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Continuum mathematical modelling of pathological growth of blood vessels

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Abstract. The present study is devoted to the mathematical modelling of a human blood vessel pathological growth. The vessels are simulated as the thin-walled circular tube. The boundary value problem of the surface growth of an elastic thin-walled cylinder is solved. The analytical solution is obtained in terms of velocities of stress strain state parameters. The condition of thinness allows us to study finite displacements of cylinder surfaces by means of infinitesimal deformations. The stress-strain state characteristics, which depend on the mechanical parameters of the biological processes, are numerically computed and graphically analysed.

Preliminary Remarks

Diseases associated with the pathological growth of the walls of blood vessels are the one of the main causes of death of the population [1,2]. At the heart of pathological growth of the vessel wall is atherosclerosis, growth processes in infectious and immune diseases, arteriolosclerosis and arteriosclerosis, hypertension, vasculitis. There are three types of vessels in the human circulatory system: arteries, veins and microcirculatory bed. The latter vessels type includes hemocapillaries, arterioles, venules and arteriolo-venular anastomoses. Arteries and veins are formed according to a similar scheme, Figure 1 [3–6].

The blood vessels growth is the thickening of the vessel wall by virtue of a pathological process. In the medical context, such growth is usually represented by an inflammatory process in the vessel wall and the process of dystrophy (accumulation of certain components in the vessel stroma). The vessel wall growth can also lead to the dystrophy process without an inflammatory reaction. Such widespread diseases as atherosclerosis and vasculitis are initiated by an inflammatory reaction leading to a chronic course and accompanying by the accumulations of lipids and proteins inside the vessel wall. Vessel remodelling process under arterial hypertension are frequently not accompanied by an inflammatory reaction, but thickening of the vessel wall occurs due to accumulation of the intercellular matrix components and active proliferation of smooth muscle cells.

Atherosclerosis is characterized by the defeats of arteries due to lipids and proteins deposition in the intima and reactive growth of connective tissue as the plaques.

The fat–protein detritus (atero) and the focal proliferation of connective tissue (sklerosis) occur due to atherosclerosis in the arteries intima and lead to the formation of an atherosclerotic



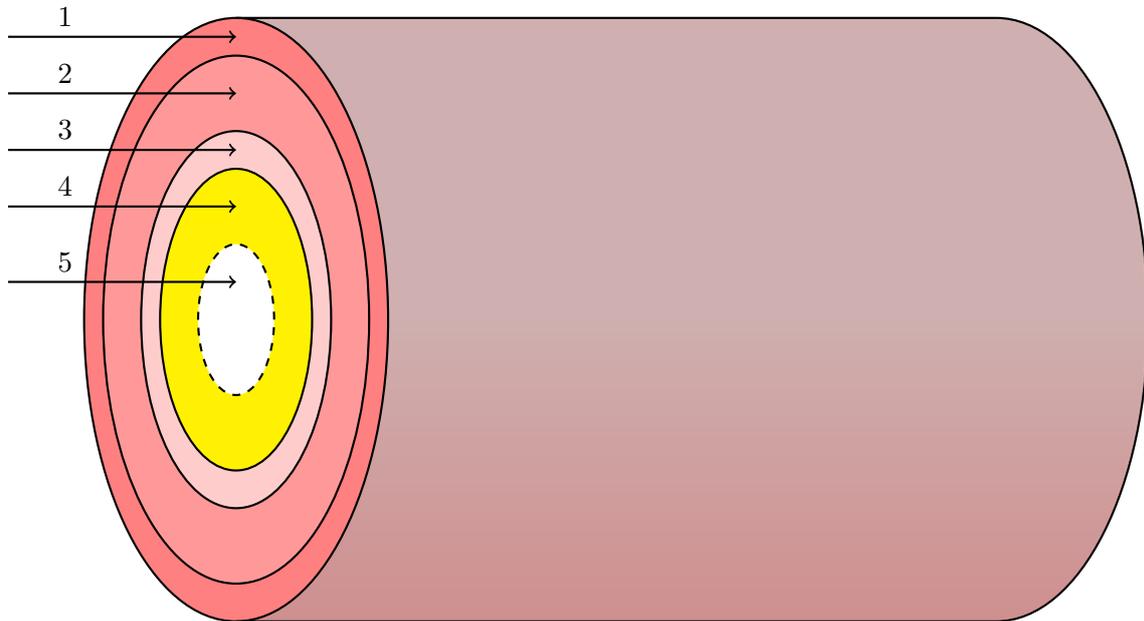


Figure 1. The scheme of a wall vessels (arteries and veins) structure. 1. Tunica adventitia is formed by a loose connective tissue. 2. Tunica media consists of muscle cells, elastic membranes and collagen. 3. Tunica intima consists of the endothelium and the elements of connective tissue located above it. 4. Growth (atherosclerosis) layer. 5. Vessel lumen.

