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

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Problem: The purpose of this work is to provide some validation methods for evaluating the hemodynamic assessment of Cerebral Arteriovenous Malformation (CAVM). This paper emphasizes the importance of validating noninvasive measurements for CAVM patients, which is designed using lumped models for complex vessel structure. Methods: The validation of hemodynamics assessment is based on invasive clinical measurements and cross-validation techniques with Philips propriety validated software's Qflow and 2D-Perfusion. Results: The modeling results are validated for 30 CAVM patients for 150 vessel locations. 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. Discussion: Modeling results were compared with clinical measurements from vessel locations of cerebral regions. Secondly, model is cross validated with Philips propriety validated software's Qflow and 2D-Perfusion. Our results shows modeling results and clinical results is nearly matching with a smaller deviation. 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.

# Computer Simulation of Cerebral Arteriovenous Malformation- Validation Analysis of Hemodynamics Parameters

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## Abstract:

Problem: The purpose of this work is to provide some validation methods for evaluating the hemodynamic assessment of Cerebral Arteriovenous Malformation (CAVM). This paper emphasizes the importance of validating noninvasive measurements for CAVM patients, which is designed using lumped models for complex vessel structure.

Methods: The validation of hemodynamics assessment is based on invasive clinical measurements and cross-validation techniques with Philips propriety validated software's Qflow and 2D-Perfursion.

Results: The modeling results are validated for 30 CAVM patients for 150 vessel locations. 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. The AVM modeling results are compared with Philips property software Qflow. The modelling results is matching nearly with 90% accuracy with Qflow results. The 2D perfusion modeling results matches nearly 88% accuracy with 2D Perfusion software.

Discussion: Modeling results were compared with clinical measurements from vessel locations of cerebral regions. Secondly, model is cross validated with Philips propriety validated software's Qflow and 2D-Perfursion. Our results shows modeling results and clinical results are nearly matching with a deviation of 10-12%

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.

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

## 1.0 Introduction:

CAVM is one of the neurovascular malformations. The cerebral vasculature of healthy normal's consists of arteries and veins which 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 patient is affected by hemodynamics changes. Invasive techniques are the current clinical procedure to measure hemodynamics of CAVM. The invasive technique is riskier to patients as CAVM get rupture. 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 [Liu 1993; Omar Saleh 2008; Yasargil MG 1987].

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.

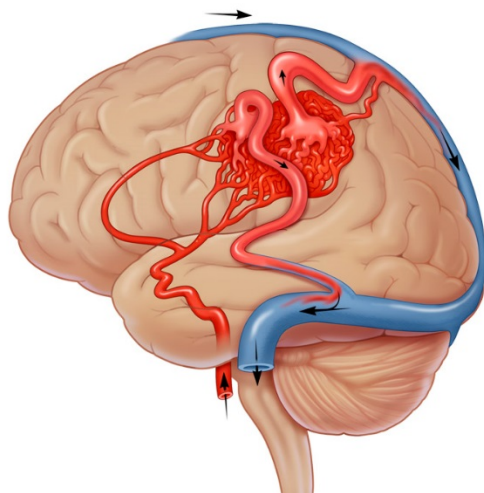
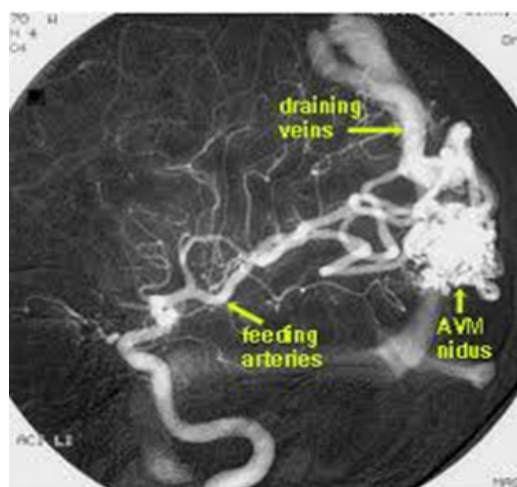



Figure 1- Cerebral Arteriovenous Malformation (CAVM).

