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Editorial Board Member of World Journal of Clinical Cases, Raden Andri Primadhi, MD, PhD, Assistant Professor, Surgeon, Department of Orthopaedics and Traumatology, Universitas Padjadjaran Medical School, Hasan Sadikin Hospital, Bandung 40161, Indonesia. randri@unpad.ac.id

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**Retrospective Study** 

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ORIGINAL ARTICLE

# Three-dimensional arterial spin labeling and diffusion kurtosis imaging in evaluating perfusion and infarct area size in acute cerebral ischemia

## Yan-Yan Jiang, Zhi-Lin Zhong, Min Zuo

Specialty type: Radiology, nuclear 430056, Hubei Province, China medicine and medical imaging Provenance and peer review: Hubei Province, China Unsolicited article; Externally peer reviewed and Technology, Wuhan 430050, Hubei Province, China Peer-review model: Single blind Peer-review report's scientific quality classification Grade A (Excellent): 0 Grade B (Very good): B Grade C (Good): C Abstract Grade D (Fair): 0 BACKGROUND Grade E (Poor): 0 P-Reviewer: Cvijic M, Slovenia; Narain R, Canada evaluation of cerebral infarction is important. Received: January 6, 2022 AIM Peer-review started: January 6, 2022

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Yan-Yan Jiang, Department of Magnetic Resonance, Wuhan Asia General Hospital, Wuhan

Zhi-Lin Zhong, Department of Radiology, Wuhan Yaxin General Hospital, Wuhan 430056,

Min Zuo, Department of Radiology, Wuhan Hanyang Hospital, Wuhan University of Science

Corresponding author: Min Zuo, BM BCh, Associate Chief Physician, Department of Radiology, Wuhan Hanyang Hospital, Wuhan University of Science and Technology, No. 53 Moohu Road, Anyang District, Wuhan 430050, Hubei Province, China. ypzm0518@163.com

Early thrombolytic therapy is crucial to treat acute cerebral infarction, especially since the onset of thrombolytic therapy takes 1-6 h. Therefore, early diagnosis and

To investigate the diagnostic value of magnetic resonance multi-delay threedimensional arterial spin labeling (3DASL) and diffusion kurtosis imaging (DKI) in evaluating the perfusion and infarct area size in patients with acute cerebral ischemia.

## **METHODS**

Eighty-four patients who experienced acute cerebral ischemia from March 2019 to February 2021 were included. All patients in the acute stage underwent magnetic resonance-based examination, and the data were processed by the system's own software. The apparent diffusion coefficient (ADC), average diffusion coefficient (MD), axial diffusion (AD), radial diffusion (RD), average kurtosis (MK), radial kurtosis (fairly RK), axial kurtosis (AK), and perfusion parameters post-labeling delays (PLD) in the focal area and its corresponding area were compared. The correlation between the lesion area of cerebral infarction under MK and MD and T2-weighted imaging (T2WI) was analyzed.

#### RESULTS

The DKI parameters of focal and control areas in the study subjects were compared. The ADC, MD, AD, and RD values in the lesion area were significantly lower than those in the control area. The MK, RK, and AK values in the lesion area were significantly higher than those in the control area. The MK/MD value in the infarct lesions was used to determine the matching situation. MK/MD < 5 mm was considered matching and MK/MD ≥ 5 mm was considered mismatching. PLD1.5s and PLD2.5s perfusion parameters in the central, peripheral, and control areas of the infarct lesions in MK/MD-matched and -unmatched patients were not significantly different. PLD1.5s and PLD2.5s perfusion parameter values in the central area of the infarct lesions in MK/MD-matched and -unmatched patients were not significantly different. PLD1.5s and PLD2.5s perfusion parameter values in the central area of the infarct lesions in MK/MD-matched and -unmatched patients were significantly lower than those in peripheral and control areas. The MK and MD maps showed a lesion area of 20.08 ± 5.74 cm<sup>2</sup> and 22.09 ± 5.58 cm<sup>2</sup>, respectively. T2WI showed a lesion area of 19.76 ± 5.02 cm<sup>2</sup>. There were no significant differences in the cerebral infarction lesion areas measured using the three methods. MK, MD, and T2WI showed a good correlation.

