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Cerebrovascular Disease and Stroke (S Silverman, Section Editor)

Vessel Wall Imaging of Cerebrovascular Disorders

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Abstract

Purpose of review High-resolution magnetic resonance vessel wall imaging (VWI) permits direct visualization of intracranial arterial wall pathology, providing diagnostic and prognostic information that is complementary to conventional imaging techniques. We highlight the most recent studies that have advanced the clinical application of VWI.
Recent findings VWI aids in distinguishing and diagnosing intracranial atherosclerotic disease (ICAD), intracranial dissections, central nervous system vasculitis, reversible cerebral vasoconstriction syndrome, and moyamoya disease. VWI may help predict recurrent stroke in ICAD, treatment effects in vasculitis, and disease progression in moyamoya. VWI also identifies ruptured intracranial aneurysms and may predict stability of unruptured aneurysms.
Summary Implementing VWI as an adjunctive imaging technique may permit earlier and noninvasive discrimination of rare vasculopathies. However the prognostic utility of VWI for more common cerebrovascular pathologies requires further validation.

Background

High-resolution magnetic resonance intracranial vessel wall imaging (VWI) improves our understanding and management of cerebrovascular disease. Conventional imaging techniques including computed tomography (CT), magnetic resonance imaging (MRI), transcranial Doppler ultrasound (TCD), and digital subtraction angiography (DSA) provide both structural and dynamic functional information about cerebrovascular

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pathology. We rely on visualizing the brain parenchyma or the vessel lumen to infer the pathology in the arterial walls. The challenge to direct visualization of the arterial wall is that the thickness ranges from 0.31 to 0.86 mm in the large proximal cerebral vessels [1], beyond the resolution of conventional imaging methods used in clinical practice. However, improvements in MR scanners and acquisition protocols now enable direct visualization of the arterial wall. High-resolution VWI sequences improve our understanding of cerebrovascular disease *in vivo* but have not yet claimed a definitive role in routine clinical practice.

The potential of VWI to provide complementary information and direct visualization of vascular pathology has ignited widespread efforts to find the most reliable and useful clinical applications. First, for ischemic stroke diagnosis, VWI can identify non-stenotic intracranial atherosclerotic disease (ICAD) to elucidate stroke mechanism and guide management. In this vein, VWI also reveals high-risk plaque features that may predict recurrent ischemic events. Secondly, VWI helps distinguish intracranial vasculopathies, specifically inflammatory vasculitis from noninflammatory vasculopathies, including ICAD, intracranial dissection, reversible cerebral vasoconstriction syndrome (RCVS), and moyamoya syndrome. Finally, VWI can identify ruptured aneurysms and may also predict stability of unruptured aneurysms. We review the most promising applications of VWI with an emphasis on the most recent literature.

Vessel wall imaging protocols

Magnetic resonance angiography (MRA) images the arterial lumen using gadolinium contrast or the blood flow within the lumen using time-of-flight sequences. As a complementary approach, VWI sequences optimize signal contrast of the arterial wall, generally by suppressing both the signal of blood within the lumen (termed "black blood" [2]) and the signal of cerebrospinal fluid (CSF) surrounding the outer wall [3]. By improving the signal contrast between the blood, the arterial wall, and the surrounding CSF, VWI reveals arterial wall pathology not detectable with angiography or conventional MRI sequences. Techniques to achieve black blood include spatial presaturation of inflowing blood [4], double inversion recovery [5], and intravoxel dephasing of flowing blood [3, 6]. The latter uses turbo spin echo pulse sequences with variable flip-angle refocusing pulses, and 3D commercial versions are available for Siemens (SPACE sequence), Phillips (VISTA sequence), and GE (CUBE sequence) 3-T scanners [7•].

Optimal image resolution is dependent on field strength, the extent of brain imaged (field-of-view), and scan time [3]. At 3-T, the first order, second order, and possibly third order cerebral arterial branches can be adequately visualized. While the wall thickness may be beyond the scanner resolution, pathologically thickened arteries may still be detected in the smaller vessels.

Two-dimensional sequences may provide better in-plane resolution, but have a smaller field-of-view, and may require targeting specific pathologic vessels. Two-dimensional sequences may be more difficult to interpret with tortuous vessels that curve obliquely through the imaging plane, particularly if there is a gap between slices. Furthermore, inadequate suppression of in-flowing blood signal can cause artifact in the lumen when the saturation plane is oblique instead of perpendicular to the vessel. Three-dimensional imaging sequences have isotropic resolution and generally have a larger field-of-view that includes all the proximal cerebral vessels. Three-dimensional imaging is preferred for diffuse vasculopathy. Two-dimensional imaging may better evaluate a specific lesion of interest [3, 8].

Multiple tissue weightings have been used, but T1 and proton density with and without contrast have yielded most results. Some studies also find T2

weighting useful to characterize atherosclerotic plaque components [9, 10]. Additional tissue weightings lengthen scan time, and the optimal combination may depend on the pathology of interest.

Intracranial atherosclerotic disease

VWI for atherosclerotic disease was pioneered in the extracranial carotid and coronary arteries, but technological advances now permit direct visualization of intracranial atherosclerosis. ICAD accounts for 8% of ischemic strokes in the USA [11] and around 50% of stroke in Asia [12]. The burden of ICAD is significant since the rate of recurrent stroke at 1 year is as high as 15–17% [13, 14]. Despite this high rate, revascularization via stenting has a higher early risk of recurrent stroke or death at 30 days (14.7%) than medical therapy with antiplatelet agents and risk factor optimization (5.8%) [15]. If we could predict which patients will have early recurrent strokes, we might identify better candidates for early revascularization. Diagnosis of ICAD currently relies on identification of arterial lumen narrowing on angiography, and severe stenosis has some predictive power for recurrent stroke [16]. However, the prevalence of ICAD may be underestimated since non-stenotic lesions may also be clinically meaningful. CT reveals atherosclerosis as arterial wall calcifications, particularly in the cavernous internal carotid segments [17]. Similarly, VWI visualizes other features of atherosclerotic plaque that have both diagnostic and prognostic significance.

VWI can identify atherosclerosis by plaque features: arterial distribution, plaque thickness, outward remodeling, plaque components, and contrast enhancement pattern. Atherosclerotic plaques are usually focal, with eccentric thickening of the arterial wall. Eccentric thickening occurs more often opposite the ostium of perforating vessels, commonly the ventral wall for both middle cerebral arteries (MCAs) and basilar artery [19–21]. Positive remodeling, or outward thickening of the arterial wall without significant lumen narrowing, is frequently seen early in ICAD [22]. A study using 7-T VWI found arterial lumen stenosis in only 27% of ICAD lesions, confirming that the extent of ICAD is underappreciated with luminal imaging [23]. Furthermore, positive remodeling is found more often in symptomatic lesions than asymptomatic lesions [22, 24] and is associated with microemboli detected on TCD [25], consistent with plaque instability. Finally, irregular plaque surface may be another marker of unstable plaque, since it is also more common in symptomatic lesions [22, 24].

The intracranial atherosclerotic plaque components identified in histopathologic studies associated with plaque instability include a thin fibrous cap, a large necrotic lipid core, and sometimes intraplaque hemorrhage [26, 27]. Plaque components identified with extracranial carotid wall imaging are challenging to visualize intracranially. However, using VWI with multiple tissue weightings, a fibrous cap can be identified as a thin T2 hyperintense band adjacent to the lumen, although inter-observer reproducibility is only moderate [10, 27]. The lipid core is poorly visualized intracranially, but intraplaque hemorrhage, when present, appears T2 hypointense and T1 hyperintense on VWI. Intraplaque hemorrhage was visualized with VWI in 4–19% of atherosclerotic lesions, but was more common in 19.6% of symptomatic lesions compared with 3.2% of asymptomatic lesions [10, 19, 27, 28]. Intraplaque hemorrhage is less common in intracranial lesions than extracranial lesions, and further prospective studies are needed to assess its predictive power for recurrent strokes.

Atherosclerotic plaques frequently enhance with gadolinium contrast on VWI, which is associated with histopathologic findings of inflammation, macrophage infiltration, increased permeability, and neovascularization of the arterial wall with vasa vasorum [29, 30]. Vasa vasorum are not present at birth in intracranial arteries, but can develop in large proximal arteries, and are associated with age and atherosclerosis [31]. Enhancement of atherosclerotic plaque is significantly associated with acute stroke in the downstream vascular territory [32, 33] and less likely to be found in asymptomatic atherosclerotic plaques. Enhancement is greatest within the first 4 weeks after stroke and declines over months [34, 35]. Enhancement may identify culprit atherosclerotic plaques, although the specificity of enhancement remains unclear.

Few studies have evaluated atherosclerotic plaque enhancement longitudinally to identify unstable plaque as a predictor of recurrent ischemic events. In a study by Kim et al. following 138 patients over a median of 18 months, 78.3% of acute strokes demonstrated plaque enhancement. Of these patients, 34% had recurrent stroke, while only 7% of patients without acute plaque enhancement had recurrence [36]. Kwee et al. performed serial VWI on 14 patients with symptomatic ICAD with a total of 55 lesions over a median of 140 days. All culprit lesions enhanced at baseline and remained enhancing at follow-up. Six recurrent ischemic events occurred and were attributable to culprit lesions. Non-culprit lesions were less likely to enhance at baseline and had overall lower enhancement grade. Enhancement declined over time in 37% (Fig. 1) [18•].

