ORIGINAL ARTICLE

Three-dimensional rotational angiography in the assessment of the angioarchitecture of brain arteriovenous malformations

Angiographie rotationnelle tri-dimensionnelle pour l’étude de l’angioarchitecture des malformations artério-veneuses cérébrales


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KEYWORDS
Brain arteriovenous malformation; Angioarchitecture; 3D rotational angiography; Vascular density

Summary
Background and purpose. — The angioarchitecture of brain arteriovenous malformations (BAVM) still remains a complex subject of study despite advances in medical imaging techniques. For this reason, the present study aimed to assess whether or not 3D rotational angiography (3DXA) might improve the assessment of BAVM.

Patients and methods. — Included prospectively were 72 patients who had undergone conventional digital subtraction angiography (DSA) and 3DXA for pretherapeutic assessment of BAVM prior to radiosurgery. Dimensional criteria, arterial-feed patterns, venous drainage, points of weakness and vascular densities (VD) of the nidus and shunt zone were studied.

Results. — 3DXA detected all arteriovenous shunts by revealing abnormal venous enhancement. Post-processing tools similar to CT and MRI may also be used to make complex 3D reconstructions. In addition, the technique provided significant help for volumetric estimations, extraction of arterial feeders and origins of draining veins, and analysis of the 3D conformation of the nidus. Furthermore, 3DXA detected significantly more points of weakness, such as intranidus aneurysms and venous anomalies (P<0.005). In 65% of cases, a gradient of vascular enhancement intensity was found between the arteries and draining veins surrounding or comprising the nidus. VD, or the percentages of space occupied by the enhanced vascular elements, was
Introduction

Despite recent advances in magnetic resonance imaging (MRI) and computed tomography (CT), digital subtraction angiography (DSA) remains the standard imaging technique for determining the angioarchitecture of brain arteriovenous malformations (BAVM) [1]. However, selective DSA has a few technical limitations. The projection of numerous vascular elements in a definite anatomical plane may lead to marked reading difficulties. Risky superselective catheterization may be required to better understand the three-dimensional (3D) structure of BAVM and to depict points of weakness in the lesion [2]. Interobserver agreement in the characterization of radioanatomical features may also vary [3,4]. In the present study, a method of complementary selective 3D rotational angiography (3DXA) was evaluated, using digital flat-panel technology to depict the angioarchitecture and spatial conformation of BAVM. The aim of the study was to evaluate 3DXA and the new-generation flat panel to determine whether or not it can improve characterization of the anatomical features of BAVM.

Patients and methods

The study was carried out in accordance with our institutional privacy policy. Prospectively included were 72 patients who underwent conventional DSA and 3DXA to assess BAVM as part of their ongoing planning of treatment by radiosurgery, whether or not the patient had already been partially treated. For these 72 patients (39 men and 33 women; mean age: 37 ± 1 years), there were 75 BAVM evaluated in both the nidus and shunt zone. VD in the shunt zone was highest in untreated patients with no history of bleeding (P < 0.005).

Conclusion. — 3DXA offers a useful approach to BAVM exploration and can improve our knowledge of lesonal angioarchitecture, necessary for the planning of therapeutic strategies.

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Vascular density of BAVM

The entire vascular density of the nidus was described as either compact ($n=45$) or diffuse ($n=30$) on angiography. With 3DXA, vascular densities within the nidus (VDN) and shunt zone (VDSZ) were estimated as percentages according to the VasNV/NV $\times 100$ and VasSZ/SZV $\times 100$ ratios, respectively (Fig. 1). Also, the volume of opacity from the embolic agent used during the previous endovascular procedure was estimated, using a similar threshold methodology as described above, then subtracted from the vascular elements. The presence of a gradient in vascular opacification intensity between the feeding pedicles and draining veins surrounding and within the nidus itself was also noted (Fig. 2). BAVM points of weakness The number of aneurysms in the proximal trunk of the circle of Willis, in the feeding pedicle and in the nidus itself was recorded. The occurrence of venous angiopathy—including venous ectasia, varicose veins, stenosis and obvious venous occlusion—as well as their number were also noted. These points of weakness were separately evaluated on selective DSA and 3DXA for further comparisons.

