



Vessel wall MR imaging for the detection of intracranial inflammatory vasculopathies

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Abstract: Intracranial vasculopathies are routinely investigated by lumen-based modalities such as magnetic resonance angiography (MRA), computed tomography angiography (CTA), and digital subtraction angiography (DSA). These techniques are useful to analyze the vessel lumen, allowing to detect vessel stenosis or occlusion. However, the primum movins of the disease, i.e., an abnormal thickening of the vessel wall, remains within the arterial wall. The vasculopathy can moreover be present without always narrowing the lumen or modifying its regularity. Hence, there is a need to detect directly and analyze vessel wall abnormalities. Development of 3D high-resolution black blood sequences for intracranial vessel wall MR imaging (VW-MRI) enabled routine clinical applications not only vasculitis, but also of intracranial atherosclerotic disease (ICAD), intracranial dissections, reversible intracranial dissections, reversible cerebral vasoconstriction syndrome (RCVS), Moyamoya disease, and intracranial aneurysms. This high-resolution intracranial VW- MRI approach is increasingly used on a clinical basis at many centers to solve diagnostic problems, especially in patients with ischemic stroke or intracranial hemorrhage. An expert consensus Guideline from the American Society of Neuroradiology provides recommendations for clinical implementation of intracranial vessel wall MRI. There are several technical aspects needed to be considered when implementing VW-MRI in intracranial vessels, including flow suppression, both in blood and cerebrospinal fluid (CSF), spatial resolution and signal-to-noise ratio (SNR). In this article, we review the technical aspects of VW-MRI, and recommend applications for vascular diseases including non-occlusive intracranial vasculopathies, Moyamoya disease, and identifying culprit plaques. We also give a focus on the utility of VW-MRI for determining stroke etiology in adults and in children and young adults.

Keywords: Vessel wall MR imaging (VW-MRI); intracranial vasculopathy; stenosis; intracranial atherosclerotic disease (ICAD)

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Introduction

Conventional arterial imaging of intracranial vessels focuses on the analysis of the vessel lumen, enabling to search for vessel irregularities, stenosis, or occlusion on angiography. Although angiography allows detecting abnormal variations of vessel lumen size, it lacks specificity as different pathologies produce similar luminal defects. Moreover, some disorders of the intracranial arteries such as intracranial atherosclerotic disease (ICAD) or vasculitis arise within the vessel wall, without always narrowing the lumen or modifying the regularity of the lumen, particularly at the initial phase.

Thanks to MR sequences designed to provide high spatial resolution with a black blood effect, it has become possible to image the vessel wall in 3 dimensions and to detect pathological changes in the wall. An early application was reported for vasculitis, where wall thickening and intramural contrast uptake were described in patients with active vasculitis affecting large brain arteries (1). Development of 3D high-resolution black blood sequences for intracranial vessel wall MR imaging (VW-MRI) enabled routine clinical applications not only vasculitis, but also ICAD, intracranial dissections, reversible intracranial dissections, reversible cerebral vasoconstriction syndrome (RCVS), Moyamoya disease, and intracranial aneurysms. There is also potential to use VW-MRI to follow disease progression and monitor treatment effects such as for vasculitis or ICAD. In this article, we review the imaging principles and pitfalls of VW-MRI, and recommend applications for vascular diseases including non-occlusive intracranial vasculopathies, Moyamoya disease, and identifying culprit plaques. We review the utility of VW-MRI for determining stroke etiology in adults with a separate focus on stroke in children and young adults.

Imaging principles and pitfalls

This high-resolution intracranial VW-MRI approach is increasingly used on a clinical basis at many centers to solve diagnostic problems, especially in patients with ischemic stroke or intracranial hemorrhage. An expert consensus Guideline (2) from the American Society of Neuroradiology provides recommendations for clinical implementation of intracranial vessel wall MRI. There are several technical aspects needed to be considered when implementing VW-MRI in intracranial vessels, including flow suppression, both in blood and cerebrospinal fluid (CSF), spatial resolution

and signal-to-noise ratio (SNR).

The primary mechanism for blood suppression effects of 3D VW-MRI is motion-induced intra-voxel dephasing (3). Blood with a wide range of velocities flowing across a magnetic field leads to the phase dispersion and signal loss. The blood suppression effect is enhanced by the use of low flip-angle refocusing pulses enabling long echo trains that promotes larger phase dispersion, especially when the flow direction is along with the frequency encoding axis (4). Additionally, the variable-flip-angle refocusing pulses introduce the formation of simulated echoes, which exhibits a complicated phase evolution leading to wide phase dispersion and strong blood suppression effect.

