DOI: 10.15825/1995-1191-2021-2-95-103

NUMERICAL AND EXPERIMENTAL JUSTIFICATION OF TRANSCATHETER AORTIC VALVE PROSTHESIS DESIGN

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Objective: to justify the design of a self-expanding transcatheter aortic valve prosthesis based on a biomaterial stabilized with ethylene glycol diglycidyl ether using numerical simulation and a series of field experiments with working prototypes to determine the consistency of the proposed design solutions. **Material and methods.** Numerical computer models of a developed aortic valve prosthesis intended for transcatheter implantation, as well as prototypes of the most promising concepts for a series of field tests, were used in the work. Computer 3D models were subjected to numerical analysis in the Abaqus/CAE environment (Dassault Systemes, France) based on the finite element method with iterative design optimization and repeated numerical experiments. Physical prototypes of the transcatheter prosthesis were subjected to a series of mechanical tests for axial and radial compression, as well as tests on a Vivitro hydrodynamic stand (Vivitro Labs, Canada) under simulated normal flow. All studies were carried out in a comparative aspect with a similar transcatheter aortic valve prosthesis (control), the CoreValve™ bioprosthesis (Medtronic, Inc., USA). **Results.** Computer simulation demonstrates the stress-strain state values that do not significantly exceed the critical levels (628 and 756 MPa versus the threshold value 1080 MPa) for two basic concepts of support frames. The fatigue strength based on the calculation of the mean and alternating stresses corresponding to normo- and hypertensive states based on the Goodman diagrams, did not reveal any evidence that the threshold values (destruction area after 200 million cycles) were exceeded. The hydrodynamic characteristics of working prototypes made on the basis of computer models correspond to the testing data of CoreValve™ clinical bioprosthesis: the effective orifice area was 1.97 cm^2, the mean transprosthetic gradient was 8.9 mm Hg, the regurgitant volume was 2.2–4.1 mL per cycle depending on the prototype model. **Conclusion.** Generally, experiments carried out showed the consistency of the concepts, including from the point of view of implementation of the leaflet apparatus based on xenogeneic tissues treated with ethylene glycol diglycidyl ether.

Keywords: transcatheter prosthesis, aortic stenosis, finite element method, fluid dynamics, numerical simulation.

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) is a minimally invasive approach, which has gained considerable acceptance in the last decade. The procedure is intended for patients with high-risk aortic stenosis, who are not eligible for surgical replacement due to significant risks associated with comorbidity and recipient age. Being much less invasive than the surgical alternative, TAVR can shorten the rehabilitation period and provide treatment for aortic stenosis in high- to moderate-risk patients [1].

Common to all FDA- and CE-approved TAVR devices is the valve material, which is made of glutaraldehyde-fixed equine or porcine pericardium. Nevertheless, the existing pool of prosthetic dysfunctions, based on this type of preservation – first of all, calcification [2] and structural degeneration [3] – prevents us from concluding that such prostheses have significantly long functioning period, and, therefore, that they can be used for low-risk patient groups. [4], for which the prosthesis should last longer. Among the methods of xenograft stabilization for cardiovascular surgery in Russia, ethylene glycol diglycidyl ether (EGDE), which is more resistant to calcification due to its chemical structure [5], has been highly recommended, and the clinical results of the use of EGDE-based heart valve prostheses confirm its durability [6]. Potentially, TAVR constructions based on this type of stabilization should not be inferior to existing glutaraldehyde-treated prostheses in terms of mechanical properties and hemodynamics. This work

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presents an experimental justification of the design of a self-expanding transcatheter aortic valve prosthesis based on an EGDE-stabilized biomaterial.

MATERIALS AND METHOD

Design input

Based on studies on TAVR features and results, analysis of design solutions of existing transcatheter valves and their shortcomings (analysis of the literature of the current state) [7, 8], analysis of new experimental prostheses [9, 10], as well as analysis of regulator requirements, the basic design characteristics of medical products were determined. The main prerequisites for the design of aortic valve prosthesis were:

– The prosthesis represents a stent-type support frame, on which three symmetrical leaflets, made of biological material and a veneer in the inflow area, are mounted.
– Structurally, the prosthesis consists of three interconnected zones that provide the functions – (1) fixation in the lumen of the annulus fibrosus or dysfunctional prosthesis; (2) preservation of the symmetrical geometry of the cusp and the possibility of its closure; (3) ensuring fixation in the sinotubular articulation area while maintaining the geometry of the cusp unchanged.
– The technology chosen for the support frame was the use of a self-expanding structure based on a superelastic titanium nickelide alloy. This solution, highly recommended in the clinical practice of TAVR, additionally, would not require the development of a complex delivery system, as in the case of alternative solution, balloon implantation.
– The prosthesis cusp must not interfere with the packaging into the delivery system, hence, have a minimum thickness, while maintaining sufficient strength and providing the necessary closure zone (co-optation), which is ensured by using EGDE-stabilized porcine xenopericardium.

