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## Review

# High-Resolution MR Intracranial Vascular Wall Imaging Technology Research and Clinical Application Progress

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## Abstract

Vascular wall imaging (VWI), as a new technology for displaying intravascular diseases, can identify intracranial artery disease even when no abnormalities are found in luminal angiography, which has good application value for the diagnosis and prediction of cerebrovascular diseases. The combination of vessel wall imaging plain scan and contrast enhancement provides more imaging and diagnostic information for intracranial atherosclerotic plaques, CNS vasculitis, reversible vasoconstriction syndrome, aneurysms, arterial dissections, and moyamoya disease than conventional luminal imaging techniques, which compensate for the lack of luminal narrowing alone. This article introduces the research progress and clinical application of vascular wall imaging technology.

**Keywords:** High-Resolution Magnetic Resonance Imaging; Vascular Wall Imaging; Intracranial Vascular Disease; Atherosclerotic Plaque.

## Introduction

Diseases producing high mortality and high disability in China are mainly ischemic stroke, and cerebrovascular diseases as one of the leading causes of stroke should be paid enough attention (1). Studies have shown that vascular wall lesions are often earlier than lumen changes. However, traditional lumen imaging techniques such as CT

angiography (CTA), MR angiography (MRA) and digital subtraction angiography (DSA) are mainly diagnosed by the degree of lumen stenosis. Blood vessels, lack of indication of early wall changes. HR-MRI VWI can display the structure of the tube wall with high resolution and analyze the characteristics of the lesion, which is of great help to the prediction and early treatment of cerebrovascular diseases.

## 1. Imaging Technology

Generally, the wall thickness of middle cerebral artery (MCA) and basilar artery (BA) is 0.2~0.3 mm. The voxel of VWI is difficult to reach at present, but the wall of the diseased vessel is often thickened, which makes the observation tube Mural lesions become possible (2). Intracranial brain parenchymal structure is complex, blood vessels are tortuous and not on the same plane, the imaging difficulty increases. Therefore, the following factors must be considered to achieve the imaging quality of the intracranial vessel wall:

### 1.1 High contrast signal-to-noise ratio and spatial resolution

High contrast signal-to-noise ratio (SNR) and spatial resolution are necessary to clearly demonstrate the lesions of the wall, and only to achieve the spatial resolution required for the thickness of the tube wall, we can diagnose whether the vessel wall is abnormal, and further measure the thickness of the tube wall, the thickness of atherosclerotic plaque.

As the field strength increases, it becomes possible to increase the signal-to-noise ratio and spatial resolution. Most of the intracranial vessel visualization is scanned on a 3.0T MRI with ultrahigh field (7.0T) FOV up to a field of view of  $250 \times 250 \times 190 \text{ mm}^3$ , allowing for isotropic vessel wall imaging with greater coverage that will show more Willis ring branch vessel reconstruction details (3). In addition, the number of head channel coils is increased to 32 or 64 channel coils, which can increase the peripheral resolution (4). Several autopsy studies have shown that 7.0T MRI is helpful in showing the substructure of plaques, and has a higher positive predictive value for distinguishing fibrous and loose calcium components. These advantages make 7.0T possible to identify the early lesions and total burden of ICAD. But 7T acquisition will also increase artifacts, and 7.0T scanning is currently in the exploratory stage (5).

### 1.2 Multi-tissue weighted imaging

The "bright blood technology" (3D-TOF-MRA) is usually used to make the flowing blood show a high signal by presetting the saturation band, which is in contrast with the stationary plaque, which is used for the location of the stenosis of the lumen and the measurement of the degree of stenosis. It is easier to distinguish between the fibrous cap showing low signal plaque and the bleeding in the plaque with high signal. However, due to factors such as blood turbulence in the blood vessel branch or the tortuous part, the blood flow signal is easily lost, and the judgment of the degree of stenosis of the official cavity is not accurate. Therefore, Gadolinium MRA is usually added for observation.

