Correcting for Partial Volume Effects in Arterial Spin Labeling Perfusion Imaging of Alzheimer's Disease

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INTRODUCTION Several imaging studies have suggested a strong link between resting cerebral blood flow (CBF) and neuropathological changes associated with Alzheimer's disease (AD)[1,2]. However, partial volume effects (PVE) are a potential confound on the quantitative interpretation of these results. PVE can be particularly problematic in elderly populations due to brain atrophy that occurs with aging. While arterial spin labeling (AS) offers several advantages over the other perfusion imaging methods, its its signal dependency on PVE is more complex because the measured signal is a ratio of two images, each of which is affected by voxel heterogeneity3. We have recently developed a linear regression algorithm that corrects for PVE in ASL imaging. The primary goal of this study was to compare PVE-corrected, *pure* gray matter, CBF images obtained from AD, mild cognitively impaired (MCI) and healthy controls (HC) using (ASL) perfusion MRI.

METHODS ***Participants***: ASL CBF images were obtained from three groups: AD (N=12, 7 males, age 70.9±9.2 years), MCI (N=13, 7 males, age 72.4±8.1 years) and HC (N=38, 18 males, age 68.6 ± 6 years). HC were recruited from family members and advertisements. For the AD group, the modified Mini Mental State score was 39.3 ± 10 and CDR 1.2 ± 0.42.. IRB approved consent was obtained from all subjects. ***Imaging acquisition***: (The following images were acquired on all subjects: (1) Single shot spin-echo EPI CAS were acquired on all subjects with: TR/TE/FA = 4s/36ms/90º, 15 slices, FOV=220 ×198 mm, matrix 64 × 51, slice thickness/gap = 8mm/1mm, labeling duration = 2000ms; post-label delay = 800ms. (2) 3DT1 SPGR structural images: TE/TR/FA = 3 ms/34 ms/45º; 100 slices, FOV = 240 × 240 mm; matrix = 256 × 256; slice thickness/gap = 1.5mm/1mm. ***Image Preprocessing***: (1) ASL control and label images were motion corrected to the first acquired image and registered to SPGR using SPM5. (2) SPGR was segmented to generate GM, WM, and CSF fractional volume maps. (3) SPGR and tissue fractional volume maps were coregistered to the EPIs. ***Partial Volume Correction***: A detailed treatment of the underlying theory and methodology of the PVE correction algorithm is given in Asllani et al.[3]. The linear regression algorithm estimates the pure tissue signals by modeling the voxel magnetization as a weighted sum of contributions from GM, WM, and CSF, and the ASL difference signal as a weighted sum of the GM and WM flow contributions. The weighting coefficients in both cases are the tissue's fractional volume obtained from posterior probability maps[3]. For each subject, linear regression was performed in subject's native space using a regression kernel size = 11x11x1 voxels and 5x5x1 voxles for control and difference ASL images, respectively[3].

RESULTS: The novelty of our method is it yields *pure*, tissue-specific 'flow density' maps. Assuming that for a given person, tissue 'flow densities' don't vary substantially across the brain, one would expect spatial distribution of these *pure* flow maps to be relatively homogenous. This expectation is qualitatively borne out in Fig.1 (2nd row) where GM flow density is quite uniform and relatively independent of the voxels's GM content in both groups. Furthermore, visual inspection shows a marked decrease in flow density in AD (Fig.1, 2nd row). Results from the ROI-analysis are shown in Fig.2. While the CBF difference between HC and AD was significant in all ROIs ($p<0.005$, $\alpha=0.05$, for all), for HC-MCI contrast, significant differences were found in the pulvinar, cingulate gyrus, and middle frontal gyrus ($p<0.01$ at $\alpha=0.05$, for all). Fig.3 shows the effect of PVE in voxelwise analysis of HC-AD contrast.

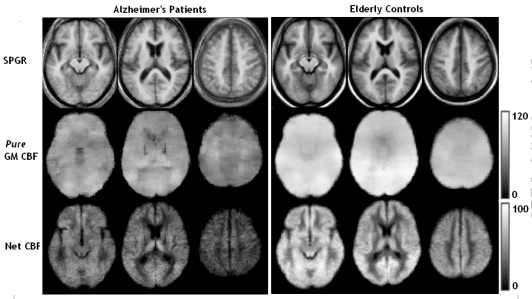

Fig.1: Images of group mean SPGR (1st row), pure GM CBF (2nd row), and net CBF image (3rd row) are shown for AD (left panel) and HC (right panel). Note the overall lower intensity of CBF in AD patients as compared to the age-matched HC. Also, note that pure GM CBF maps are independent of GM fractional volume at a given voxel thus reflecting voxel's GM flow density.

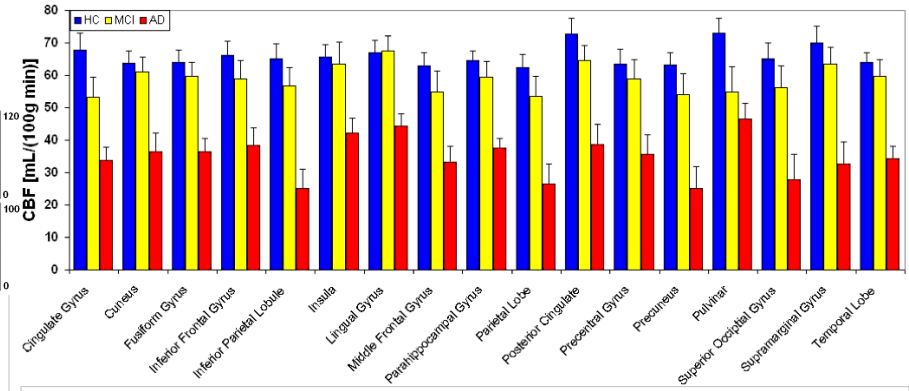

Fig2: ROI-wise average CBF values for HC, MCI, and AD are shown in bleu, yellow, and red, respectively. Bars represent ± s.d.

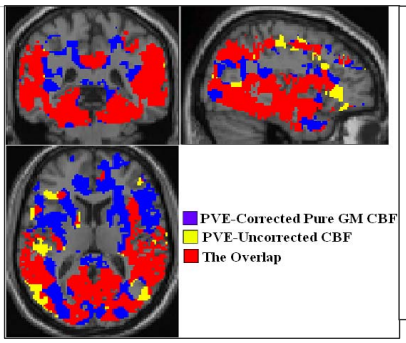

Fig.3: SPM{T} masks for HD-AC contrast ($p_{uncorrected}<0.001$). PVE corrected CBF images yielded larger areas (blue) than uncorrected (yellow) of decreased perfusion in AD as compared to HC. Overlap is shown in red.

DISCUSSION**:** We have demonstrated the utility of a PVE correction algorithm for quantification of tissue specific ASL CBF thus excluding the effect of brain atrophy in the data. A larger underestimation in CBF with the conventional method was found in the AD implying the presence of more brain atrophy in this group as compared to their age-matched counterpart. However, more work is needed to correlate the spatial distribution of the atrophy with the pattern of CBF depression.

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REFERENCES**:** [1] Alsop et al., *Neuroimage 42(4)* 2008 [2] Asllani et al. JCBFM 28(4) 2008 [3] Asllani et al. MRM, in press.

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