Acta of Bioengineering and Biomechanics
Vol. 17, No. 2, 2015

Original paper
DOI: 10.5277/ ABB-00038-2014-02

Remodelling of material structure in aortic valve leaflet

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Purpose: The goal of this study is to model changes in fibre content in aortic valve leaflet material due to mechanical stimuli. Methods: The fibre remodelling process is associated with the redistribution of the internal forces acting in the shell. The process is characterized by the occurrence of extreme stresses and strains. The load distribution function is asymmetrical. The optimization problem has been assigned the task of transferring the load imposed on the leaflet. The density of the fibres per unit surface of the middle shell was assumed to be proportional to the shell thickness, which means that fibre density along the normal direction is constant over the entire shell. Results: The model of valve leaflet loading is the distribution of the pressure generated on the leaflet shell surface by the flowing fluid. The algorithm for the redistribution of the leaflet material mass made it possible to distinguish two regions of enhanced thickness in the leaflet shell. One was localized between the commissures along the leaflet attachment, the other one in the middle part of the leaflet at the level of the commissures. A reduction in shell thickness is observed in the middle part of the leaflet, above the point of its attachment to the aorta. Conclusions: The distribution of the thickness field obtained corroborates the findings of the study reported elier. Our study on the remodelling of the valve leaflet entailed the application of the stress criterion, which visibly upgraded the functioning of the valve by improving its mechanical and hemodynamic parameters.

Key words: *aortic valve, tissue engineering, fibre reinforced material, remodelling*

1. Introduction

Remodelling has an important part in the functioning of tissues that are responsible for load transfer. The remodelling process is aimed at changing the structure of a material in order to upgrade its performance. Tissue remodelling is induced by both biological and mechanical factors. The latter act as mechanical stimuli, inducing the remodelling of the tissues whose main function entails load transfer.

Scientific reasearch into remodelling-related problems takes its roots in the mechanics of the osseous system [5]. Many investigators express the opinion that bone remodelling is predominantly induced by a mechanical stimulus. When a bone tissue is mechanically induced, its structure undergoes remodelling and adapts to the given loading set.

In the literature, much consideration has been devoted to mechanically induced remodelling of collagen fibres [6], with emphasis on the key importance of their synthesis and degradation in the aortic valve [1]. Driessen et al. [3] investigated the remodelling of collagenous fibres in the leaflet of the aortic valve. They assumed that the fibres are arranged in the directions of the principal strains, and that the density of the collagen fibres increases with the increase in the nominal strains to which they are exposed.

Driessen et al. [3] proposed a model that describes how the orientations and densities of the fibres in the aortic valve leaflet change with the progress of the mechanically induced remodelling process. They assumed that the reorientation of the fibres occurs solely in two vertical directions. They analyzed the functioning of the fibrosa layer (which is built predominantly of collagen fibres), assuming that the buckling of the leaf shell is symmetrical, and that the scheme of loading is simple, since in this case use is made of a homogeneous loading in the form of pressure. Driessen et al. [3] have developed the thesis that fibre

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Received: February 24th, 2014
Accepted for publication: June 2nd, 2014

remodelling on a micro scale results from material deformation on a macro scale. The total number of fibres increases with the increase in their average nominal tension. Boerboom et al. [1] modified Driessen's algorithm by including the capacity of the fibres for reorientation in many directions. The adopted net of fibres of an arbitrary orientation enables remodelling via fibre synthesis and degradation, which occur in the natural remodelling process.

The study reported on in this paper furthers our previous research into the structure of a physical model, which describes the functioning of natural aortic valves in terms of continuous medium mechanics. The aim of the present study was to develop a novel, original method for describing the remodelling in the aortic valve leaflet. In terms of mechanics, remodelling is an optimization problem targeted at obtaining an optimal distribution of the composite material (matrix-immersed fibres) for the aortic valve leaflet, in order to enable optimal functioning of the aortic valve in the circulatory system. The notion 'optimal functioning of the system' is included in the formal mathematical description of the optimization problem.

A key issue in describing the functioning of the aortic valve is the identification of the material of the aortic valve leaflet [7]. The three-layer structure, the collagen and elastin fibres, as well as the varying thickness of the leaflet shell, indicate that the aortic valve is best suited for performing the function of a one-way valve in the circulatory system.