### 1.3 Multi-planar 2D and 3D acquisition

VWI was performed by imaging the vessel wall in both long - and short axis directions. The 2D sequence enabled clear visualization of the tube wall in the direction perpendicular to the long axis of the vessel. Observe blood vessels through multi-planar 2D technology, which can locally show the details of vascular lesions. However, when evaluating tortuous intracranial blood vessels, 2D sequences may produce partial volume effects. But the 2D sequence can increase the contrast of the local region of interest, which has advantages for local detailed observation of the tube wall. Compared to 2D sequences, 3D sequences improved vessel wall signal-to-noise by 58% through the acquisition of isotropic data. The improvement of the signal-to-noise ratio is conducive to the multi-directional reconstruction of diseased blood vessels, and has the advantage of collecting blood vessel walls in a large range (6). However, the 3D sequence scan time is longer, which increases the possibility of motion artifacts.

Intracranial 3D-VWI imaging generally uses variable flip angle refocusing spin echo sequence, including Philips volume isotropic turbo spin-echo acquisition (VISTA), Siemens' variable flip angle Fast spin echo (sampling perfection with application -optimized contrasts by using different

flip angle evolution, SPACE) and GE's CUBE sequence. Because of its faster scanning time, larger arterial coverage and higher spatial resolution, it is used in clinical practice. Additionally, whole brain volume coverage and isotropic 0.5-mm spatial resolution scans were completed within 7 minutes of whole brain 3D IVW CMR, reaching the effect of reduced time coexisting with high resolution (7). The improved T1-weighted DANTE-SPACE sequence allows visualization of the common carotid and distal intracranial arteries in a single 3D scan, with the advantage of a wide range of acquisition vessels. The combined imaging of the vessel wall of the head and neck was first performed within 5 min using the compressed sensing sequence, which greatly reduced the imaging time (8, 9).

#### 1.4 blood suppression and CSF suppression

Blood and cerebrospinal fluid suppression can be achieved through the use of spin echo imaging, preset saturation pulses, or sequences based on double inversion recovery. The double inversion recovery sequence in the blood suppression sequence had a more satisfactory blood suppression effect, and the blood signal was suppressed, so that the inner wall lesion of the tube wall was highlighted and the structure of the plaque could be observed. The disadvantages are the tortuous shape of intracranial vessels, slow blood flow in some areas, and poor blood suppression effect, which may lead to pseudo thickening of the wall. The disadvantages are the tortuous shape of intracranial blood vessels, and effect is not good, which may cause false tube wall thickening. The pulse sequence can be added to further optimize the blood suppression effect in the TSE sequence. The Improved motion-sensitized drive balance (iMSDE) sequence uses a flow sensitive phasing gradient with low b value to suppress the residual blood flow, but it may lead to signal loss in the wall (10). Variable delays alternating with mutation for tailored excitation (DANTE) technology uses continuous low flip angle excitation pulses to zero

the flow spin signals of blood and cerebrospinal fluid (CSF). However, DANTE technology inhibits CSF and also causes a decrease in the SNR of the tube wall. Some studies have shown that 40 ° to 120 ° TSE sequence combined with 8 ° Dante angle can achieve the best display of CSF inhibition and SNR (11).

## 2. Clinical application of intracranial vascular wall

### 2.1 intracranial atherosclerotic plaque

At present, the research of intracranial vessels has shifted from the degree of lumen stenosis to the characteristics of plaque and the changes of vascular inflammation as a marker to evaluate plaque vulnerability and predict ischemic stroke. The research of atherosclerotic plaque mainly analyzes the stability of plaque from the aspects of plaque characteristics, plaque distribution, plaque reconstruction mode, plaque enhancement mode and intra plaque bleeding.

