Precision Diagnosis of Intracranial Atherosclerosis by Using High resolution MRI: Plaque Morphology and/or Components rather than Arterial Stenosis Predict Stroke Recurrence

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Declare

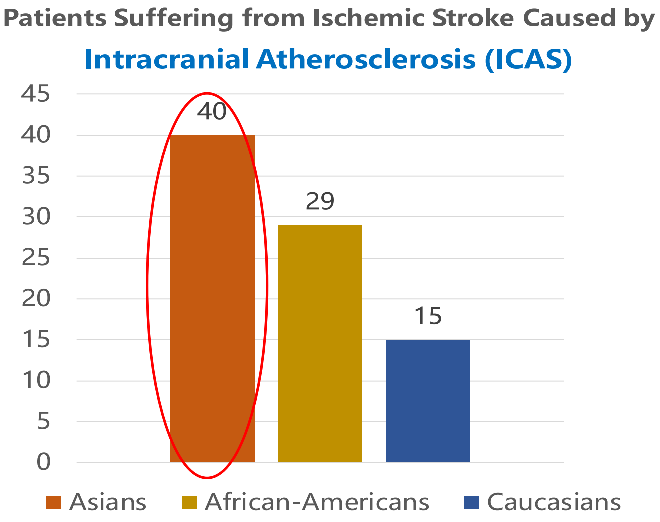
- I am working at **Department of Health Technology and Informatics (HTI), the Hong Kong Polytechnic University (PolyU).**

- ***The post-mortem study*** and ***clinical studies on stroke patients*** were conducted mainly in the Prince of Wales Hospital (PWH), ***the Chinese University of Hong Kong (CUHK)***, which have been further analyzed and drafted in PolyU.

Background

Intracranial atherosclerosis (ICAS)

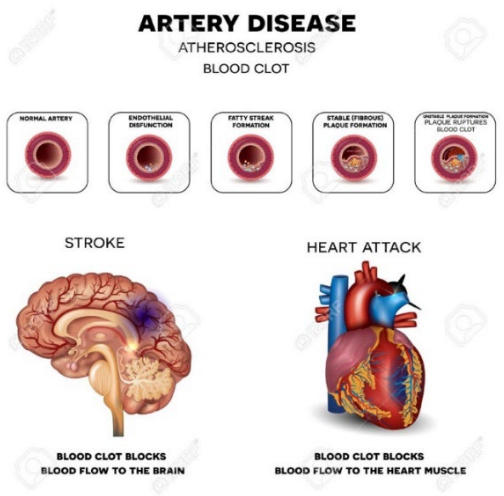
The most common etiology of ischemic stroke with *the highest rate of recurrent stroke*, especially in Asian populations.[1-5]

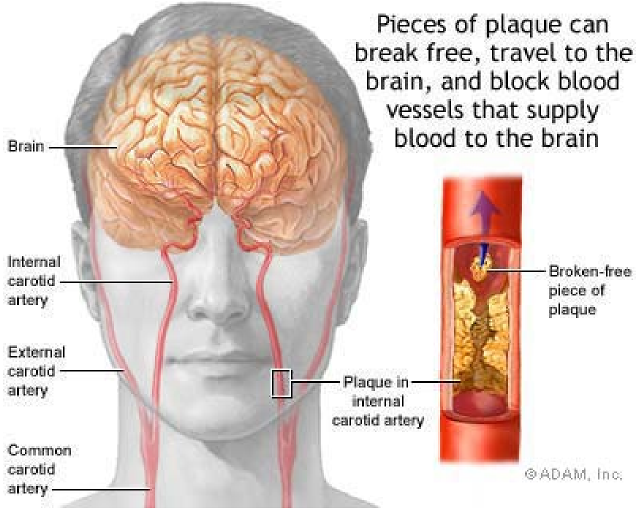


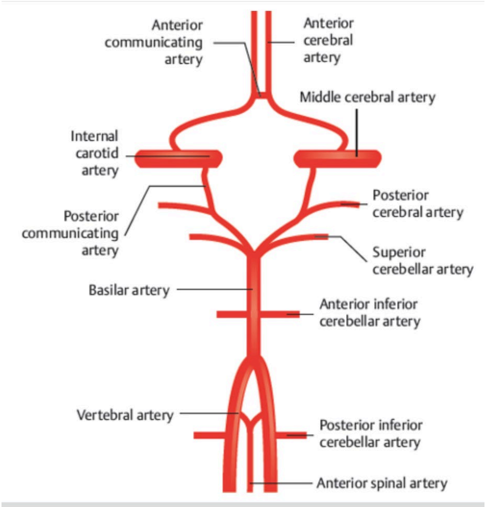
Wang, Y., et al., Prevalence and outcomes of symptomatic intracranial large artery stenoses and occlusions in China: the Chinese Intracranial Atherosclerosis (CICAS) Study. Stroke, 2014. 45(3): 663-9.
Lange, M.C., et al., Stroke recurrence in the different subtypes of ischemic stroke. The importance of the intracranial disease. Arq Neuropsiquiatr, 2018. 76(10): 649-653.

Background

Intracranial atherosclerosis (ICAS) vs. Extracranial atherosclerosis

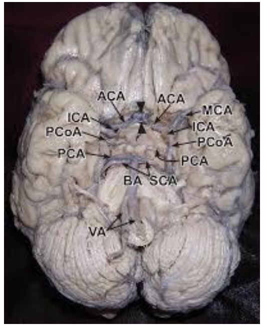






1. Bos D, et al. Atherosclerotic Carotid Plaque Composition and Incident Stroke and Coronary Events. J Am Coll Cardiol.
2. Oumer M, Alemayehu M, Muche A. Association between circle of Willis and ischemic stroke: a systematic review and meta-analysis. BMC Neurosci. 2021.