Our previous investigations have substantiated the importance of understanding the response of the leaflet tissues to the mechanical stimulus induced by the flowing fluid. The analysis of the fluid–valve interaction provides information about the distribution of the load exerted by the fluid onto the valve, as well as about the variability of this load with time [8].

A key factor in the remodelling of the leaflet structure is to define the load received by the leaflet; this load is characterized by distributions, both in space and time, which take values similar to those observed in a real process. In our present work, the determination of the loading exerted on the leaflet was preceded by a number of preliminary analyses of fluid flow through a system where the leaflet acted as a rigid obstacle. The remodelling process is formulated as an optimization problem with an objective function. The remodelling problem is analyzed using two different objective functions, each of them being physically justified. One of the objective functions refers to the rigidity of the leaflet, while the other one (which is the focus of the present research) refers to the shear stresses responsible for the degradation of the leaflet material.

Using the algorithm established for the purpose of the study and a specialized software, numerical analyses were performed to describe the remodelling of the aortic valve leaflet. This paper presents a discussion of the most significant results.

2. Materials and methods

Our previous work [7] was focused on analyzing the mechanical properties and the shell structure of the aortic valve leaflet, the Reul model being adopted as the initial geometry. The model parameters being searched were determined via optimization by minimizing the objective function, which in that case was the critical pressure. In the present study, the same class of valve leaflet geometry is made subject to analysis for comparative purposes.

The aortic valve model analyzed in this study consisted of an aorta fragment and valve leaflets (Fig. 1). Because of the symmetry planes occurring there, numerical analyses were performed for a separate fragment, which accounted for one-third of the entire system and contained one leaflet.

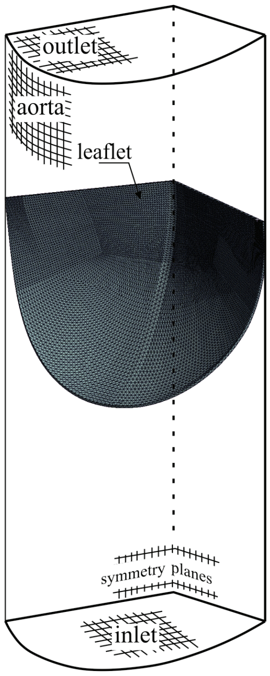

Fig. 1. Construction of the aortic valve and the aorta

The main object under analysis, the valve leaflet, was a model of a natural leaflet. A thin Kirchhoff–Love shell of varying thickness, which consisted of an isotropic material with linear elastic characteristics and a constant Poisson ratio, was adopted as the physical model of the valve leaflet [7]. The adoption of a simple model for the description of the valve leaflet does not reduce the generality of the remodelling process considered. An essential feature of the model is the non-homogeneity of the shell, which undergoes changes in the course of remodelling.

It has been assumed that the leaflet is attached stiffly to the aorta. The model contains a single leaflet only, so the contact of the leaflet with the other leaflets of the valve is not considered directly. This contact is considered indirectly while modelling the geometry of the leaflet during the phase of complete closure of the valve. Aorta is an undeformable cylinder. The model of the fluid is an incompressible Newtonian fluid characterized by density ρ and dynamic viscosity μ. The model is considered to be isothermal, viscous and incompressible. The Newtonian model of the flow can be well described be Navier–Stockes equation and the continuity equation. The character of flow is turbulent.

The only load received by the leaflet is the pressure of the surrounding fluid. The state of the valve's closure is regarded as the initial configuration of the system, where the stress in the leaflet shell is zero. The occurrence of potential stresses in the shell at the place of attachment, or under boundary conditions on the free edge, was neglected in the initial configuration. In the course of the process the load induced by the pressure of the fluid undergoes changes with time. The structure is loaded both sides. The distribution of the load in the form of a non-homogeneous pressure distribution was obtained by solving (at stage I) the independent problem of interaction between the flowing fluid and the valve shell, under conditions of ideal homogeneous parameters of the shell.