#### 2.1.1 Plaque characteristics

Atherosclerotic pathological features plaque Center for necrotic lipid, covered with platelets and fibrous cap composed of thrombus material, the surface is composed of connective tissue. Because it is hard to sample the lesions of the intracranial wall, HR-MRI VWI, as a supplement to the traditional vascular imaging technique, can effectively evaluate the lesions of the intracranial wall. Several autopsy outcomes compared with HR-MRI VWI images found that vulnerable plaque components may play a critical role in inducing ischemic stroke (12). HR-MRI VWI shows better plaque and its surface structure, and the characteristic imaging features of HR-MRI VWI can be used as a means to evaluate the vulnerability of intracranial atherosclerosis. Maarten H.T et al. found on 7T MRI that 96% of patients had at least one lesion on tube wall magnetic resonance imaging, and concluded that intracranial arteriovascular wall lesions can be used as a direct MRI marker of

atherosclerosis(3). The structure of different components of plaque assesses the vulnerability of plaque. It is verified by pathology that the lipid core of atherosclerotic plaque is a part of the plaque, which can forecast the vulnerability of the plaque, and the larger lipid core is easily damaged (12). The shape of plaque adherent growth is distinct, and the stability is also distinct. The shape of the plaque surface is used as a predictor of arterial embolism. Fang Wu et al. found that irregular fiber caps were more likely to fall off and form thrombus (13). Through a meta-analysis, Han Na Lee et al. discovered that the contrast enhancement, positive remodeling and irregular plaque signs of intracranial plaque were also used as markers of intracranial cerebrovascular disease (14).

### 2.1.2 Distribution characteristics of plaques

The configuration of blood vessels is different, leading to hemodynamic changes, and the possibility of forming arteriosclerotic plaque also has difference. Studies have indicated that the bending of blood vessels in the posterior circulation creates conditions for plaque formation. The stenosis of the vertebrobasilar artery in the posterior circulation is more likely to cause stroke, which may be related to hemodynamics (15). Shin MS et al. showed that the vertebral-basal artery angle was related to the site of plaque formation, and that basilar artery plaque was a common reason of pontine infarction. The blood flow is changed to turbulent flow at the angle of the vertebrobasilar artery due to hemodynamic influence. Therefore, the larger the angle of the vertebrobasilar artery, the possibility of plaque formation on the posterior wall of the lower pons will increase, which will further lead to the paramedian or caudal bridge Cerebral infarction. The report also measured the angle of the middle part of the basilar artery and found that as the angle enhances, the possibility of the formation of BA plaques on the horizontal side wall of the bridge increases, leading to lateral and intermediate pontine infarctions (16). The position of the plaque also has a significant impact on its

stability. Studies have shown that plaques located on the sidewall of the basilar artery often led to lateral pontine infarction (17).

### 2.1.3 Vascular remodeling mode

The pattern of vascular remodeling on VW-MRI is divided into positive remodeling and negative remodeling. The wall of the diseased vessel is thickened and grows eccentrically. With the formation of plaque on the vessel wall, the blood vessel does not directly reveal stenosis. The first manifestation is the outward expansion of the blood vessel, also known as positive remodeling, to compensate for the influence of plaque formation on blood flow. When the plaque reaches a certain volume, the body cannot adjust itself, which will cause the lumen to narrow. Studies have shown that VW-MRI can detect early tube wall alters, which has a significant advantage in the detection of early plaques, which was convenient for clinical treatment before the plaques cause vascular stenosis, thereby reducing the risk of ischemic stroke (18). Plaque can also show negative remodeling (plaque growth into the tube wall) resulting in narrowing of the lumen. The hemodynamic changes around the plaque at the vascular stenosis cause the blood flow shear stress to act on the blood vessel wall, which in turn destroys the surface of the plaque and damages the epidermal cells of the vessel wall. Inflammatory cells accumulate on the surface of the plaque, which can likely lead to the fibrous cap to fall off and form a thrombus, causing ischemic stroke (19).

### 2.1.4 Plaque enhancement

Plaque enhancement on IVW-MRI is a symbol of plaque instability and progression. Studies have shown that the enhancement of intracranial plaque reflected the degree of inflammation of the blood vessel wall, which is closely related to stroke (20). Studies have discovered that both symptomatic and non-symptomatic plaque enhancement scans both showed plaque enhancement. Therefore, it is believed that plaque enhancement is caused by inflammation of the plaque. So plaque enhancement

can be considered as an indirect marker of inflammation (17). Plaque enhancement can be divided into three grades: i) Grade 0 means no enhancement, which is described as the signal similar to or lower than that of the surrounding normal arterial vessel wall; ii) Grade 1 enhancement is described as the signal intensity is greater than no enhancement, but is more funneled than the pituitary. The signal intensity is low; iii) Grade 2 enhancement means that the signal intensity is higher than that of the pituitary funnel enhancement zone (21). Alexander et al. tried to exclude subjective factors to quantitatively measured the enhancement in order to reach a unified consensus on the images before and after the plaque enhancement (22). The enhancement and composition of BA plaques are associated with ischemic stroke (23).

