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MATHEMATICAL MODELING OF BIOMECHANICAL ELASTIC AND HYPERELASTIC PROPERTIES OF THE MYOCARDIUM

Sergey A. Muslov[1], Yury A. Vasyuk[1], Alla I. Zavialova[1], Elena Yu. Shupenina[1], Pavel Yu. Sukhochev[2], Layla Z. Guchukova[3]

[1] Russian University of Medicine, Moscow, Russia;
[2] Lomonosov Moscow State University, Moscow, Russia;
[3] Odintsovo Regional Hospital, Odintsovo, Moscow Region, Russia

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BACKGROUND: The study of mechanical properties of biological tissues is extremely informative and is one of the most important areas of biomechanics. Knowledge of these aspects of biological objects based on experimental data can become a source of new medical and technical solutions for the reconstruction of organs and the development of replacement materials.

AIM: Passive mechanical properties of isolated myocardium are compared with linear, bilinear, exponential and the most common hyperelastic models (neohookean, Mooney–Rivlin, Ogden, Yeoh, polynomial and Veronda–Westmann).

MATERIALS AND METHODS: Literature data on mechanical tests of autopsy material obtained from mongrel dogs were used as initial data. To search for the most advanced calculation algorithms the computer algebra system was used, the Mathcad 15.0 software package and the multifunctional finite element analysis application ANSYS 2022 R2 were used. Direct comparison of models was made based on mathematical statistics.

RESULTS: Among the first group of models, the results closest to the experimental data were demonstrated by the exponential model $R = 0.9958/0.9984$ (in the longitudinal/transverse direction with respect to the myocardial fibers), the lowest accuracy was demonstrated by the linear model $R = 0.9813/0.9803$. Young's moduli of linear, bilinear and exponential models and material constants of hyperelastic models are determined. The coefficient of elastic anisotropy of the myocardium, defined as the ratio of the elastic moduli of the linear model measured along and across the direction of the fibers, is equal to 2.18, which is very different from the literature data for the myocardium of the human heart. Deformation along the fibers of the heart muscle is more energy-consuming in the direction along the fibers than in the transverse direction (3.81 and 2.52 mJ/cm^3). The most accurate hyperelastic models turned out to be the 2nd order polynomial model $R = 0.9971$ and the 3rd order Yeoh model $R = 0.997$. The largest deviations and the lowest correlation coefficient between the experimental and model data were demonstrated by the simple neohookean model $R = 0.974$ with a single parameter μ. The numerical values of the parameters of hyperelastic models obtained by calculation methods used practically did not differ from each other (⩽2.16%).

CONCLUSIONS: The study demonstrated the importance of selecting the correct mechanical model for isolated myocardium. The data obtained can be useful in virtual interventions (simulations) for predicting outcomes and supporting clinical decisions, developing replacement materials and structures made of them for reconstructive operations on heart structures.

Keywords: myocardium; biomechanical models; elasticity; hyperelasticity; elastic anisotropy; bioengineering.

МАТЕМАТИЧЕСКОЕ МОДЕЛИРОВАНИЕ БИОМЕХАНИЧЕСКИХ УПРУГИХ И ГИПЕРУПРУГИХ СВОЙСТВ МИОКАРДА

С.А. Муслов[1], Ю.А. Васюк[1], А.И. Завьялова[1], Е.Ю. Шупенина[1], П.Ю. Сухочев[2], Л.З. Гучукова[3]

[1] Российский университет медицины, Москва, Россия;
[2] Московский государственный университет имени М.В.Ломоносова, Москва, Россия;
[3] Одинцовская областная больница, г. Одинцово, Московская область, Россия

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Обоснование. Исследование механических свойств биологических тканей чрезвычайно информативно и является одним из важнейших направлений биомеханики. Знание этих аспектов биологических объектов на основе опытных данных может стать источником новых медико-технических решений при реконструкции органов и разработке замещающих материалов.

Цель — пассивные механические свойства изолированного миокарда сопоставить с линейной, билинейной, экспоненциальной и наиболее известными гиперупругими моделями (неогуковской, Муни – Ривлина, Огдена, Йео, полиномиальной и Веронда – Вестманн).

Материалы и методы. В качестве исходных использованы литературные данные механических испытаний аутопсийного материала, полученного от беспородных собак. Для поиска наиболее совершенных алгоритмов расчета применяли систему компьютерной алгебры, пакет программ Mathcad 15.0 и многофункциональное приложение конечно-элементного анализа ANSYS 2022 R2. Прямое сравнение моделей производили на основе показателей математической статистики.

Результаты. Среди первой группы моделей наиболее близкие к опытным данным результаты продемонстрировала экспоненциальная модель с коэффициентом корреляции $R = 0{,}9958/0{,}9984$ (в продольном/поперечном направлении по отношению к волокнам миокарда), наименьшую точность — линейная модель, $R = 0{,}9813/0{,}9803$. Определены модули Юнга линейной, билинейной и экспоненциальной моделей и материальные константы гиперупругих моделей. Коэффициент упругой анизотропии миокарда, определенный как отношение упругих модулей линейной модели, измеренных вдоль и поперек направления волокон, установлен равным 2,18, что весьма сильно отличается от литературных данных для миокарда сердца человека. Деформация вдоль волокон сердечной мышцы более энергозатратна в направлении вдоль волокон, чем в поперечном направлении (3,81 и 2,52 мДж/см^3). Наиболее точными гиперупругими моделями оказались модели полиномиальная 2-го порядка, $R = 0{,}9971$, и Йео 3-го порядка, $R = 0{,}997$. Наибольшие отклонения и наименьший коэффициент корреляции между экспериментальными и модельными данными продемонстрировала простая неогуковская модель, $R = 0{,}974$ с единственным параметром μ. Численные значения параметров гиперупругих моделей, полученные обоими расчетными методами, практически не отличались друг от друга (⩽2,16 %).

Заключение. Исследование показало важность выбора правильной механической модели для изолированного миокарда. Полученные данные могут быть полезны при виртуальных вмешательствах (моделировании) для прогнозирования исходов и поддержки клинических решений, при разработке замещающих материалов и конструкций из них для реконструктивных операций на структурах сердца.

Ключевые слова: миокард; биомеханические модели; упругость; гиперупругость; упругая анизотропия; биоинженерия.

