Estimation of Pure Gray Matter Perfusion using Pseudo-continuous Arterial Spin Labeling and Partial Volume Correction

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Introduction

It is well-known that the reported cerebral blood flow (CBF) values in the human brain depend on the spatial resolution of the techniques, i.e. partial volume effects (PVE) between gray matter (GM) and white matter (WM). With typical spatial resolution used in MR perfusion imaging, the number of 100% GM voxels is very small with folding cortical layers of about 2-4mm thick. Therefore it is important to take PVE into account for quantifying measured CBF in the human brain as well as for comparison to animal models with little PVE. Here a strategy is proposed to correct for PVE with arterial spin labeling (ASL) measurements using pseudo-continuous ASL (PCASL) (1, 2). First, sensitivity encoding (SENSE) is used with ASL to better register with anatomical volume fraction (VF) maps. Second, long post-labeling delay (PLD, w) is used with PCASL to compensate for GM transit time with whole brain coverage. Thirdly WM ASL signal is estimated using down-sampled VF maps per slice assuming long tag-tissue exchange time (T_{ex}) with the General Kinetic Model (3). Finally the GM CBF is obtained with the removal of WM ASL signal fraction and estimated with linear regression analysis assuming T_{ex} equals image acquisition time. This approach, opposed to using higher spatial resolution, provides sufficient SNR for PCASL measurements with long PLD and benefits from natural samples of a broad range of GM VF for linear regression analysis. In addition, mis-registration and errors in volume fraction estimation are more tolerable with lower spatial resolution.

Methods

Experiments were conducted on a GE 3T Excite scanner with a 16 channel receiver coil on 3 healthy subjects under approved protocols. Labeling tag widths (τ) of 2500ms were used with PCASL and w/TR=1700/4600 or 1900/4800 ms for a 10 min scan. Extra two repeated scans were performed on one of the subjects. Parameters for PCASL include 800 μs RF with 0.05 G amplitude and 0.8/0.06 G/cm maximum/mean gradient strength. 11 or 8 axial slices of 5mm/1mm gap covering the whole brain were acquired using EPI with SENSE 3 and TE=13.2 ms with a matrix size of 66x66. A MP-RAGE volume was obtained with 1mm^3 resolution. Programs BET and FAST from the FSL package (4) were used to derive VF maps for GM, WM, and CSF. Matching VF maps were generated with proper combining and in-plane bilinear down-sampling to EPI image resolution. EPI images of fully-relaxed signals and minimum contrast (5) were obtained for estimating the magnetization of blood (M_{0b}) in signal unit (6) and for normalizing inhomogenous receive fields of array coils, respectively. Fully-relaxed WM signal and WM CBF were derived from fully-relaxed images and PCASL pairwise-subtracted average images with WM VF>0.99, respectively. Since WM has long T_{ex}, for $T_{ex} > \tau+w$, $\Delta M_{wm}(\tau+w) = 2\ \alpha M_{0b}\ cbf_{wm}\ T_{1b} \exp(-w/\ T_{1b})(1-\exp(-\tau/\ T_{1b}))$ where ΔM_{wm} is WM ASL signal, α is tagging efficiency, cbf_{wm} is WM CBF, and T_{1b} is T_1 of blood (7). Once cbf_{wm} is known, ΔM_{wm} for each slice can be calculated and pure GM ASL signal can be estimated by $\Delta M_{gm} = (\Delta M_{all} - f_{wm}\ \Delta M_{wm})/\ f_{gm}$ where ΔM_{all} is total ASL signal, f_{wm} is WM VF, and f_{gm} is GM VF for each voxel. Assuming $T_{ex} = w$ for GM, cbf_{gm}, GM CBF, can be estimated from $\Delta M_{gm}(\tau+w) = 2\ \alpha M_{0b}\ cbf_{gm}\ T_{1gm} \exp(-T_{ex}/\ T_{1b})(1-\exp(-\tau/\ T_{1gm}))$ where T_{1gm} is T_1 of GM. From the literature, it is assumed that $\alpha = 0.8$ (8), $T_{1b} = 1664$ms (9), and $T_{1gm} = 1338$ms (10). Linear regression was performed for each slice between f_{gm} and $(\Delta M_{all} - f_{wm}\ \Delta M_{wm})$ to estimated 100% cbf_{gm}.

