

## Assessment of cerebral perfusion in TIAS with unilateral middle cerebral artery stenosis using arterial spin labeling

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### ABSTRACT

**Objective:** To discuss the diagnostic value of arterial spin labeling (ASL) in the transient ischemic attack (TIA) patients with unilateral middle cerebral artery (MCA) stenosis by comparing the differences of perfusion results between dynamic susceptibility contrast enhancement (DSC) and ASL in the perfusion evaluation of unilateral MCA stenosis, and to prove that ASL would be a promising method to assess cerebral hemodynamics in future.

**Methodology:** The images of diffusion weighted imaging (DWI), DSC and ASL in 36 cases of TIA patients with unilateral MCA stenosis and 35 healthy volunteers were analyzed retrospectively to assess collateral flow in the circle of Willis, and to analyze the perfusion differences between ASL and DSC.

**Results:** The perfusion differences between lesion side and contralateral side were significant in both DSC ( $P < 0.01$ ) and ASL ( $P < 0.05$ ). Whereas, the differences of CBF between DSC and ASL in the perfusion evaluation of unilateral MCA stenosis were not significant,  $P > 0.05$ .

**Conclusion:** ASL can provide valuable information on the quality of brain perfusion in patients with unilateral middle cerebral artery stenosis. Therefore, ASL may be an alternative method in the assessment of perfusion in ischemic cerebral vascular diseases.

**KEY WORDS:** Middle cerebral artery, Arterial spin labeling, Dynamic susceptibility contrast - enhanced, Transient ischemic attack.

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### INTRODUCTION

There is a growing body of literature suggesting that patients with atherosclerotic middle cerebral artery (MCA) stenosis are at a higher risk of future ischemic stroke, and that the risk of future cerebral

ischemic events would be low if the blood flow with unilateral MCA stenosis or occlusion is compensated by circle of Willis, or by the collateral circulation from cortical artery, otherwise, the patients would suffer from cerebral ischemia and anoxaemia.<sup>1-4</sup>

Although dynamic susceptibility-weighted contrast-enhanced (DSC) magnetic resonance imaging (MRI) has been used to determine relative cerebral blood flow (rCBF) in normal and pathologic brain tissue, it requires injection of a contrast agent for imaging.<sup>5</sup> Arterial spin labeling (ASL) is one of MRI modalities capable to noninvasively assess the cerebral perfusion by labeling arterial blood with radiofrequency pulses and has the advantage of not using extrinsic contrast agents.<sup>6</sup> This modality has been successfully used to measure rCBF noninvasively in various conditions, such as normal brain tissues, epilepsy, stroke, Alzheimer's disease, and brain tumors.

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The objectives of our study were (1) to compare the perfusion data from ASL-perfusion with those from DSC-perfusion in the evaluation of the effect of collateral flow via the circle of Willis on regional hemodynamics, and (2) to examine whether ASL and DSC could yield comparable perfusion values in patients with MCA stenosis and healthy control subjects in a Chinese patient population.

## METHODOLOGY

**Patients:** This study was approved by the local ethics committee, and written informed consent was obtained from all patients. Between August 2008 and September 2009, 36 patients with transient ischemic attack (TIA) were enrolled in this study. The diagnoses were made according to the National Institute of Neurological Disorders and Stroke criteria, and were further confirmed by the clinical symptoms.<sup>7</sup> All the MCA stenosis with TIA in the thirty-six patients was confirmed by magnetic resonance angiography (MRA). The mean disease duration was 4.7 years, ranged from 0.4 to 16.4 years. The control group was recruited randomly from a hospital-based vascular screening study, consisting of thirty-five healthy volunteers without a history of neurologic disease, and without vascular pathology based on MRI or MRA detection of the brain. The participants in the control group were not on any medications prior to the study.

