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Comparison of relative CBF maps using pseudo-continuous ASL and SPECT

Peiying Liu^a, Jinsoo Uh^{a,c}, Michael D. Devous^b, Bryon Adinoff^{c,d}, and Hanzhang Lu^{a,b,c}

^aAdvanced Imaging Research Center, University of Texas Southwestern Medical Center, Texas, United States

^bDepartment of Radiology, University of Texas Southwestern Medical Center, Dallas, Texas, United States

^cDepartment of Psychiatry, University of Texas Southwestern Medical Center, Dallas, Texas, United States

^dVA North Texas Health Care System, Dallas, Texas, United States

Abstract

Pseudo-continuous arterial spin labeling (PCASL) MRI is a relatively new ASL technique and has the potential to extend the CBF measurement to all tissue types, including the white matter. However, arterial transit time (δ_a) for the white matter is not well established and a limited number of reports using multi-delay methods have yielded inconsistent findings. In the present study, we took a different approach and measured white matter δ_a , 1541 ± 173 ms (mean $\pm$ SD), by determining arrival times of exogenous contrast agent in a bolus tracking experiment. The data also confirmed δ_a of the gray matter as 912 ± 209 ms. In the second part of this study, we used these parameters in PCASL kinetic models and compared relative CBF (rCBF, with respect to the whole brain) maps to those measured using a SPECT technique. It was found that the use of tissue-specific δ_a in the PCASL model was helpful in improving the correspondence between the two modalities. On a regional level, the gray/white matter CBF ratios were 2.47 ± 0.39 and 2.44 ± 0.18 for PCASL and SPECT, respectively. On a single voxel level, the variance between the modalities was still considerable, with an average rCBF difference of 0.27.

Keywords

arterial spin labeling; cerebral blood flow; contrast agent; PCASL; perfusion; SPECT

Introduction

Arterial Spin Labeling (ASL) MRI provides a non-invasive technique to assess cerebral blood flow (CBF) (1–10). In particular, recent advances in ASL technologies, including the pseudo-continuous ASL (PCASL) method, 3D acquisition, and background suppression, have facilitated a broader application of this technique in neurological and psychiatric disorders (11–16). It has also been shown that, once a relative CBF (rCBF) map is obtained, the calculation of absolute CBF value can be feasibly achieved by using phase-contrast velocity map as a whole-brain calibration factor (17,18). A remaining challenge in ASL methodology is then how to obtain accurate rCBF maps. The present study will focus on the

measurement of rCBF with PCASL and compare the results to those of a radiotracer-based Single Photon Emission Computed Tomography (SPECT) method.

An important feature of the present study is that we pay special attention to the ability of PCASL in measuring white matter rCBF. Recent evidence suggested that PCASL may have sufficient sensitivity to reliably detect signal in the white matter, which would provide a new means to assess white matter physiology (19). However, proper quantification of ASL signal requires the knowledge of a number of parameters (e.g. T1, T2*, blood-brain partition coefficient), in particular arterial transit time (δ_a), which is the time it takes for the blood to travel from the labeling site to the imaging slice. δ_a in the gray matter has been studied extensively by fitting multi-delay ASL data to kinetic models (20–25). Such studies in the white matter, however, yielded less consistent results, presumably due to lower signal amplitude (25–28). The present study takes a different approach by using exogenous contrast agent to estimate δ_a in both gray and white matters.

This study contains two components. First, we used the time difference of Gd-DTPA bolus arrival in the labeling and imaging slices to calculate δ_a . Next, using the δ_a values obtained above, we compared the rCBF maps using a PCASL technique (3,4,29,30) to those obtained from a SPECT method. The SPECT method is insensitive to the time it takes for the tracer to reach the parenchyma, therefore can serve as a reference technique to study the transit time effect in PCASL. Spatial correspondence was assessed between the SPECT and PCASL CBF maps. The PCASL data were analyzed with two kinetic models, including a simplified model (31) and a one-compartment kinetic model (20).

