Published in final edited form as:

Invest Radiol. 2016 June ; 51(6): 365–371. doi:10.1097/RLI.0000000000000212.

Accelerated Time Resolved Contrast Enhanced MRA of Dural Arteriovenous Fistulas using Highly Constrained Reconstruction of Sparse Cerebrovascular Datasets

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Abstract

Objective—Time resolved contrast enhanced magnetic resonance angiography (TR CEMRA) is commonly used to non-invasively characterize vascular malformations. However, the spatial and temporal resolution of current methods often compromises the clinical value of the exams. Constrained reconstruction is a temporal spatial correlation strategy that exploits the relative sparsity of vessels in space to dramatically reduce the amount of data required to generate fast high resolution TR CEMRA studies. In this report we use a novel temporal spatial acceleration method termed HYPRFlow to diagnose and classify dural arteriovenous fistulas (DAVFs). Our hypothesis is that HYPRFlow images are of adequate diagnostic image quality to delineate the arterial and venous components of DAVFs and allow correct classification using the Cognard system.

Subjects and Methods—8 patients with known DAVFs underwent HYPRFlow imaging with isotropic resolution of 0.68 mm and temporal resolution of 0.75 s and 3D Time of Flight MRA (3DTOF). 3DTOF images and HYPRFlow images were evaluated by 2 readers and scored for arterial anatomic image quality. DSA was available for comparison in seven subjects and for these patients each DAVF was classified according to the Cognard system using HYPRFlow and DSA exams. DSA was considered the reference exam or gold standard.

Results—HYPRFlow imaging classification was concordant with DSA in all but one case. There was no difference in the arterial image quality scores between HYPRFlow and 3DTOF MRA (95% CI). Arterial to venous separation was rated excellent (n=3), good (n=4) or poor (n=1) and arteriovenous shunting was easily appreciated. Undersampling artifacts were reduced by using a low pass filter and did not interfere with the diagnostic quality of the exams.

Conclusion—HYPRFlow is a novel acquisition and reconstruction technique that exploits the relative sparsity of intracranial vessels in space to increase temporal and spatial resolution and provides accurate delineation of DAVF vasculature.

Keywords

Time resolved CEMRA; Constrained reconstruction; HYPRFlow; undersampled radial acquisition; dural arteriovenous fistula

Introduction

Dural arteriovenous fistulas (DAVFs) are abnormal communications between dural arteries and the dural venous system that represent 10-12% of intracranial vascular malformations. The majority of DAVFs demonstrate increased flow within the feeding vessels. There is also rapid shunting of blood from the arterial feeding vessels into the draining venous system (AV shunting). DAVFs are most commonly found in the transverse, sigmoid and cavernous sinuses. DAVFs are less aggressive in comparison to arteriovenous malformations of the brain (AVMs), which more commonly present with intracranial hemorrhage, seizure, or focal neurological deficit. Patients with DAVF typically present with more benign symptoms of pulsatile tinnitus, headache and visual symptoms. Vascular imaging plays a key role in establishing the diagnosis and excluding other etiologies for the patient's symptoms. (1, 2) Imaging of the DAVF venous drainage is particularly important because DAVFs with cortical venous drainage (CVD) can behave aggressively with annual rates of neurologic deficit of 7 - 30%, intracranial hemorrhage of 4.5 - 35%, and mortality of 11 - 45%. (2-7) Thus, vascular imaging aids in DAVF risk stratification by identifying the arterial supply and delineating the venous drainage.

Two generally accepted DAVF classification systems developed by Borden (8) and Cognard (9) stratify DAVFs based on the pattern of venous drainage. Cortical venous drainage is recognized as the most significant predictor of intracranial hemorrhage, venous infarction or cognitive decline due to venous hypertension. Borden classifies lesions by site of venous drainage and presence of CVD. The Cognard Classification is more comprehensive and describes site and direction of venous drainage, presence of CVD and cerebral venous dilatation and can therefore be used to stratify the bleeding risk (Table 1). The Cognard system was used in this study allowing for better description and stratification of findings.