My research journey in the field of stroke



ICAS: MRI vessel wall imaging & histopathology

2003 **2006** **2008** 2014 2016/**2016/2016/2016** 2017 **2021** 2023

2006 **2007** **2017/2017** **2023/2023**

IAC: CT brain & histopathology

Our research achievements on ICAS & IAC

1. **A post-mortem study (2003-2006):**
   The *Ex-vivo MRI Vessel Wall Imaging* of Histology-verified *ICAS*

2. **Clinical Studies (2014-):**
   High Resolution-MRI in **Stroke Patients**
   High Resolution-MRI in **Community dwelling adults**

3. **Clinical studies (2005-):**
   Intracranial Arterial Calcification (IAC) on *CT brain*

Our first paper on Histology of ICAS

Cerebrovasc Dis 2008;25:74–80

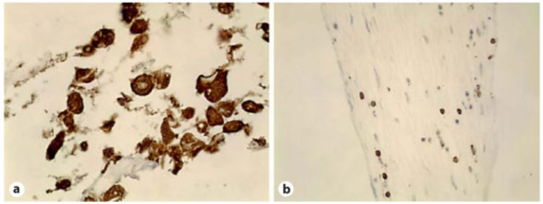
Middle Cerebral Artery Atherosclerosis: Histological Comparison between Plaques Associated with and Not Associated with Infarct in a Postmortem Study

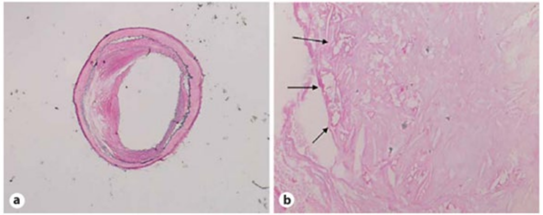
Xiang Yan Chen[a] Ka Sing Wong[a] Wynnie Wai Man Lam[c] Hai-Lu Zhao[a]
Ho Keung Ng[b]

76 autopsy cases
mean age, 74.7yrs (46-99yrs)
men: 42 (55.3%)

Table 1. Comparison of clinical risk factors between the cases with and without MCA infarctions

	Cases with infarctions in the MCA territory (n = 18)	Cases without infarctions in the MCA territory (n = 58)	p value
Age, years	76.7 ± 10.8	74.1 ± 12.8	0.437
Males	12	30	0.293
Atrial fibrillation	3	8	0.716
Ischemic heart disease	4	8	0.463
Hypertension	10	25	0.422
Diabetes	4	13	1.000
Hyperlipidemia	1	2	0.561
Never smoker	11	41	
Current smoker	3	7	1.000
Former smoker	4	10	1.0000





In addition to luminal stenosis, plaque vulnerability plays an important role in leading to brain infarctions.

Our papers on 1.5T MR vessel wall imaging of ICAS

In Vitro Assessment of Histology Verified Intracranial Atherosclerotic Disease by 1.5T Magnetic Resonance Imaging

Concentric or Eccentric?

Wen-Jie Yang, PhD; Xiang-Yan Chen, PhD; Hai-Lu Zhao, PhD; Chun-Bo Niu, MD; Yun Xu, MD, PhD; Ka-Sing Wong, MD; Ho-Keung Ng, MD

Background and Purpose—Clinical trial studies show that plaque eccentricity (symmetry) is among the plaque features that have been associated with more frequent cerebrovascular events. Plaque eccentricity of intracranial atherosclerotic disease is unclear because of lacking of cerebral artery specimens.

Methods—1.5T magnetic resonance imaging was performed in the postmortem brains to scan the cross sections of middle cerebral artery. Plaque eccentricity of histology-verified middle cerebral artery atherosclerosis was calculated on T1-weighted fat-suppressed sequence.

Results—Validated by histology, concentric atherosclerotic plaques were identified in 46 middle cerebral arteries (63.9%) on magnetic resonance imaging and eccentric plaques in 26 arteries (26.1%). Eccentric plaques showed higher maximum wall thickness and lower minimum wall thickness than concentric plaques (both $P<0.001$). Plaque burden and brain infarctions were similar between concentric and eccentric plaques.

Conclusions—Intracranial atherosclerosis presents as eccentric or concentric in geometry, which may be not linked to intracranial plaque risk. Further in vivo imaging studies are needed to identify morphological features of intracranial plaques and to verify its association with brain infarctions. **(*Stroke*. 2016;47:527-530. DOI: 10.1161/STROKEAHA.115.011086.)**

Key Words: high resolution magnetic resonance imaging ■ histology ■ intracranial atherosclerosis ■ plaque eccentricity

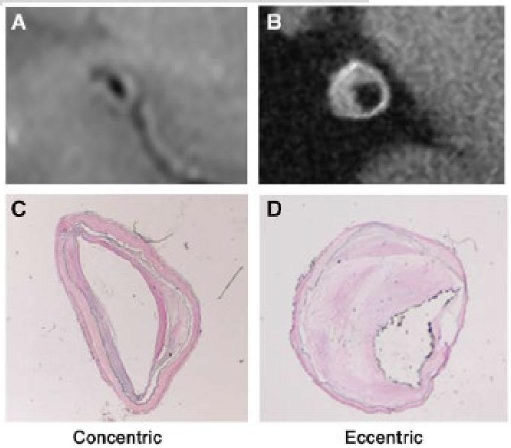


Figure. Representative magnetic resonance images and corresponding histopathologic sections of concentric and eccentric lesions. Brain magnetic resonance imaging T1-weighed fat-suppressed sequence shows examples of middle cerebral artery with concentric (**A**) and eccentric (**B**) plaques, which are verified by histopathology (**C** and **D**), respectively.

