4D Radial Acquisition Contrast-Enhanced MR Angiography and Intracranial Arteriovenous Malformations
Quickly Approaching Digital Subtraction Angiography

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Background and Purpose—The current gold standard for imaging intracranial AVMs involves catheter-based techniques, namely cerebral digital subtraction angiography (DSA). However, DSA presents some procedural risks to the patient. Unfortunately, AVM patients usually undergo multiple DSA exams throughout their diagnostic and therapeutic course, significantly increasing their procedural risk exposure. As such, high-quality noninvasive imaging is desired. We hypothesize that 4D radial acquisition contrast-enhanced MRA approximates the vascular architecture and hemodynamics of AVMs compared to conventional angiography.

Methods—Thirteen consecutive AVM patients were assessed by 4D radial acquisition contrast-enhanced MRA and DSA. The 4D rCE-MRA images were independently assessed regarding the location, nidal size, Spetzler–Martin grade, and identification of arterial feeders, drainage pattern, and any other vascular anomalies.

Results—4D rCE-MRA correctly depicted the size, venous drainage pattern, and prominent arterial feeders in all cases. Spetzler–Martin grade was correctly determined between reviewers and between the different imaging modalities in all cases except 1. The nidal size was in good correlation between the reviewers, where \( r = 0.99, P < 0.000001 \). There was very good agreement between reviewers regarding the individual scans (\( \kappa = 0.63 \) to 1), whereas the agreement between the DSA and 4D rCE-MRA images was also good (\( \kappa = 0.61 \) to 0.85).

Conclusions—We have developed a 4D radial acquisition contrast-enhanced MRA sequence capable of imaging intracranial AVMs approximating that of DSA. Image analysis demonstrates equivalency in terms of grading AVMs using the Spetzler–Martin grading scale. This 4D rCE-MRA sequence has the potential to avoid some applications of DSA, thus saving patients from potential procedural risks. (Stroke. 2009;40:2749-2753.)

Key Words: arteriovenous malformation ■ vascular ■ imaging ■ MRA ■ DSA ■ angiography

Intracranial arteriovenous malformations (iAVMs) are responsible for the majority of spontaneous intracranial hemorrhages and confer significant morbidity and mortality in young adults. Expectant management, eventual therapy, and postprocedural follow-up of iAVMs require detailed vascular imaging studies. The current gold standard for imaging iAVMs involves catheter-based techniques, namely cerebral digital subtraction angiography (DSA), mainly because of its high spatial (0.2 mm) and temporal (up to 24 frames/s) resolution capabilities. However, acquiring DSA images presents some procedural risks to the patient (0.5 to 12.2%), including the risk of thromboembolic complications, vascular injury, and exposure to radiation and iodinated-contrast dyes. Unfortunately, iAVM patients usually undergo multiple DSA exams throughout their diagnostic and therapeutic course, whether it is for preprocedural endovascular embolizations, surgical or radiosurgical planning, or follow-up imaging, which may be negative in many cases. Thus, multiple DSA examinations increase a patient’s procedural risk exposure. As such, noninvasive imaging techniques have been desired.

Noninvasive imaging of iAVMs using CT and MR angiography is not a novel concept. Historically, the major disadvantages to both techniques have been inadequate spatial resolution and their inability to acquire dynamic information, ie, the adequate separation of arterial, capillary, and venous phases. Although CT angiography has the ability to demonstrate the iAVM nidus, inadequate slice thickness and spatial resolution, absence of sufficient dynamic information, as well as exposure to ionizing radiation and iodinated contrast agents makes CT less than desirable.

