# Computer simulation of Cerebral Arteriovenous Malformation - validation analysis of hemodynamics parameters (#8828)



First submission

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# Computer simulation of Cerebral Arteriovenous Malformation-validation analysis of hemodynamics parameters

Kiran Kumar, Shashi Mehta, Manjunath Ramachandra

The purpose of this work is to provide some validation methods for evaluating the hemodynamic assessment of Cerebral Arteriovenous Malformation (CAVM). The validation of hemodynamics assessment is based on invasive clinical measurements and with cross-validation techniques. This paper emphasizes the importance of vessel calibration and validation of lumped models. The validated model was then used for two further validation tests. Firstly, model simulations were compared with measurements from vessel locations of cerebral regions. The results are validated for 150 vessel locations validation showed significantly results compared to the invasivemeasurements. Secondly, model is cross validated with Philips propriety validated software. The results are validated with 30 CAVM datasets with sensitivity of 95% and specificity of 96%.

Note: The wording in the whole text including abstract requires extensive revisions.

# Computer simulation of Cerebral Arteriovenous Malformation- validation analysis of hemodynamics parameters

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Note: The background of 3rd author was not mentioned.

## Abstract:

Note: The authors do not use headings in structured abstract.

The purpose of this work is to provide some validation methods for evaluating the hemodynamic assessment of Cerebral Arteriovenous Malformation (CAVM). The validation of hemodynamics assessment is based on invasive clinical measurements and with cross-validation techniques. This paper emphasizes the importance of vessel calibration and validation of lumped models. The validated model was then used for two further validation tests. Firstly, model simulations were compared with measurements from vessel locations of cerebral regions. The results are validated for 150 vessel locations validation showed significantly results compared to the invasive measurements. Secondly, model is cross validated with Philips propriety validated software. The results are validated with 30 CAVM datasets with sensitivity of 95% and specificity of 96%.

**Keywords:** Arteriovenous Malformation, Validation, Simulation, Hemodynamics, Cross-Validation.

## 1.0 Introduction:

Note: The authors do not follow Standard Sections in the manuscript.

CAVM is one of the neurovascular malformation. In healthy normal's, arteries and veins are connected by capillaries. In CAVM - capillaries are absent resulting in tangled cluster of vessels. The vessel geometry in CAVM is complex in nature. The CAVM patients is affected by hemodynamics changes. Current clinical procedure is for diagnosis and treatment procedure is invasive technique. The invasive technique is riskier to patients as CAVM get rupture. The figure 1 shows complex structure of CAVM. The gold standard imaging for CAVM is Digital Subtraction Angiogram (DSA), figure 2 shows the CAVM – DSA image [1-3].

In this paper, we have validated our modeling results with clinical measurements and with cross –validation techniques. We replicate actual patient condition, by simulating similar condition of patient using Matlab simulation. Lumped models are created and simulated using different signal combinations. This helps to validate our results with clinical measurements.

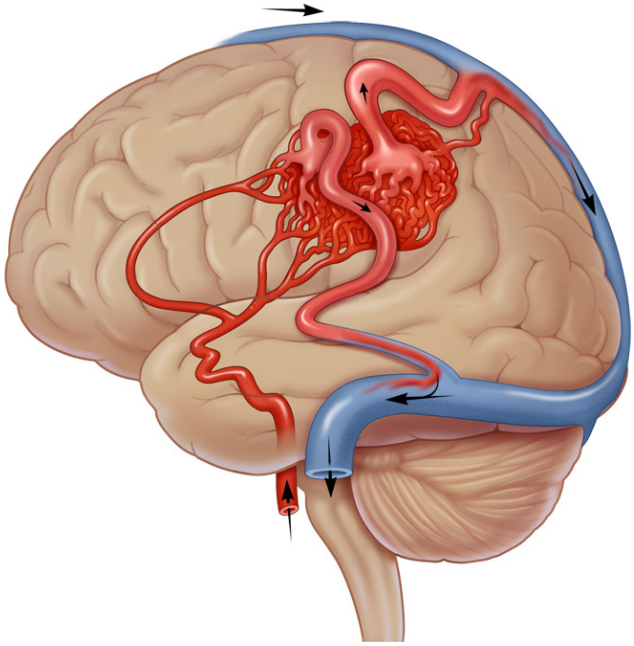


Figure 1- Cerebral Arteriovenous Malformation (CAVM).

