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Simulation Analysis for Non-invasive Measurement for Hemodynamics in Cerebral Arteriovenous Malformation Types

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Authors' contributions

This work was carried out in collaboration between all authors. Author YKK designed the study, wrote the protocol and analyses of the study. Authors SBM and MR did review of manuscript. All authors read and approved the final manuscript.

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ABSTRACT

The Cerebral Arteriovenous Malformation (CAVM) is a complex neurovascular malformation. It contains different types of complex nidus structures combinations. Each CAVM classification is of different clinical procedure and management of disease. The clinical procedure to measure hemodynamics for each CAVM classification is risky, due to complex vessel geometry may get ruptured. In this paper, we address this problem for different AVM classification and nidus complex structures combinations, by measuring hemodynamics non-invasively. The simulation of model is extended for organs other than Cerebral AVM, such as spine and lungs. The modeling results are validated with mechanical measurements. 15 CAVM patients and 20 simulated scenarios of different AVM types are studied to measure hemodynamic indices non-invasively.

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Keywords: Simulation; CAVM types; nidus; hemodynamics.

1. INTRODUCTION

The literature describes different classification of Cerebral Arteriovenous Malformation (CAVM) [1]. The CAVM classification is based on different angioarchitectural parameters. The parameters includes some of the combinations, such as CAVM size, location of AVM, number of AVM in the human body and distribution of feeding vessels, pattern of venous drainage, low and the amount of blood steal from the surrounding brain considers different clinical parameters [2-4]. These parameters influences the change in the CAVM hemodynamics and increases vessel structure complexity [5- Mikhail]. The literature shows researchers have studied the nidus type classification based on Digital Subtraction Angiogram (DSA) & Magnetic Resonance Angiogram (MRA) [6]. The AVM develops in various parts of human body such as spine and lungs and occurs in different types based on the complexity of AVM and patient condition.

The research by MingXu have studied the animal models of CAVM, however limited by clinical features considered for modeling [7]. The study by Hou on xenograft animal model for CAVM, demonstrated different nidus structure variations, however, limited by clinical validation [8].

In this paper, we proposed non-invasive methodology to model CAVM types with different Nidus geometric structures combinations. The model is based on the Windkessel model to create different lumped model for various geometric structures. We have simulated different types of AVM geometric structures of different organs and validated results with mechanical simulations. The modeling for AVM types is generic, can be extended for other organs.

2. MATERIALS AND METHODS

2.1 Study Population

The CAVM data is obtained from KMC Manipal. The subjects have given informed consent to participate in this study, which was approved by the KMC Manipal.

2.2 CAVM Structure Type Simulation

The reporting standards on CAVM by neurosurgeons [9] analyzed various types of CAVM attributes and different structures of Nidus structures. The AVM's are located in various part of human body such as spine, lungs etc. The AVM consists of various combinations of Nidus complex vessel structure. The formation of Nidus structures is different in each type of CAVM. The invasive method to acquire hemodynamics measurements for each type of AVM for various organs is difficult to clinicians and risky to patients. The proposed non-invasive method to measure hemodynamics is based on lumped model. The details of each type of CAVM structures as per Cho [10] classification are as follows:

Type 1

The cerebral vessel structure has feeding arteries, capillaries and veins but in CAVM patients arteries are shunted to veins leading to complex structure. The Type 1 CAVM structure type consists of at most 3 separate arteries shunted to a single draining vein. The three individual feeding arteries are combined to form Nidus complex structures (Fig. 1). The lumped element for Type 1 CAVM structure is based on the Nidus path starting from feeding arteries ending in a draining veins. The lumped element creation is based on the adaptive segmentation and modeling [11].

