Comprehensive Hemodynamic Evaluation of Intracranial Atherosclerotic Disease with 4D Flow MR Imaging

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Introduction: Intracranial atherosclerotic disease (ICAD) is caused by narrowing and blockage of the major intracranial vessels due to accumulation of atherosclerotic plaques within the vessel wall. It accounts for 30-50% of ischemic strokes in Asians, and 8-10% of ischemic strokes in North American Caucasians [1]. Digital subtraction angiography (DSA) is the gold standard for ICAD diagnosis and evaluation, but it is highly invasive and provides limited hemodynamic information. Non-invasive alternatives such as Transcranial Doppler Imaging or 2D phase contrast MRI are limited by regional anatomic coverage and reproducibility. The purpose of this study was to evaluate the feasibility of 4D flow MR imaging [2, 3] for the comprehensive evaluation of the impact of ICAD on intracranial hemodynamics in all major vascular territories of the brain including quantitative analysis of peak velocity and mean blood flow in the large intracranial vessels.

Methods: Twenty symptomatic ICAD patients (10 male+10 female, age=65±16 years) with mild to severe intracranial vascular stenosis were included in this study. The stenosed vessels in these patients were internal carotid artery (ICA, n=7), middle cerebral artery (MCA, n=7), vertebral artery (VA, n=2), basilar artery (BA, n=5), and posterior cerebral artery (PCA, n=3). Four patients (4/20) had multiple stenosed vessels. 4D flow data acquisition with ECG synchronization (TR/TE=5.2/2.8ms, flip angle=15º, VENC=80-100cm/s, spatial resolution=1.1×1.1×1.5mm^3, temporal resolution=42ms, acquisition time=15-20min) was performed for all patients and one healthy volunteer on 1.5T MRI scanners (Avanto, Siemens, Erlangen, Germany). 4D flow data were pre-processed using a customized Matlab program to reduce background noise and correct velocity aliasing and eddy current phase errors [4]. Intracranial hemodynamics was visualized by time-integrated 3D pathlines demonstrating the cumulative flow path over one cardiac cycle in all major intracranial arteries and veins. Color coding was used to visualize the distribution of regional blood flow velocities (Figure 1). Peak velocity (m/s) and mean blood flow (ml/s) in manually positioned planes perpendicular to the major vessels was quantified (EnSight, CEI, USA) at different vascular regions through the brain as shown in Figure 1 (top left). Due to limited spatial resolution of 4D flow MRI, locations proximal to the stenosis were used for flow quantification. Flow and peak velocity ratios (N/A) of the non-affected (normal) side versus the affected (stenosed) side were calculated in four vascular territories (ICA, MCA, PCA, and ACA) for all subjects. For the patients with BA stenosis and the normal volunteer, blood flow and peak velocity ratios (R/L) in the four vessel territories were calculated between the right and the left side vessels.

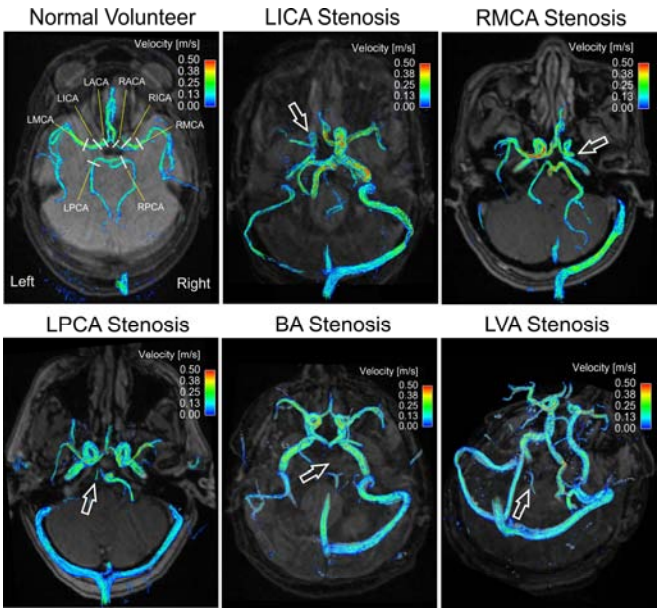

Figure 1: Intracranial hemodynamics visualized by time-integrated pathlines in one volunteer with positions labeled for flow quantification and five selected ICAD patients. Reduced blood flow velocity can be clearly appreciated in the stenosed vessels (white open arrows) in the left ICA, right MCA, left PCA, BA, and left VA, respectively.

