Susceptibility-Weighted Angiography for the Follow-Up of Brain Arteriovenous Malformations Treated with Stereotactic Radiosurgery

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ABSTRACT

SUMMARY: The criterion standard for assessing brain AVM obliteration post-radiosurgery is DSA. To explore the value of susceptibility-weighted angiography, we followed 26 patients with brain AVMs treated by radiosurgery using susceptibility-weighted angiography and DSA. Studies were evaluated by 2 independent readers for residual nidi. Susceptibility-weighted angiography demonstrated good inter-modality (κ = 0.71) and interobserver (κ = 0.64) agreement, and good sensitivity (85.7%) and specificity (85.7%). Susceptibility-weighted angiography is a useful radiation- and contrast material–free technique to follow-up brain AVM obliteration post-radiosurgery.

ABBREVIATIONS: bAVM = brain AVM; SRS = stereotactic radiosurgery; SWAN = susceptibility-weighted angiography

Brain AVMs (bAVMs) may be treated by either surgical resection, embolization, or radiosurgery. Following treatment, confirmation of complete obliteration is imperative because the risk of bleeding in incompletely obliterated lesions persists.1-3 After AVM radiosurgery, occlusion is usually achieved after 2–4 years, with regular imaging follow-up performed every 6–12 months until complete bAVM obliteration is documented.1,2

The criterion standard for evaluating post-stereotactic radiosurgery (SRS) bAVM obliteration is DSA because of its high spatial and temporal resolution.3,5 However, DSA is a high-cost, invasive procedure involving radiation and contrast media exposure, with a 1% morbidity.5,9 Noninvasive alternatives such as 3D-TOF-MRA, 3D contrast-enhanced MRA,10-12 and, lately, 4D time-resolved MRA11,13,14 have shown inferior diagnostic accuracy compared to DSA. Moreover, most entail intravenous administration of contrast material with additional cost and potential toxicity.15,16

Susceptibility-weighted angiography (SWAN) is a promising new technology that indirectly evaluates the amount of oxygen within blood vessels. As bAVMs shunt oxygenated blood from arteries to veins, bAVM draining veins appear hyperintense,17 while normal veins containing deoxygenated blood appear hypointense.18,19 SWAN demonstrates high spatial resolution that allows small normal draining veins with a diameter inferior to the size of the voxel to be visualized and is highly sensitive to small, low-flow shunts.19 Moreover, SWAN does not require administration of intravenous contrast material. We aimed to evaluate the performance of SWAN for the follow-up of patients with bAVMs treated with SRS.

MATERIALS AND METHODS

Inclusion Criteria

After institutional review board approval, all patients with bAVMs treated with SRS at the University Hospital of Nancy, France were prospectively included in a database. For the present study, patients imaged between March 2012 and May 2018 were included if they met the following criteria: 1) They had a bAVM treated by embolization and radiosurgery or radiosurgery only, 2) they were imaged during follow-up with SWAN at 1.5T or 3T and DSA, 3) both examinations were performed within a time interval of ≤6 months and without another treatment session in between, and 4) both examinations were performed at least 12 months after SRS.

The treatment strategy for each patient was based on multidisciplinary decisions involving neurosurgeons, radiotherapists, and neuroradiologists. For each patient, demographics, bleeding history, comorbidities, location of the nidus, Spetzler-Martin grade, previous treatment history, clinical symptoms, and radiosurgical parameters were recorded in a prospective database. The time intervals between SRS and SWAN imaging, SWAN imaging and DSA control were also recorded.

Imaging

After SRS treatment, each patient underwent clinical evaluation and MR imaging at 6-month intervals on either 1.5T or 3T scan-
ners (Signa 1.5T and 3T; GE Healthcare, Milwaukee, Wisconsin). The MR imaging SWAN protocol was fairly consistent: At 1.5T, the SWAN scanning parameters were the following: flip angle, 12°; TE, 80 ms; TR, 78.3 ms; slice thickness, 2.4 mm; FOV, 24 cm. At 3T, the SWAN scanning parameters were the following: flip angle, 15°; TE, 25 ms; number of echoes, 6; TR, minimum; slice thickness, 0.8 mm reconstructed in 2-mm MIP; FOV, 24 cm. DSA was performed on a biplane angiography unit (Innova; GE Healthcare) with selective contrast injections of intracranial vessels in standard projections.

