Fung's Model Constants for Intracranial Blood Vessel of Human Using Biaxial Tensile Test Results

Mohammad Shafigh, Nasser Fatouraee, Amirsaied Seddighi

***Abstract*—**Mechanical properties of cerebral arteries are, due to their relationship with cerebrovascular diseases, of clinical worth. To acquire these properties, eight samples were obtained from middle cerebral arteries of human cadavers, whose death were not due to injuries or diseases of cerebral vessels, and tested within twelve hours after resection, by a precise biaxial tensile test device specially developed for the present study considering the dimensions, sensitivity and anisotropic nature of samples. The resulting stress-stretch curve was plotted and subsequently fitted to a hyperelastic three-parameter Fung model. It was found that the arteries were noticeably stiffer in circumferential than in axial direction. It was also demonstrated that the use of multi-parameter hyperelastic constitutive models is useful for mathematical description of behavior of cerebral vessel tissue. The reported material properties are a proper reference for numerical modeling of cerebral arteries and computational analysis of healthy or diseased intracranial arteries.

***Keywords*—**Anisotropic Tissue, Cerebral Blood Vessels, Fung Model, Nonlinear Material, Plain Stress.

I. Introduction

MECHANICAL properties of arterial wall have significant effects on the functions of blood vessels since they determine the relationship between pulsatile blood flow, and the luminal cross section [1] and may be correlated to the vascular diseases like atherosclerosis [2]. Properties of living tissues are applicable for diagnostic and treatment purposes as well as in surgery [3]. Also computational modeling of cerebrovascular diseases such as aneurysms requires the structural properties of cerebral vessels as the input [4].

Factors like age, gender and smoking affects arterial properties and functions [5]-[7]. On the other hand, these properties are dependent on the structure and orientation of constituent elements of the arterial wall, mainly collagen and elastin fibers, which cause different properties in longitudinal, radial and circumferential directions and make the wall stiffer in radial than axial direction [8].

Arteries and most of the biological tissues show non-linear elastic and anisotropic properties [9]. Thus uniaxial and biaxial tests are used to determine the mechanical properties of them. Uniaxial tests are applied only to determine the tissue properties in the direction of force measurement. In the case of anisotropy, uniaxial tests will be no longer useful and comprehensive. In biaxial loading, tissue is stiffer and less nonlinear [9]. Therefore, biaxial planar tests may be proper alternatives to reach a better understanding of arterial behavior [10]-[13].

Previously the microstructure of arterial wall was not taken into account in formulation of constitutive equations traditionally used for modeling the mechanical behavior of arterial walls. That's why some researchers turned to formulate constitutive models in which some histological information is considered [14]-[17]. Constitutive equations describing nonlinearity of vessels might have a very complex form with many parameters. Hyperelastic models (for example with three parameters) have been shown to be appropriate for this purpose [18], [19].

Cerebral arteries have different structure from the other human vessels. Tunica media and tunica adventitia in cerebral arteries usually have lower thickness than other arteries of the same diameters. The amount of elastin in the media layer of cerebral arteries is less than others and the external elastic lamina, which is present between media and adventitia of other vessels, doesn't exist in cerebral arteries [20], [21].

Due to the difficulties in accessing cerebral arteries, limited sets of biomechanical data are available for them and most of studies have focused on non-cerebral vessels. Regarding to the mentioned differences between cerebral and other vessels, determining biomechanical properties of cerebral vessels through biaxial tensile tests can pave the way for further investigations.

Due to the limitations in accessing human cerebral arteries, many researchers were adopted animal specimens. Hue et al. represented stress-stretch data in the in the circumferential and axial directions from normotensive and hypertensive specimen from porcine basilar artery [22] and reported the first quantification of changes in biaxial mechanical behavior of the porcine basilar artery due to hypertension [23]. Wicker et al. tested basilar arteries from rabbits mechanically under biaxial loading conditions with and without active tone and fitted passive mechanical to a four-fiber family stress–stretch relation [24]. Nagasawa et al. studied elastic properties of the basilar artery in control and treated dogs in which 3ml of blood was injected intracisternally and observed lower elastic moduli in treated arteries which might be one of the factors affecting the development of cerebral vasospasm [25].