Our papers on 1.5T MR vessel wall imaging of ICAS

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Postmortem Study of Validation of Low Signal on Fat-Suppressed T1-Weighted Magnetic Resonance Imaging as Marker of Lipid Core in Middle Cerebral Artery Atherosclerosis

Wen-Jie Yang, PhD; Xiang-Yan Chen, PhD; Hai-Lu Zhao, PhD; Chun-Bo Niu, MD; Bing Zhang, MD, PhD; Yun Xu, MD, PhD; Ka-Sing Wong, MD; Ho-Keung Ng, MD

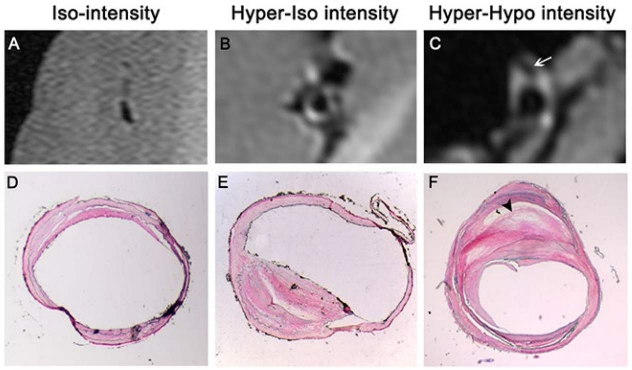
Background and Purpose—High signal on T1-weighted fat-suppressed images in middle cerebral artery plaques on ex vivo magnetic resonance imaging was verified to be intraplaque hemorrhage histologically. However, the underlying plaque component of low signal on T1-weighted fat-suppressed images (LST1) has never been explored. Based on our experience, we hypothesized that LST1 might indicate the presence of lipid core within intracranial plaques.

Methods—1.5 T magnetic resonance imaging was performed in the postmortem brains to scan the cross sections of bilateral middle cerebral arteries. Then middle cerebral artery specimens were removed for histology processing. LST1 presence was identified on magnetic resonance images, and lipid core areas were measured on the corresponding histology sections.

Results—Total 76 middle cerebral artery locations were included for analysis. LST1 showed a high specificity (96.9%; 95% confidence interval, 82.0%–99.8%) but a low sensitivity (38.6%; 95% confidence interval, 24.7%–54.5%) for detecting lipid core of all areas. However, the sensitivity increased markedly (81.2%; 95% confidence interval, 53.7%–95.0%) when only lipid cores of area ≥0.80 mm^2 were included. Mean lipid core area was 5× larger in those with presence of LST1 than in those without (1.63±1.18 mm^2 versus 0.32±0.31 mm^2; P=0.003).

Conclusions—LST1 is a promising imaging biomarker of identifying intraplaque lipid core, which may be useful to distinguish intracranial atherosclerotic disease from other intracranial vasculopathies and to assess plaque vulnerability for risk stratification of patients with intracranial atherosclerotic disease. In vivo clinical studies are required to explore the correlation between LST1 and clinical outcomes of patients with intracranial atherosclerotic disease. (***Stroke*. 2016;47:2299-2304. DOI: 10.1161/STROKEAHA.116.013398.**)

Key Words: atherosclerosis ■ lipid core ■ MCA ■ MRI ■ vessel wall imaging



Invited speech at 2016 ICAS & Invited review article on JoS

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JoS
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Journal of Stroke 2017;19(3):249-260
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Special Review

Intracranial Atherosclerosis: From Microscopy to High-Resolution Magnetic Resonance Imaging

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Intracranial atherosclerosis is one of the leading causes of ischemic stroke and occurs more commonly in patients of Asian, African or Hispanic origin than in Caucasians. Although the histopathology of intracranial atherosclerotic disease resembles extracranial atherosclerosis, there are some notable differences in the onset and severity of atherosclerosis. Current understanding of intracranial atherosclerotic disease has been advanced by the high-resolution magnetic resonance imaging (HRMRI), a novel emerging imaging technique that can directly visualize the vessel wall pathology. However, the pathological validation of HRMRI signal characteristics remains a key step to depict the plaque components and vulnerability in intracranial atherosclerotic lesions. The purpose of this review is to describe the histological features of intracranial atherosclerosis and to state current evidences regarding the validation of MR vessel wall imaging with histopathology.

Keywords Intracranial atherosclerosis; Autopsy; Histology; Magnetic resonance imaging

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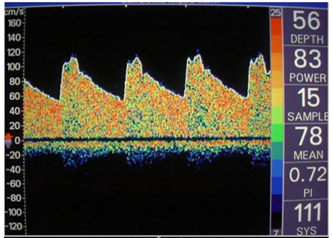
Clinical Studies:

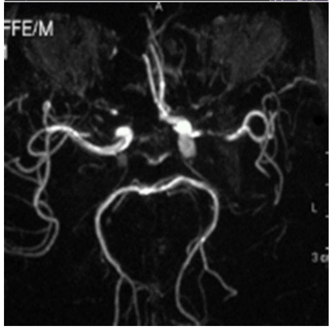
The Adoption of High Resolution-MRI in Stroke Patients

Background

How to detect ICAS?

- Transcranial Doppler (TCD)
- MRA (Magnetic Resonance Angiography)
- CTA (Computed Tomography Angiography)
- DSA (Digital Subtraction Angiography)
- **HRMRI (High-Resolution Magnetic Resonance Imaging)**





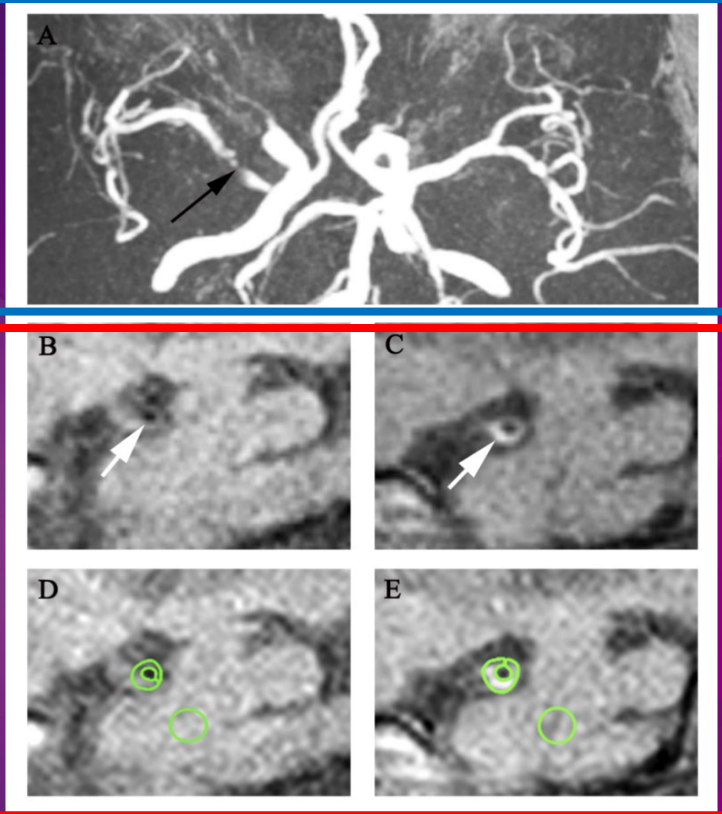


Figure 1: Representative MR images delineating enhancement index measurement. A 60-year-old man with acute stroke showed severe **right MCA stenosis** on MRA (A, white arrow). After matching pre- (B and D) and post-contrast T1w images (C and E) at the most severe narrowing site, the plaque enhancement index was **48.74%**.