plaques narrowing the vessel lumen. Arteries of large and medium calibre are more often affected by atherosclerosis than the small lumen arteries. The following stages of morphogenesis of atherosclerosis are discriminated:

- (i) *Prelipoidosis stage* is not macroscopically determined.
- (ii) *Lipoidosis stage* is characterized by focal impregnation of intima with lipids (cholesterol), lipoproteins, which leads to the formation of fat (lipid) spots and bands. Such fat spots macroscopically look like yellow areas, which sometimes can merge and form flat, elongated bands that do not rise above the surface of the intima.
- (iii) *Liposclerosis stage* when the fibroblast cells are proliferated stimulating the growth of the young connective tissue in the intima. The subsequent maturation of this tissue is accompanied by the formation of a fibrous plaques. Macroscopically fibrous plaques are dense formation having round or oval forms of white or yellowish-white flowers rising above the intima surface.
- (iv) *Atheromatosis stage.* Atheromatous masses are discriminated from the vessel lumen by a layer of mature, hyalineized connective tissue. The plaque cover is formed.
- (v) *Ulceration stage* accompanied by the formation of an atheromatous ulcer. The intima defect is covered by the thrombotic overlays.
- (vi) *Atherocalcinosis stage* is characterized by deposition in the fibrous plaques of calcium salts, i.e. their calcification (petrification). This is the final stage of atherosclerosis.

The elastosis and elastofibrosis are revealed due to hypertension in the arteries of large and medium calibre. Elastosis and elastofibrosis are sequential stages and represent hyperplasia and cleavage of the internal elastic membrane. Hyperplasia is compensatory developed in virtue of response to a persistent blood pressure increasing. Then the elastic fibres are destructed and

replaced to collagen fibres. The vessel wall is thickened and the vessel lumen is narrowed. In small vessels and arterioles, the cells produce semi-transparent masses like a hyaline cartilage. Over time, these masses are becoming denser, are thickening the walls and are narrowing the lumen.

The vessel walls growth can be described using mathematical models of volume or surface growth. Let us focus only on the processes of surface growth of thin-walled vessels. We use the ideas of the mechanics of growing bodies [7–14]. Some one-dimensional problems in frameworks of the thermoelastoplasticity are studied under conditions of axial or central symmetries in [15–20]. The principal variables of the boundary value problem for a growing body are the stress rate tensor, the strain rate tensor and the velocity vector. On the surface of growth we set a specific boundary condition depending on the curvature tensor of the growth surface and the tension and inflow rates of the incremented elements.

Some model problems for an elastic thin-walled surface-growing cylinder are considered at present work. The condition of thinness allows us to study finite displacements of cylinder points under the condition of small deformations. This, in particular, makes it possible to solve the problem with exact boundary conditions on a moving surface. The behaviour features of the main strain–stress state characteristics depending on the pressure on the inner and outer surfaces of the cylinder.

1. Boundary Value Problems Statement and Solution

Consider an infinitely long hollow elastic cylinder with internal and external radii R_1 and R_2 , respectively. The relations between the stress tensor σ_{ij} and the infinitesimal deformations e_{ij} for the isotropic elastic material are furnished by the Hooke's law

$$\begin{aligned}\sigma_{rr} &= (\lambda + 2\mu)e_{rr} + \lambda(e_{\varphi\varphi} + e_{zz}), \\ \sigma_{\varphi\varphi} &= (\lambda + 2\mu)e_{\varphi\varphi} + \lambda(e_{rr} + e_{zz}), \\ \sigma_{zz} &= (\lambda + 2\mu)e_{zz} + \lambda(e_{\varphi\varphi} + e_{rr}),\end{aligned}\tag{1}$$

where λ , μ are the Lamé parameters.

The following components of the infinitesimal strain tensor are not vanished by virtue of the hypothesis of a plane strain state

$$e_{rr} = \frac{\partial u_r}{\partial r}, \quad e_{\varphi\varphi} = \frac{u_r}{r}, \quad e_{zz} = 0,\tag{2}$$

where u_r is the radial component of the displacement vector.

