Comparison of Quantitative DSC and ASL Perfusion Methods in Human Subjects at risk for Alzheimer's Disease

G. Xu[1,2], Z. Wen[3], C. M. Carlsson[1,2], S. C. Johnson[1,2], D. Alsop[4], H. Rowley[5], W. Shin[6], T. Carroll[6], and S. B. Fain[3,5]

[1]Medicine, Univ. of Wisconsin - Madison, [2]GRECC, Madison VA Hospital, [3]Medical Physics, Univ. of Wisconsin - Madison, Madison, WI, United States, [4]Radiology, Harvard Medical School, [5]Radiology, Univ. of Wisconsin - Madison, Madison, WI, United States, [6]Biomedical Engineering, Northwestern University, Chicago, IL

Introduction:
MR perfusion imaging is being increasingly used to study *quantitative cerebral blood flow* (*qCBF*) changes in regions of the brain affected in Alzheimer's disease (AD) (1). Since brain perfusion is tightly correlated to brain metabolism and cognitive function, it is desirable to quantify baseline CBF in subjects with high risk for developing AD, and to monitor their CBF changes longitudinally. CBF and cerebral blood volume (CBV) can be simultaneously quantified using recently developed quantitative dynamic susceptibility-weighted contrast (DSC) enhanced imaging methods (2). Another potential MR method to determine qCBF is arterial spin labeling (ASL) that uses magnetically labeled blood water as an endogenous tracer. The purpose of the current study is to compare and evaluate qCBF measurements using both DSC and ASL methods in an asymptomatic group of adults at risk for AD.

Methods & Materials:
Asymptomatic middle-aged adult children of persons with AD (n=14, 10 women, age 55±8 yrs) were recruited for a statin intervention trial. Complete baseline data sets from 11 subjects are reviewed here. MR exams were performed on a 3T GE Signa scanner using a quadrature head coil. ***DSC MRI*** was performed using GRE-EPI (TR/TE/flip: 2 ms/60 ms/60o, BW = +/- 64kHz, 128 X 64 matrix over a 24X24X10 cm FOV covering the whole brain in 12 slices. Data were acquired after bolus injection of 0.1 mmol/kg Gadodiamide (Omniscan, Princeton NJ). A T1-Look-Locker sequence was played out before injection and after contrast agent concentration reached steady-state (i.e. bookend acquisition). The DSC data were processed using custom software for arterial input selection and a qCBF map was obtained by multiplying a correction factor determined from the ratio of the post- and pre- contrast T1values according to (2). ***ASL MRI*** was performed using a background suppressed pseudo-continuous arterial spin labeling (*PCASL*) sequence with a stack of variable density spiral 4ms-readout and 8 interleaves for a 48x64x48 matrix over 18x24x18 cm FOV. The continuous labeling was performed with a modification (3) of a published (4) method for multi-slice spin labeling with a single coil that virtually eliminates off-resonance errors. A labeling RF amplitude of 0.24 mG, a gradient amplitude of 1.6 mT/m, labeling duration 1.5s and post labeling delay of 1.5s were employed. Three ASL scans were averaged for the perfusion-weighted images. Equation 1 was used for the CBF quantification where ρ_b is the density of brain tissue, 1.05g/ml, α is the labeling efficiency 95% for labeling times 75% for background suppression, w is the postlabeling delay, 1.5s, tl is the labeling duration, 1.5s, $T1_a$ is the T1 of arterial blood, 1.6 s, ω_a is the density of water in blood, 0.85 g/ml, and S_l and S_c are the signal intensities in the labeled and control images, respectively. *C* is calculated from a low-resolution sensitivity map performed separately that equals the fully relaxed MRI signal intensity produced by one gm of water per ml of brain.

$$CBF = \frac{\rho_b (S_c - S_l)}{2\alpha C \omega_a T1_a \exp\left(-\frac{w}{T1_a}\right)\left(1-\exp\left(-\frac{tl}{T1_a}\right)\right)} \quad (1)$$

Analysis: Both DSC and ASL *qCBF* images were first coregistered to the standard Talairach template in AFNI software and then smoothed with 10mm Gaussian kernel. All subjects' qCBF data from both methods were averaged with the predefined ROIs in Talairach daemon including bilateral hippocampus (Hippo), parahippocampus (PH), posterior cingulate (PC), precuneus & superior parietal lobule, middle temporal gyrus (MTG) and superior frontal gyrus (SFG). Whole brain white matter (WM) and grey matter (GM) tissue masks generated based on standard T1 anatomical images from FSL software were also used to evaluate whole brain qCBF images.

