Engineering Solid Mechanics 1 (2013) 43-56

Contents lists available at GrowingScience

Engineering Solid Mechanics

homepage: www.GrowingScience.com/esm

Determining the biomechanical properties of human intracranial blood vessels through biaxial tensile test and fitting them to a hyperelastic model

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ARTICLE INFO

Article history:
Received January 20, 2013
Received in Revised form
July, 2, 2013
Accepted 6 August 2013
Available online
7 August 2013

Keywords:
Human Samples
Nonlinear Material
Cerebral Blood Vessels
Anisotropic Tissue
Plain Stress
Mooney-Rivlin Model
Experimental study

ABSTRACT

Understanding mechanical properties of healthy and unhealthy cerebral vessels is a key element in the development of their science and the relevant clinical diagnosis, prevention and treatment. Thirteen healthy samples were obtained from 23 middle cerebral arteries. The changes of force and deformation until the vessel rupture were recorded using a biaxial device. Thereafter, the stress-strain curve was plotted and fitted with a hyperelastic five-parameter Mooney-Rivlin model and the model parameters (C1, C2, C3, C4, and C5) were determined according to the best fit. For statistical comparison, the samples were divided into three age and two gender groups and subjected to non-parametric statistical analyses. Comparison of obtained results for different age groups showed that there is a significant difference between the "old" group and the other two groups (middle-aged and young). There was no significant difference between male and female groups. Therefore, the results demonstrate the changes of blood vessel wall properties with aging. The results also depicted that the arterial wall is stiffer in the circumferential direction than the axial direction. Anisotropy of cerebral vessels was confirmed by all of the tests. Therefore, the significance of the biaxial tests is in the spot light in the derived data. Moreover, good fitting of data illuminated that the use of multiple-parameter constitutive models is useful for mathematical demonstration of cerebral vessel tissue behavior. In conclusion, good fitting of data illuminated that the use of multiple-parameter constitutive models is useful for mathematical demonstration of cerebral vessel tissue behavior.

Nomenclature

Term	Description
λ_1	Stretch ratio in direction 1
λ_2	Stretch ratio in direction 2
λ_3	Stretch ratio in direction 3
C_1 to C_5	Constants of constitutive model of Fung

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doi: 10.5267/j.esm.2013.08.003

F_{11}	Force measured by load cells in direction 1
F_{22}	Force measured by load cells in direction 2
b_1 and b_2	Widths of specimens in the two directions
σ_{ii}^{model}	Cauchy stress calculated from the model
σ_{ii}^{exp}	Cauchy stress calculated based on loads applied in the test
Sij	Components of the second Piola-Kirchhoff stress tensor
Eij	Components of the Green-Lagrange strain tensor
Fij	Components of the finite strain deformation tensor
Iij	Components of the identity unit tensor
B	Function of the Finger tensor
I_3,I_2,I_1	Invariants of the function of the Finger tensor
W	Strain energy density function
S	Second Piola-Kirchhoff stress tensor
E	Green-Lagrange strain tensor
F	Finite strain deformation tensor
I	Identity unit tensor
λ_1, λ_2 & λ_3	Ratios of the function of the principal stretch
μ_1, μ_2,μ_3, α_1, α_2 &α_3	Six material parameters of hyperelastic constitutive equation

1. Introduction

Mechanical properties of arterial wall have significant effects on the functions of blood vessels since they determine the relationships between blood pressure, blood flow, and the size of arterial wall (Coulson et al., 2004). These properties are dependent on the structure and orientation of constituent elements of arterial wall with respect to each other. Due to the orientations of collagen and elastin fibers, arteries show various reactions to applied stresses in different directions and have different properties in longitudinal, radial and circumferential directions. As arteries are orthotropic materials, it is known that arterial wall is stiffer in the radial direction than the axial direction (Cox, 1984; Ally et al., 2004). Arterial walls in human body are always subjected to loading-unloading forces (pressures) which are mostly due to the pulsatile characteristic of blood flow. Factors like gender, smoking, hypertension and diabetes mellitus increase the probability of occurrence of arterial disease (Aronow et al., 1987; Lindroos et al., 1993; Steward et al., 1997; Ourie, 2001). Studying the mechanical properties of arteries is necessary since it is believed that the mechanical factors may be important in initiation of atherosclerosis (Holzapfel et al., 2000).