In general, the CSF-signal suppression effect can be attained by tailoring image contrast to T1 weighting due to its long T1 value. Implementation of an inversion recovery pre-pulse could theoretically null the CSF signal but may suffer from SNR deficiency, which is insufficient to resolve the intracranial vessel wall at 3T (3). Although DANTE-prepared VW-MRI can suppress the signal of CSF to some extent, the effect is diminished when CSF flow is below 0.1 cm/s, which is particularly problematic at CSF regions surrounding the middle cerebral arteries (5). Incorporation of a flip-down radiofrequency pulse module (e.g., anti-drive) to 3D VW-MRI has achieved enhanced CSF-signal suppression (6,7). It employs a positive 90° radiofrequency pulse at the end of the echo train to tip the transverse magnetization into the negative longitudinal plane, thereby, suppresses the transverse magnetization and minimizes signals of tissues with long T2 values (e.g., CSF).

Given the small size of intracranial vessels (normal wall thickness ranges 0.3–0.6 mm, VWI-ASNR study group has recommended an acquired resolution of 0.5 mm isotropic as a starting point for intracranial VW-MRI (2). Higher magnetic field strength (i.e., 7-T) offers the potential to increase the spatial resolution of intracranial VW-MRI, but this potential has not yet been realized (8). The 3D VW-MRI technique demonstrates high SNR-efficiency, providing a 58% improvement in SNR of vessel wall compared with 2D MRI sequence (3). The employed variable-flip-angle refocusing pulses allow for a longer echo train length without compromising signal within a relatively short scan time.

3D VW-MRI has gained popularity in the diagnosis and management of patients with cerebrovascular disease in clinical practice. The technique can, however, generate artifacts that arise from the technical caveats (e.g., slow or recirculated flow or inadequate spatial resolution). Blood

flow near the vessel wall may not be fully suppressed as the flow is often slower compared with the center of the lumen, which can cause artificial wall thickening. The slow flow in small veins can be misinterpreted as arterial wall enhancement after contrast injection. The recirculating or disturbed flow may yield plaque-mimicking flow artifacts due to incomplete flow suppression, which commonly seen in the curved and large vessel segments. Contrast-enhanced MRA is often helpful in excluding flow-related artifacts. In addition, blood suppression is more effective when the flow direction is along with the frequency encoding axis (4). Acquiring VW-MRI in multiple orientations may help to discern the artifacts caused by orientation-related incomplete flow suppression.

Inadequate spatial resolution can induce partial volume averaging. This can lead to the overestimation (9) of the wall thickness and could be misinterpreted as atherosclerotic plaque or vasculitis, in particular, with corresponding enhancement seen on contrast-enhanced VW-MRI.

Detection of non-occlusive intracranial vasculopathies

Historically, angiographic imaging has served as the reference standard for the differentiation and characterization of non-occlusive vasculopathies. Intracranial vasculopathies are routinely investigated by lumen-based modalities such as magnetic resonance angiography (MRA), computed tomography angiography (CTA), and digital subtraction angiography (DSA). These techniques are useful to analyze the vessel lumen, allowing to detect vessel stenosis or occlusion. However, the *primum movens* of the disease, i.e., an abnormal thickening of the vessel wall, remains within the arterial wall. Therefore these modalities, focusing on lumen, reflect an indirect marker of an abnormality of the vessel wall, and may be insufficient in detecting lesions that do not restrict the lumen (10). Wall thickening and intramural contrast uptake have been described as characteristic findings in patients with active cerebral vasculitis affecting large brain arteries (11,12). Several VW-MRI studies have reported that intracranial atherosclerotic lesions can also enhance on VW-MRI and the enhancement is associated with increased risk of stroke events (13-15). Therefore, lesions of different etiologies, modifying the arterial wall structure, may be detected using VW-MRI on non-contrast exams (hematoma and intracranial dissection) and after gadolinium administration (atherosclerosis, vasculitis, aneurysms...)

Furthermore, VW-MRI, combined with MR Angiography in the evaluation of suspected vasculopathies, has been shown to identify a higher number of abnormal vessel segments in comparison with 3D-TOF-MRA alone (11,13,16). This may be useful both for the detection and characterization of the intracranial arteriopathy. VW-MRI in addition to MRA significantly improves diagnostic accuracy for both per-lesion and per-patient analyses when compared to luminal imaging alone (per-lesion: 88.8% *vs.* 36.1%, $P < 0.001$, per-patient: 96.3% *vs.* 43.5%, $P < 0.001$), respectively (11). Song *et al.* (16) confirmed this hypothesis on another cohort of ≈ 100 patients.

Characterization of non-occlusive vasculopathy

Besides the importance of the detection and the characterization of the extension of an intracranial vasculopathy, different patterns of enhancement have been described for the diagnosis and subgroup differentiation of intracranial vasculopathies.