Results: Series of representative ASL and DSC qCBF images from one subject are shown in Figure 1 A & B. Group averaged qCBF maps from ASL and DSC are shown in Fig 1 C&D**.** All the regional averaged qCBF values are shown in Fig 2 for each method. The qCBF values from ASL methods across all ROIs are larger than those with the DSC method (paired *t-test, $p < 0.01$*). Averaged GM and WM qCBF values of all the subjects from both ASL and DSC methods are plotted in Fig 3. Linear regression analysis reveals high correlation in both GM and WM (*$p<0.01$*) between the values measured by these two methods.

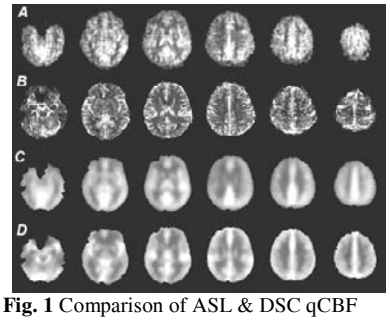

Fig. 1 Comparison of ASL & DSC qCBF images. **A & B.** representative ASL and DSC qCBF maps from one subject, respectively; **C & D.** Averaged ASL and DSC qCBF maps over all subjects, respectively.

Discussion & Conclusion: Trends in the regional perfusion data were similar between ASL and DSC results (Figs 2 and 3). However, DSC flow measures were consistently lower than ASL-derived values over all brain regions. The CBF in the posterior cingulate showed the largest difference between two methods (*$p < 0.0001$*). Such a pattern is suggestive of systematic differences in the perfusion quantification with different methods, likely related to modeling assumptions and normalization schemes. Future work comparing these new methods to a more widely accepted standard such as microspheres is needed. In conclusion, the current study shows quantitative CBF images can be reliably measured with both DSC and ASL approach. The discrepancy in CBF values from DSC and ASL methods may originate from various sources such as proper selection of arterial input function, T_1 values in the quantification model, assumption of water-exchange time between tissue and vessels, etc. Future longitudinal qCBF measurements with both DSC and ASL would provide more information about both methods' test-retest reliability/repeatability and their potential in clinical applications such as AD prevention models.

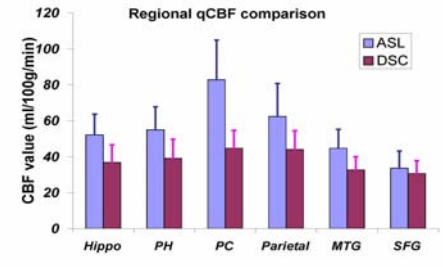

Fig. 2 Comparison of averaged qCBF values obtained by ASL and DSC methods across ROIs.

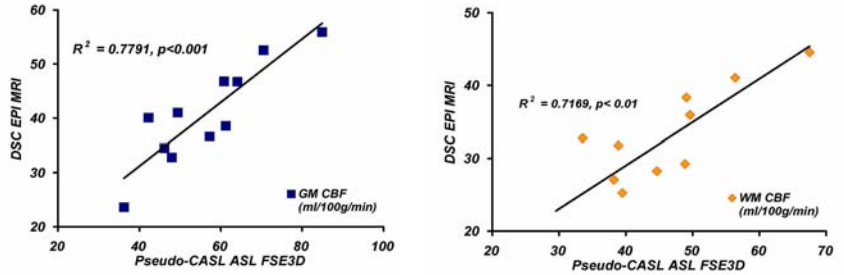

Fig. 3 Correlation between GM and WM qCBF values obtained by pseudo-CASL FSE3D sequence and DSC EPI sequence across all subjects.

Reference:
1. Alsop DC et al, Ann Neurol. 2000 Jan;47(1):93-100.
2. Shin et al, MRM 2005, 56:138-145.
3. Garcia DM et al, 13th ISMRM Miami 2005 p 37.
4. Alsop DC et al, Radiology 1998;208(2):410-416.

Acknowledgements: NIH R01 AG21155, Merit Review grant from the Department of Veterans Affairs, Wisconsin Comprehensive Memory Program Alzheimer's Disease Pilot Project and the University of Wisconsin GCRC NCRR grant M01 RR03186.