Statistical analysis

Quantitative variables were expressed as means $\pm$ standard deviation (SD). Comparisons across groups were made using the Mann—Whitney test. When groups were not independent (comparisons between angiography and 3DXA, VDN and VDSZ, Sp/Ap and Smm/Amm), the paired Wilcoxon's test was used. Multiple comparisons were made using the Kruskal—Wallis test, followed by Dunn's post-hoc pairwise test. Non-parametric correlations were calculated by Spearman's rank test except for correlations between two continuous variables, such as the NV and Sp/Ap ratio, Smm/Amm ratio and Smm. SPSS 15.0 and GraphPad 5.01 software were used for the statistical analyses. Values of $P < 0.05$ were considered significant.

Results

Global analysis of BAVM and shunt configuration

Although 3DXA does not allow for dynamic study, the presence of a shunt was always demonstrated by abnormal venous enhancement on the 3DXA acquisition. The distribution of dimensions and characteristic vascular densities in the study population are presented in Table 1. The mean $SZV/NV$ ratio was 45.1 $\pm$ 23.9% when all types of BAVM were considered. $SZV$ and $NV$ were equal or nearly so for AVF ($n=9$). In the subgroup of nidus BAVM ($n=66$), the mean $SZV/NV$ ratio was 38.6 $\pm$ 15.1% in a Gaussian distribution (not shown). This ratio was not linked to any other parameters such as therapeutic history, symptoms or vascular densities. A high positive correlation was found between NV and SZV ($P=0.924$, $P<0.001$), thereby indicating that the larger the nidus, the larger the shunt zone.
In 72% of cases, one or more feeding pedicles could be extracted from other vascular structures on 3D reconstructions (Fig. 2). However, extraction of all the feeding pedicles involved was not possible for the largest BAVM.

In addition, therapeutic history did not alter the interpretation, but the difficulty of interpretation increased significantly with the number of feeding pedicles, and the size and volume of the nidus. In contrast, in previous endovascular procedures involving opacity from embolic agents, the difficulty of interpretation was not significantly increased.

Specific BAVM features

Aneurysms and venous abnormalities tended to be more frequent in patients with a history of bleeding, but did not reach statistical significance. Also, the occurrence of hemorrhage was higher in infratentorial and deep supratentorial lesions. In about 65% of cases, a gradient of vascular enhancement intensity was present between the arteries and draining veins surrounding or comprising the nidus (Fig. 2). Although it is well known that several vascular compartments can be found within the nidus, these data were not reported in the present study because

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Dimensions and vascular densities in various types of brain arteriovenous malformations (BAVM), nidus BAVM and arteriovenous fistulae (AVF).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sp/Ap</td>
</tr>
<tr>
<td>All BAVM (n = 75)</td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>0.8</td>
</tr>
<tr>
<td>Max</td>
<td>22.5</td>
</tr>
<tr>
<td>M ± SD</td>
<td>6.5 ± 3.8</td>
</tr>
<tr>
<td>Nidus BAVM (n = 66)</td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>2.560</td>
</tr>
<tr>
<td>Max</td>
<td>22.5</td>
</tr>
<tr>
<td>M ± SD</td>
<td>7.2 ± 3.7</td>
</tr>
<tr>
<td>Arteriovenous fistulae (n = 9)</td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>0.8</td>
</tr>
<tr>
<td>Max</td>
<td>4.650</td>
</tr>
<tr>
<td>M ± SD</td>
<td>2.3 ± 1.1</td>
</tr>
</tbody>
</table>

SZV, shunt zone volume; NV, nidus volume; VDN, vascular density in entire nidus; VDSZ, vascular density in shunt zone; Sp, maximum size of nidus assessed in pixels on DSA; Ap, diameter of reference artery (carotid or basilar) assessed in pixels on DSA; Smm, maximum size of nidus assessed in mm on 3DXA; Amm, diameter of reference artery (carotid or basilar) assessed in mm on 3DXA; M ± SD, means ± standard deviation.
such compartments are much better identified by 3DXA combined with hyperselective catheterization [9].

**Vascular density**

Assessment of vascular densities within the nidus (VDN) and shunt zone (VDSZ) was always possible on 3DXA (Fig. 1). In the overall study population, the VDSZ was 40% higher than the VDN (P < 0.001). In nidus BAVM (n = 66), the VDSZ was higher than the VDN in 90% of cases (n = 60). However, VDN was marginally higher (1%) than VDSZ in six cases of nidus BAVM. In cases of AVF (n = 9), the values for VDN and VDSZ were similar (Table 1).