Materials and Methods

General

All MRI scans were performed on a 3T MRI system (Philips Medical Systems, Best, the Netherlands) using a body coil for transmission and an eight-channel array coil for reception. The two components of the study, which were the transit time study and the SPECT comparison study, were performed on separate cohorts. All subjects gave informed written consent before participating in the study. The study protocol was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center.

Transit time study

Five subjects (4 females, 1 male, 34.4 ± 6.1 years old) without history of neurological disorders participated in a bolus tracking MRI experiment. The protocol was similar to a dynamic susceptibility contrast (DSC) scan, in which a sharp bolus (5 ml/s) of Gd-DTPA (0.1 mmol/kg Magnevist®, Bayer Schering Pharma AG, Berlin, Germany) was injected intravenously while T2*-weighted MR images were acquired rapidly in the brain. A special consideration for accurate determination of δ_a was that a higher temporal sampling rate was used. Typical DSC scan uses a TR on the order of 1 second, which is too coarse for arterial transit time of 1–2 seconds. We therefore used a TR of 100 ms which allowed the simultaneous acquisition of two slices. The lower slice was at 84 mm below the anterior-commissure (AC) posterior-commissure (PC) line which was the location of the labeling plane in PCASL and provided the optimal labeling efficiency (17). The upper slice was at 10 mm above AC-PC line corresponding to typical imaging slice (see Fig 1a). The scan duration was 200 s (yielding 2000 measurements) and Gd-DTPA injection took place at 1 min after the start of scan. Other imaging parameters were: Field-of-view (FOV) 205×205 mm², matrix 64×64 , voxel size $3.2 \times 3.2 \times 5$ mm³, TE 25 ms, SENSE factor 2, and flip angle 40°.

A high resolution T_1 weighted image was acquired with the following parameters: Magnetization Prepared Rapid Acquisition of Gradient Echo (MPRAGE) sequence, TR/TE/TI=2100/3.8/1100 ms, flip angle=12°, 160 sagittal slices, voxel size=1×1×1 mm³, FOV=256×256×160 mm³, and duration 4 min. In addition, a PCASL scan with a short delay ($w=200$ ms) was acquired to delineate large vessels (24,32). Other PCASL parameters were identical to the ones used in the SPECT comparison study described below.

The raw signal time course of the bolus-tracking data is characterized by a signal drop from the baseline level upon the arrival of the Gd-DTPA bolus, followed by a gradual signal return (Fig. 2a). To estimate the bolus-arrival time, a second time course was calculated, in which the current time point together with seven points before and seven points after were used to calculate the slope of the signal change. Next, an automated algorithm was used to search for the time point at which the slope reaches 15% of the maximum slope (in this voxel) and this time point is expected to indicate the arrival of front edge of the bolus. The threshold value 15% was chosen to allow the bolus-related signal drop to be clearly distinguished from signal fluctuations associated with random noise. The algorithm was applied to each voxel in the image and a map of bolus arrival time (interpolated to 1ms temporal resolution) was obtained.

ROI-based analysis was also conducted. For the lower slice, four ROIs corresponding to left/right internal carotid and vertebral arteries were manually delineated. For the upper slice, eighteen ROIs were delineated on each dataset, which included three major categories: large blood vessel, white and gray matter. The white and gray matter was each further divided into three sections corresponding to flow territories of anterior (ACA), middle (MCA) and posterior cerebral arteries (PCA) (33–35). Two deep gray matter ROIs corresponding to basal ganglia and thalamus were also included. The white and gray matter voxels were distinguished by tissue segmentation using a T_1 -weighted image resliced from the 3D MPRAGE based on angulation and translation parameters (SPM2, University College London, UK). The separation of anterior, middle and posterior sections was conducted manually based on a flow territory atlas (33). The ROIs for deep gray matter were manually delineated. The vessel ROIs in the upper slice were defined as voxels in which relative signal in the short-delay PCASL scan was greater than 7% of equilibrium magnetization, based on a previous study (24). As an exploratory analysis, ROIs were also manually placed in the sagittal sinus to assess how long it took for the blood to travel from major arteries to major vein, although these results had no utility in PCASL quantification.