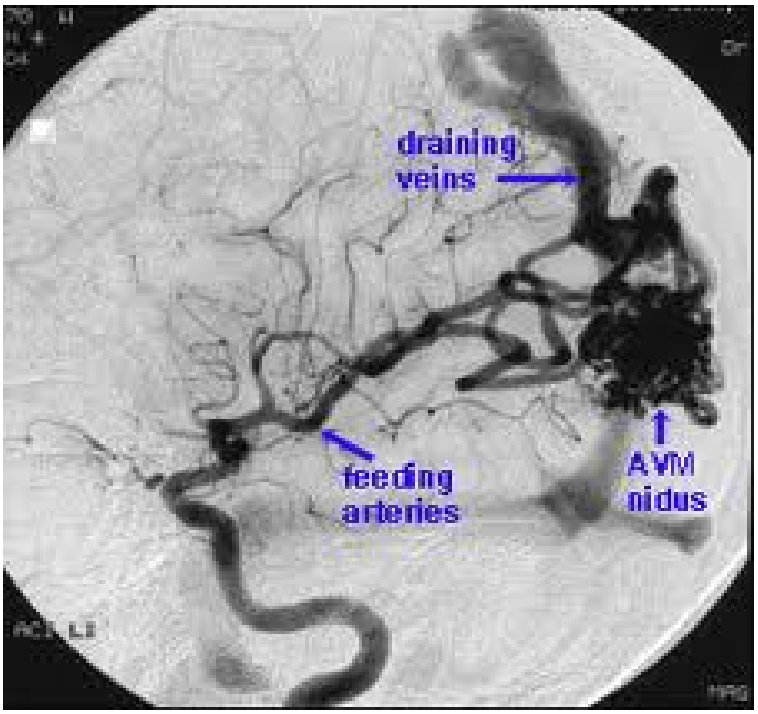



Figure 2- Digital Subtraction Angiogram of CAVM Image.

## 2.0 Methodology:

The non-invasive technique to measure hemodynamics in the complex vessel in CAVM is based on lumped model. In this paper, we focus on the different validation techniques to validate our modeling results. The non-invasive measurements are validated in two ways: Invasive technique

and Cross validation. The complex vessel structures are formed by combinations such as bifurcation, vessel feedback, vessel deformation, vessel collapsing, vessel bending, tortuosity, etc. The analysis for complex vessel structure is performed using lumped modeling [4, 5, 6]. The output pressure measurement of model is validated with invasive and cross-validation techniques.

## 2.1 **Invasive Techniques:**

The clinician performed procedure for acquire data from patient is to insert catheter from femoral artery by performing single and multi-puncture of the femoral artery, based on the patient physiological condition. The catheter is of 0.08 inch /0.2 mm with 200mm length [7]. The catheter wire is propagated slowly with various stuck-up at various bends and various structures changes of the vessels as shown in figure 3. The catheter is navigated slowly in between the path, till it reaches the CAVM vessels [8, 9].

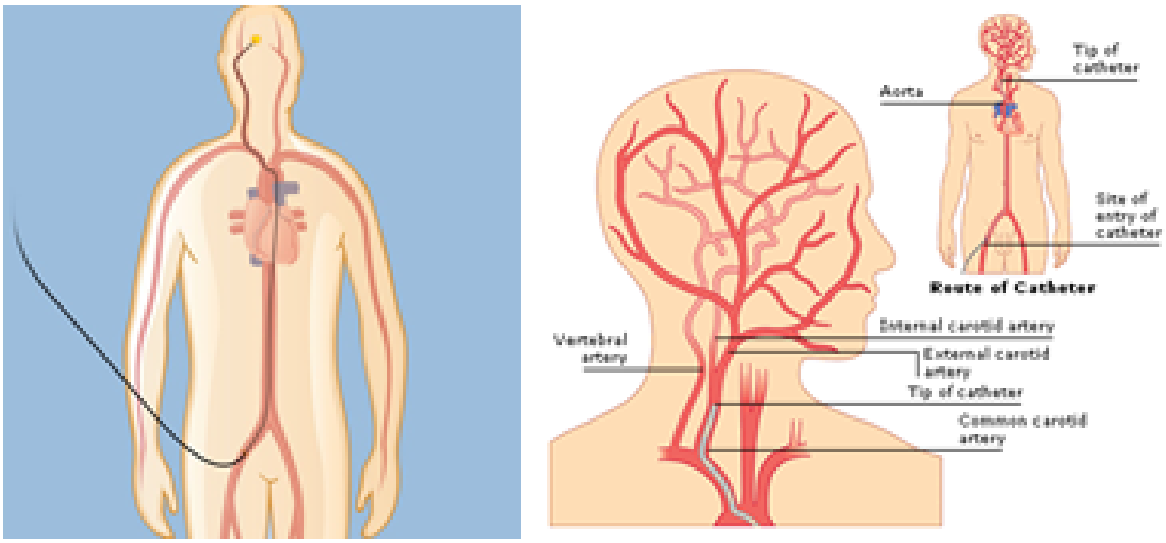



Figure 3 - Neurovascular Catheter Procedure

Note: The quality of Figure 3 is poor.