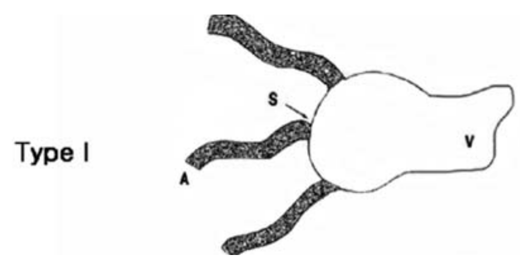

Fig. 1. Type 1 CAVM structure

Type II

The Type II CAVM structure consists of multiple arterioles shunted into a single draining vein. This structure is the complex in nature. As this type of CAVM consists of multiple feeding arteries and each feeding arteries path may not end in a draining veins, sometimes it ends in a loop structures (Fig. 2). This type of CAVM structures is more prominent in patients. The lumped model creation for these types of CAVM structures is based on the patient specific geometric structure paths. In this type of CAVM, there are multiple paths, each path is modelled independently. The steps to model each path are as follows:

- Each path is modelled separately. The path contains multiple combination of vessel geometric structure variations, each geometric variation is modeled individually and all geometric variations are interconnected together to form complete Nidus path [12].
- Repeat the above step for each different paths. This results in multiple lumped network model for each path.
- The final lumped model network is formed by interconnecting each path lumped network models. The interconnection of each lumped model is in form of T/PI section. The interconnection is challenging, as the network at the junction is complex structure combinations of all multiple Nidus paths.

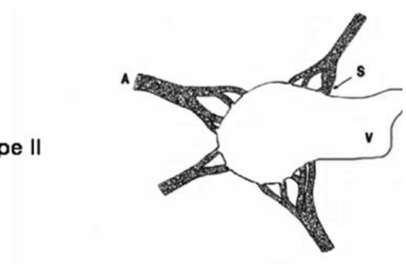

Fig. 2. Type II CAVM structure

Type IIIa

The Type IIIa is a plexiform arteriovenous shunts which contains multiple combinations of shunts between arterioles and venules. It consists of multiple individual paths for each shunts and each shunts consists of complex structures. This type of CAVM are non-dilated vessels. The clinical investigation to these CAVM is easier compared to other types as it is too fine to be punctured directly. Each individual path of each shunt is modelled separately. Each path contains complex structures in between the arterioles and venules (Fig. 3). The individual path with complex structures is subdivided in to smaller substructures. The substructures are modelled independently. The individual path is modeled by combining each substructure lumped model. The complete model for Type IIIa is formed by combination of lumped model for each path interconnected in parallel combination.

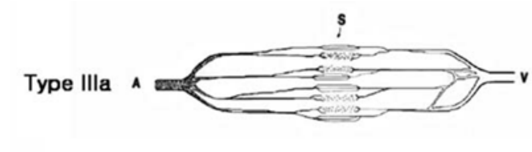

Fig. 3. Type IIIa CAVM structure

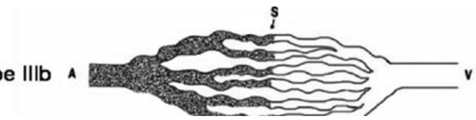

Fig. 4. Type IIIb CAVM structure

Type IIIb

The Type IIIb is the type of CAVM which are dilated in nature. This type of CAVM has multiple combinations of arteries which are dilated and interconnected to multiple dilated draining veins (Fig. 4). The dilation causes multiple complexities. The dilated vessels change the cerebral hemodynamics and result in increased pressure at Nidus. The invasive procedure for these CAVM types is risky. In this type of CAVM, the lumped model is created for each path. Each vessel path from artery to vein through nidus complex structures are modelled independently. The complete vessel structures for Type IIIb are formed by connecting each vessel path lumped model in parallel combinations. The challenge in this CAVM is variations in a flow rate and pressure variations are higher, due to dilation of vessels. This is addressed by simulation of lumped model using different input signal combinations. The Fig. 5 shows example for CAVM complex vessel structure of Type II. The feeding arteries are represented as A, B, C. Each feeding arteries is modelled separately. The lumped models for each vessel path are as follows:

2.3 Feeding Arteries Vessel A

The Vessel "A" starts from junction 10 and ends in Nidus formation. The vessel path consists of different substructures using adaptive segmentation and modeling technique. Each substructure is modelled independently for the vessel path 10-A (Fig. 6). The lumped elements are reported in (Fig. 7) for Node 10 to Node 11 and in Fig. 8 for Node 11 to Node A. The lumped elements model for vessel path Node 10 to Node A reported in (Fig. 9).