Background

Heart failure remains one of the most common causes of death worldwide, particularly among individuals aged >60 years. The biomechanical parameters and deformation properties of tissues from different heart sections should be studied for developing and selecting appropriate materials for reconstructive cardiac surgeries. The study of passive mechanical properties of hard and soft biological tissues is extremely informative and a crucial area of biomechanics. Moreover, the study of passive myocardial properties has a critical applied aspect. Knowledge derived from experimental data on the physical and mechanical aspects of biological objects is beneficial for the development of new medical and technical solutions for the reconstruction of biological tissue properties and substitute materials. Furthermore, mathematical models of biotissues do not require samples and provide researchers with opportunities to study various physiological states *in silico* (defined as computer modeling and simulation of an experiment, more often biological) without the risk to the health and life of the modeled objects [1].

Professor V.Y. Izakov, the founder of the distinctive Soviet school of myocardial biophysics, and his students recognized the significance of mathematical modeling of cardiac tissues. Their studies were based on the understanding that active elements of cardiac tissue are immersed in a specific rheological environment, including the foundational monograph [2] on experimental and computer models in cardiovascular physiology and cardiology. Regarding its mechanical properties, the myocardium is similar to polymeric materials, which are the subject of rheology. The mechanical function of the cardiac muscle and pumping function of the heart are influenced by the rheological medium. Therefore, the study of the role of this medium in the functioning of the heart in both normal and pathological conditions is crucial. Consequently, the authors analyzed the passive myocardium as a biological medium to which the experimental and theoretical apparatus of classical mechanics of deformable media, primarily rheology, i.e., from the positions of elasticity, viscosity, and plasticity, is applicable and did not consider large hyperelastic deformations characteristic to cardiac tissues.

Soft biological tissues are complex, heterogeneous (heterophase), anisotropic, physically nonlinear, and virtually incompressible (Poisson's ratio $\mu \approx 0.5$) and physiologically active structures. Sarvazyan, head of the laboratory of the Institute of Theoretical and Experimental Biophysics of the Russian Academy of Sciences, investigated the difficulty of finding the Young's modulus of soft tissues of the body. Nevertheless, recent studies have noted that solving problems of elasticity theory is benefi-

cial for overcoming the problems of diagnostics of pathologies of soft biological tissues of human body organs. Moreover, it is critical to have knowledge of deformation and strength properties of heart tissues to predict possible complications during surgical reconstructive interventions performed in prosthetics [4–6].

Methodological aspects of studying elastic properties of myocardial structures

Our understanding of the constitutive (establishing, determining, forming the basis) relations concerning the mechanical properties of the heart wall is limited. It is based on the results of uniaxial studies of samples obtained by dissection of tissues from different parts of the heart such as the ventricular trabeculae [7]. Although one-dimensional studies contribute to the understanding of the fundamentals of cardiac mechanics, their quantitative or qualitative extrapolation to intact cardiac tissue is not fully justified. For example, what is isometric in the one-dimensional case is not so in three-dimensional measurements, since the lateral edges of the specimens are not fixed during the test and can deform freely [8]. Given that the majority of the heart wall is subjected to multiaxial loads, extrapolations based on uniaxial data may not accurately reflect the true tissue stresses or strains. Moreover, Izakov et al. [2] observed that the drug behaves stiffer under biaxial tension than under uniaxial strains. Consequently, uniaxial tests provide underestimated values of tangential moduli. Moreover, theoretically, uniaxial data cannot be generalized to establish relationships for a three-dimensional model. To obtain the fundamental results to understand three-dimensional myocardial mechanics, acquiring knowledge of the myocardial properties under multiaxial loading is crucial [9–12]. Only if one assumes that the tissue is incompressible can the two-dimensional test data be generalized to obtain complete three-dimensional constitutive relations [13, 14]. Consequently, research should focus on measuring multiaxial forces and strains in isolated tissue, from which constitutive relations for the gender myocardium will then be derived. Nevertheless, uniaxial tests of biotissues remain popular among researchers because of the relative simplicity of experimental techniques and theoretical calculations. Thus, the aim of the study [7] was to determine the relationship between one- and two-dimensional stresses and strains of isolated canine myocardial tissues and study the following aspects: the degree of viscoelasticity under biaxial loading, presence and degree of anisotropy between fibers in the longitudinal and cross direction, regional heterogeneity of material properties, and specificity of the difference between the results of uniaxial and biaxial tests of the same specimen.

A brief review of studies of elastic properties and hyperelastic models of the myocardium

The mechanical properties of the myocardium are a subject of intense experimental investigation. As stated by [15], if we exclude the results on experimental objects with elastic moduli above 150 kPa (which are atypical, e.g., 400 kPa for the "systolic modulus" of dogs [16]) from the analysis, we obtain that the Young's modulus of human and mechanical properties of animal heart tissues exhibit a considerable range, spanning from 29.25 ± 9.42 to 65.10 ± 12.74 kPa ($M \pm m$). This variation is attributed to various factors, including the magnitude of deformation, measurement methods, and other variables. Importantly, there is no consensus regarding the type of elastic anisotropy observed in cardiac tissue. This is evidenced by the observed differences in the elastic moduli of myocardial sections, which depend on the direction of deformation in these sections.

Recently, alongside the conventional mechanical and ultrasound tests, other physical methods for measuring the deformation parameters of tissues have gained increasing popularity. In a study, myocardial elastography, a method based on radiofrequency (RF) correlation, was developed to assess the local distribution of strain in the heart *in vivo* [17]. A three-dimensional approach was employed to accurately measure inhomogeneities such as lesions after RF ablation or infarction. The study demonstrated that three-dimensional myocardial elastography is a valuable approach for assessing the regional distribution of deformations in three dimensions in cardiac patients and that the assessment of tissue deformations is significant in clinical cardiology, as it enables the quantitative assessment of cardiac function.

As observed in that myocardial stiffness plays a crucial role in cardiac function [18]. Currently, it can be invasively and indirectly assessed by catheter angiography. The aim of this study was to demonstrate the feasibility of quantifying right ventricular stiffness noninvasively by cardiac magnetic resonance elastography in dogs with severe congenital pulmonary valve stenosis causing right ventricular hypertrophy and to compare it with remote left ventricular myocardium. Furthermore, correlations between stiffness and selected pathophysiological parameters obtained by transthoracic echocardiography and cardiac magnetic resonance imaging were investigated.

Despite the existence of several studies on myocardial biomechanical properties, information on systematic studies of the parameters of hyperelastic properties of cardiac tissues is lacking. In a study by [15, 19], myocardial hyperelastic properties were described using the two-parameter Mooney–Rivlin model, and numerical values of the C_{10} and C_{01} co-

efficients of the model were obtained. The authors conducted an investigation into the hyperelastic properties of myocardium, using curves sourced from [4] and derived from the results of mechanical tensile tests. The study examined 80 hearts obtained from corpses of adult individuals (men and women) aged 31–70 years. The epicardium, ventricular myocardium, and endocardium samples were stretched in two directions. The authors of [20] characterized the passive mechanical properties of late fetal and neonatal pig hearts using biaxial mechanical testing as a surrogate for the mechanical properties of the human fetal heart. Samples from both right and left ventricles at late gestation from 85 days to delivery were used. Subsequently, constitutive modeling was performed using a transversal-isotropic model of the Fang and Humphrey type that factors in fiber orientation. No significant difference in mechanical stiffness was found in all age groups and between the right and left ventricular samples. The rationale for this work was to characterize the variability of myocardial stiffness during deformation.