(Adapted from http://weillcornellbrainandspine.org/condition/stroke/surgery-ischemic-stroke )

The pressure bag has the pressure sensors that are connected externally to the guided catheter. The pressure bag readings are seen in patient monitor system. After reaching vertebra, the clinician measured the pressure value, which is measured from the patient monitor. The patient monitor also shows ECG, heart rate, respiratory rate along with pressure value. The figure 4 shows the snapshot of patient monitor along with pressure values obtained from Cathlab KMC Manipal. The pressure is measured for various arteries – left external carotid artery, internal carotid artery, posterior ~~carotid~~ cerebral artery, middle ~~carotid~~ cerebral artery, near Nidus. This procedure is commonly used procedure to measure pressure at various vessels locations in Cathlab. The pressure values obtained by clinical procedure is taken as reference for validation of modeling results.

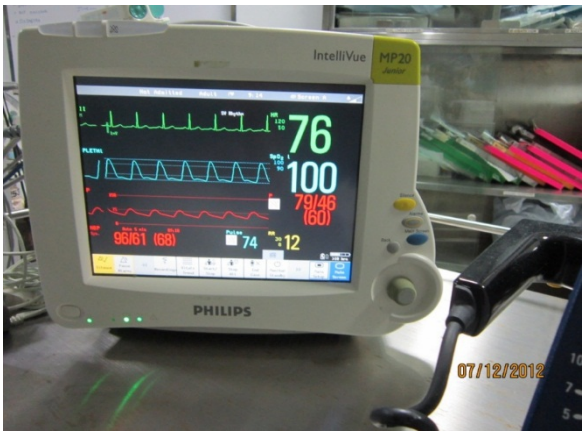



Figure 4- Clinical Pressure Measurements
(Courtesy: Kasturba Medical College & Hospital, Manipal)

## 2.2 Cross Validation:

Note: More detailed elaboration of the methods is required.

The cross validation techniques is type of validation, where the modeling results are cross validated with equivalent software, which produces same results. In our paper, we validated our results with Philips propriety software's such as Q-Flow and 2D-Perfusion analysis software.

### 2.2.1 Q-Flow Software:

The validations of complex geometries, feeding arteries are performed using Philips propriety product called Qflow. Qflow is developed and validated by Philips Healthcare. Qflow is common practice in hospitals for clinical diagnosis and treatment. This is as validated software, accepted by clinicians [10, 11]. The Qflow application requires MR Angiogram (MRA) data – Fast Field Echo (FFE) & Phase, for processing. MRA data of CAVM patient with different phase information is obtained from KMC hospital.

### 2.2.2 2D-Perfusion Software:

The modeling results are validated with Philips Propriety Cathlab software - 2D-Perfusion. The input data is DSA image. Philips validated 2D Perfusion software is a software product that provides functional information about tissues perfusion based on a digital subtraction angiography (DSA). It can visualize multiple parameters related to perfusion.

# 3.0 Results and Discussion:

Note: There is no Discussion.

## 3.1 Invasive Validation:

The invasive hemodynamics measurement inside NIDUS is risker, due to complex geometric structure of NIDUS. However, with help of clinicians in Cathlab, KMC Manipal, able to measure pressure values near locations of Nidus. The various locations are External Carotid artery, internal carotid artery, and Posterior cerebral arteries [12]. The simulation is performed for the complete path node1 to node5, refer figure 5. The pressure measurements for loop structure is shown in table 1.The model is simulated with different signal magnitude variations. The pressure measurements are validated with results of clinical simulations. The amount of percentage deviation shows the difference between the measured results and clinical results. The deviation is within acceptable range as per clinicians after validating with visual inspection.

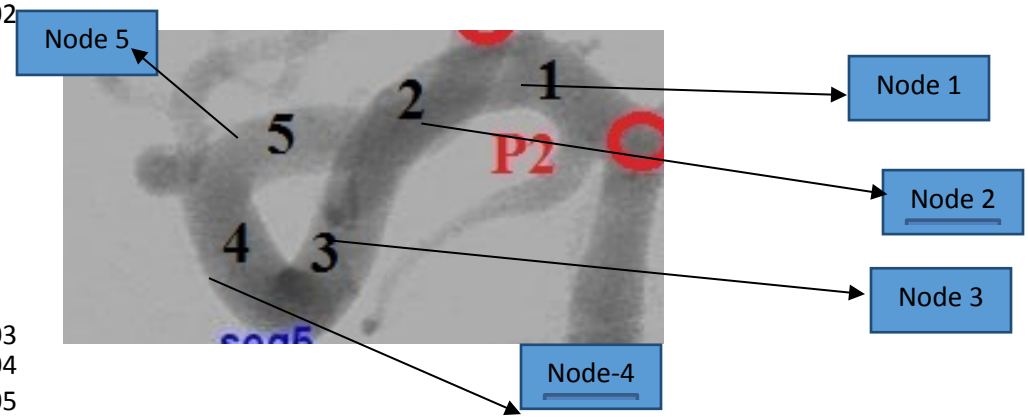



Figure 5- Complex Vessel Structure

| Nodes | Input voltage Pressure = 0.8 volt / 80mmHg | | |
|---|---|---|---|
| | Measured value | Clinical results | Deviation % |
| Node1 | 0.72v/72mmHg | 0.74v/74mmHg | 2.7 |
| Node2 | 0.7v/70mmHg | 0.72v/72mmHg | 2.7 |
| Node3 | 0.57v/57mmHg | 0.60v/60mmHg | 5 |
| Node 4 | 0.52v/52mmHg | 0.55v/55mmHg | 5.4 |
| Node5 | 0.47v/47mmHg | 0.50v/50mmHg | 6 |

