CONSTITUTIVE MODELLING OF HUMAN PERIVASCULAR ADIPOSE TISSUE

TEREZA VONAVKOVA[*], LUKAS HORNY[*], TOMAS ADAMEK[†], MARKETA KULVAJTOVA[†] AND RUDOLF ZITNY[*]

[*] Faculty of Mechanical Engineering
Czech Technical University in Prague
Technicka 4, 166 07 Praha 6, Czech Republic
e-mail: Tereza.Vonavkova@fs.cvut.cz, http://www.biomechanika.cz/

[†] Third Faculty of Medicine
Charles University in Prague
Ruska 87, 100 00 Praha 10, Czech Republic

Key words: Abdominal aorta, Constitutive modelling, Hyperelasticity, Incompressibility, Isotropy, Perivascular adipose tissue.

Abstract. The mechanical properties of adipose tissue are studied rarely despite the fact that surrounding tissue plays an important role in arterial physiology and mechanobiology. This study deals with the determination of material parameters of human perivascular adipose tissue surrounding the abdominal aorta. The selected representative experimental curve from uniaxial tensile test was used to be fitted by Ogden, Gent, and Fung hyperelastic models assuming isotropic and incompressible material of perivascular tissue. The estimated material parameters are $\mu = 0.001$ MPa and $\alpha = 28$, $\mu = 0.026$ MPa and $J_m = 0.067$, $\mu = 0.018$ MPa and $b = 31.834$, respectively. It was concluded that all applied mathematical models predicted nonlinear stress-strain relationship satisfactorily with coefficient of determination 0.995, 0.981, 0.994, respectively.

1 INTRODUCTION

One of the modifiable risk factors of mortality to cardiovascular diseases is obesity [1, 2]. The adipose tissue surrounds all blood vessels and organs and influences their mechanical state. This paper is focused on constitutive modelling of human perivascular adipose tissue that surrounds the abdominal aorta. The perivascular tissue should be taken into account in solving various types of boundary problems of abdominal aorta such as computational simulations of aneurysm or *in vivo* constitutive modeling.

The main function of fat tissue is the protection organs before trauma, and energy storage. The adipose tissue contains preadipocytes, adipocytes (fat cells), endothelial cells, monocytes/macrophages, nerve fibers and blood vessels [1-3].

The fat cells produce proteins such as adiponectin, leptin, adipokines and cytokines. Adiponectin significantly regulates metabolism of sacharides and lipids and increases the

transport of glucose and free fatty acids into muscle, liver and fat cells. Leptin is essential contribution to regulation of body weight [1-8]. Adipokines and cytokines are inflammatory proteins which may diffuse from surrounding adipose tissue into the arterial wall, where subsequently may cause endothelial dysfunction, hypercoagulability and proliferation of smooth muscle cells [1].

The aim of this study is to determine the material parameters of human perivascular adipose tissue surrounding abdominal aorta by fitting hyperelastic material models (Ogden, Gent, Fung) to uniaxial tensile test data.

2 MATERIALS AND METHODS

The human abdominal aorta specimen with perivascular adipose tissue was received from the Faculty Hospital Královské Vinohrady in Prague and was resected from cadaveric donor (male, 29 years old). Our study has been approved by the Ethics Committee of the Faculty Hospital Královské Vinohrady. The sample of perivascular tissue was manually separated from aortic wall using a scalpel and subsequently trimmed to approximately rectangular shape (Figure 1). Before the mechanical testing, reference sample dimensions (Table 1) were determined by image analysis of digital photographs (Nis-Elements, Nikon Instruments Inc., NY, USA). Axis of the adipose tissue specimen was parallel with axis of the abdominal aorta (Figure 2). The fat tissue sample was tested in air, at room temperature and 38 hours after removal from a deceased donor.

Table 1: Reference dimensions of the perivascular tissue sample from male donor aged 29 years.

