Simultaneous Measurements of Arterial Transit Times and Water Exchange Rates by Diffusion-Weighted ASL

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Introduction Changes in the exchange rate of water across the blood-brain barrier (BBB), denoted k_w, may indicate BBB dysfunction before the leakage of larger molecules, such as contrast agents, is observable. One approach for measuring k_w is to combine diffusion-weighted (DW) imaging with arterial spin labelling (ASL) to measure the vascular and tissue fractions of labelled water (1,2). k_w is determined from the vascular-to-tissue ratio by characterizing the exchange between the two pools (3). However, the accuracy of DW-ASL is affected by arterial blood contributions and the arterial transit time (τ_a) (2,4). To address these issues, we propose a two-stage method using combinations of flow-encoding gradients and post-labelling delays (τ_d) to measure τ_a and k_w. First, τ_a is determined using bipolar gradients to suppress flow in the feeding arteries with a relatively short τ_d (5). Second, k_w is determined using bipolar gradients strong enough to suppress all vascular signals and $\tau_d > \tau_a$. The aims of this study were to assess the feasibility of this two-stage method and to determine the reproducibility of the k_w measurements.

Materials and Methods Experiments were conducted on a Siemens 3.0T Verio scanner using a product 32-channel head array coil. The DW-ASL sequence incorporated pseudo-continuous ASL (pCASL), background suppression (BS) and twice-refocused spin-echo diffusion weighting (6) (Fig. 1). The pCASL labelling/control duration was 1.5s, consisting of 1600 Hanning pulses (peak/average B_1=5.3/1.8μT, duration=500μsec and peak/average G=6.0/2.3mT/m). Acquisition parameters were FOV=24cm, matrix=64x64, bandwidth =3kHz/pixel, 7/8 partial k-space, acceleration factor = 2, TR=3.5sec, TE=48ms. 8 axial slices (8 mm thickness, 2 mm gap) were acquired.

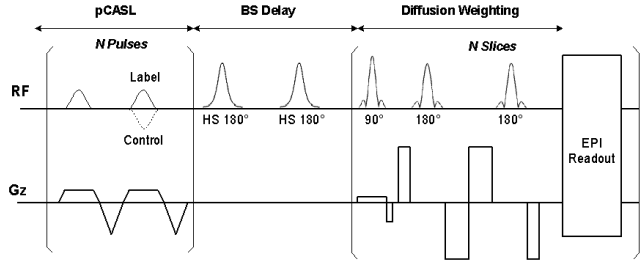

Fig. 1 Sequence diagram combining pCASL, BS and TRSE methods.

Three sets of DW-ASL data were collected, each with two b values (total scan time = 22 min). For the 1st set, b = 0 and 10 s/mm^2 and τ_d was 800ms to allow time for labelled water to reach the arterial compartment. For the 2nd and 3rd sets, b = 0 and 50 s/mm^2 – the latter value will suppress all flowing spins (4) – and τ_d was 1500ms to ensure labelled water reached the tissue compartment (i.e., capillaries and surrounding tissue). EPI images were pair-wise subtracted and time averaged to generate mean ASL images (ΔM) for each b value (32 reps / b value), from which grey matter ΔM was extracted. τ_a was determined from the ratio ΔM(b=10)/ΔM(b=0) using a two compartment model (arterial + tissue) (5). k_w was determined from the ratio ΔM(b=50)/ΔM(b=0) using an exchange model that accounts for τ_d and τ_a. k_w was determined for each set separately to assess reproducibility.

Results Figure 1 shows DW-ASL images from one subject. In this example, ΔM(b=10)/ΔM(b=0) = 0.60 and ΔM(b=50)/ΔM(b=0) = 0.78. Individual grey matter τ_a and k_w estimates from all 4 healthy subjects (mean age 27 y, 22 – 35 y) are presented in Table 1. Mean values across subjects were τ_a = 1.26 ± .09 s and k_w = 119 ± 23 min^{-1} with an average intra-subject coefficient of variation (CV) of 12%.

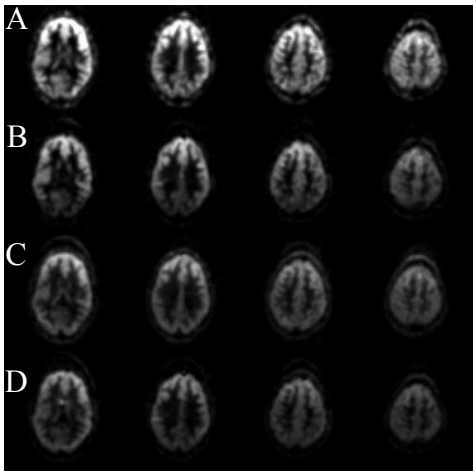

Fig. 1 DW-ASL ΔM images from one subject: (A) τ_d = 0.8s, b = 0 s/mm^2, (B) τ_d = 0.8s, b = 10 s/mm^2, (C) τ_d = 1.5s, b = 0 s/mm^2, (D) τ_d = 1.5s, b = 50 s/mm^2. 4 of 8 slices are shown.

Discussion The τ_a values agreed with previous measurements using this technique (5); however, k_w was approximately 35% lower in this study (2,4). This difference likely reflects an overestimation in the previous studies due to arterial blood contamination, which was avoided here by measuring τ_a and setting $\tau_d > \tau_a$. Since k_w is defined as the permeability-surface area (PS) product of water / microvasculature blood volume, it can be compared to PET measurements. In cortical grey matter, PS = 150 ml/100g/min (7), which is in good agreement with our results assuming a microvasculature blood volume of 1.5 ml/100g (8). A mean CV of 12% suggests that DW-ASL can measure k_w with reasonable precision, in contrast to the multi-τ_d approach (9). Since τ_a can vary between vascular territories, the next step is to determine if there are regional variations in water exchange rates.

Subject	τ_a (s)	k_w (min^{-1})	CV (%)
1	1.39	90	11
2	1.26	137	6
3	1.20	139	16
4	1.20	112	15

Table 1: Arterial transit time (τ_a) and water exchange rate (k_w) measurements from 4 subjects. Values of the coefficient of variation (CV) are from two k_w measurements obtained per subject.

Reference

[1] Silva et al., *Magn Reson Med* 1997;38:232-7. [2] Wang et al., *J Cereb Blood Flow Metab* 2006;27: 839-50. [3] St Lawrence et al., *Magn Reson Med* 2000;44:440-9. [4] St Lawrence, *Proc ISMRM*, 2008;16:188 [5] Wang et al., *Magn Reson Med* 2003;50:599-607 [6] Wang, *Proc ISMRM*, 2007;15:2974 [7] Herscovitch et al., *J Cereb Blood Flow Metab* 1987;7:527-42 [8] Pawlik Brain Res 1981;208: 35-58 [9] Carr etl al. *Magn Reson Med* 2007;58:281-289