Table 1- Loop Structure Pressure Measurements and Analysis

### 3.2 Cross Validation Techniques:

#### 3.2.1 Q-Flow Validation:

The study is validated by comparing results of Qflow results with modeling results. The Qflow processing results are velocity components for specific node/region. The velocity is converted to pressure values and compared with our modeling results. The figure 5 shows the MRA image of CAVM patient with velocity results for the drawn region of interest in cerebral vascular region. The table 3 shows comparison results modeling and Qflow results along with amount of difference between them. The Qflow validation analysis is performed for each phase acquisition of MRA of CAVM patient. The table 4 shows the pressure values for various phase & vessel regions along with comparison analysis with modelling results along with difference between them.

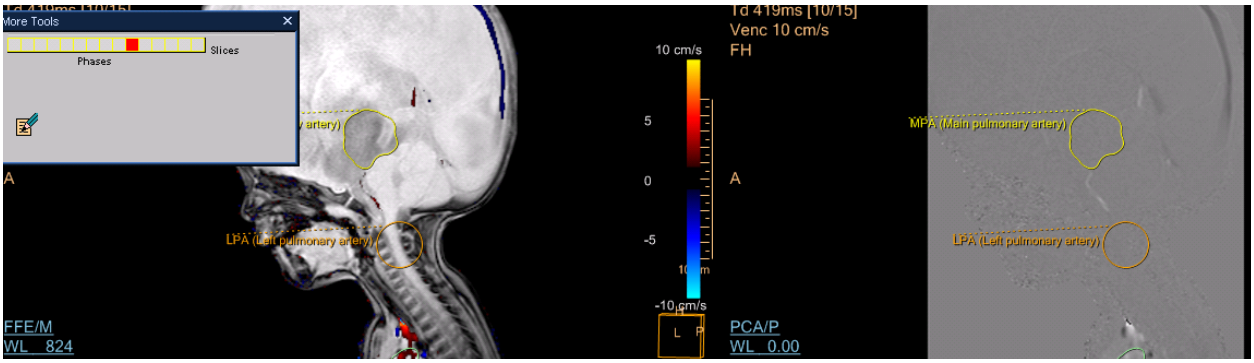



Figure 5- Qflow analysis with node locations

Note: MPA and LPA here are "pulmonary" arteries?

Pre-requisite: Conversion of maximum velocity to volts

| Vessel location as per figure 5 | Flow outputs Peak velocity as per Qflow outputs in volts | Electrical Network – Modeling output | Deviation % |
|---|---|---|---|
| Input | 0.02Volts – input voltage (Qflow initial velocity –max 200cm/s) | 0.0187Volts | 6.5 |
| Location 1 | 0.012 volts | 0.01 volts | 0.001 |
| Location 2 | 0.003 volts | 0.0225 | 0.0195 |

Table 3: Qflow validation with modeling results

Note: Table 2 is missing.

Conversion factor:
Input location: mean – 0.4cm/s = 0.03Volts – input voltage
Location 1- 0.2cm/s-0.015 volts
Location 2- 0.1cm/s-0.01 volts

| Phase 3: | | | |
|---|---|---|---|
| Vessel locations as per figure 5 | Flow outputs Mean velocity (in volts) | Electrical Network Modeling output | Deviation % |
| Input | 0.03 | 0.0278 | 0.0022 |
| Location 1 | 0.015 | 0.01 | 0.005 |
| Location 2 | 0.01 | 2x10-4 | 0.0098 |

| Phase 5: |
|---|

| Vessel locations as per figure 5 | Flow outputs Mean velocity | Electrical Network Modeling output | Deviation % |
|---|---|---|---|
| Input | 0.05 | 0.0489 | 0.011 |
| Location 1 | 0.035 | 0.030 | 0.005 |
| Location 2 | 0.02 | 0.018 | 0.002 |

| Phase - 8 | | | |
|---|---|---|---|
| Vessel locations as per figure 5 | Flow outputs Mean velocity | Electrical Network Modeling output | Deviation % |
| Input | 0.35 | 0.337 | 0.013 |
| Location 1 | 0.28 | 0.268 | 0.012 |
| Location 2 | 0.19 | 0.178 | 0.012 |