Pattern and distribution are the two main features of enhancement that can vary depending on the etiology. The pattern may be concentric, eccentric, or focal and nodular. The distribution may also be solitary or multifocal. MRA abnormalities can be found in the presence of abnormal vessel wall enhancement with either a decrease in size of the outer diameter at the lesion site (negative remodeling) or with a normal to increase in diameter (positive remodeling) (17,18).

Atherosclerotic plaque

Histopathological studies of the composition of plaques offer strong evidence that intraplaque hemorrhage and inflammation are significant risk factors for ischemic symptoms, regardless of stenosis severity (17).

This evidence highlights the role of plaque imaging and plaque phenotyping in risk stratification and clinical decision making in addition to stenosis parameters, and have been mainly validated with histopathological evidence from resected atherosclerotic lesions of the bulbar carotid artery.

However, although thinner, intracranial vessels have already been studied with post gadolinium VW MRI in more than 20 studies and several meta-analyses (13,14,19,20) focused on the determination of markers of intracranial culprit plaque. These studies typically exclude other causes of stroke, such as atrial fibrillation, severe cervical carotid stenosis, or vasculitis. The main VW MRI findings of

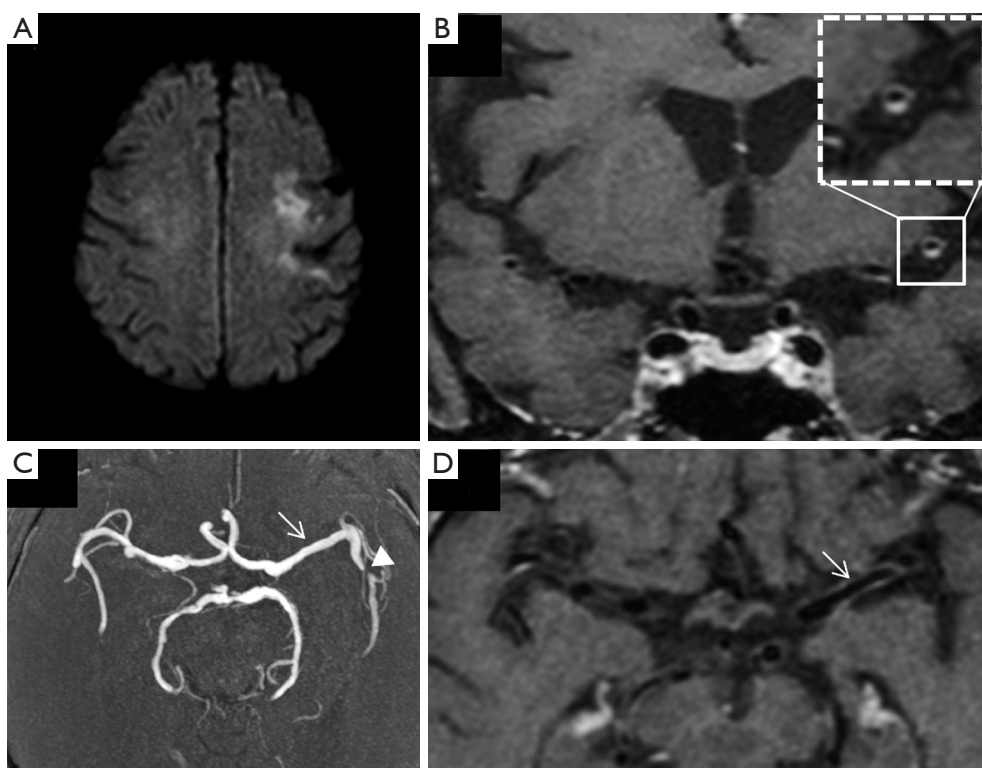


Figure 1 ICAD related stroke. A 65-year old male with an acute stroke. There is restricted water diffusion on DWI of the left MCA territory (A). VW-MRI at one week, showing an eccentric enhancing ICAD of the left MCA (B), there is an MCA preocclusive stenosis on 3D Time-of-flight (C, arrowhead). In contrast, the other portions of the MCA are neither stenosed (C, arrow) nor enhancing (D, arrow). ICAD, intracranial atherosclerotic disease; DWI, diffusion weighted imaging; VW-MRI, vessel wall MR imaging.

ICAD plaque are eccentric enhancement of the plaque with a variable length of involvement remaining most frequently focal (11,15,21). In patients with recent stroke, multiple studies have reported an association between T1 post-contrast plaque enhancement and the symptomatic status of the ICAD plaque (Figure 1).

Lee *et al.* (14) reported that intracranial plaque with contrast enhancement, positive remodeling, and wall irregularity were significantly more likely to be associated with ischemic stroke at the corresponding territory. On a meta-analysis, using a random effects model, Gupta *et al.* (19) reported that infarction was 10 times more likely in tissue supplied by an enhancing artery than in tissue supplied by nonenhancing arteries. Overall in their study, 59% of the culprit plaques were enhancing versus 23% of the non-culprit plaques.