The fibre remodelling process is associated with the redistribution of the internal forces acting in the shell while the valve is working. The process is assumed to take place only during the systole phase, which is characterized by the occurrence of extreme stresses and strains. Because of the non-homogeneous and complex nature of the load distribution, it is necessary to take into account the possibility that the buckling of the leaflet and the distribution of the function describing the state of the shell will be asymmetrical.

To obtain numerical solutions, nonlinear-geometric analyses were performed using the finite element method and (in most instances) the Ansys system. Applying the method of one-way interaction between the fluid and the leaflet structure necessitated the assumption that the fluid affects the shell of the leaflet whereas the shell does not affect the fluid; it only acts as a rigid obstacle to the fluid (an obstacle with a time-dependent geometry).

The optimization problem consisted in finding the optimal distribution of the physical structure (density of the net of fibres immersed in the matrix), which has been assigned the task of transferring the load imposed on the leaflet during the valve functioning cycles. The density of the fibres per unit surface of the middle shell was assumed to be proportional to the shell thickness, which means that fibre density along the normal direction is constant over the entire shell [9].

The dynamic process being analyzed, formulated in terms of continuous medium mechanics, was solved numerically by the finite element method. For the adopted discrete model MES the following design vector variable was defined

$$\mathbf{b} = (h_{(1)}, h_{(2)}, ..., h_{(e)}, ..., h_{(e_{\max})})^{\mathrm{T}} \tag{1}$$

where $h_{(e)}$ is shell thickness on the e-th element.

Vector **b** is a discrete representation of the function describing the distribution of the leaflet shell thickness, which can also be interpreted as the distribution of fibre density per unit surface of the shell.

The optimization algorithm was established at the following additional limitations:

- the total mass (volume) of the leaflet shell is steady,
- the local thickness of the shell can vary over a defined range with respect to the average value.

The objective function $F(\mathbf{b})$ was the minimum of the average shear stress in the valve leaflet when the valve was fully opened. The objective function formulated in this way has a significant physical meaning. Because of the three-layer structure of the leaflet shell, the extreme shear stresses in the middle layer contribute largely to the degree of its effort. In the case of stress concentration, there is probability that the delamination phenomenon, and consequently the degradation of the shell, will occur.

The optimization problem was solved in two stages.

Stage I

The valve model was analyzed on the assumption that the thickness of the leaflet shell h_0 is constant, the mechanical parameters of the material being E = 10 MPa, ν = 0.45. Analysis was performed of the process of fluid flow through a part of the aorta (multistep analysis). The process was divided into time steps Δt_k (k = 1, 2, ..., n), where $\Delta t_k = t_k - t_{k-1}$. For each time step two analyses were performed:

- analysis of fluid flow, where the leaflet was considered as a rigid body of a given geometry,
- static analysis of the leaflet shell considered as an elastic body loaded with the fluid pressure resulting from the analysis of fluid flow,
- in the subsequent time step the geometry of the leaflet was actualized, taking into account the deformations produced by previous loadings.

The geometry of the leaflet was defined by structural points, which well characterize the state of deformation at the point in time t.

As a result of calculations, n pressure distributions, $\mathbf{p}_k(\mathbf{x})$, were obtained, where k = 1, 2, ..., n. These are the pressure distributions obtained at the end of the k-th time step at the points in time t_1, t_2, ..., t_n. The set of shell load distributions established as shown above was used during stage II (Fig. 2).

Stage II

The optimization problem is solved during stage II, where a convergent solution is obtained in successive