The original geometry of the support frame should allow laser cutting from a small-diameter 6 mm (18 Fr) tube for subsequent packaging in a minimal profile delivery system.

Concepts

Components of the developed prosthesis were designed through a series of numerical experiments to assess the main functional characteristics – radial forces, stress-strain state, and fatigue-strength characteristics. For this purpose, two primary concepts of a stent-based support frame were developed: "classical" and "inclined" cell topology. The main difference in the second case was the inclination of three cell rows – two in the inflow area and one in the outflow. Such a feature, presumably, should provide a special pattern for subsequent pre-implantation packaging into the delivery system – due to the twisting of the support frame. Support frame models, implemented in the form of two-dimensional sweeps for subsequent formation of volumes, were built in the SolidWorks (Dassault Systemes, France) design software (computer-aided design).

Numerical Simulation

The resulting concepts were subjected to numerical analysis in the Abaqus/CAE environment (Dassault Systemes, France) based on the finite element method with iterative design optimization and repeated numerical experiments. For this purpose, C3D8 hex element grid (a general-purpose 3D hexagonal element, fully integrated with 8 nodes, n = 105,000) was obtained on the basis of three-dimensional models. The study was performed for a series of load tests, including:

1) Giving the final shape to the support frame (Fig. 1, a, b) from the initial 6 mm to the final geometry of variable diameter, fitting size 25 mm for the area containing the cusps. The criterion for the consistency of the design was the absence of elements with high stress values exceeding the ultimate strength of the material (σ = 1522.4 MPa [11]).
2) Axial stiffness test of the inflow area (Fig. 1, b) to assess fixation forces at 75% relative to the original diameter. The resulting stress-strain curves were evaluated.
3) Radial compression test (Fig. 1, b) to assess the force with which the device will exert pressure on the annulus fibrosus in the implanted state, in particular, in the cardiac conduction system passage area, i.e. the area responsible for the occurrence of the left bundle branch block.
4) The cyclic fatigue test based on the average and alternating stress diagrams – the ability of the structure to withstand prolonged alternating load – demonstrated for the final models the ability to operate without node destruction under the action of normal and elevated pathological pressures – up to 160 mmHg (0.21 kPa).

Real-life experiments

The developed drawings of the support frames formed the basis for the prototypes of two versions of the TAVR prosthesis: one based on the "classical" design and two based on the "inclined" design (Fig. 2, a). Titanium nickelide tubes with 6 mm diameter and 0.5 mm wall thickness were manufactured by laser cutting, with subsequent shaping by heat treatment with a phase trans-

formation temperature of 17 ± 3 °C and surface treatment by mechanical and electrochemical polishing.

The obtained support frames were subjected to a series of mechanical tests for axial and radial compression in comparison with the control – a CoreValve™ bioprosthesis support frame (Medtronic, Inc., USA) of the same standard size. For this purpose, the specimens were placed in plate clamps or radial grips of ZwickRoell universal testing machine (ZwickRoell, Germany) and compressed by 75% in axial (Fig. 3, a) and radial (Fig. 3, b) directions, with registration of force-deformation curves.

To create the cusp and the lining, the templates were designed, according to which the necessary components were made by laser cutting using the thickness mapping of EGDE-stabilized porcine xenopericardium. Then, by consecutive mounting of all elements of the prosthesis on the support frame with the help of sutures according to well-known methods, working prototypes of prostheses (Fig. 2, b) were made for hydrodynamic tests under real-life experiments on a stand. Hydrodynamic characteristics were studied in a Vivitro pulsating flow setup (Vivitro Labs, Canada), in which normal blood flow was simulated: 70 mL stroke volume, 5 L/min cardiac output, and 120/80 mm Hg pressure. Results: the effective orifice area, maximum and mean transprosthetic gradients, and regurgitant volume were recorded for 10 steady-state cycles. A 25-size commercial CoreValve™ bioprosthesis was used as control values.