M. Shafigh is with the Biomedical Engineering Department, Sciences and Research Branch, Islamic Azad University, Hesarak, Tehran, I.R. Iran; Postal Code: 1477893855; (corresponding author, phone: +98-21-44440506; fax: +98-21-44440505; e-mail: Shafigh_Mohammad@yahoo.com).

N. Fatouraee is with the Biological Fluid Mechanics Research Laboratory, Biomechanics Department, Biomedical Engineering Faculty, Amirkabir University of Technology (Tehran Polytechnic), Tehran, Iran. (e-mail: Nasser@aut.ac.ir).

A. Seddighi is with the Functional Neurosurgery Research Center, Shohadae Tajrish Hospital, Shahid Beheshti University of Medical Sciences, (e-mail: A_Sedighi@sbmu.ac.ir).

The study by Monson et al. was one of the few studies on human cerebral vessels. They investigated the biaxial properties of cerebral vessels by applying internal pressure through inflation and used Fung's hyperelastic model to describe them [26].

Scott et al. have done Static pressure-volume curves on intracranial several saccular aneurysms and major cerebral arteries from human autopsies and their reported experimental data were used by several researchers later [27]. Seshayer et al. reported the first multiaxial mechanical data on human saccular aneurysms and used a subdomain inverse finite element method to estimate the best fit material parameters to Fung-type pseudostrain energy function [28]. Later Toth et al. also investigated the biomechanical properties of strips from human cerebral aneurysms from surgery and cadavers by making uniaxial and biaxial measurements [29].

Therefore due to the authors' knowledge, there is no definite data regarding hyperelastic model parameters for cerebral vessels subjected to a biaxial test in a plane stress method. Thus the present study was carried out to determine the coefficients mentioned above and also to investigate the affecting factors. This is also one of the first studies providing the stress-stretch curves for cerebral vessels in two directions.

II. Materials And Methods

A. Developing a Dedicated Biaxial Tensile Test Device

Regarding the dimensions of samples and the range of applied forces, a biaxial tensile test device was designed and developed. The device can keep the tissue wet at temperature of 37°C during test so that its properties do not change due to evaporation. Tensile forces are measured by two 2 channels 16 bit with 5 to 8 sample/s ADC and load cell conditioners, for UMAA 2 kgf load cell (Dacell Co., Ltd, Korea Corporation, Korea). The required tensile forces, in this device, are applied by four micro stepper motors with a resolution of 0.36 degrees and with a nominal torque of 1.2kg.cm (Autonics Corporation, Gyeonggi-do, Korea). Four drivers were used to drive the stepper motors (Autonics model MD5-H14). For visual measurement of the tissue deformation, a USB digital microscope camera was used (300X zoom, 30 Hz and resolution of 480×640). All images were processed through freeware package called ImageJ (formerly, NIHImage). The end distance between clamps was considered as the reference measure of sample length in two mutually perpendicular directions. Due to the small dimensions of the specimens, staining of tissue was not applicable. So to prevent errors due to the slip of the tissue in the clamps grip, the clamp displacements were calculated according to the known pitch of the screw and rotation degree of stepper motors every 0.2 seconds and these displacements were compared with the stretch of tissue obtained by images. In case of any difference between the displacement of the clamps and the stretch of the tissue, the data of the specimen were deleted as this discrepancy was due to slip of the tissue.

TABLE I
MATERIAL CONSTANTS DERIVED FROM BEST FITTING OF EXPERIMENTAL DATA TO THE HYPER-ELASTIC FUNG MATERIAL MODEL

Fung constants	Specimens: age/gender								
	53M	87F	18M	45M	30F	80F	78M	35M	Average
c	0.232	0.355	0.367	0.361	0.483	0.052	0.173	0.366	0.313
a_1	0.515	3.998	1.764	0.659	5.234	12.968	10.234	1.994	2.898
a_2	1.560	0.754	0.775	0.963	0.0163	0.0379	0.013	1.558	1.186
a_3	0.400	0.140	0.120	0.099	1.078	0.960	0.780	0.810	0.130
Anisotropy	0.470	0.220	0.480	0.710	0.170	0.071	0.072	0.840	0.430

B. Samples Preparation and Test Procedure

Thirteen samples were obtained from 23 middle cerebral arteries (MCA) extracted according to a special protocol from 20 human cadavers whose death wasn't due to injuries or diseases of cerebral blood vessels. These samples were tested by our biaxial tensile device within 12 hours after their resection. Before resecting the samples, we asked the families of the deceased to sign a consensus form.