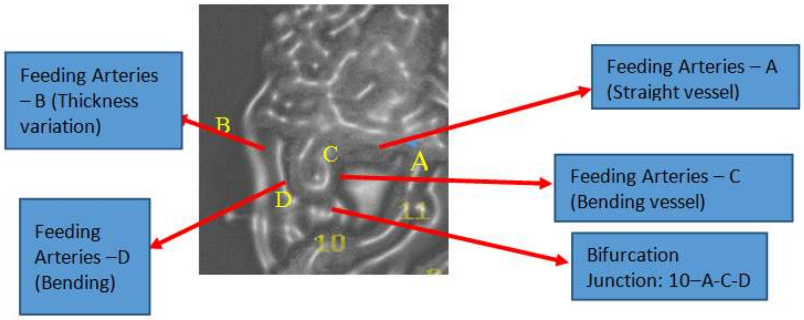

Fig. 5. Type II CAVM vessel structure

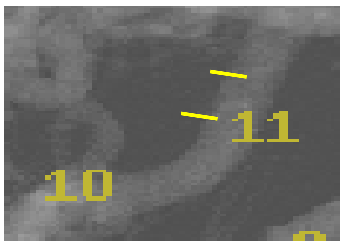

Fig. 6. Vessel path structure- Node 10 to Node A

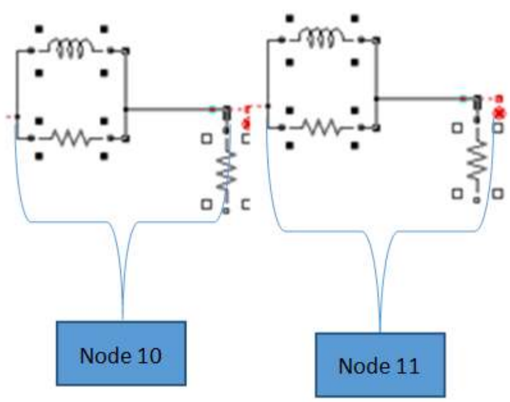

Fig. 7. Lumped elements for Nodes

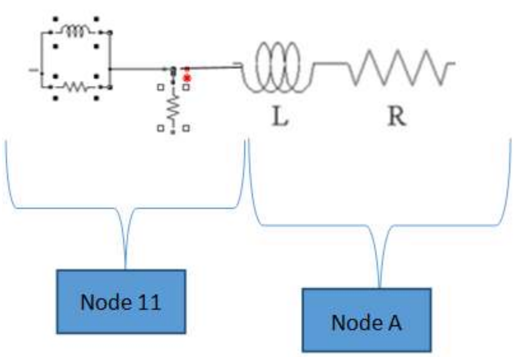

Fig. 8. Lumped elements for Node 11 to Node A

2.4 Feeding Arteries Vessel C

The vessel "C" is modelled for the location starts from Node 10 to Node "C" (Fig. 10). The vessel structure for Node10-Node"C" is of bending geometry. The lumped model for Node 10- Node "C" (Fig. 11).

2.5 Feeding Arteries Vessel D

The vessel "D" is modelled for location Node 10-Node D (Fig. 12).The lumped model for Node 10-Node D (Fig. 13).

2.6 Feeding Arteries Vessel B

The vessel "B" is modelled for location Node 10-Node B (Fig. 14). The lumped model for Node 10- Node B (Fig. 15). The complete lumped model for complete path combinations is the feeding arteries bifurcation junction to Nidus complex structure formation. The lumped network is formed by parallel combination of (Node 10-Node A) || (Node 10-Node C) || (Node 10-Node D) || (Node 10-Node B) (Fig. 16).The lumped network equations are explained in Appendix A.

2.7 Signal Simulations

The different types of CAVM is simulated by different signal combinations. This will simulate actual patient conditions of CAVM with different Nidus structure types and geometric vessels combinations. The signal combinations replicate flow and pressure variations inside CAVM types. In case of Type II and Type IIIb, the complexity of vessel structures is comparably higher than other types. The signal simulations for these types of CAVM patients, helps to analyze each specific part of CAVM using lumped element for specific geometric variations. The input signals to lumped model are varied for both magnitude and phase signals (Fig. 17).