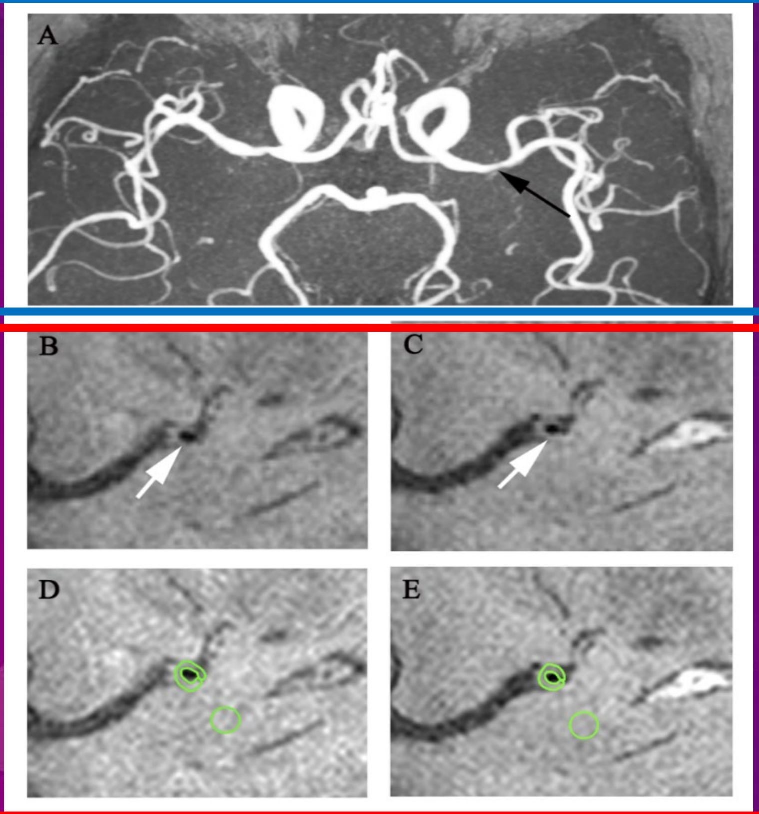


Figure 2: Representative MR images delineating enhancement index measurement. A 65-year-old man with acute stroke showed **severe left MCA stenosis** on MRA (A, white arrow). After matching pre- (B and D) and post-contrast T1w images (C and E) at the most severe narrowing site, the plaque enhancement index was **2.82%**.

Magnetic Resonance Imaging of Plaque Morphology, Burden, and Distribution in Patients With Symptomatic Middle Cerebral Artery Stenosis

Nikki Dieleman, MSc*; Wenjie Yang, MD*; Jill M. Abrigo, MD; Winnie Chiu Wing Chu, MD, PhD; Anja G. van der Kolk, MD, PhD; Jeroen C.W. Siero, PhD; Ka Sing Wong, MD, PhD; Jeroen Hendrikse, MD, PhD; Xiang Yan Chen, MD, PhD

Background and Purpose—Intracranial atherosclerosis is a major cause of ischemic stroke worldwide. Intracranial vessel wall imaging is an upcoming field of interest to assess intracranial atherosclerosis. In this study, we investigated total intracranial plaque burden in patients with symptomatic middle cerebral artery stenosis, assessed plaque morphological features, and compared features of symptomatic and asymptomatic lesions using a 3T vessel wall sequence.

Methods—Nineteen consecutive Chinese patients with ischemic stroke and transient ischemic attack (mean age: 67 years; 7 females) with a middle cerebral artery stenosis were scanned at 3T magnetic resonance imaging; the protocol included a time-of-flight magnetic resonance angiography and the T1-weighted volumetric isotropically reconstructed turbo spin echo acquisition sequence before and after (83%) contrast administration. Chi-square tests were used to assess associations between different plaque features. Statistical significance was set at $P<0.05$.

Results—Vessel wall lesions were identified in 18 patients (95%), totaling 57 lesions in 494 segments (12% of segments). Lesions were located primarily in the anterior circulation (82%). Eccentric lesions were associated with a focal thickening pattern and concentric lesions with a diffuse thickening pattern ($P<0.001$). When differentiating between asymptomatic and symptomatic lesions, an association ($P<0.05$) was found between eccentricity and asymptomatic lesions, but not for enhancement or a specific thickening pattern. Symptomatic lesions did not have any specific morphological features.