There was a positive correlation between VDN and VDSZ (P = 0.693, P < 0.01), indicating that the higher the vascular density within the nidus, the higher the vascular density within the shunt zone. A positive correlation was also found between VDSZ and NV and VDSZ and SZV, as well as between VDN and SZV (P = 0.28–0.32 and P < 0.01, respectively), indicating that the larger the BAVM, the greater the vascular density within the shunt zone. On the other hand, there was no significant correlation between VDN and NV or between vascular densities and the total number of feeding pedicles.

Considering the subgroup of untreated patients, VDSZ was 45% lower in patients with, compared with those without, a bleeding history (P < 0.01). A similar tendency was found for VDN, but did not reach statistical significance (P = 0.08). However, no difference between VDN and VDSZ was found in terms of seizures.

Multiple comparisons of VDSZ, VDN, NV, SZV, SZV/NV ratio and the difference between VDSZ and VDN were performed in four patient subgroups: treated patients with no bleeding history (T + H-); treated patients with a bleeding history (T + H+); untreated patients with no bleeding history (T-H-); and untreated patients with a bleeding history (T-H+) (Table 2; Fig. 3). The SZV/NV ratio did not differ across the four groups. The highest statistically significant values of VDSZ were found in the T-H+ group compared with the T+H- and T+H+ groups after Dunn’s post-hoc test. This means that having BAVM not reshaped by a bleeding or treatment history was associated with a higher vascular density within the shunt zone with a threshold at around 40% (Fig. 3). However, no significant difference was found between these groups in VDN. The difference between VDSZ and VDN was greatest in the T-H- group, which was statistically significant compared with the T + H- and T + H+ groups, suggesting that treatment modifies mainly the shunt zone and not necessarily the areas surrounding it. Also, NV and SZV were significantly different in the four groups: BAVM in T-H+ were twice as large as those in T-H-. In addition, seizure rates did not differ across these subgroups (data not shown).

**Venous drainage**

Non-parametric multiple comparisons of the three venous-drainage configurations (superficial, deep, and both superficial and deep) were performed for VDN, VDSZ, SZV/NV ratio, incidence of bleeding and incidence of seizures (Table 3). VDN and VDSZ were lowest in the deep venous-drainage configuration, which also showed the highest incidence of hemorrhage. Seizure occurrence was more frequent

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**Table 2** Multiple comparisons of brain arteriovenous malformation volumes and vascular densities according to bleeding and treatment history.

<table>
<thead>
<tr>
<th></th>
<th>T-H- (n = 14)</th>
<th>T-H+ (n = 15)</th>
<th>T + H- (n = 22)</th>
<th>T + H+ (n = 24)</th>
<th>P (Kruskal–Wallis)</th>
<th>Post-hoc (Dunn’s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDSZ</td>
<td>51.01 ± 12.3</td>
<td>34.50 ± 15.8</td>
<td>35.98 ± 11.8</td>
<td>41.55 ± 10.4</td>
<td>0.003</td>
<td>T-H- vs T-H+</td>
</tr>
<tr>
<td>VDN</td>
<td>31.95 ± 12.5</td>
<td>23.09 ± 10.9</td>
<td>27.66 ± 8.6</td>
<td>32.00 ± 9.4</td>
<td>0.058</td>
<td>T-H+ vs T + H+</td>
</tr>
<tr>
<td>NV (mm³)</td>
<td>7035 ± 9839</td>
<td>2518 ± 2151</td>
<td>18,056 ± 29,134</td>
<td>19,513 ± 33,867</td>
<td>0.032</td>
<td>—</td>
</tr>
<tr>
<td>SZV (mm³)</td>
<td>2390 ± 3390</td>
<td>791.7 ± 616</td>
<td>7579 ± 13,829</td>
<td>9024 ± 21,211</td>
<td>0.007</td>
<td>T-H+ vs T + H+</td>
</tr>
<tr>
<td>SZV/NV ratio</td>
<td>36.1 ± 12.2</td>
<td>49.6 ± 33.1</td>
<td>44.6 ± 21.2</td>
<td>47.9 ± 24.3</td>
<td>0.526</td>
<td>—</td>
</tr>
<tr>
<td>VDSZ–VDN</td>
<td>19.1 ± 7.6</td>
<td>11.4 ± 9.7</td>
<td>8.3 ± 8.2</td>
<td>9.5 ± 7.9</td>
<td>0.005</td>
<td>—</td>
</tr>
</tbody>
</table>

Data are presented as means ± SD; T-H-, no bleeding history in untreated patients; T-H+, bleeding history in untreated patients; T + H-, no bleeding history in treated patients; T + H+, bleeding history in treated patients; NV, nidus volume; SZV, shunt zone volume; VDSZ, vascular density in shunt zone; VDN, vascular density in entire nidus; VDSZ–VDN = difference between VDSZ and VDN.