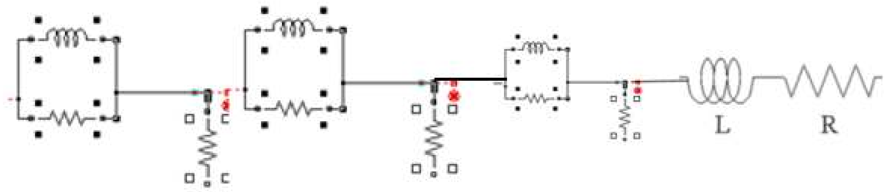

Fig. 9. Complete Lumped network model for vessel path

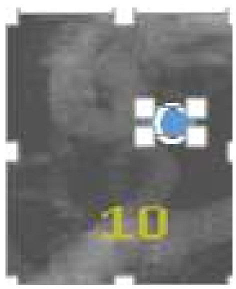

Fig. 10. Vessel path structure Node 10 – Node "C"

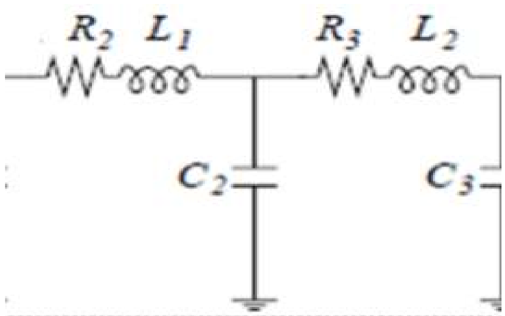

Fig. 11. Lumped Model Node 10-Node "C"

Fig. 12. Vessel path structure Node 10-Node D

2.8 Simulation of Complex Path Structures

The different combinations of vessel complex structures is derived from different types of AVM from various anatomical location such as spine AVM, pulmonary AVM [13]. The vessel path creation is based on vessel path navigation, obtained from clinical data. In some cases, vessel path are derived with help of clinicians by visual inspection. The path structures are derived based on adaptive segmentation and modeling methodology (Fig. 18). The lumped model is created for patient specific nidus structure path with different complex geometric structures. The proposed non-invasive method to measure hemodynamics can be extended for other AVM in other organs. However, we didn't get Type IIIa CAVM types. The data is combination of Type I and Type II. The Type IIIb is subset of Type II. The validation is performed using mechanical simulation only not with clinical measurements.

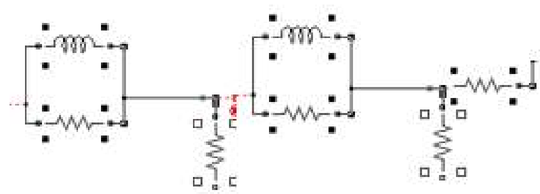

Fig. 13. Lumped model for Node10-Node D

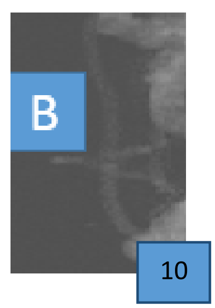

Fig. 14. Vessel path structure "B"