Several studies noted that the intensity of enhancement was different when comparing enhancing plaques, leading to or qualitative or quantitative evaluation of the enhancement.

Qiao *et al.* (18) proposed to test an ordinal scale with three levels of enhancement of the ICAD plaque compared to that of the pituitary infundibulum. She concluded that the higher the grade, the higher is the probability of the plaque to be the culprit for stroke.

Quantitative analysis (22) of the enhancement, comparing pre and post-contrast intensity values of the ICAD plaque, support this hypothesis and found that the percentage increase in enhancement after contrast was significantly higher for symptomatic plaques (63 vs. 23%, $P=0.001$). An analysis of different plaque features found that high signal on T1-weighted images, wall thickening pattern, and a high degree of postcontrast enhancement were associated with culprit plaque (23).

As suggested by a recent study (24), the wall enhancement in ICAD lesions is variable over time. Contrast enhancement of ICAD can persist months after the ischemic event. Preliminary results (21) suggest that follow-up improves accuracy in identifying culprit

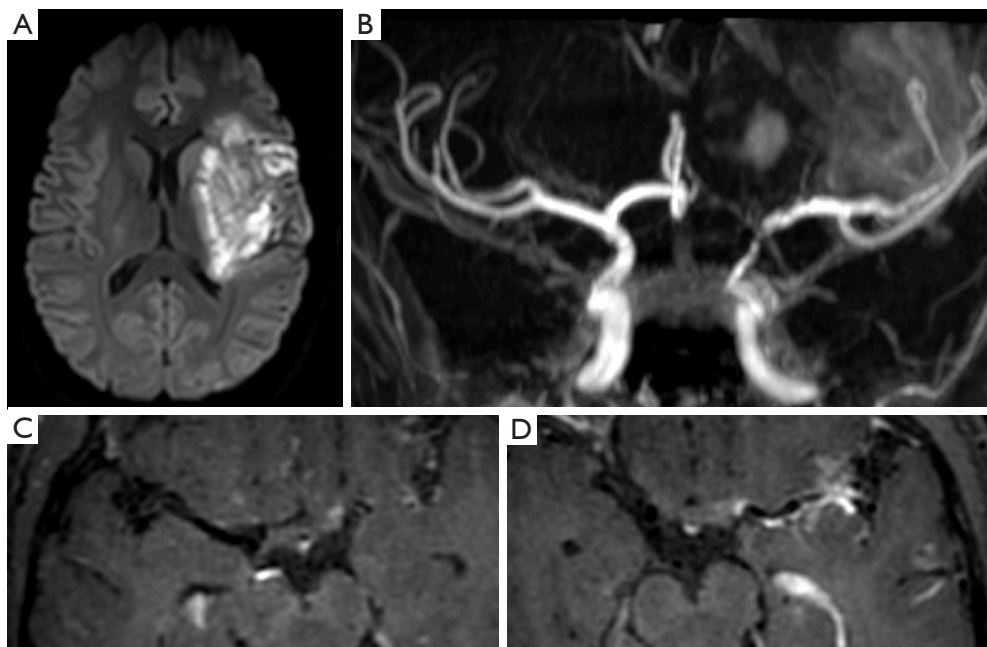


Figure 2 Varicella-Zoster vasculitis responsible for stroke in a 20-year-old male. Stroke with secondary hemorrhagic components (A, DWI), multiple intracranial stenoses on 3D Time-of-Flight (B), with sub-occlusion of the terminal portion of the ICA, and A1 segment. On VW-MRI, No enhancement of the vessel wall of the right MCA (C), irregularities of the left MCA with strong circumferential enhancement in favour of vasculitis (D). The family of the patient reports a previous Varicella Zoster infection three weeks prior to the stroke. DWI, diffusion weighted imaging. DWI, diffusion weighted imaging; VW-MRI, vessel wall MR imaging.

plaques. Lack of enhancement at baseline or a decrease in enhancement at follow-up may suggest that the plaque is not the culprit.

Systemic vasculitis and primary angiitis of the central nervous system

Cerebral vasculitis is defined as inflammation of arterial walls leading to progressive obstruction of the lumen, increased coagulation, and hence risk of stroke. Primary angiitis of the central nervous system (25) can occur as an idiopathic disorder restricted to the CNS, but most often, vasculitis is associated with systemic connective tissue disorders or may be secondary to non-inflammatory process: infection, neoplasm, drugs, or radiation therapy (26,27).

The 2012 Chapel Hill Consensus Conference categorized vasculitis in terms of size of the involved arteries (small, medium, or large vessels) and associated pathologic lesions (27).

The angiographic diagnosis of vasculitis depends on the presence of one or multiple stenoses of brain vessels. Straightening and kinking of arteries can be seen as consequences of the induration and stiffening of the

vascular walls.

