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# Vessel Wall MRI for Targeting Biopsies of Intracranial Vasculitis

S.R. Zeiler, Y. Qiao, C.A. Pardo, M. Lim, and B.A. Wasserman



## ABSTRACT

**SUMMARY:** Central nervous system vasculitides are elusive diseases that are challenging to diagnose because brain biopsies have high false-negative rates. We sought to test the ability of contrast-enhanced, high-resolution 3D vessel wall MR imaging to identify vascular inflammation and direct open biopsies of intracranial target vessels and adjacent brain parenchyma. Eight of 9 specimens revealed vascular inflammation. We conclude that vessel wall MR imaging can identify inflamed intracranial vessels, enabling precise localization of biopsy targets.

**ABBREVIATIONS:** CNSV = CNS vasculitis; VWMRI = vessel wall MR imaging

We operationally define central nervous system vasculitis (CNSV) as any inflammatory vasculopathy producing non-atheromatous inflammation of intracranial vessels either directly (eg, primary CNS vasculitis) or indirectly via inflammation of CNS parenchyma with secondary vascular involvement (eg, as seen with infections, tumors, and certain autoimmune conditions). A variety of pathogenic processes leading to CNSV may have similar or overlapping clinical presentations and can mimic noninflammatory vasculopathies on conventional MR imaging or CT (eg, atherosclerosis, dissection, and reversible cerebrovascular vasoconstriction syndrome).<sup>1,2</sup> Thus, a biopsy should be performed for a definitive diagnosis and to identify the cause of the underlying inflammation,<sup>1,3,4</sup> especially because immunosuppressive therapy has adverse effects.<sup>5</sup>

Unfortunately, despite MR imaging and digital subtraction angiography (DSA) having high sensitivities for CNSV (60%–100%), specificity estimates range from 14% to 60%<sup>6,7</sup> and 19% to 36%<sup>7–9</sup> for DSA and MR imaging, respectively. For MR imaging, this sensitivity is likely secondary to flow artifacts and partial volume averaging constraints.<sup>10</sup> Furthermore, intracranial blood

vessel biopsy has a high false-negative rate (<50%)<sup>9,11</sup> because of patchy involvement of relevant pathology.<sup>3,12,13</sup>

We hypothesized that vessel wall MR imaging (VWMRI)<sup>14</sup> can identify inflamed intracranial vessels and precisely localize biopsy targets, thus aiding in the diagnosis of CNSV and its attendant pathology.

## MATERIALS AND METHODS

### Patients

We present 9 patients (On-line Tables 1 and 2) consecutively admitted to the Johns Hopkins stroke service between 2012 and 2016 for ischemic stroke with clinical concern for CNSV and no reasonable explanation for a noninflammatory cause.<sup>4</sup> Work-up for hypercoagulable state, rheumatologic disease, malignancy, cardiac dysfunction, and infection was unremarkable for all patients except patient 6, which revealed Varicella zoster virus immunoglobulin G in the CSF. All 9 patients referred with intent to biopsy underwent VWMRI and subsequent biopsy and were therefore included in this prospective study and consecutively entered into our data base. The institutional review board approved this study and provided an exemption to allow the inclusion of de-identified data for patients from whom we did not receive written consent because the VWMRI was performed as part of clinical care.

### MR Imaging Examination Protocol

VWMRI examinations were performed up to 7 days before biopsy (mean, 2.2 days) on a 3T MR imaging scanner (Magnetom Skyra; Siemens, Erlangen, Germany) using a 32-channel head coil. Fiducial markers were placed, and a standardized MR imaging protocol was implemented for all patients that included a 3D time-of-

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flight MRA (acquired resolution,  $0.5 \times 0.5 \times 0.55 \text{ mm}^3$ ), pre- and postcontrast 3D VWMRI (acquired resolution,  $0.5 \times 0.5 \times 0.5 \text{ mm}^3$ ), and a 3D contrast-enhanced MRA (acquired resolution,  $0.52 \times 0.52 \times 1.04 \text{ mm}^3$ ) of the intracranial vessels (On-line Fig 1). Diffusion-weighted images of the brain were obtained for all patients, and susceptibility-weighted images (acquired resolution,  $0.70 \times 0.70 \times 1.50 \text{ mm}^3$ ) were obtained for 5 of the 9 examinations. Postcontrast T1 echo-spoiled gradient-echo images were obtained for surgical navigation.