Conclusions—Our results lead to a 2-fold conclusion: (1) The classification system of both thickening pattern and distribution of the lesion can be simplified by using distribution pattern only and (2) differentiation between symptomatic and asymptomatic atherosclerotic lesions was possible using intracranial vessel wall imaging. (*Stroke*. **2016;47:00-00. DOI: 10.1161/STROKEAHA.116.013007.**)

Key Words: atherosclerosis ■ brain ■ magnetic resonance imaging ■ stroke

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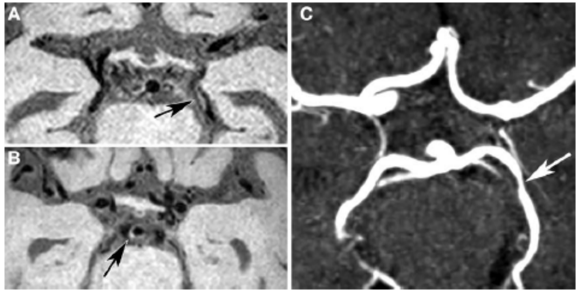

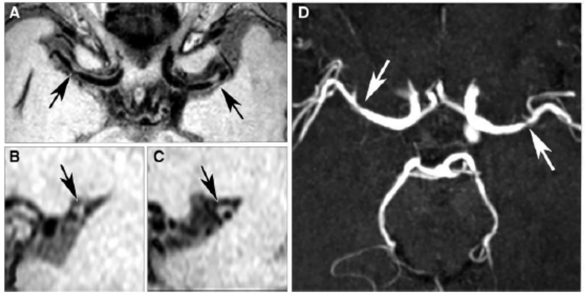

HRMRI studies in stroke patients

- **HMRF project (1 May 2017- 30 April 2019)**

  Precision medicine in Intracranial Atherosclerosis: Delineating Plaque stability by Novel High resolution MRI to Improve Personalized Treatment for Stroke Patients

- **GRF (1 October 2016-30 September 2019)**

  Evolution of Intracranial Large Artery Stenosis in Patients with and without RNF213 Genetic Variant: A Prospective Study Using High Resolution MRI Vessel Wall Imaging and MR Angiography

The flow chart of patient selection

武汉市第一医院
神经内科

From 2014 to 2020, stroke patients with intracranial large artery stenosis diagnosed by routine cerebral angiography (**n=190**)

Remark:
HR-MRI scanning protocol started at the BA level (2014-2015), while modified to cover the intracranial segments of the bilateral VAs from 2016 to 2020.

Excluded (n=54):
- Subacute IS/TIA (n=25);
- Chronic IS/TIA (n=29).

Patients with acute IS/TIA (n=136)

Excluded (n=11):
- Poor image quality (n=6);
- Other etiologies (n=5).

Patients with acute IS/TIA due to intracranial large artery atherosclerosis (n=125)

Excluded (n=29):
- Incomplete imaging scan of the intracranial VAs.

Excluded (n=18):
- No MCA atherosclerotic lesions identified by HR-MRI.

Patients with MCA atherosclerotic lesions identified by HR-MRI (n=107)

Patients with intracranial large-artery atherosclerotic lesions identified by HR-MRI (n=96)

In Section One
Research on MCA atherosclerosis

In Section One
Research on ICAS

Excluded (n=28):
- Absence of the VA or the BA on MRA (n=8);
- No vertebrobasilar atherosclerotic lesions identified by HR-MRI (n=20).

Patients with vertebrobasilar atherosclerotic lesions identified by HR-MRI (n=68)

In Section Two
Research on vertebrobasilar artery atherosclerosis

HMRF-funded project:

Objectives:

- This study aimed to ***evaluate the association between plaque features (morphology and/or components) assessed by HRMRI*** and ***the short/long-term outcomes*** of ischemic stroke or TIA patients with ICAS.

- The goal was to determine specific parameters of plaque features with the best predictive efficacy for stroke recurrence.

HMRF-funded project:

Methods:

- ***Consecutive patients with acute ischemic stroke*** were included.
- ***3T MRI*** was used to perform vessel wall imaging before and after contrast administration.
- ***Imaging analysis***: luminal stenosis, plaque burden, plaque eccentricity and plaque enhancement index and signal intensity were assessed in bilateral middle cerebral artery (MCA), vertebral artery (VA) and the basilar artery (BA) .
- ***Regular follow-up*** was performed within one year after stroke onset.

HMRF-funded project:

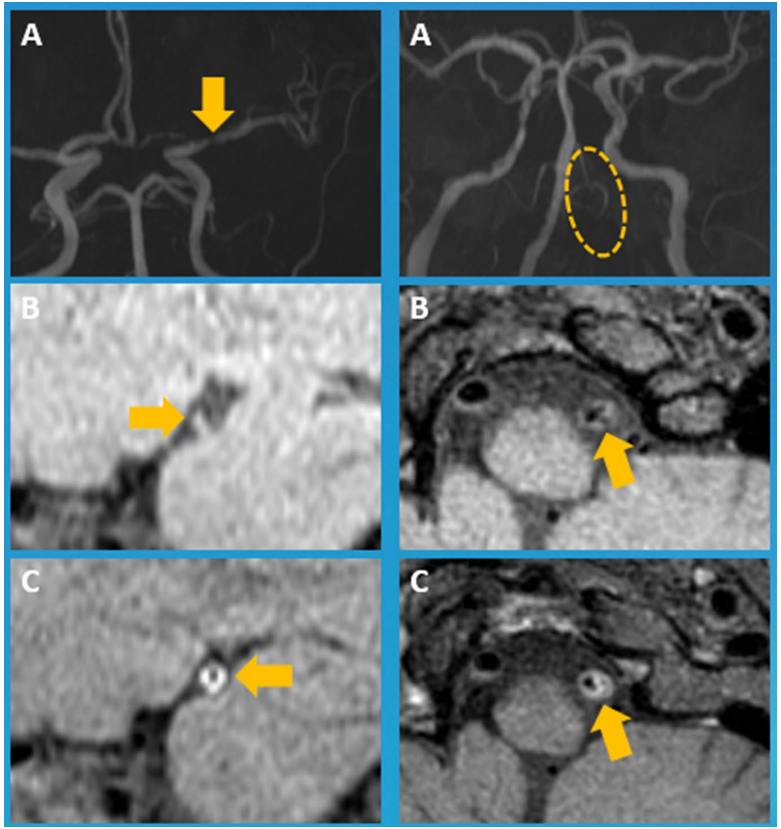

Figure 1 (The LEFT). Left MCA stenosis (A). HRMRI indicates hyper-intensity on pre-contrast image (B) and enhancement on post-contrast image (C) at the lesion site.

Figure 2 (The RIGHT). Signal void in left VA's region (A). HRMRI indicated hypo-intensity on pre-contrast image (B) and enhancement on post-contrast image (C) at the lesion site.