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**Figure 3** Vascular densities within the shunting zone (VDSZ) according to therapeutic and bleeding history (H = bleeding history, T = previous therapeutic session done, N = none).
Table 3  Multiple comparisons of vascular density, SZV/NV x 100 ratios, VDSZ/VDN ratios and occurrence of hemorrhage or seizures according to venous-drainage patterns.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>n</th>
<th>Bleeding (%)</th>
<th>Seizures (%)</th>
<th>VDN ± SD</th>
<th>VDSZ ± SD</th>
<th>SZV/NV ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial</td>
<td>40</td>
<td>37.5%</td>
<td>40%</td>
<td>29.9 ± 10.7</td>
<td>42.6 ± 14.6</td>
<td>46.1 ± 25.4</td>
</tr>
<tr>
<td>Deep</td>
<td>22</td>
<td>77.3%</td>
<td>4.5%</td>
<td>24.2 ± 9.4</td>
<td>33.1 ± 11.6</td>
<td>44.9 ± 26.1</td>
</tr>
<tr>
<td>Both</td>
<td>13</td>
<td>53.9%</td>
<td>23.1%</td>
<td>34 ± 9</td>
<td>45.2 ± 7.1</td>
<td>42.5 ± 14</td>
</tr>
<tr>
<td>P (Kruskal–Wallis)</td>
<td>0.0117</td>
<td>0.0105</td>
<td>0.0116</td>
<td>0.0076</td>
<td>0.9453</td>
<td></td>
</tr>
<tr>
<td>Post-hoc (Dunn’s)</td>
<td>Superficial vs deep</td>
<td>Superficial vs deep</td>
<td>Both vs deep</td>
<td>Superficial vs deep</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as means ± SD or percentages; SZV, shunt zone volume; NV, nidus volume; VDN, vascular density in entire nidus; VDSZ, vascular density in shunt zone.

with superficial venous drainage than with deep venous drainage. However, the highest values of VDN and VDSZ were observed in patients with both superficial and deep venous drainage.

Comparison of DSA and 3DXA

A significant correlation between NV and maximum diameters, as evaluated by angiography and 3DXA ($P = 0.879$, $P < 0.01$), was found. The Sp/Ap ratio (6.57) was significantly higher ($P < 0.01$) than the Smm/Amm ratio (6.25), and both the VDN and VDSZ of compact BAVM on angiography were 30% higher ($P < 0.001$) than in diffuse BAVM.

The number of aneurysms and venous anomalies detected during interpretation was significantly higher ($P = 0.035$ and $P < 0.005$, respectively) with 3DXA ($n = 34$ and $n = 60$, respectively) vs DSA ($n = 20$ and $n = 47$, respectively), especially for intranidus aneurysms ($n = 20$ with 3DXA vs $n = 6$ with DSA, $P < 0.001$; Fig. 4). In contrast, in a few cases ($n = 5$), angiography revealed lesions undetected by 3DXA (venous abnormalities in four cases and an aneurysm in one).

Discussion

According to the literature, 3DXA is used mostly for the assessment of cerebral aneurysms [10]. As 3DXA can provide substantial additional information on BAVM [11], we performed 3DXA routinely for BAVM exploration prior to radiosurgery. Such use of contrast is well tolerated even in the pediatric population [12]. A single 3DXA acquisition enables assessment of the entire BAVM conformation and can eliminate multiple oblique angiography injections, thereby helping to decrease the overall contrast load used for angiographic explorations. Furthermore, the patient’s radiation dose is reduced, as the 3DXA radiation dose is significantly lower than that of biplanar DSA [13], especially with the use of a flat-panel detector [14]. Flat-panel technology is currently replacing image-intensifier technology, as it increases sensitivity to X-rays and offers a potential reduction in radiation dose. The dynamic is also improved and stays linear across a very wide range [15]. The key parameter that describes the efficiency of a flat panel is the detective quantum efficiency (DQE), which can reliably describe the spatial resolution of an X-ray imaging detector in the presence of noise, parallax and blurring [16]. With a normal arterial 3DXA acquisition, there is no venous enhancement, whereas veins can be enhanced on CT-angiography and post-contrast MR-angiography. Therefore, venous opacification on 3DXA is the hallmark of an arteriovenous shunt. Thus, even small cortical or small deep fistulae can be detected and analyzed with 3DXA. Likewise, following venous structures back to the nidus helps to delineate the origins of draining veins in the search for the targeted shunt zone. Points of weakness, such as aneurysms and venous anomalies, may be related to a greater risk of rupture [17,18], and are more accurately identified by 3DXA than by angiography, and 3DXA can also detect more aneurysms and venous lesions. However, our present results need to be confirmed by further studies that include interobserver agreement in multireader readings, as is currently done with DSA [3,4]. In our present study, these points of weakness were not significantly linked to a bleeding history.