To prevent damages to vessels, brain of the deceased were first removed completely. Then all cerebral vessels were separated from soft tissue by an experienced neurosurgeon. To standardize the tests, the 10mm proximal segment of MCA was resected for all specimens. Thickness of specimens was measured with a vernier caliper. Then the specimens were cut to 5×5 mm^2 with a special cutter. To reach a uniform stress distribution, special clamps were designed that could grip tissues with dimensions as small as 5×5 mm^2 directly. These light clamps were then attached to the load cells. During the test, the samples were stored in 0.9% physiological saline heated by a heater to 37°C. The specimens, after attachment to the four clamps, were stretched simultaneously in two dimensions (four directions). Low rate of loading with selecting the strain rate at 0.02mm/s in all tests was considered for a quasi-static test.

C. Fung Hyperelastic Model

Most experimental data are generally analyzed with the help of a strain energy density function. If there is a one-to-one relationship between strain and stress, then the theory of elasticity states that there exists a strain energy density function W, from which the stresses can be computed from the strains as follows [11], [18], [30]:

$$S_{ij} = \frac{\partial W}{\partial E_{ij}} \tag{1}$$

$$E_{ij} = \frac{1}{2}\left(F_{ij}.F_{ij}^{T} - I_{ij}\right) \tag{2}$$

where S_{ij}, E_{ij}, F_{ij}, I_{ij} are the components of the second Piola-Kirchhoff stress tensor (S), E is the Green-Lagrange strain tensor, F is the deformation gradient tensor, and I is the identity unit tensor, respectively.

The Fung strain energy function model W was used:

$$W(Q) = \frac{1}{2}c(e^{Q} - 1) \tag{3-a}$$

$$Q(E) = a_1 E_{11}^2 + a_2 E_{22}^2 + 2a_3 E_{11} E_{22} \tag{3-b}$$

where c, a_1, a_2, a_3 are model parameters [31].

The force-displacement curve for each specimen was obtained in two mutually perpendicular directions. The experimental stresses for specimens were calculated as follows:

$$\sigma_{11}^{\exp} = \lambda_1 \frac{F_{11}}{b_1 t} \tag{4}$$

$$\sigma_{22}^{\exp} = \lambda_2 \frac{F_{22}}{b_2 t} \tag{5}$$

where λ_1 and λ_2 are stretch ratios, F_{11} and F_{22} are forces measured by load cells, t is thickness of specimen, and b_1 and b_2 are widths of specimens in the two directions. The stress components were then calculated as follows:

$$\sigma_{11}^{\text{model}} = \{\frac{1}{2}c\lambda_1^2\left[a_1(\lambda_1^2 - 1) + a_3(\lambda_2^2 - 1)\right] * e^{\frac{1}{4}\left[a_1(\lambda_1^2-1)^2 + a_2(\lambda_2^2-1)^2 + 2a_3(\lambda_1^2-1)(\lambda_2^2-1)\right]}\} \tag{6}$$

$$\sigma_{22}^{\text{model}} = \{\frac{1}{2}c\lambda_2^2\left[a_2(\lambda_2^2 - 1) + a_3(\lambda_1^2 - 1)\right] * e^{\frac{1}{4}\left[a_1(\lambda_1^2-1)^2 + a_2(\lambda_2^2-1)^2 + 2a_3(\lambda_1^2-1)(\lambda_2^2-1)\right]}\} \tag{7}$$

Experimental data then were fitted to (6) and (7) using least-squares Levenberg–Marquardt algorithm and the parameters of constitutive model c, a_1, a_2, a_3 obtained for each date set. Anisotropy is calculated as follows:

$$Anisotropy = \min\left[\frac{a_1 + a_3}{a_2 + a_3}, \frac{a_2 + a_3}{a_1 + a_3}\right] \tag{8}$$

III. Results

Experiments were performed on total numbers of 8 human MCA specimens. Average thickness of vessels was considered 0.6mm and the cross sectional area was 3 mm^2 under tension.