53    Figure 2- Digital Subtraction Angiogram of CAVM Image.

## 54    2.0 Methodology:

55    The non-invasive technique to measure hemodynamics in the complex vessel in CAVM is based
56    on lumped model. In this paper, we focus on the different validation techniques to validate our
57    modeling results. The non-invasive measurements are validated in two ways: Invasive technique
58    and Cross validation. The complex vessel structures are formed by combinations such as
59    bifurcation, vessel feedback, vessel deformation, vessel collapsing, vessel bending, tortuosity, etc.
60    The analysis for complex vessel structure is performed using lumped modeling [Kumar, Mehta &
61    Ramachandra, 2014; Kumar, Mehta & Ramachandra, 2013a; Kumar, Mehta & Ramachandra,
62    2013b]. The output pressure measurement of lumped model is validated with invasive and cross-
63    validation techniques for 30 CAVM patients, with 150 vessel locations.
64
65    2.1 **Invasive Techniques:**

66         The clinical procedure to acquire data from patient, is to insert catheter from femoral artery
67    by performing single and multi-puncture in the femoral artery. The catheter is of 0.08 inch /0.2
68    mm with 200mm length [Omar Saleh 2008]. The catheter wire is propagated slowly with various
69    stuck-up at various bends and various structure changes of the vessels as shown in figure 3. The
70    catheter is navigated slowly in between the path, till it reaches the CAVM vessels [Valavanis et.al,
71    2005]. The ethical clearance is received for this study. The KMC Manipal has approved the
72    clearance for this study.

73

74    Figure 3 - Neurovascular Catheter Procedure

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

76    The pressure bag has the pressure sensors that are connected externally to the guided catheter. The
77    pressure bag readings are shown in patient monitor system. After reaching required vessel location,
78    the clinician measure the pressure value from the patient monitor. The patient monitor also shows
79    ECG, heart rate, respiratory rate along with pressure value. Figure 4 shows a patient monitor along
80    with pressure values obtained from Cathlab KMC Manipal. The pressure is measured for various
81    arteries – left external cerebral artery, internal carotid artery, posterior cerebral artery, middle

82  cerebral artery, near Nidus [Standring 2008]. This procedure is used to measure pressure at various
83  vessels locations in Cathlab. The pressure values obtained by clinical procedure is taken as
84  reference for validation of modeling results.

85

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

88  **2.2 Cross Validation:**

89  The cross validation techniques is a type of validation, where the modeling results are cross
90  validated with equivalent software, which produces same results. In our paper, we validated our
91  results with Philips propriety software such as Q-Flow and 2D-Perfusion analysis software.
92

93  **2.2.1 Q-Flow Software:**
94  The validations of complex geometries, feeding arteries are performed using Philips propriety
95  product called Qflow. Qflow is developed and validated by Philips Healthcare. Qflow is commonly
96  used in hospitals for clinical diagnosis and treatment. This is as validated software, accepted by
97  clinicians [Lotz J 2002; Kondo 1991]. The Qflow application requires MR Angiogram (MRA)
98  data – Fast Field Echo (FFE) & Phase, for processing. MRA data of CAVM patient with different
99  phase information is obtained from KMC hospital. The MR Angiogram is an imaging technique
100 to obtain phase, flow analysis of the patient. The MRA for cerebral patients gives cerebral flow
101 parameters. Using Qflow software, we obtain the velocity of the blood flow. The velocity is
102 converted to pressure, which is used for our validation analysis. Our study have approximated
103 conversion between the velocities to pressure. This approximation results in loss of accuracy,
104 which is analyzed in Results section.

105 **2.2.2 2D-Perfusion Software:**

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

110 **Statistical Analysis:**

111    Mean flow, diameter, and pressure were compared between modeling results and with
112 clinical/cross validation measurements, using independent 2-tailed Student t test. Refer Appendix

113    1 for t test results. Exponential regression analysis was used to assess the relationship between
114    blood flow, vessel diameter, and pressure between them. Univariate analysis is used to assess the
115    relationship between vessel diameter, vessel cross-sectional area, AVM volume, AVM pressure,
116    and AVM flow results was performed with linear or exponential regression.. Two-way tables were
117    verified using Fisher's exact test, and regular logistic regression was used to evaluate the
118    association between pressure and diameter variation in the vessel. All analyses were performed
119    with SPSS (Version 22; IBM Inc.)[Anna M. Fica et.al 2014].
120        Node voltage outputs were expressed as mean value ±Standard deviation. A total of 30
121    AVM patients were studied with evaluation of 150 vessels locations as node point. The statistical
122    analysis for various node output of loop structure is shown in table 5. -The statistical analysis
123    shows that the average error rate less than 0.05 and mean square error is lesser compared to other
124    simulation results. A P-value<0.05 was considered significant (refer Appendix 1 for results). The
125    standard deviation for each node is less than 0.05, compared to other simulation results. This shows
126    that proposed model based on non-invasive technique has advantages than other simulation
127    techniques.

