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

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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 subacute 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=3156/40 ms, 3.1 mm x 3.1 mm x 5.0 mm, FOV: 200 mm x 200 mm x 96 mm, half k-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 (ATTearly) and delayed (ATTdelay) 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).

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 Tmax 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.

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

References