RESULTS

Numerical simulation

The following characteristics were obtained from numerical analysis of load tests:

1) Giving the final shape to the support frame from the initial 6 mm to the final geometry of variable diameter, up to 22–31 mm with a fitting size of 25 mm did

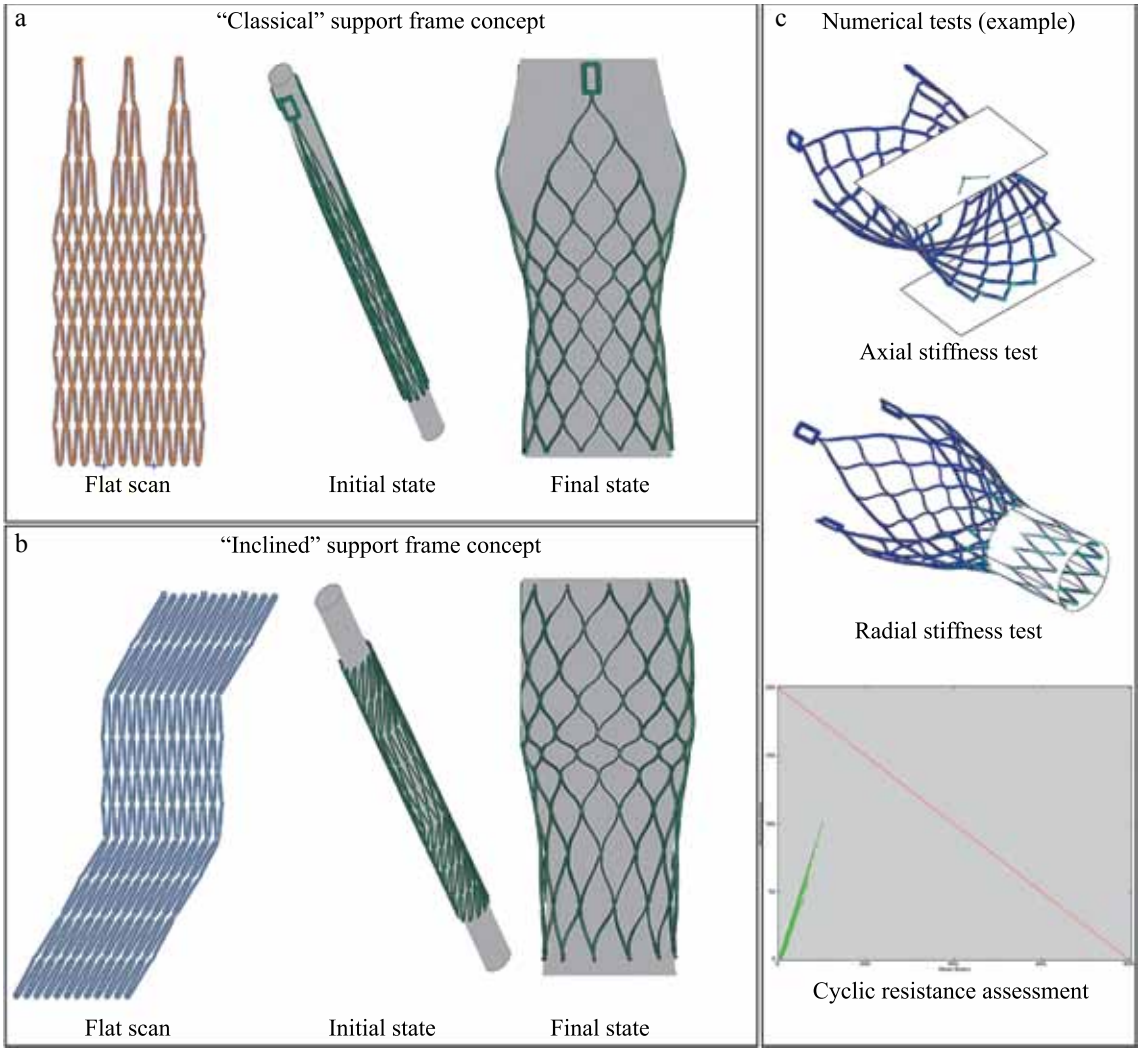

Fig. 1. Two primary concepts of a support frame based on stents "classical" (a) and "inclined" (б) topology of cells, computer models: initial flat sketch for laser cutting machine; initial state, similar to the manufactured one; final state obtained by the finite element method; в – an example of numerical tests for design optimization: axial stiffness test with slabs; radial stiffness test with a cylindrical surface; alternating stress diagram for evaluating cycle durability

not cause a critical increase in the stress-strain state of the nodes: the average weighted value of node stress was 341 (110–628) and 258 (53–756) MPa depending on the concept at the threshold level (1080 MPa), taken as the ultimate strength of titanium nickelide (Fig. 4, b).