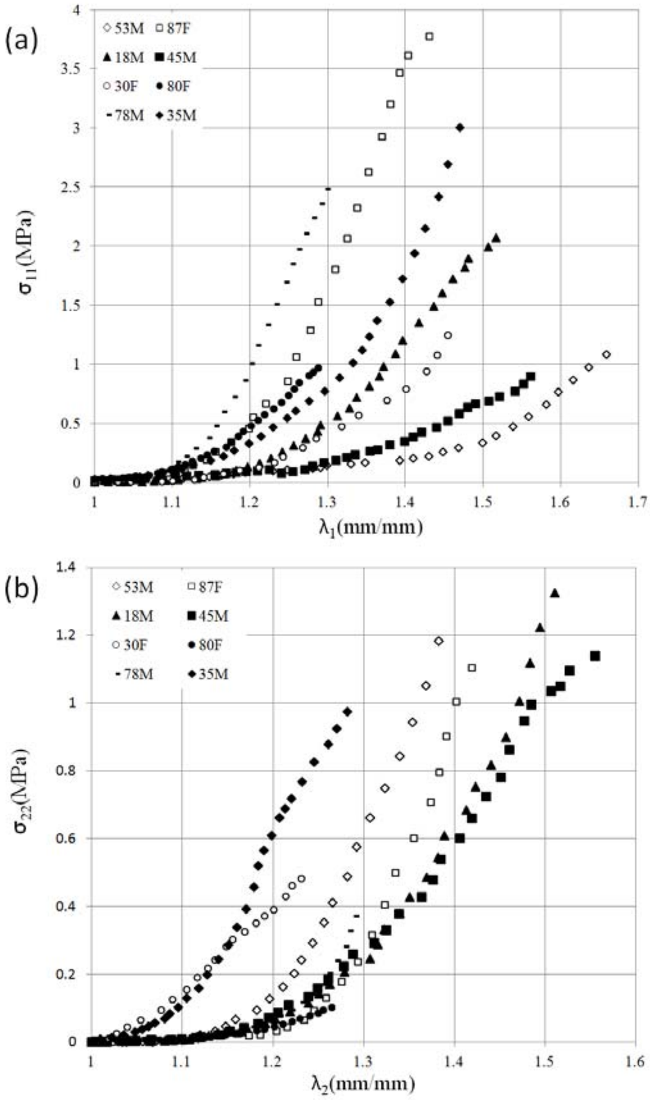

Fig. 1 Stretch-stress curves obtained from the biaxial mechanical testing of all specimens in circumferential (a) and axial (b) directions

Force-displacement data obtained from mechanical tests were converted to stretch-stress curves through (4) and (5). Fig. 1 shows the stretch-stress curves obtained from the biaxial mechanical testing of all specimens in circumferential (a) and axial (b) directions respectively. The data series' name in all figures is containing age and gender information (e.g. M53 is a 53-year-old Male). It was evident that arteries were noticeably stiffer in circumferential versus axial direction. This observation represents that uniaxial testing is not sufficient for determining mechanical properties of blood vessels and it is necessary to consider the anisotropic behavior of arterial tissue in testing or modeling studies (Table I).

Experimental data then were fitted to a three parameters Fung material model through (7) and (8) as mentioned before. Table I represents the best-fit material parameters for all the existing data and the averaged values were calculated in the last column.

Deriving best-fit material constants, stretch-stress curves were obtained and illustrated in Fig. 2 for all specimens. Also the mean biaxial stretch-stress curve for human MCA is obtained from average Fung constants mentioned in Table I and sketched in Fig. 2 as well.