The external elastic lamina, evident in transition area between tunica media and tunica adventitia of other vessels, does not exist in cerebral arteries. Thickness of the two main layers, tunica media and tunica adventitia, in cerebral arteries are usually less than the arteries of the same diameters. The amount of elastin in tunica media of cerebral arteries is less than other vessels (Busby & Burton, 1965; Stehbens, 1972, Sekhar & Heros, 1981). Many factors are effective in determining the behavior of soft tissues, particularly cerebral vessels. Arteries and most of the biological tissues show non-linear elastic properties. From mechanical point of view, cerebral arteries are anisotropic (Shadwick et al., 1999).

For describing biological tissues, uniaxial and biaxial tests are used. 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. For example, mechanical properties of blood vessels samples in circumferential and axial directions are different due to their anisotropic structure. In biaxial loading, tissue is stiffer and its nonlinearity is less (Dixon et al., 2003). Therefore, biaxial and planar tests may be good alternatives to reach a better understanding of arterial behavior (Guccione et al., 1991; L'italien et al., 1994; Okamoto et al., 2002; Criscione et al., 2003; Sun et al., 2003, Lu et al., 2005; Criscione et al., 2005). Simulations of tissues mechanical behavior are applicable for diagnostic and treatment purposes as well as in surgery (Dumoulin & Cochelin, 2000;

Gourisankaran & Sharma, 2000; Laroche & Delorme, 2006; Gasser & Holzapfel, 2007; Kiousis et al., 2007; Wu et al., 2007). Moreover, constitutive models of wall arteries shall be able to reveal the mechanical behavior of healthy and diseased tissues (Ottensmeyer et al., 2004).

Computational modeling for prediction of cerebral aneurysm growth and rupture requires the biomechanical properties of cerebral vessels as input parameters (Feng et al., 2004). For better understanding of the injuries and disease procedures, modeling methods are also used but limited sets of biomechanical data are available for cerebral vessels. In the past, the structural pattern of arterial wall has not been taken into account in formulation of the constitutive equations that are used traditionally for modeling the mechanical behavior of arterial wall. That is why some researchers turned to formulate constitutive models in which some histological information is considered (Holzapfel et al., 1996; Keshaw, 2001; Gasser et al., 2002; Ogden, 2004). Therefore, the material properties involved can be related to the histological structure of arterial walls. Due to nonlinearity of mechanical properties of arterial wall, constitutive equations describing nonlinearity might have a very complex form with many parameters. Therefore, to formulate elastic properties of arterial walls some assumptions were taken into consideration including ideal cylindrical geometry, homogeneity of material, incompressibility, cylindrical orthotropy and hyperelasticity (Holzapfel & Weizsacker, 1998; Prendergast et al., 2003; Schulze-Bauer and Holzapfel, 2003; Gleason et al., 2004; Holzapfel et al., 2004; Holzapfel, 2005; Virues-Delgadillo et al., 2006).

Hyperelastic models have been shown to be appropriate for prediction of vessel behavior (Humphrey et al., 1990a). Three-parameter Mooney-Rivlin model has been used for modeling the vessels and has had a good fitting to experimental data (Humphrey et al., 1990b). For a more precise fitting, the five-parameter Mooney-Rivlin model is used (Monson et al., 2008). Therefore, obtaining biomechanical properties of cerebral vessels is a significant step toward understanding the mechanisms causing the blood vessel injuries such as cerebral aneurysms. Since most of the studies on the biomechanical properties of blood vessels focus on non-cerebral vessels and regarding to the differences between cerebral vessels and other vessels, determining biomechanical properties of cerebral vessels through biaxial tensile test can smooth the way for further investigations.

The study performed by Monson et al. (2008) is one of the few studies on the cerebral vessels. They investigated the biaxial properties of cerebral vessels by applying internal pressure through inflating the vessels and using the hyperelastic model of Fung et al (1971), but they did not use the plane stress method, as we did, to obtain the biaxial properties of cerebral vessels. Since in the literature, as far as the authors know, there is no definite data regarding hyperelastic model parameters for cerebral vessels subjected to a biaxial test in a plane stress method and there is no study about the effect of gender and age on the mechanical properties of cerebral vessels, the present study was carried out to determine the coefficients mentioned above and also to investigate the effects of mentioned factors on the mechanical properties of cerebral vessels. This is also one of the first studies providing the stress-strain curve for cerebral vessels in two directions.

