Current uses of intracranial vessel wall imaging for clinical practice: a high-resolution MR technique recently available

Usos atuais do estudo de parede vascular intracraniana na prática clínica: uma técnica de RM de alta resolução recentemente disponível

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ABSTRACT

Intracranial vessel wall imaging plays an increasing role in diagnosing intracranial vascular diseases. With the growing demand and subsequent increased use of this technique in clinical practice, radiologists and neurologists should be aware of the choices in imaging parameters and how they affect image quality, clinical indications, methods of assessment, and limitations in the interpretation of these images. Due to the improvement of the MRI techniques, the possibility of accurate and direct evaluation of the abnormalities in the arterial vascular wall (vessel wall imaging) has evolved, adding substantial data to diagnosis when compared to the indirect evaluation based on conventional flow analyses. Herein, the authors proposed a comprehensive approach of this technique reinforcing appropriated clinical settings to better use intracranial vessel wall imaging.

Keywords: Magnetic Resonance Imaging; Stroke; Intracranial Arteriosclerosis; Vasculitis.

INTRODUCTION

Noninvasive studies of intracranial arteries have been available since the first techniques of Doppler ultrasound, Computed Tomography Angiography (CTA), Magnetic Resonance Angiography (MRA) were developed. However, all these procedures are based on direct evaluation of the vascular lumen. In general, a possible abnormality in an artery is an inference to an abnormal flow within it. Therefore, just an indirect evaluation is obtained1.

Due to the improvement of the magnetic resonance imaging (MRI) techniques, the possibility of accurate and intrinsic

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evaluation of the abnormalities in the arterial vascular wall has evolved. This can narrow the differential diagnosis and improve diagnostic accuracy for various intracranial artery diseases, beyond that achievable from the indirect information obtained from luminal angiography. For the best use of this new diagnostic modality, aiming at the standardization of the procedure, a consensus on its acquisition technique and utilities was recently reported.1

In addition to the technical details for the implementation of this recent complementary tool, the consensus also established some scenarios where its use may be advantageous, adding value to the therapeutic planning and follow up of each case in the clinical routine. Herein, the authors proposed a comprehensive approach of this technique, reinforcing the appropriate clinical settings to better use this technique.

Magnetic resonance techniques to acquire arterial vascular wall imaging

It is important to comprehend the study of intracranial vascular wall, also known as vessel wall imaging (VWI), as an additional sequence to flow analyses of intracranial arterial studies, not to replace them. Currently, VWI is a complementary tool, since it allows the combined evaluation of flow and arterial walls.2

Some basic principles permeated its development, being perhaps the most important and the one which most extended its development, the high spatial resolution acquired particularly in 3 Tesla MR scanners. It is essential, since the thickness of the wall of the largest intracranial vessels present calibers ranging from 0.2 to 0.3 mm, approximately 1/10 the lumen diameter of the vessels.3 The blood signal saturation inside the vessels was also an indispensable requirement, as well as the cerebrospinal fluid (CSF) that surrounds them, so that an adequate characterization of the vascular wall can be acquired independently using high-resolution vessel wall imaging (HR-VWI).4

The need for sequences to assess the signal of the most varied tissues and substances in the intracranial arterial compartment became fundamental. Accordingly, T1-weighted volumetric (TIWI 3D) acquisitions before and after Gadolinium administration form the basis of a HR-VWI imaging study. It is worth noting that, in some cases, T2-weighted image (T2WI) sequences and proton density (PD), and also others are required for the complementary analysis according to the clinical scenario (Table 1).

Nevertheless, it is essential to be aware of some peculiar artifacts of this technique. For instance, slow flow in some areas inside the vessel might still produce a signal, which can lead to plaque mimicking artifacts in the context of VWI. Thus, new sequences and parameters have been developed to minimize these pseudo abnormalities, such as Motion-Sensitized Driven Equilibrium (MSDE) and Delay Alternating with Nutation for Tailored Excitation (DANTE).

These techniques are focus on the black-blood (BB) effect that has been used to suppress even more blood and CSF signal on the TIWI sequence.