A comprehensive examination of the application of biomechanical models to investigate the passive properties of myocardium under finite strain was presented by Avazmohammadi et al. [21]. The authors provided the constitutive equations of the models and classified them according to symmetry groups (isotropic, transversally isotropic, and orthotropic) and by the parameters on which they were based (equality of invariants of the strain tensor $W = \Psi(I_i)$ or strain components $W = \Psi(E_{ij})$; the authors' designations are preserved). However, a review of the literature revealed that majority of models are relatively uncommon and have not been widely used in the field of large deformation mechanics. An exception to this is the Holzapfel–Ogden model, which has been presented in the literature as the Holzapfel model [1] or the Ogden model [22]. Furthermore, the review did not include a comparative analysis of the accuracy of approximation of passive myocardial properties by different models.

In investigated the mechanical response of passive sheep myocardium obtained from three different regions of the heart [1]. Tissue samples from the central regions of the left and right ventricles and from the interventricular septum were obtained. The results demonstrated that the Choi–Vito and Fang models exhibited the greatest fit to the left ventricle, whereas the Holzapfel, polynomial (anisotropic), and four-fiber family models demonstrated the greatest fit to the right ventricle. The authors observed that two of the six models applied were associated with the use of the Green–Lagrange tensor and four with the use of I_k strain invariants. For more than 30 years, the Fang model has been widely used to characterize the nonlinearity of soft biological tissues. However, there has been no systematic discussion on the statistical parameters of either elastic or hyperelastic models of myocardial structures.

The present study aimed to identify the mechanical properties of passive myocardial tissues by analyzing the most well-known elastic and hyperelastic models.

Materials and methods

In this study, computer models were compared with experimental data obtained by scientists from the Johns Hopkins Medical Institute (1983) [7]. The study material was obtained from 49 non-breed dogs weighing approximately 20 kg that had previously received anesthesia. Sodium heparin (2000 units) was administered intravenously to suppress thrombus formation in myocardial vessels before heart extraction from the animal. Following extraction, the heart was immediately rinsed and immersed in ice-cold oxygenated saline for several minutes before sectioning. The anterior and posterior free walls of the left ventricle and basal and apical halves (above and below the equator), were examined. Strains in the central part of the specimen were measured to minimize edge artifacts. Differences in thickness within each specimen were minimized by sampling. Flat slices of the free wall of the left ventricular heart were studied under mechanical biaxial and uniaxial tests. Epicardial and endocardial specimens were not used owing to the presence of substantial coronary vessels and trabeculations, respectively.

The deformation properties of myocardial tissues were investigated using the computer algebra system Mathcad 15.0 and the application program package ANSYS 2022 R2. The linfit and genfit functions were employed to determine the parameters of linear and exponential functions, respectively, and the correlation coefficients, which were calculated using the corr Mathcad 15.0 function. The fit of the model data to the experimental data in the ANSYS 2022 R2 package was evaluated using the Error Norm for Fit function in the absolute error position.

In the construction of adequate phenomenological numerical deformation models of biological tissues, the function $\sigma = \sigma(\varepsilon)$ is selected, where σ is the applied mechanical stress and ε is the relative strain. This function is preferred because it minimizes the discrepancies between calculated and experimental data. The linear model, also called Hooke's law, is a common choice owing to its relative simplicity and the uniqueness of the parameter, Young's modulus $E = \sigma/\varepsilon$. Moreover, a multiphase model, such as a two-phase bilinear model with two Young's moduli, E_1 and E_2, is commonly used. This model reflects the bimodular nature of deformation properties observed in biological tissues. Indeed, soft biotissues are com-

posite materials composed of components with different mechanical properties. Therefore, it is not surprising that such a material exhibits complex mechanical behavior. As evidenced by the literature data, at the initial stage of tissue deformation, the elastin matrix with elasticity modulus E_1 is responsible for elasticity, acting as a bearing element. Collagen fibers are included in the deformation process later, only at $\varepsilon = \varepsilon_{cr}$. They are significantly stiffer and initiate the increase of the total Young's modulus of the tissue up to E_2. In the historical context, other functions $\sigma = \sigma(\varepsilon)$ are defined by the following formulas: $\varepsilon^2 = a\sigma^2 + b\sigma$ (Wertheim, 1847) [24], $\varepsilon = a\sigma^n$ (Morgan, 1960) [25], $\sigma = k\varepsilon^d$ and $\sigma = B[e^{m\varepsilon} - 1]$ (Kenedi, 1964) [26], and $\varepsilon = C + k\sigma^b$ and $\varepsilon = x + y \lg \sigma$ (Ridge and Wright, 1964) [27]. These formulas were proposed, but were not widely recognized. The authors of proposed the regression functions $Stress = ae^{b(strain)} + c$ to approximate the experimental σ–ε curves of the left ventricular myocardium of Sprague–Dawley rats during mitral regurgitation [28]. They used the three-parameter dependence $stress = A[\exp B(stretch\ ratio) - 1] + C$ [7]. The exponential approximation is recommended by biomechanists because of the high degree of correlation observed between experimental and calculated data [29, 30]. Furthermore, the efficacy of the *e*-approximation is supported by considerable evidence indicating the exponential nature of the *J*-dependence of stress–strain $\sigma = \sigma(\varepsilon)$ observed in the majority of soft biological tissues [31, 32]. Additionally, the exponential function is the most popular because it describes the hardening effect of soft tissue deformation.

In our study of myocardial deformation properties, the experimental σ–ε curves [7] were approximated by various functions (Table 1).

Table 2 shows the formulas used to determine the values of elastic moduli in the bilinear and exponential model.

Furthermore, the present study examined the differences in myocardial tissue isolated from the left ventricular wall by comparing six hyperelastic models: the neohookean, Mooney–Rivlin, Ogden, Yeoh, polynomial, and Veronda–Westmann models. Table 3 summarizes the constitutive equations of these models.

Electron microscopic study was performed using a Hitachi 12A microscope.