2) The axial stiffness test (Fig. 4, a) of the inflow area yielded values ranging from 11.3 to 17.1 N as the total force to estimate the fixation forces.
3) The radial compression test (Fig. 4, a) showed similar findings, with radial forces for the "classical" and "inclined" concepts – 12.4 and 16.8 N, respectively, with slightly higher values for the CoreValve™ bioprosthesis (up to 21.3 N) [12].
4) Cyclic fatigue test showed that the resulting alternating stresses do not exceed 36–50 MPa. The average stress variations, taking into account the previously formed stress-strain state, are 410–513 MPa – below the ultimate fatigue strength (S-N curves 400 MPa [13]).

Real-life experiments

It was shown that the maximum axial force in the case of the developed support frames was 12.8–15.6 mm, depending on the geometry and, in general, weakly depended on the frame area. For the control case, the CoreValve™ bioprosthesis, there was a clear dependence of forces on the prosthesis area: 12.4 N for the inflow area and 7.58 N for the outflow area. The 75% radial compression force generated for the experimental prostheses was also shown to be weakly dependent on the prosthesis area, being 11.6–17.0 N, while in the control case it ranged from 20.6 N (inflow area) to 8.1 N (outflow area). In all cases, a clear hysteresis dependence of the frame properties under loading and unloading was obtained – formation of a specific stress-strain curve loop that is characteristic of titanium nickelide. It was shown that the ranges of forces created by the support frames in a real-life experiment, firstly, agree with the findings of numerical experiments, which made it possible to verify computer simulation, and secondly, agree well with the properties of the commercial CoreValve™ prosthesis, which is widely used in in TAVR clinical practice in Russia.

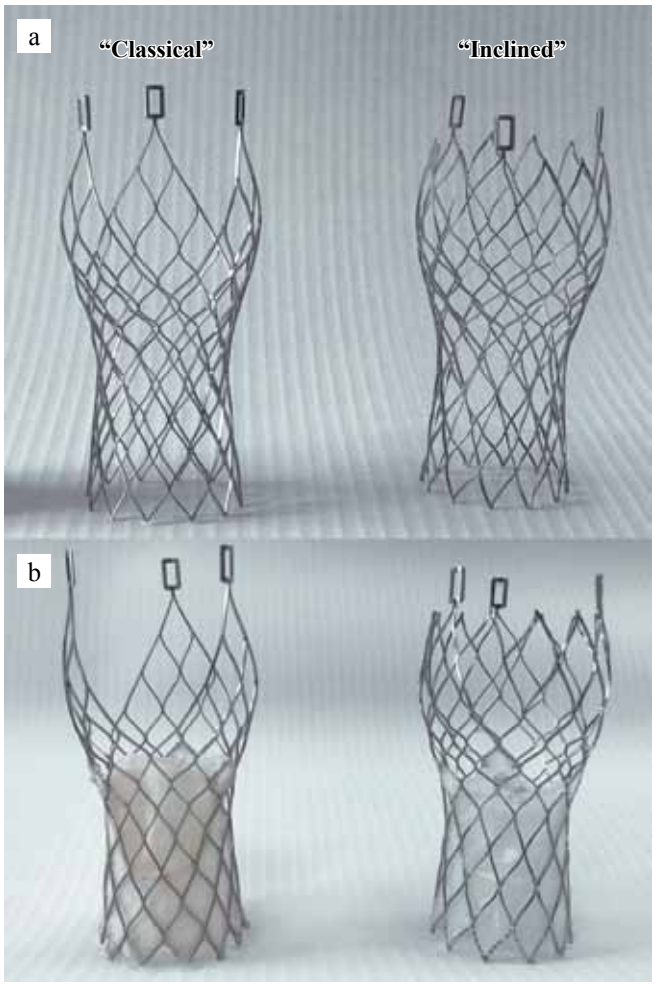

Fig. 2. Supporting frames and prototypes of TAVR-prostheses, containing a valve apparatus and facing of the inflow zone, of two concepts: based on the "classic" cell and "inclined"

Quantitative results of the hydrodynamic study are shown in Table.