HMRF-funded project:

Results:

- Among ***132 recruited patients***, 293 ICAD lesions were identified, including ***86 symptomatic*** and ***207 asymptomatic lesions***.
- ***Symptomatic ICAD*** had ***higher degree of stenosis*** (73.75 ± 18.27% vs. 61.78 ± 21.07%, $p<0.001$), ***higher plaque burden*** (84.82 ± 10.58% vs. 77.48 ± 11.58%, $p<0.001$) and ***slightly higher prevalence of eccentric plaque*** (70.9% vs. 59.9%, $p=0.075$), compared with asymptomatic ICAD.
- During 1-year follow-up, ***11 patients*** had recurrent stroke.

HMRF-funded project:

	ICAD of patients with recurrent stroke (n=26)	*ICAD of patients without recurrent stroke (n=267)*	*p value*
Symptomatic lesion	*7 (26.9%)*	*29 (29.6%)*	*p=0.776*
Stenosis (%)	*60.28 ± 22.07*	*65.79 ± 20.85*	*p=0.231*
Plaque burden (%)	*78.91 ± 10.69*	*79.71 ± 11.88*	*p=0.623*
Enhancement index (%)	*25.41 ± 24.93*	*30.50 ± 28.03*	*p=0.219*
Hypo intensity	*6 (23.1%)*	*86 (32.2%)*	*p=0.781*
Hyper intensity	*3 (11.5%)*	*94 (35.2%)*	*p=0.014*
Eccentric plaque	*15 (57.7%)*	*170 (63.7%)*	*p=0.546*

HMRF-funded project:

Conclusions:

- ***Characterized by HRMRI***, ***luminal stenosis*** and ***morphological features*** of individual lesions in the intracranial vessel wall may play a synergetic effect on the occurrence and recurrence of stroke.

- The study findings suggest that ***both luminal stenosis and plaque morphology/components*** play a synergistic role in stroke occurrence.

Our publications on HR-MRI vessel wall imaging

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frontiers in Neurology

Regression of Plaque Enhancement Within Symptomatic Middle Cerebral Artery Atherosclerosis: A High-Resolution MRI Study

Wen-Jie Yang[1], Jill Abrigo[2], Yannie Oi-Yan Soo[3], Simon Wong[2], Ka-Sing Wong[3], Thomas Wai-Hong Leung[3], Winnie Chiu-Wing Chu[2] and Xiang-Yan Chen[4]**

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Objective: Contrast enhancement is a vital feature of the intracranial atherosclerotic plaque on high-resolution magnetic resonance imaging (HRMRI), but its clinical significance is still unclear. We aimed to quantitatively assess plaque enhancement patterns in the middle cerebral artery (MCA) atherosclerotic plaque.

Methods: We conducted a cross-sectional study by prospectively recruiting stroke or transient ischemic attack patients with $>30\%$ of MCA stenosis of either side. All patients underwent contrast-enhanced HRMRI scans. Enrolled patients were classified into acute phase (<4 weeks), subacute phase (4–12 weeks) and chronic phase (>12 weeks) groups based on the time interval from stroke onset to imaging scan. Plaque enhancement index was calculated for each MCA lesion at the maximal narrowing site.

Results: We identified a total of 89 MCA plaques [53 (60%) symptomatic and 36 (40%) asymptomatic; 57 (64%) acute, 18 (20%) subacute and 14 (16%) chronic] in 58 patients on HRMRI. Among the acute lesions, symptomatic plaques had a significantly stronger plaque enhancement than asymptomatic plaques (symptomatic vs. asymptomatic: 38.9 ± 18.2 vs. 18.2 ± 16.2, $p < 0.001$). Among the symptomatic lesions, plaque enhancement diminished with increasing time after stroke onset (38.9 ± 18.2, 22.0 ± 22.8, and 5.0 ± 10.1 for acute, subacute, and chronic phase, respectively; $p = 0.001$).

Conclusion: Plaque enhancement in the acute atherosclerotic plaque is closely related to recent ischemic events. In symptomatic atherosclerosis, plaque enhancement regresses over time after ischemic stroke, which may offer the potential to monitor the plaque activity in intracranial atherosclerosis using HRMRI.

Keywords: intracranial atherosclerosis, magnetic resonance imaging, stroke, inflammation, middle cerebral artery, plaque enhancement

Our publications on HR-MRI vessel wall imaging

武汉市第一
医院神经内科

Plaque Wall Distribution Pattern of the Atherosclerotic Middle Cerebral Artery Associates With the Circle of Willis Completeness

Jia Li[1], Lu Zheng[2], Wen-Jie Yang[3], Cheuk-Yin Sze-To[4], Thomas Wai-Hong Leung[5] and Xiang-Yan Chen[1]*

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Objective: Investigating the relevance of the incomplete circle of Willis (COW) to the plaque wall distribution in the atherosclerotic middle cerebral arteries (MCAs) through utilizing high-resolution magnetic resonance imaging (HR-MRI), and its potential clinical impact.

Methods: This hospital-based study enrolled consecutive adult patients with acute ischemic stroke or transient ischemic attack, who received a 3.0T Achieva MR system scanning. The COW completeness was evaluated on MR angiography imaging, including anterior (A) and posterior (P)-COW sections. The MCA plaque wall distribution was assessed on HR-MRI. The occurrence of perforator infarction was detected on diffusion-weighted imaging.

Results: Among 87 patients (mean age = 62.39 ± 11.64 years old) with atherosclerotic plaques in the MCA M1 segments, the incomplete COW types were more prevalent than the complete COW type (incomplete P-COW, 83.9%; incomplete A-COW, 36.8%; complete COW, 8.1%). The incomplete A-COW had more inferior but fewer ventral plaques of MCA atherosclerosis than the complete A-COW, while the incomplete P-COW had fewer inferior MCA plaques than the complete P-COW. Moreover, symptomatic MCA plaques causing perforator infarctions were more likely to locate on the superior wall.

Conclusion: Our findings suggested that the COW completeness could influence the vessel wall distribution of the MCA plaques, among which the superior plaques of symptomatic MCA atherosclerosis was associated with branch occlusive disease.