#### CONCLUSION

DKI parameters showed significant difference between the focal and control areas in patients with acute ischemic cerebral infarction. 3DASL can effectively determine the changes in perfusion levels in the lesion area. There was a high correlation between the area of the infarct lesions diagnosed by DKI and T2WI.

**Key Words:** Magnetic resonance; Multi-delay 3D arterial spin labeling; Diffusion kurtosis imaging; Acute ischemic cerebral infarction; Perfusion; Nerve function

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**Core Tip:** Through the analysis and research of patients in the hospital, we have concluded that diffusion kurtosis imaging (DKI) parameters show that there is a significant difference between the lesions of patients with acute ischemic cerebral infarction and the control area. Three-dimensional arterial spin labeling can effectively determine the changes in the perfusion level of the diseased area. The infarct size diagnosed by DKI is highly correlated with T2-weighted imaging.

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#### INTRODUCTION

Cerebral infarction mainly occurs in geriatric patients, and it is a common clinical cerebrovascular disease with high disability and fatality rates. Therefore, it can severely affect patients' quality of life and health. Clinical practice has demonstrated that early and effective thrombolytic therapy can significantly improve the prognosis of patients with acute cerebral infarction, and that treatment options vary according to the severity of the infarction[1]. Therefore, it is important to explore effective methods for the accurate diagnosis of cerebral infarction to improve the treatment modalities and prognosis.

Magnetic resonance imaging (MRI) has important advantages in the diagnosis of central nervous system diseases due to its high soft tissue resolution. Multi-delay three-dimensional arterial spin labeling (3DASL) can accurately evaluate cerebral blood flow (CBF). Diffusion kurtosis imaging (DKI) is a clinical imaging method used to describe the non-Gaussian diffusion of water molecules in tissues; it can accurately reflect the complexity and heterogeneity of neural tissue microstructure by quantifying the diffusion characteristics of water molecules[2,3]. Our study aimed to investigate the diagnostic value of magnetic resonance multi-delay 3DASL and DKI in evaluating the perfusion and infarct area size in patients with acute cerebral ischemia.

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## MATERIALS AND METHODS

#### Baseline data

A total of 84 patients who experienced acute cerebral ischemia from March 2019 to February 2021 in our hospital were selected. The inclusion criteria were as follows: Patients (1) Aged 57-82 years; (2) diagnosed with unilateral acute ischemic cerebral infarction (diagnostic criteria of the Fourth National Academic Conference on Cerebrovascular Diseases in 1996)[4]; (3) with dizziness, vomiting, limb numbness, and headache as the main clinical manifestations; (4) who were hospitalized within 24 h of the onset of the disease and who underwent MRI; and (5) who provided informed consent before the relevant examination. The exclusion criteria were as follows: Patients with (1) Cerebrovascular hemorrhagic diseases (hypertensive cerebral hemorrhage, aneurysm, arterial malformation); (2) intracranial tumors; (3) a history of craniotomy; (4) a history of acute myocardial infarction and had an implanted pacemaker placed less than 3 mo previously; (5) cochlear implants and other such complications; (6) mental illness and hyperthyroidism; and (7) a history of drug allergy. The study tender and related materials was implemented after the decision of the medical ethics committee.

#### MRI and data collection

A 3DASL scan was performed using our MRI scanner (1.5 T, 8-channel cranial coil) from the cranial top to the lower margin of the foramen magnum. Conventional transverse T1-weighted imaging, T2weighted imaging (T2WI), and coronal fat-suppressed (FS) + fluid-attenuated inversion recovery imaging were performed. The 3DASL sequence adopted 3D spiral fast spin echo technology. The scanning parameters were as follows: echo time (TE), 10.5 ms; repetition time (TR), 4548 ms; labeling delay time, 1.5; layer thickness, 4 mm; and post-labeling delay (PLD), 1525. The CBF values of PLD1.5s and PLD2.5s were obtained.