Results and discussion

Elastic modules

In the longitudinal direction, the experimental graph of σ–ε tensile tests of specimens and calculated curves plotted using linear, bilinear, and exponential functions are presented in Fig. 1. The experimental

Table 1 / Таблица 1

Elastic models used in the study
Упругие модели, использованные в исследовании

Model	Mathematical formulation
Linear	$\sigma = E\varepsilon$
Bilinear	$\sigma = E_1\varepsilon + E_2(\varepsilon - \varepsilon_{cr})\theta(\varepsilon - \varepsilon_{cr})$
Exponential	$\sigma = a(e^{b\varepsilon} - 1)$

N o t e: E, Young's modulus in the linear model; $E_1 = E_{min}$, $E_2 = E_{max}$, Young's moduli in the bilinear model; θ, a step function of Heaviside, equal to zero for negative values of the argument and one for positive values; parameters a and b correspond to the greatest accuracy of approximation of the exponential model; $e \approx 2.72$, the base of natural logarithms.

Table 2 / Таблица 2

Elastic modulus of linear, bilinear, and exponential models
Модули упругости линейной, билинейной и экспоненциальной моделей

Model	Mathematical formulation
Linear	E
Bilinear	$E_1 = E_{min} = ab$, $E_2 = E_{max} = abe^{b\varepsilon_{max}}$
Exponential	$E(\varepsilon) = E_{max} = abe^{b\varepsilon}$, $E_{avg} = \frac{1}{\varepsilon_{max} - 0}\int_0^{\varepsilon_{max}} E(\varepsilon)d\varepsilon = \frac{1}{\varepsilon_{max}}\int_0^{\varepsilon_{max}} abe^{b\varepsilon}d\varepsilon = \frac{a}{\varepsilon_{max}}\int_0^{\varepsilon_{max}} (e^{b\varepsilon_{max}} - 1)$

Table 3 / Таблица 3

List of hyperelastic models used in the study
Список гиперупругих моделей, использованных в исследовании

Model	Mathematical formulation	Source
Neohookean	$\sigma = 2\mu\left(\lambda^2 - \frac{1}{\lambda}\right)$	[33, 34]
Mooney–Rivlin	$\sigma = 2C_{10}\left(\lambda - \frac{1}{\lambda^2}\right) + 2C_{01}\left(1 - \frac{1}{\lambda^3}\right)$	[33]
Ogden	$\sigma = \sum_{p=1}^{n} \mu_p \left(\lambda^{\alpha_p} - \lambda^{-\frac{1}{2}\alpha_p}\right)$	[22]
Yeoh	$\sigma = 2\left(\lambda - \frac{1}{\lambda^2}\right)\sum_{i=1}^{n} iC_i(I_1 - 3)^{i-1}$	[35]
Polynomial, five-parameter	$\sigma = 2(\lambda - \lambda^{-2})[C_{10} + C_{01}\lambda^{-1} + 2C_{20}(\lambda^2 + 2\lambda^{-1} - 3) + 2\lambda^{-1}C_{02}(2\lambda + \lambda^{-2} - 3) + 3C_{11}(\lambda - 1 - \lambda^{-1} + \lambda^{-2})]$	[36]
Veronda–Westmann	$\sigma = 2C_1C_2\, e^{C_2(\lambda^2 + 2\lambda^{-1} - 3)}(\lambda - \lambda^{-2}) + 2C_3(1 - \lambda^{-3})$	[37]

N o t e: σ, conditional stresses; $\lambda = \varepsilon + 1$, coefficients (multiplicities) of deformation; the rest, material constants of hyperelastic models.

graph of σ–ε and regression curves for the transverse direction exhibit a similar appearance.

Table 4 presents the parameters of the deformation and strength properties of the three elastic models used.

Table 4 illustrates that myocardial tissues exhibit greater stiffness in the longitudinal direction than in the transverse direction, as evidenced by deformation and strength parameters (E_{avg}, 145.92 and 70.174 kPa). In the longitudinal direction, the myocardial tissues show increased stiffness (σ_{max} 9.557 and 7.358 kPa), whereas in the transverse direction, they display elevated plasticity (ε_{max} 0.101 and 0.067), which is consistent with the experimental data [7].

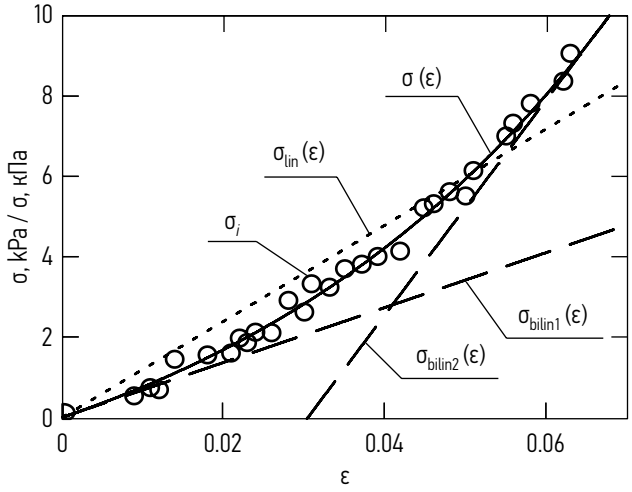

Fig. 1. Longitudinal direction. Stress-strain graphs of myocardial models: linear σ_{lin}, bilinear σ_{bilin} (with 2 elastic modules E_1 and E_2) and exponential σ(ε). The points σ_i represent experimental data, ε is the relative deformation

Рис. 1. Направление вдоль волокон. Графики напряжение – деформация моделей миокарда: линейной σ_{lin}, билинейной σ_{bilin} (с двумя модулями упругости E_1 и E_2) и экспоненциальной σ(ε). Точки σ_i — опытные данные, ε — относительная деформация

The differential Young's modulus of the myocardium in the exponential model is incremental; that is, it increases with strain. The calculated modulus in the longitudinal/transverse direction exhibited a minimum at baseline (68.33/23.93 kPa), a maximum at $\varepsilon = \varepsilon_{max}$ (267.43/155.03 kPa), and an E_{max}/E_{min} ratio (an index of nonlinearity of elastic properties) of 3.91/6.48. These results slightly differ from those obtained for biaxial testing of the pig fetal heart (15.20 ± 6.28/7.21 ± 4.80 and 83.89 ± 51.80/34.81 ± 31.78 kPa, E_{max}/E_{min} = 5.52/4.82) and significantly differ from the known data for other biotissues, for example, for the oral mucosa ($E_1 = 0.15$, $E_2 = 16.5$ MPa [38]) and periodontal ligament ($E_1 = 0.05$, $E_2 = 10$ MPa, $\varepsilon_{cr} = 0.075$ [39]). The parameters of the relationship $\sigma = a(eb^{\varepsilon} - 1)$ were calculated with $a = 3.359/1.307$ kPa and $b = 20.343/18.317$ (determined using the genfit Mathcad 15.0 function).