DISCUSSION

Designing a new transcatheter aortic valve prosthesis is a complex task that requires investigation and justification of the geometry and properties of all its components – the support frame, the cusp, and the subsequent

Table

Hydrodynamic characteristics of the studied prostheses

Indicator	"Classical" design	"Inclined" design	Control
Effective orifice area, cm^2	2.17 ± 0.32	1.97 ± 0.21	2.34 ± 0.11
Maximum transprosthetic gradient, mm Hg	13.9 ± 6.5	17.5 ± 8.8	10.4 ± 6.2
Mean transprosthetic gradient, mm Hg	7.1 ± 3.8	8.9 ± 4.3	5.1 ± 2.1
Regurgitant volume, mL/cycle	2.2 ± 1.8	4.1 ± 2.3	2.8 ± 2.6

Note. All data are presented as mean ± standard deviation, calculated over 10 steady-state hydrodynamic cycles.

validation of the assembled structure. The present study demonstrates an analysis of the two most important risks for TAVR – excessive pressure on the areas of the cardiac conduction system around the annulus fibrosus and hemodynamic efficiency. The first aspect determines the possibility of conduction abnormalities – primarily atrioventricular block resulting from mechanical compression, while the second determines the development of para- and transprosthetic regurgitation due to loose engagement of the prosthesis with the surrounding tissues or violations of the leaflet geometry. Clinical experience with the use of self-expanding TAVR prostheses demonstrates the prevalence of these two effects in the complication structure of this type of prosthetic repair [14].

The study of mechanical properties and stress-strain states through numerical and real-life experiments, demonstrates the consistency of the proposed concepts. The arising internal forces (stress) do not reach critical values, constituting much lower amplitudes even for loaded structural nodes. The value of such a "safety margin", on one hand, does not cause risk of failure of the prosthesis sections, even with additional loads (bends during the passage of the patient's vascular bed), on the other hand, it makes it possible for in-depth optimization of the design: changes in the geometric parameters of the cell, i.e., potential reduction in the prosthesis diameter in the pre-implantation state – the delivery system profile. External forces generated by the support frame in the radial and axial directions are largely consistent with the control – the CoreValve™ clinical bioprosthesis, which, despite complications, has a high evidence base for its effectiveness. It can be assumed that the proposed design will demonstrate similar fixation results in the aortic valve lumen. The concepts show lower radial forces in the annulus fibrosus, suggesting a lower risk of compression of the conduction system. However, this thesis should be confirmed by an extended series of experiments, including assessing the fixation reliability. Fatigue modeling data showed a slight change in the stress in the systole-diastole cycle for both models, suggesting that the frame is functioning in an "infinite" range and predicting com-