The MR imaging diagnosis relies on both the detection of vascular stenosis by 3D time of flight MRA and circumferential enhancement on VW-MRI (28). The enhancement can be either pencil-thin or thick, extending beyond the margin of the vessel wall (11,12). One or multiple stenoses can be identified, and their detection can be sensitized by the presence of circumferential enhancement on VW-MRI. The ability of vascular MR imaging to identify vasculitis relates to the size of the affected vessels (29).

Proximal involvement has been observed (30) in sarcoid, giant cell arteritis (GCA), systemic sclerosis, primary angiitis of the central nervous system, and infectious disease, foremost among which is Varicella Zoster vasculitis (Figure 2), frequently affecting M1 segment, responsible of basal ganglia infarcts. This can occur after primary or reactivated Varicella Zoster virus infection and in patients who are immunocompetent or immunosuppressed (31). Other infectious vasculitis etiologies are bacterial meningitis by pneumococcus and meningococcus, tuberculosis, Treponema pallidum, Borrelia burgdorferi, and fungus (27).

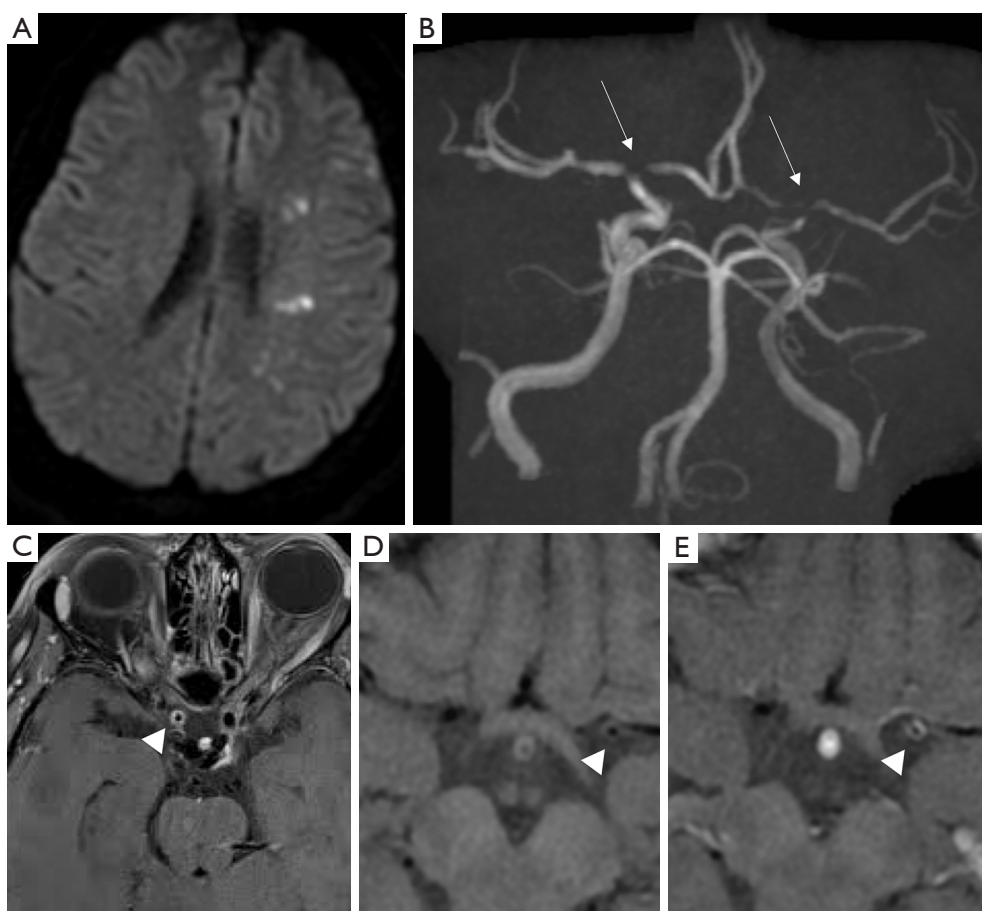


Figure 3 Giant cell arteritis and intracranial vasculitis. A 72-year-old male with transient amaurosis of the right eye, headaches, and pain while chewing. No diabetes mellitus, no arterial hypertension, high sedimentation rate. DWI (A) demonstrates ischemic spots with restricted water diffusion in the left MCA territory. Intracranial stenoses on 3D Time-of-Flight (B, white arrows) of the bilateral terminal portion of the ICA, M1 and A1 segments are present. Post-contrast VW-MRI (C,E) compared to pre-contrast VW-MRI (D) shows circumferential vessel wall enhancement of the stenosed intracranial vessels (arrow head), in favour of a vasculitis. The biopsy of the temporal artery confirmed the diagnosis of giant cell arteritis. DWI, diffusion weighted imaging; VW-MRI, vessel wall MR imaging.

