# DETECTING AGE-RELATED CHANGES IN RESTING CBF USING CASL MRI

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**INTRODUCTION** Even in the absence of Alzheimer's Disease and other recognized brain diseases, aging is associated with impairment in several brain functions[1,2]. While the underlying mechanisms of these functional changes are still under investigation, hypoperfusion has been recognized as an important factor[3]. Typically, studies of brain perfusion have relied on PET and SPECT imaging methods, which, in addition to high cost and low availability, require injection of exogenous radioactive tracers that are uncomfortable and potentially harmful. Continuous arterial spin labeling (CASL) is a non-invasive, feasible and cost-effective MRI technique that provides absolute quantification of CBF with reproducibility, resolution and contrast comparable to PET[4]. The goal of this ongoing study is to quantify and map-out changes in baseline CBF due to normal aging.

**METHODS** ***Subjects*** **-** Resting CBF images from a group of young subjects (n=11, age= 27 ± 3 years, 4 males) were compared with those from a group of healthy elderly (n=12, age= 71 ± 7 years , 5 males). All elderly subjects were classified as non-demented and without serious cognitive impairment. Written consent was obtained as approved by the institutional IRB. ***MRI-*** Images were acquired on a 1.5T scanner (Philips) using a standard transmit-receive coil. SE-EPI CASL images were acquired with: TR/TE=4s/36ms, θ=90º, FOV=220x198 mm$^2$, acq. matrix=64x58, 13 slices (8mm/1mm-gap), post-labeling delay (PLD) of 800ms, and slice acq. time 64ms. Adiabatic inversion of water spins and correction for off-resonance effects were achieved as per Alsop *et al.*[5]. The labeling plane was positioned 100mm inferior to the center of the imaging volume. 30 control/label pairs were acquired for each subject. A high resolution, 3D T1 (SPGR): TE/TR=3 ms/34 ms, θ =45°, 100 slices (1.5mm/1mm-gap), FOV=240x240mm$^2$, acq. matrix=256x256, was also acquired in each subject. All EPI images were motion corrected, co-registered to the corresponding SPGR, and spatially normalized to MNI standard space using SPM99. Each control-label pair yielded a % signal change image and a CBF image, using the formula of derived by Alsop *et al.*[5] but correcting for slice-dependency of PLD. ***Analysis –*** Voxel-by-voxel *t*-statistic ($\alpha_{uncorrected}$=0.001) was calculated using SPM99. Region based analysis was done on ROIs obtained from published atlas[6]; these ROIs were selected due to their known involvement in aging of the brain[1,2]. Only voxels with posterior probability of gray matter, P[GM] > 0.8 were included in the ROI analysis.

**RESULTS** ***Voxelwise analysis –*** SPM{T} maps ($\alpha_{uncorrected}$=0.001) for the voxelwise CBF contrast (Young -Elderly) presented in Fig.1 show areas of CBF depression in elderly in the frontal and temporal regions in good agreement with their involvement in functional aging of the brain[1,2]. The largest significant group-difference was found in the Middle Temporal Gyrus (T=6.99, MNI position [66, -50, 0].) ***ROI analysis*** –Average CBF values for each ROI are shown in Fig.2 in blue and red for young and elderly, respectively. For simplicity, only left hemisphere ROIs are shown; there was no effect of brain laterality. The largest group-difference in CBF was found in Left Precuneus (31.5 mL/100g*min) and Sup. & Mid. Frontal Gyrus (28 mL/100g*min), representing a 32% CBF decrease in elderly in both cases. Except for hippocampus, all other ROI CBF differences were statistically significant ($p<0.05$ at $\alpha$=0.05). Globally, GM CBF in elderly and youngs were 68.8 and 90.5 (mL/100g*min), respectively, representing a 24% difference due to age (one-tailed *t*-test, $p<0.00001$, $\alpha$=0.05). Fig.3 shows a graph of global GM CBF vs. age. GM CBF was found to decrease at ~ 0.49% per year, in very good agreement with PET data[7] and a previous ASL study by Parkes et al., which reported a decrease of 0.45%[8].