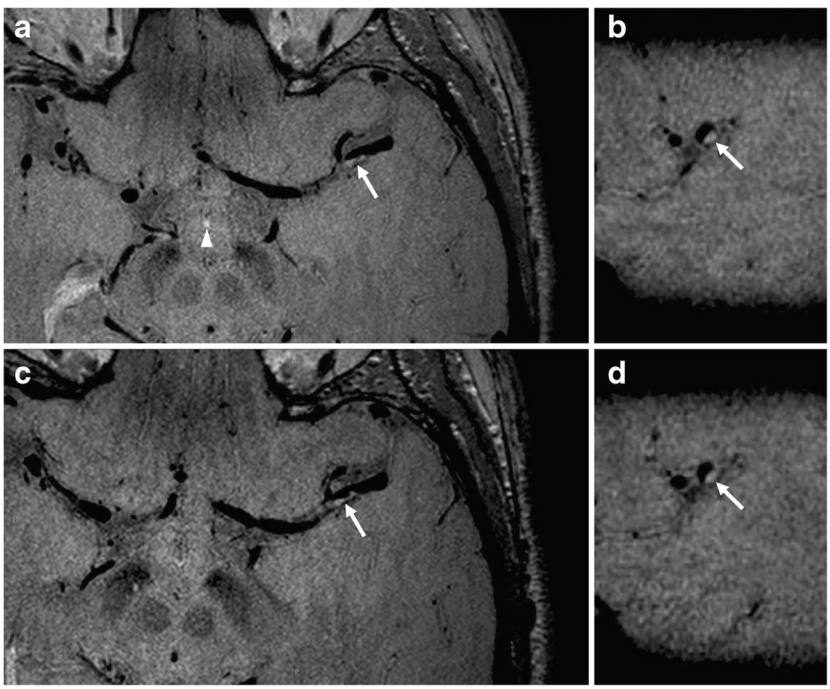

Fig. 1. Intracranial atherosclerotic disease. Reprinted with permission from Kwee et al., European Society of Neuroradiology [18•]. "Persistent grade 1 enhancement of a culprit plaque in the M2 segment of the left middle cerebral artery in a 49-year-old male patient who experienced a transient ischemic attack 8.2 months before the baseline scan. Post-contrast reconstructions in the axial plane and perpendicular to flow direction of the middle cerebral artery at baseline (**a**, **b**) and after 13.6 months (**c**, **d**) show a plaque (arrows) with persistent enhancement greater than that of normal intracranial arteries elsewhere but less than that of the pituitary infundibulum (arrowhead in **a**)."

While focal plaque enhancement may discern atherosclerotic mechanism, clinical interpretation is key. Regardless of stroke mechanism, all patients who underwent mechanical thrombectomy were found to have some degree of arterial wall enhancement, and many treated with only medical therapy also demonstrated wall enhancement (up to 40%) [37, 38]. In these cases, enhancement may reflect endothelial trauma due to mechanical thrombectomy, thrombosis, or thrombolytic treatment [39]. Vessel wall enhancement should be interpreted cautiously after acute stroke since it may be an expected finding, as opposed to focal plaque enhancement, which may have more prognostic value.

In summary, VWI reveals atherosclerotic plaques with focal, eccentric wall thickening, outward remodeling, and variable enhancement. Symptomatic lesions are more likely to have enhancement, outward remodeling, irregularity, and intraplaque hemorrhage, suggesting plaque instability. Enhancement is prevalent, particularly immediately post-stroke, but may predict stroke recurrence if focal and localized to plaque. Longitudinal studies are needed to define temporal changes in atherosclerotic plaque features and determine the added value of VWI to identify unstable plaques, predict stroke recurrence, and monitor treatment efficacy in ICAD.

Intracranial dissections

Dissections of the cervical arteries are well described as a leading cause of stroke in younger patients [40]. But isolated intracranial arterial dissections are poorly characterized. Previously thought to be rare, intracranial arterial dissections are now better visualized with VWI. With more widespread use of VWI and the ability to distinguish dissection from other intracranial vasculopathies, we hope to better understand the risk factors, consequences, and management of intracranial dissections

Isolated intracranial arterial dissections are reported more frequently in Asian populations [42, 43•, 44•], with nearly all large case series originating from China, Japan, or Korea. Genetics, a higher prevalence of intracranial atherosclerosis, or diagnostic techniques may account for this geographic difference [45]. Compared with those with extracranial dissections, patients with intracranial dissections were more likely to be older or hypertensive and less likely to identify a precipitating trauma [43, 46]. However, compared with patients with intracranial atherosclerotic lesions, those found to have isolated intracranial dissections were younger with fewer atherogenic risk factors [41••].

Intracranial arterial dissections are most commonly found in the vertebral arteries, in the V4 segment, near the origin of the posterior inferior cerebellar artery (PICA), and more often in the non-dominant vertebral artery [46]. The internal carotid artery at the C6 segment is the next most common location [44•]. These segments mark the transition from extradural to intradural, where the external elastic lamina terminates. However, dissections are found in all intracranial arteries [43] and may be underdiagnosed. One Japanese study reported that 43% of isolated anterior cerebral artery strokes were due to dissection, confirmed by follow-up angiography [47].

Intracranial dissections can present as either ischemic or hemorrhagic stroke. Ischemic lesions may result from artery-to-artery embolism, local branch

occlusion, in-situ thrombosis, or hemodynamic impairment [43]. Subarachnoid hemorrhage may occur, particularly when the dissection involves the media and adventitia, leading to formation of a dissecting aneurysm. Hemorrhage is more likely to result from posterior circulation dissection and has a high rate of recurrence [48]. Intracranial dissections accounted for 1.5–10.5% of nontraumatic subarachnoid hemorrhages on histopathology in several studies of Asian populations [49].

Diagnosing dissections is challenging with conventional, luminal imaging, often requiring serial scans to evaluate for resolution, or confounded by complete vessel occlusion. VWI improves identification of intracranial dissection by several distinct features: an intimal flap or double lumen, an intramural hematoma, outer diameter enlargement with crescent shape, stenosis and dilatation ("pearl and string sign"), and variable wall enhancement (Fig. 2) [50–53]. Compared with time-of-flight MRA alone, VWI improved detection of intracranial dissection from 11 to 22% [54].

The increasing use of VWI will shed more light on the natural history and appropriate management of intracranial dissections. Shin et al. report the prospective use of VWI for Korean patients with symptomatic intracranial stenosis of undetermined etiology. In this population, dissection accounted for 36% of lesions, while the remaining were determined to be atherosclerotic stenoses. While 90-day functional outcomes were similar, dissection was associated with a lower risk of recurrent events (6.2% vs. 18.6%), and a higher rate of improvement in the stenosis on follow-up imaging (50.7% vs. 11.6%) [41••]. It is possible that prior treatment trials of intracranial stenoses have misidentified dissecting lesions, and that VWI may better select patients for

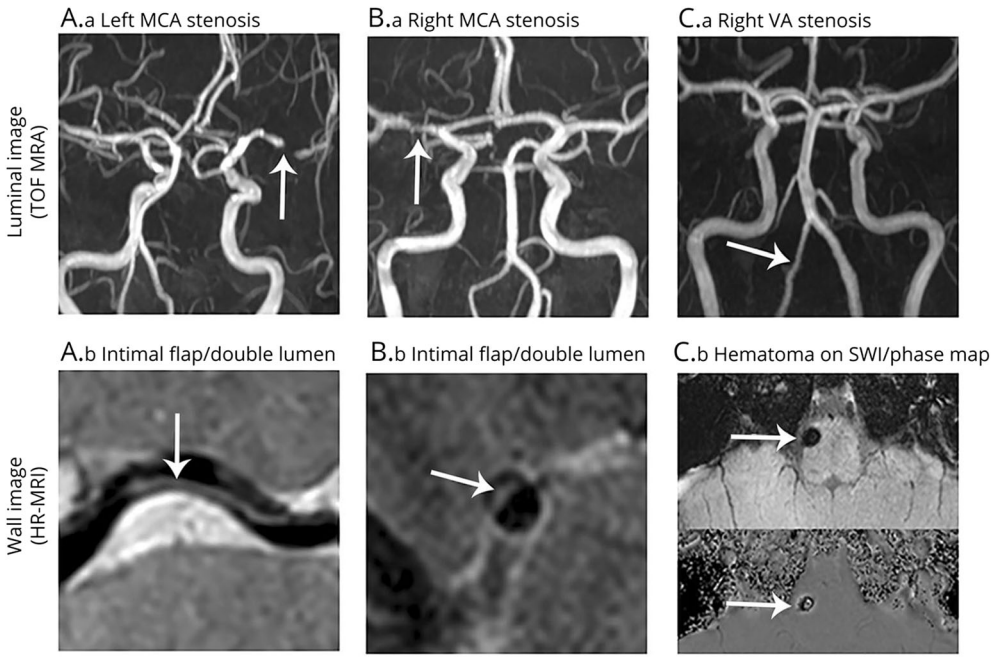

Fig. 2. Reprinted with permission from Shin et al., American Academy of Neurology [41••]. "Examples of patients with no typical changes of dissection on luminal imaging (A.a, B.a, C.a, arrows) but with high-resolution MRI findings of dissection (A.b, B.b, C.b, arrows)."

intervention. However, there is likely overlap with dissecting atherosclerotic plaques, for which treatment of atherosclerotic risk factors is still beneficial.

