3 T Pulsed Arterial Spin Labeling MRI Reveals Perfusion Deficits in Patients with Minor Stroke or Transient Ischaemic Attack

B. J. MacIntosh[1], A. C. Lindsay[2], I. Kylintireas[2], J. M. Lee[2], M. D. Robson[2], J. Kennedy[3], R. P. Choudhury[2], and P. Jezzard[1]

[1]Clinical Neurology, FMRIB Centre, Oxford, Oxfordshire, United Kingdom, [2]Department of Cardiovascular Medicine, John Radcliffe, [3]Acute Stroke Programme, Nuffield Department of Clinical Medicine, John Radcliffe

Introduction

Several studies have demonstrated that DWI lesion conspicuity is related to the duration of transient ischaemic attack (TIA) symptoms [1, 2]. In minor ischaemic stroke or TIA (minS/TIA) the perfusion deficit will resolve over the time span of several days to one week [3, 4]. The relationship between a DWI lesion and perfusion deficit, however, remains controversial, motivating the further development of clinical perfusion imaging. Arterial spin labeling (ASL) is a promising perfusion technique that does not rely on injection of a contrast agent. The goal of this study was to investigate the clinical utility of a whole brain 3D gradient and spin echo (GRASE) pulsed ASL implementation [5, 6] that incorporates multiple inversion times (TI). The present study extends from previous clinical ASL work in acute stroke using continuous ASL [7] by asking whether perfusion deficits can be seen during acute and sub-acute presentation of patients with minS/TIA. Arterial transit time (ATT) maps are also calculated from the multiple-inflow ASL data and we hypothesize that these maps provide an additional imaging marker of ischaemia.

Methods

11 minS/TIA patients (median age: 70 ± 12 years; 4 females) were scanned using a 3 T Siemens MRI scanner and a 12-channel head coil. The median time to scan was 3 days post clinical presentation. The imaging protocol consisted of: DWI to delineate acute lesions, fluid-attenuated inversion recovery (FLAIR), and time-of-flight angiography. ASL data were acquired in 7 minutes 34 s to estimate cerebral blood flow (CBF) as well as arterial transit times (ATT) on a voxel basis. Doppler ultrasound was performed to characterize the degree of carotid disease and revealed 30% stenoses or greater in all patients. A physician performed the clinical assessments with a NIH Stroke Scale (NIHSS) and Rankin Score at the time of assessment as well as follow up scans in a subset of patients. Informed consent was obtained from all patients under a protocol approved by the relevant ethical committee.

GRASE-ASL data were collected at 9 inversion times i.e. TI=[500: 250: 2500 ms]. ASL imaging parameters include: 8 controls and 8 tag volumes, TR/TE=3156/40ms, 3.1 mm x 3.1 mm x 5.0 mm, FOV: 200 mm x 200 mm x 96 mm, half k_z-space coverage; 64 x 64 x 24 matrix size. A coregistration algorithm was developed using FSL tools [8] to correct for head motion during the ASL scans. A single compartment kinetic model was fit to the ASL data using Matlab, producing estimates and confidence intervals for CBF [mL/100g/min] and ATT [s]. ATT maps were partitioned using a “k-means clustering” algorithm into two k-means clusters: early (ATT_{early}) and delayed (ATT_{delay}) transit times. ATT maps were assessed for symmetry between the two hemispheres using the following metric: (# of voxels in affected hemisphere minus # of voxels in unaffected hemisphere) / (total # of voxels in the ATT map). An asymmetry = 1 indicates all voxels are in the affected hemisphere.

Results

Stroke/TIA impairment levels were low with a mean NIHSS of 1 ± 1.1. Accordingly, DWI lesion volumes were found to be small (mean 7 ± 14.2 mL). Inter-operator reliability in delineating the DWI lesion was good (Kappa = 0.80). Despite the good clinical condition of the patients scanned, and the small average DWI volumes, perfusion deficits were evident in 73% of patients (8 of 11). Motion correction significantly improved the z-statistics of the CBF and ATT estimates ($P < 0.001$ and $P < 0.02$, respectively). Using an automated clustering approach, voxels were identified on the basis of early or delayed ATT (Fig. 1). Despite a diagnosis of minS/TIA using conventional imaging / clinical scores, the asymmetry metric demonstrated that delayed ATT voxels were significantly more likely to reside in the affected hemisphere ($P < 0.05$; Fig. 2).