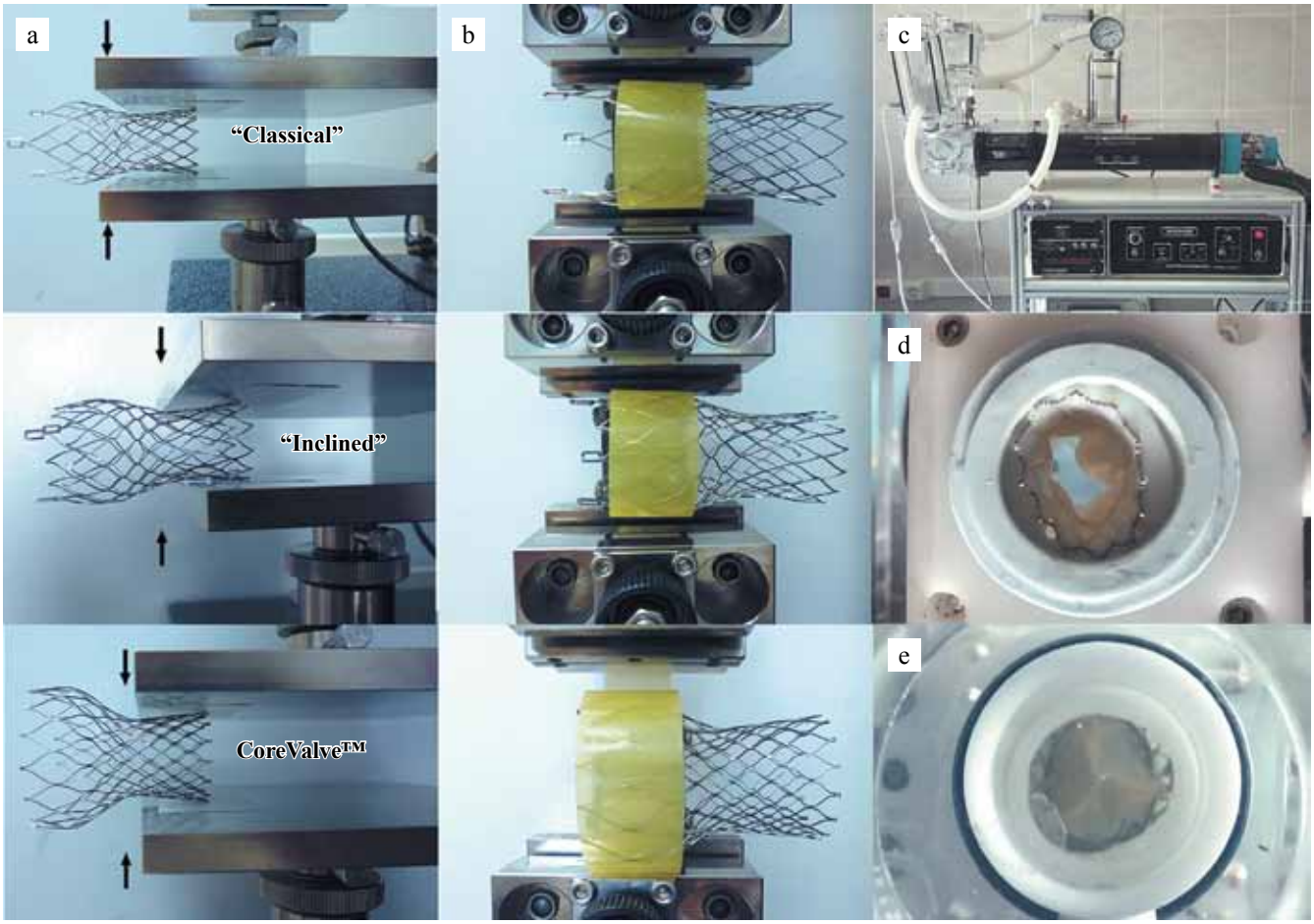

Fig. 3. Setting up full-scale experiments with prototypes of supporting frames and working prototypes of an assembled prosthesis: а – study of mechanical properties in a universal testing machine for axial compression; б – the same for radial compression; в – stand for hydrodynamic testing of prostheses; г – view from the inflow zone of the prototype valve prosthesis installed in the hydrodynamic stand; д – view from the outlet zone to the closed flap apparatus

pliance with the requirements to withstand 200 million systole-diastole cycles without failure.

In vitro hydrodynamic characteristics are the main indicator of bioprosthesis performance; in a comparative aspect, they show generally satisfactory results. Comparison of the performance of glutaraldehyde-stabilized xenopericardial leaflets (CoreValve™ control bioprosthesis) and the concepts in question based on EGDE-stabilized biomaterial confirmed the acceptability of the latter for TAVR prostheses. Quantitative characteristics – effective orifice area and the transprosthetic gradient determining the opening of the cusp, indicate sufficient elasticity and mobility of the leaflets. The regurgitant volume, comparable both with bioprostheses for open intervention [15, 16], and with the control, in turn, confirms the cusp closure tightness and creation of tight contact with the annulus fibrosus in vitro model.

CONCLUSION

The series of studies carried out demonstrates the consistency of the developed support frame concepts, including from the point of view of implementing the cusp based on EGDE-treated xenotissues. Validation of working prototypes in the hydrodynamic evaluation unit in a comparative aspect with the clinical specimen of a similar TAVR bioprosthesis confirmed the satisfactory functional characteristics of the models developed.

The study was funded by a grant from the Russian Science Foundation (project No. 18-75-10061) on the topic "Research and Implementation of the Concept of Robot-Assisted Minimally Invasive Aortic Valve Repair".

The authors declare no conflict of interest.