2. Materials and methods

2.1 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. This device is able to perform a quasi-static test with proper force sensitivity. The clamps of this device are able to directly hold samples with dimensions of $\geq 5\times5$ mm^2. The device can keep the tissue wet during the 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 (Analogue to Digital Converter) and load cell conditioners, for UMAA 2 kgf load cell (Dacell Co., Ltd, Korea Corporation, Korea) attached to the aluminum clamps with a precision of 16 bits. The required tensile forces in this device are applied by four micro stepper motors (made by Autonics Corporation, Gyeonggi-do, Korea) with a resolution of 0.36 degrees and with a torque of 1.2 kg.cm. For visual measurement of the tissue deformation, a USB digital microscope camera (with zoom: 300X, frequency: 30 Hz and resolution: 480×640) was used in the test device. Four drivers were used to start the stepper motors (Autonics model MD5-H14). Data sent by our controller are transferred to a computer and saved there. For synchronizing the results, the data of load cells and cameras were both written simultaneously with a frequency of 5 Hz in a Python programmed code and saved. After completion, the device was calibrated with standard balance weights. Moreover, we tested successfully a silicon sample with known properties to validate our device measurements.

2.2 Strain Energy Density Function

Most experimental data are generally analyzed using the strain energy density function. It is a scalar measure of the energy stored in the material as a result of deformation. 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 (Humphrey et al., 1990b; Sun et al., 2003; Monson et al., 2008):

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

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

where Sij, Eij, Fij, Iij are the components of the second Piola-Kirchhoff stress tensor (s), the Green-Lagrange strain tensor (E), the finite strain deformation tensor (F) and the identity unit tensor (I), respectively.

The most common strain energy density functions used to determine the mechanical properties of an artery are the functions of the Finger tensor (B) or more explicitly in terms of its invariants (I_3, I_2, I_1) (Sun et al., 2003). The Finger tensor B gives us the relative local change in area within the sample and is defined as:

$$B = F.F^{T}. \tag{3}$$

The finite strain deformation tensor (F) is defined as $F = \partial x/\partial x'$, where x' and x are the initial and current configurations, respectively. The invariants of this tensor are given by:

$$I_1 = \mathrm{trB}, \tag{4}$$
$$[(trB)^2 - trB^2] = (1/2)\ I_2, \tag{5}$$
$$I_3 = det\ B\ . \tag{6}$$

For an incompressible material I_3=1. Tr and det refer to transpose of a matrix and determinant of a matrix, respectively.

2.2.1 Hyperelastic models

2.2.1.1 Mooney-Rivlin model

Mooney-Rivlin model (Mooney, 1940; Rivlin, 1948) used in this work includes 5 parameters. This model was used before in many studies for blood vessels (Ally et al., 2004). The strain energy function used was also employed before by Humphrey et al., (1990b), to describe the non-elastic pseudolinear behavior of myocardium (Humphrey et al., 1990b; Monson et al., 2008).

$$W(I_1 {\textstyle'} I_2) = C_1(I_2 - 1)^2 + C_2(I_2 - 1)^3 + C_3(I_1 - 3) + C_4(I_2 - 1)(I_1 - 3) + C_5(I_1 - 3)^2, \tag{7}$$

where W is the strain energy function, I_1 and I_2 are invariants of right Cauchy deformation tensor, and C_1-C_5 are empiric constants to be fitted.

2.2.1.2 Other models developed to describe the behavior of arteries

Several researchers have developed many mathematical expressions that describe the stress-strain relationship for mechanical tests, but the most common are those based on polynomial or exponential functions. A three dimensional strain energy function which is appropriate for the analysis of thick-walled tubes or a two dimensional strain energy function can be used for modeling the mechanical properties of arteries. Some of these functions are described below:

Ogden (Keshaw, 2001) proposed an isotropic, hyperelastic constitutive equation that has six material parameters (three dimensional: μ_1, μ_2,μ_3, and three non-dimensional: α_1, α_2,α_3), which is a function of the principal stretch ratios, λ_1,λ_2 and λ_3. Another three dimensional strain energy function was developed by Humphrey et al. (1990b) and Monson et al. (2008). For doing that, they based their development on the extension of the two dimensional strain energy function proposed by Fung et al., (1971). Until now, the architecture of the arterial wall has not been considered in the formulation of the constitutive equations that are conventionally used to model the mechanical behavior of the arterial wall. That is why several researchers (Holzapfel et al., 1996; Holzapfel et al., 2000) have formulated constitutive models which incorporate some histological information. Hence, the material parameters involved may be associated with the histological structure of the arterial walls.

2.3. Test method

Thirteen samples were obtained from 23 middle cerebral arteries (MCA) extracted according to a special protocol from 20 human cadavers whose death was not due to injuries or diseases of cerebral blood vessels. These samples were subjected to the test by our biaxial tensile device within 12 hours after their resection. Before resecting the samples, the families of the deceased were asked to sign a consensus form. To reach a uniform stress distribution, special clamps were designed such that could grip tissues with dimensions as small as 5×5 mm^2 directly. These lightweight clamps were then attached to the load cells. In order to prevent damages of the vessels, brain of the deceased were first removed completely. Then all cerebral vessels were separated from soft tissue by an expert neurosurgeon. To standardize the tests, 10mm proximal segment of MCA was resected for all specimens. To maintain the physiological conditions and freshness of samples, all the tests were done on the day of acquiring samples. Specimens were stored in physiological saline 0.9%. Thickness of specimens was measured with a vernier caliper. Then the specimens were cut to 5×5 mm^{2}with a special cutter. 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) by the movement of four stepper motors (Fig. 1).