**Image Analysis**

Two independent senior readers (S.B. and R.A.), with >20 years of experience in diagnostic and interventional neuroradiology each, reviewed the axial SWAN examinations randomly and confirmed the presence or absence of a remaining arteriovenous shunt, that is, the presence of hypersignal within the nidus or a draining vein. Readers were blinded to baseline and follow-up clinical data, DSA imaging, bAVM location, and treatments received. In case of disagreement, consensus was reached by a third senior neuroradiologist (S.F.). Results were recorded separately and used to determine interobserver and intermodality agreement.

DSA studies were reviewed in consensus by 2 other senior readers. Total obliteration of the bAVM was defined as the complete absence of the nidus, normalization of the afferent and efferent vessels, and a normal circulation time. Any remaining nidus, regardless of its size, was considered “patent,” including the existence of early-filling draining veins.

**Statistical Analysis**

Quantitative variables were described as median and interquartile ranges, whereas qualitative variables were described as numbers and percentages. Intermodality and interobserver agreement was calculated using the χ² statistic. All analyses were completed using commercial statistical software (SPSS, Version 23.0; IBM, Armonk, New York).

**RESULTS**

Twenty-six patients fulfilled the inclusion criteria (Fig 1). Patient demographics are shown in Table 1. Two patients underwent 2 sets of imaging at different time points that were included in the analysis. Before SRS, 23 patients were embolized with a mixture of n-BCA and glue; and 1, with Onyx (Covidien, Irvine, California).

**Interobserver Agreement**

For SWAN examinations, the 2 observers agreed on the existence of a residual nidus in 23 of 28 cases (82.1%), resulting in good interobserver agreement (χ² = 0.64; 95% CI, 0.36–0.92) (Figs 2 and 3). Table 2 shows the interpretations according to the 2 readers and the consensus reading. Two disagreements corresponded to nidus remnants of millimetric size. Three more disagreements corresponded to occluded nidi that contained faint hyperintense spots.

**Intermodality Agreement**

The consensus reading for SWAN showed agreement regarding residual nidi in 24/28 (85.7%) cases, resulting in good intermodality agreement (χ² = 0.71; 95% CI, 0.455–0.974). Two unseen nidi (false-negative cases) were very small (Fig 4). One false-positive case was due to a large intranidal calcification that was obvious on plain CT (Fig 5). Another false-positive case was a corpus

### Table 1: Characteristics of the 26 patients

| Characteristics               | Number (Percent) |
|-------------------------------|------------------|
| Age (yr)                      | 33 (22–42)       |
| Sex, male                     | 17 (65.4%)       |
| BAVM location                 |                  |
| Supratentorial                | 24 (92.3%)       |
| Infratentorial                | 2 (7.7%)         |
| Spetzler-Martin grade         | 1 (1–II)         |
| Presentation                  |                  |
| Hemorrhage                    | 20 (76.9%)       |
| Seizure                       | 4 (15.4%)        |
| Headache                      | 5 (19.2%)        |
| Neurologic symptoms           | 1 (3.8%)         |
| Type of treatment             |                  |
| Embolization then radiosurgery| 22 (84.6%)       |
| Radiosurgery                  | 2 (7.7%)         |
| Surgery then embolization then radiosurgery | 2 (7.7%) |
| Time intervals                |                  |
| Delay between last treatment and SWAN (mo) | 34 (27.7–46.8) |
| Delay between SWAN and DSA (days) | 3 (3–65)        |

*Continuous variables are presented as proportion and percentage; categoric variables are described as median and first and third quartiles.