In GCA, VW MRI allows to analyze intracranial arteries (Figure 3) and external branches of the carotid artery, such as the superficial temporal artery, looking for circumferential enhancement. Interestingly, Rhéaume *et al.* (32) reported in a correlation of imaging and histopathological findings in patients with suspected GCA, that normal findings on scalp artery MRI are very strongly associated with negative temporal artery biopsy findings. This finding suggests that MRI could be used as the initial diagnostic procedure in GCA, with temporal artery biopsy being reserved for patients with abnormal MRI findings. Zeiler *et al.* (12) showed the post-contrast 3D high resolution VW-MRI can be used to identify inflamed intracranial vascular targets

for biopsy, greatly improving the diagnostic accuracy of biopsies for CNSV.

Vasculitis affecting medium-sized arteries are caused by a wide spectrum of disorders (30), such as panarteriitis nodosa (33), lupus erythematosus (34), Behcet's disease (35). Although VW-MRI is useful to detect abnormal enhancing segments in vasculitis, it cannot however distinguish between these disorders (12).

Detecting wall thickening and vessel wall enhancement may also serve as biomarkers of treatment efficacy. However, as reported by Reichenbach *et al.* on a controlled trial of GCA patients under tocilizumab (36), vessel wall enhancement normalized in only one-third of patients yet

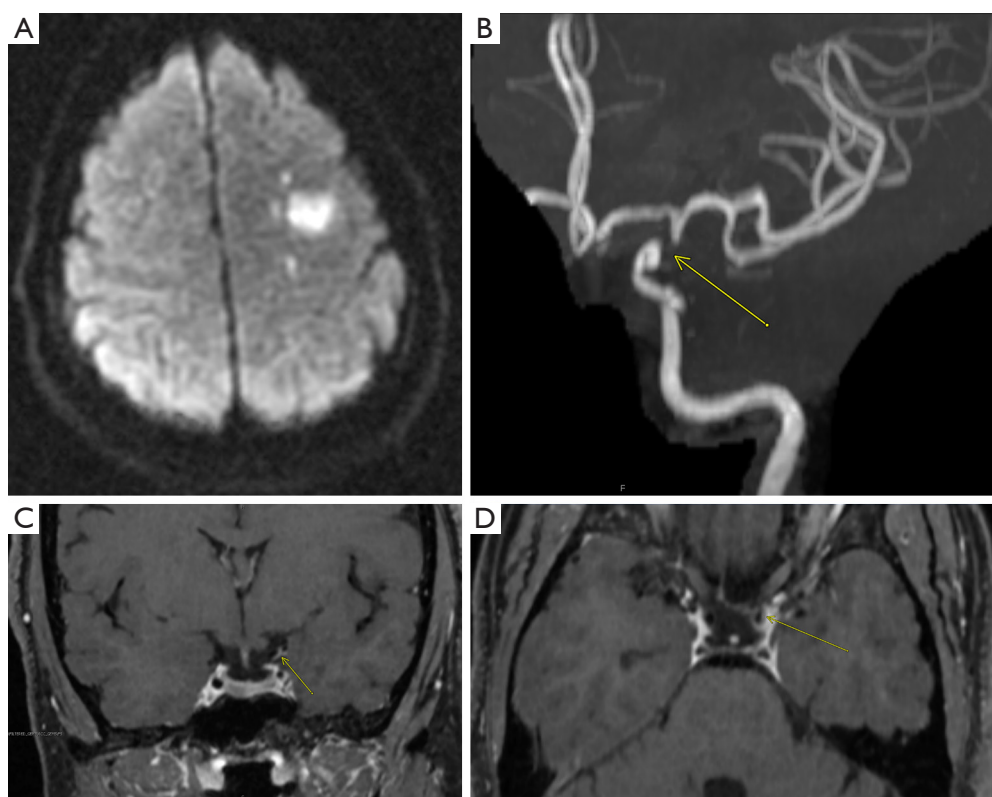


Figure 4 A 45-year-old female with stereotyped stroke symptoms. DWI (A) of the brain performed six months prior, demonstrates restricted water diffusion of the MCA territory. Recent MRA (B) of the brain shows a lack of flow-related enhancement of the supraclinoid ICA, reflecting severe stenosis. VW-MRI post gadolinium coronal view (C) and axial view (D) demonstrate eccentric enhancement of the supraclinoid ICA (C) and circumferential enhancement of the ICA (D). DWI, diffusion weighted imaging; VW-MRI, vessel wall MR imaging.

presenting a complete clinical and laboratory remission. Hence, whether these signals are of prognostic importance remains to be determined.

