Published in final edited form as:

World Neurosurg. 2019 June ; 126: 405–412. doi:10.1016/j.wneu.2019.02.131.

Serial Quantitative and Qualitative Measurements of Flow in Vein of Galen Malformations Using 4D Flow MRI (PC-VIPR): Case Report

Yiping Li, MD¹, Raheel Ahmed, MD, PhD¹, Leonardo A Rivera-Rivera, PhD³, James A Stadler III, MD¹, Patrick Turski, MD², Beverly Aagaard-Kienitz, MD^{1,2}

¹Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

²Department of Radiology, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

³Department of Medical Physics, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

Keywords

vein of galen malformation; phase contrast imaging; cerebral blood flow; interventional; novel imaging sequence; Time resolved MRI; novel imaging application; endovascular

Introduction

Vein of Galen malformation (VOGM) is a congenital arterial-venous fistula that develops during weeks 6-11 of fetal life manifested by persistent abnormal shunting of arterial blood into an embryonic deep venous system. VOGMs often present at birth with high-output cardiac failure or in early infancy with hydrocephalus, seizures, or progressive neurologic impairment.

Historical interventions aimed at direct ligation or intravascular closure of VOGMs resulted in high morbidity and mortality¹. Elucidation of cerebral hemodynamics and improvements in neonatal endovascular techniques have significantly improved clinical outcomes¹. Current

Corresponding Author: Beverly Aagaard Kienitz, MD, University of Wisconsin-Madison School of Medicine and Public Health, Clinical Science center, 600 Highland Avenue, Madison, WI, 53792-3252, USA, Telephone: 608-263-8328, Fax: 608-262-6214, baagaard-kienitz@uwhealth.org.

Author Contributions:

Conception and design: Li, Aagaard-Kienitz Acquisition of data: Li, Aagaard-Kienitz, Rivera-Rivera Analysis and interpretation of data: Li, Ahmed, Aagaard-Kienitz, Rivera-Rivera, Turski Drafting the article: Li, Ahmed, Aagaard-Kienitz Critically revising the article: Li, Ahmed, Aagaard-Kienitz, Rivera-Rivera, Turski. Reviewed submitted version of manuscript: all authors.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The current study is not supported by any sources of funding

Oral podium presentation at American Society of Neuro Radiology, Long Beach CA, 2017

expert consensus advocates staged, trans-arterial embolization². This enables gradual obliteration of the vascular shunt and minimizes risk of acute changes in cerebral hemodynamics due to abrupt closure of feeding arterial pedicles or the draining deep venous system.

However, timing for therapeutic interventions and patient selection remains controversial. Treatment evaluation is often based on clinical assessment of neurological and systemic sequelae². Conventional angiography remains the gold standard technique to assess the location and extent of persistent fistulae and their real-time flow patterns that can objectively guide surgical decision making. Diagnostic angiography however, carries a high procedural risk in neonates, infants, and young children¹. Non-invasive techniques for serial and reproducible assessment of cerebrovascular hemodynamics to objectively guide clinical decision making are lacking.

Phase Contrast Vastly under sample Isotropic Projection reconstruction (PCVIPR) is a quantitative 4D flow MR technique which radially under samples k -space allowing for accelerated acquisition times and high-resolution angiography. 4D flow MRI with PCVIPR permits the assessment of blood flow rates and pressure changes by relating these parameters to the velocity field captured at multiple phases of the cardiac cycle in a volumetric acquisition using three-directional velocity encoding^{5, 6}.

We report our initial results, based on a novel application of 4D-Flow MRI, using a highly accelerated PCVIPR technique. We demonstrate its preliminary application and feasibility for serial non-invasive assessment of angioarchitecture, arterial flow patterns, and venous pressure gradients before and after embolization of VOGMs in a cohort of pediatric patients¹.