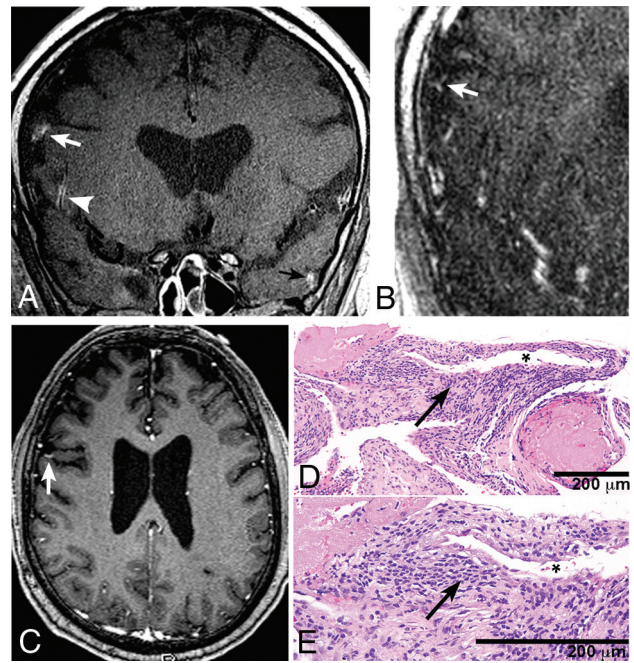
The 3D-VWMRI sequence design was previously described, and T1-weighting was implemented to highlight contrast enhancement (TR/TE, 800/25 ms; turbo factor, 30; echo spacing, 5.6 ms; generalized autocalibrating partially parallel acquisition acceleration, 2; FOV,  $160 \times 160 \text{ mm}^2$ ; number of averages, 1.4).<sup>14,15</sup> VWMRI was acquired in a coronal plane (112 slices [56 mm]; 9.5-minute acquisition time) and, after contrast administration, was oriented in multiple planes (axial [80 slices, 40 mm; 7.5-minute acquisition time], coronal, and in some cases, sagittal) to enable greater coverage of intracranial vessels, including distal branches. Contrast-enhanced MRA images were acquired during the intravenous administration of gadobutrol (Gadavist; Bayer Schering Pharma, Berlin, Germany; 0.1 mmol/kg) with arterial and venous phase acquisitions, and postcontrast VWMRI acquisitions began 5 minutes after contrast administration.

### MR Imaging Analysis

All MR imaging examinations were analyzed by a neuroradiologist (B.A.W.) using a PACS. 3D-VWMRI was reconstructed in multiple obliquities and was used to visually identify vascular inflammation (present/absent) based on segmental, concentric enhancement of the vessel wall and/or circumferential, periaventricular enhancement following a vessel segment. Evidence of atherosclerotic features including calcification, a fibrous cap and lipid core, or focal, noncircumferential wall thickening excluded the diagnosis of vasculitis. The 3D-TOF MRA and contrast-enhanced MRA acquisitions were reconstructed and coregistered with the VWMRI sequence to isolate the vessel of interest in long and short axes. Because the lumen of very small vessels could not always be identified on VWMRI, small-vessel involvement was suspected on the basis of the linear configuration of inflammatory enhancement (Figure) and was corroborated by the identification of a lumen on the reconstructed contrast-enhanced MRA and TOF MRA source images or the susceptibility-weighted images when available. Diffusion-weighted imaging (on present and prior examinations) was used to exclude foci of enhancement due to subacute infarction. The inflamed vessel segments were then reviewed with the neurology and neurosurgical services to reach a consensus on a vessel target that avoided eloquent areas, was superficial, and was preferably venous.

### Biopsy Procedure

Open biopsy was performed with the patient under general anesthesia using fiducial markers. The target vessel and adjacent brain parenchyma were biopsied with the aid of an image-guidance system (Brainlab Cranial Navigation Systems; Brainlab, Feldkirchen, Germany). M.L. was able to identify and biopsy a vessel at the identified coordinates.