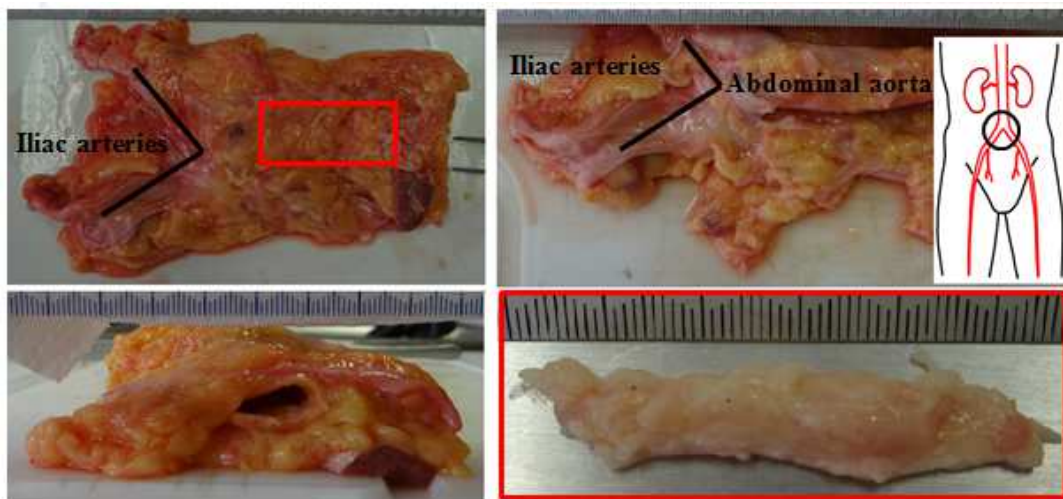| Donor	Age [years]	Sex	Reference dimensions (mean ± SD)		
			Thickness [mm]	Width [mm]	Cross-section [mm^2]
M29	29	Male	7.998 ± 0.295	6.456 ± 0.456	51.640

Figure 1: Sample of the human abdominal aorta and iliac arteries with surrounding perivascular adipose tissue.

2.1 Kinematics of uniaxial tensile test

Consider x and X, respectively, denoting the position vector of material particle in some reference (undeformed) configuration β_r and some deformed (current) configuration β. Motion of a continuum body is shown in Figure 2. The mapping from reference to current configuration is described by [9]

$$x = \chi(X, t), \tag{1}$$

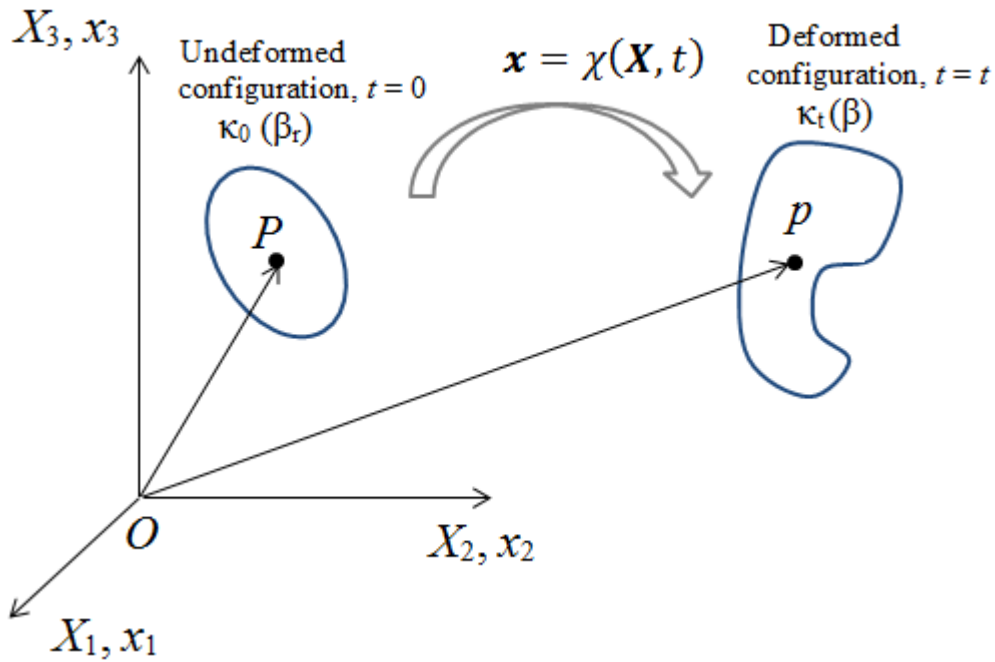where χ is the function describing the motion.