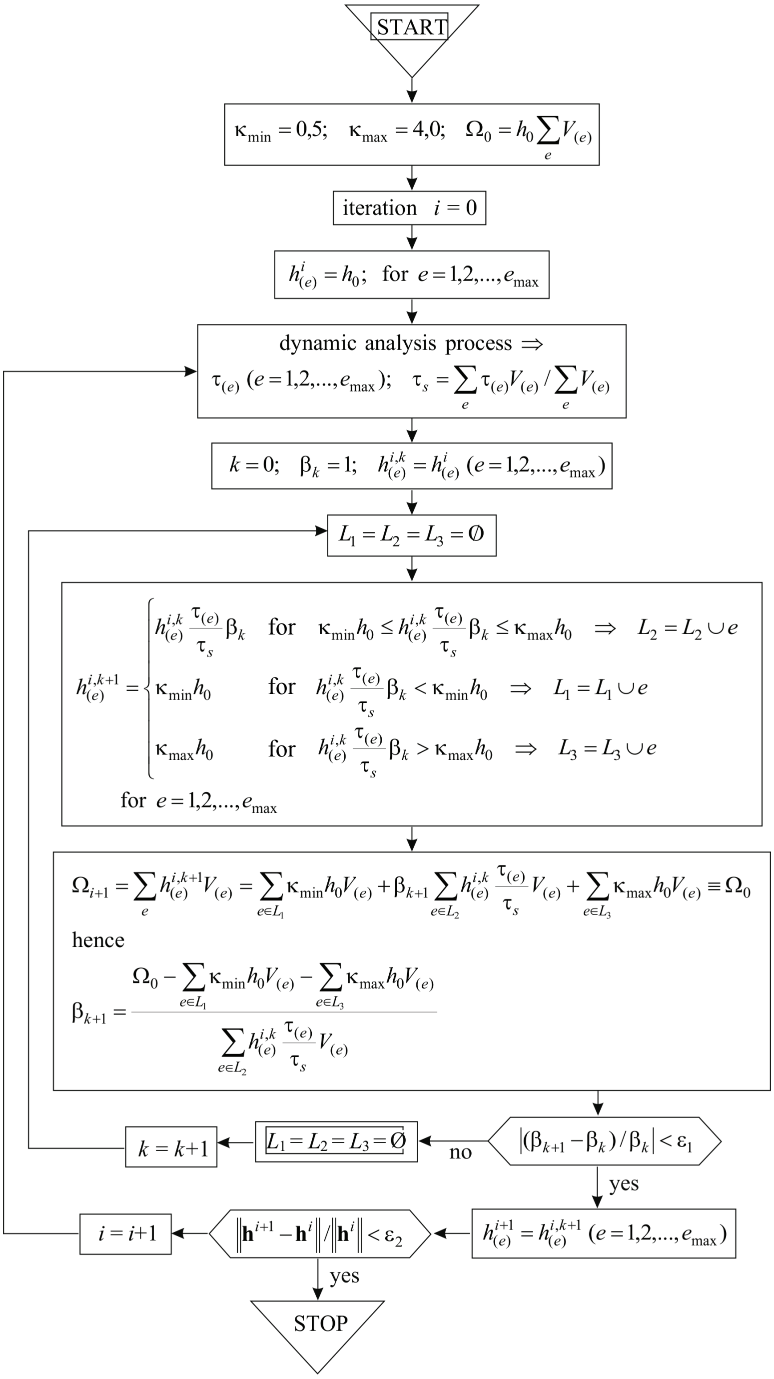

Fig. 2. Block diagram of the optimization problem solution

iterative steps, in accordance with the objective function assumed.

During each iterative step a dynamic analysis is performed of the process of valve opening; the loading applied consists of the pressure distributions derived from stage I. In the subsequent time steps, the loading applied to the shell occurs in the form of pressure with the following distribution

$$\mathbf{p}(\mathbf{x}, t) = \mathbf{p}_k(\mathbf{x}) \quad \text{for} \quad t \subset (t_{k-1}, t_k) \tag{2}$$

and the loading is temporarily constant in the *k*-th time step.

Each iterative step involves the following operations:

- the distribution of the shell thickness is given: thickness $h_{(e)}$ is sought for each finite element (*FE*),
- the process of valve opening is made subject to dynamic analysis, with the assumption that load distribution is time-dependent: $\mathbf{p}(\mathbf{x}, t)$. The results of analysis are stress and strain distributions in each particular *FE*, special consideration being given to the determination of the shear stresses on the surface of the middle shell, τ_{xz}, τ_{yz}, and to the determination of the resultant of those stresses, $\tau_{\max} = \sqrt{\tau_{xz}^2 + \tau_{yz}^2}$, at selected points of the *FE*, such as: (a) the centre of the *FE*, (b) the nodal points of the *FE*, (c) the integration points,
- the average value of the maximal shear stress, $\tau_{(e)}$, in the *FE* is determined,
- the average value of the shear stress on the leaflet shell is determined

$$\tau_s = \sum_e \tau_{(e)} V_{(e)} / \sum_e V_{(e)} \,,$$

- leaflet mass redistribution is obtained by defining a new shell thickness distribution according to the procedure specified in the block diagram.