**Protocol for MRI:** All MRI images were acquired on a 3.0T whole body scanner (Trio Tim, 3.0T, Siemens Medical System) with twelve channel head surface coil. The parameters consisted of axial T<sub>1</sub>-weighted imaging (T<sub>1</sub>WI) [T<sub>1</sub> flair, time to repetition (TR)/time to echo (TE)=400/2.46 ms], axial T<sub>2</sub>-weighted imaging (T<sub>2</sub>WI) (TR/TE=5,000/93 ms), and diffusion weighted imaging (DWI) (TR/TE=3,800/93 ms, b values=1,000 s/mm<sup>2</sup>, matrix=128×128, slice=19, slice thickness= 1.5 mm, and a scan time of 77 s). Before perfusion weighted imaging (PWI), axial T2-wighted fluid-attenuated inversion recovery (FLAIR) imaging (TR/TE=8,000/93ms, TI=2,371ms, matrix=512×256, field of view=220×200mm) was performed with 5 mm contiguous slices. Axial ASL and DSC echo planar imaging (EPI) PWI had 19 slices, 5mm thickness with an interslice gap of 1 mm and an imaging matrix 128×128. Additional for PWI, a gadolinium-based contrast agent (25 ml of 0.5 mol/L Gadovist or 25 ml of 0.5 mol/L Omniscan) was injected, with imaging starting 10 seconds after the start of contrast injection, continuing for 77 seconds, and collecting 50 measurements of 19 axial slices.

**Image Processing:** All the MRI images were processed blinded to clinical and any other laboratory findings. DWI and PWI data were spatially coregistered with the use of SPM8 (the Wellcome Trust Centre for Neuroimaging, London, UK).

CBF map was obtained immediately after each ASL scan. In order to get the DSC-PWI images, all original images were transferred into perfusion software bag to get a concentration-time curve. The AIF from the fitted data were defined by averaging the concentration-time data from voxels corresponding to the lumina.

**Statistical Analysis:** Statistical analysis was performed with SAS 9.2 (SAS Institute, Cary, NC). All continuous parameters were summarized by mean±SDs, and all categorical parameters were summarized as proportions. To compare between-group differences the two-sample t-test was used for continuous variables and the chi-square test was employed for categorical variables. The paired t-test was used to compare lesion volume and rCBF between lesion side and contralateral normal side with ASL-PWI and DSC-PWI in those with MCA stenosis, as well as rCBF between ASL-PWI and DSC-PWI in healthy volunteers. A Bonferroni adjustment was used to account for multiple testing. The p-values reported are two-sided. A p-value <0.05 indicated statistical significance.

## RESULTS

Seventy-one participants were included in this study. Among them, 36 were patients with MCA stenosis (23 were men; mean age: 61.8±12.3 years), and 35 were healthy controls (23 were men, mean age: 59.3±11.7 years). Demographic and clinical

Table-I: Demographic and Clinical Characteristics of Patients with Middle Cerebral Artery Stenosis & Controls

Characteristics	TIA's with MCA stenosis (N=36)	Control (N=35)	P value group
Age, years(mean±SD)	61.8±12.3	59.3±11.7	0.384
Male sex (%)	63.9	60.0	0.758
Hypertension (%)	47.2	11.4	0.001*
Diabetes mellitus (%)	33.3	5.7	0.003*
Previously Smoking (%)	11.1	5.7	0.414
Currently Smoking (%)	33.3	14.3	0.06
History of stroke (%)	22.2	5.7	0.046*
Atrial fibrillation (%)	25.0	2.9	0.007*
History of myocardial infarction	27.8	0.0	0
Hypercholesterolemia (%)	19.4	11.4	0.351
Congestive heart failure (%)	19.4	0.0	0

TIAS=transient ischemic attack;

\*Statistically significant difference.

characteristics of participants with or without middle cerebral artery stenosis are presented in Table-I.

There was no statistical difference in the lesion volume between ASL-PWI and DSC-PWI ( $p>0.05$ ). There were significant differences in rCBF between the lesion side and contralateral normal side in both ASL-PWI and DSC-PWI, however, the differences in rCBF in the lesion side or in the contralateral normal side between ASL-PWI and DSC-PWI were not significant ( $p>0.05$ ) (Table-II).

An example of an ASL and DSC MRI investigation of a patient with a unilateral symptomatic MCA stenosis as shown in Fig.1. Decreased CBF is found in the hemisphere ipsilateral to the MCA stenosis both in ASL-PWI and in DSC-PWI.

### DISCUSSION

TIA is defined as a sudden onset of neurological symptoms that are of vascular etiology and resolve within 24 hours.<sup>8</sup> TIA onset was believed to have no injury in the past. While the assumption that TIAs are associated with complete resolution of brain ischemia leaving no permanent brain injury is false. Recently, more and more evidence has proved that TIA is not a benign condition and that the risk of a subsequent stroke is high within the next 48 hours of symptom onset.<sup>9</sup> A large number of TIAs come from the unilateral MCA stenosis. So we should seek a routine clinical practice to determine whether a TIA patient needs therapeutic treatment. Because serial (at baseline and at the end of follow-up) computed tomography scanning was not performed routinely, some asymptomatic cerebrovascular events might have been missed. Therefore, it is important to assess the CBF in the patients with MCA stenosis.