Figure 2: A Change of shape or volume of the body (deformation) from undeformed configuration β_r to deformed configuration β.

The deformation gradient tensor is described by equation [9]

$$\mathbf{F} = \frac{\partial \chi}{\partial X}. \tag{2}$$

In case of incompressible material can be determinant of the deformation gradient expressed as [9]

$$\det \mathbf{F} = \lambda_1 \lambda_2 \lambda_3 = 1, \tag{3}$$

where λ are the principal stretches and index 1 indicates direction of the loading force, λ_2 and λ_3 are transversal stretches.

For an isotropic material during uniaxial tensile test can be written the following relationship [10]

$$\lambda_2 = \lambda_3. \tag{4}$$

From equation (3) and (4) implies [10]

$$\lambda_2 = \frac{1}{\sqrt{\lambda_1}}. \tag{5}$$

The deformation gradient when considering incompressibility and isotropy is [10]

$$\mathbf{F} = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \frac{1}{\sqrt{\lambda_1}} & 0 \\ 0 & 0 & \frac{1}{\sqrt{\lambda_1}} \end{pmatrix}. \tag{6}$$

The right Cauchy-Green strain tensor is generates from the deformation gradient [9]

$$\mathbf{C} = \mathbf{F^T F}, \tag{7}$$

where ^{T} represents transpose of a second-order tensor.

2.2 Constitutive modelling

The strain energy density function for the hyperelastic Ogden [11], Gent [12], and Fung [13] model is expressed as

$$W_{\text{Ogden}} = \frac{\mu}{\alpha}(\lambda_1^\alpha + \lambda_2^\alpha + \lambda_3^\alpha - 3), \tag{8}$$

$$W_{\text{Gent}} = -\frac{1}{2}\mu J_m ln\left(1 - \frac{I_1 - 3}{J_m}\right), \tag{9}$$

$$W_{\text{Fung}} = \frac{1}{2}\frac{\mu(e^{b(I_1 - 3)} - 1)}{b}, \tag{10}$$

where $\lambda_1, \lambda_2, \lambda_3$ are the principal stretches and $I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2$ is the first invariant of the right Cauchy-Green strain tensor. μ, α, J_m, b are material parameters. μ is positive stress-like material parameter corresponding at infinitesimal strain in shear modulus. α, J_m, b are dimensionless material constants which indicate strain stiffening of material.

The Cauchy stress tensor for incompressible material is given by constitutive equation [11]

$$\boldsymbol{\sigma} = \mathbf{F}\frac{\partial W}{\partial \mathbf{F}} - p\mathbf{I}, \tag{11}$$

where $\mathbf{F}$ is the deformation gradient, $\mathbf{I}$ is the unit tensor. p is the Lagrange multiplier which is interpreted as the hydrostatic pressure resulting from the incompressibility constrain $\sigma_{22} = 0$.