Time-of-flight magnetic resonance angiography (TOF-MRA), which uses the physiological properties of blood flow, was...
Table 1. Characteristics of Patients Imaged With Intracranial AVMs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Location</th>
<th>Presentation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33</td>
<td>F</td>
<td>R medial parietal</td>
<td>Hemorrhage</td>
<td>GK</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>M</td>
<td>R cerebellar</td>
<td>Incidental</td>
<td>Surgery</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>M</td>
<td>L inferior frontal</td>
<td>Vertigo</td>
<td>GK</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>F</td>
<td>L cerebellar</td>
<td>L facial numbness</td>
<td>GK</td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>F</td>
<td>L TPO</td>
<td>Headache</td>
<td>GK/surgery</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>R</td>
<td>R posterior frontal</td>
<td>Incidental</td>
<td>GK</td>
</tr>
<tr>
<td>7</td>
<td>52</td>
<td>F</td>
<td>L posterior frontal</td>
<td>Hemorrhage</td>
<td>GK</td>
</tr>
<tr>
<td>8</td>
<td>42</td>
<td>R</td>
<td>Medial occipital</td>
<td>Seizure</td>
<td>GK/surgery</td>
</tr>
<tr>
<td>9</td>
<td>31</td>
<td>F</td>
<td>L parietal</td>
<td>Hemorrhage</td>
<td>GK</td>
</tr>
<tr>
<td>10</td>
<td>24</td>
<td>M</td>
<td>R posterior frontal</td>
<td>L parasthesias</td>
<td>GK</td>
</tr>
<tr>
<td>11</td>
<td>65</td>
<td>M</td>
<td>R posterior frontal</td>
<td>Seizure</td>
<td>Embo/surgery</td>
</tr>
<tr>
<td>12</td>
<td>50</td>
<td>M</td>
<td>R cerebellar</td>
<td>Ataxia</td>
<td>Embo/surgery</td>
</tr>
<tr>
<td>13</td>
<td>54</td>
<td>F</td>
<td>L mesial temporal</td>
<td>Hemorrhage</td>
<td>GK</td>
</tr>
</tbody>
</table>

TPO indicates tempo-parieto-occipital; GK, gamma knife; Embo, embolization.

Stereotactic DSA imaging was performed on a Neurostar biplane angiography unit (Siemens AG Healthcare Sector) by selective contrast injection of all territories feeding the iAVM at 6 frames/s in standard orthogonal anteroposterior, lateral, and oblique projections.

4D rCE-MRA was performed on a 3T Whole-body MR-scanner (MAGNETOM Trio, Siemens AG Healthcare Sector, Erlangen, Germany) within 2 to 4 weeks of the DSA examination. A single injection of intravenous gadolinium (0.1 mmol/kg, Magnevist, Berlex) for each anatomic (sagittal and coronal) plane was used and injected at a rate of 4 mL/s. Our 4D rCE-MRA acquisition technique included radial k-space undersampling and pseudorandom view ordering, sliding scale windowing, and a sliding mask subtraction technique.16,17 We achieved a field of view (FOV) of 220×220×75 mm with pixel resolution of ~1 mm with the temporal resolution at the equivalent of 6 frames per second by imaging the sagittal and coronal planes separately. A dynamic series of maximum-intensity-projection (MIP) images were generated in the sagittal and coronal planes and stored on a workstation.

The 4D rCE-MRA images were independently assessed by a neuroradiologist, a neurosurgeon, and an interventional radiologist blinded to the patient and clinical information. No image sequences were viewed together, ie, DSA and MRA images from the same patient were viewed 2 to 3 weeks apart. An iAVM imaging questionnaire was provided to each physician regarding the location, nidal size, Spetzler–Martin (SM) grade, identification of arterial feeders, drainage pattern, and any vascular anomalies, eg, flow-related aneurysms, venous stenosis, and varices. Each response was assigned a yes (1) or no (0) value except for the nidal size, which was a numeric value in centimeters. Each binary categorical response (eg, presence of deep drainage) was compared between DSA and MRA images as well between the 3 reviewers using a 2 reviewer Kappa analysis. The intra- and interreviewer Kappa analysis was performed using the MiniTab statistics program (Minitab Inc).

Results

Thirteen consecutive patients were assessed by 4D rCE-MRA and DSA. The patient demographics are listed in Table 1 (Mean age was 44.2±14.7 with a male to female ratio of 6:7). DSA demonstrated 10 supratentorial and 3 infratentorial (cerebellar hemisphere) iAVMs.

4D rCE-MRA correctly depicted the size, venous drainage pattern, and prominent arterial feeders in all cases. SM grade was correctly determined between reviewers and between the different imaging modalities in all cases except one, where the size of the nidus was underestimated resulting in an SM grade that was greater than the grade assigned using DSA images. The nidus size was in good correlation between the reviewers (Supplemental Figure I, available online at http://stroke.ahajournals.org), where r=0.99, P<0.000001, and 4D RACE MRA=0.93 DSA +0.14 cm. There was very good agreement between raters regarding the individual scans.