Technique

Subjects

Between July 2016 and July 2018, 4 pediatric patients (age range 6-30 months) harboring VOGMs underwent PCVIPR imaging at the University of Wisconsin Hospitals and Clinics. Imaging and clinical management data was collected and evaluated with informed consent

Procedure

All endovascular procedures were performed using bi-plane angiography under general anesthesia. Systemic blood pressure was maintained at age normalized ranges. Standard guide catheters, microcatheters, and embolic materials were used for embolization with systemic heparinization to prevent thromboembolic complications.

Imaging

Patients were scanned using a 3.0T clinical MRI system (MR750, GE Healthcare, Waukesha, WI) with an eight-channel head coil (Excite HD Brain Coil, GE Healthcare, Waukesha, WI). Volumetric, time-average PC MRI data with three-directional velocity encoding were acquired with PC VIPR. The imaging parameters include: velocity encoding = 80cm/s, imaging volume = 22x22x16 cm³, isotropic spatial resolution = 0.7mm³,

repetition time/echo time = 7.4/2.7 ms, 14,000 projection angles, scan time ~ 7 minutes, flip angle = 10°, bandwidth = ±83.3 kHz. Magnitude and velocity data were generated using an offline reconstruction software for all subjects.

Technical Application

Patient #1 was a 6-month old girl referred due to significant developmental delay. She was found to have a mural type VOGM with secondary ventriculomegaly, venous hypertension and significant cortical volume loss. She underwent serial PCVIPR imaging before (baseline PCVIPR imaging, Figure 1A) and after multiple endovascular interventions. The PCVIPR imaging following stage 1 trans-arterial embolization of multiple feeding pedicles indicated moderate reduction of inflow into the primitive vein of Markowski. Flow quantification on PCVIPR imaging reflected the expected post-treatment hemodynamic changes (Figure 1B). Further staged trans-venous embolization of the vein of Markowski enabled significant decrease of flow across the fistula as evidenced on pressure changes visualized on PCVIPR images (Figure 1C). Embolization with documented decreased flow and pressure on PCVIPR correlated with a significant improvement in neurological function from somnolent and no purposeful activity to increased alertness, increased interaction with parents, vocalization and improved motor function. Due to the acute flow reduction and severe jugular bulb/vein outflow stenosis, the patient developed progressive sinus thrombosis necessitating anticoagulation and antiplatelet therapy. The child was clinically stable and following 3 months of anticoagulation, follow-up PCVIPR imaging demonstrated a near-quadruple flow recruitment over this time period (Figure 1D). Given these new PCVIPR findings additional embolization procedures were planned.

Patient #2 is a 30-month old girl who presented with progressive macrocephaly and mild developmental delay. Imaging indicated a mural type VOGM fed primarily by multiple right posterior thalamic perforator branches off the posterior cerebral artery. Baseline PCVIPR imaging was obtained (Figure 2A). PCVIPR imaging following Stage 1 trans-arterial embolization showed modest reduction of inflow into the vein of Markowski (Figure 2B). Repeat imaging (Figure 2C), after Stage 2 embolization with closure of the largest feeding artery as well as a portion of the vein of Markowski, demonstrated normalization of flow and pressure within the right internal carotid artery and the posterior communicating artery. Her scheduled Stage 3 embolization was delayed due to respiratory illness. Although she was neurologically stable, PCVIPR imaging obtained 4 months after Stage 2 embolization, demonstrated universally increased venous and basilar flow with increased pressure in the venous outflow (Table 2).

Following residual embolization and complete occlusion of the Vein of Markowski during Stage 3, PCVIPR (Figure 2, D) accurately demonstrated absence of venous flow. This illustrative example demonstrates the utility of PCVIPR in demonstrating how non-invasive interim measurements of elevated PCVIPR pressure or flow during staged treatments help determine the optimal timing of further therapeutic embolizations in an otherwise developmentally stable child. Identification of elevated PCVIPR pressure or increasing flow measurements, similar to her pre-treatment measurements, therefore assisted in dictating timing for subsequent embolization.