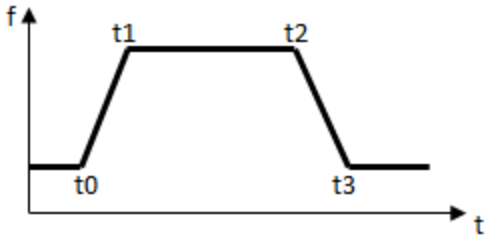
| Phase 11 | | | |
|---|---|---|---|
| Vessel locations as per figure 5 | Flow outputs Mean velocity | Electrical Network Modeling output | Deviation % |
| Input | 0.40 | 0.382 | 0.018 |
| Location 1 | 034 | 0.329 | 0.011 |
| Location 2 | 0.31 | 0.291 | 0.019 |

Table 4: CAVM -MRA flow study for various phases & CSF region

**3.2.2 2D-Perfusion validation:**

. 2D Perfusion can be used for identification of perfusion alterations in blood vessel perfusion behavior e.g. in CAVM. The following are the list of parameters that are used for validation with modeling outputs:

- Model fit to the Time density Curve:




- Time of Arrival = t0
- Time to Peak = (t1+t2) / 2
- Wash-in rate:

$$r = \frac{f(t0) - \frac{\int_{t1}^{t2} f(t)dt}{t2 - t1}}{tp - t0} = \frac{(t2 - t1)f(t0) - \int_{t1}^{t2} f(t)dt}{(t2 - t1)(tp - t0)}$$

- Width = (t2+t3)/2 - (t0+t1)/2
- Area under Curve:

$$A = \int_{t0}^{t3} (f(t) - f0)dt$$

- Mean Transit Time:

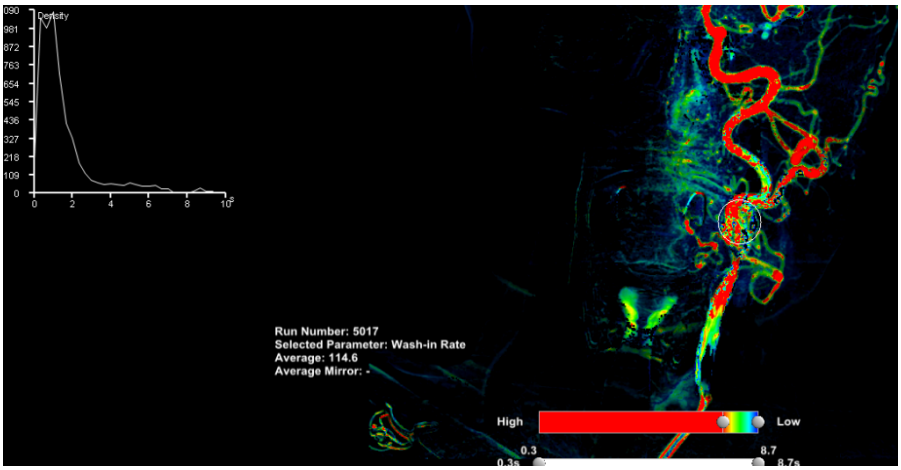
$$MTT = \frac{\sum_{i=0}^{3} t_i f(t_i)}{\sum_{i=0}^{3} f(t_i)}$$

These clinical parameters are the output of perfusion software. These parameters are converted in to the electrical equivalent for validation analysis, the details are as follows:

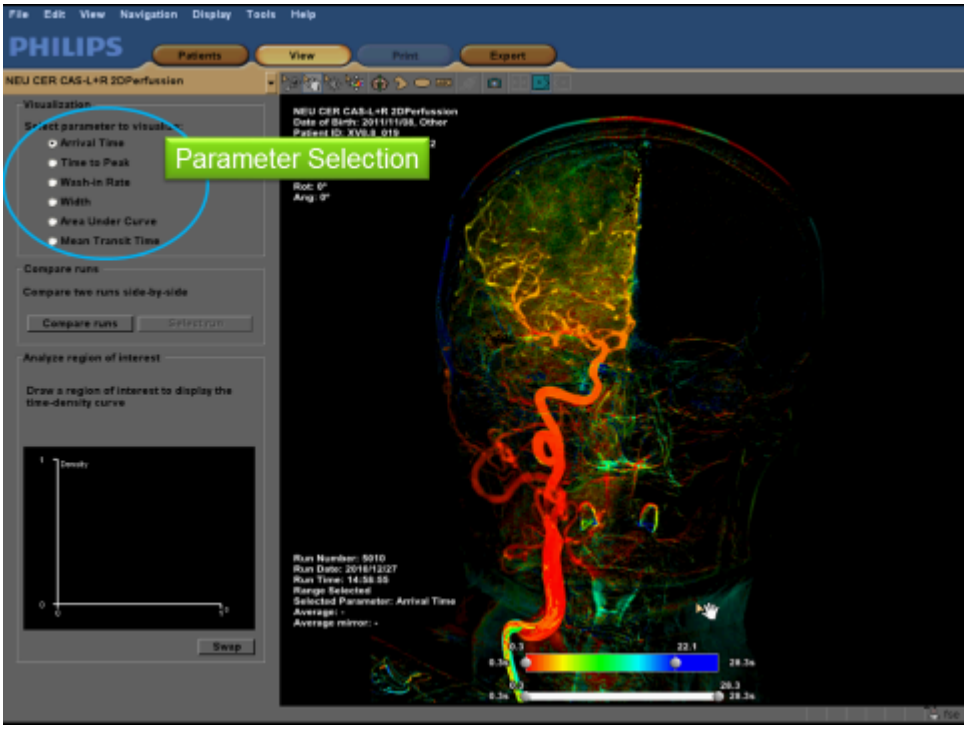
- Cerebral Blood flow (CBF) ~ Wash in Rate- Flow rate ~ current
- Cerebral Blood Volume (CBV) ~ Area under Curve / Width – velocity ~ pressure
- Mean Transit Time (MTT) ~ CBV / CBF = (Area under Curve / Width) / Wash in Rate-Friction coefficient ~ Resistance