The components of the stress tensor satisfy the equation of equilibrium

$$\frac{\partial \sigma_{rr}}{\partial r} + \frac{\sigma_{rr} - \sigma_{\varphi\varphi}}{r} = 0.\tag{3}$$

One can transform the equilibrium equation (3) by determining the deformations from equation (1) in terms of the stresses by

$$\frac{\partial}{\partial r} \left(2\sigma_{rr} + r \frac{\partial \sigma_{rr}}{\partial r} \right) = 0.\tag{4}$$

A general solution of the equation (4) constitutes the radial stress depending on radius and undefined functions A, B

$$\sigma_{rr} = A + \frac{B}{r^2}.\tag{5}$$

The angular stress $\sigma_{\varphi\varphi}$, axis one σ_{zz} and radial displacement u_r define according to (1)–(5)

$$\sigma_{\varphi\varphi} = A - \frac{B}{r^2}, \quad \sigma_{zz} = \frac{\lambda A}{(\lambda + \mu)}, \quad u_r = \frac{Ar}{2(\lambda + \mu)} - \frac{B}{2\mu r}. \quad (6)$$

The lateral surface of the cylinder is subjected to a stationary loading pressure

$$\sigma_{rr}(R_1) = p_1, \quad \sigma_{rr}(R_2) = -p_2. \quad (7)$$

The relations for an undefined functions A and B are derived by the solution of the boundary conditions system (7) in forms

$$A = -\frac{p_1 R_1^2 + p_2 R_2^2}{R_2^2 - R_1^2}, \quad B = \frac{R_1^2 R_2^2 (p_1 + p_2)}{R_2^2 - R_1^2}. \quad (8)$$

The equations (5)–(8) determine the stress-strain state parameters before the growth. Suppose at time $t = 0$ on the inner surface of the cylinder the new material is adding with the velocity $v = v(t)$

$$\begin{aligned} \dot{\sigma}_{rr}(R_1(t)) &= -\frac{v(t)\tau(t)}{R_1(t)}, \\ R_1(t) &= R_1 - v(t)t, \\ \dot{\sigma}_{rr}(R_2) &= 0. \end{aligned} \quad (9)$$

Herein the dot denotes the speed of the considered variable, which can be determined as a partial derivative with respect to time within the frameworks of the infinitesimal deformations approach; $\tau(t)$ is the circumferential tension of the adding layer at the moment of joining to the cylinder surface. For a correct description of the stress-strain state evolution under the conditions of continuous growth $t > 0$ it is necessary to transform governing equations by replacing all variables on its velocities (1)–(3). After that we obtain following solution in terms of the velocities

$$\begin{aligned} \dot{\sigma}_{rr} &= X(t) + \frac{Y(t)}{r^2}, \quad \dot{\sigma}_{\varphi\varphi} = X(t) - \frac{Y(t)}{r^2}, \\ \dot{\sigma}_{zz} &= \frac{\lambda X(t)}{(\lambda + \mu)}, \quad \dot{u}_r = \frac{X(t)r}{2(\lambda + \mu)} - \frac{Y(t)}{2\mu r}. \end{aligned} \quad (10)$$

Unknown functions $X(t)$ and $Y(t)$ can be computed by the solution of the system (9) in following form

$$X(t) = \frac{R_1(t)v(t)\tau(t)}{R_2^2 - R_1^2(t)}, \quad Y(t) = -\frac{R_1(t)v(t)\tau(t)R_2^2}{R_2^2 - R_1^2(t)}. \quad (11)$$

The relations for stresses and displacements after integrating on time the equations (10) taking into account the boundary conditions (5)–(6) read by

$$\begin{aligned} \sigma_{rr} &= A + \frac{B}{r^2} + \int_0^t \left(X(s) + \frac{Y(s)}{r^2} \right) dt, \\ \sigma_{\varphi\varphi} &= A - \frac{B}{r^2} + \int_0^t \left(X(s) - \frac{Y(s)}{r^2} \right) dt, \\ \sigma_{zz} &= \frac{\lambda}{(\lambda + \mu)} \left(A + \int_0^t X(s) dt \right), \\ u_r &= \frac{Ar}{2(\lambda + \mu)} - \frac{B}{2\mu r} + \left(\int_0^t \frac{X(s)r}{2(\lambda + \mu)} - \frac{Y(s)}{2\mu r} \right) dt. \end{aligned} \quad (12)$$