*Calculated for 28 datasets because 2 patients had 2 separate SWAN/DSA follow-ups.
callosal AVM with multiple adjacent arteries that gave the impression of hyperintense draining veins (Fig 6). Univariate statistics failed to show any association between false diagnostic results and Spetzler-Martin grade ($P = 0.64$; 95% CI, 0.37–0.92), AVM location ($P = 0.64$; 95% CI, 0.37–0.92), previous hemorrhage ($P = 1$), and previous embolization ($P = 0.27$).

**Diagnostic Value of SWAN**

The diagnostic accuracy of SWAN for a residual nidus reached a sensitivity of 85.7%, a specificity of 85.7%, a positive predictive value of 85.7%, and a negative predictive value of 85.7%.

**DISCUSSION**

The role of SWAN in the post-SRS follow-up of bAVMs has not been studied, to our knowledge. Our results show that SWAN has good intermodality ($\kappa = 0.71$; 95% CI, 0.45–0.97) and interobserver ($\kappa = 0.64$; 95% CI, 0.37–0.92) agreement compared with DSA, with a sensitivity of 85.7%, specificity of 85.7%, positive predictive value of 85.7%, and negative predictive value of 85.7%.

Although SWAN has good diagnostic accuracy, given its actual limitations, a negative SWAN finding cannot assert with certainty whether a bAVM is completely obliterated. However, it may guide imaging follow-up of patients with bAVMs treated with SRS without the need for intravenous injection of gadolinium and may potentially help avoid some unnecessary DSA examinations. After bAVM SRS, SWAN may be performed annually until the findings become negative (ie, until there is no residual shunt visible) and the final result can be confirmed by DSA.

Using SWAN, we found spots of increased signal intensity for residual arteriovenous shunts and patent draining veins in 12 of 14 (85.7%) residual nidi diagnosed by DSA (Fig 2). This hyperintense pattern has been noted in previous SWAN studies of non-treated bAVMs. At high blood velocities, the hypesignal within the nidus and the venous drainage are partially related to an inherent TOF effect of SWAN at 1.5T and 3T.\(^\text{19,20}\) At lower blood velocities, higher blood-oxygen levels and a lack of paramagnetic phase shift linked to direct arterial-to-venous shunt inside the nidus appears to be mainly responsible for the hyperintensity.\(^\text{19}\)

False-negative diagnoses of a residual nidus on SWAN occurred in 2 cases of residual nidi of millimetric size (Fig 4). False-positive diagnoses of a nidus remnant occurred in 2 patients. In one, a hyperintense signal in a fully occluded nidus was produced by susceptibility artifacts from a large calcified area visible on plain CT (Fig 5). In the other patient, multiple hyperintense normal vessels near the occluded bAVM that proved to be normal arteries gave the false impression of hyperintense small draining veins (Fig 6). This pitfall may be avoided by the use of multplanar reformations to distinguish draining veins and arteries.\(^\text{19}\)

In the present study, 20 of 26 (76.9%) bAVMs had previously bled and contained hemosiderin. However, this was not found to be detrimental to the diagnosis of a residual bAVM nidus ($P = 1$). \textit{n-}BCA glue was used as an embolic agent in 23 of 26 bAVMs before SRS. When injected, \textit{n-}BCA glue is mixed with Lipiodol (Guerbet, Roissy, France), an oil-based contrast agent that could exhibit high signal on T1- and T2-weighted images. However, in the present series, previous embolization was not related to the false diagnosis of a nidus remnant ($P = 0.27$). One patient had been embolized with Onyx, but the remaining bAVM nidus was correctly diagnosed as patent. Previous embolizations could obscure the margin of the nidus or result in a fragmented nidus and thereby mislead to a false negative diagnosis. Although, in the present series, glue did not interfere with the diagnostic accuracy.
of SWAN, the potential for diagnostic pitfalls related to the use of ethylene copolymer–based embolic agents should be investigated in larger series.

