable transfer time maps could be derived for all subjects. Water transfer time maps from one patient are shown in fig. 1. A ROI analysis was done on all subjects. Resulting averaged values are shown in table 1. Confidence intervals are calculated based on the standard deviations within ROIs.

Discussion: We introduced a novel T2-based ASL approach and demonstrated feasibility to assess the temporal dynamics of water transit between the vasculature and the brain, modeled as two compartments characterized by different transverse relaxation rates. A comparison to literature values from PET (1.5 ml/g/s) [4] shows good agreement in the case of grey matter, while white matter values show significant differences (PET: 0.8 ml/g/s). Limitations to the method are neglecting backflow and throughflow effects which presumably lead to apparently faster transfer in larger vessel regions, and the dependence on long TI and high SNR for regions with slow exchange. This is crucial in the case of white matter and leads to largely inaccurate values. A direct comparison with PET H2O-15 could help validate the absolute permeability values. To the best of our knowledge, this ASL study is the first to derive full-brain maps of the temporal exchange dynamics of labeled blood water via T2 relaxation on the human brain. Potential applications range from diagnosis to monitoring disease progression, generally in all diseases affecting the blood-brain-barrier.

References: [1] Wang J, Fernandez-Seara MA, Wang S, St Lawrence KS.: JCBF 2007;27(4):839-849.; [2] Li KL et.al. MRM 2005; 53 (3):511-518. [3] Liu P, Uh J, Lu H. MRM 2010. [4] Parkes LM, Tofts PS.MRM 2002;48(1):27-41. [5] Günther, M., K. Oshio and D. A. Feinberg (2005). MRM 54(2): 491-8. [6] Gregori J, Günther M, Schuff N, Proc. ISMRM 17 (2009) 3624

	GM_L	GM_R	OC	MSC	WM_L	WM_R	GM	WM
$T_{bl\rightarrow ex}$	470±80	350±40	1620±220	880±100	3020±620	3140±670	830±60	3080±240
PS	2.54±0.41	3.43±0.36	0.74±0.10	1.37±0.16	0.40±0.08	0.38±0.08	1.45±0.11	0.39±0.03

Tab. 1: Table containing mean $T_{bl\rightarrow ex}$ values in [ms] with 95% confidence intervals. PS values are listed in [ml/g/min]