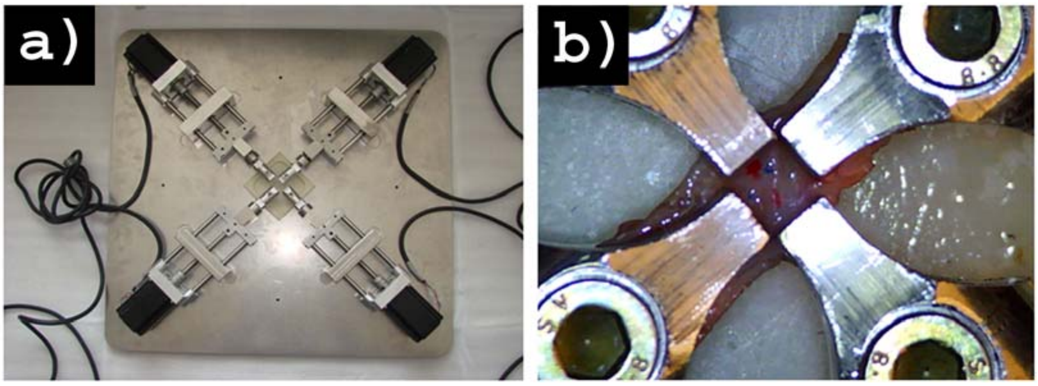

Fig. 1. Biaxial tensile test device (a) and cerebral vessel specimen under loading (b)

The rate of 0.02 mm/s was chosen for applying the tension in quasi-static tests. Force and displacement data were recorded in 0.2 second intervals (i.e. frequency of 5 Hz). Due to low rate of loading (the strain rate was 0.02 mm/s in all tests), there was no need to consider the specimens as viscous materials. Information of patients were gathered and collected. Then, to compare the specimens, three age groups were formed according to the standard of blood vessel diseases as follows:

Group A: Young people under 45 years old
Group B: Middle-aged people ranging from 45 to 65 years old
Group C: Old people above 65years old

In order to measure the strains, a digital microscope camera, (installed above and perpendicular to the specimens) was used. To synchronize the data, images of the camera and data of the load cells were acquired with a frequency of 5 Hz. As the data and images were synchronous, 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. Thus 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. These displacements were also compared with the stretch of tissue obtained by images by means of Image J freeware. In the case of any difference between the displacement of the clamps and the stretch of the tissue, the data were deleted as this discrepancy was due to slip of the tissue.

2.4. Data processing

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

$$\sigma_{11}^{exp} = \lambda_1 \frac{F_{11}}{b_1 t}, \tag{8}$$

$$\sigma_{22}^{exp} = \lambda_2 \frac{F_{22}}{b_2 t}, \tag{9}$$

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

$$\sigma_{11}^{model} = 2\lambda_1 c_1(\lambda_1 - 1) + 3\lambda_1 c_2(\lambda_1 - 1)^2 + \lambda_1 c_4\left({\lambda_1}^2 + {\lambda_2}^2 + {\lambda_3}^2 - 3\right) + 2\left({\lambda_1}^2 - {\lambda_3}^2\right)\left[c_3 + c_4(\lambda_1 - 1) + 2c_5\left({\lambda_1}^2 + {\lambda_2}^2 + {\lambda_3}^2 - 3\right)\right], \tag{10}$$

$$\sigma_{22}^{model} = 2\left({\lambda_2}^2 - {\lambda_3}^2\right)\left[c_3 + c_4(\lambda_1 - 1) + 2c_5\left({\lambda_1}^2 + {\lambda_2}^2 + {\lambda_3}^2 - 3\right)\right], \tag{11}$$

where C_1 to C_5 are constants of constitutive model. For proper fitting of empirical constants and model parameters, an algorithm was written using COBYLA (Powell, 1998) (an acronym of Constrained Optimization BY Linear Approximations). COBYLA algorithm employs linear approximations to the objective and constraint functions. These approximations are formed by linear interpolation at n+1 points in the space of the variables. The interpolation points are regarded as vertices of a simplex. In our routine, it is reduced from 1 to 10^{-8}. COBYLA minimizes the difference between the experimental stresses and the model stresses obtained based on Eq. (10) and Eq. (11) using the following equation:

$$\underset{c_i}{\boldsymbol{Min}} \sum_{n=1}^{f_n}\left[\left({\sigma_{11}}^{model} - {\sigma_{11}}^{exp}\right)^2 + \left({\sigma_{22}}^{model} - {\sigma_{22}}^{exp}\right)^2\right], \tag{12}$$

where σ_{ii}^{model} is Cauchy stress calculated from the model for a specified deformation, σ_{ii}^{exp} is Cauchy stress calculated based on the loads applied in the test, deformation gradient tensor and specimen geometry. Parameters C_1 to C_5 were calculated by COBYLA algorithm with an initial guess of (1,1,1,1,1) and after applying 10 million times iterations of optimization program. The optimization program stops reaching the convergence threshold of 10^{-8}, otherwise it is implemented for 10 million times. In all of our tests, the convergence threshold was reached before 10 million times.

2.5. Analysis of statistical results

The wall mechanical properties of cerebral vessels of the circle of Willis for these hyper-elastic coefficients were studied using the mean value of variables categorized based on age and gender and were compared using the non-parametric Mann-Whitney U (Mann & Whitney, 1947) test (for gender categories) and the non-parametric Kruskal-Wallis (Wallis, 1952) test (for the investigated age categories). The levels of significance in these statistical tests were set on 0.05. The SPSS software version 19 was used for statistical analysis.

3. Results

3.1 Statistical population

Regarding the gender distribution, most of the specimens in this research, i.e. 53.8 % (7 persons), were female samples and the rest (6 persons, 46.2%) were male samples. Regarding the age distribution, most of the specimens (6 specimens or 38.5%) belonged to middle-aged party. The distribution of specimens of young and old groups was 30.75% (4 people in each group), Tables 1 to 4 summarize the information of samples used for experimental study of this research.

Table 1. Specifications of tested specimens

Total number of specimens	13
Ratio of male/female	6/7
Average age	57.23
Age range	18-87
Average thickness of MCA vessels	0.6 mm

Table 2. Age classification

Group	Average age	Ratio of male/female	Number of specimens
A: Young	34.5	3/1	4
B: Middle-aged	54.2	2/3	5
C: Old	83	2/2	4

Table 3. The abundance distribution related to (gender) variable

Levels	Abundance	Percentage
Male	6	46.2
Female	7	53.8
Total	13	100

Table 4. The abundance distribution related to (age) variable

Levels	Abundance	Percentage
Old	4	30.75
Middle-aged	5	38.5
Young	4	30.75
Total	13	100

3.2. Mechanical test

After carrying out mechanical tests and data processing, the average thickness of the specimens and the average cross sectional area under tension were 0.6 mm and 3 mm^2, respectively. Table 5 provides the amounts of C_1 to C_5 under various range of tensions.

Table 5. The abundance distribution related to (age) variable

Hyperelastic coefficients	Range of tension (MPa)	Average amount
C_1	[-1.27 to 0.79]	0.2567
C_2	[-2.83 to 8.84]	1.3348
C_3	[-0.33 to 0.06]	-0.2950
C_4	[-1.1 to 21.1]	0.0377
C_5	[-0.11 to 0.22]	0.0455

To facilitate the analysis, the results have been reported based on age and gender in Table 6.

Table 6. Mann-Whitney U (comparison of hyperelastic coefficients in biaxial test with emphasize on gender)

Hyperelastic coefficients	Gender	Number	Average of ranks	Sum of the ranks	Mann-Whitney U	Amount of Z	Level of significance
C_1	Male	6	8	48	15	-0.857	0.445
	Female	7	6.14	43			
C_2	Male	6	7.17	43	20	-0.143	0.945
	Female	7	6.86	48			
C_3	Male	6	7.33	44	19	-0.286	0.836
	Female	7	6.71	47			
C_4	Male	6	5.67	34	13	-1.143	0.295
	Female	7	8.14	57			
C_5	Male	6	8.17	49	14	-1	0.366
	Female	7	6	42			

- The Mann-Whitney U test is used to assess whether two independent groups are significantly different from each other.
- The level of significance shows the probability of the results being down to chance.
- Z is the number of standard deviations.

