When Perfusion Meets Diffusion – in vivo Measurement of Water Extraction and Permeability in Human Brain

J. Wang[1], K. S. St Lawrence[2], M. Fernandez-Seara[1], J. A. Detre[1]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]Lawson Health Research Institute, London, ON, Canada

Introduction While water was initially considered as a freely diffusible tracer in arterial spin labeling (ASL) perfusion MRI, emerging evidence suggested a limited degree of water exchange between the vascular (capillary) and tissue compartments (1, 2). Quantification of water extraction fraction and permeability is important for accurate perfusion quantification in ASL methods, and may provide clinically relevant information regarding the functional status of the microvasculature. In this study, water extraction fraction was estimated by differentiating the amount of labeled water in the vascular and tissue space based on their distinct diffusion characteristics, using diffusion weighted (DW) ASL perfusion MRI. By resorting to the single-pass approximation (SPA) model (3), we further estimated the water permeability of human brain.

Materials and Methods The DW perfusion sequence was a hybrid of the amplitude modulated continuous ASL technique (4) and a twice-refocused spin-echo (TRSE) diffusion sequence (5) (Fig. 1). The tagging/control duration for ASL was 2.6s. Two delay times (0.8 and 1.2s) between the labeling pulse and image acquisition were employed. Two pairs of bipolar gradients were applied along the slice direction, with the RF refocusing pulses dividing each bipolar pair. Series of b values were tested, i.e., b=0, 25, 50, 100, 150, 200 and 300 s/mm^2 for 0.8s delay, and b=0, 10, 25, 50, 100 and 200 s/mm^2 for 1.2s delay. The durations of the four lobes of bipolar gradients were optimized to minimize eddy currents. MR scanning was conducted on a Siemens 3.0T Trio whole-body scanner, using a standard Tx/Rx head coil. Nine healthy subjects (5 females, age 22-33yrs) participated in the experiment, with 5 undergoing scans with 0.8s delay and the rest 4 scanned with 1.2s delay. Acquisition parameters were: FOV=22cm, matrix=64x64, bandwidth=3kHz/pixel, 6/8 partial K-space, TR=4sec, TE=60 and 55ms for 0.8 and 1.2s respectively. Four slices (6mm thickness with 3mm gap) were acquired from inferior to superior in a sequential order, and each slice acquisition took about 90ms. Each ASL scan (with a particular b value) including 80 acquisitions took 5.5 minutes.

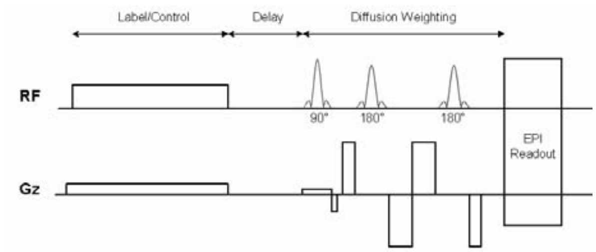

Fig. 1 Diagram of the hybrid sequence combining CASL and TRSE methods.

The raw EPI images were separated into label and control pairs and then pair-wise subtracted. Temporal fluctuations in the difference ASL image series were minimized using an algorithm based on principal component analysis, followed by averaging across the image series to form the mean ASL perfusion images (ΔM). The mean ΔM and raw EPI (M) signals were measured within the gray matter (GM) ROIs (segmented using SPM99), and were fitted according to a biexponential model. Simulation was carried out based on the SPA model including two compartments of capillary and brain tissue. A numerical technique was used which divided a single capillary transit of the labeled spins (defined as capillary space, Vc, divided by cerebral blood flow, f) into small, consecutive time segments (n=200) to allow calculation of exchange effects in a stepwise fashion. Assumed T1s for brain tissue (gray matter) and blood at 3.0T were 1.26 and 1.49s, and T2s were 80, 120 and 40ms for brain tissue (gray matter), arterial and venous blood respectively. The arterial transit time (ATT) was assumed to be 1.4s. The ratio of extravascular (Se) and capillary (Sc) ASL signals was calculated while three parameters were systematically varied in the SPA model, i.e., permeability surface product (PS), Vc and f .