The DKI sequence scanning parameters were as follows: TR, 6000 ms; layer thickness, 5 mm; TE, minimum; layer spacing, 1.5 mm; field of vision, 240 mm × 240 mm; matrix, 96 × 130; diffusion direction, 15; and B = 0, 1000, and 2000 s/mm<sup>2</sup>. The images obtained were analyzed by the supporting software for the following DKI parameters: apparent diffusion coefficient (ADC), axial tensor (AD), mean diffusion coefficient (MD), radial tensor (RD), mean kurtosis (MK), radial kurtosis (RK), and axial kurtosis (AK).

#### Image and data processing

The original data were processed using a GEMR processing workstation. Two imaging physicians with a senior professional title in our hospital agreed to select the infarction area, abnormal ASL perfusion area, mismatching area, and corresponding contralateral normal brain tissue as regions of interest (ROIs). The CBF value of each ROI area and the ADC value were measured and calculated.

#### Statistical analysis

In this study, the DKI parameters, CBF values under PLD1.5s and PLD2.5s, and other measurement indices were consistent with the approximate normal distribution or the normal distribution by a normal distribution test, and they are expressed as mean ± SD. The *t*-test was used for group comparisons. The Statistical Package for the Social Sciences (version 21.0; IBM, Armonk, NY) was used for data analysis. The inspection level was  $\alpha = 0.05$ .

#### RESULTS

#### Comparison of baseline data between the joint and control groups

The age, body mass index, and time from onset to admission of the study subjects were 57-82 (average,  $68.8 \pm 5.8$ ) years,  $23.8 \pm 2.1$  kg/m<sup>2</sup>, and 9-24 (average,  $14.2 \pm 4.0$ ) h, respectively. The study subjects included 48 males and 36 females. A total of 27 and 30 patients smoked and consumed alcohol, respectively. Moreover, 29, 15, 16, and 34 patients had hypertension, diabetes, coronary heart disease, and hyperlipidemia, respectively. The National Institutes of Health Stroke Scale (NIHSS) score within 24 h after admission ranged from 11–18 points, and the average NIHSS score was  $14.8 \pm 2.2$  points.

#### Comparison of DKI parameters between the lesion and control areas

The DKI parameters of the focal and control areas in the study subjects were compared. The ADC, MD, AD, and RD values in the lesion area were significantly lower than those in the control areas (P < 0.05). The MK, RK, and AK values in the lesion area were significantly higher than those in the control area (P < 0.05) (Table 1).

#### Comparison of perfusion parameters between the lesion and control areas under different PLDs

The CBF values of the focal area of the study subjects at PLD1.5s and PLD2.5s were significantly lower than that of the control area (P < 0.05). The results are presented in Table 2 and Figure 1.



Table 1 Comparison of diffusion kurtosis imaging parameters between the lesion and control areas (mean ± SD)				
Indexes	The lesion area ( <i>n</i> = 84)	The control area ( <i>n</i> = 84)	<i>t</i> value	P value
ADC	576.3 ± 94.2	756.0 ± 102.1	-11.856	0.000
MD	$0.651 \pm 0.150$	$0.847 \pm 0.167$	-8.003	0.000
AD	$0.830 \pm 0.167$	$1.305 \pm 0.204$	-16.513	0.000
RD	$0.531 \pm 0.093$	$0.644 \pm 0.122$	-6.751	0.000
AK	$1.281 \pm 0.224$	$0.760 \pm 0.115$	18.964	0.000
MK	$1.256 \pm 0.241$	$0.922 \pm 0.207$	9.636	0.000
RK	$1.328 \pm 0.304$	$0.987 \pm 0.185$	8.782	0.000

ADC: Apparent diffusion coefficient; MD: Average diffusion coefficient; AD: Axial diffusion; RD: Radial diffusion; AK: Axial kurtosis; MK: Average kurtosis; RK: Radial kurtosis.