Central nervous system vasculitis

Perhaps the best application of VWI is diagnosing central nervous system (CNS) vasculitis. CNS vasculitis may be idiopathic primary angiitis of the CNS (PACNS) or secondary to infectious or systemic rheumatologic etiologies. CNS vasculitis presents with headache (43–64%), altered cognition (50%), focal neurologic deficit (40%), seizure (17%), infarct (81%), or hemorrhage (11%) [55, 56]. Diagnostic certainty is critical because CNS vasculitis is potentially devastating, and the treatment for PACNS is aggressive immunosuppression, which also bears risk. However, CNS vasculitis is challenging to diagnose, typically requiring a combination of conventional brain MRI sequences, MRA or CTA, DSA, lumbar puncture, and brain biopsy. DSA has a sensitivity of 60–90% [56, 57] but a low specificity of 6–30% [56, 58, 59]. DSA may be normal in small-vessel vasculitis and can have a similar angiographic appearance to other noninflammatory cerebral vasculopathies: RCVS, ICAD, or moyamoya syndrome. Lumbar puncture may be normal in 12–20% [56, 57, 59]. The gold standard for diagnosis is brain biopsy, which carries additional risk of permanent neurologic complication around 1–2% [60, 61], and still only has a sensitivity of 50–75% [8, 56, 57, 62] due to heterogeneous vessel involvement. Clinical characteristics may favor a diagnosis of vasculitis, such as progressive cognitive decline and seizures, or else point toward other entities such as thunderclap headache in RCVS, or multiple uncontrolled atherosclerotic risk factors in ICAD. However, VWI provides complementary information about arterial thickening and vessel inflammation to support the diagnosis of vasculitis, plan targeted biopsies, or otherwise suggest an alternative diagnosis, thereby sparing brain biopsy.

The VWI features of vasculitis include multifocal, segmental, smooth, concentric enhancement and thickening of the vessel walls [63–65]. Enhancement can be seen in areas of stenosis on MRA, or in non-stenotic segments (Fig. 3). Even where the lumen is not visualized on VWI, a pattern of periadventitial linear enhancement can be seen that coincides with the location of smaller vessels [65]. Enhancement can also be seen in the parenchyma or leptomeninges [8]. The sensitivity of wall enhancement is 67–100% while the specificity is 40–48% [8, 66, 67•] depending on the pattern and population being studied. Eiden et al. compared 2D to 3D VWI techniques and found similar sensitivities and specificities, but found more parenchymal and leptomeningeal enhancement with 3D VWI [8]. Kesav et al. evaluated 49 recent stroke patients with symptomatic stenosis and were able to reclassify 47.3% of strokes of unknown etiology based on T1 VWI wall thickening, enhancement pattern, and T2 signal. One hundred percent of patients with inflammatory vasculopathy had diffuse concentric wall thickening on T1 imaging, and 92.3% had diffuse concentric enhancement (one had heterogeneous enhancement). In contrast, patients with ICAD all had focal eccentric T1 thickening while 84.2% had focal eccentric enhancement [67•].

VWI improves the diagnostic yield of brain biopsy for CNS vasculitis by revealing better stereotactic targets. Non-targeted biopsies have lower yield

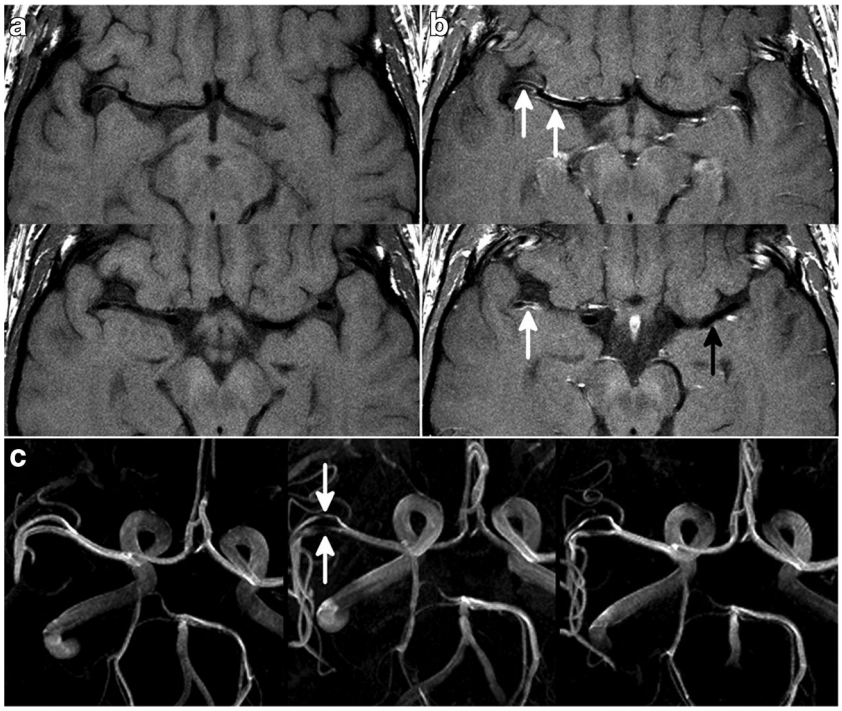

Fig. 3. Central nervous system vasculitis. Reprinted with permission from Mandell et al., American Heart Association [63]. "Axial T1-weighted vessel wall MRI pre-gadolinium (**a**) and post-gadolinium (**b**) at presentation demonstrates arterial wall thickening and enhancement (arrows). MR angiogram at the time of vessel wall imaging (middle image in **c**) shows narrowing of the right middle cerebral artery (arrows) compared with an MR angiogram obtained 2 months earlier (left image in **c**). Follow-up angiogram 3 months after vessel wall MRI (right image in **c**) shows persistent narrowing."

compared with MRI lesion-targeted biopsies [61]. In one study, none of six non-targeted right frontal biopsies were diagnostic, while 78% of lesion-targeted biopsies were diagnostic [68]. Zeiler et al. used VWI features of segmental, concentric wall enhancement, or circumferential periadventitial enhancement to target image-guided brain biopsy in 9 patients, and found vascular inflammation in 8 [65]. Given their success, VWI should be considered in pre-surgical planning for brain biopsy in large-to-medium vessel CNS vasculitis.

The long-term prognosis for CNS vasculitis is variable, and the optimal duration of immunosuppressive treatment is unknown, so therapy is tailored to clinical relapses. But serial VWI holds promise in predicting disease activity. Obusez et al. followed 6 patients treated for vasculitis, and at 11 to 16 months, 4 showed persistent enhancement, 3 of which also had persistent wall thickening. One of these patients still had active symptoms at follow-up. Meanwhile, 2 showed resolution of enhancement, wall thickening, and stenosis at about 7 months and were asymptomatic or stable [64]. Two case reports of PACNS tracked response to immunosuppressive treatment with clinical improvement and found decrease or resolution of wall enhancement at 6 and 9 months [69, 70]. These cases suggest that VWI features follow the clinical course in CNS vasculitis, but prospective trials are needed to determine if VWI can improve management.

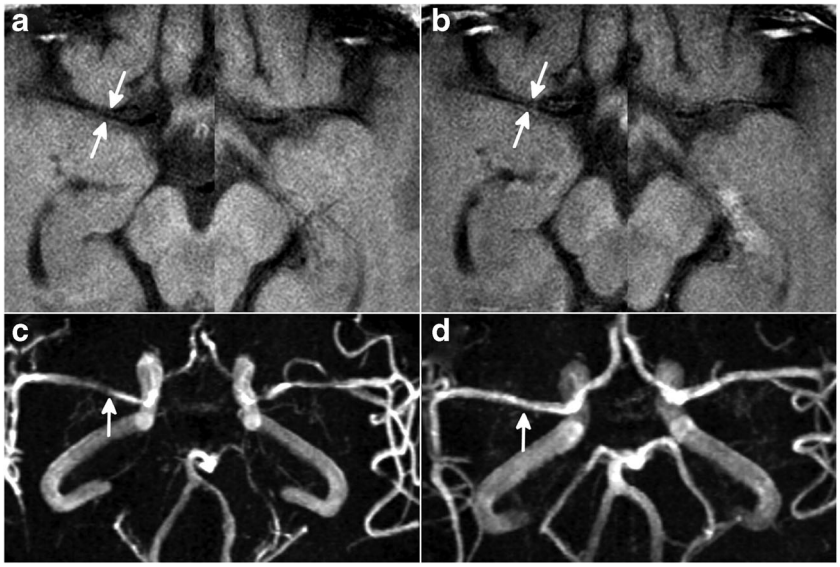

Fig. 4. Reversible cerebral vasoconstriction syndrome. Reprinted with permission from Mandell et al., American Heart Association [63]. "Axial T1-weighted vessel wall MRI pre-gadolinium (**a**) and post-gadolinium (**b**) at presentation demonstrates arterial wall thickening (arrows) but has absent/minimal arterial wall enhancement. Note the slice positioning is different for the right and left middle cerebral artery images. MR angiography at presentation (**c**) shows segmental narrowing of the anterior, middle (arrow), and posterior cerebral arteries bilaterally. Three-month follow-up angiogram (**d**) shows resolution of arterial narrowing."