The myocardial elastic anisotropy coefficient, defined as the ratio of elastic moduli of the linear model measured along and across the fibers, was found to be 119.627/55.016 kPa = 2.18. This value coincides with the literature data (1.2–2.6) [40], which also demonstrated that in rat myocardium, the right ventricular tissue shows more pronounced anisotropic behavior than the left ventricular tissue and interventricular septum. The authors employed the ratio of maximum tangent modulus values along and across myocardial fibers as an index of anisotropy.

Table 4 / Таблица 4

Parameters of linear, bilinear, and exponential models of deformation and strength properties of myocardial tissues. Mathcad 15.0

Параметры линейных, билинейных и экспоненциальных моделей деформационных и прочностных свойств тканей миокарда. Mathcad 15.0

Direction relative to fibers	Deformation properties of the model							Strength properties (experience)	
	exponential			linear	bilinear				
	a, kPa	b	E_{avg}, kPa	E_{lin}, kPa	E_1, kPa	E_2, kPa	ε_{cr}	ε_{max}	σ_{max}, kPa
Longitudinal	3.359	20.343	145.92	119.627	68.33	267.43	0.041	0.067	9.557
Transverse	1.307	18.317	70.174	55.016	23.93	155.03	0.066	0.101	7.358

N o t e: ε_{cr}, deformation corresponding in the bilinear model to the point where $\sigma_{bilin1} = \sigma_{bilin2}$ (Fig. 1), at which the elastin mechanism of deformation of soft biological tissues is replaced by the collagen mechanism.

Table 5 / Таблица 5

Statistical indicators of exponential models of myocardial tissues, Mathcad 15.0

Статистические показатели экспоненциальных моделей тканей миокарда, Mathcad 15.0

Direction relative to fibers	Standard deviation *SD*, kPa	Maximum absolute error, kPa	Maximum relative error δ, %	Correlation coefficient *R*
Longitudinal	0.048	0.078	5.517	0.9958*
Transverse	0.018	0.028	3.47	0.9984*

*The correlation coefficient of the linear and bilinear models was 0.9812/0.9787.

In an isotropic material, the mechanical properties are consistent in all directions of deformation. In contrast, an anisotropic material exhibits its mechanical properties that vary depending on the direction of deformation. Orthotropic material represents a special case of anisotropy, where changes occur in three mutually orthogonal directions. This phenomenon is further observed in the myocardium [41]. While a healthy myocardium can be considered orthotropic, a significant degree of anisotropy, although not orthotropy, is observed in scar tissue. This was established by a study evaluating the mechanical properties of rat myocardium in response to myocardial infarction. The equiaxial stretching test revealed a continuous increase in elastic modulus within 28 days after myocardial infarction when the tissue was stretched perpendicular to the fibers, whereas no differences were found when stretching parallel to the fibers [42].

The specific strain work of the specimens, geometrically equal to the area under the curve $\sigma(\varepsilon)$, was calculated as a definite integral:

$$W = \frac{1}{\varepsilon_{max} - 0} \int_0^{\varepsilon_{max}} \sigma(\varepsilon) d\varepsilon.$$

Along the fibers, it was 3.81, whereas across, it was 2.52 mJ/cm^3. Thus, deformation along the fibers of cardiac muscle is more energy-consuming in the direction along the fibers than across, further indicating the presence of elastic anisotropy in the myocardium.

Table 5 presents statistical parameters that demonstrate the efficacy of the exponential model in the analysis of deformation properties of myocardial tissues. The mean squared error of the e-approximation was 0.048/0.018 (in the longitudinal/transverse direction relative to fibers), maximum absolute error was 0.078/0.028, and maximum relative error was 0.055/0.034. The correlation coefficient between experimental and model data was 0.9958/0.9984, indicating that the exponential model ($\sigma = a(eb^{\varepsilon} - 1)$) is sufficiently acceptable.

Hyperelastic models

All soft biological materials, including passive myocardial tissues of humans and animals, are hyperelastic [34]. However, the parameters of the hyperelastic properties of myocardium have not been studied in detail. In this study, the parameters of the main hyperelastic models are considered in the packages of specialized programs Mathcad 15.0 and ANSYS 2022 R2. These packages were used simultaneously to search for the most optimal calculation algorithms.

The model myocardial curves are presented in a summary plot (Fig. 2). The numerical parameters of the models are provided in Tables 6 (longitudinal direction) and 7 (transverse direction), and the statistical metrics are presented in Table 8.

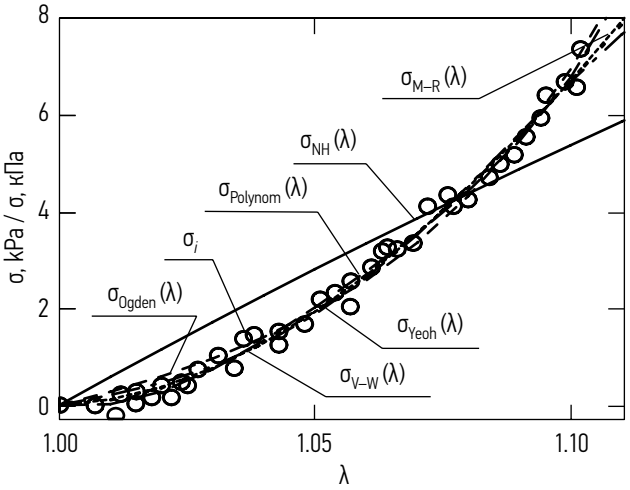

Fig. 2. Cross myocardial fibers direction. Experimental points (σ_i) and model curves of 6 hyperelastic models used: neohookean (NH), Mooney–Rivlin (M–R), Ogden (Ogden), Yeoh (Yeoh), polynomial (Polynom) and Veronda–Westmann (V–W). λ — strain coefficient

Рис. 2. Направление поперечно волокнам миокарда. Опытные точки (σ_i) и модельные кривые шести использованных гиперупругих моделей: неогуковской (NH), Муни – Ривлина (M–R), Огдена (Ogden), Йео (Yeoh), полиномиальной (Polynom) и Веронда – Вестманн (V–W). λ — коэффициент деформации

Notably, the difficulty associated with the application of most hyperelastic models is that the parameters of such models often lack physical meaning. Consequently, such models are challenging to approximate. This issue can be most effectively addressed in the NH (μ is the shear modulus) and two-parameter Mooney–Rivlin ($2C_{10} + 2C_{01} = \mu_0 \approx E_0/3$) models. The more accurate the initial shear modulus and approximate equality are, the more incompressible the hyperelastic material is. As is known, almost all soft biological tissues are incompressible (Poisson's ratio: 0.5) or close to it. Nevertheless, an analysis of Tables 6–8 enables us to draw some conclusions.