Table 2 Comparison of cerebral blood flow values between the lesion area and control area under different parameters of different delay time after labeling (mean ± SD, mL/100 g/min)

Groups	n	PLD1.5s	PLD2.5s
Focal area	84	22.64 ± 5.81	$14.03 \pm 3.91$
Control area	84	34.51 ± 7.03	37.58 ± 7.76
<i>t</i> value		-11.929	-24.839
<i>P</i> value		0.000	0.000

PLD: Perfusion parameters post-labeling delays.



Figure 1 Histogram of cerebral blood flow values of the lesion and control areas under parameters of different delay time after labeling 1.5 s and 2.5 s. <sup>a</sup>P < 0.05 vs control areas. CBF: Cerebral blood flow; PLD: Parameters of different delay time.

#### Comparison of PLD1.5s perfusion parameters of MK/MD-matched and -unmatched infarct lesions

The MK/MD value in the infarct lesions was used to determine the matching situation. MK/MD < 5mm was considered matching, whereas  $MK/MD \ge 5$  mm was considered mismatching. The PLD1.5s perfusion parameters in the central, peripheral, and control areas of the infarct lesions in MK/MDmatched and -unmatched patients were not significantly different (P > 0.05). The PLD1.5s perfusion parameter values in the central area of infarct lesions in MK/MD-matched and -unmatched lesions were significantly lower than those in peripheral and control areas (P < 0.05) (Table 3).

Table 3 Comparison of parameters of different delay time after labeling 1.5s perfusion parameters of average kurtosis/average diffusion coefficient-matched and unmatched infarct lesions (mean ± SD, mL/100 g/min)				
Lesion area	MK/MD unmatched ( <i>n</i> = 48)	MK/MD matched ( <i>n</i> = 36)	t value	P value
Central are	16.33 ± 4.75	$17.50 \pm 4.82$	-1.110	0.270
Peripheral area	26.95 ± 5.30 <sup>a,d</sup>	28.03 ± 5.47 <sup>a,d</sup>	-0.912	0.365
Unmatched area	25.73 ± 5.54 <sup>a,d</sup>	-		
Matched area	$34.60 \pm 6.95^{\rm d}$	$34.12 \pm 6.85^{d}$	0.315	0.753
<i>F</i> value	29.064	28.551		
<i>P</i> value	0.000	0.000		

 $^{a}P < 0.05 vs$  the control area.

 $^{d}P < 0.05 vs$  the central area.

MK: Average kurtosis; MD: Average diffusion coefficient.

#### Comparison of PLD2.5s perfusion parameters of MK/MD-matched and -unmatched infarct lesions

The PLD2.5s perfusion parameters in the central, peripheral, and control areas of the infarct lesions in MK/MD-matched and -unmatched patients were not significantly different (P > 0.05). The values of the PLD2.5s perfusion parameters in the central area of infarct lesions in MK/MD-matched and -unmatched patients were significantly lower than those in peripheral and control areas (P < 0.05) (Table 4).

#### Results of low perfusion area measurement

The MK map showed an infarct area of  $20.08 \pm 5.74$  cm<sup>2</sup>, and the MD map showed an area of  $22.09 \pm 5.58$  cm<sup>2</sup> in the study subjects. T2WI showed a lesion area of  $19.76 \pm 5.02$  cm<sup>2</sup>. There were no significant differences in the cerebral infarction areas measured using these three methods (F = 2.094, *P* = 0.227). MK, MD, and T2WI showed a good correlation (*r* = 0.617, *r* = 0.620, *P* < 0.05) (Figure 2A and B).

#### Case introduction

A 67-year-old male patient was admitted to the hospital due to dizziness, vomiting, and limb dysfunction for 12 h (Figure 3).

#### DISCUSSION

The traditional method used for clinical diagnosis of cerebral infarction relies on computed tomography (CT), which evaluates the absorption of different types of radiation by different tissues. However, some studies[5-7] have suggested that CT diagnosis and evaluation of cerebral infarction often cannot be performed within 6 h of onset, thus affecting the treatment.

