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1. Introduction

Intracranial atherosclerotic stroke (ICAS) is responsible for ischemic stroke in 10~33%,1-3 ICAS occurs in association with various stroke mechanisms, such as in situ thrombotic occlusion, artery-to-artery embolism, hemodynamic insufficiency, and branch occlusion.4 Various radiologic stroke patterns are associated with ICAS, from single and small subcortical perforator infarctions to multiple cortical infarctions [Figure 1].5,6

The characteristics of ICAS and the role of MRI and magnetic resonance angiography (MRA) are discussed herein.

Fig. 1. Various mechanisms of stroke in patients with intracranial atherosclerosis.
2. Hemodynamic characteristics of ICAS

Despite of the diversity in stroke mechanisms of ICAS, ICAS has unique hemodynamics features compared to other stroke subtypes.

2.1 Pre-stroke hemodynamic status in patients with intracranial atherosclerosis

The balance of occlusion and collaterals determines the hemodynamic circumstance or blood flow changes that challenge the brain. Depending on the time course, such changes may have radically discrepant effects. Collateral circulation is a potent determinant of recurrent stroke risk in symptomatic ICAS, demonstrating a protective role with severe stenoses and identifying more unstable milder stenosis. In addition, there are increasing evidences that ischemic preconditioning can induce tolerance by raising the threshold of tissue vulnerability in human brain. Although ischemic brain injuries resulting from focal decrease in perfusion cause ischemic brain damage, patients with preceding less severe ischemic stimuli (i.e. transient ischemic attacks) showed less likely to have stroke and more likely to have good outcome after stroke. Longstanding hemodynamic compromise which was frequently observed in intracranial atherosclerosis may elicit collateral development and preconditioning to adapt to recurrent ischemia. Thus, it is conceivable that patients with intracranial atherosclerosis may be ‘prepared’ and ‘preconditioned’ for the risk of subsequent stroke.

2.2 Hemodynamic feature in patients with ICAS

The most common techniques for imaging the ischemic penumbra in acute ischemic patients are (a) combined diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) and (b) combined DWI and MRA. ICAS had a typical PWI–DWI (a large mismatch region but less severe hypoperfusion) and MRA–DWI mismatch profiles (a stenosis or occlusion of large intracranial vessels but a small core region), which have been reported to be associated with favorable outcomes after recanalization therapy. The differences in PWI–DWI and MRA–DWI mismatch profiles between ICAS and other stroke mechanisms may be related to differences in pretreatment collateral flow status. Moreover, patients with ICAS had increased CBV when compared to patients with cardioembolic stroke. Patients with ICAS had a good collateral grade than those with other subtypes.

2.3 Stroke evolution, outcomes and recurrence after ICAS

There were two types of stroke evolution had different pathophysiological mechanisms. Specifically, the large mild perfusion delay was associated with new lesions, whereas the large initial DWI lesions and a severe perfusion delay were associated with lesion growth. Because patients with ICAS had relatively mild perfusion delay in their pretreatment MRI that were related to mostly multiple and small recurrent lesions, they may had minimal infarct growth. Similarly, ICAS as a stroke mechanism resulted in favorable clinical outcomes. Benign pretreatment MR profiles which were associated with good collaterals of ICAS patients may explain these results.
Fig. 2. Typical examples of intracranial atherosclerotic stroke. Initial MR shows typical PWI (B)-DWI (A) (a large salvageable area but less severe hypoperfusion) and MRA (C)-DWI (A) (a severe stenosis of right middle cerebral artery (white arrow) but a small core region). Digital subtraction angiography (D) demonstrates a severe stenosis in the same location (arrow head, arterial phase) and adequate leptomeningeal collateral flow from right anterior cerebral artery (black arrows, capillary phase). Follow-up DWI (E) reveals minimal infarct growth.

On the contrary, recurrent ischemic lesions during the first week after the onset of stroke in ICAS are relatively frequent compared to other stroke subtypes. In clinical aspects, many patients with ICAS have recurrent cerebral ischemic events despite standard medical therapy with antiplatelet agents or oral anticoagulants. The pattern of recurrence differed between intracranial and extracranial atherosclerotic stroke. Unlike the patients with carotid atherosclerosis who were unpredictable with respect to the site of recurrence and degree of preexisting stenosis, patients with ICAS usually recurred within the same territory as the index stroke which was associated with progression of stenosis. Collateral circulation is a potent determinant of recurrent stroke risk in symptomatic ICAS, demonstrating a protective role with severe stenoses and identifying more unstable milder stenosis.

