Pulsed Arterial Spin Labeling for CBF MRI in Non-Human Primate Model of Stroke

Kai-Hsiang Chuang[1], Elaine Manigbas[2], Douglas Collins[2], Flordeliza de Villa[2], Rosario Perez[2], and Lynn Collura[2]
[1]*Magnetic Resonance Imaging Group, Singapore Bioimaging Consortium, A*STAR, Singapore, Singapore, Singapore,* [2]*Maccine Pte Ltd, Singapore, Singapore, Singapore*

Introduction

Rodent models have been widely used to understand the pathological progression of stroke, to identify biomarkers, and to assess treatment effects. However, due to the very different structure and function of rodent brain and vascular system, non-human primate (NHP) models are preferable. Typically perfusion and diffusion MRI have been used for diagnosis and prognosis of stroke. While arterial spin labeling (ASL) perfusion imaging has been widely applied in stroke studies on human and rodents, similar study on NHPs are still limited. Quantitative cerebral blood flow (CBF) using ASL has been suffering from low signal-to-noise ratio (SNR). To achieve suitable SNR, previous studies on ASL CBF in NHP used continuous ASL either with neck labeling coils (1) or the pseudo-continuous approach (2). A recent study demonstrated using pseudo-continuous ASL to measure CBF in a middle cerebral artery occlusion (MCAO) model in baboon (2). In this study, we assessed using pulsed ASL for CBF measure in a MCAO model in the cynomolgus macaque (*Macaca fascicularis*).

Method

The study was approved by local Institutional Animal Care and Use Committee. Three female macaques (ages 13, 15, and 4 y/o) were used. Animals were anesthetized by ketamine, followed by maintenance under 2% isoflurane. Transient MCAO was induced by applying an aneurysmal clip at the left MCA for 3 hours. The MRI was conducted before and 24 hr after the stroke on a 3T MRI (Trio, Siemens, Germany) with an 8-channel monkey brain array (Rapid Biomed, Germany) for receiving. Diffusion weighted imaging was acquired with spin-echo EPI of TR = 5000ms, TE = 85ms, b = 1000mm^2/s. ASL was obtained by PICORE with a C-FOCI labeling slab of 10 cm and 1 cm gap. Gradient echo EPI of TR = 3000ms, TE = 13ms, matrix = 64x56, resolution = 3x3x4 mm^3 was used to acquire 10 ascending slices across the brain. To assess the arterial transit time, TI was varied from 100 to 1800 ms. For quantitative CBF measurement, Q2TIPS with TI1 = 700ms, TI1s = 800ms, and TI2 = 1600ms was used. CBF quantification was calculated based on a reference image with same acquisition setting but with TR = 10s (2). Region-of-interest (ROI) analysis was conducted on temporal lobes, sensorimotor areas, and visual areas.

Results

Good perfusion signal was obtained in all animals. Fig.1 presents the perfusion signals at various TI from a temporal lobe ROI that shows transit time increased by ~500ms after MCAO. The transit time before occlusion ranged from 500 to 1000 ms across the brain. One day after transient MCAO, the transit time increased by up to 600ms. Fig.2 shows CBF maps of an animal with reduction of CBF on the ipsi-lesional side that is more extensive than the lesion shown in the FLAIR image but comparable to the extent of reduced ADC.

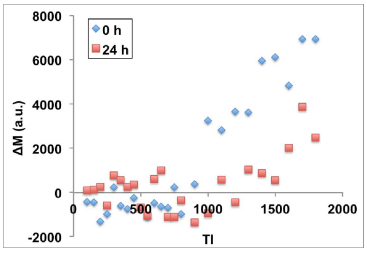

Fig.1 Perfusion difference signal, Δ M, at various inversion times.

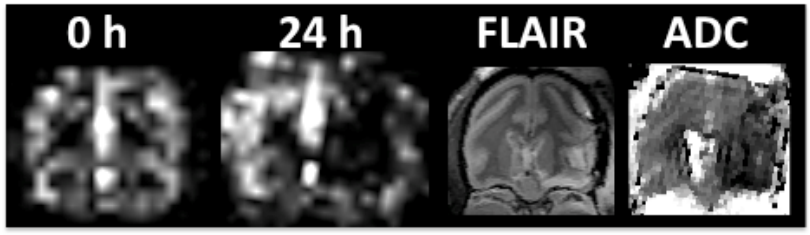

Fig.2 Extensive CBF reduction is observed 1 day after transient MCAO.

Discussion

In this study we evaluated the feasibility of quantitative CBF in NHP before and after transient MCAO using a pulsed ASL technique. While suitable signal quality could be achieved using the standard PICORE ASL sequence, the large variation of arterial transit time before and after MCAO posed a challenge for quantification. One day after the MCAO, the very long transit time caused hyperintensity in artery and underestimation of CBF due to the insufficient TI2 used. To allow more accurate quantification, various TI and/or very long TI2 would be needed.

Reference

1. Doung TQ, Methods 50: 125–135, 2010.
2. Wey HY, et al, Open Neuroimag J, 5: (S 2-M2) 147-152, 2011.
3. Çavuşoğlu M, et al, Magnetic Resonance Imaging 27: 1039–1045, 2009.