### 2.1.5 Bleeding in the plaque

Intraplaque hemorrhage is a direct sign of plaque instability and progression, and is intently related to ischemic stroke. Studies have used HR-MRI's T1-weighted fat suppression image (HST1) to observe whether there is a high signal in the middle cerebral artery plaque, which is judged as hemorrhage. And found that it is easier to find intra-plaque hemorrhage in symptomatic plaques (24).

### 2.2 Central nervous system arteritis

Central Nervous System Arteritis (PACNS) is a vascular inflammatory disease that mainly affects the central nervous system, leading to intracranial hypoperfusion, which eventually leads to ischemic stroke. Imaging manifestations include thickening of the wall of the lesion, narrowing and occlusion of the lumen (25). The pathology mainly manifests as destruction of the arterial media. It may be the primary disease of the tube wall, or it may be inflammation of the tube wall caused by autoimmunity or infection. On VW-MRI, central nervous system arteritis is manifested as thickening of multiple short-segment vessels and annular

enhancement on enhanced scanning, which is different from the eccentric enhancement of atherosclerotic vessel wall. HR-MRI VWI has major support in diagnosing the activity of vasculitis. Pathology has confirmed that inflammation increases the permeability of the vascular endothelium and the extravasation of the contrast agent. The imaging shows that the lesions of active vasculitis are enhanced (26). Central nervous system arteritis is difficult to diagnose. Due to sampling errors, even intracranial biopsy has a high false-negative rate. HR-MRI VWI can be used to locate inflamed blood vessels and determine their biopsy targets, improving accuracy (27). Studies have found that negative results of superficial arteries cannot rule out vasculitis. The reason may be that it is difficult to obtain materials for aortic biopsy, and that superficial arteries cannot reflect the diseased state of aortic arteries. In addition, studies also pointed out that VW-MRI was expected to be used as an auxiliary method for CNS arteritis biopsy. Nonetheless, for intracranial arterioles, the existing VWI voxels have not yet reached the requirements for imaging of the distal end small vessel walls. In addition, the intracranial arterioles are easy to sample, and biopsy is still an important tool for disease diagnosis. Therefore, VW-MRI has a significant merit in diagnosing vasculitis of the large arteries (26, 28).

### 2.3 Reversible cerebral vasoconstriction syndrome

The clinical treatment of reversible cerebral vasoconstriction syndrome (RCVS) and central nervous system arteritis is completely different. RCVS is treated with calcium channel blockers, while central nervous system arteritis is treated with steroids and immunosuppressive agents. Therefore, it is major for the clinic to identify the two diseases as soon as possible and adopt the appropriate treatment plan in time.

High-resolution vascular wall MRI contrast enhancement makes it possible to distinguish between vasoconstriction and central vasculitis.

Because RCVS is a kind of arterial dystonia, the pathological manifestation is that the overlap of spastic vascular cells increases. When the lumen is narrowed to 60%, the wall thickness increases by nearly 500%. The HR-MRI VWI shows that only the wall is thickened but no enhancement, which accord with pathology. The pathology of the PACNS lesion showed peripheral inflammatory cell infiltration, and the image showed that the tube wall was thickened and enhanced (29). Some studies have further conducted time and spatial follow-up of RCVS and PACNS, and found that the HRMRI wall type of RCVS and PACNS changed over time. Compared with the long-term stable wall disease of PACNS, RCVS showed a short-term reversal of internal wall stenosis. And found that the imaging characteristics of PACNS, including wall thickening and eccentric enhancement, involving the scattered distribution of multiple vessels. The imaging feature of RCVS is thickening of the vessel wall without enhancement, the feature accumulates all diseased blood vessels (30). In addition, if the RCVS lesion involves vasculitis, the MR-enhanced image will also be enhanced. Therefore, the distinction between RCVS and arteritis should be combined with other clinical features.