The Cauchy stress acting in the direction of axial force during uniaxial tensile loading for incompressible material can be express by equations (8) for Ogden, (9) for Gent, and (10) for Fung model

$$\sigma_{\text{mod}}^{\text{Ogden}} = \mu \lambda_1^\alpha - \mu \left(\frac{1}{\sqrt{\lambda_1}} \right)^\alpha, \tag{12}$$

$$\sigma_{\text{mod}}^{\text{Gent}} = \frac{\mu J_m \left(\lambda_1^3 - 1 \right)}{J_m \lambda_1 + 3\lambda_1 - \lambda_1^3 - 2}, \tag{13}$$

$$\sigma_{\text{mod}}^{\text{Fung}} = \frac{\mu}{\lambda_1} e^{\frac{b(\lambda_1 + 2)(\lambda_1 - 1)^2}{\lambda_1}} \left(\lambda_1^3 - 1 \right). \tag{14}$$

2.3 Uniaxial tensile test protocol

The multipurpose testing machine (Zwick/Roell, Ulm, Germany) was used for measurement of mechanical properties of human perivascular tissue (Figure 3a). Values of sample deformations were determined by built-in video extensometer by means of the distance of transverse marks on the sample surface (Figure 3b). Current force (U9B, ± 25 N, HBM, Darmstadt, Germany) and video extensometer data were recorded into the controlling computer. Four loading cycles were realized at constant velocity of the clamp 0.2 mm/s.
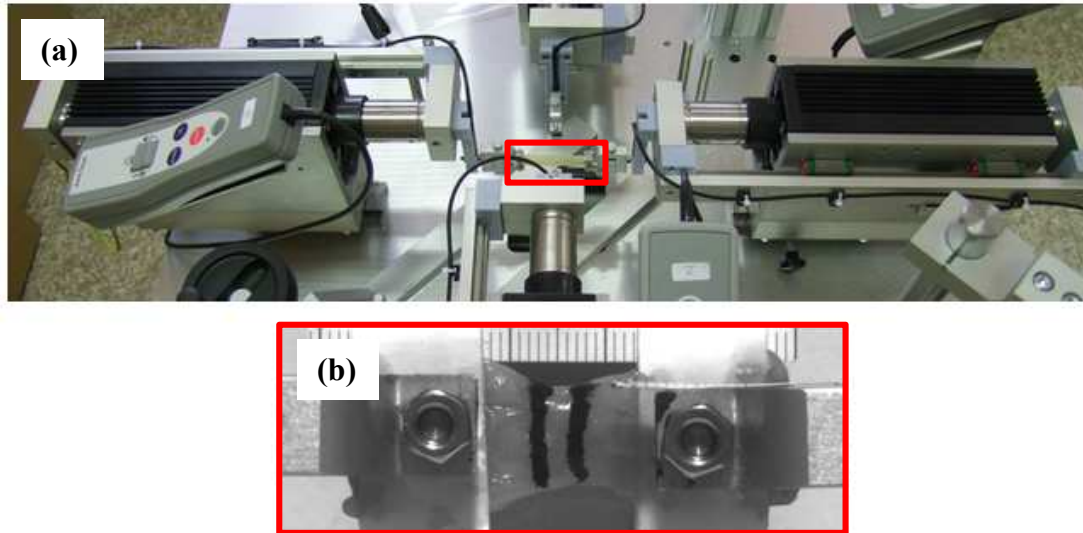

Figure 3: (a) The multipurpose testing machine for uniaxial tensile test.
(b) The tested sample of human perivascular tissue in the jaws of the multipurpose testing machine with transverse marks for the strain measurement.

In the case of uniaxial tensile tests, incompressible and isotropic material is the Cauchy stress expressed as [10]

$$\sigma_{\text{exp}} = \lambda_1 \frac{f}{A}. \tag{15}$$

2.4 Optimization

The material parameters (μ, α, J_m, b) have been determined by means of nonlinear least squares regression method. The objective function Q was minimized in Maple (Maplesoft, Waterloo, Canada)

$$Q^2 = \sum_{i=1}^{n} \left(\sigma_{\text{exp}_i} - \sigma_{\text{mod}_i} \right)^2, \tag{16}$$

where n is the number of observation points.