Table 7. Kruskal-Wallis (comparison of hyperelastic coefficients in biaxial test with emphasize on age range)

Hyperelastic coefficients	Age range	Number	Average of ranks	Chi-square	Degrees of freedom	Level of significance
C_1	old	4	7	0.267	2	0.875
	Middle-aged	5	6.40			
	Young	4	7.75			
C_2	old	4	10.50	8.40	2	0.015
	Middle-aged	5	3.20			
	Young	4	8.25			
C_3	old	4	7.25	5.38	2	0.068
	Middle-aged	5	4.20			
	Young	4	10.25			
C_4	old	4	4	7.24	2	0.027
	Middle-aged	5	10.60			
	Young	4	5.50			
C_5	old	5	10.25	6.86	2	0.032
	Middle-aged	4	3.60			
	Young	5	8			

- The degree of freedom is the number of groups minus 1.
- the chi-squared distribution is the distribution of a sum of the squares of the independent standard normal random variables.

4. Discussion and conclusion

To investigate the hypothesis that the vessel properties change in various age and gender groups, the data obtained from these groups were compared statistically. According to Table 7 and with emphasize on the values of U and due to small difference in the significance level of α=0.05, it can be stated that there is no considerable difference between the hyperelastic coefficients C_1 to C_5 in female and male groups subjected to the biaxial test. Therefore, the average amounts of stresses and strains reported in this study can be used simultaneously for both groups. According to the results in Table 8 and with emphasize on the values of Z, there is a meaningful difference between the hyperelastic coefficients C_2 and C_5 in significance levels of α=0.01 and α=0.05. Regarding the ranks of hyperelastic coefficients C_2 and C_5 in the "old" group (10.50 and 10.25, respectively) are greater than those of the “young” and “middle-aged” groups, it can be concluded that the amounts of hyperelastic coefficients C_2 and C_5 in biaxial test are greater in “old” group. This underscores the increase in vessel stiffness with aging. There is also a noticeable difference in hyperelastic coefficients C_4 in significance level of α=0.05. As the average of ranks for this coefficient is in the middle-aged group (10.60) greater than those of the old and young groups, thus the amount of hyper-elastic coefficient C_4 is greater in middle-aged group.

The maximum values of C_2 in the old group were 3.34 MPa (average value of this group was: 1.35 MPa). The maximum values of C_5 in the old group were 0.19 MPa (average value of this group was -0.052 MPa). The maximum values of C_4 in middle-aged were 1.21MPa (with average of 0.684 MPa). In general, the vessels in the male group had a stiffer behavior than those of female group (Table 7).
By computing the modulus of elasticity in the range of physiological stresses inside vessels, it was found that the tangent modulus in axial direction is in the range of 0.5 and 1.4 MPa (with average value of 0.82 MPa) and in circumferential direction is in the range of 0.6 and 1.6 MPa (with average of 0.87 MPa). By comparing the curves of mechanical behavior obtained for the tested cerebral vessels in axial and circumferential directions and their corresponding slopes, it was found that these vessels are stiffer in circumferential direction than in axial direction.

Regarding the results of biaxial test and the small size of specimens studied, the obtained data are a proper reference for numerical modeling of cerebral vessels in cases of accidents, the head trauma and the aneurysms. The average values reported in this investigation can be used regardless of gender. Experimental data related to the biaxial test of cerebral vessels, as far as the authors know, had not been available in literature. By the way, the Monson’s study was performed by applying the internal pressure through inflation and there was no categorization in it based on gender and age (Monson et al., 2008). The most important accomplishment of the present study was the determination of mechanical properties of cerebral vessels of the Willis circle through biaxial test and demonstration of differences and changes of properties with aging in addition to the comparison of vessel mechanical properties between genders (see Figs. 2-8).

Overall, good fitting of data illuminated that the use of multiple-parameter constitutive models is useful for mathematical demonstration of cerebral vessel tissue behaviour. It is finally noted that according to measurement protocol, many of the specimens did not have acceptable data for reporting since removing the cerebral vessels and separating them from the surrounding soft tissue without being damaged was intricate very difficult. Hence, from 23 specimens obtained from 20 cadavers, only the data of 13 specimens were acceptable and reportable. Carrying out extensive tests on various categories yields more comprehensive information.