## 2.4 Aneurysma

The image of aneurysm showed a localized bulging of the diseased lumen. Pathological reports indicate that compared with undamaged aneurysms, abundant macrophages and lymphocytes infiltrate in the acutely damaged aneurysm due to the repair of the vessel wall, which leads to increased instability of the aneurysm (31). HR-MRI VWI enhanced scanning has great significance for clinical judgment of the risk of acutely damaged aneurysms, and it is convenient for doctors to intervene early in the risk of rupture of aneurysms (32). Abundant studies have shown that inflammation of the vessel wall may accelerate the rupture of aneurysms. HR-MRI VWI enhanced scanning has a great advantage in the assessment of aneurysm progression and stability. Vessel wall

enhancement has been widely recognized as a biomarker of unstable aneurysms, and unenhanced aneurysms may predict a stable, undamaged state (32, 33). However, some studies have shown that stable tumors in some cases also have enhancements, indicating that enhanced scanning has high sensitivity but lacks specificity for aneurysms. In addition, the slow blood flow in the fluid may also cause blood flow artifacts, suggesting that clinicians cannot judge its instability based on the enhancement of the tumor. The study subdivided the tumor enhancement mode into four grades (no enhancement, focal enhancement, thin-wall enhancement, and thick-wall enhancement) in order to conduct a more accurate analysis of aneurysm stability. Significantly, the 3 grade enhancement has high specificity for the diagnosis of tumor stability (34).

Most studies are exploring the relationship between tumor cavity and stability, but certain studies try to find whether there is a relationship between the thickness of the aneurysm wall and its stability. The high resolution and high signal-to-noise ratio of HR-MRI VWI images provide the possibility to measure tumor wall thickness. As the magnet strength increases, 7T MRI has higher CNR and spatial resolution. Studies have found that the partial volume effect of the tumor is related to its own signal intensity. Although the current VW-MRI voxel does not reach the display less than 1mm tube wall, the algorithm is used to calculate whether the tumor wall thickness is consistent with the pathological results, which makes it possible to measure the tumor wall thickness (35).

## 2.5 Moyamoya disease

Moyamoya disease is a chronic cerebrovascular disease in which unilateral or bilateral internal carotid arteries are progressively narrowed, occluded and produce abundant collateral circulation. Moyamoya disease is an important cause of transient ischemic attack (TIA) in children and adolescents. Although DSA is the gold standard for diagnosing Moyamoya disease, because it is an

invasive examination and requires a contrast agent, it is difficult to avoid the danger of invasive examination.

As a non-invasive examination, VWI can show more diagnostic information. Histopathology believes that Moyamoya disease is a thinning of the vascular media and no inflammatory cell infiltration (36). However, subsequent studies showed that, compared with eccentric enhancement of atherosclerosis, the imaging features of Moyamoya disease showed constriction of the middle cerebral artery and concentric enhancement of the end of the internal carotid artery. In addition, thickening of the tube wall was rare, and the tube wall was negatively remodeled. The enhancement of the atherosclerotic wall indicates the presence of inflammation or new blood vessels in the lesion. The higher enhancement of symptomatic moyamoya disease also reflects the active angiogenesis in the lesion. Studies have found that the degree of wall enhancement in moyamoya disease can predict acute ischemic infarction, and the enhancement of the intracranial wall can be used as an important marker for assessing its stability (37, 38).

Sometimes Moyamoya disease can coexist with atherosclerotic disease called Moyamoya syndrome. VWI can better distinguish Moyamoya syndrome from Moyamoya disease. Moyamoya syndrome is characterized by eccentric enhancement of the lumen and negative remodeling of the lumen. Studies have found that moyamoya disease has a higher probability of cerebral hemorrhage, which may be due to the forced dilation of its collateral circulation vessels and increased intravascular wall pressure. In patients with moyamoya syndrome, intracranial hemorrhage is less likely to be caused by blood in the lesion. It is caused by changes in rheological pressure and has guiding significance for clinical treatment (39). Moyamoya disease requires lumen recanalization, and Moyamoya syndrome requires active drug treatment. It is very important to distinguish between the two as soon as possible to facilitate the clinical selection of appropriate treatment strategies.