Moreover, some limitations have been reported in the literature. Most of them are related to the interpretive experience and an adequate imaging acquisition, leading to normal variations being misinterpreted as a disease; another limitation was the long acquisition time that lead to a motion artifact that could not be repaired afterward.

Relevance of the HR-VWI in the differential diagnoses

The characterization of luminal narrowing of intracranial vessels in conventional sequences makes it possible to demonstrate arterial stenosis. However, the list of etiologies remains long, with distinct treatments and prognoses.

Classically, the stenotic pattern may help us to restrict the differentials, as observed in the "beading pattern" and in the "multifocal alternating vasoconstriction and dilation/normal caliber vessels", which increase the suspicion for vasculitis and posterior reversible cerebral vasoconstriction syndrome (RCVS), respectively. In turn, multiple focal stenosis, in an elderly patient with multiple ischemic sequelae, increases the possibility of intracranial atheromatous plaques. Despite that, all these inferences remain an indirect analysis with limited specificity for a singular clinical setting.

Conversely, HR-VWI allows the direct characterization of the mural arterial abnormalities, which generate those

### Table 1. Protocol suggested to acquire vessel wall imaging and supported sequences according to different clinical scenario.

<table>
<thead>
<tr>
<th>Suggested VWI imaging protocol</th>
<th>3D TOF MR angiography</th>
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<tr>
<td>Fluid-attenuated inversion recovery (FLAIR)</td>
<td>3D T1 VWI sequence pre- and post-contrast</td>
</tr>
<tr>
<td>Diffusion-weighted imaging (DWI)</td>
<td>CUBE (GE)</td>
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<tr>
<td>SPACE (Siemens)</td>
<td>VISTA (Philips)</td>
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Imaging techniques

- FOV (mm): 200 × 167 × 160
- Acquisition orientation: transverse
- Acquisition spatial resolution: 1 × 1 × 1
- Reconstructed spatial resolution (mm³): 0.96 × 0.96 × 1.0
- TR/TE/TI (msec): 8.5/3.9/1016
- Flip angle (degrees): 8
- Oversampling factor: 1.4
- Readout bandwidth (Hz): 189.8
- No. of signals acquired: 1
- Sensitivity encoding factor: 3 (RL)
- Acquisition time: 2 min 29 sec

Additional sequences (according to clinical scenario):
- Meningitis (FLAIR+Gd)
- Vasculitis (SWI+Gd, T1 pre+post Gd, perfusion sequences, +/- non-enhanced CT)
- Focal lesions (Perfusion sequences, spectroscopy)
- Arterial dissection (cervical MRA)
recognizable angiographic patterns. Consequently, adding data for an earlier and more accurate diagnosis, supporting effective approaches for treatment and a better-defined prognosis.

Moreover, HR-VWI has also been used to study the aneurysm wall and its susceptibility to rupture according to the enhancement pattern. However, the discussion of this specific finding is beyond the scope of this article and it will not be discussed herein. Other clinical scenarios such as investigating the activity of Moyamoya disease are also not discussed in this paper, since few patients have been included in recent studies.

Clinical scenarios in which HR-VWI add value to already available conventional methods

**Intracranial atheromatous disease**

Intracranial atherosclerotic disease is currently recognized as a common cause of ischemic stroke worldwide, particularly prevalent in Asian, African, and Hispanic populations. The pattern of ischemic involvement may occur in two main types: atherothrombotic, due to the continuous and gradual growth of the plaque, or atheroembolic, due to embolism of atheromatous plaque debris (artery-to-artery embolism). Until then, the possibility of diagnosing the disease was restricted to the demonstration of the luminal narrowing of intracranial arteries, attributable to intracranial plaques. Thus, the earlier phase of the positive remodeling of atheromatous plaques development on vessel walls was neglected. Furthermore, the characterization of focal luminal narrowing by probable atheromatous plaques in asymptomatic patients did not allow the definition of adequate primary prevention, due to the impossibility of establishing a real risk.