3DXA also permits identification of a gradient of vascular enhancement intensity between the arteries and draining veins surrounding or comprising the nidus. Such information may be helpful for highlighting precisely the transitional points of arteriovenous connections to target the shunt zones.

In assessments of BAVM size, angiography showed a tendency to overestimate the maximum diameter, as Sp/Ap...
and Smm/Amm diverged significantly in our study. Another advantage of 3DXA is that it obviates the need for multiple hyperselective catheterization to characterize the nidus and feeding pattern, especially during the planning of endovascular procedures [19], as already described for arteriovenous malformations of the spine [20]. As a result, the duration and irradiation of pretherapeutic angiography are both likely to be reduced. However, superselective catheterization, the most accurate technique for evaluation of BAVM [2], is still needed for the most complex lesions.

In the present study, a shunt zone was delineated within the entire nidus, which contains more than shunt vascular elements only. The nidus is usually defined as a tangled bundle of abnormal vessels linked by one or more fistulæ [7]. However, in the present study, we identified a ‘strategic nidus’ that corresponded to the area of arteriovenous connection, excluding vascular elements such as vascular loops and vascular structures distant from the pathological arteriovenous shunts. In the literature, there is usually no distinction made between the entire nidus and such a strategic nidus. For this reason, we introduced the concept of a ‘shunt zone’ that corresponds to the target of endovascular and radiosurgical treatments. Interestingly, our results showed that, in nidus BAVM, the SZV/NV ratio is not linked to either a bleeding or treatment history, or lesional vascular density.

A noteworthy contribution of 3DXA is the assessment of BAVM vascular density, the percentage of space occupied by vascular elements enhanced within the nidus and shunt zone. Vascular density is usually greater in the shunt zone than in the entire nidus except in AVF where, by definition, there is no difference between the nidus and shunt zone [6]. Furthermore, vascular densities are highest in BAVM with both superficial and deep venous drainage. It can be assumed that a dense BAVM is likely to have numerous venous outflows. Another noteworthy finding of the present study is that vascular density in the shunt zone (VDSZ) was greater in BAVM that had not been reshaped by rupture and previous treatment. In contrast, the vascular density in the entire nidus did not differ whatever the treatment or bleeding history. However, the difference between VDSZ and VDN was greatest in untreated patients with no bleeding history. It can be assumed that any bleeding or treatment history will reduce vascular density within the shunt zone, but not in the entire nidus. Furthermore, a low VDSZ with a threshold < 40% might be linked to a higher risk of rupture, based on the results of comparisons of the bleeding histories of untreated patients (Fig. 3). These data were supported by analyses of venous-drainage patterns. Indeed, the VDSZ was lowest for the deep venous-drainage configuration, which showed a greater prevalence of hemorrhage, as it is classically described, than the other configurations. However, as also seen in Fig. 3, the VDSZ was not statistically different in treated patients with or without a history of bleeding. This might be a consequence of vascular remodelling due to treatment.

**Conclusion**

Three-dimensional rotational angiography with the new-generation flat panel provides a novel approach to BAVM characterization that can improve our understanding of lesional angioarchitecture necessary for planning a therapeutic strategy. The technique combines slice-imaging benefits with multiple reconstructions from volumetric acquisitions with unequalled spatial resolution. It may also improve the efficiency of BAVM exploration compared with selective DSA alone, and should reduce both the duration and amount of radiation of pretherapeutic angiography. It allows a virtual microdissection of each component of BAVM—from the feeding pedicle, through the nidus and shunt zone, and into the draining veins—thus leading to a better understanding of the 3D conformation of the lesion. It also offers the possibility of estimating vascular densities in the nidus and shunt zone, a unique feature that may vary according to treatment and bleeding history. This means that it can be used to characterize BAVM and follow their evolution to better understand the natural history of these anomalies. Furthermore, the implementation of 3DXA data as a computer-assisted surgical tool during endovascular procedures should facilitate arterial catheterization and improve the achievement of treatment targets.

**Conflict of interest statement**

None.

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