At the beginning of the iteration process the initial thickness of the *FE* is $h_{(e)} = h_0$ in the model.

The final point of each iteration step (i.e., the point in time t_f) is determined as follows:

- for the first iteration, several points, $\mathbf{x}_j$ (j = 1, 2, ..., m), on the free edge of the leaflet are selected; they form the contour of the open leaflet and, at the same time, constitute the base for the measure of the orifice area during the systole phase equal to A_0 (A_0 is the area between the extreme radii, $\mathrm{O}\mathbf{x}_1$ and $\mathrm{O}\mathbf{x}_m$, and the broken curve, which connects consecutive points of the set $\mathbf{x}_j$),
- during any further iteration, the displacements of selected points on the leaflet edge are determined, and the orifice area during the systole phase, A_k, is calculated; this area is selected for the point of timein such a way that $|A_k - A_0| \le \varepsilon_A = 0.01$.

Because of the limitations of the optimization problem, the thicknesses for the particular *FE* of the shell are chosen by internal iteration. The block diagram of the optimization problem solution is specified in Fig. 2.

3. Results

The solution to the problem of remodelling a net of collagen fibres being part of the aortic valve leaflet structure was based on two assumptions, which in our opinion are of importance.

The model of valve leaflet loading is the distribution of the pressure generated on the leaflet shell surface by the flowing fluid. It is assumed that the distribution of this loading can be obtained through the one-way interaction of the fluid with the shell. Such loading distribution is determined primarily by the time-dependent variability of the pressure of the fluid at the input of the valve, and to a lesser degree by the distribution of the shell thickness. The time-dependent variability of the loading distribution obtained in this way at stage I for the shell of a constant thickness is regarded as a signal inducing the remodelling of the leaflet material. Examples of pressure distributions for a closed and an open leaflet are shown in Fig. 3.

The other important assumption adopted for the analysis of the redistribution process pertains to the choice of the criterion for the remodelling of the leaflet material. Considering the function of the valve in the circulatory system, it has been assumed that the criterion should refer to the reliability of the system's functioning. As the system works under dynamic conditions, the minimization of the shear stress gradients (accounting for the delamination of the shell) reduces the extent of the shell's effort and thus exerts a direct impact on the durability of the system. The criterion has been incorporated into the objective function of the iteration process at stage II.

With the algorithm for the redistribution of the leaflet material mass it was possible to distinguish two regions of enhanced thickness in the leaflet shell. One was localized between the commissures along the leaflet attachment to the aorta, the other one in the middle part of the leaflet at the level of the commissures. A reduction in shell thickness is observed in the middle part of the leaflet, above the point of its attachment to the aorta. Upon optimization, a symmetrical distribution of the thickness field is observed on the leaflet shell (Fig. 4).

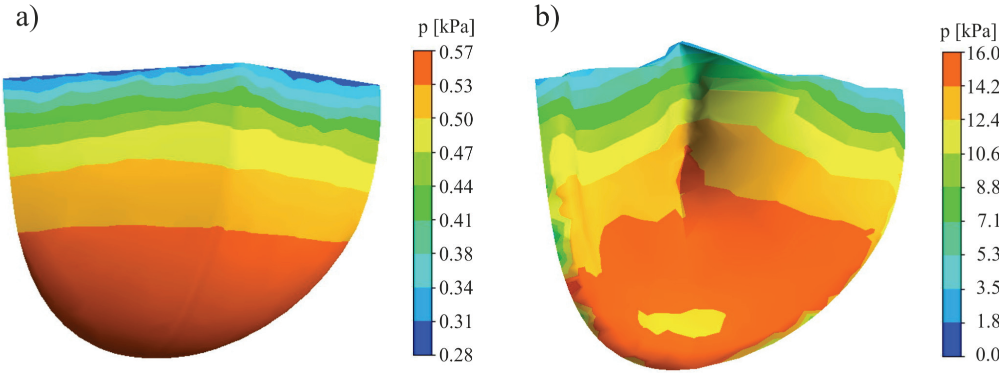

Fig. 3. Distribution of load in the form of pressure: (a) closed valve, (b) opened valve