For example, the inequalities $\partial^2 W/\partial\lambda^2 > 0$, where W is the strain energy, or $\partial\sigma/\partial\lambda > 0$ (Hill [43] and Drucker [44] conditions) serve as a criterion for the mechanical stability of hyperelastic models in uniaxial tension. These inequalities indicate restrictions on the model parameters. For the two-parameter Mooney–Rivlin model, these restrictions are reduced to the inequality $C_{10} + C_{01} > 0$. Figure 2 and Tables 6 and 7 show that these inequalities are satisfied, indicating that this model is mechanically stable and can be applied in the whole range of deformations. All other elastic and hyperelastic models are stable (Figs. 1 and 2).

Tables 6 and 7 reveal that the only parameter of the NH model μ differs by a factor of two between the two program packages. This discrepancy is possibly due to the different forms of recording the constitutive equation of this model in *ANSYS* 2022 *R2* and Mathcad 15.0 (Table 3). Thus, this issue should be clarified.

Table 8 illustrates that the polynomial model exhibited the least discrepancy between the model and experimental data, with a mean square error of 0.198 kPa, maximum absolute error of 0.447 kPa, maximum relative error of 4.682 %, correlation coefficient between experimental and model data of 0.9971, and residual parameter (*ANSYS* 2022 *R2*) of 1.235. The simple NH model exhibited the greatest discrepancies (mean square error of 0.821 kPa, maximum absolute error of 1.191 kPa, maximum relative error of 16.182 %, correlation coefficient between experimental and model data of 0.974, and residual parameter of 26.984). The Yeoh, Veronda–Westmann, and Ogden models demonstrated a high correlation between experimental and calculated data ($R = 0.997$).

Comparison with literature data

In conclusion, we compare the modeling results presented in this report with those obtained by [15] from the Mooney–Rivlin model based on the data of Ostrovsky et al. [4] in the study of the elastic properties of the myocardium of hearts taken from adult human cadavers. The elastic modules (E_{lin}, E_1, E_2 и E_{avg}) of human myocardium were found to be 2.77 ± 1.22 times smaller in modulus, and the type of elastic anisotropy was found to be opposite (less and more than unity: 0.86 and 2.18). It is plausible that this phenomenon was initially observed by Izakov et al., who noted that preparations from the outer layer of the ventricles exhibited greater stiffness across the fibers, whereas preparations from the inner layer demonstrated greater stiffness along the fibers [2]. The coefficients of the two-parameter Mooney–Rivlin models C_{10} and C_{01} exhibited a significant discrepancy from those obtained in this study. In the longitudinal direction, the average difference was 8.03 times less, whereas in the transverse direction, the average difference was 5.27 times less. We believe that this discrepancy may be attributed to several factors, including the methodological peculiarities in the preparation of biomaterial samples for the study, such as sectioning and fixation, which prevent the destruction and preservation of tissues prior to measurements. Additionally, differences in the methods of mechanical testing, particularly regarding strain rate, and in the calculated formulas of elastic properties may contribute to this discrepancy. It appears that the tested samples were from different localizations. Furthermore, the human heart is anatomically distinct from the dog heart. Additionally, according to Ref. [45], the directions of myocardial muscle fibers are not straightforward to determine.

Table 6 / Таблица 6

Parameters of hyperelastic myocardial models in the longitudinal direction of the fibers
Параметры гиперупругих моделей миокарда в направлении вдоль волокон

Hyperelastic model (constant models)	Calculation method	μ, kPa	α	C_{10}, C_1, kPa	C_{01}, C_2, kPa	C_{20}, C_3, kPa	C_{02}, kPa	C_{11}, kPa
Neohookean (μ)	Mathcad	20.862	–	–	–	–	–	–
	ANSYS	41.72	–	–	–	–	–	–
Mooney–Rivlin (C_{10}, C_{01})	Mathcad	–	–	281.004	–272.88	–	–	–
	ANSYS	–	–	281.004	–272.88	–	–	–
Ogden (μ, α)	Mathcad	1.74	27.83	–	–	–	–	–
	ANSYS	1.74	28.66	–	–	–	–	–
Yeoh (C_1, C_2, C_3)	Mathcad	–	–	12.817	625.399	$-6.60 \cdot 10^3$	–	–
	ANSYS	–	–	12.817	625.399	–6600.9	–	–
Polynomial (C_{10}, C_{01}, C_{20}, C_{02}, C_{11})	Mathcad	–	–	$1.36 \cdot 10^3$	$-1.36 \cdot 10^3$	$-1.37 \cdot 10^6$	$-1.56 \cdot 10^6$	$2.93 \cdot 10^6$
	ANSYS	–	–	$1.36 \cdot 10^3$	$-1.36 \cdot 10^3$	$-1.37 \cdot 10^6$	$-1.57 \cdot 10^6$	$2.94 \cdot 10^6$
Veronda–Westmann (C_1, C_2, C_3)	Mathcad	–	–	35.562	3.815	–124.57	–	–

Table 7 / Таблица 7

Parameters of hyperelastic myocardial models in the transverse fiber direction
Параметры гиперупругих моделей миокарда в направлении поперек волокон

Hyperelastic model	Calculation method	μ, kPa	α	C_{10}, C_1, kPa	C_{01}, C_2, kPa	C_{20}, C_3, kPa	C_{02}, kPa	C_{11}, kPa
Neohookean (μ)	Mathcad	9.823	–	–	–	–	–	–
	ANSYS	19.65	–	–	–	–	–	–
Mooney–Rivlin (C_{10}, C_{01})	Mathcad	–	–	128.252	–127.59	–	–	–
	ANSYS	–	–	128.252	–127.59	–	–	–
Ogden (μ, α)	Mathcad	0.716	24.174	–	–	–	–	–
	ANSYS	0.739	24.716	–	–	–	–	–
Yeoh (C_1, C_2, C_3)	Mathcad	–	–	3.351	241.665	$-1.9 \cdot 10^3$	–	–
	ANSYS	–	–	3.351	241.664	$-1.9 \cdot 10^3$	–	–
Polynomial (C_{10}, C_{01}, C_{20}, C_{02}, C_{11})	Mathcad	–	–	228.36	–230.35	$5.4 \cdot 10^4$	$6.03 \cdot 10^4$	$-1.1 \cdot 10^5$
	ANSYS	–	–	228.36	–230.36	$5.4 \cdot 10^4$	$6.03 \cdot 10^4$	$-1.1 \cdot 10^5$
Veronda–Westmann (C_1, C_2, C_3)	Mathcad	–	–	–549.82	–0.262	–144.08	–	–