For each ROI, an averaged time course was obtained and the bolus arrival time was determined as described above. δ_a was then calculated as the difference in bolus arrival times between the ROI in the upper slice and the feeding artery in the lower slice. Considering the flow territory of individual feeding artery, the posterior gray and white matter used the subtraction of bolus arrival time in the vertebral artery whereas all other ROIs used the internal carotid's arrival time. δ_a values were compared across ROIs with Analysis-of-variance (ANOVA), followed by post-hoc pair-wise comparisons. A corrected P value of 0.05 or less is considered significant.

PCASL and SPECT comparison study

Ten subjects (7 females, 3 males, 39.3 ± 9.4 years old) without history of neurological disorders underwent both a PCASL MRI scan and a SPECT scan. The gap between the two sessions was 0–10 days with a mean value 3.2 ± 3.4 days. Both PCASL and SPECT images covered the whole brain. The PCASL MRI scans used the following parameters: labeling duration 1650 ms, labeling RF flip angle 18°, RF interval 1ms, the labeling plane was located 84 mm below the AC-PC line as optimized previously (17), TR/TE=4151/14 ms, post-labeling delay time (w) = 1525 ms for the bottom slice with an increase of 35 ms for

each additional slice, matrix size 80×80, in-plane resolution 3×3 mm², 27 slices with the bottom slice at 55 mm below the AC-PC line, slice thickness 5 mm, no gap, 30 pairs of labeled and control images, duration 4.1 minutes. In addition, a T₁-weighted MRPAGE scan was performed during the MRI session using sequence parameters identical to those described in the “Transit time study”.

For the SPECT study, a total of 20 mCi of CBF tracer Technetium-99m hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO) (GE Healthcare, Princeton, New Jersey, USA) was administered over 30 s and followed by a 10 ml saline flush over 30 s. SPECT scans were obtained 90 min after ^{99m}Tc HMPAO administration to allow time for tracer activity to clear from blood and non-brain tissues. The SPECT image was acquired with a PRISM 3000S three-headed SPECT camera (Picker International, Cleveland) with ultra-high-resolution fanbeam collimators, positioned 13–13.5 cm from the axis of rotation (36). Projection data were acquired in a 128×128 matrix in 3° increments using a 20% wide centered energy window. The SPECT scan duration was 20 min. Image reconstruction were performed in the transverse domain by using filtered back-projection. The CBF-weighted images were filtered to a spatial resolution of 10×10×10 mm³. The images were corrected for incomplete extraction of the radio-tracer by using a permeability-surface-area (PS) model (37–39), in which $CBF_{corrected} = CBF_{uncorrected} / (1 - \exp(-PS/CBF_{corrected}))$. PS for the ^{99m}Tc-HMPAO tracer was assumed to be 91 ml/100g/min according to the literature (37,39,40).

For data processing, PCASL image series were realigned to the first volume using SPM2. Pair-wise subtraction was conducted for the label and control images, and the difference images were averaged over multiple measurements. The PCASL and SPECT data of each subject were spatially transformed to a template CBF map available in SPM2, which is in the standard space established by Montreal Neurological Institute (MNI). To match the spatial resolution between the two modalities, the PCASL data were smoothed using a Gaussian kernel with full-width-half-maximum (FWHM) of 10 mm.

