A Pipeline for ASL Quantification and Regional Statistical Analysis: Application to Young Onset Alzheimer's Disease. *Jack Highton (UCL), Dr Jonathan Schott (UCL), Dr Enrico De Vita (KCL), Dr David Thomas (UCL)*

Arterial Spin Labelling (ASL) is a non-invasive MRI method to measure cerebral blood flow (CBF) with great potential to assist in early dementia diagnosis – which may allow emerging pharmaceuticals to be administered earlier with greater effect. However, difficulties in quantitative consistency frustrate the definition of robust ASL biomarkers. Here, raw ASL data acquired from patients with Young Onset Alzheimer's Disease (YOAD) was analysed, using a pipeline optimised for the particular acquisition protocol and a novel statistical approach.

Method The YOAD cohort consisted of 28 patients with typical AD, 14 with posterior cortical atrophy (PCA), and 24 control subjects. ASL images were acquired using a multi-shot 3D GRASE PASL sequence with with the following parameters: matrix size=64x64x30; resolution=3.8x3.8x4mm; TI1=800ms; TI2=2000ms - alongside 5s saturation recovery images with the same readout scheme to allow CBF quantification. 1mm isotropic resolution T1-weighted MPRAGE images were acquired for structural information. These were used along with a novel registration pipeline to handle the opposite contrast properties of T1-weighted and saturation recovery images. CBF maps were segmented into eight major grey matter brain regions to compare regional differences in patients and controls.

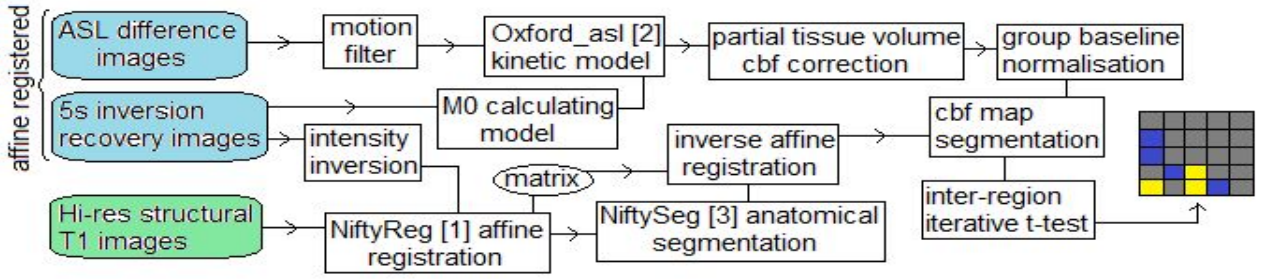

Figure 2 - A summary of the image processing pipeline.

Results

Key				
	1 Frontal Lobe	**3** Parietal Lobe	**5** Insular Lobe	**7** Hippocampus
	2 Temporal lobe	**4** Occipital Lobe	**6** Limbic Lobe	**8** Basal Ganglia and Ventral Diencephalon

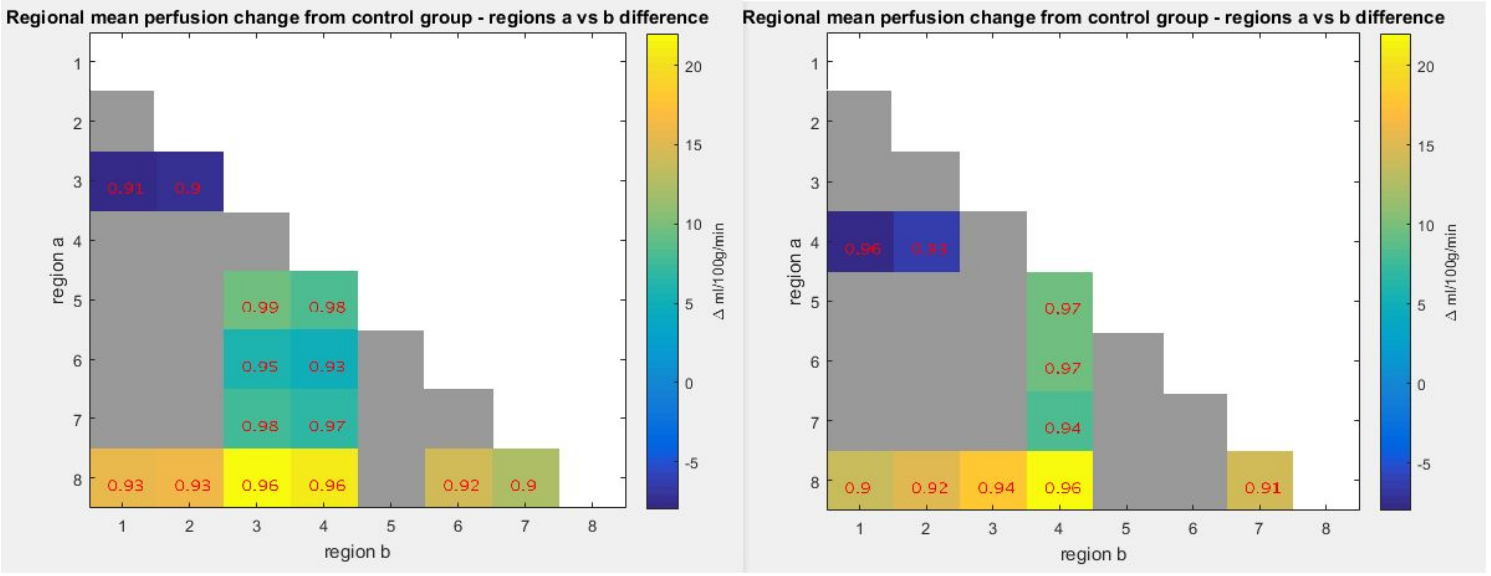

Figure 1 – Novel cohort analysis approach showing statistically significant relative differences in CBF change relative to health controls in key brain regions, within the two main separate diagnosed condition groups. For example in both typical AD and PCA, the CBF difference between basal ganglia (region 8) and occipital GM (region 4) was significantly greater in the patients than in the control group. The maximum confidence interval where significance was still found is shown by the red numbers.

Conclusion

As expected by current understanding [3], distinctive patterns of CBF change were observed in the YOAD patients: in typical AD, larger differences were observed between the parietal/occipital lobes and other brain regions in patients than in controls; in PCA, these increased CBF differences were more restricted to the occipital lobe only. In both groups, perfusion was significantly reduced in all cortical regions relative to the deep brain regions, suggesting this contrast may be a robust global biomarker.

[1][3] Modat, et al. (2014). Global image registration using a symmetric block- matching approach. J. of Medical Imaging, 1(2), 024003
[2] Chappell MA, et al. Variational Bayesian inference for a non-linear forward model. IEEE Trans. on Signal Processing 57(1):223-236, 2009.
[3] Lehmann M, Melbourne A, Dickson JC, et al A novel use of arterial spin labelling MRI to demonstrate focal hypoperfusion in individuals with posterior cortical atrophy: a multimodal imaging study J Neurol Neurosurg Psychiatry Published Online First: 05 January 2016.