Patient #3 was a full term infant with a choroidal VOGM who developed congestive heart failure 5 days after birth requiring multiple staged embolization procedures. The initial pre-operative MR scans were performed at an outside hospital without PCVIPR and also were before we were using PCVIPR for VOGM at our hospital. Figure 4 demonstrates PCVIPR imaging after several staged embolizations had been performed (A), the final completion embolization (B) and a 15 month follow-up MR confirming durability of the embolization repair (C). Table 3 demonstrates quantitative measurements of pressure changes from interim to final embolization and 15 month follow-up.

Patient #4 was a full term infant whose VOGM lesion was detected prenatally with ultrasound; on pre-operative MR imaging the VOGM was shown to be a mixed but predominantly mural VOGM. Figure 5 demonstrates her pre-operative PCVIPR imaging. The lesion was treated at another center that did not perform PCVIPR.

Discussion

VOGM is a rare congenital arteriovenous fistula which drains into an aberrant primitive deep venous system with nearly 100% mortality if left untreated^{1, 3}. Lasjaunias et al proposed the Bicetre evaluation score based on clinical assessment of VOGM sequelae to guide initiation and timing of therapeutic intervention^{2, 3}. Their contribution has improved our understanding of VOGMs and significantly reduced therapeutic complications associated with improper timing or inadequate assessment of these patients. Various radiographic biomarkers that portend poor prognosis include venous outflow obstruction, absence of collateral venous drainage and high flow choroidal type fistulas⁴. These factors in addition to hydrocephalus, encephalomalacia, and cerebral edema suggest a poor natural history and are indications for surgical intervention.

Therapeutic intervention aims to reduce arteriovenous shunting below a certain threshold to prevent further neurologic or multi-organ deterioration while avoiding progressive outflow obstruction which can cause intracranial hemorrhage or venous infarction. The maintenance of cerebrovascular homeostasis within a fine balance during treatment is challenging especially due to lack of quantitative and qualitative flow/pressure measurements through the arterial venous fistula to guide management.

Moreover, serial radiographic assessments are imperative because the underlying angioarchitectural changes are often dynamic with varying periods of stability between ultimate progressions. Small feeding pedicles previously unseen on diagnostic images can rapidly progress resulting in new or advancing clinical symptoms. To date, diagnostic cerebral angiography remains the gold standard modality due its superior anatomic and qualitative imaging quality. Its significant limitation is the absence of reproducible quantitative data and invasive nature especially in the infant population. There is growing interest in developing non-invasive modalities to quantitatively assess cerebral hemodynamics to guide therapeutic decision making.

PCVIPR is a novel 4D flow MRI technique which uses non Cartesian 3D radial undersampling for an accelerated acquisition while providing isotropic spatial resolution^{5, 6}.

This 4D flow MRI technique has potential utility in assessing patients with VOGMs by providing blood flow patterns, directionality and pressure gradients across a fistulous point while maintaining exceptional temporal and spatial resolution for anatomic and qualitative assessments, all within a single acquisition. Importantly, rapid acquisition obviates the need for frequent anesthetic sedation for serial imaging. Our group has previously demonstrated a high degree of correlation between invasive pressure measurements and PCVIPR-based flow assessment in intracranial aneurysms ($R = 0.82$, $P < 0.01$)⁷ and dural arteriovenous fistulas⁸.

We therefore implemented 4D flow MRI in VOGM patients to assess its potential for obtaining anatomic and physiologic flow data across the arterial venous fistula before and after endovascular embolization. We also compared these results to stump pressures recorded in-vivo inside the vein of Markowski using a microcatheter prior and subsequent to coil embolization⁹. We found a decrease in mean arterial pressure from 97 mmHg pre-treatment to 65 mmHg on immediate post-coiling evaluation. These findings reflect the decrement in venous pressure gradients documented on subsequent PCVIPR imaging. This high degree of association corroborates our previous results and suggests PCVIPR has a potential role in quantifying extent of embolization, estimating changes in arterial venous flow patterns and guiding timing for therapeutic intervention based on actual hemodynamic characteristics^{7, 8}. To our knowledge, our experience demonstrates the first application of non-invasive anatomical and physiological arterial venous fistula measurements for VOGM infants.