Two relative CBF maps were generated from the PCASL data for comparisons with the SPECT map: a simplified kinetic model of Chalela et al. assuming that the labeled spins stay inside blood compartment and do not enter tissue (31); and a one-compartment model of Alsop et al. (20). The calculation of CBF weighted signal in the simplified model used only one assumption that arterial blood T_{1a}=1664 ms (41). The CBF signal was calculated as:

$$S_{PCASL} = (Control - Label) / \exp(-w/T_{1a}) \quad [1]$$

where w is the post-labeling delay time. The S_{PCASL} of each voxel was then divided by the whole-brain-averaged S_{PCASL} to obtain the rCBF map. In the one-compartment model, the CBF weighted signal was calculated as (20):

$$S_{PCASL} = (Control - Label) / \left\{ T_1 / \lambda \cdot [\exp(\min(\delta_a - w, 0)/T_1) - \exp((\delta_a - w - \tau)/T_1)] \cdot \exp(-\delta_a/T_{1a}) \cdot \exp(-TE/T_2^*) \right\}$$

where τ is the labeling duration, λ is the blood-brain partition coefficient, T_1 and T_2^* are the brain tissue relaxation times, and T_{1a} is the T_1 of arterial blood. Table 1 shows assumptions on gray and white matter model parameters. Note that the white matter δ_a value was previously not well established, and was one of the contributions of the present study. For each voxel, the actual model parameters were estimated based on its gray/white matter probability as:

$$C_{Voxel} = P_{Gray} \cdot C_{Gray} + P_{White} \cdot C_{White} \quad [3]$$

where C is either T_1 , T_2^* , λ , or δ_a in Eq. [2] and P is the tissue probability. The tissue probability was obtained by performing tissue segmentation on the T_1 -weighted anatomic image using SPM2.

Gray and white matter ROIs were manually placed on five representative axial slices, from which rCBF values were obtained. Caution was used in the ROI drawing to avoid voxels near gray/white boundary, so that partial volume effect could be minimized. The gray/white matter rCBF ratio was compared across modalities using a paired Student t test. Voxel-by-voxel comparison between PCASL and SPECT relative maps was conducted by assessing scatter plot between the two modalities. The scatter plot used a $10 \times 10 \times 10$ mm³ voxel volume consistent with the image spatial resolution. To quantify the discrepancy between the two rCBF maps, a mean difference index, D , was calculated as (42):

$$D = \sqrt{\frac{1}{N} \sum_{i=1}^N (rCBF_{PCASL,i} - rCBF_{SPECT,i})^2} \quad [4]$$

where $rCBF_{PCASL,i}$ and $rCBF_{SPECT,i}$ are PCASL rCBF and SPECT rCBF values, respectively, for a voxel i , and N is the total number of voxels in the brain.

We further identified brain regions that showed significant differences between the two modalities by conducting a voxel-wise Student t test (SPM2) for the PCASL and SPECT rCBF maps. A threshold of $P < 0.001$ and cluster size of > 1.6 cm³ (200 voxels) was used to identify significant clusters.

Results

Figure 1 shows representative bolus-tracking images before and after the contrast agent injection, demonstrating sufficient signal and contrast even using a relatively short TR of 100 ms. Figure 2a shows time courses of MR signals in different ROIs. Voxels corresponding to large arteries showed an early and large bolus-associated signal drop due to high blood content, and they also manifested greater signal fluctuation due to cardiac pulsation. The signal decrease in the gray and white matter occurred at a later time with a smaller amplitude (Figure 2a). Figure 2b shows a representative map of bolus arrival time. No laterality in arrival times was observed. Thus, the left and right ROIs were combined. The Gd-DTPA bolus arrived at the internal carotid arteries slightly before vertebral arteries (by 297 ± 233 ms, $P = 0.047$). δ_a was then calculated from the arrival time differences. Table 2 listed the δ_a values by tissue types and ROIs. One-way ANOVA revealed a significant difference in δ_a across vessel, gray and white matter. Post-hoc pair-wise comparisons also showed a pattern of increasing δ_a across these tissue types (corrected $P < 0.05$). Within the gray matter, a significant difference was observed across sub-regions ($P < 0.001$) with MCA territory having the shortest δ_a and thalamus having the longest δ_a . No differences in δ_a were observed across white matter sub-regions. The transit time from internal carotid artery to sagittal sinus was considerably longer, as expected (Table 2).