Previously investigators have demonstrated that DAVFs can be detected and classified using currently available methods of time resolved contrast enhanced magnetic resonance imaging (TR CEMRA). (10-14) These reports did not attempt to delineate small vessel anatomy but did establish that noninvasive imaging could be used as a screening tool to confirm the presence of a DAVF. Subsequent work using acceleration methods of parallel imaging and a combination of keyhole imaging with segmented k space ordering technique for TR CEMRA demonstrated improved delineation of DAVF arterial feeder anatomy and venous drainage but were limited by SNR as acceleration and spatial resolution increased. (14-16)

In this report, a novel constrained reconstruction method termed HYPRFlow was used to provide TR CEMRA images with spatial resolution of 0.68mm isotropic and temporal resolution of 0.75 s and whole brain coverage. Previous reports have demonstrated the value of using radial undersampling and highly constrained reconstruction (HYPRFlow) to characterizing brain AVMs. (17-19)

Subjects and Methods

Subjects

The project was reviewed and approved by the Institutional Review Board and performed in compliance with the Health Insurance Portability and Accountability Act regulations. All patients signed informed consent documents approved by the local Investigational Review Board. Patients were selected from the Interventional Neuroradiology and Endovascular Neurosurgery service undergoing evaluation for DAVF. The subject population varied in age from 42 to 80 with 2 female and 6 male subjects. The clinical presentations included pulsatile tinnitus (n=6), seizures (n=1) and headache (n=1). Digital subtraction angiography (DSA) exams were available for comparison in seven patients. HYPRFlow exams were obtained using a 3T MR imaging system (Discovery 750, GE Healthcare, Waukesha, Wisconsin) with an 8-channel head coil (HD Brain Coil, GE Healthcare).

Imaging Methods

The novel imaging protocol in this report uses a non-Cartesian 3D radial acquisition for dynamic and static imaging. The 3D radial sampling strategy allows for significant acceleration due to the incoherent nature of undersampling artifacts (vastly undersampled radial projection reconstruction = VIPR). The radial imaging methods used in this report have been previously described. (20, 21)

HYPRFlow images are derived from data acquired during three radial acquisitions. The first is a 60 second non contrast mask, the second a high temporal resolution 60 second dynamic series obtained during the first pass of a contrast bolus through the cerebrovascular system. The third scan is a static exam with high spatial resolution that is used as the spatial constraint for HYPR-LR reconstruction. For the dynamic and static scans the background tissue signal is subtracted to sparsify the datasets resulting in only the vascular structures being present within the imaging volumes.

Dynamic Scan

The dynamic contrast enhanced 3D radial scan (CE VIPR) was obtained using the following imaging parameters: FOV = 22cm³, TR/TE = 3.0/0.4 ms, bandwidth = 125 kHz, 64 points from the center to the edge of the *k*-space for each projection, frame rate 0.5s; total acquisition window = 0.75 seconds, spatial resolution 1.7×1.7×1.7mm. Gadobenate dimeglumine (MultiHance, Bracco Diagnostics, Princeton, New Jersey) was injected at 3 mL/s, and the contrast dose was 0.1 ml/kg followed by a 20-mL saline flush.

Static Scan

The static scan is obtained as a five point phase contrast MRA using a radial acquisition (PC VIPR). (22) The imaging parameters for the postcontrast PC VIPR were the following: FOV 22 cm³, TR/TE = 7/2.5 ms, VENC 80 cm/s, BW = +/- 62.5 kHz. The readout matrix was 320 points per projection, and the spatial resolution for the phase contrast study was 0.68 mm³ isotropic. Ten thousand radial projections were acquired within approximately 5.35 minutes.

For comparison of spatial resolution, 3DTOF MRA exams were obtained using 4-5 overlapping slabs, (TR /TE = 25/2.5 ms), 24cm FOV, Cartesian encoding, zero filling, voxel size 0.5mm isotropic. 3DTOF was selected to allow comparison of the HYPRFlow arterial anatomy with the highest resolution MRA method commercially available. Digital Subtraction Angiography (DSA) exams were obtained using a Siemens Artis Zee biplane system. DSA was considered the reference or gold standard. The biplane DSA injections were obtained with temporal resolution ranged from a minimum of 2 frames per second to six frames per second. Selective injections were performed to provide precise anatomic characterization of the DAVFs.