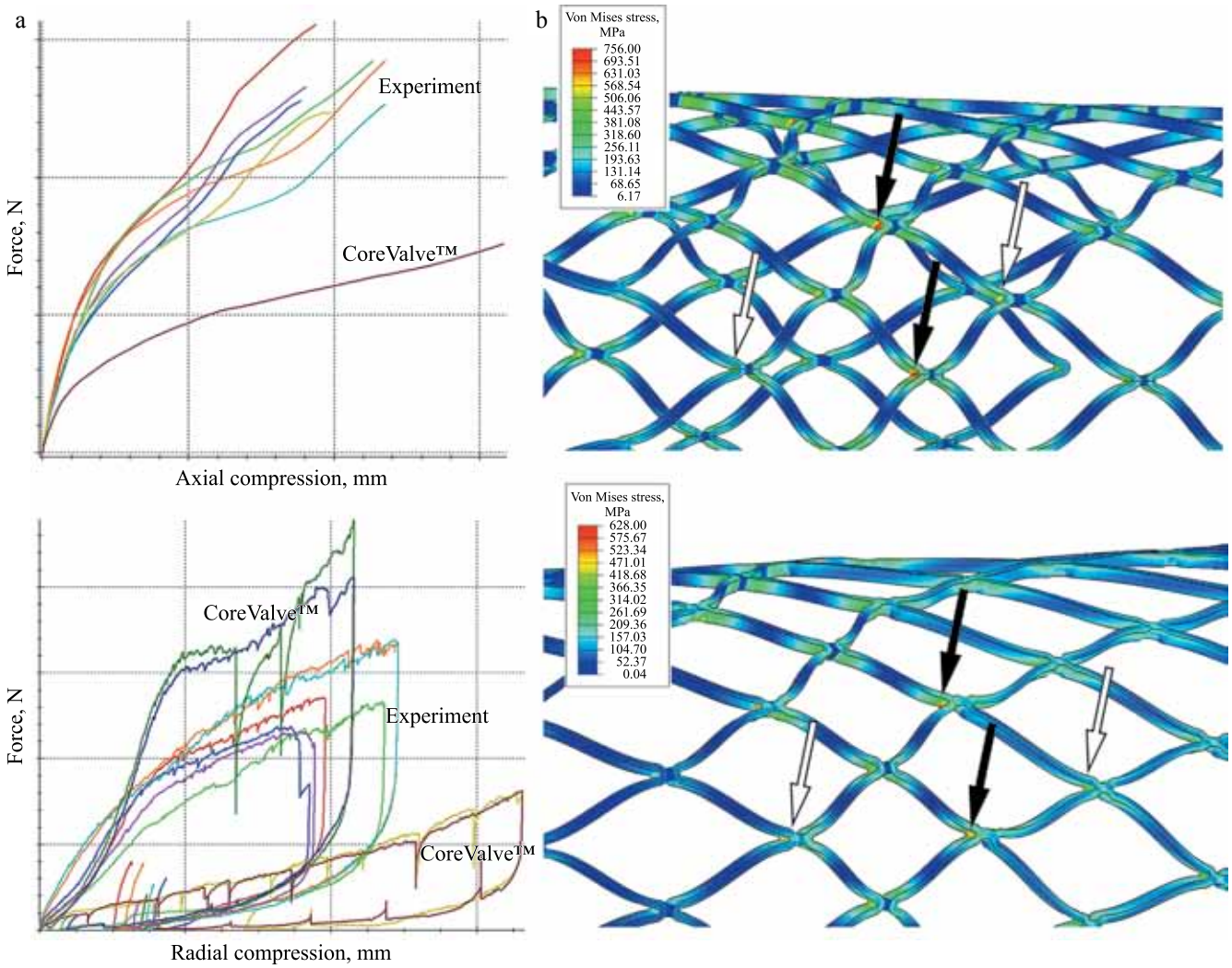

Fig. 4. Test results: a – full-scale assessment of mechanical properties in a universal testing machine in comparison with a control – a commercial bioprosthesis CoreValve ™; б – numerical assessment of the stress-strain state of the support frame models, black arrows indicate nodes with maximum von Mises stress values, white – with moderate ones