Figure 3a shows rCBF maps from SPECT and from PCASL using various models. Gray and white matter rCBF ratio from the ROIs is plotted in Figure 3b. The ratio using the simplified model was found to be significantly higher than that of SPECT (multiple-comparison-corrected $P < 0.005$), suggesting a potential estimation bias using this model. The one-compartment model, on the other hand, yielded results relatively consistent with the SPECT (paired t test, $P = 0.7$). Thus it seems that the use of the more comprehensive model is necessary for proper calculation of rCBF map. In addition, it was found that knowledge of δ_a in both gray and white matter is needed in order to avoid tissue-specific bias in the rCBF

map. When identical δ_a was used for gray and white matter (assuming 912 ms for both tissue types), the gray/white CBF ratio was considerably under-estimated ($P < 0.001$) (Figure 3b).

Scatter plots between SPECT and each of the PCASL rCBF maps are shown in Figure 4. The slopes for the fitting curves were 1.13, 1.04, and 1.01, respectively. The mean difference index, D , between SPECT and PCASL maps was 0.26, 0.27, and 0.29, respectively.

Figure 5 shows the results of voxel-wise statistical comparison between SPECT and one-compartment PCASL rCBF. It can be seen that, despite a general agreement between these two modalities, systematic differences are still present in certain brain regions.

Discussion

The present study aims to investigate model and parameter-related issues in PCASL quantification and to compare it to a radiotracer-based method. We first provided an estimation of an important kinetic parameter in ASL, the arterial transit time, for the white matter. Using these values for rCBF quantification, it was found that tissue-specific δ_a considerations can improve its correspondence to SPECT results and that the one-compartment model appears to provide a more accurate estimation of CBF compared to the simplified model. After accounting for these factors, the PCASL CBF maps were found to show good agreement with the SPECT method.

It is well known that arterial transit time is a key parameter in the calculation of CBF in ASL. Previous considerations on this topic have primarily focused on the gray matter, the transit time of which has been studied extensively with multi-delay continuous or pseudocontinuous ASL experiments and a range of values have been reported, e.g. Alsop et al. (~600 ms) (20), Ye et al. (~500 ms) (22), Gonzalez-At et al. (651–1200 ms) (21), Mildner et al. (~1600 ms) (23), Liu et al. (938 ± 156 ms) (24). Other studies have measured transit time in Pulsed ASL methods (43–46). The gray matter transit time obtained in this study (912 ± 209 ms) is in excellent agreement with a previous report using multiple delay times at similar slice locations (24).

For the white matter, our contrast agent approach estimated an averaged white matter transit time of 1541 ms, which is consistent with reports by van Gelderen et al. that the white matter transit time is 650 ms longer than that of the gray matter (47). Our values are longer than those measured with multi-delay methods, e.g. 350–1000 ms in Parkes and Toft. 2002, 700–1200 ms in Kimura et al. 2004, 1070–1490 ms in Qiu et al. 2010, and 990 ms in Kiziak et al. 2008. A possible reason for the discrepancy is that the gap between our labeling and imaging planes was 94 mm whereas the previous studies tended to use a smaller gap. Compared to previous contrast agent studies (47–49), we also used a higher temporal sampling rate (100 ms) which allowed the detection of small time differences across arteries and across sub-regions. For example, the Gd-DTPA bolus was found to arrive at the vertebral arteries later than internal carotid arteries, probably reflecting their differential vessel dimensions. The MCA perfusion territory was found to have an earlier bolus arrival compared to ACA and PCA regions, presumably again associated with the vessel sizes.

The simplified PCASL model assumes that T_1 decay of the labeling follows the relaxation of the blood, while in reality the decay is faster due to the shorter tissue T_1 . Thus, the use of the simplified model generally results in an under-estimation of the CBF weighted signals. Furthermore, because white matter T_1 is shorter than gray matter T_1 , the degree of under-estimation is greater for the white matter. Consequently, in terms of rCBF values, the gray matter is over-estimated while the white matter is under-estimated when the simplified model is used. In addition to the T_1 differences among blood, gray and white matter, the

time fraction in which the spins experience these T_1 's is also an important factor, which is determined by δ_a . If the longer white matter δ_a is not accounted for, white matter CBF signal would be over-estimated. Then, in the rCBF map, white matter rCBF values will be over-estimated and the gray matter values will be under-estimated.