Intracranial atheromatous plaques develop through a process of deposition of fats in the intimal layer of the arteries, and their formation begins through endothelial injuries due to the risk factors to which an individual has been exposed. Plaque growth does not occur homogeneously on the vessel wall and eccentric growth is usually observed, resulting in a consequent focal luminal reduction of the vessel.

Currently, HR-VWI enables us to reveal the growth pattern and composition of the atheromatous plaque on the vessel walls. Therefore, an eccentric abnormality on the arterial wall has been assumed to be an atheromatous plaque with a good correlation with the degree of luminal stenosis demonstrated in addition to conventional flow imaging studies. In this setting, it is crucial that pre-contrast HR-VWI analyses detect a focal and eccentric wall abnormality as well as its content with intrinsic components and their variable MR signal intensity (intermediate to high) that allows to demonstrate, for instance, the stages of hemoglobin degradation. In this context, intraplaque focal hyperintensity on T1WI might reveal hemorrhagic content by recent intraplaque bleeding, which makes it more vulnerable.

The study of post-contrast HR-VWI demonstrates the degree of neovascularization and inflammatory activity present on the plaques and may also be a predictor of additional vulnerability (Figure 1).

Thus, based on the HR-VWI findings, one can not only identify an intracranial atheromatous plaque as the real cause of the arterial stenosis, but also estimate its vulnerability and, therefore, the requisites for a more aggressive approach (Figure 2).

**Noninfectious vasculitis**

Vasculitis results from an inflammation of the vessel wall, being divided into two large groups: infectious and noninfectious; the first one is due to a direct invasion of the pathogen to the vessel wall, leading to an inflammatory reaction process, whereas in the second group there is no identification of a specific pathogen.

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**Figure 1.** Male, 75 years old, suspected of recurrent transitory ischemic attacks. Axial MIP MRA (A) demonstrates bilateral stenosis on the middle cerebral arteries (M1 segments — white arrows), more prominent on the right side. (B) vessel wall imaging sequence pre- (superior image) and post-contrast (inferior image) showing bilateral atheromatous plaques with intraplaque haemorrhage on the left, depicted by spontaneous parietal T1 hyperintensity on pre-contrast sequence. On the right, the inset shows typical eccentric pattern of enhancement for atheromatous plaques, also demonstrating culprit intracranial atherosclerotic lesion.
The Revised International Chapel Hill Consensus Conference Nomenclature (2012) establishes a nomenclature of the types of vasculitis according to the size of the vessels affected; and their involvement may vary, ranging from arterioles and venules to large vessels of the supra-aortic trunk.

Primary angiitis of the central nervous system (PACNS) is due to an alteration in the vascular wall restricted to intracranial vessels, associated with rather variable clinical and laboratory scenarios. In addition, for its diagnosis, it is necessary to exclude a systemic disease which may also involve the central nervous system (CNS) secondarily, with systemic (secondary) vasculitis. Imaging studies are essential, since the characterization of vascular abnormalities, whether angiographic or histopathological, is included in the current diagnostic criteria.

MRI findings of a CNS vasculitis, whether primary or secondary, are quite variable, since they can result in different combinations of vascular, parenchymal and/or leptomeningeal involvement, often becoming nonspecific. Conventional angiographic studies, whether through MRA, CTA or digital subtraction angiography (DSA), may demonstrate areas of luminal narrowing with variable multifocal irregularities or dilation in the intracranial arteries. In addition to the low sensitivity of these studies, all these features are not specific for vasculitis. False-negative rates reached as much as 2/3 of the patients who had the final diagnosis established through histopathology.

However, CNS vasculitis can be spatially heterogeneous, and false-negative biopsies might also occur. Therefore, HR-VWI could also be used to identify a peripherally located inflamed vessel to target for biopsy.

Thus, HR-VWI allows the direct characterization of a parietal thickening, as well as an intense and homogeneous gadolinium enhancement, adding higher accuracy to the finding, increasing the sensitivity of the MR techniques, either for the definition of a presumptive diagnosis, or for a more precise choice of biopsy site, directing the procedure and optimizing its diagnostic results (Figure 3).