Reversible cerebral vasoconstriction syndrome

VWI may play a complementary role in diagnosing RCVS. Similar to CNS vasculitis, RCVS can also present with headache (96%), focal neurologic deficit (40%), infarct (28%), or hemorrhage (46%). Unlike CNS vasculitis, RCVS more often presents with a thunderclap headache (89% vs. 6% in vasculitis) and brain MRI may show vasogenic edema (25% vs. 0% in vasculitis). Angiographic similarities include multivessel, segmental narrowing and dilatation, and differences can be subtle [55, 71]. In RCVS, clinical presentation and noninvasive imaging findings are often sufficient to diagnose RCVS even without DSA, but many patients will still undergo lumbar puncture, brain biopsy, or empiric immunosuppressive therapy prior to correct diagnosis [55].

VWI, as a complementary, noninvasive, diagnostic approach, can distinguish RCVS from PACNS [63, 64] and ICAD [72]. VWI in RCVS shows diffuse uniform or concentric wall thickening with mild or no contrast enhancement (Fig. 4). In 3 studies comparing a total of 38 patients with RCVS with 31 patients with CNS vasculitis, all patients with RCVS had absent or minimal enhancement (grade 0) (79%) or mild enhancement (grade 1) (21%). In the vasculitis group, 1 patient (3%) had no enhancement, 6 patients (19%) had mild enhancement (grade 1), and 25 patients (80%) had the highest grade of enhancement (present or grade 2). When present, enhancement was diffuse in both RCVS and vasculitis. Arterial wall thickening and stenosis were seen in 74% of patients with RCVS and 97% of patients with vasculitis. Notably, of 12 patients with RCVS followed with VWI at 1.5 to 3.5 months, 11 (92%) had a

resolution of wall enhancement and thickening, and one had near-resolution [63, 64, 72]. In summary, the absence of wall enhancement may be the most important distinguishing feature of VWI for distinguishing RCVS or vasculitis and may prevent the potentially deleterious use of empiric glucocorticoid treatment [73] or brain biopsy in this population.

Moyamoya

The unique arterial wall features and collateralization found in moyamoya syndrome or moyamoya disease (MMD) are easily seen with VWI and can be leveraged to improve diagnoses and potentially predict disease progression. MMD is a chronic noninflammatory, occlusive arteriopathy characterized by progressive stenosis affecting predominantly the bilateral terminal internal carotid arteries [74]. As stenoses progress, neovascularization leads to the development of wispy basal collaterals. While steno-occlusive disease causes borderzone strokes or seizures [75], neovascularization can lead to intracerebral hemorrhage [75, 76]. MMD presents in childhood or middle-adulthood; is ten times more common in East Asians, twice as common in women; and is familial in 10–15% of cases. Moyamoya syndrome occurs when progressive stenoses are secondary to systemic disease such as diabetes, ICAD, sickle-cell disease, cranial irradiation, Down syndrome, or neurofibromatosis type I [75].

VWI in MMD reveals negative arterial remodeling with concentrically smaller outer wall diameter, wall area, and remodeling index compared with other chronic vasculopathies (Fig. 5) [77–79]. Arterial shrinkage is related to moyamoya staging [79]. Furthermore, collateral vasculature can be seen directly around the area of stenosis [79]. Kim et al. used VWI to measure outer wall diameters of stenotic MCAs to discriminate etiology in a group of 12 patients with MMD and 20 patients with ICAD. An outer wall diameter threshold of 2.39 mm provided 90% sensitivity, while a threshold of 2.48 mm provided 100% specificity [78].

Findings on VWI enhancement patterns in moyamoya are more nuanced. Kim et al. found that patients with MMD have concentric occlusive lesions that rarely enhance (28.6%) compared with ICAD (76.5%) [78]. However, Ryoo et al., in a larger sample, found that diffuse concentric enhancement is often found in MMD (90.6%). However, the diffuse concentric enhancement pattern in MMD was distinct from patients with ICAD, who had predominantly focal eccentric enhancement localized at the stenosis [77]. Strong vessel enhancement in MMD is associated with acute infarct and may also predict disease progression [80, 81••]. Roder et al. evaluated 31 MMD patients with VWI longitudinally and found that while 69% had no or mild wall enhancement, which was associated with disease stability, 17% had strong wall enhancement, which was associated with clinical progression within 6 months [81••]. Muraoka et al. studied 24 patients with MMD with repeat MRI VWI at an interval of 6 months and found that strong wall enhancement was an independent predictor of progression of luminal stenosis on imaging, with an odds ratio of 36 [82].

Finally, the diagnostic utility of VWI in moyamoya was confirmed in a small study by Mossa-Basha et al., who found that adding a multi-contrast VWI protocol (including T1 pre- and post-contrast and T2) to conventional MRI and MRA improved the inter-reader agreement from 11 to 82% when

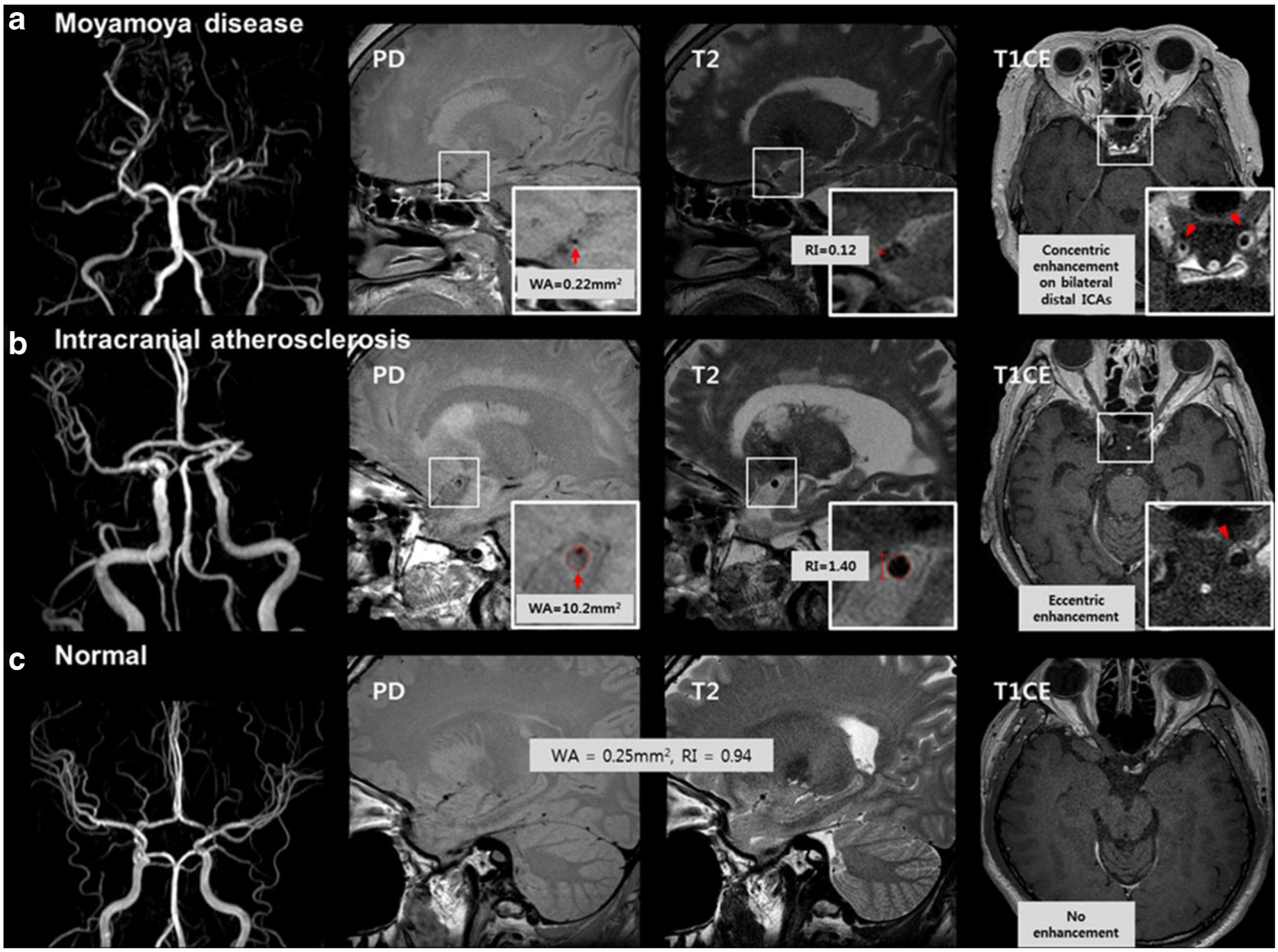

Fig. 5. Moyamoya disease. Reprinted with permission from Ryoo et al., American Heart Association [77]. "Cases of moyamoya disease (MMD), intracranial atherosclerotic disease (ICAD), and a normal control showing different high-resolution MRI findings. **a** MMD showing shrinking middle cerebral artery (MCA; arrows) and concentric enhancement on bilateral distal internal carotid arteries (ICAs; arrowheads). **b** Thick MCA with positive remodeling (arrows) in ICAD. Enhancement of the left distal ICA is eccentric (arrowhead). **c** Normal control has MCA without shrinkage or plaque and no enhancement on distal ICAs." PD, proton density; T1CE, T1 contrast-enhanced; WA, wall area; RI, remodeling index.

distinguishing MMD from moyamoya syndrome due to ICAD or vasculitis [83]. In summary, while terminal ICA shrinkage on VWI, particularly smaller outer wall diameter, is an important diagnostic feature for MMD, enhancement patterns may be useful for predicting clinical or radiographic disease progression.