Table 8 / Таблица 8

Statistical parameters of hyperelastic models
Статистические параметры гиперупругих моделей

Hyperelastic model	Calculation method	Direction relative to fibers	Standard deviation *SD*, kPa	Maximum absolute error, kPa	Maximum relative error δ, %	Correlation coefficient *R*
Neohookean	Mathcad	Longitudinal	0.804	1.07	11.195	0.98
		Transverse	0.821	1.191	16.182	0.974
	ANSYS	Longitudinal	18.763*			
		Transverse	26.984*			

End of Table 8 / Окончание таблицы 8

Hyperelastic model	Calculation method	Direction relative to fibers	Standard deviation *SD*, kPa	Maximum absolute error, kPa	Maximum relative error δ, %	Correlation coefficient *R*
Mooney–Rivlin two-parameter	Mathcad	Longitudinal	0.226	0.548	5.738	0.997
		Transverse	0.213	0.404	5.485	0.995
	ANSYS	Longitudinal	1.488*			
		Transverse	1.818*			
First-order Ogden	Mathcad	Longitudinal	0.22	0.397	4.152	0.9967
		Transverse	0.277	0.571	7.759	0.9931
	ANSYS	Longitudinal	1.399*			
		Transverse	3.070*			
Second-order Yeoh	Mathcad	Longitudinal	0.214	0.475	4.975	0.997
		Transverse	0.238	0.495	6.727	0.994
	ANSYS	Longitudinal	1.355*			
		Transverse	2.271*			
Second-order polynomial	Mathcad	Longitudinal	0.206	0.447	4.682	0.9971
		Transverse	0.198	0.495	6.725	0.9961
	ANSYS	Longitudinal	1.235*			
		Transverse	1.571*			
Veronda–Westmann	Mathcad	Longitudinal	0.214	0.467	4.885	0.9968
		Transverse	0.212	0.45	6.117	0.9955

* Residual (ANSYS parameter).

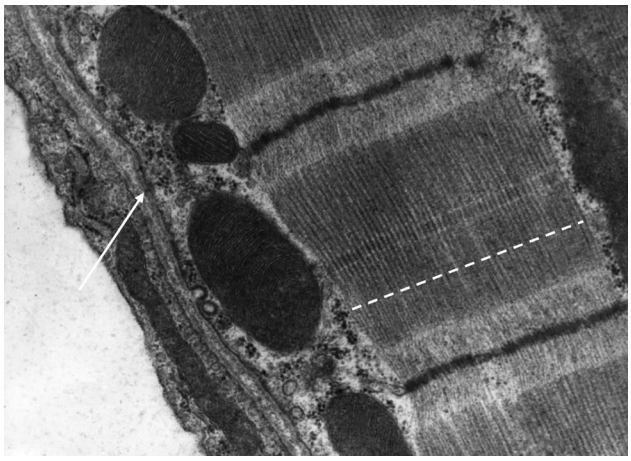

Fig. 3. Myofibril, mitochondria and paravasal connective tissue. Longitudinal section of a cardiomyocyte fragment. Transmission electron microscopy, ×13,000. Arrow points to connective tissue next to a blood microvessel, the dotted line is the cut line in Fig. 4

Рис. 3. Миофибрилла, митохондрии и паравазальная соединительная ткань. Продольный срез фрагмента кардиомиоцита. Трансмиссионная электронная микроскопия, ×13000. Стрелка указывает на соединительную ткань рядом с кровеносным микрососудом, пунктирная линия — линия среза на рис. 4

Figures 3 and 4 present electron microscopic images of myocardial slices longitudinally and transversely to its fibrous structures. In the myocardium, fibrillar structures of connective tissue origin, namely, collagen and elastic fibers, are scant. They are localized mainly in narrow connective tissue layers between myocardial muscle cells (cardiomyocytes) and accompanying blood vessels (arrow in Figure 3). The main volume is occupied by muscle cells, which belong to the transverse striated muscle tissue with the characteristic transverse striation. This striation of myofibrils is based on sequences of regularly repeating units, called sarcomeres. Each sarcomere is represented by a set of contractile filaments composed of actin (thin) and myosin (thick) filaments. These filaments interact with each other during contraction. The efficiency of contraction largely depends on the ordered packing of thick and thin filaments, which is most clearly demonstrated on cross sections (Fig. 4). This ordered packing is hexagonal, which is the most densely packed structure.

The extent to which the collective contractile structures of cardiomyocytes influence the physicomechanical properties of the myocardium, particularly the parameters under investigation, remains

uncertain. Hence, an exclusively passive mechanical response of the tissue cannot be assumed.

Finally, a considerable degree of dispersion was observed in the data pertaining to the parameters of elastic and hyperelastic models within a single series of measurements [1]. Regarding the values of myocardial elastic modules established in this study, they were found to be in satisfactory agreement with the reduced range (without atypical values) of 29–65 kPa, as previously established in Ref. [15] based on an analysis of literature data.

Conclusions

1. The results of modeling the biomechanical properties of isolated myocardium using elastic and hyperelastic phenomenological models are presented. Numerical values of the parameters of linear, bilinear, and exponential models and of the main hyperelastic models (neohookean, Mooney–Rivlin, Ogden, Yeoh, polynomial, and Veronda–Westmann models) for uniaxial stretching of specimens along and across fibers were obtained.
2. The myocardium cannot be considered as an isotropic tissue; its deformation behavior cannot be represented by models that do not factor in fiber orientation. The elastic and hyperelastic properties of the myocardium are anisotropic and depend on the preferential orientation of the tissue fibers. The coefficient of elastic anisotropy, defined as the ratio of the elastic moduli of a linear model measured along and across the fiber direction, was 2.18, and deformation along myocardial fibers is more energy-consuming than across fibers (3.81 and 2.52 mJ/cm^3).
3. The errors of the models have been examined. Among the elastic models of passive myocardium, the exponential model is the most suitable to approximate the experimental data; among the hyperelastic models, the polynomial, Yeoh, Veronda–Westmann, and Ogden models are the most suitable to approximate the experimental data (the correlation coefficient between experimental and calculated data of all the above models was $R > 0.99$).
4. All investigated models are mechanically stable as they satisfy the Hill and Drucker conditions $\partial^2 W/\partial\lambda^2 > 0$, $\partial\sigma/\partial\lambda > 0$ (W, internal energy of the material; σ, mechanical stress; and λ, strain ratio), and can be applied over the entire strain range.
5. The present study demonstrates the importance of selecting an appropriate model for isolated myocardium. The established numerical characteristics can be used for accurate computer modeling of myocardial mechanical function in virtual interventions and in future work on emulation of elastic and hyperelastic properties of passive myocardial tissue. Moreover, the results can be used for developing replacement materials for reconstructive surgeries and applied in cardiac tissue engineering.