The characterization of a concentric and homogeneous parietal thickening of intracranial arteries on HR-VWI does not allow distinguishing between primary and secondary vasculitis. However, it has been assumed to be a distinctive feature for the differential diagnosis to be acquired, in most cases, with diseases which simulate vasculitis, such as RCVS, sarcoidosis, and lymphoproliferative diseases.
**Infectious vasculitis**

An important relevant differential to be considered, mainly in developing countries, corresponds to the vasculitis caused by infectious pathogens. Bacteria, fungi, and viruses could be all implied in infectious intracranial vessels.

Neurotuberculosis is an aggressive form of extrapulmonary disease that is more common in patients coinfected with HIV and/or in those with multi drug-resistant forms. Cerebral vessels may be affected primarily (more common) or related to an active meningial inflammation that could cause vasospasm, both leading to vessel stenosis and cerebral infarction. The hallmark pathologic feature of infectious intracranial tuberculous is the presence of cisternal meningitis with prominent exudate in the basilar meninges (leptomeningitis). HR-VWI could clearly demonstrate the proximal vessels parietal inflammation that commonly leads to stenosis and, consequently, parenchymal infarctions. Clinical correlation, CSF analysis, and MRI features are crucial to the recognition and differentiation of PACNS.

Emerging infections, including neurosyphilis, should be included in the differential diagnosis of infectious vasculitis, particularly in the group of meningovascular variants of this disease. It is a distinct form of neurosyphilis characterized by a combination of chronic syphilitic meningitis and arteritis, leading to a meningo-encephalopathic syndrome with superimposed cerebrovascular or myelovascular events. It results in an injury to the blood vessels of the leptomeninges, brain, and spinal cord, leading to infarctions, with histopathological findings similar to autoimmune arteritis, such as lupus erythematosus or polyarteritis nodosa.

Neurosyphilis has been called the great mimicker as it clinically manifests as an acute stroke syndrome or, more commonly, as a subacute illness. Two types of arteritis have been described: Heubner arteritis, the most common form, affecting medium and large arteries, and Nissl-Alzheimer arteritis, affecting small arteries. Both types might result in vessel occlusion and secondary ischemia (Figure 4). There are no specific radiological findings for meningovascular syphilis, even when HR-VWI is adopted. MRI techniques may show multiple areas of brain or spinal cord infarction, meningeal thickening and abnormal Gd-enhancement, including unspecific perivascular concentric abnormalities. Angiographic imaging methods often reveal varying degrees of segmental, concentric steno-occlusive arteriopathy.

Particular attention has been devoted to Varicella-zoster virus (VZV) vasculopathy, which is also known in the setting of viral vasculopathies as a particular granulomatous vasculitis by VZV, being related with the occurrence of transient ischemic attacks and stroke, with intracranial artery involvement demonstrated on neurovascular imaging in up to 70% of the cases. Angiography studies often reveal unspecific stenosis as a multifocal VZV vasculopathy in the distal internal carotid or middle cerebral arteries, associated or not with extracranial involvement of superficial temporal arteries mimicking giant cell arteritis.

Pathologic tissue analysis and CSF studies to detect the VZV might reveal signs of inflammation and viral antigens mostly in the arterial affected adventitia and media. While treatment reduces further stroke, the course of resolution of arterial inflammation and stenosis is unknown. HR-VWI findings include various patterns of stenosis, vessel wall concentric thickening, usually with Gd-enhancement, predominantly in terminal internal carotid artery segments and in the M1 segment of the middle cerebral...
arteries (Figure 5). Follow-up imaging using HR-VWI may show reducing stenosis, associated with reduced vessel wall concentric thickening and/or Gd-enhancement at multiple times after treatment, being a potential tool to assist in the diagnosis and treatment follow-up of VZV vasculopathy27.