Intracranial aneurysms

VWI provides better visualization of intracranial aneurysms to identify and risk-stratify this common but devastating cerebrovascular pathology. Unruptured intracranial aneurysms are prevalent in 3.2% of the adult population [84], and aneurysmal subarachnoid hemorrhage has a high rate of morbidity and mortality [85]. Risk factors for rupture include site, greater size, shape, prior rupture, female

sex, Japanese or Finnish ancestry, tobacco use, and elevated blood pressure. Large population studies of unruptured aneurysms have led to the development of risk calculators to help guide management, including the ISUIA calculator, the PHASES score, and the ELAPSS score [86–88]. While the annual risk of rupture for a small aneurysm is low [90], aneurysms less than 5 mm still account for half of all aneurysmal subarachnoid hemorrhages [91]. Risk of rupture is balanced with the risk of aneurysm coiling or clipping, which may depend on aneurysm site and morphology. Since VWI provides detail of the aneurysmal wall not available via other imaging modalities, it holds promise as a noninvasive tool to improve aneurysm identification, risk-stratification, and management.

Aneurysmal wall enhancement (AWE) is an imaging feature distinct to VWI that may be complementary to morphological changes seen with conventional angiography for risk stratification. Other features such as size and morphology are easily gleaned from angiographic techniques. Aneurysmal wall thickness measurements are unreliable with VWI resolution, since the aneurysm wall is typically much thinner than the healthy arterial wall. So AWE has been the primary focus of most VWI studies. Histopathologic correlation studies found that AWE in unruptured aneurysms correlated with wall thickening, development of vasa vasorum, and macrophage infiltration [92•]. Enhancement may also reflect atherosclerotic changes that contribute to aneurysm growth in older patients.

While smaller studies found no AWE in unruptured aneurysms, larger studies found that 18–38.4% of asymptomatic, unruptured aneurysms enhance [89•, 92•, 93, 94•]. AWE is associated with aneurysm size [95–98], irregular shape [97], and a higher PHASES score [96, 97, 99]. AWE is also more common when neurologic symptoms are present [89, 97, 100–102]. In a large meta-analysis by Texakaladis et al., AWE was significantly associated with aneurysm instability, as defined by growth, neurologic symptoms, or rupture. Sensitivity of enhancement was 95%, and negative predictive value was 96.2%, although specificity was only 62.7% and positive predictive value only 55.8% [103].

Few studies have evaluated the predictive power of AWE longitudinally. Edjlali et al. evaluated 241 patients with 307 unruptured aneurysms with VWI who had repeat angiography at 6 months. Enhancement, graded 0 to 3, was significantly associated with unstable aneurysms at baseline (symptomatic or recent morphologic change) or growth at 6 months. Only 4 stable aneurysms grew at 6 months. Enhancement was found in 71% of unstable aneurysms, and only 38.4% of the 276 stable aneurysms that remained stable at 6 months. Using grade 3 enhancement yielded greater specificity at 84.4% (Fig. 6) [89•]. Vergouwen et al. followed 57 patients with 65 unruptured aneurysms for a median of 27 months. At baseline, 29% of aneurysms enhanced. Only 4 aneurysms, all enhancing, grew or ruptured by follow-up [104]. Matsushige et al. evaluated 60 unruptured aneurysms with serial angiography over at least 2 years (mean 49 months). While 10% had shown expansion prior to the study period, 45% of the aneurysms grew, 48% of which had AWE. However, when growth was distinguished as whole sac expansion vs. daughter sac formation, enhancement was more common in 82% of those with daughter sac formation. Meanwhile, only 28% of stable aneurysms enhanced [105•]. These data suggest that lack of enhancement predicts aneurysm stability, but enhancement has only modest specificity or predictive power.

Finally, AWE on VWI is found in 88.5–100% of ruptured aneurysms, and enhancement has been proposed as a way to identify ruptured aneurysms when

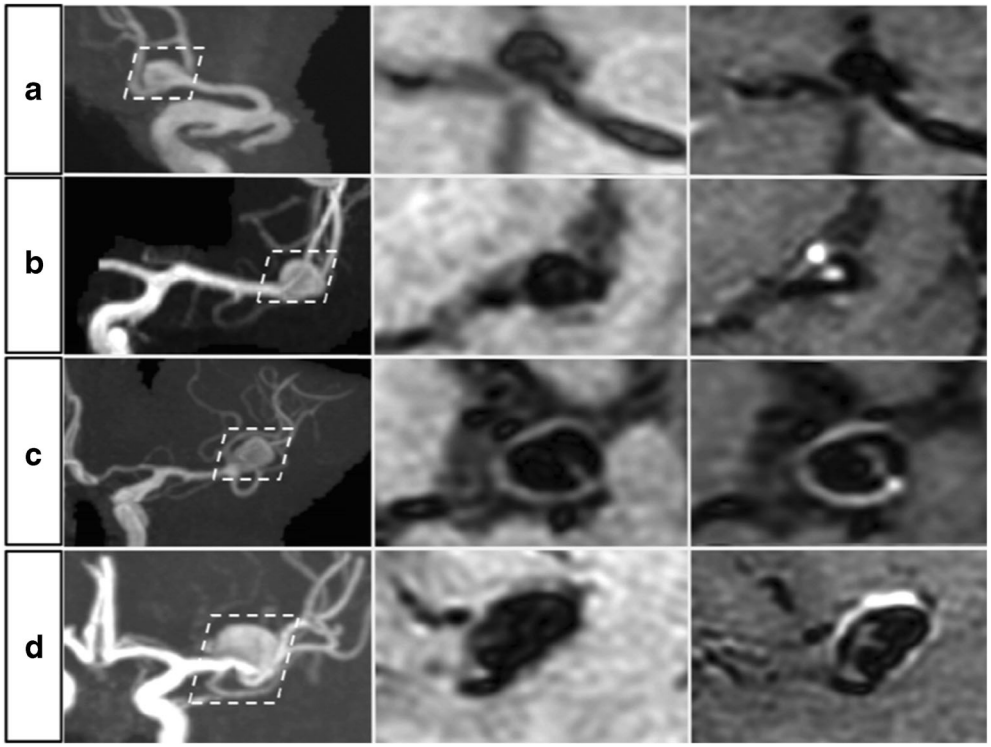

Fig. 6. Reprinted with permission from Edjlali et al., Radiological Society of North America [89•]. "Grading of aneurysm wall enhancement. For each aneurysm represented on a row, a 3D time-of-flight MRA is shown in the left column, a 3D T1-weighted fast-spin-echo image is in the middle column, and a 3D T1-weighted fast-spin-echo image obtained after enhancement with gadolinium chelate is shown in the right column. **a** Grade 0: non-enhancing anterior communicating artery aneurysm. **b** Grade 1: focal thick wall enhancement of a middle cerebral artery aneurysm. **c** Grade 2: thin and circumferential wall enhancement of a middle cerebral artery aneurysm. **d** Grade 3: thick (> 1 mm) and circumferential wall enhancement of a middle cerebral artery aneurysm. Focal enhancement greater than 1 mm within otherwise thin circumferential aneurysmal wall enhancement was grade 3."

multiple aneurysms are present [89•, 93, 94•, 106, 107]. Enhancement can be circumferential or focal. Focal enhancement may reflect intraluminal thrombus and the point of rupture [105•]. Few studies have used VWI to identify the bleeding source when DSA is negative. Vergouwen et al. evaluated 7 patients with perimesencephalic hemorrhage with VWI at 7 T and found no arterial wall abnormalities [108]. Coutinho et al. used the 3-T VWI in 11 patients with non-perimesencephalic subarachnoid hemorrhage with normal angiograms. Seven patients had wall enhancement, but 5 were considered nonspecific or unrelated. The other 2 had focal abnormalities of the outer margin of the basilar artery, which could have been a ruptured blood blister aneurysm, a thrombosed aneurysm, or just loculated extramural blood. The authors concluded that VWI did not change management [109]. Further prospective studies are needed to determine the value of VWI in cryptogenic subarachnoid hemorrhage.

Conclusion

In summary, VWI can provide new insights into cerebrovascular pathologies not readily apparent on conventional angiographic imaging. Commercially

available MRI pulse sequences for 3D isotropic, whole-brain, VWI should hasten the widespread adoption of this technique. The noninvasive nature of VWI and the complementary information it provides make it suitable for distinguishing intracranial vasculopathies, particularly when the diagnosis is in question and DSA and biopsy are being considered. Clinicians should be familiar with VWI features of ICAD, intracranial dissection, CNS vasculitis, RCVS, and moyamoya, since VWI may spare unnecessary invasive testing, or identify a better biopsy site. While VWI holds promise for predicting recurrent strokes in ICAD and rupture or growth of intracranial aneurysms, its utility should be confirmed in large, prospective, longitudinal studies. Future studies should evaluate the utility of VWI in monitoring disease activity and treatment effects for ICAD and CNS vasculitis.