DKI technology analyzes the motion of water molecules in tissues in a non-Gaussian distribution, which is closer to the real motion characteristics of water molecules, and is an extension of magnetic resonance diffusion tensor imaging and magnetic resonance diffusion-weighted imaging[8,9]. In our study, the ADC, MD, AD, and RD values in the lesion area were significantly lower than those in the control group, whereas the MK, RK, and AK values were significantly higher than those in the control group. DKI was more prone to uneven signals due to the large variation in DKI parameters when taken soon after the cerebral infarction occurred, suggesting that DKI has a higher sensitivity in differentiating ischemic brain injuries and can be used as an indicator of complexity and heterogeneity of the changes in the microenvironment inside the cerebral infarction tissue. The movement of water molecules in brain tissue is restricted by the cell membrane, organelles, axons, and myelin sheath; therefore, water molecules in brain tissue cannot show the ideal normal distribution diffusion movement because of restricted movement. Therefore, DKI is more sensitive to pathological changes in brain tissue after ischemia than DWI and DTI, and it is conducive for a more comprehensive analysis of the micro-structural changes in cerebral infarction[10-12].

3DASL technology is a type of perfusion imaging with total brain volume coverage and can be used to determine the appropriate treatment method for stroke. In this study, the CBF values of the focal area in the study subjects at PLD1.5s and PLD2.5s were significantly lower than that of the control area. 3DASL is a non-invasive and quantitative diagnostic method, which can accurately evaluate blood flow in the entire brain, determine the blood flow status of the local infarction area, quantitatively analyze blood flow velocity, and evaluate the establishment of collateral circulation, which is of crucial significance for the formulation of a treatment plan and the evaluation of its curative effect[13-15].

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Table 4 Comparison of parameters of different delay time after labeling 2.5s perfusion parameters of average kurtosis/average diffusio
coefficient-matched and unmatched infarct lesions (mean ± SD, mL/100 g/min)

Lesion area	MK/MD unmatched ( <i>n</i> = 48)	MK/MD matched (n = 36)	t value	P value
Central area	11.50 ± 3.89	$12.28 \pm 4.03$	-0.896	0.373
Peripheral area	$25.84 \pm 6.03^{a,d}$	26.71 ± 5.94 <sup>a,d</sup>	-0.659	0.512
Unmatched area	21.76 ± 5.20 <sup>a,d</sup>	-		
Control area	37.85 ± 7.54	$38.90 \pm 7.41^{d}$	-0.636	0.526
<i>F</i> value	41.025	43.008		
<i>P</i> value	0.000	0.000		

 $^{a}P < 0.05 vs$  the control area.

 $^{d}P < 0.05 vs$  the central area.

MK: Average kurtosis; MD: Average diffusion coefficient.



Figure 2 Correlation between the average kurtosis, the average diffusion coefficient, and the area of cerebral infarction on T2-weighted imaging. A: Correlation between the average kurtosis and the area of cerebral infarction; B: Correlation between the average diffusion coefficient and the area of cerebral infarction. MD: Average diffusion coefficient; MK: Average kurtosis; T2WI: T2-weighted imaging.



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Figure 3 A 67-year-old male patient was admitted to the hospital due to dizziness, vomiting, and limb dysfunction for 12 h. Magnetic resonance imaging examination was performed within 4 h after admission, and the patient was diagnosed with acute cerebral infarction in the left frontal lobe. A: The diffusion-weighted imaging image and the focal area of cerebral infarction showing high signal performance; B: The color map of cerebral perfusion, showing significant hypoperfusion in the infarct lesion area; C: T2-weighted imaging, with the infarct area indicated by the white arrow showing high signal intensity (Arrow).