The model is validated with 15 DSA data of CAVM patients. The results are nearly matching with accuracy of 85%. The effect of conversion approximation of software have effect of accuracy between modeling results, yet the results are acceptable by clinicians after visual inspection. The snapshot of 2D-Perfusion along with clinical parameters is shown in figure 6, are as follows:

193


Density
Run Number: 5017
Selected Parameter: Wash-in Rate
Average: 114.6
Average Mirror: -
High
Low
0.3
8.7

194


File Edit View Navigation Display Tools Help
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Time to Peak
Wash-in Rate
Width
Area Under Curve
Mean Transit Time
Parameter Selection
Compare runs
Compare two runs side-by-side
Compare runs
Spectrum
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Draw a region of interest to display the time-density curve
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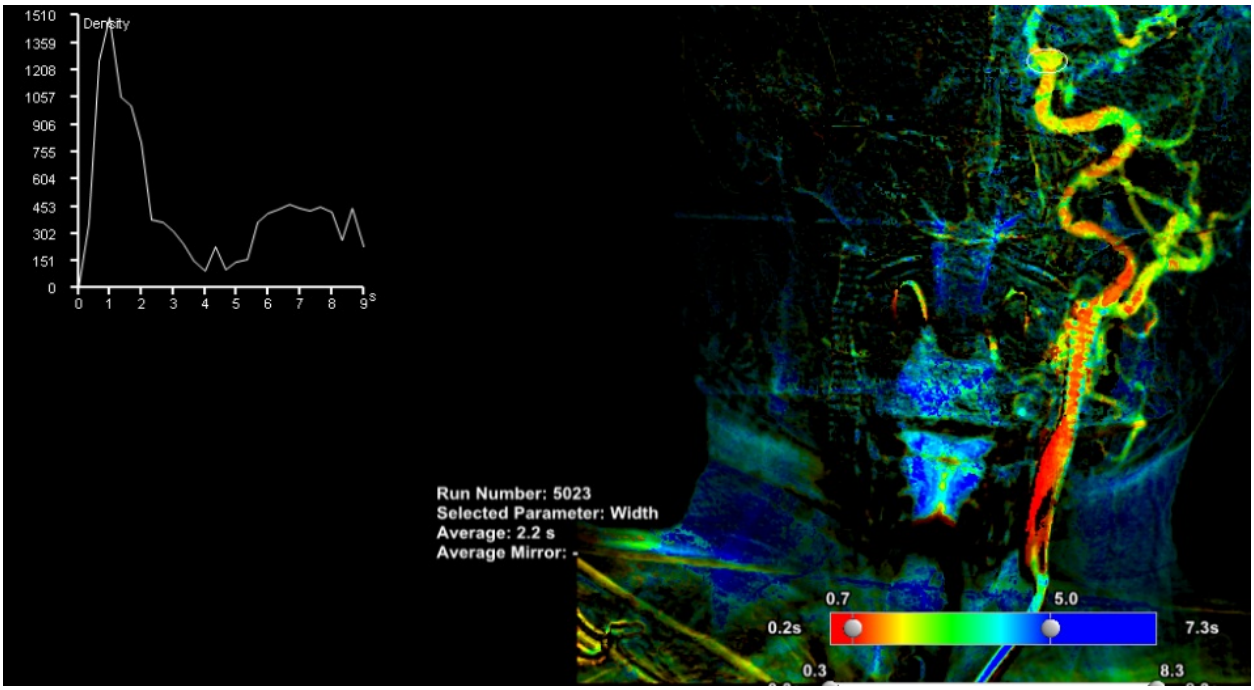
22.1
28.3