Patient #1 developed progressive venous thrombosis following second embolization due to a rapid and extensive inflow reduction into the vein of Markowski and severe jugular bulb/vein outflow stenosis. This child was successfully treated with anticoagulation without sequelae; however, large changes in venous pressure gradients across fistulous sites can result in devastating complications. Evaluation of PCVIPR flow/pressure changes following embolization in additional patients is necessary to assess the usefulness of this technique in guiding the extent and timing of endovascular intervention. PCVIPR may also shed light on the particular arterial venous hemodynamic patterns associated with development of poor outcome predictors such as venous outflow obstruction, venous hypertension and arterial steal. The relative speed of PCVIPR acquisitions also facilitates its prospective wider clinical use especially in the pediatric population.

Use of PCVIPR, as seen in our initial patients as a proof of concept, demonstrates the potential utility of this technique in assessing flow and pressure changes with treatment and, in future, guiding the extent and timing of intervention. Considerable further investigation is needed to quantify pressure gradient changes following staged treatments in normal and pathologic vascular conditions and develop pressure parameters to guide therapeutic decision making in future. In addition to the Bicetre Evaluation Score, PCVIPR flow and venous pressure measurements could guide intervention.

Conclusion

Vein of Galen malformation (VOGM) hemodynamics induce cerebrovascular dysfunction through arterial steal and venous hypertension resulting in poor clinical outcomes. At

present there is a lack of non-invasive techniques to evaluate cerebral hemodynamics in VOGMs. We demonstrate a proof of concept that the application of qualitative and quantitative data from 4D flow MRI/PCVIPR imaging can serve as a non-invasive biomarker and, with future investigation, may prove to be a reliable indicator of treatment success and/or disease progression. If true, MRI PCVIPR may be used in the future to help objectively guide management decisions in patients with VOGMs.

Acknowledgements

The authors would like to thank the University of Wisconsin Department of Neurosurgery and Radiology for their guidance and support. Grant support was provided by NINDS R01NS066982 and NIA R01AG021155.

Glossary

PCVIPR	Phase Contrast Vastly undersampled Isotropic PROjection imaging
VOGM	vein of galen malformation
4D Flow MRI	time-resolved 3D phase contrast MRI

References

1. Khullar D, Andeejani AM, Bulsara KR. Evolution of treatment options for vein of Galen malformations. *J Neurosurg Pediatr.* 2010 11;6(6):444–51 [PubMed: 21039167]
2. Lasjaunias PL, Chng SM, Sachet M, Alvarez H, Rodesch G, Garcia-Monaco R. The management of vein of Galen aneurysmal malformations. *Neurosurgery.* 2007 4;60(4):393
3. Frawley GP, Dargaville PA, Mitchell PJ, Tress BM, Loughnan P. *Arch Dis Child Fetal neonatal Ed.* 2002 9;87(2):144–9
4. Geibprasert S, Krings T, Armstrong D, Terbrugge KG, Raybaud CA. Predicting factors for the follow-up outcome and management decisions in vein of Galen aneurysmal malformations. *Childs Nerve Syst.* 2010 1;26(1):35–46
5. Gu T, Korosec FR, Block WF, Fain SB et al. PCVIPR: a high-speed 3D phase-contrast method for flow quantification and high-resolution angiography. *Am J Neuroradiol.* 2005 4;26(4):743–9 [PubMed: 15814915]
6. Johnson K, Lum D, Turski P, et al. Improved 3D phase contrast MRI with off-resonance corrected dual echo VIPR. *Magn Reson Med* 2008; 60: 1329–1336. [PubMed: 19025882]
7. Moftakhar R, Aagaard-Kienitz B, Johnson K, Turski PA et al. Noninvasive measurement of intra-aneurysmal pressure and flow pattern using phase contrast with vastly undersampled isotropic projection imaging. *Am J neuroradiol.* 2007 10;28(9):1710–14. [PubMed: 17885239]
8. Rivera-Rivera LA, Johnson KM, Turski PA, Wieben O. Pressure Mapping and Hemodynamic Assessment of Intracranial Dural Sinuses and Dural Arteriovenous Fistulas with 4D Flow MRI. *Am J neuroradiol.* 2018, 39 (3) 485–487. [PubMed: 29269408]
9. Fleischer LH, Young WL, Pile-Spellman J, et al. Relationship of transcranial Doppler flow velocities and arteriovenous malformation feeding artery pressures. *Stroke.* 1993;24(12): 1897–1902. [PubMed: 8248974]