Vertebrobasilar Junction Angle Over 90°: A Potential Imaging Marker Associated With Vertebrobasilar Atherosclerosis

Jia Li[1,2], Wen-Jie Yang[3], Lu Zheng[4], Heng Du[2], Winnie Chiu-Wing Chu[5], Thomas Wai-Hong Leung[6] and Xiang-Yan Chen[2]*

[1] *Department of Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China,* [2] *Department of Health Technology and Informatics, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China,* [3] *Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland, Baltimore, Baltimore, MD, United States,* [4] *Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China,* [5] *Department of Imaging and Interventional Radiology, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China,* [6] *Division of Neurology, Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China*

Objective: Whether the cerebral vascular variations play an important role in the progression of intracranial atherosclerosis is yet largely unclear. We aimed to investigate the relationship between the magnitude of the vertebrobasilar junction (VBJ) angle and the imaging features of vertebrobasilar artery atherosclerosis.

Methods: Adult patients with acute ischemic stroke or transient ischemic attack undergoing a 3.0-tesla vessel wall magnetic resonance imaging (VW-MRI) scanning were consecutively included. Imaging features of vertebrobasilar artery atherosclerosis were assessed on the reconstructed short axis of VW-MRI at the most stenotic site. The VBJ angle degree was measured on magnetic resonance angiography and classified into the angle ≥90° or <90°.

Results: Among 68 patients (mean age = 63.5 ± 9.4 years old; 63.2% were male) with vertebrobasilar atherosclerosis, 33 had a VBJ angle ≥90° and 35 had a VBJ angle <90°. Compared to the vertebrobasilar plaques with VBJ angle <90°, those with VBJ angle ≥90° had a heavier plaque burden (84.35 vs. 70.58%, $p < 0.001$) and higher prevalence of intraplaque hemorrhage (17.1 vs. 3.3%, $p = 0.01$). In the regression analyses, the VBJ angle ≥90° was also robustly associated with plaque burden (odds ratio, 1.11; 95% confidential interval, 1.043–1.18; $p = 0.001$) and intraplaque hemorrhage (odds ratio, 5.776; 95% confidential interval, 1.095–30.46; $p = 0.039$) of vertebrobasilar atherosclerosis.

Conclusion: The VBJ angle over 90° might aggravate the vessel wall condition of the atherosclerotic vertebrobasilar arteries, which might serve as a potential risk factor for vertebrobasilar atherosclerosis.

Our publications on HR-MRI vessel wall imaging

Association of Plaque Morphology With Stroke Mechanism in Patients With Symptomatic Posterior Circulation ICAD

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Abstract

Background and Objectives

Although the main mechanisms of stroke in patients with intracranial atherosclerotic disease (ICAD)—perforating artery occlusion (PAO) and artery-to-artery embolism (AAE)—have been identified and described, relatively little is known about the morphology of the symptomatic plaques and how they differ between these 2 mechanisms.

Methods

We prospectively recruited patients with acute ischemic stroke in the posterior circulation that was attributable to ICAD. Fifty-one eligible patients were enrolled and underwent magnetic resonance imaging before being assigned to the PAO or AAE group according to probable stroke mechanism. Plaque morphological properties including plaque length, lumen area, outer wall area, plaque burden, plaque surface irregularity, vessel wall remodeling, and plaque enhancement were assessed using high-resolution MRI. Plaque morphological parameters of both PAO and AAE groups were compared using nonparametric tests. A binary logistic regression model was used to identify independent predictors while a receiver operating characteristic curve tested the sensitivity and specificity of the model.

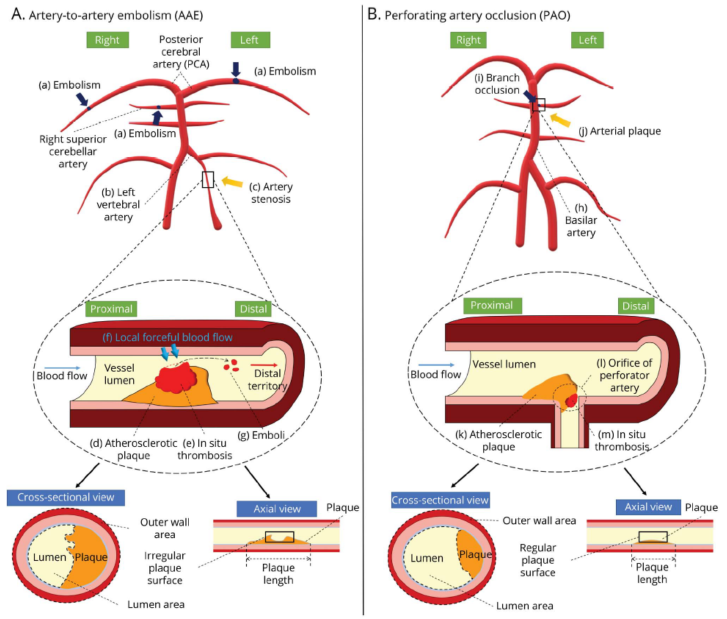
Results

Among patients who met the imaging eligibility criteria, 38 (74.5%) had PAO and 13 (25.5%) had AAE. Plaque length was shorter (6.39 interquartile range [IQR, 5.18–7.7]1 mm vs 10.90 [IQR, 8.18–11.85] mm, $p < 0.01$) in patients with PAO. Plaque burden was lower in PAO group (78.00 [IQR, 71.94–86.35] % vs 86.37 [IQR, 82.24–93.04] %, $p = 0.04$). The proportion of patients with plaque surface irregularity was higher in patients with AAE than in patients with PAO (19/38, 50.00% vs 12/13, 92.30%, $p = 0.008$). Plaque length was significantly associated with the PAO mechanism (adjusted OR 0.57, 95% CI, 0.41–0.79).

Discussion

Intracranial atherosclerotic plaque morphology differs between patients with PAO and those with AAE. Plaque with shorter length, lower plaque burden, and regular surface is more likely to cause PAO.