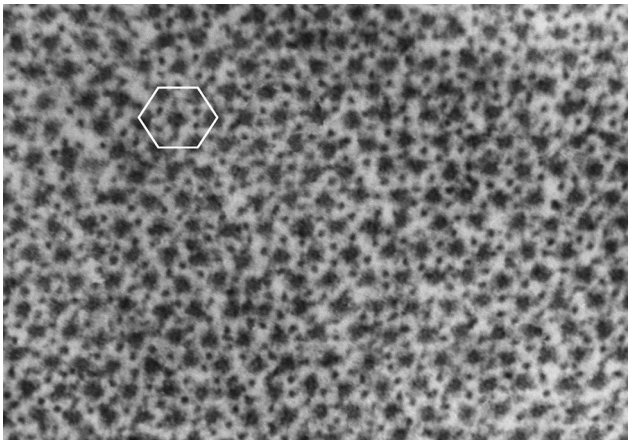

Fig. 4. Cross section of a myofibril. Transmission electron microscopy, ×60,000. Mutual hexagonal packing of thick and thin myofilaments. The cut was made approximately at the level indicated by the dotted line in Fig. 3

Рис. 4. Поперечный срез миофибриллы. Трансмиссионная электронная микроскопия, ×60 000. Взаимная гексагональная упаковка толстых и тонких миофиламентов. Срез проведен примерно на уровне, обозначенном пунктиром на рис. 3

Additional information

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Author contribution. All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Personal contribution of each author: *S.A. Muslov* — GC-MS, concept and design of the study, calculations in the Ansys 2022 R2 package, analysis and interpretation of data, writing the manuscript; *Yu.A. Vasyuk* — GC-MS, editing the manuscript, providing text and graphic material on the structure of the myocardium, making final corrections; *A.I. Zavialova* — collection and processing of materials for the review part of the article, proofreading of the manuscript; *E.Yu. Shupenina* — collection and processing of materials for the review part of the article; *P.Yu. Sukhochev* — calculations in the computer algebra system Mathcad 15.0, data analysis, preparation of graphic material in accordance with the requirements of the editor; *L.Z. Guchukova* — collecting and processing materials for the review part of the article, editing the manuscript for spelling and syntax errors, editing the list of publications.

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Информированное согласие на публикацию. Персональные медицинские данные и фотографии в статье отсутствуют.

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Information about the authors / Информация об авторах

Russian University of Medicine, Moscow, Russia
ФГБОУ ВО «Российский университет медицины» Минздрава России, Москва, Россия

Sergey A. Muslov — Cand. Sci. (Physics and Mathematics), Dr. Sci. (Biol.), Professor of the Department of Normal Physiology and Medical Physics.
ORCID: 0000-0002-9752-6804;
eLibrary SPIN: 7213-2852;
e-mail: muslov@mail.ru

Сергей Александрович Муслов — канд. физ.-мат. наук, д-р биол. наук, профессор кафедры нормальной физиологии и медицинской физики.
ORCID: 0000-0002-9752-6804;
eLibrary SPIN: 7213-2852;
e-mail: muslov@mail.ru

Yury A. Vasyuk — MD, Dr. Sci. (Med.), Professor, Scientific Secretary, Head of the Department of Hospital Therapy No. 1, Honored Doctor of the Russian Federation, Honored Worker of Higher Education of the Russian Federation.
ORCID: 0000-0003-2913-9797;
eLibrary SPIN: 2265-5331;
e-mail: yvasyuk@yandex.ru

Юрий Александрович Васюк — д-р мед. наук, профессор, ученый секретарь, заведующий кафедрой госпитальной терапии № 1, заслуженный врач РФ, заслуженный работник высшей школы РФ.
ORCID: 0000-0003-2913-9797;
eLibrary SPIN: 2265-5331;
e-mail: yvasyuk@yandex.ru

Alla I. Zavialova — MD, Cand. Sci. (Med.), Assistant Professor, Department of Hospital Therapy No. 1, Head of the Therapeutic Department of the Kuskovo Medical Center.
ORCID: 0009-0001-1727-4388;
eLibrary SPIN: 4883-7130;
e-mail: allaz05@list.ru

Алла Ивановна Завьялова — канд. мед. наук, доцент кафедры госпитальной терапии № 1, заведующая терапевтическим отделением КМЦ «Кусково».
ORCID: 0009-0001-1727-4388;
eLibrary SPIN: 4883-7130;
e-mail: allaz05@list.ru

Elena Yu. Shupenina — MD, Cand. Sci. (Med.), Professor of the Department of Hospital Therapy No. 1.
ORCID: 0000-0001-6188-4610;
eLibrary SPIN: 2090-9938;
e-mail: eshupenina@mail.ru

Елена Юрьевна Шупенина — канд. мед. наук, профессор кафедры госпитальной терапии № 1.
ORCID: 0000-0001-6188-4610;
eLibrary SPIN: 2090-9938;
e-mail: eshupenina@mail.ru

Lomonosov Moscow State University, Moscow, Russia
ФГБОУ ВО «*Московский государственный университет имени М.В.Ломоносова*», *Москва, Россия*

Pavel Yu. Sukhochev — Researcher at the Laboratory of Mathematical Support for Simulation Dynamic Systems, Department of Applied Research, Faculty of Mechanics and Mathematics.
ORCID: 0000-0002-8004-6011;
eLibrary SPIN: 7780-8694;
e-mail: ps@moids.ru

Павел Юрьевич Сухочев — научный сотрудник лаборатории математического обеспечения имитационных динамических систем отдела прикладных исследований механико-математического факультета.
ORCID: 0000-0002-8004-6011;
eLibrary SPIN: 7780-8694;
e-mail: ps@moids.ru

Information about the authors / Информация об авторах

Odintsovo Regional Hospital, Moscow, Russia
ГБУЗ МО «Одинцовская областная больница», Москва, Россия

Layla Z. Guchukova — general practitioner.
ORCID: 0009-0007-2150-6034;
eLibrary SPIN: 8280-0970;
e-mail: Gucci.loca@mail.ru

Лайла Заурбековна Гучукова — врач-терапевт.
ORCID: 0009-0007-2150-6034;
eLibrary SPIN: 8280-0970;
e-mail: Gucci.loca@mail.ru

✉ Corresponding author / Контактное лицо

Sergey A. Muslov / Сергей Александрович Муслов
Address: 20 building 1 Delegatskaya St., Moscow, 127473, Russia
Адрес: Россия, 127473, Москва, Делегатская ул., д. 20, стр. 1
E-mail: muslov@mail.ru