**Reversible Cerebral Vasoconstriction Syndrome**

This heterogeneous clinical and radiological condition has a recognizable presentation characterized by severe onset thunderclap headache and multifocal vasoconstriction of the cerebral arteries that must be reversible within 3 months8,28. RCVS may be triggered spontaneously or present a provocative exogenous trigger, such as vasoactive drugs (amphetamines, alcohol, nicotine, cocaine, marijuana), postpartum status, blood transfusions, neoplasms (pheochromocytoma, paraganglioma), trauma, as well as less common causes, such as arterial dissection, antiphospholipid antibody syndromes and thrombotic thrombocytopenic purpura27,28.

The pathophysiology of RCVS remains unknown, but changes in the vascular tone have been pointed out as a fundamental mechanism. Typically, RCVS has a benign course, but permanent sequelae and dysfunctions, such as complications of ischemic events and intracranial hemorrhages, has also been reported28. Additional clinical conditions have been associated to RCVS, including epileptic seizures, encephalopathy, focal neurologic deficit, altered mental status, transient ischemic attacks, ischemic insults, intracranial hemorrhage, cerebral edema, and posterior reversible encephalopathy syndrome (PRES).

The classical role of MRI in patients with RCVS includes the demonstration of vasoconstriction in angiographic studies; differentiation with alternative diagnoses, such as vasculitis and subarachnoid hemorrhage secondary to aneurysm rupture; and surveillance of potential complications such as hemorrhage, vasogenic edema, and ischemia. Angiographic studies, whether through MRA, CTA or DSA, classically demonstrate a pattern of multifocal alternating vasoconstriction and dilation/normal caliber vessels. Currently, HR-VWI has elucidated that the areas of arterial stenosis, already demonstrated angiographically, result from focal circumferential thickening, which is generally not associated with post-contrast Gd-enhancement29. Nevertheless, the occurrence of concentric thickening with subtle homogeneous Gd-enhancement has been reported, not invalidating the diagnosis of RCVS. In addition to the prompt recognition of RCVS, HR-VWI is confident to distinguish this self-limited condition from the more intense and thicker pattern of Gd-enhancement that predicts the diagnosis of intracranial vasculitis30.

Despite the differentiation between RCVS and intracranial vasculitis having been recently reported, their distinctive treatment and prognosis reinforce the need to use new MR techniques, particularly HR-VWI, to prospectively recognize these disorders. The current recommended treatment for RCVS is the immediate suspension of the exogenous triggering factor and the introduction of symptomatic medication (including analgesics), blood pressure control, and proper treatment in case of epileptic seizures31.
Intracranial dissection

Arterial dissection occurs due to a hematoma in the wall of a cervical or an intracranial artery. Intracranial dissection is usually observed as an extension of cervical dissection, but it can also occur as an isolated intracranial abnormality.

This condition is a remarkable cause of ischemic stroke in young patients, being ischemic stroke and subarachnoid hemorrhage the most frequent clinical presentations. Approximately 70% of intracranial artery dissection occurs in the vertebral artery. Typical imaging findings are intramural hematoma, double lumen, and intimal flap.

Current literature recommends the use of HR-VWI in suspected cases, particularly for its accurate delineation of the lumen and wall of intracranial arteries, depicting curvilinear hyperintensity on T2-weighted images (intimal flap), separating the true lumen from the false one. Also, eccentric arterial wall thickening with characteristic signals of blood (intramural hematoma) is depicted, whose signal characteristics evolve with time (Figure 6).

FINAL CONSIDERATIONS

This new HR-VWI MR technique has been created to be used in the identification of symptomatic non-stenotic intracranial arterial diseases, as well as in the recognition of differential diagnoses of vascular luminal abnormalities.
Additionally, HR-VWI has increased MRI accuracy to demonstrate inflammatory activity in vasculitis, and also the vascular involvement by intracranial pathogens.

Despite the growing clinical use of HR-VWI, with additional advantages to previous scenarios, any new complementary diagnostic tool should follow a strictly established imaging protocol, with well-defined technical parameters according to the specialized medical literature, always respecting clinical indications, and also the premises of a learning curve of inexperienced observers.

References


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