## 2.6 Arterial dissection

Arterial dissection is a vascular disease in which the intima of the blood vessel is separated from the wall of the vessel and blood flows through it to form a fake lumen in the artery. Intimal damage leads to local formation of thrombus, unstable thrombus shedding to block the distal blood vessels, or local lumen narrowing, which leads to insufficient blood supply to the brain tissue, which eventually leads to ischemic stroke or TIA (40).

Compared with DSA invasive examination, HR-MRI can be used as a non-invasive method to diagnose dissection, and high-resolution VWI can help outline important anatomical details or show lesions that are not obvious from other imaging modes. Provide guidance on the early detection and treatment of the disease (40). Typical manifestations include stripped valve, double-lumen sign, intramural hematoma, and aneurysmal dilation. Studies have conducted time-series exploration on isolated anterior cerebral artery dissection, and found that the hemoglobin product in intramural hematoma is a paramagnetic effect, which is mainly found in the subacute late stage. Therefore, it can be used as one of the gold standards for the diagnosis of intracranial dissection. 80% of cases in the acute phase were found to have aneurysm-like expansion on T2-weighted HRVWI, and the imaging manifestations of subacute early aneurysm-like expansion reached 100%. Therefore, it is concluded that small intramural hematoma and aneurysm expansion on HRVWI provide evidence for the early diagnosis of anterior cerebral artery dissection (41).

## 3. Conclusion and Prospective

The application of high-resolution magnetic resonance VWI in cerebrovascular diseases can make up for the lack of traditional angiography that only shows the lumen. As a non-invasive diagnostic tool, it has high spatial resolution, signal-to-noise



ratio and contrast signal-to-noise ratio. Its blood and cerebrospinal fluid suppression technology can show the thickened arterial wall and the surface structure of the diseased vessel wall, provide technical support for the early diagnosis of abnormal wall, and have important significance in the diagnosis of intracranial artery disease, differential diagnosis and stroke prediction.

However, there are still various problems waiting to be resolved in this area. There is no uniform standard for the diagnosis of the characteristics of vascular lesions. For example, the description of atherosclerotic plaque on the enhancement degree of the vessel wall and the vascular remodeling index is only a subjective judgment. Various manufacturers and researchers do not have a unified standard for the description of lesion scanning parameter settings and various feature measurements, and further standardization of operation and diagnosis is still needed. How are these measurement indicators quantitatively correlated with the occurrence, development and severity of acute ischemic stroke, which still need us to continue to explore. In addition, blood vessel wall imaging scan time is long, it is easy to produce motion artifacts, and blood and cerebrospinal fluid suppression technology can easily cause fake thickening of the wall in tortuous blood vessels where blood flow is slow, which also limits the general application of this technology. Therefore, HR-MRI VWI technology still needs further exploration by researchers. It is believed that with technological advancement, VWI will provide more effective information for the prediction of stroke caused by intracranial diseases. Achieve early detection and early treatment, and improve the survival rate of patients.

## Declarations

### 1) *Consent to publication*

We declare that all authors agreed to publish the manuscript at this journal based on the

signed Copyright Transfer Agreement and followed publication ethics.

### 2) *Ethical approval and consent to participants*

Not applicable.

### 3) *Disclosure of conflict of interests*

We declare that no conflict of interest exists.

### 4) *Funding*

None

### 5) *Availability of data and material*

We declare that the data supporting the results reported in the article are available in the published article.

### 6) *Authors Contributions*

Authors contributed to this paper with the design (SBL), literature search (MJS), drafting (MJS), revision (MJS and SBL), editing (MJS) and final approval (SBL).

### 7) *Acknowledgement*

None

### 8) *Authors' biography*

None.

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