**FIGURE.** High-resolution vessel wall MR imaging protocol for identifying a surgical target in a 33-year-old man with suspected intracranial vasculitis. A coronal reconstruction of a 3D-VWMRI sequence (acquired resolution, 0.5 mm isotropic, A) shows evidence of vasculitis, including circumferential enhancement and thickening of the wall of a small branch of the right MCA (white arrowhead) and of small cortical veins (arrow). The right frontal cortical vein (white arrow), confirmed to be a vein on the venous phase of the contrast-enhanced MRA (B), was selected as the target. Note that the vessel is identified on the 3D echo-spoiled gradient-echo sequence (C, arrow) acquired for surgical navigation but does not appear abnormal (D and E). Hematoxylin-eosin-stained biopsy section shows significant transmural inflammation (arrows) of the blood vessel wall. The lumen is indicated by asterisks.

## RESULTS

### Biopsy Results

The targeted blood vessel and surrounding brain tissue were obtained from each patient (On-line Table 2). Blood vessel biopsy analysis from 8 of the 9 patients revealed vascular inflammation via direct tissue examination (Figure and On-line Fig 2). The etiology of CNSV for patients 1, 2, 3, and 9 was primary CNS angitis; for patient 4, it was amyloid- $\beta$ -related angitis; and for patient 6, it was Varicella zoster virus vasculitis. Although we confirmed perivascular inflammation for patients 7 and 8, we were unable to find a cause. Brain biopsy specimens showed no evidence of parenchymal inflammation in all except patient 7. The vessel specimen from patient 5 did not reveal inflammation but instead a multitude of thickened blood vessels with amyloid deposition. There were no postoperative complications.

Standard MR imaging T1 postcontrast studies (Figure and On-line Fig 2) as well as MRA, CTA, and DSA studies (On-line Table 1) did not prospectively identify the target pathology that was identified by VWMRI and eventually biopsied.<sup>16</sup>

## DISCUSSION

We present the first reported study to use 3D-VWMRI at 3T for identifying CNSV. Notably, we show that VWMRI can be used to direct biopsies of inflamed intracranial vessels with high accuracy

(89% in our series), which is a substantial improvement over the standard approach (sensitivities as low as 36% in prior studies).<sup>3,7,9,17</sup> The success of our study was largely attributable to our ability to implement a 3D high-resolution VWMRI sequence that enables evaluation of a large volume of intracranial vessels, maximizing the number of potential targets that could then be reviewed for accessibility and safety.

There are several limitations of this study: 1) Although the VWMRI sequence was acquired using a TR of 800 ms to produce T1-weighting, some inherent proton-density weighting could not be eliminated, and this issue accounted for areas of mild hyperintense signal from remote white matter ischemic injury. We acquired precontrast VWMRI to help distinguish this hyperintensity from true enhancement surrounding small parenchymal vessels. Consequently, we confirmed vascular enhancement only when postcontrast signal was unequivocally high, so vessels with milder postcontrast signal were excluded from consideration. 2) The 3D-VWMRI sequence can result in inadequate flow suppression, depending on the size and orientation of the vessel.<sup>18</sup> We acquired the 3D-VWMRI sequence in multiple planes, so most vessels were captured in the long axis relative to the scan orientation. Furthermore, we used contrast-enhanced MRA images to confirm patency of the lumen. 3) Shifting of vascular structures from the craniotomy and opening of the dura could lead to false-negative specimen analyses. Nevertheless, in our cohort, every patient except patient 5 was confirmed to have CNSV on biopsy. VWMRI was unable to distinguish inflammation located in the transmural or perivascular space.

## CONCLUSIONS

Our data indicate that VWMRI can be used to target and improve the yield of biopsy in patients with CNSV. We suggest that biopsy remains instrumental in tailoring therapy because VWMRI was unable to distinguish among primary, infectious, and/or any etiology leading to perivascular inflammation.