RCVS

Recurrent thunderclap headache is the most common symptom of patients with RCVS, for which the main differential diagnosis is subarachnoid hemorrhage. RCVS is supposedly due to a transient disturbance in the control of cerebrovascular tone and often resolves spontaneously within 3 months. More than half the cases occur postpartum or after exposure to adrenergic or serotonergic drugs. It can be difficult to distinguish RCVS from other arteriopathies since most lack a gold standard diagnostic test and are similarly associated with headache and stroke. Early discrimination is important because of management differences: in RCVS, CSF examination and brain biopsy have little utility

other than to exclude mimics. Although the prototypical demographics and classic presentation of RCVS (most commonly seen in young or middle-aged females with numerous described risk factors) differ from CNS vasculitis, diagnostic uncertainty may remain after conventional luminal imaging in some cases. It is important to differentiate between the two diagnoses because RCVS does not require anti-inflammatory or immunosuppressive treatment. As a non-inflammatory disease, RCVS has been described as presenting with non enhancing concentric wall thickening (11,37) corresponding to the areas of multifocal segmental arterial narrowing. However some cases have also been reported as presenting marked enhancement, highlighting the limited specificity of lack of enhancement in RCVS (11).

Moya-moya vasculopathy

Moyamoya syndrome is a vasculopathy exclusive to the

vasculature of the brain that results in significant stenosis of the proximal intracranial vessels. This abnormality results in decreased flow to the brain and is associated with an increased risk of ischemic and hemorrhagic stroke. In an effort to compensate for lack of flow, collateral vessels develop near the internal carotid artery apex, cortical apex, and brain perforating vessels in the basal ganglia.

The syndrome occurs in a bimodal chronology and is common in children who are approximately five years of age and adults 40–50 years (38–40). The reported incidence-rate ratios is 4.6 for Asian Americans, 2.2 for blacks, and 0.5 for Hispanics, as compared with whites (41).

While ischemic events are common in children, hemorrhagic is common in adults. Ischemia is commonly associated with areas of border zone circulation related to ICA stenosis and MCA stenosis. Hemorrhage, on the other hand, occurs 10–40% of cases and is frequent in the basal ganglia with intraventricular extension, or subarachnoid hemorrhage.

The pathophysiology of Moyamoya has always been intriguing for neuropathologists, it is a non-inflammatory and non-atheromatous disease of the intracranial circulation that shows fibrocellular thickening of the wall, irregular undulation of the internal elastic laminae, medial thinness and a decrease in the outer diameter (41–43).

Approximately 10% of individuals with MMD exhibit a familial occurrence and is associated with other genetically related diseases such as collagen disorders, Down syndrome, neurofibromatosis, and sickle cell (44).

The diagnosis of Moyamoya relies heavily on symptoms and imaging characteristics. CT imaging could demonstrate border zone infarcts, hypodensities in the basal ganglia, or be entirely normal in some patients. CT angiography may demonstrate the classical vessel characteristics of narrowing of the supraclinoid segment of the ICA, proximal, anterior cerebral arteries, middle cerebral arteries, and later proliferation of collateral vessels. The Suzuki grading system describes the stages of Moyamoya (45).

MR angiography is a very sensitive technique that besides demonstrating acute strokes, also demonstrates multiple abnormalities of the intracranial circulation of patients with Moyamoya syndrome, and may provide brain perfusion data that can guide a surgeon's approach. Newer MRI technology, such as VW-MRI, has identified unknown features of the disease in its different phases.

A multi-contrast vessel-wall MRI protocol with luminal imaging could help differentiate between moyamoya disease, atherosclerotic-moyamoya syndrome and

vasculitic-moyamoya syndrome significantly better than luminal imaging alone (46). It has also been reported that Moyamoya disease may also have different presentations depending on the phase of the disease. The most common pattern to be identified has been concentric enhancement on bilateral distal internal carotid arteries and shrinkage of a middle cerebral artery, regardless of symptoms (47). The same group reported that eccentric enhancement corresponded with acutely infarcted territories, which is a link to vulnerable lesions in Moyamoya disease (Figure 4). There is also evidence of lower vessel wall cross-sectional area in patients with Moyamoya disease compared to vessels of patients with ICAD.