HYPRFlow reconstruction

The details of the HYPR LR reconstruction have been reported in detail (23) and the following concise summary is quoted from a previous publication. (18)

“The constrained reconstruction can be formulated as the temporal weighting image (I_w^t) multiplied by the constraint (I_C) as following:

$$I_H(t) = I_w^t \cdot I_C = \frac{I_t \otimes K}{I_C^t \otimes K} \cdot I_C$$

where I_t is a reconstructed time frame image from the dynamic scan, I_C^t is the phase contrast constraint (PC VIPR). I_C^t is the reprojected constraint along the same trajectory as the current time frame image I_t , and K is the convolution kernel. A threshold (5%) is selected to and applied to the denominator to provide protection against zero in the denominator. Undersampling streak artifacts are reduced by first applying a low pass filter to the time frame images producing temporal weighting images. The convolution operation is performed in k-space. The equivalent kernel size in image space is about $10 \times 10 \times 10$ pixels. In order to compensate for the signal variations due to the high undersampling, a tornado shaped filter was used with 0.5 s at the center of k-space and 0.75 s at the cutoff frequency of the local kernel being applied. (0.5s scan time but 0.75 s data acquisition window).

The constraint is the high resolution PC VIPR angiogram, which provides the vascular map with high spatial resolution and high SNR. When the PC VIPR constraint is multiplied by the dynamic images obtained during the first pass of the contrast agent, the result is a time series of high spatial resolution MR angiographic images (0.68 mm^3) with the contrast kinetic features of high temporal resolution (0.75 s). The PC VIPR velocity data can also be used for flow analysis. (24) The entire acquisition is obtained in a clinically acceptable imaging time of 5.35 minutes. HYPRFlow reconstruction takes 30-45 minutes and requires noncommercial software.” (Figure 1)

Image Analysis

The 3DTOF and HYPRFlow images were retrospectively reviewed by two readers. Arterial image quality was scored as (1) no or poor visualization; (2) vessels can be identified but the image quality is not adequate for diagnostic purposes; (3) adequate to good image quality with diagnostic quality vessel delineation; (4) excellent image quality and vessel delineation.

The vessels that were scored included the anterior cerebral artery A2/A3 segments; middle cerebral artery M2/M3 segments; posterior cerebral artery P2/P3 segments; internal maxillary arteries (IMA); middle meningeal arteries (MMA); and occipital arteries (OA).

Arteriovenous shunting was determined by qualitatively comparing the arrival of contrast in the transverse sinus to arrival of contrast in the cortical and deep veins. If the transverse sinus enhanced prior to enhancement of the cortical or deep veins this was considered evidence of dural arteriovenous shunting. The exams were categorized as arteriovenous shunt present or absent.

Arteriovenous separation was scored as (1) poor arteriovenous separation with no or one frame without venous overlap; (2) good arteriovenous separation with at least two frames with delineation of the arterial component without venous overlap and (3) excellent arteriovenous separation with at least 3 arterial frames without venous overlap.

Venous anatomy was assessed by comparing the HYPRflow venous outflow assessment and Cognard Classification to the DSA based venous outflow and Cognard classification. (Table 1) Artifacts in the HYPRFlow images due to radial undersampling were categorized as (1) none or minimal artifacts and the images are of diagnostic quality or (2) significant or severe artifacts that degrade images to a level that the exam is no longer of diagnostic quality.

Statistical Analysis

Paired t-test and computed 95% confidence intervals (CI) for the difference in arterial image quality scores for 3DTOF vs HYPRFlow were performed. The paired t test was chosen because it gives an estimate of the mean difference as opposed to a binary decision of significant versus non-significant. This is based on the recommendation of our statistician to move away from significance testing and instead report mean difference estimations. We selected this approach because with small samples it is hard to assess distributional assumptions and the t-test is well-known to be robust to mild violations in the assumptions, especially if data are independent, as in our case. (24-26)

Cohen's kappa was used to assess inter-observer agreement. Weighted kappa with square weights was obtained for ordinal variables (AV separation, undersampling artifacts), and no weights were used for binary variables (AV shunting).

Results

Vascular anatomic image quality scores were compared between 3DTOF and HYPRFlow and in no instance did the mean difference attain significance within the 95% confidence interval. The confidence intervals were for anterior cerebral artery A2/A3 segments: 0.38 mean difference 95% CI, 0.24 to 0.99; for middle cerebral artery M2/M3 segments: 0.25 mean difference 95% CI, 0.34 to 0.84; for posterior cerebral P2/P3 segments: 0.38 mean difference 95% CI, (0.24 to 0.99); for MMG, IMA and OA 0.00 mean difference 95% CI.