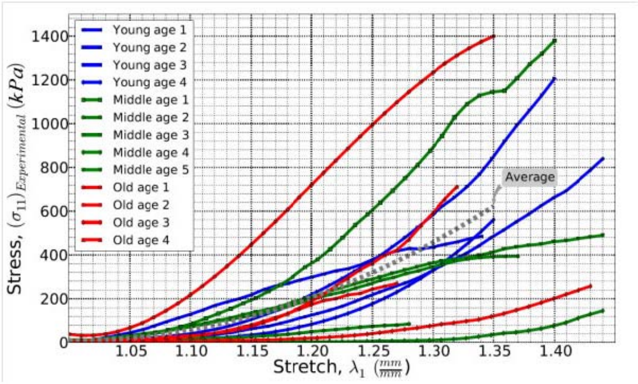

Fig. 2. Stress-strain curve in axial direction for all of the studied specimens based on the age group along with the average curve

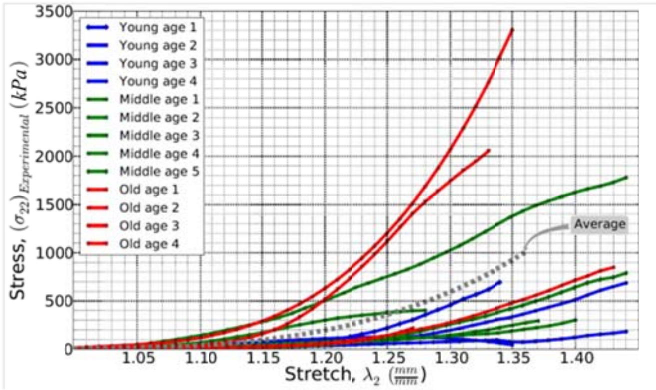

Fig. 3. Stress-strain curves in circumferential direction for all of the studied specimens based on the age group along with the average curve

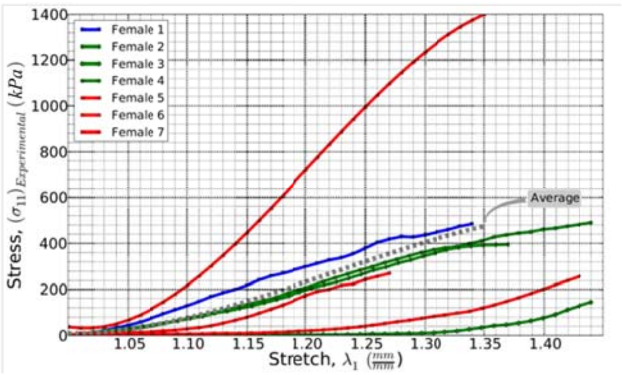

Fig. 4. Stress-strain curves in axial direction for all of the female specimens studied along with the average curve

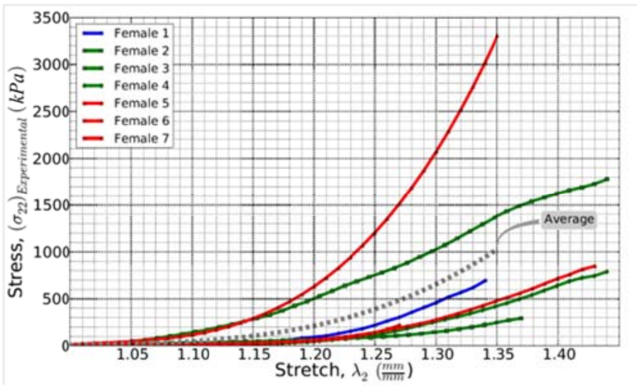

Fig. 5. Stress-strain curves in circumferential direction for all of the studied female specimens along with the average curve

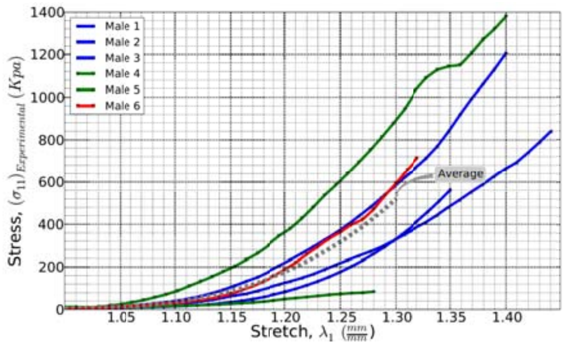

Fig. 6. Stress-strain curves in axial direction for all of the male studied specimens along with the average curve

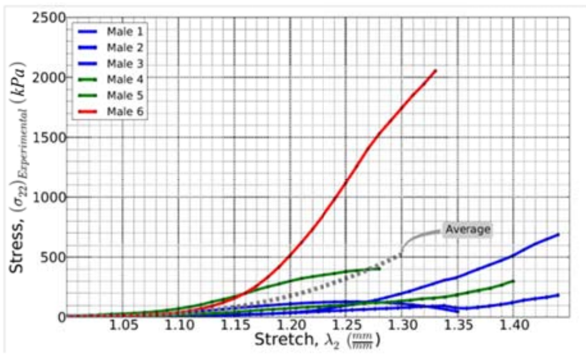

Fig. 7. Stress-strain curves in circumferential direction for all of the studied male specimens along with the average curve