Several previous studies have compared earlier ASL methods to PET (26,50,51) and to SPECT (52). A recent report also compared the PCASL technique to a $H_2^{15}O$ PET method (53). While both the present study and the earlier study demonstrated a correlation between PCASL and radio-tracer methods, they are different in a number of aspects. First, the study of Xu et al. did not account for transit time differences between the gray and white matter. Instead, a simplified model of Chalela et al. (31) was used for quantification which assumed identical T_1 values for blood and tissues. As shown in our results, the simplified model yielded less than optimal correspondence with the gold-standard method. Second, the sample size of the earlier study was relatively small and also included a mixture of patients and controls. Finally, the PET/PCASL comparison of Xu et al. was conducted in elderly subjects and the effect of brain atrophy on the validation results was not clear.

Our data suggest that PCASL quantification may benefit from using a more realistic model, in which the model parameters, e.g. T_1 , T_2^* , λ and δ_a , are varied on a voxel-by-voxel basis using assumed values for pure gray and white matter together with tissue probability from high-resolution T_1 -weighted image. One contribution of this work is the determination of δ_a in the white matter. However, we do not recommend the measurement of δ_a for each subject who undergoes ASL scan, because the procedure requires the use of exogenous contrast agent, which nullifies the advantage of the convenience of ASL. One can also divide the tissue into subregions (e.g. based on flow territory) and use region-specific (in addition to tissue-specific) δ_a values listed in Table 2. This strategy would, however, require additional assumptions on flow territory maps and would also be susceptible to errors associated with normal variations in cerebral arteries of the Circle of Willis (34). We also recognize that different slices may have different δ_a , thus the use of a single δ_a value for one tissue type cannot account for this variation. We note, however, that the across-slice differences (24) are expected to be smaller than the gray/white differences (47). In our opinion, a tradeoff strategy is to use model parameters based on tissue probability to achieve best possible estimation while acknowledging that systematic bias could still be present due to imperfection in model and parameter considerations (24,25,54–56).

The findings from the present study should be interpreted in view of a few limitations. First, the two components of the study were conducted on separate cohorts. Should the experiments be performed on the same subjects, the δ_a values obtained in the bolus-tracking study would have been more relevant for the PCASL quantification and an improved correspondence between PCASL and SPECT may be observed. The study will also benefit from a direct comparison between transit times determined with bolus-tracking and those from multi-delay ASL. Second, as the SPECT method used in the present study did not employ arterial sampling, it was not possible to obtain absolute CBF values. On the other hand, as stated at the beginning of this report, alternative methods are available for the relative-to-absolute conversion and the goal of the present study was to identify an optimal approach to estimate a relative CBF map. Another limitation is that our study has primarily focused on healthy control subjects, but no patient populations were included. Patients with cerebrovascular diseases may have longer arterial transit times (57). In these patients, a bolus-tracking transit time measurement is recommended for accurate CBF estimation. Alternatively, one can lengthen the post-labeling delay time (e.g. to 2.5–3 seconds) in ASL to ensure a full arrival of the labeled spins. This is, however, achieved at the cost of the SNR of the data. Finally, the calculation of rCBF used a number of assumptions based on

relaxation parameters in the literature (42,58,59). We have also tested to use values in other reports (60,61), and found that the findings were qualitatively comparable.

Conclusions

The present study determined arterial transit time in brain tissue using a bolus-tracking approach. White matter transit time was found to be significantly greater than that of the gray matter. The use of tissue-specific model parameters was helpful in improving the correspondence between PCASL and SPECT results. One-compartment PCASL model yielded more accurate estimation of rCBF, compared to a simplified model. Despite the need for further improvement in its quantification, PCASL-derived rCBF after accounting for transit time offers an excellent choice for a fast, convenient, and noninvasive measurement of perfusion in the human brain.