Although not statistically significant, the mean image quality scores were higher for the 3DTOF for the anterior, middle and posterior cerebral artery segments. There was good

inter-observer agreement on the anatomic vascular image quality scoring for all vascular regions for both 3DTOF (kappa range 0.7 -1.0) and HYPRFlow (kappa range 0.78 -1.0).

Both readers considered arterial-to venous separation as excellent in three cases (at least 3 frames without significant venous overlap) good in four cases (at least 2 frames without significant venous overlap), and poor in one case with an unusually large fast fistula and venous filling present on the very early images. All HYPRFlow exams were considered of diagnostic image quality with no significant radial undersampling artifacts and excellent inter observer agreement in the assessment of radial artifacts (kappa=1.0). (Figures 2 and 3) Arteriovenous shunting defined as early transverse sinus enhancement was identified by HYPRFlow in 7/8 cases by both readers. In one instance, a small mixed dural / pial malformation with near normal dural sinus opacification rate was scored as poorly visualized A-V shunting.

Venous drainage and the Cognard Classification

The number of subjects in each category based on DSA were grade I (n=2), grade 2a (n=1), grade 2a+b (n=1), and grade 4 (n=2). One subject had a complex lesion felt to be a mixed dural and pial malformation which could not be definitively classified using the Cognard system. However, the venous outflow as determined by DSA and HYPRFlow was concordant in this case. The Cognard classification and venous outflow anatomy as determined by HYPRFlow imaging was concordant with DSA in 5/6 cases. In one case there was a small amount of retrograde flow into the cavernous sinus through the inferior petrosal sinus that was identified on DSA but not on HYPRFlow and therefore the Cognard classification was discordant. (Figure 4) One subject in the study did not have a DSA exam. This patient underwent multiple corroborating CTA, MRV and TR CEMRA (TRICKS) studies and was diagnosed with a type 1 DAVF, which was concordant with the HYPRFlow classification. Table 2

Discussion

DAVFs often have small arterial feeders and rapid arteriovenous shunting necessitating both high spatial and temporal resolution for characterization. A noninvasive MRA technique that can accurately characterize DAVFs would reduce the need for DSA and thus limit the patient exposure to ionizing radiation, minimize risk of renal injury or allergic reaction, and avoid the DSA procedure risk of iatrogenic stroke. This would be especially useful for the more benign type I lesions which often do not require treatment.

Current Cartesian based methods have limitations due to the use of time consuming phase encoding. In order to address the need for acceleration investigators have used segmented central k-space ordering, k-t BLAST, k-t SENSE and other spatial temporal correlation strategies to obtain temporal resolution of 1.8 s and spatial resolution of $1 \times 1 \times 1.5 \text{ mm}^3$. (27, 28) However, at this resolution it is conceivable that small arterial feeders and venous reflux could be missed in complex DAVFs. Another promising 4D MRA technique for characterizing DAVFs is pseudo-continuous arterial spin labeling (pcASL). This technique does not require contrast and eliminates the potential risk of nephrogenic systemic fibrosis. Investigators have been able to achieve $0.5 \times 0.5 \times 0.6 \text{ mm}^3$ spatial resolution and 300

millisecond temporal resolution with this technique. (29) A major disadvantage of this technique is difficulty characterizing venous anatomy due to the short T1 of the labelled spins. Improved depiction of late filling DAVF vessels has been addressed using a variable flip angle pcASL technique. (16)

Contrast enhanced 3DTOF MRA provides an alternative approach by first obtaining a non contrast 3DTOF scan followed by a contrast enhanced 3DTOF exam. The advantage of this approach is that the arterial system is visual on the non contrast exam without venous overlap. In cases of high flow fistulas the location of the arteriovenous shunting can also be identified on the non contrast images. The contrast enhanced 3DTOF exam combines in flow enhancement and T1 shortening of blood to provide a high resolution scan of the arterial and venous system allowing for delineation of the venous drainage of the DAVF. However, this method does not provide information on contrast filling dynamics and suffers from overlapping structures and contrast enhancing non vascular structures such as the dural sinus wall. (30, 31)