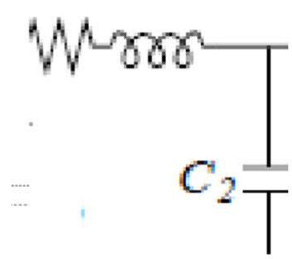

Fig. 15. Lumped Model for Node 10-Node B

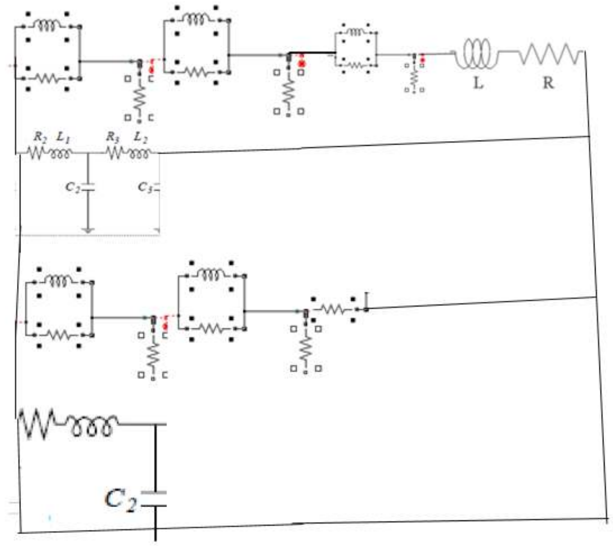

Fig. 16. CAVM Type II complete lumped model

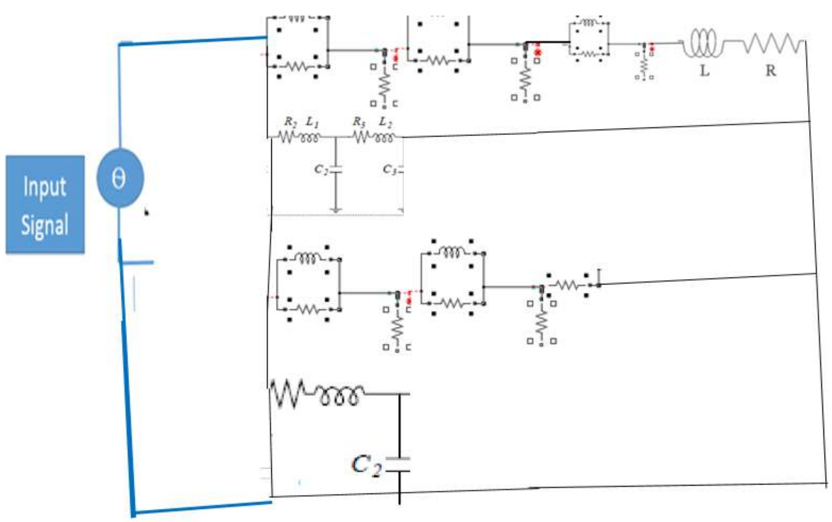

Fig. 17. Signal Simulations for CAVM Type II lumped model

3. RESULTS

3.1 Validation with Mechanical Simulation

The CAVM types are modeled using lumped models and results are compared with mechanical simulations. The mechanical software used is Comsol Pipe flow module software. The extracted nidus path of any vessel network is modelled using adaptive segmentation and lumped modeling. The results are compared with mechanical simulation and comparison is performed for the amount of percentage deviation. Fig. 19 shows the Type I feeding artery vessel structure. This CAVM has three feeding arteries inputs namely vessels path - 3, 7, 6. Each vessel path is modelled separately. The lumped model network is created independently for each path and interconnected to form a complete vessel path for CAVM Type I structure (Fig. 20). The complete lumped model is simulated for signal variations (Fig. 21). The Table 1 shows that for various node locations in Fig. 21, pressure values are measured. The node is simulated for different pressure signals such as 80 mmHg, 100 mmHg. The node outputs for each input represents the output voltage/pressure for given input. The node output is compared with mechanical simulations. The amount of percentage deviation between them is calculated.