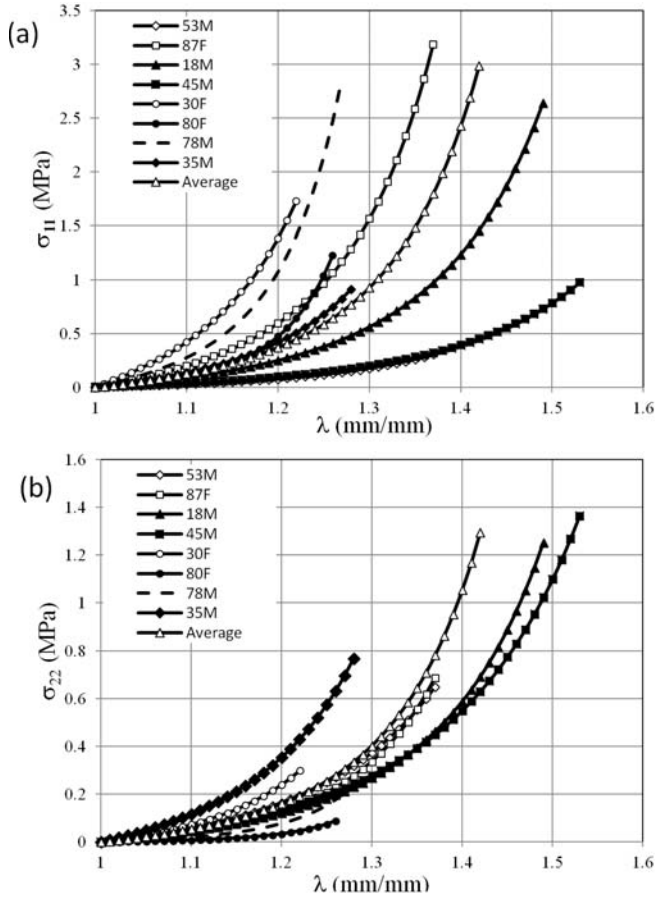

Fig. 2 Stretch-stress curves obtained from the derived constants in circumferential (a) and axial (b) directions ($\lambda = \lambda_1 = \lambda_2$)

To validate the fitting method, the experimental data and model curves which were obtained from derived material constants were illustrated together in Fig. 3 for the youngest and oldest cases. It can be seen that predicted models are in agreement with experimental data.

IV. Discussion

In the present study the mechanical properties of cerebral vessels located in the circle of Willis were determined through biaxial mechanical tests and the effect of age and gender has been analyzed.

According to the lack of biaxial data and related material constants of cerebral vessels, the present study can be a proper reference for numerical modeling of cerebral arteries in cases of accidents, head trauma or arterial diseases such as intracranial aneurysms.

Due to the difficulties of removing the cerebral vessels and separating them from the surrounding soft tissue without being damaged, many specimens did not give acceptable data for reporting. Hence from 25 specimens obtained from 22 cadavers, only the data of 8 specimens were acceptable and reportable.

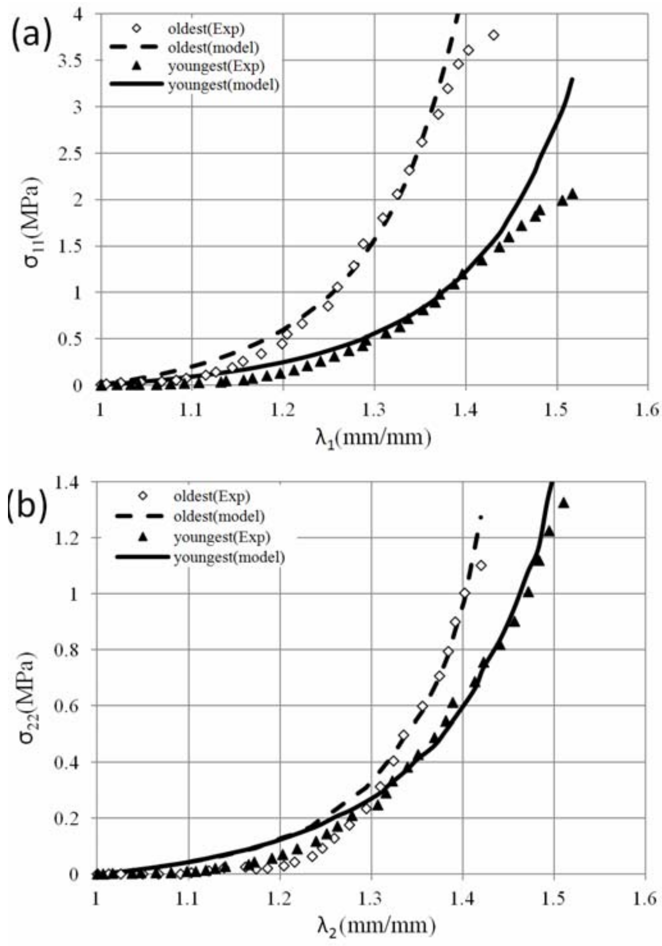

Fig. 3 Comparison of stretch-stress curves of obtained model and experimental data in circumferential (a) and axial (b) directions