Lee et al\textsuperscript{21} assessed the diagnostic accuracy of 3D-TOF and T1 postcontrast MR imaging for the diagnosis of residual post-SRS treated bAVMs and found sensitivities ranging from 76.7\% to 84.9\% and specificities from 88.9\% to 95\%. Other authors have studied the accuracy of time-resolved MRA and have found sen-

Table 2: Detection of nidus remnant on SWAN compared with DSA\textsuperscript{a}

| DSA          | SWAN Reader 1 |         | SWAN Reader 2 |         | Consensus Reading |         |
|--------------|---------------|---------|---------------|---------|-------------------|---------|
|              | Patent        | Obliterated | Patent        | Obliterated | Patent | Obliterated |
| Patent (n = 14) | 11           | 3        | 11            | 2        | 12                | 2       |
| Obliterated (n = 14) | 5           | 9        | 3             | 12       | 2                 | 12      |
| Sensitivity (%) | 68.7         | 78.6     | 85.7          | 85.7     | 85.7              |         |
| Specificity (%) | 75           | 85.7     | 85.7          | 85.7     |                   |         |
| PPV (%)       | 78.6         | 84.6     | 85.7          | 85.7     |                   |         |
| NPV (%)       | 64.3         | 80       | 85.7          | 85.7     |                   |         |

Note:—PPV indicates positive predictive value; NPV, negative predictive value.

\textsuperscript{a} Prevalence of nidus remnant after SRS for bAVM.

FIG 4. A 32-year-old man with a right parietal AVM with hemorrhagic presentation, partially embolized with glue. SWAN imaging 3.5 years after SRS (white arrow, A) fails to show a very small residual nidus that was depicted by DSA (black arrow, B).

FIG 5. A 60-year-old man with a left parietal AVM with hemorrhagic presentation that was partially embolized with glue. SWAN imaging 4 years after SRS shows an amorphous area of hyperintensity within the nidus (white arrow) that was diagnosed as a nidus remnant, but the DSA findings were negative. B, CT shows extensive calcification (white arrow) inside the AVM scar.
The clear advantage of SWAN

Nevertheless, a head-to-head comparison with these techniques is warranted.

The diagnosis and management of brain arteriovenous malformations. *Neurology* 2013;81:1530–7

**REFERENCES**

1. Pierot L, Cognard C, Spelle L. Cerebral arteriovenous malformations: evaluation of the hemorrhagic risk and its morbidity [in French]. *J Neurol Neurosurg Psychiatry* 2004;75:565–71

2. Novakovic RL, Lazzaro MA, Castonguay AC, et al. The diagnosis and management of brain arteriovenous malformations. *Neurolog Clin 2013*;31:749–63

3. Maruyama K, Kawahara N, Shin M, et al. The risk of hemorrhage after radiosurgery for cerebral arteriovenous malformations. *J Neurosurg* 2012;116:1468–74

4. Oppenheim C, Meder JF, Trystram D, et al. Radiosurgery of cerebral arteriovenous malformations: an early angiogram needed? *AJNR Am J Neuroradiol* 1999;20:475–81

5. Steiner L, Lindquist C, Adler JR, et al. Clinical outcome of radiosurgery for cerebral arteriovenous malformations. *J Neurosurg* 1999;84:18–22

6. Dawkins AA, Evans AL, Wattam J, et al. Complications of cerebral angiography: a prospective analysis of 2,924 consecutive procedures. *Neuroradiology* 2007;49:753–59

7. Heiserman JE, Dean BL, Hodak JA, et al. Neurologic complications of cerebral angiography. *AJNR Am J Neuroradiol* 1994;15:1401–07

8. Earnest F 4th, Forbes G, Sandok BA, et al. Complications of cerebral angiography: prospective assessment of risk. *AJR Am J Roentgenol* 1984;142:247–53

9. Bendszus M, Koltzenburg M, Burger R, et al. Silent embolism in diagnostic cerebral angiography and neurointerventional procedures: a prospective study. *Lancet* 1999;354:1594–97

10. Heidenreich JO, Schilling AM, Unterharnscheidt F, et al. Assessment of 3D-TOF-MRA at 3.0 Tesla in the characterization of the angioarchitecture of cerebral arteriovenous malformations: a preliminary study. *Acta Radiol* 2007;48:678–86