The quality of the regression was evaluated by means of the coefficient of determination

$$\rho^2(\sigma) = 1 - \frac{\sum_{i=1}^{n} \left(\sigma_{\text{mod}_i} - \sigma_{\text{exp}_i} \right)^2}{\sum_{i=1}^{n} \left(\sigma_{\text{exp}_i} - \text{Mean}\left(\sigma_{\text{exp}_i} \right) \right)^2}. \tag{17}$$

3   RESULTS

The reference dimensions (Table 1) were determined as a mean value of six measurements of geometrically non-uniform sample (width, thickness and cross-section area).

The uniaxial tensile test data (the stress-stretch relationship) fitted by models (8), (9), (10) are displayed in Figure 4. The estimated material parameters, α = 28 and μ = 0.001 MPa, J_m =0.067 and μ = 0.026 MPa, b = 31.834 and μ = 0.018 MPa, respectively, are summarized in Table 2. The goodness of fit of the nonlinear regression analysis is indicated by the coefficients of determination which are included in Table 2.

Table 2: Material parameters obtained from Ogden, Gent and Fung model and coefficient of determination.

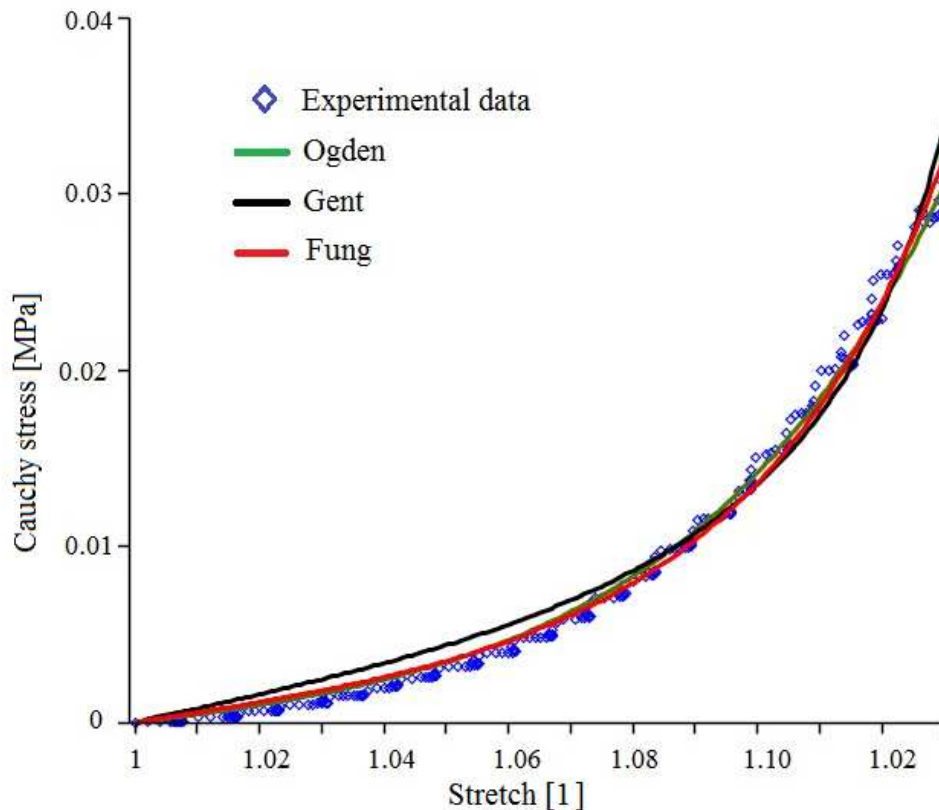| Hyperelastic model	Material parameter μ [MPa]	Material parameter α, J_m, b [-]	Coefficient of determination
Ogden	0.001	28	0.995
Gent	0.026	0.067	0.981
Fung	0.018	31.834	0.994

Figure 4: Results of the nonlinear regression analysis.