128
129    Table 5: Statistical analysis for various node output of loop structure
130    `
131

| Quantification Parameters (for figure 5 loop structure) | Node1 Output voltage | Node2 output voltage | Node3 output voltage | Node4 output voltage | Node5 output voltage |
|---|---|---|---|---|---|
| Count | 12 | 11 | 10 | 9 | 8 |
| Minimum | 3.49 | 3.5 | 3.6 | 3.2 | 3.02 |
| Maximum | 5.2 | 5.1 | 4.9 | 4.8 | 4.7 |
| Mean | 3.4159 | 3.4159 | 3.4159 | 3.4159 | 3.4159 |
| Standard deviation (range) | 0.05 | 0.04 | 0.05 | 0.044 | 0.047 |
| Mean Squared Error | 9.869587728 | 9.869587728 | 9.868770939 | 9.9225 | 9.93 |

132

## 3.0 Results and Discussion:

### 3.1 Invasive Validation:

135        The invasive hemodynamics measurement inside NIDUS is risky, due to complex
136    geometric structure of NIDUS. However, with help of clinicians in Cathlab, KMC Manipal; able
137    to measure pressure values near locations of Nidus using guided micro catheter.  The various
138    measured locations are external carotid artery, internal carotid artery, and posterior cerebral artery.
139    The simulation is performed for the complete path node1 to node5, refer figure 5. The pressure
140    measurements for loop structure is shown in table 1.The model is simulated with different signal
141    magnitude variations.
142

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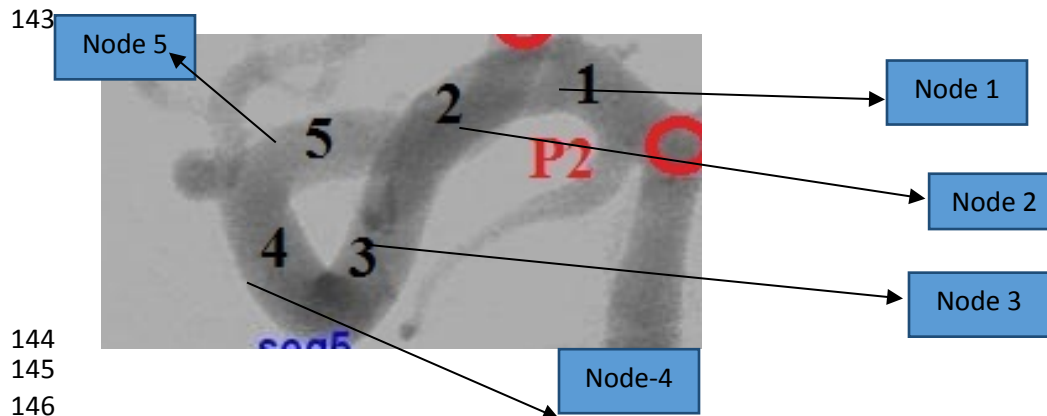
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145
146
147
148    Figure 5- Complex Vessel Structure

149
150    Table 1- Loop Structure Pressure Measurements and Analysis

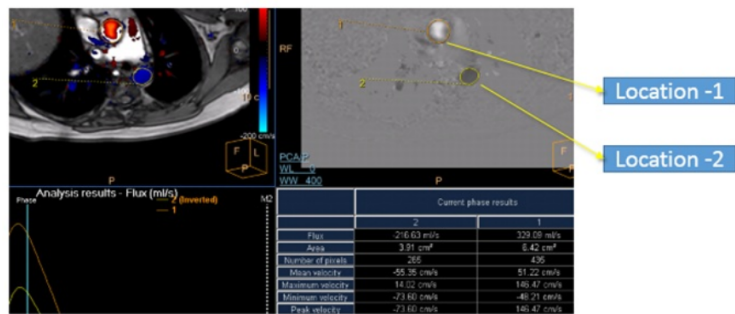
151
152

| Nodes | Input voltage  Pressure = 0.8 volt / 80mmHg | | |
|---|---|---|---|
| | Measured value | Clinical  results | Percentage 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 |

153    The table 1 shows modeling results are validated against clinical measurements. The input
154    voltage/pressure used for simulation is 80mmHg/0.8 volts.  Each node represents corresponding
155    cerebral vessel location. Each node is modeled using lumped elements and the corresponding node
156    outputs are compared against clinical measurements.   The percentage deviation in table 1,
157    represents the amount of percentage difference between the modeling results and clinical results.