Compliance with Ethical Standards

Conflict of Interest
Kyle C. Kern declares that he has no conflict of interest.
David S. Liebeskind declares that he has no conflict of interest.

Human and Animal Rights and Informed consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Harteveld AA, Denswil NP, Van Hecke W, Kuijf HJ, Vink A, Spliet WGM, et al. Ex vivo vessel wall thickness measurements of the human circle of Willis using 7T MRI. Atherosclerosis. 2018;273:106–14.
2. Edelman RR, Chien D, Kim D. Fast selective black blood MR imaging. Radiology. 1991;181:655–60.
3. Lindenholz A, Van Der Kolk AG, Zwanenburg JJM, Hendrikse J. The use and pitfalls of intracranial vessel wall imaging: how we do it. Radiology. 2018;286:12–28.
4. Felmlee JP, Ehman RL. Spatial presaturation: a method for suppressing flow artifacts and improving depiction of vascular anatomy in MR imaging. Radiology. 1987;164:559–64.
5. Song HK, Wright AC, Wolf RL, Wehrli FW. Multislice double inversion pulse sequence for efficient black-blood MRI. Magn Reson Med. 2002;47:616–20.
6. Busse RF, Brau ACS, Vu A, Michelich CR, Bayram E, Kijowski R, et al. Effects of refocusing flip angle modulation and view ordering in 3D fast spin echo. Magn Reson Med. 2008;60:640–9.
7.• Mandell DM, Mossa-Basha M, Qiao Y, Hess CP, Hui F, Matouk C, et al. Intracranial vessel wall MRI: principles and expert consensus recommendations of the American Society of Neuroradiology. *AJNR Am J Neuroradiol*. 2017;38:218–2.

This review provides consensus recommendations for VWI by highlighting imaging protocol recommendations and grading the applicability of adjunctive VWI for various cerebrovascular disorders.

8. Eiden S, Beck C, Venhoff N, Elsheikh S, Ihorst G, Urbach H, et al. High-resolution contrast-enhanced vessel wall imaging in patients with suspected cerebral

vasculitis: prospective comparison of whole-brain 3D T1 SPACE versus 2D T1 black blood MRI at 3 Tesla. PLoS One. 2019;14:e0213514.
9. Xu W-H, Li M-L, Gao S, Ni J, Zhou L-X, Yao M, et al. In vivo high-resolution MR imaging of symptomatic and asymptomatic middle cerebral artery atherosclerotic stenosis. Atherosclerosis. 2010;212:507–11.
10. Yang WQ, Huang B, Liu XT, Liu HJ, Li PJ, Zhu WZ. Reproducibility of high-resolution MRI for the middle cerebral artery plaque at 3 T. Eur J Radiol. 2014;83:e49–55.
11. Sacco RL, Roberts JK, Boden-Albala B, Gu Q, Lin I-F, Kargman DE, et al. Race-ethnicity and determinants of carotid atherosclerosis in a multiethnic population: the Northern Manhattan Stroke Study. Stroke. 1997;28:929–35.
12. Wong LKS. Global burden of intracranial atherosclerosis. Int J Stroke. 2006;1:158–9.
13. Sing WK, Huan L. Long-term mortality and recurrent stroke risk among Chinese stroke patients with predominant intracranial atherosclerosis. Stroke. 2003;34:2361–6.
14. Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, et al. Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. N Engl J Med. 2005;352:1305–16.
15. Derdeyn CP, Chimowitz MI, Lynn MJ, Fiorella D, Turan TN, Janis LS, et al. Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial. Lancet. 2014;383:333–41.
16. Kasner SE, Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, et al. Predictors of ischemic stroke in the territory of a symptomatic intracranial arterial stenosis. Circulation. 2006;113:555–63.
17. Arenillas JF, Dieleman N, Bos D. Intracranial arterial wall imaging: techniques, clinical applicability, and future perspectives. Int J Stroke. 2019;0:174749301984094.
18.• Kwee RM, Qiao Y, Liu L, Zeiler SR, Wasserman BA. Temporal course and implications of intracranial atherosclerotic plaque enhancement on high-resolution vessel wall MRI. Neuroradiology. 2019;61:651–7. https://doi.org/10.1007/s00234-019-02190-4.
Atherosclerotic plaque enhancement on VWI may have predictive value in ICAD. Symptomatic, culprit plaques were more likely to enhance, and all 6 recurrent ischemic events were attributed to culprit plaques.
19. Sui B, Gao P, Lin Y, Jing L, Qin H. Distribution and features of middle cerebral artery atherosclerotic plaques in symptomatic patients: a 3.0 T high-resolution MRI study. Neurol Res. 2015;37:391–6.
20. Xu W-H, Li M-L, Gao S, Ni J, Zhou L-X, Yao M, et al. Plaque distribution of stenotic middle cerebral artery and its clinical relevance. Stroke. 2011;42:2957–9.
21. Huang B, Yang W-Q, Liu X-T, Liu H-J, Li P-J, Lu H-K. Basilar artery atherosclerotic plaques distribution in symptomatic patients: a 3.0T high-resolution MRI study. Eur J Radiol. 2013;82:e199–203.
22. Chung GH, Kwak HS, Hwang SB, Jin GY. High resolution MR imaging in patients with symptomatic middle cerebral artery stenosis. Eur J Radiol. 2012;81:4069–74.
23. Van Der Kolk AG, Zwanenburg JJM, Brundel M, Biessels GJ, Visser F, Luijten PR, et al. Intracranial vessel wall imaging at 7.0-T MRI. Stroke. 2011;42:2478–84.
24. Zhao D-L, Deng G, Xie B, Ju S, Yang M, Chen X-H, et al. High-resolution MRI of the vessel wall in patients with symptomatic atherosclerotic stenosis of the middle cerebral artery. J Clin Neurosci. 2015;22:700–4.
25. Shi M-C, Wang S-C, Zhou H-W, Xing Y-Q, Cheng Y-H, Feng J-C, et al. Compensatory remodeling in symptomatic middle cerebral artery atherosclerotic stenosis: a high-resolution MRI and microemboli monitoring study. Neurol Res. 2012;34:153–8.
26. Chen XY, Wong KS, Lam WWM, Zhao H-L, Ng HK. Middle cerebral artery atherosclerosis: histological comparison between plaques associated with and not associated with infarct in a postmortem study. Cerebrovasc Dis. 2008;25:74–80.
27. Zhao D-L, Li C, Chen X-H, Ju S, Deng G, Xie B, et al. Reproducibility of 3.0T high-resolution magnetic resonance imaging for the identification and quantification of middle cerebral arterial atherosclerotic plaques. J Stroke Cerebrovasc Dis. 2019;28:1824–31.
28. Xu W-H, Li M-L, Gao S, Ni J, Yao M, Zhou L-X, et al. Middle cerebral artery intraplaque hemorrhage: prevalence and clinical relevance. Ann Neurol. 2012;71:195–8.
29. Yuan C, Kerwin WS, Ferguson MS, Polissar N, Zhang S, Cai J, et al. Contrast-enhanced high resolution MRI for atherosclerotic carotid artery tissue characterization. J Magn Reson Imaging. 2002;15:62–7.
30. Millon A, Boussel L, Brevet M, Mathevet J-L, Canet-Soulas E, Mory C, et al. Clinical and histological significance of gadolinium enhancement in carotid atherosclerotic plaque. Stroke. 2012;43:3023–8.
31. Aydin F. Do human intracranial arteries lack vasa vasorum? A comparative immunohistochemical study of intracranial and systemic arteries. Acta Neuropathol. 1998;96:22–8.
32. Qiao Y, Zeiler SR, Mirbagheri S, Leigh R, Urrutia V, Wityk R, et al. Plaque enhancement 2014 cerebrovasclular events. Radiology. 2014;271:534–42.
33. Gupta A, Baradaran H, Al-Dasuqi K, Knight-Greenfield A, Giambrone AE, Delgado D, et al. Gadolinium enhancement in intracranial atherosclerotic plaque and ischemic stroke: a systematic review and meta-analysis. J Am Heart Assoc. 2016;5:e003816.
34. Vergouwen MDI, Silver FL, Mandell DM, Mikulis DJ, Swartz RH. Eccentric narrowing and enhancement of symptomatic middle cerebral artery stenoses in patients with recent ischemic stroke. Arch Neurol. 2011;68:338–42.

35. Skarpathiotakis M, Mandell DM, Swartz RH, Tomlinson G, Mikulis DJ. 3T MRI 2012 ICAS plaque enhancement in ischemic stroke. Am J Neuroradiol. 2013;34:299–304.
36. Kim J-M, Jung K-H, Sohn C-H, Moon J, Shin J-H, Park J, et al. Intracranial plaque enhancement from high resolution vessel wall magnetic resonance imaging predicts stroke recurrence. Int J Stroke. 2016;11:171–9.
37. Power S, Matouk C, Casaubon LK, Silver FL, Krings T, Mikulis DJ, et al. Vessel wall magnetic resonance imaging in acute ischemic stroke: effects of embolism and mechanical thrombectomy on the arterial wall. Stroke. 2014;45:2330–4.
38. Abraham P, Pannell JS, Santiago-Dieppa DR, Cheung V, Steinberg J, Wali A, et al. Vessel wall signal enhancement on 3-T MRI in acute stroke patients after stent retriever thrombectomy. Neurosurg Focus. 2017;42:E20.
39. Renu A, Laredo C, Lopez-Rueda A, Llull L, Tudela R, San-Roman L, et al. Vessel wall enhancement and blood-cerebrospinal fluid barrier disruption after mechanical thrombectomy in acute ischemic Stroke. Stroke. 2017;48:651–7.
40. Lee VH, Brown RD, Mandrekar JN, Mokri B. Incidence and outcome of cervical artery dissection: a population-based study. Neurology. 2006;67:1809–12.
41.•• Shin J, Chung J-W, Park MS, Lee H, Cha J, Seo W-K, et al. Outcomes after ischemic stroke caused by intracranial atherosclerosis vs dissection. Neurology. 2018;91:e1751–9. https://doi.org/10.1212/WNL.0000000000006459.