V. Conclusions

In the present study the mechanical properties of middle cerebral artery has been determined through biaxial mechanical tests which were performed on total numbers of 8 human specimens. Experimental data then were fitted to a three parameters Fung material model and the average best fit material constants were reported. The obtained stretch-stress curves of model were compatible with the original data. It can be concluded that arteries are noticeably stiffer in circumferential versus axial direction and this represents the necessity to consider the anisotropic behavior of blood vessels. The reported material properties can be a proper reference for numerical modeling of cerebral arteries in cases of trauma or accidents and also in computational analysis of healthy or diseased intracranial arteries considering the interaction between the vessel wall and blood flow, and can be beneficial in prediction of vessel resistance and rupture. Furthermore, the present results provide reliable data for mechanical properties data bank of cerebral vessels.

ACKNOWLEDGMENT

The authors would like to thank Malikeh Nabaei and Aisa Rasuli for their excellent assistance throughout this project.

REFERENCES

[1] R. J. Coulson, M. J. Cipolla, L .Vitullo, N. C. Chesler, "Mechanical properties of rat middle cerebral arteries with and without myogenic tone," *J. Biomech Eng*, 2004, 126, pp. 76-81.
[2] G. A. Holzapfel, T. C. Gasser, R. W. Ogden, "A new constitutive framework for arterial wall mechanics and a comparative study of material models," *J. Elasticity,* 2000, 61, pp. 1-48.
[3] V. Gourisankaran, M. G. Sharma, "The finite element analysis of stresses in atherosclerotic arteries during balloon angioplasty," *Crit Rev Biomed Eng,* 2000, 28 (1-2), pp. 47-51.
[4] Y. Feng, S. Wada, K. Tsubota, T. Yamaguchi, " Growth of intracranial aneurysms arising from curved vessels under the influence of elevated wall shear stress a computer simulation study," *JSME Int. J. Ser. C*, 2004, Series C. 2004, 47(4), pp. 1035–1042.
[5] W. S. Aronow, K.S. Schwartz, M. Koenigsberg, " Correlation of serum lipids calcium, and phosphorus, diabetes mellitus and history of systemic hypertension with presence or absence of calcified or thickened aortic cusps or root in elderly patients," *Am J Cardiol* 1987, 59 (9), pp. 998-9.
[6] M. Lindroos, M. Kupari, J. Heikkila, R. Tuilvis, "Prevalence of aortic valve abnormalities in the elderly: An echocardiography study of a random population sample," *Am J Cardiol,* 1993, 21(5), pp. 1220-5.
[7] K. Ourie, "Peripheral Arterial Disease," *Lancet,* 2001, 358(9289), pp. 1257-64.
[8] C. Ally, A. J. Reid, P. J. Prendergast, "Elastic behavior of porcine coronary artery tissue under uniaxial and equibiaxial tension," *Ann Biomed Eng,* 2004, 32(10), pp. 1355-64.
[9] S. A. Dixon, R. G. Heikes, R. P. Vito, "Constitutive modeling of porcine coronary arteries using designed experiments," *J. Biomech Eng,* 2003, 125(2), pp. 274-9.
[10] S. H. Lu, M. S. Sacks, S. Y. Chung, D. C. Gloeckner, R. Pruchnic, J. Huard, W. C. Degroat, M. B. Chancellor, "Biaxial mechanical properties of muscle derived cell seeded small intestinal submucosa for bladder wall reconstitution," *Biomaterials,* 2005,26(4), pp. 443-9.
[11] J. C. Criscione, M. S. Sacks, W. C. Hunter, "Experimentally tractable pseudoelastic constitutive law for biomembranes," *J. Biomech Eng,* 2003, 125 (1), pp. 94-9.
