Comparison of 3D Multi-inversion Time Arterial Spin Labeling and Digital Subtraction Angiography in the Evaluation of Cerebral Collateral Circulation

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Numerous studies have established the relationship between collateral flow and the reduction of stroke volumes secondary to improved cerebral perfusion, associated with improved prognosis [1–3]. The development of new neuroimaging techniques has enhanced the assessment of cerebral blood flow (CBF), cerebral perfusion and collateral circulation through noninvasive means. While digital subtraction angiography (DSA) remains the standard of care for evaluation of the intracranial circulation [4], the examination is invasive and expensive. The advent of magnetic resonance arterial spin labeling (ASL) has provided a completely noninvasive and quantitative ability to measure CBF and perfusion through the use of endogenous magnetically labeled arterial water protons as a tracer. 3D multitemporal arterial spin labeling (3D mTI-ASL) is a prototype sequence based on pulsed ASL method using flow-sensitive alternating inversion recovery (FAIR) labeling [5].

In this study, we compared the performance of DSA and 3D mTI-ASL in evaluating collateral circulation, respectively, in the same group cohort of patients.

Patients hospitalized in the stroke unit of Beijing Tiantan Hospital were screened continuously from October 2014 to February 2015. Included patients had a diagnosis of transient ischemic attack (TIA) or ischemic stroke within 30 days and moderate-to-severe stenosis or occlusion of the internal carotid artery or other intracranial arteries (defining as the rate of stenosis is >50% based on Warfarin Aspirin Symptomatic Intracranial Disease (WASID) criteria [6]). Patients with severe stenosis or occlusion of the

posterior circulation and the external carotid artery were excluded in our study. All the patients provided informed consent, and the ethics committee approved the study protocol.

All DSA was performed with the use of Siemens Artis zee biplane fluoroscopy (Siemens Healthcare GmbH, Forchheim, Germany). The results of DSA were read by a senior physician. The evaluation of collateral circulation was based on the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) [7] Collateral Flow Grading System.

All patients underwent MR examination on a MAGNETOM Skyra 3-Tesla scanner (Siemens Healthcare GmbH, Erlangen, Germany) with a 20-channel head-neck coil. Multi-TI ASL was performed using a prototype sequence, and all ASL source images (ASL-SI) were postprocessed inline after the ASL scan to obtain perfusion related parameters. Parameters based on 3D mTI-ASL were relative cerebral blood flow (rCBF) and the bolus arrival time (rBAT). Using MRICron software (<http://people.cas.sc.edu/rorden/mricron/index.html>) provided CBF and BAT values from every region of interest, and rCBF and rBAT in every section were calculated as the quotient between the values from ischemic and contralateral regions of interest. All ASL-SI processing was performed by two radiologists, who were blinded to collateral circulation assessment based on DSA. (Figure S1).

Interobserver agreement for ASL assessment was calculated with Pearson's correlation, coefficient, and interclass correlation coefficient. The consistency between ASL and DSA was calculated with Cohen's kappa value. For all analyses, a two-tailed probability value

Table 1 Baseline demographics of enrolled patients

	Total patients (n = 25)	Good collaterals (n = 11)	Poor collaterals (n = 14)	P value
Age (y)	55.6 ± 8.40	54.6 ± 7.02	57.3 ± 8.98	0.430
Male	13 (52.0%)	6 (46.2%)	7 (53.8%)	0.665
Clinical feature				
Time to onset (d)	19.7 ± 8.30	20.9 ± 7.48	18.7 ± 9.13	0.543
NIHSS	3.32 ± 5.08	6.45 ± 5.41	1.57 ± 3.92	0.015
mRS	1.18 ± 1.40	2 ± 1.48	0.64 ± 1.51	0.017
Medical history				
Hypertension	19 (76.0%)	8 (72.7%)	11 (78.6%)	0.747
DM	7 (28.0%)	4 (36.4%)	3 (21.4)	0.43
CHD	6 (24.0%)	3 (27.3%)	3 (21.4)	0.747
Hyperlipidemia	12 (48.0%)	5 (45.5%)	7 (50%)	0.984
Tobacco	15 (60.0%)	7 (63.6%)	8 (57.1%)	0.736
Alcohol	11 (44.0%)	5 (45.5%)	6 (54.5%)	0.923
Imaging features				
Complete Willis circle	10 (40.0%)	7 (70.0%)	3 (30.0%)	0.753
Location of stenosis				0.529
ICA	11 (44.0%)	5 (45.5%)	6 (54.5%)	—
MCA	14 (56.0%)	6 (42.9%)	8 (57.1%)	—
ACA	0	—	—	—
Rate of stenosis (%)	0.80 ± 0.12	0.80 ± 0.11	0.80 ± 0.12	0.960
Length of stenosis (mm)	9.66 ± 5.59	11.7 ± 6.81	8.03 ± 3.92	0.103

of $P < 0.05$ was considered statistically significant. Statistical analysis was performed using SPSS 19.0 (IBM SPSS Statistics, version 19, Chicago, IL, USA).