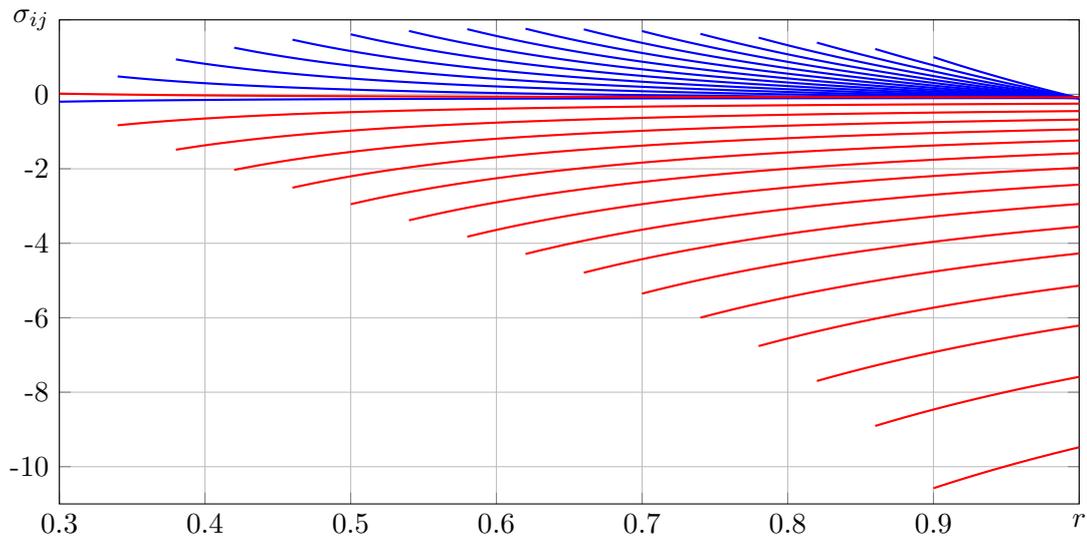


Figure 2. Stresses in the growth cylinder at different times

2. Numerical Results Discussion

The calculations were carried out for various values of the growing layer size $R_1(t)$ and the growth layer tension level $\tau(t)$. For the case of $v(t) = const$ and $\tau(t) = const$ it is established that the growth tension level τ level has a key influence on the formation of the final stress-strain state of the material. Figure 2 illustrates the radial stress field (blue) and circumferential one (red) during the growth. The stresses are vanished on the inner surface $R_1(t)$ for a certain value of growth layer tension τ during the inner cylinder wall growth. On Figure 3 is shown the radial displacement in the process of the inner cylinder wall growth. Calculations were carried out with the following material dimensionless parameters

$$\tau = 6, \quad \lambda = 4, \quad \mu = 2, \quad v = 0.1, \quad p_1 = 1, \quad p_2 = 0.1, \quad R_1 = 0.9, \quad R_2 = 1.$$

The stresses concentration caused by the influence of internal pressure can be computed in the absence of initial growth tension in the adding layer by formulae (5) and (8). The stresses concentration caused by the high level of the initial growth tension during the narrowing of the vessel lumen are calculated. Thus, it is possible to conclude, that on the one hand, with correct initial parameters of the growing process, it is possible to achieve a minimum effect of the internal pressure in the vessel on its walls deformation. To another hand, a certain growth regime is capable of causing irreversible deformation and fracture vessel wall.

Conclusions

- The constitutive and governing equations of the linear elasticity have been furnished as a tool for mathematical modeling of blood vessels growth.
- The boundary value problem of the surface growth of an elastic thin-walled cylinder has been solved.
- The stresses concentration caused by the different levels of the initial growth tension during the narrowing of the vessel lumen have been calculated.
- The stress-strain state characteristics, which depend on the mechanical parameters of the biological processes, are numerically computed and graphically analysed.

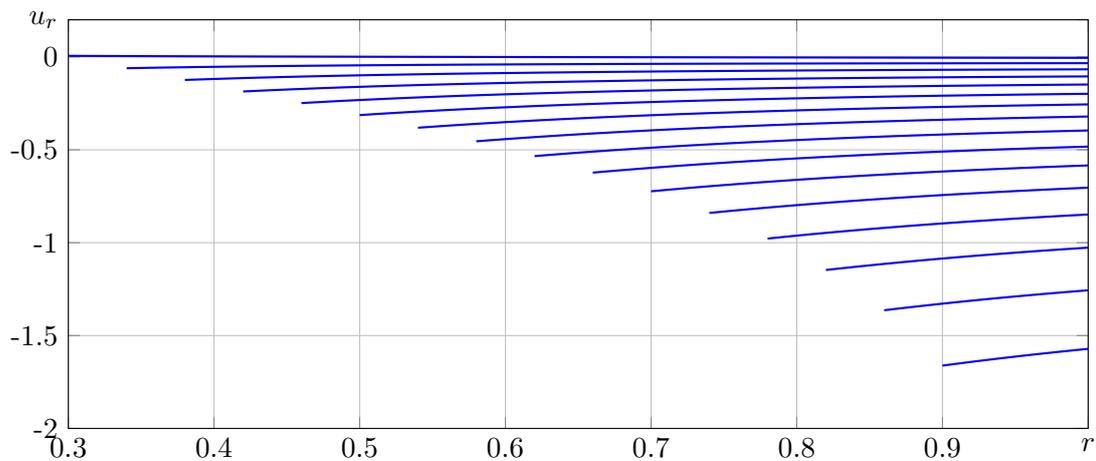


Figure 3. Displacement in the growth cylinder at different times

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