3. Vascular imaging in patients with ICAS

3.1 Vascular studies for luminal imaging

Digital subtraction angiography (DSA) is the current gold standard for the diagnosis of intracranial atherosclerosis. However, DSA is invasive and carries the risk of stroke. Along with transcranial Doppler (TCD) and computed tomographic angiography (CTA), MRA is
less invasive techniques and has emerged as a more popular modality for visualization of intracranial vessels [Figure 3].

Fig. 3. A patient with intracranial stenosis on the left proximal middle cerebral artery. (A) DSA, (B) CTA, (C) TOF MRA, and (D) TCD findings.

Two MRA techniques used to detect intracranial stenosis are the 3D time-of-flight (TOF) MRA and contrast-enhanced MRA (CE-MRA). The Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) trial compared the accuracy of TOF MRA with DSA. SONIA demonstrated that TOF MRA have a good negative predictive value (89-93%) for excluding the presence of 50 to 99% intracranial atherosclerotic stenosis but relatively low positive predictive value (54-65%). CE-MRA is less studies for intracranial vessels because of technical issues. It has been thought that CE-MRA can lessen the problem of overestimation of the length and degree of stenosis, a common obstacle with 3D-TOF MRA by decreased dependence of flow signal intensity and T1 shortening effects of fat and calcium. However, recent studies suggested that TOF MRA provides comparable diagnostic performance with CE-MRA for intracranial stenosis with development of various TOF MRA sequence.

Recent advances in MRI techniques enable visualization of small perforating vessels originated from large intracranial arteries [Figure 4 D]. The Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial investigators showed that the degree of stenosis (the presence of severe stenosis of ≥70%) was associated with subsequent ischemic stroke in the territory of the stenotic artery. On the contrary, not only stenosis of severe degree but also stenosis of a milder degree on the symptomatic vessels should be taken into account, especially in patients with deep infarcts (branch occlusive disease). Physicians may consider a mild degree of stenosis to be irrelevant. However, large intracranial arteries have many
deep perforators, and mild stenosis may occlude these deep perforators' orifices, resulting in stroke in the absence of plaque rupture or platelet activation. A follow-up study of patients with various subtypes of ischemic stroke demonstrated that, in patients with diagnoses of lacunar stroke at the time of their index strokes, physicians often found intracranial stenoses upon these patients' recurrences.34

Fig. 4. Application of high resolution MRI. Contrast-enhanced MRI for plaque image (A-C), and 7-tesla MRA for small perforating arteries (D) and pial branches of leptomeningeal collaterals (E).

3.2 MRI for wall/plaque image

Patients with ICAS often have tandem lesions. Based on MRA, 65 out of 238 patients (27.3%) had coexistent asymptomatic intracranial stenosis. During a mean follow-up period of 1.8 years, 5 ischemic strokes (5.9%) occurred in the asymptomatic intracranial atherosclerotic stenosis territory (risk at 1 year=3.5%).35 Thus, it is important to differentiate ‘high-risk’ stenosis and so called ‘stable’ (low-risk) stenosis. There has been a growing body of interest in the role of MRI for imaging the vessel wall or the plaque. Autopsy series observed atherosclerotic plaques in intracranial vessels of 45.5-62.5% of subjects.36,37 High-resolution MRI could provide the information on the presence and the volume of plaque.38, 39 Plaque was clearly identified as plaque enhancement after gadolinium injection [Figure 4 A~C].39