This Korean study used VWI to evaluate acute stroke patients with focal, intracranial stenoses of unclear etiology and identified more than one third as intracranial dissections by their imaging criteria. Compared with atherosclerotic lesions, patients with dissections had similar 90-day outcomes, but were less likely to have recurrent events and more likely to have improvement in the focal stenosis on follow-up imaging.

42. Asaithambi G, Saravanapavan P, Rastogi V, Khan S, Bidari S, Khanna AY, et al. Isolated middle cerebral artery dissection: a systematic review. Int J Emerg Med. 2014;7:44.
43. Kwon JY, Kim N-Y, Suh DC, Kang D-W, Kwon SU, Kim JS. Intracranial and extracranial arterial dissection presenting with ischemic stroke: lesion location and stroke mechanism. J Neurol Sci. 2015;358:371–6.
44.• Debette S, Compter A, Labeyrie M-A, Uyttenboogaart M, Metso TM, Majersik JJ, et al. Epidemiology, pathophysiology, diagnosis, and management of intracranial artery dissection. *Lancet Neurol*. 2015;14:640–5.

This article summarizes the current literature on spontaneous intracranial artery dissections, which are rare but are being detected more commonly with VWI, particularly in Asian populations.

45. Bang OY, Toyoda K, Arenillas JF, Liu L, Kim JS. Intracranial large artery disease of non-atherosclerotic origin: recent progress and clinical implications. J Stroke. 2018;20:208–17.
46. Shin DH, Hong JM, Lee JS. Nasim R, Sohn S Il, Kim SJ, et al. Comparison of potential risks between intracranial and extracranial vertebral artery dissections. Eur Neurol. 2014;71:305–12.
47. Sato S, Toyoda K, Matsuoka H, Okatsu H, Kasuya J, Takada T, et al. Isolated anterior cerebral artery territory infarction: dissection as an etiological mechanism. Cerebrovasc Dis. 2010;29:170–7.
48. Ono H, Nakatomi H, Tsutsumi K, Inoue T, Teraoka A, Yoshimoto Y, et al. Symptomatic recurrence of intracranial arterial dissections. Stroke. 2012;44:126–31.
49. Ro A, Kageyama N, Abe N, Takatsu A, Fukunaga T. Intracranial vertebral artery dissection resulting in fatal subarachnoid hemorrhage: clinical and histopathological investigations from a medicolegal perspective. J Neurosurg. 2009;110:948–54.
50. Takano K, Yamashita S, Takemoto K, Inoue T, Kuwabara Y, Yoshimitsu K. MRI of intracranial vertebral artery dissection: evaluation of intramural haematoma using a black blood, variable-flip-angle 3D turbo spin-echo sequence. Neuroradiology. 2013;55:845–51.
51. Chung J-W, Kim BJ, Choi BS, Sohn CH, Bae H-J, Yoon B-W, et al. High-resolution magnetic resonance imaging reveals hidden etiologies of symptomatic vertebral arterial lesions. J Stroke Cerebrovasc Dis. 2014;23:293–302.
52. Han M, Rim NJ, Lee JS, Kim SY, Choi JW. Feasibility of high-resolution MR imaging for the diagnosis of intracranial vertebrobasilar artery dissection. Eur Radiol. 2014;24:3017–24.
53. Gao PH, Yang L, Wang G, Guo L, Liu X, Zhao B. Symptomatic unruptured isolated middle cerebral artery dissection: clinical and magnetic resonance imaging features. Clin Neuroradiol. 2016;26:81–91.
54. Park MS, Cha J, Chung J-W, Seo W-K, Kim G-M, Bang OY. Arterial dissection as a cause of intracranial stenosis in East Asians. J Am Coll Cardiol. 2017. p. 2205–6.
55. Singhal AB, Topcuoglu MA, Fok JW, Kursun O, Nogueira RG, Frosch MP, et al. Reversible cerebral vasoconstriction syndromes and primary angiitis of the central nervous system: clinical, imaging, and angiographic comparison. Ann Neurol. 2016;79:882–94.
56. Salvarani C, Brown RD, Calamia KT, Christianson TJH, Weigand SD, Miller DV, et al. Primary central nervous system vasculitis: analysis of 101 patients. Ann Neurol. 2007;62:442–51.
57. Hajj-Ali RA, Singhal AB, Benseler S, Molloy E, Calabrese LH. Primary angiitis of the CNS. Lancet Neurol. 2011;10:561–72.
58. Harris KG, Tran DD, Sickels WJ, Cornell SH, Yuh WT. Diagnosing intracranial vasculitis: the roles of MR and angiography. AJNR Am J Neuroradiol. 1994;15:317–30.
59. Duna GF, Calabrese LH. Limitations of invasive modalities in the diagnosis of primary angiitis of the central nervous system. J Rheumatol. 1995;22:662–7.
60. Chu CT, Gray L, Goldstein LB, Hulette CM. Diagnosis of intracranial vasculitis: a multi-disciplinary approach. J Neuropathol Exp Neurol. 1998;57:30–8.

61. Alrawi A, Trobe JD, Blaivas M, Musch DC. Brain biopsy in primary angiitis of the central nervous system. Neurology. 1999;53:852–5.
62. Calabrese LH, Dodick DW, Schwedt TJ, Singhal AB. Narrative review: reversible cerebral vasoconstriction syndromes. Ann Intern Med. 2007;146:34–44.
63. Mandell DM, Matouk CC, Farb RI, Krings T, Agid R, Willinsky RA, et al. Vessel Wall MRI to differentiate between reversible cerebral vasoconstriction syndrome and central nervous system vasculitis: preliminary results. Stroke. 2012;860–2. https://doi.org/10.1161/STROKEAHA.111.626184
64. Obusez EC, Hui F, Hajj-ali RA, Cerejo R, Calabrese LH, Hammad T, et al. High-resolution MRI vessel wall imaging: spatial and temporal patterns of reversible cerebral vasoconstriction syndrome and central nervous system vasculitis. AJNR Am J Neuroradiol. 2014;35:1527–32.
65. Zeiler SR, Qiao Y, Pardo CA, Lim M, Wasserman BA. Vessel wall MRI for targeting biopsies of intracranial vasculitis. AJNR Am J Neuroradiol. 2018;39:2034–6.
66. Pfefferkorn T, Linn J, Habs M, Opherk C, Cyran C, Ottomeyer C, et al. Black blood MRI in suspected large artery primary angiitis of the central nervous system. J Neuroimaging. 2013;23:379–83.
67.• Kesav P, Krishnavadana B, Kesavadas C, Sreedharan SE, Rajendran A, Sukumaran S, et al. Utility of intracranial high-resolution vessel wall magnetic resonance imaging in differentiating intracranial vasculopathic diseases causing ischemic stroke. Neuroradiology. 2019;61:389–96.

This study evaluated VWI for diagnosing vasculopathy in the setting of recent stroke with symptomatic stenosis. Adding VWI allowed reclassification of 47.3% of the subjects with stroke of undetermined etiology. Diffuse concentric vs. focal eccentric wall thickening and/or enhancement provided excellent discriminatory power between ICAD and inflammatory vasculopathy.