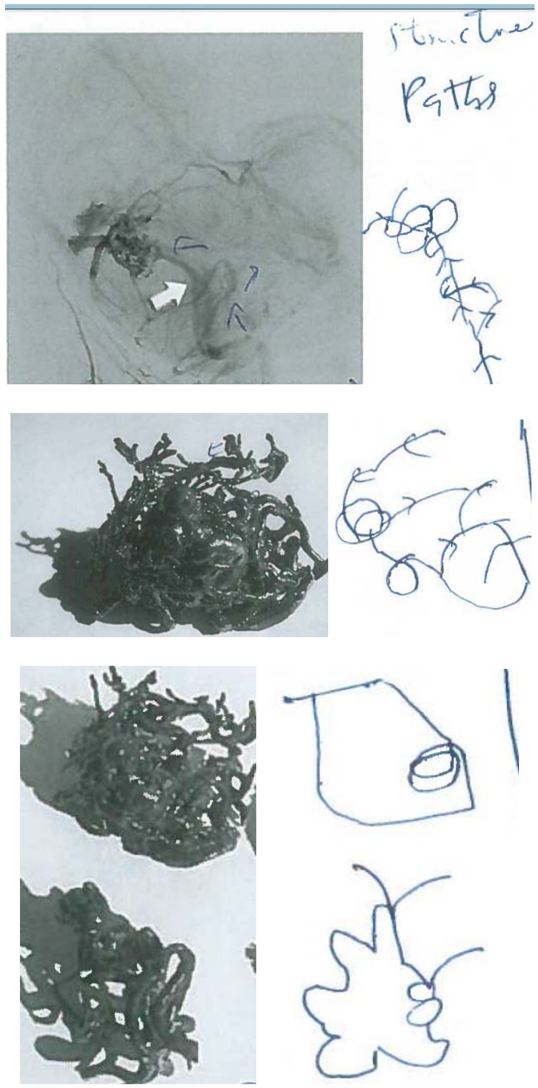

Fig. 18. Simulated path structures variations

4. DISCUSSION

This study involves modeling of the various types of CAVM structures and different types of Nidus geometric structures variations. The lumped model is created using Windkessel model for each vessel segment. The vessel is modeled to represent each smaller geometry variation of complete Nidus. The proposed methodology is extended to other AVM present in organs other than CAVM.

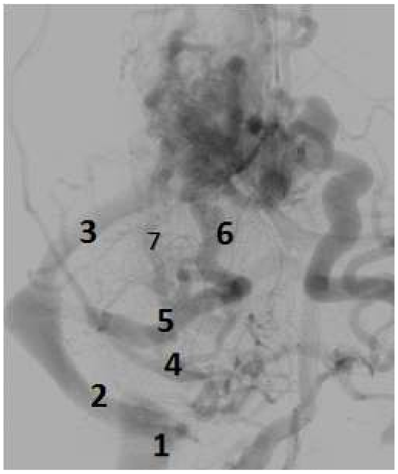

Fig. 19. CAVM Type I structure

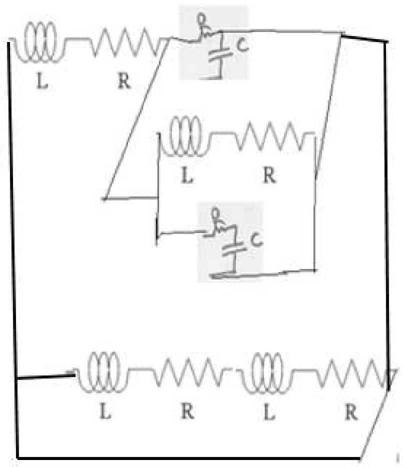

Fig. 20. Lumped Model for CAVM Type I structure

The literature shows different AVM types based on the morphology of AVM found in patients. However the authors have studied clinical invasive procedure to measure hemodynamics for AVM classifications [14]. The proposed lumped model based non-invasive for CAVM types is unique and novel. The vessel model is created using vessel diameter and length. The Windkessel lumped network is created for each AVM type. These models help to analyze the flow variations by simulating models with different voltage/pressure variations, to create similar patient conditions in CAVM. The sub-segmented vessels are represented as nodes of a complex lumped networks. The network consists of different vessel geometry variations and all are interconnected to form integrated model of complete