Highlights

- In-vivo flow and pressure measurements during angiography corroborate changes in flow and pressures obtained from PCVIPR imaging
- PCVIPR has a potential role to quantify extent of embolization with surgical outcomes based on hemodynamic characteristics which would be a novel approach in treatment of cerebrovascular diseases.
- PCVIPR could be used to guide the extent and timing of surgical intervention by objectively quantifying cerebrovascular changes following embolization.

Figure 1.

Patient 1 was a 6-month-old girl with developmental delay and an underlying mural-type vein of Galen malformation with secondary ventriculomegaly, venous hypertension, and volume loss. Color pressure maps (mm Hg) of baseline PCVIPR imaging (**A**) were obtained identifying the vein of Galen (*VoG*), straight sinus (*SS*), and torcular herophili (*TH*). Stage 1 transarterial transfemoral embolization of multiple feeding pedicles enabled moderate reduction of inflow into the primitive vein of Markowski (**B**). Further staged transvenous transfemoral embolization of the vein of Markowski enabled significant decrease of flow across the fistula; basilar artery (*BA*) (**C**). Follow-up *Phase Contrast Vastly undersampled Isotropic PROjection* demonstrated marked progressive recruitment of flow over the past 3 months (**D**).

Figure 2.

Patient 2 was a 30-month-old girl who presented with enlarging head circumference and mild developmental delay found to have a mural-type vein of Galen malformation fed primarily by multiple right posterior thalamic perforator branches off the posterior cerebral artery. Color pressure maps (mm Hg) of baseline *Phase Contrast Vastly undersampled Isotropic PROjection* (PCVIPR) imaging were obtained; outflow measurement locus identified by arrow (A). Stage 1 transarterial embolization of a single medium-sized feeding pedicle was performed with modest reduction of inflow into the vein of Markowski (B). (C)

Normalization of flow and pressure within the right internal carotid artery and across the posterior communicating artery after stage 2 embolization. **(D)** Interval imaging before final, stage 3 embolization indicated increased venous outflow. **(E)** After final treatment, PCVIPR accurately depicts the absence of venous outflow.

Figure 3.
Grayscale angiogram showing Patient 2 anatomic landmarks for blood flow and pressure drops (P) quantification. Similar landmarks were used for all the patients.

Figure 4.

Patient 3 was a full-term baby who developed postnatal new-onset congestive heart failure with diastolic flow reversal of blood from the thoracic aorta and ductus arteriosus. Imaging showed a choroidal vein of Galen malformation (VoGM) with feeders from the anterior cerebral artery, bilateral posterior choroidal and posterior cerebral arteries, and left paramedian pericallosal and superior cerebellar artery, respectively. (A) Interim imaging after multiple staged embolizations showed remnant fistula feeders from feeders from bilateral posterior choroidal and posterior cerebral arteries with early venous drainage via

the median prosencephalic vein and subsequently the transverse and sigmoid sinuses. **(B)** Final closure of the VoGM was undertaken through embolization of the straight sinus with elimination of early venous shunting thereafter. **(C)** Follow-up imaging, 15 months later, shows stable resolution of arteriovenous shunting.

Figure 5.

Patient 4 was a full-term baby, with a prenatal vein of Galen malformation (VoGM) diagnosis through fetal magnetic resonance imaging (MRI). Postnatal MRI showed a mural VoGM with feeders from pericallosal artery, posterior communicating, choroidal and posterior cerebral arteries. Color pressure maps (mm Hg) of baseline *Phase Contrast Vastly undersampled Isotropic PROjection* (PCVIPR) imaging were obtained. Axial, coronal, and sagittal reconstructions demonstrate the predominant arterial supply from bilateral posterior choroidal vessels arising from posterior cerebral arteries. Additional supply is evident from the single pericallosal artery. The draining falcine sinus tapers at the torcular herophili. The family pursued treatment at another center, and follow-up PCVIPR imaging is not available.