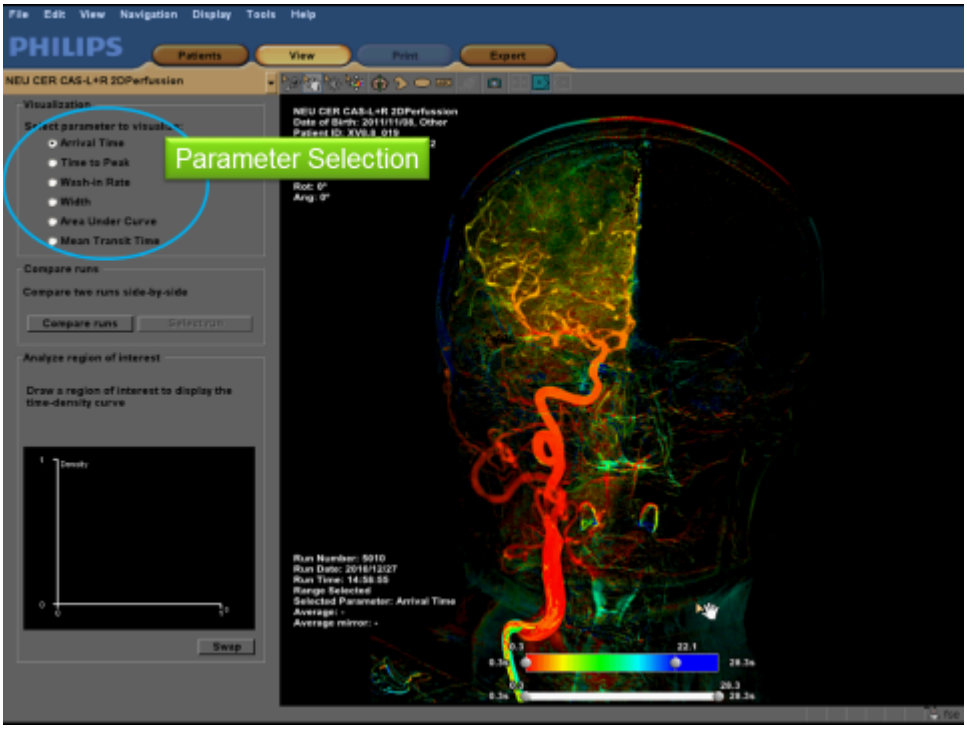




Figure 6- 2D-Perfusion analysis

The table 5 shows validation analysis for various locations of vessels along with percentage deviation.

| Vessel location as per figure 6 | Cerebral Blood Volume (Pressure in volts) | Electrical Network Modeling output | Deviation % |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Input | 0.12Volts | 0.115Volts | 4.1 |
| Location 1 | 0.22 volts | 0.209 volts | 5 |
| Location 2 | 0.43 volts | 0.415 volts | 3.4 |

Table 5- 2D Perfusion – Cross validation.

Statistical Analysis:

Mean flow, diameter, and pressure were compared between modeling results and with clinical/cross validation measurements, using independent 2-tailed Student t test. Exponential regression analysis was used to assess the relationship between blood flow, vessel diameter, and pressure between them. Univariate analysis is used to assess the relationship between vessel diameter, vessel cross-sectional area, AVM volume, AVM pressure, and AVM flow results was performed with linear or exponential regression. All the collected data were submitted to usual descriptive statistical analyses. Two-way tables were checked by using Fisher's exact test, and regular logistic regression was used to evaluate the association between pressure and diameter variation in the vessel. All analyses were performed with SPSS (Version 22; IBM Inc.)[13].

| Quantification Parameters | Node1 Output voltage | Node2 output voltage | Node3 output voltage | Node4 output voltage | Node5 output voltage |
|---|---|---|---|---|---|
| Count | 12 | 12 | 12 | 12 | 12 |
| Minimum | 3.4159 | 3.4159 | 3.4159 | 3.4159 | 3.4159 |
| Maximum | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 |
| Sum | 19.42477 | 19.42477 | 19.42477 | 19.42477 | 19.42477 |
| Mean | 4.4159 | 3.4159 | 3.4159 | 3.4159 | 3.4159 |
| Median | 3.14159 | 3.14159 | 3.1414 | 3.15 | 3.15 |
| Mode | N/A | N/A | 3.1414 | N/A | N/A |
| Range | 0 | 0 | 0.00018 | 0 | 0 |
| Interquartile range | 0 | 0 | 0.00018 | 0 | 0 |
| Standard deviation (range) | 5.43896E-16 | 5.43896E-16 | 5.43896E-16 | 0 | 0 |