Disclosures: Ye Qiao—UNRELATED: Patents (Planned, Pending or Issued): 3D high-resolution intracranial vessel wall imaging technique, US Patent Application 13/922,111. Michael Lim—UNRELATED: Consultancy: Bristol-Myers Squibb, Merck, TocaGen, Stryker; Grants/Grants Pending: Bristol-Myers Squibb, Accuray, Agenus\*; Patents (Planned, Pending or Issued): for radiation and immunotherapy. Bruce A. Wasserman—OTHER RELATIONSHIPS: Patent No. 13/922,111 for the 3D high-resolution vessel wall MRI technique used in this study. No financial gain (ie, no royalties or licenses). \*Money paid to the institution.

## REFERENCES

- Birnbaum J, Hellmann DB. **Primary angiitis of the central nervous system.** *Arch Neurol* 2009;66:704–09 Medline
- Jennette JC, Falk RJ, Bacon PA, et al. **2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides.** *Arthritis Rheum* 2013;65:1–11 CrossRef Medline
- Salvarani C, Brown RD Jr, Calamia KT, et al. **Primary central nervous system vasculitis: analysis of 101 patients.** *Ann Neurol* 2007;62:442–51 CrossRef Medline
- Marsh EB, Zeiler SR, Levy M, et al. **Diagnosing CNS vasculitis: the case against empiric treatment.** *Neurologist* 2012;18:233–38 CrossRef Medline
- Néel A, Pagnoux C. **Primary angiitis of the central nervous system.** *Clin Exp Rheumatol* 2009;27:S95–107 Medline
- Kadkhodayan Y, Alreshaid A, Moran CJ, et al. **Primary angiitis of the central nervous system at conventional angiography.** *Radiology* 2004;233:878–82 CrossRef Medline
- Chu CT, Gray L, Goldstein LB, et al. **Diagnosis of intracranial vasculitis: a multi-disciplinary approach.** *J Neuropathol Exp Neurol* 1998;57:30–38 CrossRef Medline
- Calabrese LH, Duna GF. **Evaluation and treatment of central nervous system vasculitis.** *Curr Opin Rheumatol* 1995;7:37–44 Medline
- Duna GF, Calabrese LH. **Limitations of invasive modalities in the diagnosis of primary angiitis of the central nervous system.** *J Rheumatol* 1995;22:662–67 Medline
- Antiga L, Wasserman BA, Steinman DA. **On the overestimation of early wall thickening at the carotid bulb by black blood MRI, with implications for coronary and vulnerable plaque imaging.** *Magn Reson Med* 2008;60:1020–28 CrossRef Medline
- Cupps TR, Moore PM, Fauci AS. **Isolated angiitis of the central nervous system: prospective diagnostic and therapeutic experience.** *Am J Med* 1983;74:97–105 Medline
- Alreshaid AA, Powers WJ. **Prognosis of patients with suspected primary CNS angiitis and negative brain biopsy.** *Neurology* 2003;61:831–33 CrossRef Medline
- Miller DV, Salvarani C, Hunder GG, et al. **Biopsy findings in primary angiitis of the central nervous system.** *Am J Surg Pathol* 2009;33:35–43 CrossRef Medline
- Qiao Y, Steinman DA, Qin Q, et al. **Intracranial arterial wall imaging using three-dimensional high isotropic resolution black blood MRI at 3.0 Tesla.** *J Magn Reson Imaging* 2011;34:22–30 CrossRef Medline
- Qiao Y, Guallar E, Suri FK, et al. **MR imaging measures of intracranial atherosclerosis in a population-based study.** *Radiology* 2016;280:860–68 CrossRef Medline
- Salvarani C, Brown RD Jr, Calamia KT, et al. **Angiography-negative primary central nervous system vasculitis: a syndrome involving small cerebral vessels.** *Medicine (Baltimore)* 2008;87:264–71 CrossRef Medline
- Berlit P, Kraemer M. **Cerebral vasculitis in adults: what are the steps in order to establish the diagnosis? Red flags and pitfalls.** *Clin Exp Immunol* 2014;175:419–24 CrossRef Medline
- Jara H, Yu BC, Caruthers SD, et al. **Voxel sensitivity function description of flow-induced signal loss in MR imaging: implications for black-blood MR angiography with turbo spin-echo sequences.** *Magn Reson Med* 1999;41:575–90 CrossRef Medline