# Cerebral blood flow in Alzheimer's disease by Arterial Spin Labeling QUASAR

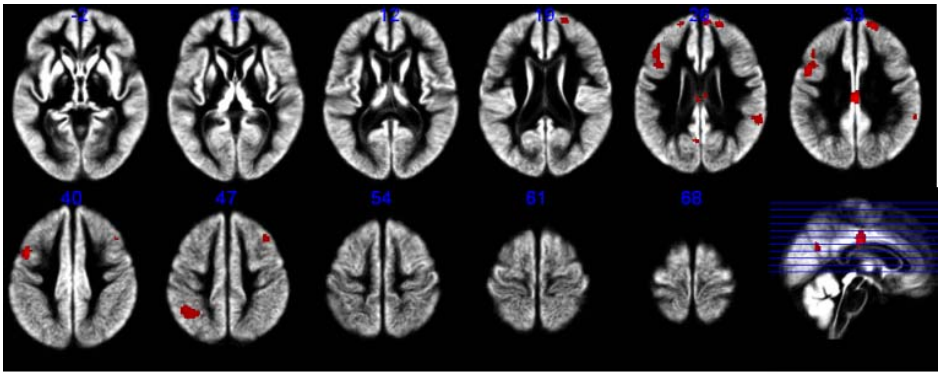
**H. Mak[1], Q. Chan[2], Z. Zhang[1], E. Petersen[3], D. Qiu[1], X. Golay[4], and L-W. Chu[5]**

[1]Diagnostic Radiology, University of Hong Kong, Hong Kong, Hong Kong, [2]Philips Healthcare, [3]Clinical Imaging Research Centre, National University of Singapore, Singapore, Singapore, [4]UCL Institute of Neurology, Univeristy College of London, United Kingdom, [5]Medicine, University of Hong Kong, Hong Kong

Background:
Arterial Spin Labeling (ASL) is quantitative and effective in detection of cerebral blood flow abnormalities in Alzheimer's disease (AD) [1]. Here, we attempt to employ the QUASAR ASL pulse sequence [2,3] to compare whole brain cerebral blood flow (CBF) in AD and cognitively normal elderly subjects in a Chinese population. Currently, there is no definite diagnostic biomarker for the assessment of AD. Earliest 18-fluoro-deoxyglucose positron emission tomography (18F-FDG-PET) found hypometabolism affecting the temporal and parietal association areas [4]. As glucose metabolism is thought to be directly related to cerebral blood flow [5], we employ ASL as an indirect marker of glucose metabolism in patients with AD and compare them to normal elderly subjects. The utility of ASL in distinguishing various stages of AD from amnesic mild cognitive impairment (MCI) preceding dementia to fully developed dementia for prognostication, selection and monitoring of treatment is also of clinical importance.

Method:
13 patients with AD and 15 normal elderly subjects had Magnetic Resonance Imaging (MRI) scans on a 3.0T Philips Achieva scanner. The QUASAR sequences consisted in a Look-Locker-based EPI sequence with the following parameters: TR/TE 4000/22 ms, FOV 240 mm, Matrix 64 x 64, $\alpha = 35°$, 7 axial 6mm slices with 2mm gap, labeling slab = 150 mm, with a gap to the closest slice of 15mm. The first image was acquired at a delay of 40ms, while 13 consecutive time points were measured at intervals of 300ms; thus yielding ten time points ranging from 40 up to 3640ms. In order to cover the whole brain, two separate blood flow acquisitions were obtained, with overlap of 1 slice. The ASL data were analyzed using institutional specially-designed software to calculate the CBF and R1 map. The preprocessing and statistical analyses were carried out with SPM5 (statistical parametric mapping software, Wellcome Trust Centre for Neuroimaging, London, UK) implemented in MATLAB (Mathworks Inc., Natick, MA, USA). Preprocessing included co-registration, and normalization to the standard space of the Montreal Neurological Institute (MNI) brain. R1 map was co-registered with the T1W images, followed by spatial normalization. The normalization parameters derived were applied to the CBF maps of the same subject. For creating a single CBF map of the upper and lower stacks, a scaling factor was introduced to adjust their differences due to position of saturation band and scanning area. The CBF maps were then spatially smoothed with an isotropic 8mm full width at half maximum (FWHM) Gaussian filter. Two-sample Student's *t*-test (one-sided) was performed on normalized CBF maps between AD subjects and their controls using SPM5, including covariate with gray matter, extent threshold at 15 voxels, threshold at $P<0.01$ uncorrected for multiple comparisons.

Findings:
The average age and MMSE scores of the case and control groups were 75.3 (SD+/-6.75) & 70.8 (SD+/-5.99) years and 16.3 (SD+/-4.55) & 28.4 (SD+/-1.99) respectively. There is no significant difference in age (p=0.068) but significant difference in MMSE score between the 2 groups.




There are significant decreases in CBF in AD as compared to cognitively normal elderly controls (after adjustment for gray matter volumes) in the following regions (highlighted as red colour in figure) i.e. middle & posterior cingulate, bilateral inferior frontal, bilateral superior frontal, right inferior parietal and left superior temporal gyri.

Discussion:
Using QUASAR ASL, we found significant decrease in regional CBF in our local cohort with moderate AD (MMSE 16.3). Findings showed a characteristic distribution of impaired perfusion, analogous to previous PET studies showing hypometabolism in the angular gyrus [4], posterior cingulate and precuneus [6], frontolateral association cortex [7] of patients with early and moderate AD. A recent study using ASL (DIPLOMA-II) found different patterns of hypoperfusion in distinct subgroups of MCI, further suggesting that cognitive impairment is related to cerebral hypoperfusion [8]. Functional MRI (fMRI) is a promising tool in assisting diagnosis and prognosis in AD, MCI and at risk population. A reduction of functional activation in the mesial temporal lobe and temporal parietal regions has been demonstrated on a variety of memory tasks [9]. Conversely, lateral frontal activity has been shown to increase in AD patients during verbal retrieval, suggestive of under recruitment compensatory mechanism [10]. As compared to PET, ASL uses electromagnetic labeling of the naturally occurring water in the blood to acquire images sensitive to flow, it is non-invasive and can be used to monitor drug responses by repeated scanning. ASL is also more versatile than fMRI, as it does not require any task performance. In summary, QUASAR ASL may be a useful adjunct for prognostication and monitoring of therapeutic intervention in AD.

References: [1] Alsop DC et al. Ann Neurol 2000; 47:93-100. [2] Petersen ET et al, MRM 2006;55: 219-32. [3] Petersen ET et al, Proc. ISMRM 2007; #2688. [4] Benson DF et al, Arch Neurol 1983; 40: 711-14. [5] Sokoloff L et al. J Neurochem 1977; 28: 897-916. [6] Minoshima S et al. Ann Neurol 1997; 42: 85-94. [7] Salmon E et al. J Nucl Med 1994; 35: 391-98. [8] Chao L et al. Alzheimer Dis Assoc Disord 2009; 23: 245-252. [9] Smith CD et al. Neurology 1999; 53: 1391-96. [10] Grady GL et al. J Neurosci 2003; 23: 986- 93.