| | | | | | |
|---|---|---|---|---|---|
| Standard deviation (Population) | 5.44089E-16 | 5.44089E-16 | 5.44089E-16 | 0 | 0 |
| Variance (Sample) | 3.95823E-31 | 3.95823E-31 | 3.95823E-31 | 0 | 0 |
| Variance (Population) | 1.97215E-31 | 1.97215E-31 | 1.97215E-31 | 0 | 0 |
| Sum of Squares | 39.60876318 | 39.60876318 | 39.60876318 | 39.60876318 | 31.7675 |
| Mean Squared Error | 9.869587728 | 9.869587728 | 9.868770939 | 9.9225 | 9.93 |
| Root Mean Squared Error | 3.14159 | 3.14159 | 3.141460001 | 3.15 | 3.151 |
| Mean Absolute Deviation | 4.44089E-16 | 4.44089E-16 | 8E-05 | 0 | 0 |
| Skewness | 2.449489743 | 2.449489743 | 1.732050808 | 65535 | 65535 |
| Standard error of Skewness | 1.224744871 | 1.224744871 | 1.224744871 | 1.224744871 | 1.224744871 |
| Excess Kurtosis | 65535 | 65535 | 65535 | 65535 | 65535 |
| Standard Error of Kurtosis | 65535 | 65535 | 65535 | 65535 | 65535 |
| Jacque-Bera Test Stat | 65535 | 65535 | 65535 | 65535 | 65535 |
| Durban-Watson Test Stat | 0 | 0 | 1.6416E-09 | 0 | 0 |

Table 6: Statistical analysis for various node output of loop structure

Note: This table is difficult to interpret.

Node voltage outputs were expressed as mean value ±Standard deviation. A P-value<0.05 was considered significant. A total of two AVM patients were studied with evaluation of 150 vessels locations as node point were evaluated for complex structure, with accuracy of 89%. The

statistical analysis for various node output of loop structure is shown in table 6. Refer figure 3, for node details.

Conclusion:

In this paper, we have validated our modeling results with clinical measurements. The new approach for cross-validation is proposed, by validating our results with validated product in clinical environment. The results are validated for 150 vessel locations validation showed significantly results compared to the invasive measurements. Secondly, model is cross validated with Philips propriety validated software. The results are validated with 30 CAVM datasets with sensitivity of 95% and specificity of 96%.

Note: The sensitivity and specificity appear abruptly.

References:

[1]. Liu et.al. Recursive tracking of vascular networks in angiograms based on the detection-deletion scheme. IEEE Trans Med Imaging. 1993; 12(2):334-41.

[2] Omar Saleh et.al. Arteriovenous Malformation, complications, and perioperative anesthetic management. M.E.J. Anesth 2008; 19 (4): 737-56.

[3].Yasargil MG. Association of aneurysms and AVM. In: Yasargil MG, ed. Microneurosurgery. Vol IIIA Stuttgart: George Thieme Verlag, 1987:182-189.

[4] Y.Kiran Kumar, Shashi Mehta, and Manjunath Ramachandra. Cerebral Arteriovenous Malformation Modeling. Advanced Science, Engineering and Medicine. 2014; 6:105-107.

[5] Y.Kiran Kumar, Shashi Mehta, and Manjunath Ramachandra: Review Paper: Cerebral Arteriovenous Malformations Modelling. International Journal of Scientific and Engineering Research 2013, 4:129-139.

[6] Y.Kiran Kumar, Shashi Mehta, Manjunath Ramachandra: Lumped Modelling of Bifurcation – Cerebral Arteriovenous Malformation. International Journal of Applied Information Systems 2013; 6:19-21.

[7] Omar Saleh et.al. Arteriovenous Malformation, complications, and perioperative anesthetic management. M.E.J. Anesth 2008; 19 (4): 737-56.

[8].Yasargil MG. Association of aneurysms and AVM. In: Yasargil MG, ed. Microneurosurgery. Vol IIIA Stuttgart: George Thieme Verlag, 1987:182-189.

[9] Ondra SL, Troupp H, George ED, Schwab K: The natural history of symptomatic arteriovenous malformations of the brain: A 24 year follow-up assessment. J Neurosurg 1990; 73:387-391.

[10] Lotz J et.al. Cardiovascular Flow Measurement with Phase-Contrast MR Imaging: Basic Facts and Implementation. RadioGraphics 2002; 22:651–671.

[11]Kondo et.al. Right and left ventricular stroke volume measurements with velocity-encoded cine MR imaging: invitro and in vivo validation. AJR Am J Roentgenol. 1991; 157(1):9-16.

269 [12] Standring. Gray's Anatomy: The Anatomical Basis of Clinical Practice, 40th Edition,
270 Churchill Livingstone, 2008.

271 [13] Anna M. Fica, Derek B.Inghamb, Maciej K. Ginalskic, Andrzej J. Nowakd,Luiz C. Wrobelea.
272 Modelling and optimization of the operation of a radiant Engineering Bristol, United Kingdom
273 Centre for CFD. Medical Engineering & Physics 2014; 36(1):81-87