11. Lim HK, Choi CG, Kim SM, et al. Detection of residual brain arteriovenous malformations after radiosurgery: diagnostic accuracy of contrast-enhanced four-dimensional MR angiography at 3.0 T. *Br J Radiol* 2012;85:1064–69

12. Uluu E, Temizoz O, Albayram S, et al. Contrast-enhanced MR 3D angiography in the assessment of brain AVMs. *Eur Radiol* 2006;16:367–78

13. Soize S, Bouquin F, Kadiolika K, et al. Value of 4D MR angiography at 3T compared with DSA for the follow-up of treated brain arteriovenous malformation. *AJNR Am J Neuroradiol* 2014;35:1903–09

14. Hadizadeh DR, Kukuk GM, Steck DT, et al. Noninvasive evaluation of cerebral arteriovenous malformations by 4D-MRA for preoperative planning and postoperative follow-up in 56 patients: comparison with DSA and intraoperative findings. *AJNR Am J Neuroradiol* 2012;33:1095–101

15. Kanda T, Ishii K, Kawaguchi H, et al. High signal intensity in the dentate nucleus and globus pallidus on unenhanced TI-weighted MR images: relationship with increasing cumulative dose of a gadolinium-based contrast material. *Radiology* 2014;270:834–41

**FIG 6.** A 19-year-old man with a left frontal AVM with hemorrhagic presentation that was partially embolized with glue. A, SWAN imaging 5 years after SRS shows hyperintense vessels (white arrow) near the AVM that were mistakenly diagnosed as a nidus remnant. B, Digital subtraction angiography findings were negative.
16. Mawad H, Laurin LP, Naud JF, et al. Changes in urinary and serum levels of novel biomarkers after administration of gadolinium-based contrast agents. Biomark Insights 2016;11:91–94 CrossRef Medline

17. Jagadeesan BD, Delgado Almandoz JE, Moran CJ, et al. Accuracy of susceptibility-weighted imaging for the detection of arteriovenous shunting in vascular malformations of the brain. Stroke 2011;42:87–92 CrossRef Medline

18. Hodel J, Rodallec M, Gerber S, et al. Susceptibility weighted magnetic resonance sequences "SWAN, SWI and VenoBOLD": technical aspects and clinical applications [in French]. J Neuroradiol 2012;39:71–86 CrossRef Medline

19. Hodel J, Blanc R, Rodallec M, et al. Susceptibility-weighted angiography for the detection of high-flow intracranial vascular lesions: preliminary study. Eur Radiol 2013;23:1122–30 CrossRef Medline

20. Schmitz BL, Aschoff AJ, Hoffmann MHK, et al. Advantages and pitfalls in 3T MR brain imaging: a pictorial review. AJNR Am J Neuroradiol 2005;26:2229–37 Medline

21. Lee KE, Choi CG, Choi JW, et al. Detection of residual brain arteriovenous malformations after radiosurgery: diagnostic accuracy of contrast-enhanced three-dimensional time of flight MR angiography at 3.0 Tesla. Korean J Radiol 2009;10:333–39 CrossRef Medline

22. Saini J, Thomas B, Bodhney NK, et al. Susceptibility-weighted imaging in cranial dural arteriovenous fistulas. AJNR Am J Neuroradiol 2009;30:E6 CrossRef Medline

23. Noguchi K, Kuwayama N, Kubo M, et al. Intracranial dural arteriovenous fistula with retrograde cortical venous drainage: use of susceptibility-weighted imaging in combination with dynamic susceptibility contrast imaging. AJNR Am J Neuroradiol 2010;31:1903–10 CrossRef Medline

24. Gasparetto EL, Pires CE, Domingues RC. Susceptibility-weighted MR phase imaging can demonstrate retrograde leptomeningeal venous drainage in patients with dural arteriovenous fistula. AJNR Am J Neuroradiol 2011;32:E54 CrossRef Medline

25. Letourneau-Guillon L, Krings T. Simultaneous arteriovenous shunting and venous congestion identification in dural arteriovenous fistulas using susceptibility-weighted imaging: initial experience. AJNR Am J Neuroradiol 2012;33:301–07 CrossRef Medline