Constraints in Absolute Quantification of Cerebral Blood Flow Using Arterial Spin Labeling fMRI

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Introduction:
Voxel tissue heterogeneity affects quantification of CBF as measured with arterial spin labeling MRI through: 1) partial volume effects (PVE), and 2) conversion of ASL raw signal (%) to units of CBF (mL/100g*min). Recently, a linear regression method that yields pure, tissue-specific CBF images independent of voxels' tissue content has been developed[1]. The regression coefficients are based on voxel tissue factional volumes obtained via the segmentation of a high resolution structural image.
The purpose of this study was to investigate the effects of tissue segmentation and voxel heterogeneity on quantification of CBF using ASL MRI. The advantages and pitfalls of using the PVE-correction method over the conventional ASL in detecting of focal changes in CBF were also investigated.

Methods:
MPRAGE (TR/TE=6.7/3.1ms, FA=8°, TI=0.8s, resolution=.8x.8x.9mm^3) were acquired on 8 subjects (age=25.2 ± 4.1 years, 3 males) on a 3T Philips scanner. To investigate the effect of image modality on tissue segmentation, on one subject an additional structural image, SPGR (TR/TE=25/1.9ms, FA=30°, resolution=.9x.9x.9mm^3), was acquired. These images were then used to obtain gray matter (GM), white matter (WM) and CSF tissue posterior probability maps (P_{GM}, P_{WM}, P_{CSF}) using SPM5's unified segmentation algorithm. Simulation: (1) CBF images were simulated as follows: CBFnet=(P_{GM}*f_{GM})+(P_{WM}*f_{WM}), where f_{GM} and fWM denote GM and WM CBF assumed 107 and 28 mL/100g·min, respectively[1], with P_{GM}, P_{WM}, and P_{CSF} obtained via segmentation of MPRAGE and SPGR, independently. (2) SE EPI ASL control images (resolution=3.5x3.5x8mm^3) were simulated assuming tissue magnetization ratios: m_{CSF}:m_{GM}:m_{WM}=1.7:1.2:1.0[1]. The label images were simulated to represent the same flow baselines as in (1). A 15% ΔCBF activation was simulated with activation kernel = 5x5x1 voxels centered at various locations across the brain. EPIs were analyzed to yield CBF images using both the conventional and the PVE-correction method with varying regression kernel sizes[1].

Results:
Fig.1 shows the effect of image modality used for tissue segmentation on quantification of CBF. The two segmentation outputs resulted in a voxelwise CBF difference of -79 to +79 mL/100g·min across the brain. The effect was more pronounced in cortical regions and less severe in deep white matter (Fig.1C). Fig. 2 demonstrates the effect of inter-subject variability in tissue content when the same image modality was used for tissue segmentation. The effect of spatial smoothing caused by PVE-correction algorithm is shown in Fig 3A for various regression kernel sizes. The number of voxels incorrectly appearing as 'activated' due to the smoothing effect = $[(n+N-1)^2-n^2]$ where n and N denote the length of the activation and regression kernels, respectively (Fig.3B).

Conclusions:
1) For a given subject, quantification of CBF using ASL perfusion MRI was confounded by the modality of high-resolution image used to obtain voxel-wise tissue fractional volumes. 2) Inter-subject variability in GM, which could reflect a true physiological distribution in GM content across the population or a confound of image processing, affects the overall measured variability in ASL CBF. 3) PVE-corrected ASL is superior to the conventional method in detecting activation ΔCBF.

References:
Asllani, I (2008), 'Regression Algorithm Correcting for Partial Volume Effects in Arterial Sin Labeling MRI', *Magnetic Resonance in Medicine*, vol. 60, no. 6, pp. 1362-1371.

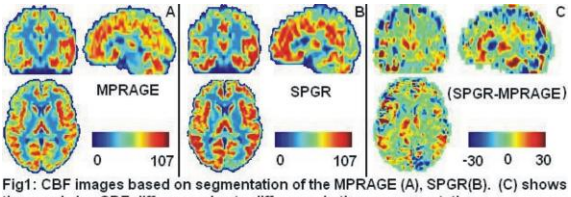

Fig1: CBF images based on segmentation of the MPRAGE (A), SPGR(B). (C) shows the voxelwise CBF difference due to difference in tissue segmentation.

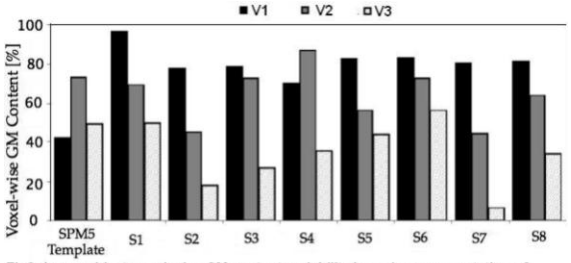

Fig2: Inter-subject voxel-wise GM content variability based on segmentation of MPRAGE images using SPM5's segmentation algorithm. V1, V2 and V3 represent voxels in the MNI space[3.5,0,-16],[-3.5,-31.5,-8], and [7,-24.5,-40], respectively. Data are compared with the GM content in the SPM5 template.

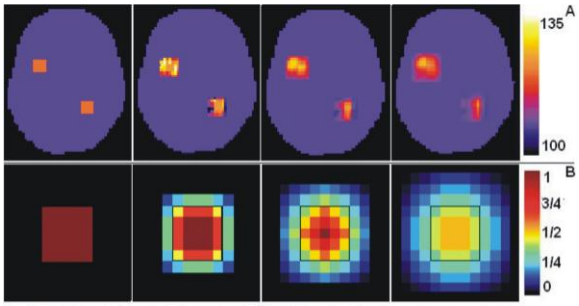

Fig3: (A) Effect of smoothing on a 15% CBF activation kernel centered at two spatially distinct voxels ([-35,3.5,8] PGM=0.8, PWM=0.15, PCSF=0.05 and [28,-52.5,8] PGM=0.39, PWM=0.39, PCSF=0.22) and analyzed with varying regression kernel sizes, 3x3, 5x5 and 7x7, left to right, respectively. Note that spatial smoothing effect of activation depends on the local tissue distribution. The theoretical activated region is shown on the leftmost pannel. (B) Shows fraction of regression kernel voxels overlaing with the activated ROI at various locations.