158
159    **3.2 Cross Validation Techniques:**

160
161    **3.2.1 Q-Flow Validation:**
162    The study is validated by comparing against Qflow results with modeling results. The Qflow
163    processing results are velocity components for specific node/region.  Lumped model is created for
164    specific node/region. The lumped model is simulated for same input used in Qflow application.
165    Figure 6 shows MRA image of CAVM patient with velocity results for the drawn region of interest
166    in cerebral vascular region. Table 2 compares modeling results against Qflow results along with
167    amount of difference between them. The Qflow validation analysis is performed for each phase

168 acquisition of MRA of CAVM patient. The table shows various locations such as location 1,
169 location 2, depicts the pressure measurements at corresponding location for various phases.
170

175 Figure 6- Qflow analysis with node locations

177 Pre-requisite: Conversion of maximum velocity to volts

179 Table 2: Qflow validation with modeling results

| Vessel location as per figure 6 | 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 |

183 Table 3 shows pressure values obtained from each phase of MRA flow study compared against
184 with our modeling results. The percentage deviation shows amount of variation between modeling
185 results with Qflow pressure results. The reason for deviation is due to conversion factor from
186 velocity to pressure values.

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

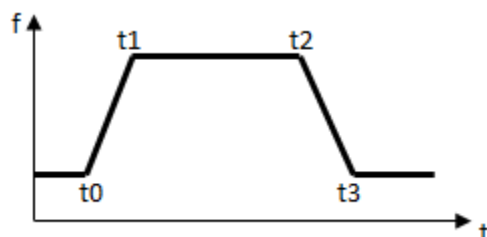
193 Table 3: CAVM -MRA flow study for various phases & CSF region

| Phase 3: | | | |
|---|---|---|---|
| Vessel locations as per figure 6 | 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 - 8 | | | |
|---|---|---|---|
| Vessel locations as per figure 6 | Flow outputs Mean velocity (in volts)* | 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 |

**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:

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

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

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

223
224 • Mean Transit Time:

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

225

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

228 ➢ Cerebral Blood flow (CBF) ~ Wash in Rate- Flow rate ~ current

229 ➢ Cerebral Blood Volume (CBV) ~ Area under Curve / Width – velocity ~ pressure

230 ➢ Mean Transit Time (MTT) ~ CBV / CBF = (Area under Curve / Width) / Wash in
231    Rate-Friction coefficient ~ Resistance

232 The model is validated with 15 DSA data of CAVM patients. The results are nearly matching with
233 an accuracy of 85%. The accuracy of modeling results is affected due to approximations in
234 conversion of clinical to electrical parameters. Figure 7 shows snapshot of 2D-Perfusion along with
235 clinical parameters.

236

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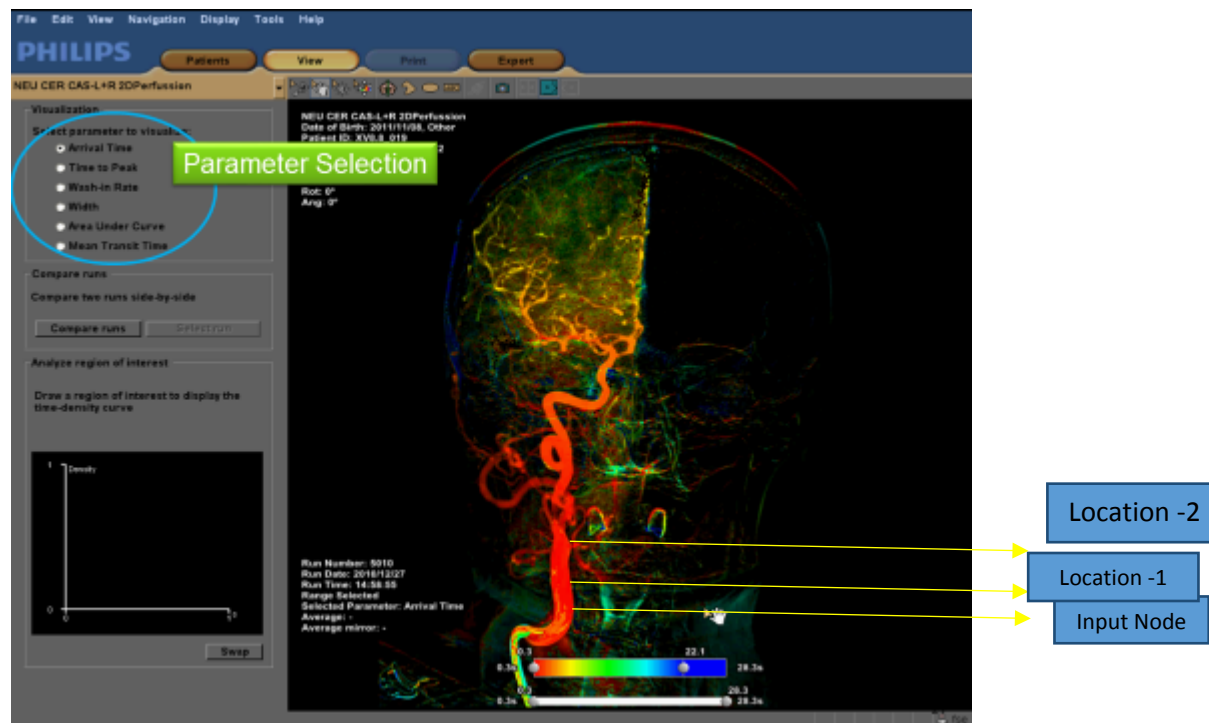
239    Figure 7- 2D-Perfusion analysis