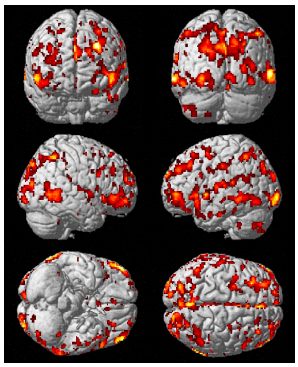

**Fig.1**: SPM{T} maps thresholded at T=3.5 (p<0.001, uncorrected) for CBF (Young-Elderly)

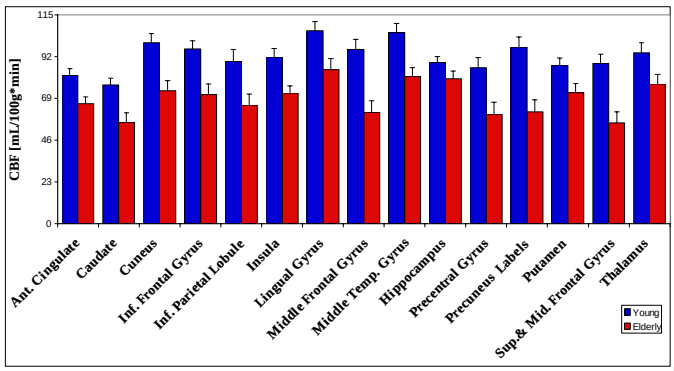


**Fig. 2**: ROI group average CBF for young (blue) and elderly (red). Error bars represent s.e.

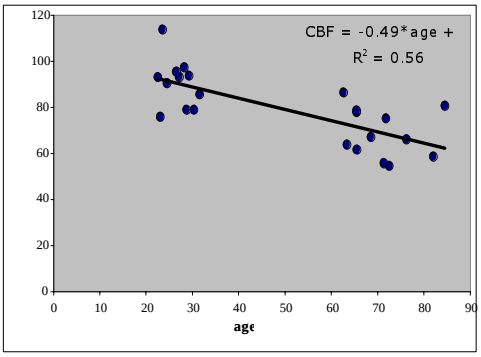


**Fig.3**: Graph of global GM CBF vs. age. Solid line represents the best fit.

**DISCUSSION:** Both voxelwise and region-based analysis of CASL CBF images showed marked decrease in elderly in areas of the brain such as prefrontal cortex, caudates, and thalamus involved in impairment of verbal, visual, and language processing associated with normal aging. Globally GM was found to be ~ 24% lower in elderly. The results presented here are in good agreement with data from quantitative PET, which indicates an independence of findings on the image modality employed thus pointing toward an underlying true physiological effect of aging. However, both PET and ASL suffer substantially from partial voluming effects. Although care was taken in this study to include only voxels with P[GM] >0.8, it is quite possible that the overall CBF decrease observed is at least partially due to brain atrophy associated with normal aging, which would exacerbate the effects of partial voluming present in CBF imaging. These effects could explain some of the inconsistencies that have been observed in perfusion studies of brain aging, with several studies reporting no change[9]. Future work is needed to investigate the effects of partial voluming in the age-related CBF imaging.

**REFERENCES: 1**. Beason-Held LL et al., *Neurob. Aging* (2006), **2.** Zarahn E. et al., *Neurob Aging 28 (2007)*, **3.** Bentourkia et al., *J Neurol Sciences 181* (2000), **4.** Golay X et al., *Top Magn Reson Imag.* 15 (2004).), **5.** Alsop DC & Detre JA, *JCBFM*, 16(6) (1996), **6.** Maldjian JA et al., *Neuroimage 21* (2004), **7.** Leenders KL et al., Brain 113 (1990), **8.** Parkes L. et al., MRM 51 (2004), **9**. Biagi L. et al., *JMRI 25* (2007)