4 DISCUSSION

This article is focused on the constitutive modelling of human perivascular adipose tissue. The sample of perivascular tissue from donor, 29 year old men (M29), was subjected to uniaxial tensile test at post mortem interval 38 hours (Figure 1). It has been observed nonlinear behavior with large deformations typical for biological materials (Figure 4). The experimental stress-stretch curve was used to fit three hyperelastic models (Ogden, Gent, Fung) assuming isotropic and incompressible material of the tissue (Figure 4). Material parameters (Table 2) of perivascular adipose tissue were obtained for each model applying a nonlinear regression analysis. We concluded that all applied material models predicted the uniaxial tensile test data satisfactorily.

To the best of authors´ knowledge, this is the first study which offers materials parameters for human perivascular adipose tissue surrounding abdominal aorta. In the literature, we can find studies dealing with mechanical properties of adipose tissue located in other areas of the body. Sommer et al. [14] found constitutive parameters from biaxial tensile tests of 8 samples $(c, k_1, k_2, \varphi, \kappa)$ and triaxial shear test with 6 specimens of subcutaneous adipose tissue $(c, k_1, k_2, \varphi, \nu, \kappa)$. Holzapfel-Gasser-Ogden hyperelastic model that includes incompressibility and anisotropy defined by two families of collagen fibers was used to determine the material parameters.

Material models are part of commercial FEM software, therefore the results of our study could be included in stress analysis of the human abdominal aorta with surrounding perivascular adipose tissue or simulation of aneurysm.

ACKNOWLEDGEMENT

REFERENCES

[1] Verhagen SN, Visseren FLJ (2011) Perivascular adipose tissue as cause of atherosclerosis. Atherosclerosis 214:3-10. doi:10.1016/j.atherosclerosis.2010.05.034.

[2] Chan JM, Rimm EB, Colditz GA, Stampher MJ, Willett WC (1944) Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care 17 (9):961-969.

[3] Hauner H (2004) The new concept of adipose tissue function. Physiol Behav 83(4):653-8. doi:10.1016/j.physbeh.2004.09.016.

[4] Arita Y, Kihara S, Ouchi N et al. (1999) Paradoxical decrease of an adipose-specific protein, adiponectin,in obesity. Biochem Biophys Res Commun; 257 (1): 79–83.

[5] Yamauchi T, Kamon J, Minokoshi Y et al. (2002) Adiponectin stimulates glucose utilization and fattyacid oxidation by activating AMP-activated protein kinase. Nat Med; 8 (11): 1288–1295.

[6] Haluzik M (2002) Poruchy výživy a leptin. Praha: Grada Publishing.

[7] Hotta K, Funahashi T, Arita Y et al. (2000) Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. Arterioscler Thromb Vasc Biol; 20 (6): 1595–1599.

[8] Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW, Jr. (2003) Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest; 112 (12): 1796–1808

[9] Ogden RW (2003) Nonlinear Elasticity, Anisotropy, Material Stability and Residual stresses in Soft Tissue. Biomechanics of Soft Tissue in Cardiovascular Systems. 441: 65-108. doi: 10.1007/978-3-7091-2736-0.

[10] Taber LA (2004) Nonlinear Theory of Elasticity: Applications in Biomechanics. ISBN:9812387358. World Scientific.

[11] Ogden RW (1982) Elastic deformations of rubberlike solids. In Mechanics of Solids (The Rodney Hill 60th Anniversary Volume), pages 499–538. Wheaton and Co.

[12] Gent AN (1996) New constitutive relation for rubber. Rub. Chem. Technol. 69:59–61.

[13] Demiray H. (1972) A note on the elasticity of soft biological tissues. J. Biomech. 5(3):309-11.

[13] Taber LA (2004) Nonlinear Theory of Elasticity: Applications in Biomechanics. ISBN: 9812387358. World Scientific.

[14] Sommer G, Eder M, Kovacs L, Pathak H, Bonitz L, Mueller Ch, Regitnig P, Holzapfel GA (2013) Multiaxial mechanical properties and constitutive modeling of human adipose tissue: A basis for preoperative simulations in plastic and reconstructive surgery Acta Biomat 9:9036-9048. doi: 10.1016/j.actbio.2013.06.011.