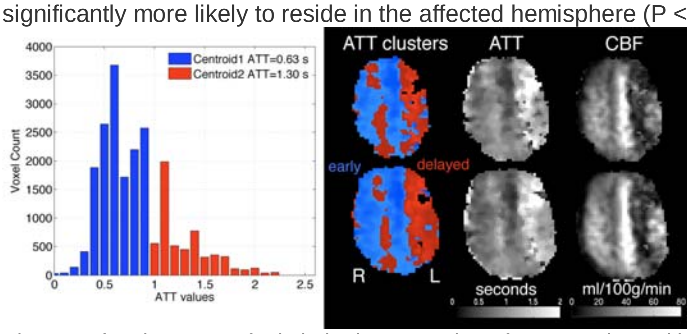

Fig. 1. Left: Histogram of whole-brain ATT values from a patient with right side weakness and 97% left internal carotid artery stenoses. A DWI infarct was seen in left frontal/parietal lobes. Automated K-means clustering separate early and delayed voxels. Right: ATT cluster maps are shown in blue (early) and delayed (red). Gray scale ATT and CBF maps show a large left hemisphere perfusion deficit.

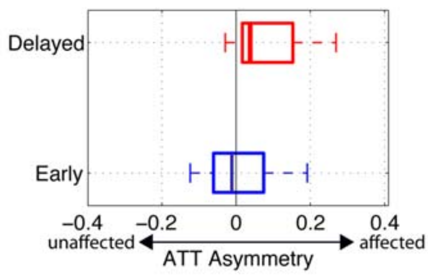

Fig. 2. Group box plots (N=11 patients) show delayed ATT voxels are more likely to reside in the affected hemisphere when compared with early ATT voxels (P < 0.05).

Discussion

Multiple-TI PASL produced reliable maps of CBF and ATT. The advantages of multiple-TI include: 1) reduced error in CBF arising from unknown transit delays, 2) avoidance of the use of an injected contrast agent, and 3) the ability to map ATT across the brain. Z-statistics of ATT maps were far greater than those from the CBF maps ($t = 7.4$, $DOF = 13$; $P < 0.00001$). We demonstrate that it is possible to detect perfusion abnormalities in patients with relatively minor clinical syndromes using multi-TI PASL and on the basis of the ATT maps alone. ATT is analogous to the T_{max} metric that is the result of dynamic susceptibility contrast (DSC) perfusion MRI. Future work will be to increase the patient cohort size and incorporate follow-up scans (data not shown) to corroborate these preliminary findings.

References

1. Crisostomo, R.A., M.M. Garcia, and D.C. Tong. Stroke, 2003. 34(4): p. 932-7. **2.** Kidwell, C.S., J.R. Alger, F. Di Salle, et al. Stroke, 1999. 30(6): p. 1174-80.
3. Fiehler, J., M. Foth, T. Kucinski, et al. Stroke, 2002. 33(1): p. 79-86. **4.** Fiehler, J., M. von Bezold, T. Kucinski, et al. Stroke, 2002. 33(10): p. 2421-5.
5. Gunther, M., K. Oshio, and D.A. Feinberg. Magn Reson Med, 2005. 54(2): p. 491-8. **6.** MacIntosh, B.J., K.T. Pattinson, et al. J Cereb Blood Flow Metab, 2008.
7. Chalela, J.A., D.C. Alsop, J.B. Gonzalez-Atavales, et al. Stroke, 2000. 31(3): p. 680-7. **8.** Jenkinson, et al. Neuroimage, 2002. 17(2): p. 825-41.