240    Table 4 represents cross validation analysis for various vessel locations such as location -1,
241    location-2 (refer figure 7).  Modeling results are compared against 2D Perfusion software.  The
242    amount to percentage deviation is calculated for each cross validation comparison.

243

244

245    Table 4- 2D Perfusion – Cross validation.
246

| Vessel location as per figure 7 | 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 |

256
257
258    Discussion:
259

260    The clinical procedure to measure hemodynamics in CAVM is invasive procedure. The current
261    procedure is risky, as catheter may rupture, can cause patient death [Erzhen Gao a, William L.

262  Young 1998; WayneWakeland 2008.].  The -researchers explained different models based on
263  invasive techniques for hemodynamics analysis [Cattivelli 2008] but limited by measurement of
264  radius calculation for specific arteries. Kuebler analyzed the regional cerebral blood flow based on
265  non-invasive technique, however limited by cerebral circulation only.  Kienzler et al analyzed
266  various methods for validation of noninvasive pressure measurements, but limited by data points.

267  The  proposed  non-invasive  methodology  address  the  clinical  procedure  to  measure
268  hemodynamics, by simulating the actual patient condition using lumped model. The modeling
269  results are validated with clinical invasive measurements. Our results show that simulated results
270  are approximately matching with the actual clinical measurements .The reason for deviation is due
271  to conversion factor from velocity to pressure values.  A total of 30 CAVM patients and    150
272  vessel locations were validated with invasive measurements and with cross validation (Qflow).
273  The statistical analysis shows mean square error rate for 150 vessel locations is less than 0.05,
274  shows a statistically significant evidence. The modeling results is approximately matching with
275  Qflow results. The reason for deviation is due to conversion factor from pressure to velocity
276  parameter.

277  In validation of 2D-Perfusion, the data is limited to 15 DSA images, as this software requires
278  specific type of DSA acquisition to process. With the 15 patients, we validated and quantified our
279  modeling results with 2D-Perfusion. The results are nearly matching with accuracy of 85%. The
280  reason for deviation of modeling results with 2D perfusion is due to approximation of parameters
281  used for modeling.

282  The cross validation is a novel approach for CAVM validation. Qflow and 2D-perfusion software's
283  implementation is based on mechanical simulation. The lumped modeling results nearly matching
284  with  Philips  propriety  software's,  confirms  the  matching  of  results  between  electrical  and
285  mechanical simulation. To reach significant evidence>98%, we require more data for our
286  validation work. The limitation of this work, is the usage of multiple approximated conversions of
287  application specific compared against modeling results. This work can be extended for different
288  geometry using three dimensional volume data and require optimization of conversion factors to
289  increase the accuracy of modeling results.

290

291  Conclusion:

292        In this paper, we have validated CAVM modeling results, created using lumped networks
293  with clinical measurements and with cross validation techniques. The new approach for cross-
294  validation is proposed in this paper. The modeling results by validating our results with validated
295  produc t in clinical environment. The results are validated for 30 CAVM patients with 150 vessel
296  locations validation shows nearly matching significantly results compared to the invasive
297  measurements and with Philips propriety validated software's. This method seems to be safe and
298  reliable.
299

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345

346  Appendix 1:

347
348      Attached excel for the results of t-test and other statistical analysis.
349

Output Pressures at
different Nodes.xlsx

350