MR perfusion technique including ASL-PWI and DSC-PWI can provide information about brain tissue ischemia. In this study, we used an ASL technique to make it possible to assess noninvasively the cerebral perfusion condition by using magnetically labeled blood as an endogenous contrast agent. Because of more and more concerns about the use of ionizing radiation and contrast

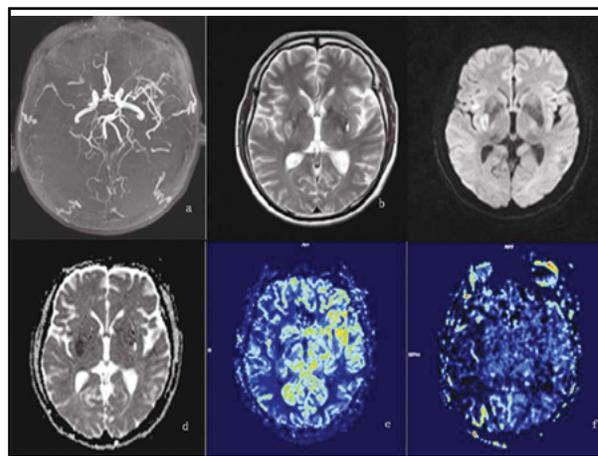


Fig.1: The right MCA occlusion in a 57-year-old man. MR images showed that the right MCA was occluded (a), and the right basal regions showed hyperintense on T2-weighted images (b) and DWI (c), while apparent diffusion coefficient value in the affected areas was decreased (d). The CBF of DSC-perfusion (e) showed the hypoperfusion areas corresponding with that of ASL-perfusion (f). And the hypoperfusion areas corresponds grossly with the DWI lesion but underestimates the penumbral hypoperfusion.

agents in the patients with renal insufficiency, ASL may be a prospective noninvasive alternative in the assessment of the cerebral hemodynamics.<sup>10</sup>

To determine the area of maximal perfusion impairment, we use parametric rCBF maps since they show a lack of perfusion affecting both gray and white matter to a similar degree.<sup>11</sup> Our findings in the present study show the capability of noninvasive ASL to quantify CBF in patients with MCA stenosis with use of data obtained to compensate for delayed collateral flow. With use of this ASL method, we observed a significant decrease in CBF in the hemisphere ipsilateral to the MCA stenosis as compared with both the CBF in the contralateral hemisphere and the CBF in the control subjects. In both the control subjects and the contralateral hemisphere of the patients with MCA stenosis, we observed a mean CBF of 55-60 mL/min per 100g of tissue. Although ASL CBF measurements are highly correlated with CBF measurements obtained with other techniques, ASL is well known to yield slightly overestimated CBF

Table-II: Comparisons of Ischemic Lesion Measurements Derived from ASL-PWI and DSC-PWI Methods in MCA Stenosis Patients and Controls.

Parameter	ASL-PWI		DSC-PWI		ASL-PWI healthy volunteers	DSC-PWI healthy volunteers
	Lesion side	Contralateral normal side	Lesion side	Contralateral normal side		
Perfusion-weighted imaging						
Lesion volume(mL)	86.3±57.5	-	84.5±71.6	-	-	-
rCBF(mL/100g/min)	30.4±8.2#	58.3±11.4#	28.7±12.8#	54.2±9.5#	56.8±10.7#	55.2±9.8#

\* data are summarized as mean±standard deviation. \*\* #:  $p>0.05$

values in the gray matter owing to the presence of label in the vasculature.<sup>12</sup> The CBF decrease measured in the gray matter of the flow territory of the MCA ipsilateral to the MCA stenosis is in agreement with the findings in previously performed positron emission tomography (PET) and xenon-based perfusion imaging studies.<sup>13</sup>

The most important finding of our study was that hypoperfusion could be assessed with ASL MRI in patients with or without a symptomatic MCA stenosis. In patients with a unilateral MCA stenosis, reduced CBF measured by ASL in the flow territory distal to an MCA stenosis corresponds with those observation by DSC MR studies. So assessment of the cerebral perfusion with ASL would be used in future to select those patients who are at risk of stroke and need stent planting. Furthermore, as the reduced clearance of emboli in patients with perfusion, this technique could not only be useful to identify patients at risk of hemodynamics events, but also be useful to predict embolic stroke.<sup>14</sup>