MRI for plaque imaging is a potentially promising tool that can be used in clinical practice for patients with ICAS. First, this can be useful in evaluating the mechanisms of stroke, i.e. demonstrating the presence of intracranial plaque in patients with cryptogenic stroke. High-resolution MRI to determine the presence of plaque revealed that MRI detects basilar artery plaques in 42% of patients with pontine infarctions and normal basilar angiograms.38 Second, this technique can help physician to identify the vulnerable plaque in the intracranial vessels. A recent study showed that all patients with ICAS have eccentric enhancing plaques when imaging is performed within weeks to months of cerebral infarcts within the artery territory, but none of asymptomatic plaques had enhancement.40 Moreover, remodeling mode of intracranial atherosclerosis can be identified using high-resolution MRI. It has been well known that atherosclerotic narrowing of arterial lumen is not a simple consequence of enlargement of atherosclerotic burden.41 Recent investigations with patients with intracranial atherosclerotic stenosis revealed that some compensatory enlargement of vessels (positive remodeling) which is associated with more lipid-rich
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plaques\textsuperscript{42, 43} was more frequently observed in symptomatic patients compared with asymptomatic ones.\textsuperscript{44, 45} Lastly, risk factors for the presence of intracranial plaque have been reported\textsuperscript{36} and several drug therapies (i.e. statin) could modify plaque stability. In addition, the effects of such therapeutic intervention could be monitored using high-resolution MRI.

### 3.3 Collateral image

MRA can evaluate the cerebral collateral circulation in the circle of Willis. With phase contrast MRA, flow direction information can be obtained by the phase changes in blood water protons in the different arterial segments of the circle of Willis.\textsuperscript{46} Although MRA have moderate to good diagnostic performance for the presence of collateral flow via the anterior circle of Willis, MRA tends to underestimate the presence of collateral flow with respect to the posterior communicating artery. Compared to conventional angiography which is considered as a gold standard for the assessment of collaterals, MRA collateral flow measurements via the anterior part of the circle of Willis yielded a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 83\%, 77\%, 78\%, 82\% and 80\%, respectively. On the other hand, MRA collateral flow measurements via the posterior communicating artery yielded a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 33\%, 88\%, 89\%, 31\% and 47\%, respectively.\textsuperscript{47-49} Recently, vessel-encoded arterial spin labeling technique was developed to assess collateral circulations.\textsuperscript{50-52}

Beside the collateral circulation via the circle of Willis, leptomeningeal collaterals also play an important role in patients with ICAS. The leptomeningeal collateral can be visualized using a dedicated MRI method (subtracting the image of the first movement map).\textsuperscript{53} Beside the vessel images, various MRI parameters can indirectly reflect the collateral status, e.g. DWI, PWI, and FLAIR. We found that, compared to the large cortical DWI pattern, the deep-infarcts pattern exhibited less severe hypoperfusion related to good collateral flows.\textsuperscript{54} In addition, distal hyperintense vessels on fluid-attenuated inversion recovery image likely represent excessively slow flow induced by retrograde collateral flow distal to the occlusion of a proximal artery, and may be associated with leptomeningeal collaterals and response to thrombolysis.\textsuperscript{55, 56} A recent study using 7-tesla MRI directly visualized the pial branches, indicating the possibility of assessment of leptomeningeal collaterals with high-resolution MRA [Figure 4 E].\textsuperscript{57}

### 4. Conclusion

Patients with ICAS often received the same treatment as those with extracranial carotid atherosclerosis. However, there are accumulating evidences that hemodynamic features as well as stroke mechanisms may differ between ICAS and other stroke subtypes.\textsuperscript{24, 58, 59} Using MRI techniques to understanding pathophysiology, hemodynamic status, and vascular pathology (via both luminal and wall imaging) will allow the future development of rational stroke therapies for patients with ICAS.

### 5. References


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As MRI has paved its role in diagnostic angiography, MRA has the potential to provide more physiological and pathophysiological data over the disease in addition to the anatomical information. This book is divided into three sections. The first section discusses the basics of MRI angiography. It starts with focus on the contrast agents that are mainly used in MR angiography with detailed discussion of advantage and limitations of different types of contrast. The second chapter is oriented more towards the technical consideration that contribute to good quality examination, both the non contrast and contrast based sequences from black to bright blood imaging, contrast enhanced MRA, review of clinical application of MRA in different body systems and MR venography. The second section reviews the clinical application of MRI mainly in the head and neck and brain ischemia imaging. The new high resolution intracranial plaque imaging of the branch athermanous disease, to the hemodynamic of intracranial atherosclerotic stroke and quantitative MRA imaging in neurovascular imaging, are the topics in this section. Also this section covers the future prospective and the new frontiers MRI angiography is exploring. In the third section, MRA of aortic disease in children with emphasis on cardiac MRA.

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