Time resolved contrast enhanced magnetic resonance angiography combined with innovative MR sampling and reconstruction techniques such as constrained reconstruction and non Cartesian trajectories, provides important advances in the noninvasive characterization of DAVFs. Constrained reconstruction exploits the relative sparsity of vessels in space to reduce the amount of temporal data required to generate high resolution TR CEMRA exams. (32)

By using a spatial constraining image set (PC VIPR) to reconstruct each individual time frame obtained during the dynamic series (CE VIPR), HYPRFlow is able to take advantage of the high SNR from the constraining image. The rapid whole brain acquisition time frames obtained in the dynamic series are therefore not bound by a SNR affected by the acquisition time of the dynamic series. By separating temporal (dynamic series) and spatial resolution (PC VIPR constraint) into two scans HYPRFlow maximizes each. HYPRFlow is able to achieve a temporal resolution of 0.75 s and spatial resolution of 0.68 mm isotropic in clinically acceptable total scan time of 6 min. This technique has been used with success to characterize AVMs, which similarly to DAVFs requires high spatial and temporal resolution due to their rapid arteriovenous shunting and small feeding vessels. (18, 19) HYPRFlow is well suited for characterizing AVMs and DAVFs because whole brain coverage allows the whole lesion to be characterized which is possible because the relative sparsity of vessels in 3D space allows for the use of undersampling techniques such as radial acquisition (VIPR). Previous work has demonstrated that use of the HYPR reconstruction method provides improved SNR compared to radially sampling k -space with a sliding window reconstruction method (33)

Our pilot clinical study demonstrates that it is feasible to characterize DAVF using the constrained reconstruction HYPRFlow method. The major advantage of HYPRFlow is the ability to characterize venous drainage which is the main determinant of DAVF prognosis and classification. The Cognard classification of DAVFs by HYPRFlow was concordant with DSA in 5/6 cases and the venous outflow anatomy was concordant in 6/7 cases. In the one discordant case there was subtle reflux through the inferior petrosal sinus, only seen on

selective arteriography, which was not detected by HYPRFlow. (Figure 4) The presence of the inferior petrosal drainage classified the DAVF as type IIa instead of the HYPRFlow classification of a type I lesion. HYPRFlow arterial anatomic image quality was also rated equivalent to 3DTOF.

Although HYPRFlow imaging is well suited for imaging DAVFs, there are limitations to our study. First, as a clinical pilot feasibility study there was a small number of subjects and our initial experience will have to be further validated in a larger study group. In addition, the arterial vasculature was not compared between the two techniques in a normal subjects control group. Although HYPRFlow has improved spatial resolution compared to previously used TR CEMRA techniques, DSA is still superior for delineating subtle venous reflux in small vessels as we saw in one case where reflux through the inferior petrosal sinus was only seen with selective arterial catheterization at DSA. Patient motion occurring between the dynamic scan and the static scan can compromise the reconstruction due to misregistration of the two scans. If the scans are not severely degraded, manual coregistration of the two scan can reduce this problem.

Complex or slow flow can lead to spin dephasing with the PC VIPR constraining image which is another limitation of HYPRFlow imaging. For example, in one patient with a complex DAVF in the region of the torcular herophilli there was difficulty visualizing multiple small arterial feeders on the HYPRFlow images using the PC-VIPR as a constraint. In certain instances it may be advantageous to weight the PC VIPR constraint by incorporating a portion of the non velocity dependent magnitude data from the PC VIPR acquisition. (34) Alternatively, a CE-VIPR constraint can be obtained which also does not have velocity dependence . (Figure 5)

In conclusion, HYPRFlow is a promising technique for the non-invasive characterization of DAVFs. Arterial HYPRFlow images compared favorably with 3DTOF and venous imaging was concordant with DSA in 6/7 cases. The most significant limitation of the technique is the potential for signal loss in the PC VIPR constraining image data either due to dephasing from complex flow or poor visualization of very slow flow vessels due to the velocity dependence of the PC VIPR scan. However, HYPRflow has the additional advantage that the velocity data from the PC VIPR exam can be used to measure velocity, flow and display streamline flow in each arterial pedicle and venous drainage pathway, thus improving the characterization of DAVFs by isolating the arterial and venous components. (35)