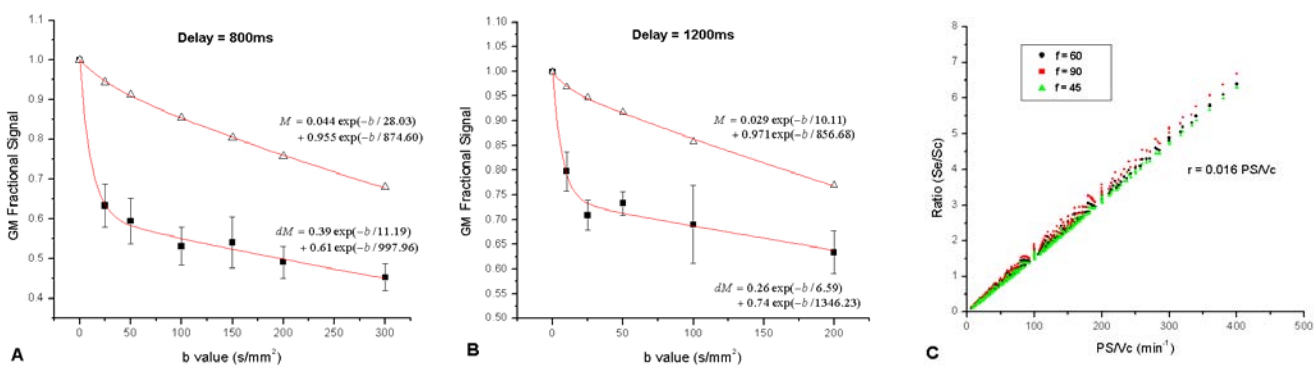

Fig. 2 The attenuation curves of M and ΔM signals with b values acquired using (A) 0.8s and (B) 1.2s delay. (C) Simulation results showing linear relationship between Se/Sc and PS/Vc at 3 different flow rates.

Results The ΔM signal curves (Fig. 2A&B) apparently consisted of a fast and a slow decaying component. With the delay time of 0.8s, the fitted water extraction fraction was 61%, which increased to 74% with a prolonged delay of 1.2s (p=0.05). A relatively clean separation of the fast and slow components of the ΔM attenuation curve could be achieved with the b value of 50s/mm^2, at which there was only less than 2% signal of the fast component while the slow component still retained more than 95% of the signal. The estimated pseudo-ADC of the slow component of the ΔM signal curve (0.00100 and 0.00074 mm^2/s for 0.8 and 1.2s delay) seemed lower than their counterparts of the M signal curve (0.00114 and 0.00117 mm^2/s for 0.8 and 1.2s delay). However, no statistically significant difference (p>0.1) was detected. The SPA model simulation showed a very good linear relationship between Se/Sc and PS/Vc (r= 0.998), when the delay time is equal to or slightly shorter than the ATT (Fig. 2C). In our experiment, data acquired with the delay time of 1.2s generally satisfied the above presumption, and the estimated mean PS/Vc was 193.28 ± 50.17 min^{-1} from four subjects. PS/Vc images could be derived from a minimum of two-point ASL measurement with b=0 and 50s/mm^2.

Discussion The present study added support to a limited exchange rate of blood water across the brain blood barrier. In contrast to earlier studies employing a short or no post-labeling delays (1), the fast decay observed in our study should be attributed primarily to labeled spins in arterioles and capillaries, since a relatively long delay time was applied to minimize the effect of arterial contribution. The challenge for estimating water extraction and permeability using the DW ASL method is adequate SNR especially in the presence of large diffusion gradients. Future development may take advantage of several latest technical advancements of ASL to reliably image water permeability.

Reference

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