There are several technical limitations in present study. First, a general drawback of ASL MR perfusion imaging is the low signal-to-noise ratio, which is caused by subtraction of the unlabeled from the labeled images to obtain the perfusion images.<sup>15</sup> The use of higher magnetic field strengths results in increased SNR at ASL MR imaging. Second, the scan time was longer than seven minutes. The noise of echo planar imaging was so loud that even normal person could not endure, not mentioning the TIA patients caused by unilateral MCA stenosis. Finally, ASL had only one parameter, CBF. Whereas, DSC could produce rCBV, rCBF, MTT and rTTP. Even though it has the mentioned drawbacks, ASL-perfusion as a noninvasive method can evaluate the cerebral flow volume in the TIAS caused by unilateral MCA stenosis, and the ASL technique has a promising future.

### CONCLUSION

In conclusion, changes in CBF are highly correlated with changes in arterial blood transmit time. Therefore, the described method may broaden the clinical use of ASL as a completely noninvasive and quantitative approach to image cerebral hemodynamics.

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### REFERENCES

1. Bogousslavsky J, Barnett HJ, Fox AJ, Hachinski VC, Taylor W. Atherosclerotic disease of the middle cerebral artery. *Stroke* 1986;17:1112-1120.
2. Arenillas JF, Molina CA, Montaner J, Abilleira S. Progression and clinical recurrence of symptomatic middle cerebral artery stenosis: a long-term follow-up transcranial Doppler ultrasound study. *Stroke* 2001;32:2898-2904.
3. Wong KS, Li H, Lam WW, Chan YL, Kay R. Progression of middle cerebral artery occlusive disease and its relationship with further vascular events after stroke. *Stroke* 2002;33:532-536.
4. Yoon W, Seo JJ, Cho KH, Kim MK, Kim BC, Park MS, et al. Symptomatic middle cerebral artery stenosis treated with intracranial angioplasty: experience in 32 patients. *Radiology* 2005;237(2):620-626.
5. Weber MA, Günther M, Lichy MP, Delorme S, Bongers A, Thilmann C, et al. Comparison of arterial spin-labeling techniques and dynamic susceptibility-weighted contrast-enhanced MRI in perfusion imaging of normal brain tissue. *Invest Radiol* 2003;38(11):712-718.
6. The European Carotid Surgery Trialists Collaborative Group. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998;351:1379-1387.
7. Wolf RL, Detre JA. Clinical neuroimaging using arterial spin-labeled perfusion magnetic resonance imaging. *Neurotherapeutics* 2007;4:346-359.
8. Rivers CS, Wardlaw JW, Am Itage PA. Do acute diffusion and perfusion-Weighted MRI lesions identify final infarct volume in ischemic stroke [J]. *Stroke* 2006;37(1):98-104.
9. Penfield JG, Reilly RF, Jr. What nephrologists need to know about gadolinium. *Nat Clin Pract Nephrol* 2007;3:654-668.
10. Sadowski EA, Bennett LK, Chan MR, Wentland AL, Garrett AL, Garrett RW. Nephrogenic systemic fibrosis: risk factors and incidence estimation. *Radiology* 2007;243:148-157.
11. Deibler AR, Pollock JM, Kraft RA, Tan H, Burdette JH, Maldjian JA. Artery spin-labeling in routine clinical practice, part 2: hypoperfusion patterns. *AJNR Am J Neuroradiol* 2008;19:1235-1241.
12. Acco RL, Adams R, Albers G. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke* 2006;37:577-617.
13. Simon JE, Bristow MS, Lu H. A novel method to derive separate gray and white matter cerebral blood flow measures from MR imaging of acute ischemic stroke patients. *J Cereb Blood Flow Metab* 2005;(9):1236-1243.
14. Forster A, Szabo K, Hennerici MG. Pathophysiological concepts of stroke in hemodynamic risk zone: do hypoperfusion and embolism interact? *Nat Clin Pract Neurol* 2008;4:216-225.
15. Sallustio F, Kern R, Gunther M. Assessment of intracranial collateral flow by using dynamic arterial spin labelling MRA and transcranial color-coded duplex ultrasound. *Stroke* 2008;39:1894-1897.

### Authors Contribution:

**Dan Tong:** Study concept and design.

**Hongwei Zhou, Jing Wang:** Analysis and interpretation of data.

**Yi Yang, Mingchao Shi:** Critical revision of the manuscript for important intellectual content and study supervision.

**Hongwei Zhou, Yang Liu:** Acquisition of data and drafting of the manuscript.