Acknowledgments

Funding source: NIH RO1NS066982

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Abbreviations

VIPR	Vastly undersampled projection reconstruction using 3D radial encoding
CE VIPR	a dynamic time resolved series of whole brain acquisitions obtained during the first pass of a contrast bolus using undersampled 3D radial encoding
TR CEMRA	Time resolved contrast enhanced MRA
PC VIPR	a highly accelerated phase contrast MRA obtained using 3D radial encoding
4D Flow MRI	flow and velocity data obtained from a peripheral or cardiac gated phase contrast MRA

HYPR LR	an algorithm that improves the SNR and spatial resolution of a dynamic series of images by using a reference scan to constrain the dynamic images
HYPRFlow	a series of angiographic images that are reconstructed from two datasets one dynamic series with high temporal resolution and one static dataset with high spatial resolution.

Figure 1.

HYPRFlow Image reconstruction. Top row: Dynamic time-resolved 3D radial CE-VIPR images. Following acquisition of a precontrast mask, 60 whole-brain 3D radial scans are obtained every 0.5 seconds and reconstructed using a 0.75 second acquisition window during the first passage of a contrast bolus. The precontrast mask is used to subtract the background stationary tissue to sparsify the dataset. A low pass filter is then applied to the dynamic series to suppress undersampling streak artifacts. Immediately following the dynamic scan a 5.35 minute 3D radial phase-contrast MRA is obtained (PC VIPR). HYPR LR reconstruction is then applied using the PC VIPR flow images to constrain the dynamic weighted images and generate the HYPRFlow images (bottom row).

Figure 2.

Cognard Type IV dural AVF. Top Row: Selective left external carotid artery DSA shows filling of a posterior branch of the middle meningeal artery (arrow) during the arterial phase (A), which connects via a dural fistula directly into a dilated (>5 mm diameter) cortical vein (dashed arrow) (B,C). The fistula ultimately drains into the superior sagittal sinus (arrow) (D). Bottom Row: Corresponding HYPRFlow images at similar time points in the angiographic series (E-H).

Figure 3.

Cognard Type IIa dural AVF. Top Row: 3DTOF images in the axial plane (projection slab thickness (A) 10mm, (B) 20mm and (C) 60mm) demonstrating multiple arterial feeders from the left external carotid artery, the largest are the left occipital artery and posterior branch of the middle meningeal artery (arrows). (A-C). HYPRFlow images (axial projections of entire head) clearly demonstrate the arterial supply and early venous filling of the left transverse sinus and fully characterize the DAVF. The drainage is antegrade into the transverse and sigmoid sinus (D-F)

Figure 4.

Cognard Type IIa dural AVF. Additional images in the sagittal plane of the same patient as figure 3. DSA of the left common carotid injection demonstrate that the arterial supply to the DAVF is predominantly from the left occipital artery (arrow) (A). Selective arteriogram of the left occipital artery (B) revealed subtle reflux through the inferior petrosal sinus (dashed arrow), which is not visualized on the 3DTOF (C) or HYPRFlow images (D-F).

Figure 5. Cognard Type I dural AVF. Left: HYPR reconstruction using PC VIPR constraint. Right: HYPR images using a CE VIPR constraint. Note improved conspicuity of very slow flow vessels within the dura (arrow). Using PC VIPR as the constraint adds a velocity dependence to the reconstruction.

Table 1

Cognard Classification

Type	Venous Drainage
I	Antegrade venous drainage into dural sinus
IIa	Retrograde venous drainage into dural sinus only
IIb	Retrograde venous drainage into cortical vein only
IIa + IIb	Retrograde venous drainage into dural sinus and cortical vein
III	Direct drainage into cortical vein without venous ectasia
IV	Direct drainage into cortical vein with venous ectasia
V	Drainage into spinal perimedullary veins

Venous ectasia: defined as venous dilation larger than 5 mm diameter and three times larger than the diameter of the draining vein.

Table 2

Cognard Classification by HYPR and DSA

Subject	HYPR	DSA
1	I	None
2	Mixed dural/pial fistula	Mixed dural/pial fistula
3	I	IIa
4	IV	IV
5	I	I
6	IV	IV
7	IIa+b	IIa+b
8	I	I