REFERENCES

1. *Kamioka N, Wells J, Keegan P, Lerakis S, Binongo J, Corrigan F et al.* Predictors and clinical outcomes of nextday discharge after minimalist transfemoral transcatheter aortic valve replacement. *JACC Cardiovasc Interv.* 2018; 11: 107–115. doi: 10.1016/j.jcin.2017.10.021.
2. *Rodriguez-Gabella T, Voisine P, Puri R, Pibarot P, Rodes-Cabau J.* Aortic bioprosthetic valve durability: incidence, mechanisms, predictors, and management of surgical and transcatheter valve degeneration. *J Am Coll Cardiol.* 2017; 70: 1013–1028. doi: 10.1016/j.jacc.2017.07.715.
3. *Wang M, Furnary AP, Li HF, Grunkemeier GL.* Bioprosthetic aortic valve durability: a metaregression of published studies. *Ann Thorac Surg.* 2017; 104: 1080–1087. doi: 10.1016/j.athoracsur.2017.02.011.
4. *Dasi LP, Hatoum H, Kheradvar A, Zareian R, Alavi SH, Sun W et al.* On the mechanics of transcatheter aortic valve replacement. *Ann Biomed Eng.* 2017; 45: 310–331. doi: 10.1007/s10439-016-1759-3.
5. *Zhuravleva IYu, Karpova EV, Oparina LA, Kabos N, Ksenofontov AL, Zhuravleva AS et al.* Xenopericardum, preserved by di- and pentaepoxides: molecular mechanisms of crosslinking and mechanical properties of biomaterial. *Circulatory pathology and cardiac surgery.* 2018; 22 (3): 56–68. doi: 10.21688/1681-3472-2018-3-56-68. [In Russ, English abstract].
6. *Barbarash LS, Rogulina NV, Rutkovskaya NV, Odarenko YuN, Kokorin SG.* Experience with the use of epoxy-treated biological prostheses in mitral valve disease in patients younger than 65 years of age. *Thoracic and cardiovascular surgery.* 2019; 61 (2): 114–122. doi: 10.24022/0236-2791-2019-61-2-114-122. [In Russ, English abstract].
7. *Rotman OM, Bianchi M, Ghosh RP, Kovarovic B, Bluestein D.* Principles of TAVR valve design, modelling, and testing. *Expert Rev Med Devices.* 2018; 15 (11): 771–791. doi: 10.1080/17434440.2018.1536427.
8. *Cahill TJ, Chen M, Hayashida K, Latib A, Modine T, Piazza N et al.* Transcatheter aortic valve implantation: current status and future perspectives. *Eur Heart J.* 2018; 39 (28): 2625–2634. doi: 10.1093/eurheartj/ehy244.
9. *Bogachev-Prokofiev AV, Zhuravleva IYu, Sharifulin RM, Zheleznev SI, Demidov DP, Kliver EE, Karaskov AM. In vitro* implantation of the first domestic transcatheter prosthesis in the native mitral valve. *Circulatory pathology and cardiac surgery.* 2018; 22 (1): 22–28. [In Russ, English abstract].
10. *Rotman OM, Kovarovic B, Chiu WC, Bianchi M, Marom G, Slepian MJ, Bluestein D.* Novel Polymeric Valve for Transcatheter Aortic Valve Replacement Applications: *In vitro* Hemodynamic Study. *Ann Biomed Eng.* 2019; 47 (1): 113–125. doi: 10.1007/s10439-018-02119-7.
11. *Marrey R, Baillargeon B, Dreher ML, Weaver JD, Nagaraja S, Rebelo N, Gong XY.* Validating Fatigue Safety Factor Calculation Methods for Cardiovascular Stents. *J Biomech Eng.* 2018; 140 (6): 10.1115/1.4039173. doi: 10.1115/1.4039173.
12. *Tzamtzis S, Viquerat J, Yap J, Mullen MJ, Burriesci G.* Numerical analysis of the radial force produced by the Medtronic-CoreValve and Edwards-SAPIEN after transcatheter aortic valve implantation (TAVI). *Med Eng Phys.* 2013; 35 (1): 125–130. doi: 10.1016/j.medengphy.2012.04.009.
13. *Robertson SW, Pelton AR, Ritchie RO.* Mechanical fatigue and fracture of Nitinol. *International Materials Reviews.* 2012; 57 (1): 1–37. doi: 10.1179/1743280411Y.0000000009.
14. *Alfadhli J, Jeraq M, Singh V, Martinez C. Updates* on transcatheter aortic valve replacement: Techniques, complications, outcome, and prognosis. *J Saudi Heart Assoc.* 2018; 30 (4): 340–348. doi: 10.1016/j.jsha.2018.07.002.
15. *Klyshnikov KYu, Ovcharenko EA, Maltsev DA, Zhuravleva IYu. Comparative* characteristics of hydrodynamic indicators of bioprostheses of heart valves "UniLine" and "PeriCor". *Clinical physiology of blood circulation.* 2013; 1: 45–51. [In Russ, English abstract].
16. *Marquez S, Hon RT, Yoganathan AP.* Comparative hydrodynamic evaluation of bioprosthetic heart valves. *J Heart Valve Dis.* 2001; 10 (6): 802–811.

The article was submitted to the journal on 16.07.2020