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Abbreviations used

PCASL	Pseudo-continuous arterial spin labelin
SPECT	Single Photon Emission Computed Tomography
CBF	cerebral blood flow
rCBF	relative cerebral blood flow
DSC	dynamic susceptibility contrast
ACA	anterior cerebral arteries
MCA	middle cerebral arteries
PCA	posterior cerebral arteries
ICA	internal carotid arteries

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Figure 1.

Representative images from the transit time study. (a) An illustration of slice locations. Two slices were acquired during each measurement of 100 ms. The lower slice was located 84 mm below the AC-PC line, corresponding to the labeling plane in PCASL. The upper slice was located 10 mm above AC-PC line corresponding to a typical imaging slice in PCASL. (b) An example of images of the upper slice before and after the arrival of contrast agent bolus. (c) An example of images of the lower slice before and after the arrival of contrast agent bolus. Red arrows indicate the internal carotid arteries.

Figure 2.

Bolus arrival times obtained from the transit time study. (a) Signal time courses in the internal carotid arteries (ICA), gray and white matter in a representative subject. The injection of the contrast agent took place at time 60 s. The signals have been normalized to the pre-contrast levels for each ROI. Large fluctuations in the ICA are associated with cardiac pulsation effects. (b) Map of bolus arrival time. The arrival time was shown in reference to the start of the scan. The ventricle regions did not yield reliable fitting. Thus, the values in ventricles were excluded from the display. A pre-contrast image is shown on the right panel for anatomical reference.

Figure 3. Comparison between SPECT and PCASL results. (a) Relative CBF maps using SPECT, PCASL with a simplified model, PCASL with a one-compartment model, and PCASL with one-compartment model using gray matter δ_a only, respectively. The images have been averaged across subjects (N=10). (b) Gray matter to white matter CBF ratio. The gray/white ratio with the simplified model was significantly greater than SPECT ($P<0.005$). That of the one-compartment model using gray matter δ_a only was smaller than SPECT ($P<0.001$). The results using one-compartment model with tissue specific δ_a were not different from SPECT ($P=0.74$). Error bars indicate the standard deviations across subjects.

Figure 4.

Scatter plot between group-averaged SPECT and PCASL rCBF maps. The rCBF maps were down-sampled to a voxel size of $10 \times 10 \times 10 \text{ mm}^3$ in accordance with their intrinsic spatial resolution. The color of the symbols represents the gray matter probability of individual voxel, demonstrating that the gray matter voxels are distributed in the upper right corner whereas the white matter voxels are clustered in the lower left corner. The black line indicates the fitted curve.

Figure 5. Brain regions showing significant differences between SPECT and PCASL rCBF maps. Voxels with $P < 0.001$ and cluster size $> 1.6 \text{ cm}^3$ are shown in color. Both positive and negative contrasts are shown.

Table 1

Parameter assumptions used in the one-compartment ASL model

	δ_a (ms)	T_1 (ms)	T_2^* (ms)	λ (ml/g)
Arterial blood	--	1664 ^b	--	--
Gray matter	912 ^a	1165 ^c	53 ^d	0.98 ^f
White matter	1541 ^a	750 ^c	47 ^e	0.86 ^f

^a determined in the transit time study^b Lu et al. (41)^c Lu et al. (59)^d Uh et al. (42)^e Wansapura et al. (60)^f Herscovitch et al. (58)

Table 2

Arterial transit times (in ms) of different brain regions (mean ± standard deviation).

Gray Matter				White Matter			Arterial Vessels	Venous Vessels
912±209				1541±173			425±119	4882±503
ACA	MCA	PCA	Thalamus	ACA	MCA	PCA		
959±206	805±190	1196±149	1685±277	1677±1022	1430±472	1634±347		

* ACA – anterior cerebral artery
* MCA – middle cerebral artery
* PCA – posterior cerebral artery