Table 2. MRA/DSA Comparison Inter-Reviewer Kappa Values

<table>
<thead>
<tr>
<th>Reviewer 1</th>
<th>Reviewer 2</th>
<th>Reviewer 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.61</td>
<td>0.63–1</td>
<td>0.5–1</td>
</tr>
<tr>
<td>0.62–1</td>
<td>. . .</td>
<td>0.63–1</td>
</tr>
<tr>
<td>0.5–1</td>
<td>0.63–1</td>
<td>. . .</td>
</tr>
</tbody>
</table>

Table 3. MRA/DSA Comparison Intra-Reviewer Kappa Values

<table>
<thead>
<tr>
<th>Reviewer 1</th>
<th>Reviewer 2</th>
<th>Reviewer 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.86</td>
<td>0.68</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Materials and Methods

Consecutive iAVM patients who were scheduled to undergo stereotactic radiosurgery as well as patients who presented to the neurovascular clinic with prior DSA imaging were enrolled in a HIPPA-compliant IRB-approved study to undergo a 4D rCE-MRA scan during a 12-month period. The inclusion criteria for patients were presence of a previously untreated iAVM, aged between 12 to 75 years old, and normal (GFR >60) renal function. Patients were only excluded if they did not meet the above criteria or chose not to participate in the study. No in-hospital patients were examined.
and the agreement between the DSA and 4D rCE-MRA images was also good ($\kappa=0.61$ to 0.85; Table 3). Figures 1 and 2 represent case examples. Figure 3 demonstrates the discovery of an incidental aneurysm on both DSA and 4D rCE-MRA images.

**Discussion**

**Imaging**

We have found that the vascular architecture and hemodynamics of iAVMs can be determined using 4D rCE-MRA exams. Intracranial AVMs present a unique challenge for MRA because of the high-flow hemodynamics, i.e., AV shunt transit times on the order of $\approx0.5s$. As such, conventional dynamic MR signal acquisition techniques, e.g., contrast-enhanced timing-robust angiography (CENTRA), keyhole and parallel imaging, and sensitivity encoding (SENSE), have improved the temporal resolution of MRA; however, these techniques have been less successful at achieving the necessary temporal resolution required to adequately separate the hemodynamic phases of iAVMs, i.e., separate arterial and venous phases. Several groups have reported temporal resolutions equivalent to image acquisition speeds as low as $\approx600ms/frame$. However, acquiring adequate temporal resolution comes at the expense of spatial resolution, which for iAVMs requires high spatial resolution. Only recently, however, has sufficiently high spatial resolution been achieved using novel acquisition sequences such as rapid radial undersampling techniques.

MR undersampling techniques, although aiding in the improvement of the temporal resolution in recent reports of dCE-MRA of iAVMs, have still been ultimately limited by the necessity of enough contrast signal to capture all of the relevant physiological information within the time frame desired. To maintain both an acceptable signal-to-noise ratio along with adequate temporal resolution, we used a combination of several MR techniques, namely radial undersampling, sliding window reconstruction, and sliding mask subtraction. Radial undersampling involves sampling a higher density of the center of k-space, where the concentration of image energy resides, and less of the outer parts. Each radially acquired line of the image contains the center of k-space, in contrast to Cartesian sampling, which does not, and thus allows fewer acquisitions without significant signal loss. Further, this technique has been shown to increase the temporal resolution with minimal degradation of spatial resolution. The sliding window reconstruction technique allows multiple frames between 2 consecutive independent acquisitions to be reconstructed by combining data from the 2 acquisitions. As a result, each reconstructed frame has an equal amount of data but involves various combinations of

![Figure 1](image1.png)

**Figure 1.** Comparison of DSA and 4D rCE-MRA images in a patient with a deep iAVM associated with a verix. White box in 4D rCE-MRA image shows magnified area represented by insert row. Numbers represent approximate elapsed time between frames in all rows. Arrow in 0.2-s frame demonstrates initial nidal filling. Arrow in 0.4-s frame points to venous verix, arrowhead points to main draining vein.