In total, 25 patients met the final inclusion criteria, which included 13 (52%) males and 12 (48%) females, with an age range from 35 to 75 years. Baseline of demographic information, clinical information, and imaging features is shown in Table 1.

Good correlation was found in the measurement of AOI in both CBF and BAT. Measurement of AOI in CBF found the Pearson's correlation coefficient to be 0.871 ($P < 0.001$), while the interclass correlation coefficient was 0.846 ($P < 0.001$). Measurement of AOI in BAT found the Pearson's correlation coefficient to be 0.904

($P < 0.001$), and the interclass correlation coefficient was 0.9 ($P < 0.001$) (Figure 1).

After analyzing the correlation between DSA and the parameters of ASL, we found that rCBF may be associated with the quality of collateral circulation (Table 2). A high AUC for rCBF values and collateral circulation status was observed. The ROC curve-derived optimum cutoff value for rCBF to discriminate between good and poor collateral status was 0.82 (sensitivity, 78.6%; specificity, 72.7%; $P < 0.001$; AUC, 0.799, 95% CI: 0.614–0.984). Using this cutoff value for rCBF to discriminate between good and poor collateral status, patients were divided into two groups based on the assessment system of ASL, with

Figure 1 Bland–Altman plot of rCBF and rBAT by two radiologists. Measurement of rCBF and rBAT in different observers showed high consistency. SD, standard deviation.

Table 2 Correlation between parameters of ASL and collateral circulation status

	Total (n = 25)	Poor collaterals (n = 11)	Good collaterals (n = 14)	P value
CBF of AOI (mL/100 g/min)	97.6 ± 60.0	103 ± 68.7	93.2 ± 30.5	0.633
BAT of AOI (s)	978 ± 274	948 ± 367	1002 ± 185	0.631
rCBF	0.82 ± 0.10	0.77 ± 0.12	0.86 ± 0.05	0.034
rBAT	1.23 ± 0.25	1.25 ± 0.22	1.14 ± 0.31	0.342

11 patients in the poor collateral group and 14 patients in the good collateral group. The consistency of collateral circulation grouping between DSA and ASL was high (Kappa value = 0.675, $P = 0.001$). The result of comparison of DSA and ASL was given in Table S1.

ASL is an MR imaging method that enables the measurement of tissue perfusion without using exogenous contrast agents by magnetically tagging water molecules in actively flowing blood [8,9]. Using this method, 3D mTI-ASL has proved to be useful to evaluate cerebral perfusion and collateral circulation. In the evaluation of collateral perfusion in steno-occlusive diseased patients, 3D mTI-ASL was found to significantly correlate with DSA ($k = 0.675$, $P < 0.0001$). Furthermore, good intraobserver agreement has been demonstrated with the 3-D mTI-ASL evaluation system (Pearson's correlation coefficient: 0.871 in CBF, 0.904 in BAT; $P < 0.001$), revealing its reproducibility.

Current cerebral perfusion methods used in clinical practice, including single-photon emission computed tomography (SPECT) [10], perfusion computed tomography (PCT) [11], and MRI, especially dynamic susceptibility contrast-enhanced MR imaging (DSC-MRI), require intravenous injection of either radioactive tracers or contrast agents. The development of ASL allows quantitative measurement of cerebral blood flow without the reliance on intravenous access or use of contrast media [6]. The noninvasive nature also allows for repeat imaging without the risks associated with contrast agents [12].

This study also has some limitations. First, the final sample size of the study was small, and future research and validation will need to be based upon a larger population. Another limitation of this study is the selection of patients with isolated internal carotid artery and/or M1 occlusion as these results cannot necessarily be considered representative of all ischemic stroke patients.

Based on the results, we found that 3D mTI-ASL revealed a similar quantification of collateral circulation compared to DSA, providing a novel and noninvasive method to evaluate this important clinical finding. This study and radiologic method warrants future validation in a larger sample size of ischemic stroke patients.

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Conflict of Interest

The authors declare no conflict interest.

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Supporting Information

The following supplementary material is available for this article:

Data S1. ASL Acquisition.

Figure S1. Illustrated pictures showed the process of evaluating the status of collaterals.

Table S1. Collateral status as defined by DSA and ASL assessment systems.