The comparison of the PLD1.5s and PLD2.5s perfusion parameters between the two groups showed that the values of the PLD1.5s perfusion parameters in the central area of infarct lesions in MK/MD-matched and -unmatched patients were significantly lower than those in the peripheral and control areas. 3DASL, as a whole-brain non-invasive volume perfusion evaluation technology, can provide quantitative and accurate whole-brain blood perfusion information and help in the precise and early

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diagnosis and treatment of stroke. Moreover, the selection of the PLD is important for the analysis of ASL results. PLD1.5s showed the perfusion behavior and the compensatory ability of rapid collateral circulation and PLD2.5s showed the perfusion result. The results of this study also suggested that 3DASL can effectively evaluate and determine the infarct area[16].

The results of the low perfusion area measurement indicated that MK, MD, and T2WI showed no significant differences in the measurement of the area of cerebral infarction lesions in the study subjects, suggesting that these three modalities showed good correlation. The MK and MD values are dependent on the complexity of the tissue microstructure in the ROI and are the most representative parameters of DKI, which can show the degree of limited diffusion of water molecules and the complexity of tissue microstructure. The more complex the structure, the more evident the limited diffusion of water molecules and the larger the MK and MD values [17-20]; whereas there was a significant increase in CBF value on T2WI of the cerebral infarction area, which was closely correlated with MK, MD, and T2WI.

#### CONCLUSION

In conclusion, the difference in DKI parameters between the focal and control areas in patients with acute ischemic cerebral infarction is significant, which is important for the diagnosis of infarction. 3DASL can effectively determine the changes in perfusion levels in the lesion area. There was a high correlation between the area of the infarct lesions diagnosed by DKI and T2WI.

## ARTICLE HIGHLIGHTS

#### Research background

Early thrombolytic therapy is crucial to treat acute cerebral infarction, especially since the onset of thrombolytic therapy takes 1-6 h. Therefore, early diagnosis and evaluation of cerebral infarction is important.

#### Research motivation

This study explored the methods for assessing perfusion and infarct size in patients with acute cerebral ischemia.

#### Research objectives

The study aimed to investigate the diagnostic value of magnetic resonance multi-delay threedimensional arterial spin labeling (3DASL) and diffusion kurtosis imaging (DKI) in evaluating the perfusion and infarct area size in acute cerebral ischemia patients.

#### Research methods

Eighty-four patients who experienced acute cerebral ischemia from March 2019 to February 2021 were included.

#### Research results

The apparent diffusion coefficient, average diffusion coefficient (MD), axial diffusion, and radial diffusion values in the lesion area were significantly lower than those in the control area. The average kurtosis (MK), radial kurtosis, and axial kurtosis values in the lesion area were significantly higher than those in the control area. parameters post-labeling delays (PLD) 1.5s and PLD2.5s perfusion parameters in the central, peripheral, and control areas of the infarct lesions in MK/MD-matched and -unmatched patients were not significantly different. PLD1.5s and PLD2.5s perfusion parameter values in the central area of the infarct lesions in MK/MD-matched and -unmatched patients were significantly lower than those in peripheral and control areas. There were no significant differences in the cerebral infarction lesion areas measured using the three methods.

#### Research conclusions

DKI parameters showed significant difference between the focal and control areas in patients with acute ischemic cerebral infarction. 3DASL can effectively determine the changes in perfusion levels in the lesion area. There was a high correlation between the area of the infarct lesions diagnosed by DKI and T2-weighted imaging.

#### Research perspectives

3DASL and DKI have broader application value in assessing perfusion and infarct size in patients with acute cerebral ischemia.



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#### FOOTNOTES

Author contributions: Jiang YY and Zhong ZL contributed equally to this study, and should be regarded as co-first authors, Jiang YY and Zhong ZL designed the study and collected the data; Zuo M drafted the manuscript, Zuo M and Jiang YY analyzed and interpreted data.

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#### Country/Territory of origin: China

**ORCID number:** Yan-Yan Jiang 0000-0001-7831-6775; Zhi-Lin Zhong 0000-0002-9215-3578; Min Zuo 0000-0001-7205-1462.

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