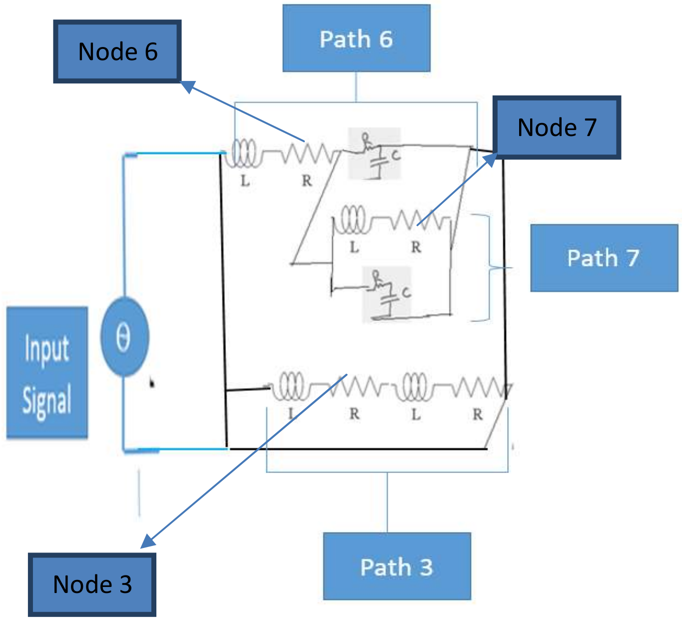

Fig. 21. Signal simulation for complete lumped model

Table 1. Comparison analysis between modeling results and mechanical simulations

Nodes as shown in Fig. 21	Input voltage Pressure = 0.8 volt / 80 mmHg			Input voltage Pressure = 1 volt / 100 mmHg		
	Measured value	Mechanical results	Deviation %	Measured value	Mechanical results	Deviation %
Node 3	0.7 v/70 mmHg	0.66 v/66 mmHg	5.7	0.90 v/90 mmHg	0.87 v/87 mmHg	3.3
Node 6	0.63 v/63 mmHg	0.60 v/60 mmHg	4.7	0.88 v/88 mmHg	0.86 v/86 mmHg	2.2
Node 7	0.60 v/60 mmHg	0.55v/55 mmHg	8.3	0.85 v/85 mmHg	0.82 v/82 mmHg	3.5

complex Nidus path. The combined Nidus vessel network is used to analyze flow variations by simulating using various transient signals combinations. The simulated results and measurements of resulting flow variation at different nodes of lumped model are validated using mechanical simulations results. This model is used only for assessing the flow variations in a complex vessel structure not for the prediction analysis.

The complex structure of AVM is common in all its types, irrespective of organ or location. Since network formation using Windkessel is generic, it can be applied for any type of AVM of any organ. The proposed logic to create model and its analysis for flow variations of any type of AVM of other organs still hold good.

5. CONCLUSION

The objective of this study is to measure hemodynamics for different CAVM types and Nidus structures variations. The proposed methodology based on non-invasive method, using lumped model address the problem faced by clinicians. The present clinical procedure to measure AVM hemodynamics measurement by invasive procedure is risky as Nidus may get rupture, which is evident in Type II and Type IIIb patients. In this paper, we have created a lumped model for Nidus for different CAVM structures and non-cerebral organs such as spine and lungs to measure hemodynamics non-invasively. The modeling results are validated with mechanical results, however, the limitation of this study is the absence of clinical validation for modeling results for spine and pulmonary AVMs.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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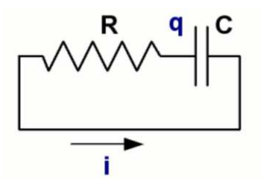
APPENDIX A

The lumped model are solved by Runge Kutta Method 4th order method. The lumped model creates a set of differential equations, which are solved are using Runge Kutta Method. Runge-Kutta method, which is based on formulas derived by using an approximation to replace the truncated Taylor series expansion.

The steps to solve differential equations are as follows:

1. Apply KVL, KCL to the created lumped network models.
2. The differential equations are generated for each loop as per KVL.
3. Solve KVL equations using Runge Kutta Method
   The following example shows solution for simple lumped model.



Using Ohm's and Kirchhoff's laws, we get the formula for current i:

i = -1/(R C) q

Because i = dq/dt, we obtain the first order differential equation:

dq/dt = 1/(R C) q

Knowing the charge q0 at the instant t0, we would like to find the time variation of the charge, which is an unknown function q = q (t). Despite the fact that an analytical formula for this function exists, we want rather to get numerical approximations of q = q (t). Among many methods invented to solve such initial problems, fourth-order Runge-Kutta method is more applicable for our analysis. Having a function of the first derivative and an initial condition:

dy/dt = f (t, y), y (t0) = y0

The Runge-Kutta method finds the next value yn+1 from the present value yn with the help of following equation:

yn+1 = yn + h/6 (k1 + 2 k2 + 2 k3 + k4)

Where h is a selected time interval and coefficients k1 to k4 are:

k1 = f(tn, yn)
k2 = f(tn + h/2, yn + h/2 k1)
k3 = f(tn + h/2, yn + h/2 k2)
k4 = f(tn + h, yn + h k3)

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