Results

Three slices of ASL images are shown in **Fig. 1** with w=1900 ms (top), together with GM VF maps (middle) and $f_{wm} > 0.7$ WM mask overlapped on the ASL images to show the alignments. Except some top and bottom slices and part of the frontal lobe area, the alignments are excellent. **Fig. 2** shows the linear regression of an example slice. The dotted red lines represent 95% confidence interval. The 'outlier' voxels in green are marked on the corresponding ASL image and are mostly on the edge of brain, most likely due to misalignments or errors in VF estimation due to incomplete removal of meninges and skull. The correlation coefficient (cc) of the linear regression and estimated pure GM CBF is shown in **Fig. 3**. The cc values are higher toward the middle of the slices consistent with the fact that the edge slices are less aligned. Lower cc values often accompany larger non-zero offsets where the regression line intersects y-axis, indicating improper accounting for residual signal mostly likely WM. The repeated scans on subject 1 are highly reproducible and the two PLD used show minimum difference, indicating the PLD is mostly sufficient long. Without the WM VF correction, the cc values decrease significantly. Moreover, the cc values can be increased to about 0.9 by masking out the 'outlier' voxels outside the 95% confidence intervals. The mean 100% GM CBF is 107±12 ml/100 ml/min from slices with cc>0.7 and the 100% WM CBF is 13±1 ml/100 ml/min.

Discussion and Conclusion

Highly correlated data demonstrate the power of this approach with typical low spatial resolution images. It takes advantage of the fact that 100% WM voxels are readily available and are mostly contiguous and less prone for mis-alignment. With sufficient long PLD for GM and the assumed long T_{ex} for WM, the perfusion quantification is simplified and less dependent on the accuracy in estimating T_{ex}. Although it is assumed that the tag for WM is still in the vasculature, the estimate can be close if the tag is already in the perfused voxels, a reasonable assumption for large voxels. If the estimated WM CBF is correct, the ratio of GM/WM perfusion becomes 8:1 with the correction for PVE. The identification of 'outlier' voxels can potentially be a mean to detect GM tissues with abnormal perfusion and may ultimately provide diagnostic purposes. It may also provide insight into the relationship of PVE and high perfusion measurements in young children. In conclusion, we have demonstrated a way to quantify ASL CBF in the human brain and estimate pure GM perfusion with robust performance.

References

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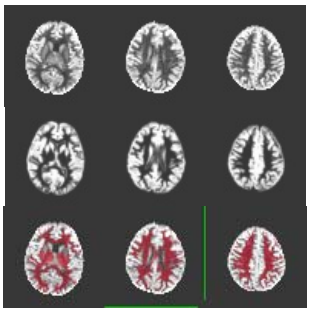

Fig. 1. ASL images (top), VF maps (middle), and WM mask overlapped (bottom).

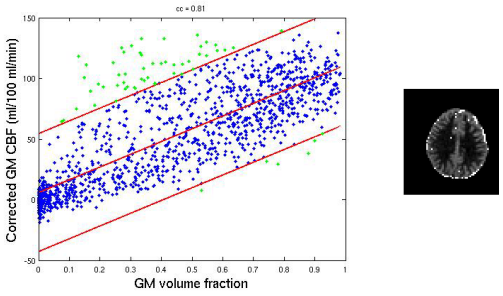

Fig. 2. Linear regression of an example slices. The 'outlier' voxels (green) are shown as bright marks in image (right).

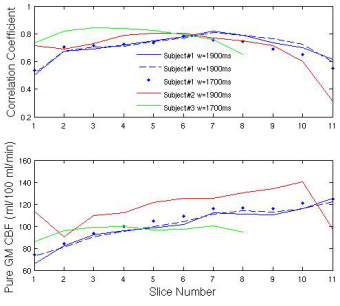

Fig. 3. The correlation coefficient (cc) and estimated pure GM CBF.