Applications for determining stroke etiology

In adults

As we have shown, patterns and intensity of post gadolinium enhancement of vascular lesions using postcontrast VW-MRI have been used to differentiate between intracranial vasculopathies. Its application to detect the cause of stroke is therefore promising, especially in cryptogenic stroke, for which no cause of stroke has been detected. Indeed, in at least 30% of cases, the exact etiology of stroke cannot be determined using existing investigative protocols (48). Adding VW-MRI may therefore help to detect etiologies that cannot be diagnosed using only luminal angiograms. In the adult stroke population, several studies have already tested the utility of intracranial high-resolution VW MRI in differentiating intracranial vasculopathic diseases causing stroke (49–52). Yet, the diagnostic utility of VW-MRI in the work-up of ischemic stroke still remains a subject of debate, namely on its impact regarding patient outcomes (53). Kesav *et al.* (49) reported a large number of stroke etiology reclassification due to the use of VW-MRI in cases originally classified as “undetermined” etiologies. In this cohort, compared to the TOAST classification, VW-MRI reclassified 5/49 patients from undetermined etiology to determined etiology, mainly by diagnosing ICAD plaques. This was reinforced in a larger cohort of 205 patients (50), in which 116/205 patients were reclassified as presenting an ICAD plaque thanks to the analysis of VW-MRI. Hence, ICAD is under diagnosed when only analyzing the lumen (54). ICAD might therefore be the most frequent underdiagnosed etiology of stroke in the cryptogenic stroke population. An important question would be to know the temporal course of enhancement of ICAD and whether

enhancement would sign a link depending on the delay from stroke symptoms onset. Kwee *et al.* (21) reported that follow up could help improving accuracy in identifying culprit plaques, as they present enhancement that persists during follow-up, whereas non culprit plaque or do not enhance at baseline or present a decrease in enhancement during follow up. Beside stroke related ICAD diagnosis, VW-MRI can highlight previously described pattern of lesions suggesting underlying causes such as vasculitis or RCVS (11).

The specificity of VWI in children and young adults with stroke

Ischemic and hemorrhagic stroke represent a significant burden in the pediatric population, with long-term medical and psychosocial consequences (55,56). In this age group, vascular imaging plays a central role in the diagnosis and etiologic classification of underlying processes that largely differ from those found in the adult population (57).

Arteriopathy, for instance, is amongst the predominant causes of arterial ischemic strokes in children and may include Moya Moya Disease or Moya Moya syndromes, focal cerebral arteriopathy (FCA) of childhood or post-varicella arteriopathy, intracranial arterial dissection, and less commonly primary angiitis of the central nervous system. As these arteriopathies may present acutely, or at early stages, with overlapping or quasi-similar radiological aspects (58-60), they are very difficult to discriminate from each other using purely luminal imaging techniques (59). Collaterals, either from deep perforators or from leptomeningeal arteries, are known to be an important discriminant but bear imperfect diagnostic and prognostic capacities. Yet, it is critical to correctly classify the underlying processes, which may have dissimilar ischemic recurrence rates, mid-long term evolution, and be approached with different treatment strategies.

Still, the role of VW-MRI in childhood arteriopathies remains poorly understood, as data only begin to be reported. Recently, Stence *et al.* categorized vessel wall enhancement on a 3 grade scale (none, mild, strong) at the site of luminal abnormalities detected using 3T MRA in a cohort of 16 children with acute ischemic stroke (61). They reported that strong vessel enhancement at baseline was associated with arteriopathy progression, while no enhancement was associated with milder evolutions. Of important note, they also showed that patients treated with steroid courses were more likely to have decreased

enhancement at follow-up. Two recent studies (62,63) aimed to explore the clinical characteristics and diagnostic utility of VW-MRI in children with acute ischemic stroke and Pediatric Focal Cerebral Arteriopathy-Inflammatory Subtype. The authors did not find associations between specific patterns of enhancement and underlying etiologies. In this report, there was a tendency for children with VW enhancement to be older, but possibly reflecting technicalities in the acquisition. As such, those studies highlight the potential role of VW-MRI imaging in care intensity stratification for childhood intracranial arteriopathies, and its importance as a longitudinal biomarker during follow up under anti-inflammatory or etiology-specific treatments. But further work is needed to assess the utility of vessel wall imaging in pediatric arterial ischemic stroke and arteriopathies.

Indeed, there remains a considerable knowledge gap to fill before VW-MRI may inform disease targeted strategies, prognostication, and ultimately influence the outcome.

Conclusions

Vessel wall imaging has provided information beyond the epiphenomena of luminal narrowing in the evaluation of intracranial arteriopathies. As described in this review article, VW-MRI is a noninvasive imaging method that has proved to be useful in the detection of inflammatory changes of the intracranial arteries and veins that are frequent in certain arteriopathies. This information is undoubtedly useful for clinicians and stroke neurologists in the workup of patients with acute stroke. Further work is necessary for many areas; these include the use of VW-MRI as a biomarker for immunosuppressive therapy response, prediction of aneurysmal rupture based on aneurysmal wall enhancement, the clinical use of VW-MRI in the pre-stenotic phase of atheromatous disease, increased resolution, and faster sequences are also needed for our acutely ill patients. Radiologist should be knowledgeable of the normal patterns and pitfalls of vessel wall enhancement and the main morphological characteristics of vessel wall lesions.

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