Table 1.

Flow Measurements Through Treatment Course for Patient 1

Flow (mL/second) Measurement Location	Preembolization	Post First Embolization	Post Second Embolization
Straight sinus	6.51 ± 0.4	2.13 ± 0.9	1.72 ± 0.1
Basilar artery	3.98 ± 0.1	1.28 ± 0.3	0.63 ± 0.1

Table 2.

Pressure and Flow Measurements Through treatment course for patient 2

P (mm Hg) Measurement Location	Preembolization	Post First Embolization	Post Second Embolization	Pre Third Embolization	Post Third Embolization
Venous outflow (from end of aneurysm to end of left transverse sinus)	+0.123 ± 0.04	NA	-0.081 ± 0.02	-0.100 ± 0.01	NA
Left ICA (from cervical ICA to carotid siphon)	-0.501 ± 0.06	-0.620 ± 0.04	-0.371 ± 0.01	-0.248 ± 0.02	-0.431 ± 0.03
Right ICA (from cervical ICA to carotid siphon)	-1.028 ± 0.07	-0.644 ± 0.08	-0.353 ± 0.01	-0.004 ± 0.02	-0.440 ± 0.01
Basilar (from vertebral union to superior cerebellar artery)	-0.042 ± 0.01	-0.043 ± 0.07	-0.063 ± 0.03	-0.117 ± 0.04	-0.068 ± 0.02
Flow mL/second Measurement Location	Pre Embolization	Post First Embolization	Post Second Embolization	Pre Third Embolization	Post Third Embolization
Venous outflow	14.3 ± 0.1	13 ± 0.4	8.51 ± 0.2	9.66 ± 0.2	NA
Left ICA	6.27 ± 0.3	7.86 ± 0.4	7.05 ± 0.3	6.72 ± 0.2	5.84 ± 0.1
Right ICA	7.91 ± 0.2	8.95 ± 0.5	7.53 ± 0.2	6.83 ± 0.2	4.75 ± 0.3
Basilar	10.0 ± 0.1	10.8 ± 0.4	7.31 ± 0.2	8.66 ± 0.1	5.01 ± 0.2

ICA, internal carotid artery; NA, not applicable.

Table 3.

Pressure and Flow Measurements Through Treatment Course for Patient 3

P (mm Hg) Measurement Location	Post Interim Embolization	Post Final Embolization	Follow-Up at 15 Months
Venous outflow (from end of aneurysm to end of left transverse sinus)	-0.056 ± 0.01	NA *	NA *
Left ICA (from cervical ICA to carotid siphon)	-0.134 ± 0.02	-0.474 ± 0.02	-0.599 ± 0.02
Right ICA (from cervical ICA to carotid siphon)	-0.115 ± 0.02	$+0.015 \pm 0.01$	-0.054 ± 0.01
Basilar (from vertebral union to superior cerebellar artery)	-0.378 ± 0.04	-0.357 ± 0.03	-0.242 ± 0.01
Flow mL/second Measurement Location	Post Interim Embolization	Post Final Embolization	Follow-Up at 15 Months
Venous outflow	6.61 ± 0.1	NA *	NA *
Left ICA	4.18 ± 0.2	3.89 ± 0.2	3.73 ± 0.1
Right ICA	4.42 ± 0.1	4.71 ± 0.1	4.56 ± 0.3
Basilar	3.15 ± 0.1	1.96 ± 0.1	1.98 ± 0.1

Quantitative measurements of pressure changes following serial embolizations indicate correlation with clinical course and Phase Contrast Vastly undersampled Isotropic PROjection imaging. ICA, internal carotid artery.

* Measurement not possible due to lack of vessel signal.