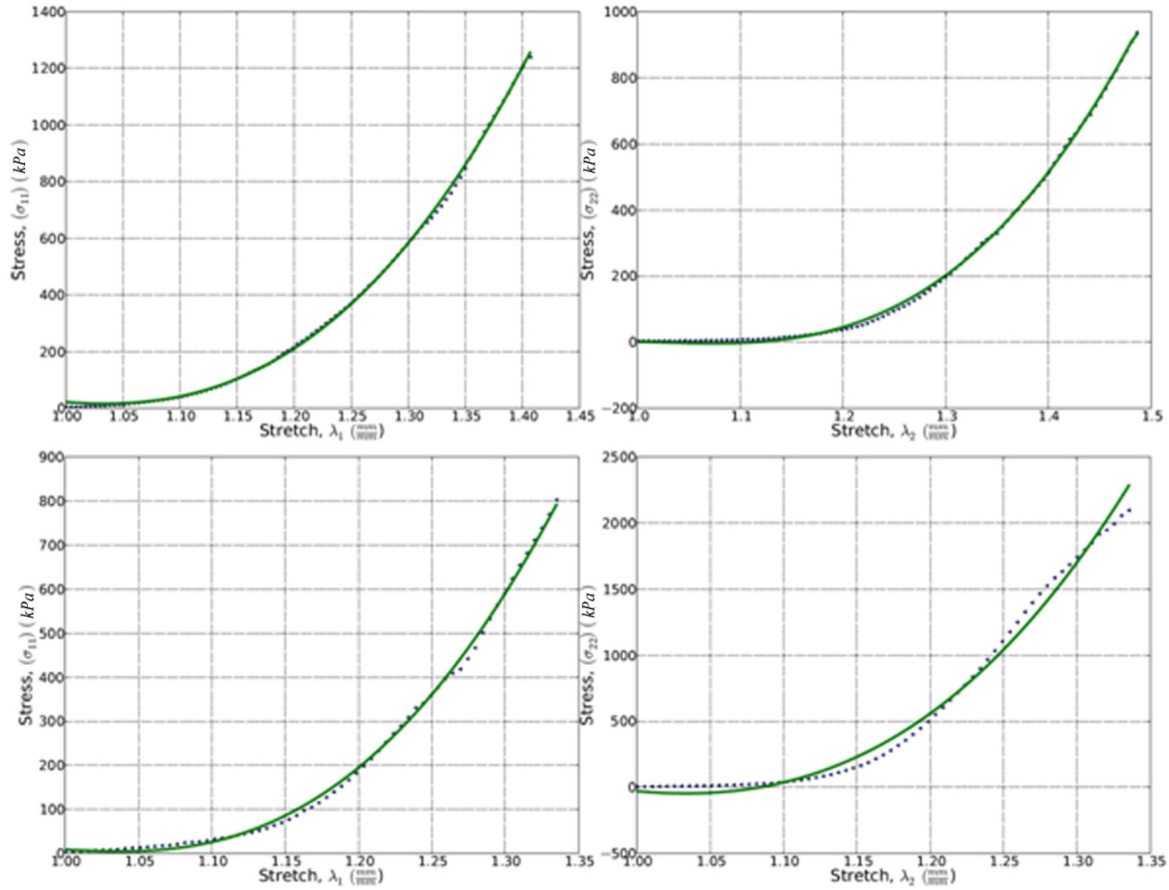

Fig. 8. Comparison of some specimens subjected to tension in two directions along with the fitted model. Dots show the experimental data and the solid line is the result of mathematical model

Specimens were studied in gender and age groups. The specimens of "old" group were stiffer than those of other groups and this confirmed the variation of wall mechanical properties of vessels with aging. There was no significant difference between male and female groups. Studying the biomechanical behavior of cerebral vessels is useful for modeling and predicting the behavior of vessel in cases of accidents and cerebral aneurysms. Knowing the stress-strain behavior of cerebral vessels can be beneficial in prediction of vessel resistance and rupture time by numerical and computational modeling. Further studies on biomechanical properties of cerebral vessels can help the understanding of the biomechanical conditions leading to occurrence and rupture of aneurysms during traumas and accidents. Biomechanical properties of cerebral vessels can be a helpful prediction of indices for more comprehensive studies through simulations of wall structure-fluid interaction based on imaging so that patients can be informed of rupture risk according to these expert assessments (Nabaei & Fatouraee, 2012). This can also be helpful in creation of the numerical simulation software which will lead to better understanding of changes of wall mechanical properties of cerebral vessels. Furthermore, researches conducted in this study provide reliable data for mechanical properties of cerebral vessels.

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