Figure 2 Mechanisms of Artery-to-Artery Embolism (AAE) and Perforating Artery Occlusion (PAO)



(1) The left diagram shows that AAE leads to the infarct pattern of multiple embolisms (A) in separate distal territories (cortical and subcortical) of the culprit artery. The left vertebral artery (B) with stenotic lesion (C) is the culprit artery segment. Beginning with fissuring of the fibrous cap of the atherosclerotic plaque (D), in situ thrombosis (E) can be formed rapidly. During this process, local forceful blood flow (F) may break up a part of the thrombus and carry the emboli (G) to distal arteries. (2) The right diagram shows PAO mostly caused by eccentric plaque associated with small single subcortical infarct. A branch of the basilar artery (H) with relatively normal vessel lumen is occluded (I) due to atherosclerotic plaque (J). PAO mainly results from the protrusion of the atherosclerotic plaque (K) of the parent artery into the orifice of the perforator artery (L), in which secondary thrombosis (M) can be formed.

Editorial by Prof. Caplan L.R.

EDITORIAL

Intracranial Plaque Imaging

Louis R. Caplan, MD

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Among 900,000 annual strokes and transient ischemic attacks, up to 10% are attributable to intracranial atherosclerosis (ICAS).[1] The recurrence rate in these patients is 15% per year.[1] In a recent autopsy study from Paris, France, that involved a systematic analysis of intracranial and extracranial arteries, the aortic arch, and the heart in 339 consecutive autopsies of patients with stroke, the study population had very significant ICAS.[2] Intracranial plaques were found in 62% of patients with brain infarction and intracranial arterial stenoses in 43%. In those patients with at least 1 intracranial plaque-inducing luminal stenosis >30%, the stenosis was considered causal in 5.8% because of the presence of superimposed clot on ulcerated plaques; 27% of these patients had stenoses graded 30%–75%.[2]

RELATED ARTICLE

Research Article
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1) This study provides additional evidence that high-resolution intracranial plaque morphology can provide information about stroke mechanism and paints a more complete picture of plaques: their location, size, regularity, and extent and locale of luminal compromise.
2) Recognizing these plaque details helps with diagnosis and can also inform the interventionalist before placing stents or other devices in and through lumens bordered by intracranial arterial plaques.

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Clinical Studies

The Application of High Resolution-MRI in community-dwelling adults

Opening Minds • Shaping the Future
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A Community-based Study

Project title:
Intracranial Atherosclerotic Disease and Cerebral Small Vessel Disease among Middle-Aged and Older Adults: a Community-based Study

Among middle-aged and older population, we aim

1) to investigate the prevalence and clinical relevance of *intracranial atherosclerosis (ICAS)* using 3.0T MRI.

2) to detect the prevalence of *cerebral small vessel disease (CSVD)* and its correlation with intracranial atherosclerosis

A Community-based MRI Study

Start From Nov. 2022

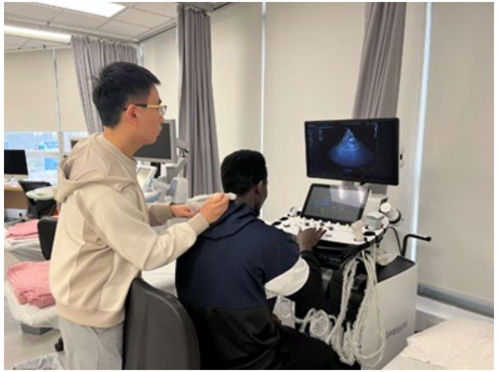
The lesions caused by intracranial atherosclerosis (ICAS) on MRA and HRMRVWI and

Imaging markers of small vessel disease multiple sequences on MRI

Imaging analysis

Each vessel lesion and SVD identified and recorded for data analysis

TCCD and carotid duplex
Cerebrovascular reactivity (CVR)



Approach and Objectives

Conducting a well-designed community-based **MRI** project.

Explored existing literature through systematic review and meta-analysis

Using **TCCD and carotid ultrasound** for vascular hemodynamics, MRI for brain structure.

Analyse current and previous data for a holistic impression on **ICAS and CSVD**

Subjects and Methods

In **stroke-free** adults

Little is known how

ICAS + CSVD

Contributes to

Cognitive decline

Cerebrovascular reactivity (CVR)

measures

brain vessels' response to changes in metabolic demand

could explain

underlying mechanisms

Problem: **Breath-holding CVR_{BH}** and **hyperventilation CVR_{HV}** assessment techniques are practically challenging for critically ill patients.

Research Objectives: To investigate how each parameter influences **cognitive deterioration** and to explore the alternative vascular metrics **to evaluate underlying mechanisms for early detection and precise diagnosis.**

(Terborg et al., 2000, Miller et al., 2019, Lasek-bal, 2012)

Suggestions:

- Our findings highlight the impact of **intracranial atherosclerosis** on **cognitive performance**, ***independent of small vessel disease*** as indicated by WMH or even other cerebrovascular risk factors**.**

- The **mediating role of WMH and diastolic blood pressure** in the relationship between **CVR and ICAS** suggests that the preservation of ***white matter integrity and blood pressure management*** could be crucial in mitigating cerebrovascular and cognitive deteriorations.

- **CVR_{BH} and CVR_{HV}** reflect different hemodynamic mechanisms of vasodilatation and vasoconstriction, respectively. CVR_{BH} and CVR_{HV} are independent of each other.

Summary:

In applying **MR vessel wall imaging** for for optimizing the diagnosis and treatment of ischemic stroke

1) The Ex-vivo MRI (***1.5T***) Vessel Wall Imaging of Histology-verified ICAS

2) ***3T*** MR vessel wall imaging ***in stroke patients***

3) ***3T*** MR vessel wall imaging ***in community-based study***

Clinical Impacts:

- The study demonstrates ***that HRMRI can enhance the diagnosis and management of ICAS*** by providing detailed insights into plaque morphology and components.
- This advancement ***allows for more precise risk stratification and targeted treatment strategies***.
- The findings advocate for ***the integration of HRMRI into clinical practice and health policy***, promoting the use of advanced imaging techniques in stroke prevention and management to optimize healthcare services and improve population health.

Acknowledgement

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