68. Miller DV, Salvarani C, Hunder GG, Brown RD, Parisi JE, Christianson TJ, et al. Biopsy findings in primary angiitis of the central nervous system. Am J Surg Pathol. 2009;33:35–43.
69. Saam T, Habs M, Pollatos O, Cyran C, Pfefferkorn T, Dichgans M, et al. High-resolution black-blood contrast-enhanced T 1 weighted images for the diagnosis and follow-up of intracranial arteritis. Br J Radiol. 2010;83:182–4.
70. Tsivgoulis G, Papadimitropoulos GN, Lachanis S, Palaiodimou L, Zompola C, Antonellou R, et al. High-resolution intracranial vessel wall imaging in monitoring treatment response in primary CNS angiitis. Neurologist. 2018;23:188–90.
71. Ducros A. Reversible cerebral vasoconstriction syndrome. Lancet Neurol. 2012;11:906–17.
72. Mossa-Basha M, Hwang WD, De Havenon A, Hippe D, Balu N, Becker KJ, et al. Multicontrast high-resolution vessel wall magnetic resonance imaging and its value in differentiating intracranial vasculopathic processes. Stroke. 2015;46:1567–73.
73. Singhal AB, Topcuoglu MA. Glucocorticoid-associated worsening in reversible cerebral vasoconstriction syndrome. Neurology. 2017;88:228–36.
74. Kim JS. Moyamoya disease: epidemiology, clinical features, and diagnosis. J Stroke. 2016;18:2–11.
75. Scott RM, Smith ER. Moyamoya disease and moyamoya syndrome. N Engl J Med. 2009;360:1226–37.
76. Iwama T, Morimoto M, Hashimoto N, Goto Y, Todaka T, Sawada M. Mechanism of intracranial rebleeding in moyamoya disease. Clin Neurol Neurosurg. 1997;99(S2):S187–90.
77. Ryoo S, Cha J, Kim SJ, Choi JW, Ki C-S, Kim KH, et al. High-resolution magnetic resonance wall imaging findings of moyamoya disease. Stroke. 2014;45:2457–60.
78. Kim YJ, Lee DH, Kwon JY, Kang DW, Suh DC, Kim JS, et al. High resolution MRI difference between moyamoya disease and intracranial atherosclerosis. Eur J Neurol. 2013;20:1311–8.
79. Yuan M, Liu Z, Wang Z, Li B, Xu L, Xiao X. High-resolution MR imaging of the arterial wall in moyamoya disease. Neurosci Lett. 2015;584:77–82.
80. Wang M, Yang Y, Zhou F, Li M, Liu R, Guan M, et al. The contrast enhancement of intracranial arterial wall on high-resolution MRI and its clinical relevance in patients with moyamoya vasculopathy. Sci Rep. 2017;7:44264.
81.•• Roder C, Hauser T-K, Ernemann U, Tatagiba M, Khan N, Bender B. Arterial wall contrast enhancement in progressive moyamoya disease. J Neurosurg. 2019;1–9. American Association of Neurological Surgeons. https://doi.org/10.3171/2019.2.JNS19106.

This study of moyamoya disease evaluated arterial wall enhancement as a predictor of clinical progression within 6 months. Lack of enhancement had a negative predictive value of 95%.

82. Muraoka S, Araki Y, Taoka T, Kawai H, Okamoto S, Uda K, et al. Prediction of intracranial arterial stenosis progression in patients with moyamoya vasculopathy: contrast-enhanced high-resolution magnetic resonance vessel wall imaging. World Neurosurg. 2018;116:e1114–21.
83. Mossa-Basha M, de Havenon A, Becker KJ, Hallam DK, Levitt MR, Cohen WA, et al. Added value of vessel wall magnetic resonance imaging in the differentiation of moyamoya vasculopathies in a non-Asian cohort. Stroke. 2016;47:1782–8.
84. Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. Lancet Neurol. 2011;10:626–36.
85. Nieuwkamp DJ, Setz LE, Algra A, Linn FHH, de Rooij NK, Rinkel GJE. Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to

age, sex, and region: a meta-analysis. Lancet Neurol. 2009;8:635–42.

86. Wiebers DO, Whisnant JP, Huston J 3rd, Meissner I, Brown RDJ, Piepgras DG, et al. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet. 2003;362:103–10.

87. Greving JP, Wermer MJH, Brown RDJ, Morita A, Juvela S, Yonekura M, et al. Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. Lancet Neurol. 2014;13:59–66.

88. Backes D, Rinkel GJE, Greving JP, Velthuis BK, Murayama Y, Takao H, et al. ELAPSS score for prediction of risk of growth of unruptured intracranial aneurysms. Neurology. 2017;88:1600–6.

89.• Edjlali M, Guedon A, Ben Hassen W, Boulouis G, Benzakoun J, Rodriguez-Regent C, et al. Circumferential thick enhancement at vessel wall MRI has high specificity for intracranial aneurysm instability. Radiology. 2018;289:181–7. https://doi.org/10.1148/radiol.2018172879.

This large study of ruptured and unruptured aneurysms used VWI to differentiate stable and unstable aneurysms. Unstable aneurysms with neurologic symptoms, or morphological changes over time, were associated with grade 3 wall enhancement, while lack of enhancement had an excellent negative predictive value of 94%.

90. Korja M, Kaprio J. Controversies in epidemiology of intracranial aneurysms and SAH. Nat Rev Neurol. 2015;12:50.

91. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet. 2002;360:1267–74.

92.• Shimonaga K, Matsushige T, Ishii D, Sakamoto S, Hosogai M, Kawasumi T, et al. Clinicopathological insights from vessel wall imaging of unruptured intracranial aneurysms. Stroke. 2018;49:2516–.

This study provides histopathologic correlation VWI findings for 9 unruptured aneurysms that underwent surgical clipping. Aneurysmal wall enhancement on VWI was associated with thickening of the vessel wall, development of vasa vasorum, and abundant macrophages.

93. Nagahata S, Nagahata M, Obara M, Kondo R, Minagawa N, Sato S, et al. Wall enhancement of the intracranial aneurysms revealed by magnetic resonance vessel wall imaging using three-dimensional turbo spin-echo sequence with motion-sensitized driven-equilibrium: a sign of ruptured aneurysm? Clin Neuroradiol. 2016;26:277–83.

94. Hu P, Yang Q, Wang D-D, Guan S-C, Zhang H-Q. Wall enhancement on high-resolution magnetic resonance imaging may predict an unsteady state of an intracranial saccular aneurysm. Neuroradiology. 2016;58:979–85.

95. Tian B, Toossi S, Eisenmenger L, Faraji F, Ballweber MK, Josephson SA, et al. Visualizing wall enhancement over time in unruptured intracranial aneurysms using 3D vessel wall imaging. J Magn Reson Imaging. 2019;50:193–200.

96. Zhu C, Wang X, Degnan AJ, Shi Z, Tian B, Liu Q, et al. Wall enhancement of intracranial unruptured aneurysm is associated with increased rupture risk and traditional risk factors. Eur Radiol. 2018;28:5019–26.

97. Lv N, Tang H, Chen S, Wang X, Fang Y, Karmonik C, et al. Morphological parameters related to aneurysm wall enhancement in patients with multiple intracranial aneurysms. World Neurosurg. 2018;114:e338–43.

98. Ishii D, Matsushige T, Sakamoto S, Shimonaga K, Akiyama Y, Okazaki T, et al. Decreased antiatherogenic protein levels are associated with aneurysm structure alterations in MR vessel wall imaging. J Stroke Cerebrovasc Dis. 2019;28:2221–7.

99. Hartman JB, Watase H, Sun J, Hippe DS, Kim L, Levitt M, et al. Intracranial aneurysms at higher clinical risk for rupture demonstrate increased wall enhancement and thinning on multicontrast 3D vessel wall MRI. Br J Radiol. 2019;92:e20180950.

100. Fu Q, Guan S, Liu C, Wang K, Cheng J. Clinical significance of circumferential aneurysmal wall enhancement in symptomatic patients with unruptured intracranial aneurysms: a high-resolution MRI study. Clin Neuroradiol. 2018;28:509–14.

101. Omodaka S, Endo H, Niizuma K, Fujimura M, Inoue T, Endo T, et al. Circumferential wall enhancement in evolving intracranial aneurysms on magnetic resonance vessel wall imaging. Neurosurgery. 2018;82:638–44.

102. Wang G x, Gong M f, Zhang D, Lei S, Yin J b, Gong Z l, et al. Wall enhancement ratio determined by vessel wall MRI associated with symptomatic intracranial aneurysms. Eur J Radiol. 2019;112:88–92.

103. Texakalidis P, Hilditch CA, Lehman V, Lanzino G, Pereira VM, Brinjikji W. Vessel wall imaging of intracranial aneurysms: systematic review and meta-analysis. World Neurosurg. 2018;117:453–458.e1.

104. Vergouwen MDI, Backes D, van der Schaaf IC, Hendrikse J, Kleinloog R, Algra A, et al. Gadolinium enhancement of the aneurysm wall in unruptured intracranial aneurysms is associated with an increased risk of aneurysm instability: a follow-up Study. Am J Neuroradiol. 2019;40:1112–6.

105.•• Matsushige T, Shimonaga K, Mizoue T, Hosogai M, Hashimoto Y, Kaneko M, et al. Focal aneurysm wall enhancement on MRI indicates intraluminal thrombus and the rupture point. World Neurosurg. 2019;127:e578–8.

This study followed 60 aneurysms over a mean of 49 months with VWI and found that aneurysmal wall enhancement was

associated with aneurysm growth, particularly with the development of daughter sac formation.

106. Matouk CC, Mandell DM, Gunel M, Bulsara KR, Malhotra A, Hebert R, et al. Vessel wall magnetic resonance imaging identifies the site of rupture in patients with multiple intracranial aneurysms: proof of principle. Neurosurgery. 2013;72:492–6.
107. Cornelissen BMW, Leemans EL, Slump CH, Marquering HA, Majoie CBLM, van den Berg R. Vessel wall enhancement of intracranial aneurysms: fact or artifact? Neurosurg Focus. 2019;47:E18.
108. Vergouwen MDI, Hendrikse J, van der Kolk AG, Wermer MJH, Versluis MJ, Biessels GJ, et al. 7Tesla vessel wall imaging of the basilar artery in perimesencephalic hemorrhage. Int J Stroke. 2015;10:E31.
109. Coutinho JM, Sacho RH, Schaafsma JD, Agid R, Krings T, Radovanovic I, et al. High-resolution vessel wall magnetic resonance imaging in angiogram-negative non-perimesencephalic subarachnoid hemorrhage. Clin Neuroradiol. 2017;27:175–83.

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