Results: Time-integrated pathlines illustrate the blood flow patterns and velocity distributions for one healthy volunteer and five selected ICAD patients who had moderate left ICA, severe right MCA, severe left PCA, severe BA, and severe left VA stenosis, respectively (Figure 1). For the normal volunteer, large intracranial vessels can be clearly appreciated and the blood flow velocity distribution was coherent across the vessels (Table 1). In contrast, stenosed vessels (white open arrows) had clearly decreased blood flow and velocity (mostly blue) compared with their normal contralateral vessels (mostly from green to red). Table 1 summarized the blood flow and peak velocity ratios in the four vascular territories for the 20 ICAD patients and one normal volunteer. For the patient with ICA (or MCA) stenosis, we observed highly asymmetric blood flow and peak velocity in the MCA (or ICA), PCA and ACA between the non-affected and affected hemispheres. We also noted that the blood flow ratios in PCA (0.71±0.21; 0.76±0.24) were opposite to the ratios in ICA (2.98±1.98; 2.46±2.14) and MCA (2.41±2.46; 3.50±2.47) for ICA and MCA stenosis, which indicated intracranial blood flow redistribution due to regional stenotic lesions. However, the impact of regional PCA and BA stenosis on the hemodynamics in other vessel territories (e.g. ICA, MCA) were not significant. In addition, we found that the blood flow in the stenosed vessels (ICA: 3.30±1.71ml/s; MCA: 1.20±0.52ml/s) were significantly lower compared with the normal contralateral vessels (ICA: 6.72±1.83ml/s; MCA: 3.65±0.82ml/s) in two subgroups with ICA ($p=0.005$) and MCA ($p<0.001$) stenosis.

Table 1: Blood Flow and peak velocity ratios for four pairs of vessels in 20 ICAD patients and one normal volunteer

Stenosed Vessels	Blood Flow Ratios (N/A or R/L)*				Peak Velocity Ratios (N/A or R/L)*			
	ICA	MCA	PCA	ACA	ICA	MCA	PCA	ACA
ICA (n=7)	2.98±1.98	2.41±2.46	0.71±0.21	5.67±6.85	1.95±1.08	1.34±0.57	0.86±0.27	1.11±0.66
MCA (n=7)	2.46±2.14	3.50±2.47	0.76±0.24	0.77±0.39	1.60±1.16	1.58±0.62	0.95±0.53	0.80±0.23
PCA (n=3)	1.04±0.20	0.96±0.23	1.65±0.82	0.92±0.40	1.05±0.44	0.95±0.09	1.10±0.24	0.72±0.32
VA (n=2)	0.77±0.43	1.09±0.25	1.86±0.05	0.99**	0.81±0.21	1.00±0.17	0.72±0.22	0.90**
BA (n=5)	0.98±0.45	1.04±0.36	0.92±0.22	0.75±0.38	1.20±0.38	1.01±0.21	1.08±0.14	0.89±0.35
Volunteer (n=1)	1.06	0.95	0.99	1.29	0.81	0.94	1.03	0.78

Note: *N/A: the ratios of the non-affected side versus the affected (stenosed) side for ICA, MCA, PCA, and VA stenosis; R/L: the ratios of the right to the left side for BA stenosis and the normal volunteer; **One ACA was not available for quantification.

Discussion: The results in this study demonstrated the feasibility and potential of 4D flow MR imaging for the evaluation of intracranial hemodynamics in a study with 20 ICAD patients. Our findings demonstrated significant impact of regional stenotic lesions on the hemodynamics in other vascular territories. 3D visualization of the whole intracranial vasculatures using time-integrated pathlines provides an overview of the blood flow patterns and distribution of blood flow velocities in all MR visible brain vessels. Combined evaluation of the qualitative flow dynamics and quantitative hemodynamic markers may provide additional insight into the pathophysiology and risk stratification for ICAD patients. In addition, 4D flow imaging may be useful for the monitoring of intracranial hemodynamics for ICAD patients at pre- and post-interventions. A primary limitation of 4D flow imaging is its inability to measure the hemodynamics inside severely stenosed lesions. Further development on improving the velocity sensitivity to slow flow (e.g. dual VECN [5]) and spatial resolution is required to make the stenosis visible in 4D flow imaging.

References: [1] Khan M, et al. Stroke Research and Treatment 2011, Article ID 282845. [2] Markl M, et al. J Magn Reson Imaging 2012; 36:1015-1036. [3] Markl M, et al. J Cardiovasc Magn Reson 2011; 13:7. [4] Bock J, et al. ISMRM 2008; 16:3053. [5] Nett EJ, et al. J Magn Reson Imaging 2012; 35:1462-1471.