[12] R. J. Okamoto, J. E. Wagenseil, W. R. Delong, S. J. Peterson, N. T. Kouchoukos, "Mechanical properties of dilated human ascending aorta," *Ann Biomed Eng,* 2002, 30(5), pp. 624-35.
[13] G. J. L'Italien, N. R. Chandrasekar, G. M. Lamuraglia, W. C. Pevec, S. Dhara, D. F. Warnock, W. M. Abbott, "Biaxial elastic properties of rat arteries in vivo: Influence of vascular wall cells on anisotropy," *Am J Physiol,* 1994, 267(2 Pt 2), pp. H574-9.
[14] G. A. Holzapfel, R. Eberlein, P. Wriggers,, H. Weizsacker, "Large strain analysis of soft biological membranes: Formulation and finite element analysis," *Comput Methods Appl Mech Eng,* 1996, 132(1-2), pp. 45-61.
[15] R. W. Ogden, *Nonlinear Elastic Deformations*, 1st Ed, New York, Dover Publication,1997.
[16] M. A. Zulliger, P. Fridez, K. Hayashi, N. Stergiopulos, "A strain energy function for arteries accounting for wall composition and structure," *J. Biomech*, 2004, 37(7), pp. 989-1000.
[17] T. C. Gasser, C. A. Schulze-Bauer, G. A. Holzapfel, "A three dimensional finite element model for arterial clamping," *J. Biomech Eng,* 2002,124.
[18] J. D. Humphrey, R. K. Strumpf, F. C. P. Yin, "Determination of a constitutive relation for passive myocardium: a new functional form," *J. Biomech Eng*, 1990,112.
[19] J. D. Humphrey, R. K. Strumpf, F. C. P. Yin, "Determination of a constitutive relation for passive myocardium: II. Parameter estimation," *J . Biomech Eng*, 1990, 112(3), pp. 340-6.
[20] W. E. Stehbens, "Pathology of the Cerebral Blood Vessels," *St Louis, MO: CV Mosby*, 1972, pp. 351–470
[21] D. E. Busby, A. C. Burton, "The effect of age on the elasticity of the major brain arteries," *Can J Appl Physiol Pharmacol*, 1965, 43(2),pp. 185-202.
[22] J. J. Hu, S. Baek, J. D. Humphrey, "Strain behavior of the passive basilar artery in normotension and hypertension," *J. Biomech*, 2007, 40(11), pp. 2559-63.
[23] J. J. Hu, T. W. Fossum, M. W. Miller, H . Xu, J. C. Liu, J. D. Humphrey, "Biomechanics of the porcine basilar artery in hypertension," *Ann Biomed Eng*, 2006, 35, pp. 19-29.
[24] B. K. Wicker, H. P. Hutchens, Q. Wu, A. T. Yeh, J. D. Humphrey, "Normal basilar artery structure and biaxial mechanical behavior," *Comput Methods Biomech Biomed Engin,* 2008, 11, pp. 539–551.
[25] S. Nagasawa, H. Handa, Y. Naruo, K. Moritake, K. Hayashi, "Experimental cerebral vasospasm arterial wall mechanics and connective tissue composition," *Stroke*, 1982, 13, pp. 595-600.
[26] K. Monson, *Mechanical and failure properties of human cerebral blood vessels*, Ph.D. Thesis, University of California, Berkeley, USA, 2001.
[27] S. Scott, G. G. Fergosun, M. R. Roach, "Comparison of the elastic properties of human intracranial arteries and aneurysms," *Can J Appl Physiol Pharmacol*, 1972, 50, pp. 328-32.
[28] P. Seshaiyer, F. P. K. Hsu, A. D. Shah, S. K. Kyriacou, J. D. Humphrey, "Multiaxial mechanical behavior of human saccular aneurysms," *Comput Methods Biomech Biomed Engin*, 2001, 4, pp. 281-289.
[29] K. Toth, "Analysis of the mechanical parameters of human brain aneurysm," *Acta Bioeng Biomech*, 2005, 7,pp. 1-21.
[30] K. L. Monson, N. M. Barbaro, G. T. Manley, "Biaxial response of passive human cerebral arteries," *Ann Biomed Eng*, 2008, 36, pp. 28-41.
[31] Y. C. Fung, K. Fronek, P. Patitucci, "Pseudoelasticity of arteries and the choice of its mathematical expression," *Am J Physiol,* 1979, 237, pp. 620–631.