![Figure 2](image2.png)

**Figure 2.** Comparison of DSA and 4D rCE-MRA images in a patient with a small infratentorial iAVM. White box in 4D rCE-MRA image shows magnified area represented by insert row. Numbers represent approximate elapsed time between frames in all rows. Arrow in 0.2-s frame demonstrates initial nidal filling. Arrowhead in 0.2-s frame represents en passage vessel identified. Arrowhead in 0.6-s frame points to small draining vein.
The sliding mask subtraction technique allows the continuous subtraction of stagnant signal similar to digital subtraction angiography, which allows the dynamic phases of iAVM filling to be separately imaged. When these images are put together in a series, the dynamic filling of iAVMs can be clearly delineated with both high spatial and temporal resolution.

**Limitations**

The limitations of this study are several-fold. The current spatial resolution of 4D CE-MRA is just on the order of ≈1 mm, less than that of DSA. Although many intracranial AVMs involve arterial feeders (<1 mm) that may not be completely resolved using this 4D CE-MRA technique, this limitation did not affect the grading of the iAVMs examined in this study, as arterial feeder size or location are not considered in the classification system. Further, current improvements in contrast agents and signal acquisition techniques continue to increase the visualization of these small arterial feeders. In the cases of iAVMs which involve the deeper parts of the brain, namely the thalamus, basal ganglia, and brain stem that are notorious for having arterial feeders that are even beyond the spatial resolution of DSA, 4D CE-MRA may not be as useful a technique. However, the shape and volume of the nidus, which is what is used for stereotactic radiosurgery planning, could possibly be delineated. Lastly, iAVMs imaged with 4D CE-MRA are shown to fill with contrast simultaneously from all arterial feeders, which could possibly obscure some arterial feeders in the same imaged plane, given that only the MIP images are used. However, this limitation can be overcome by either multiplane or 3D-rotational imaging, which is currently being examined at our institution.

Several limitations regarding the future implementation of such an MR technique for imaging iAVMs exist. Many patients, including those with iAVMs, cannot undergo routine MR imaging because of the presence of ferromagnetic aneurysm clips, devices, or implants. Furthermore, medical comorbidities, such as severe renal failure, put patients at risk for nephrogenic systemic fibrosis, a serious syndrome involving extensive fibrosis of skin, joints, and internal organs associated with exposure to gadolinium. Therefore, caution must be undertaken with renal patients by either decreasing the amount of contrast used or abandoning the use of contrasted imaging altogether. Fortunately, this syndrome is rare and even rarer in the young patients that often present with iAVMs. Moreover, contrast agents continue to improve in terms of increased signal (higher relaxivity) at lower doses, thus reducing the patients’ risks for this rare syndrome.

**Future Considerations**

While DSA imaging of iAVMs will unlikely ever be replaced as long as endovascular options in their treatment exist, several clinical applications of this 4D CE-MRA sequence are possible. Some centers continue to use stereotactic DSA in conjunction with MRI to plan radiosurgical treatment of iAVMs and other vascular lesions, including dAVFs. Given the high correlation of SM grade between the 2 imaging modalities, this would allow radiosurgical planning using these MRA sequences and avoid any DSA procedural risks. Furthermore, DSA is an invasive procedure which requires increased costs compared to the acquisition of these image sequences. These studies are currently underway at our institution. Another important potential clinical application is using the 4D CE-MRA sequences for preoperative planning. Localization of specific details of the angio-architecture can be difficult and potentially problematic when working near/around eloquent areas of the brain. Having the ability to visualize the high-definition angio-architecture overlaid onto either cortical brain images or diffusion-tensor maps could allow the neurosurgeon to avoid unnecessary surgical complications. Furthermore, these sequences can be used in conjunction with stereotactic-guidance such that important aspects of the iAVM nidus or corresponding vasculature can be noted throughout the resection. Finally, iAVM patients often require multiple follow-up images, where some institutions still perform routine DSA. Although MR has been shown to be a viable option with regard to postradiosurgical treatment of iAVMs, this imaging modality could potentially improve the detection of residual nidus or early draining veins and minimize the number of DSA procedures required.

**Summary**

We have developed a 4D CE-MRA sequence capable of imaging intracranial AVMs at sufficiently high spatial resolution and a temporal resolution at the equivalent of a frame rate acquisition of at least 6 frames/s, approximating that of DSA. Image analysis demonstrates equivalency in terms of grading iAVMs using the SM grading scale. This 4D CE-MRA sequence has the potential to avoid some applications of DSA, thus saving patients from potential procedural risks. Further use of this MRA sequence in different clinical applications is currently underway.
Disclosures

None.

References


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