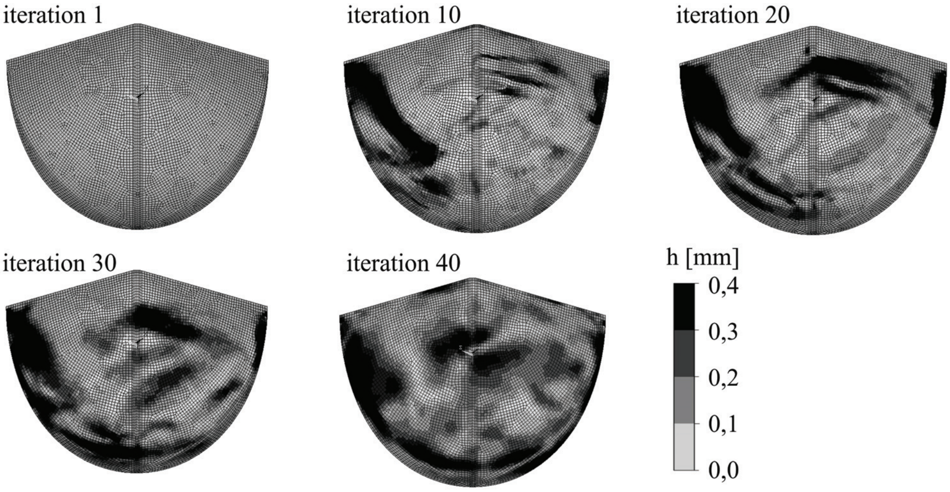

Fig. 4. Change of the thickness distribution during the optimization process

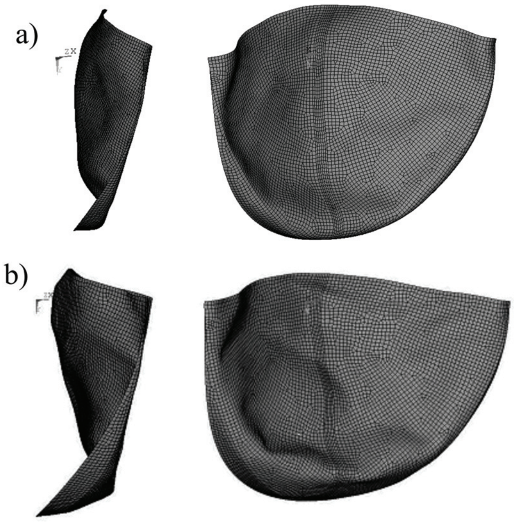

Fig. 5. Leaflet deformation:
(a) constant thikness, (b) optimized thikness

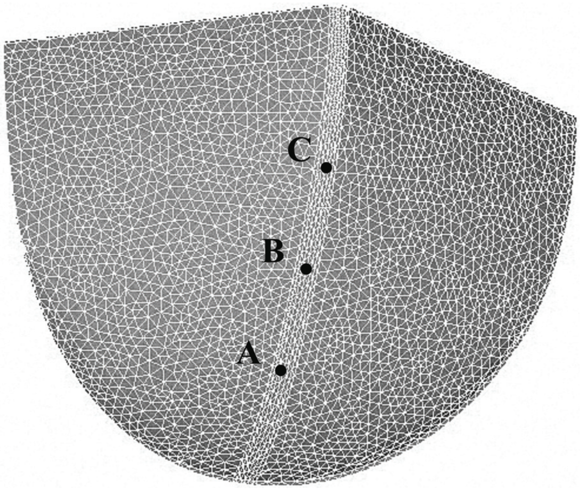

Fig. 6. Nodal points located on the symmetry axis of the leaflet

The optimization process did not deteriorate the hemodynamic parameters of the valve. The deformations recorded before and after analysis displayed similar properties (Fig. 5). To gain information on how the remodelling of the material affected the functioning of the aortic valve, dynamic analysis was carried out, which aimed at assessing the time required for the full opening of the valve. The valve opening

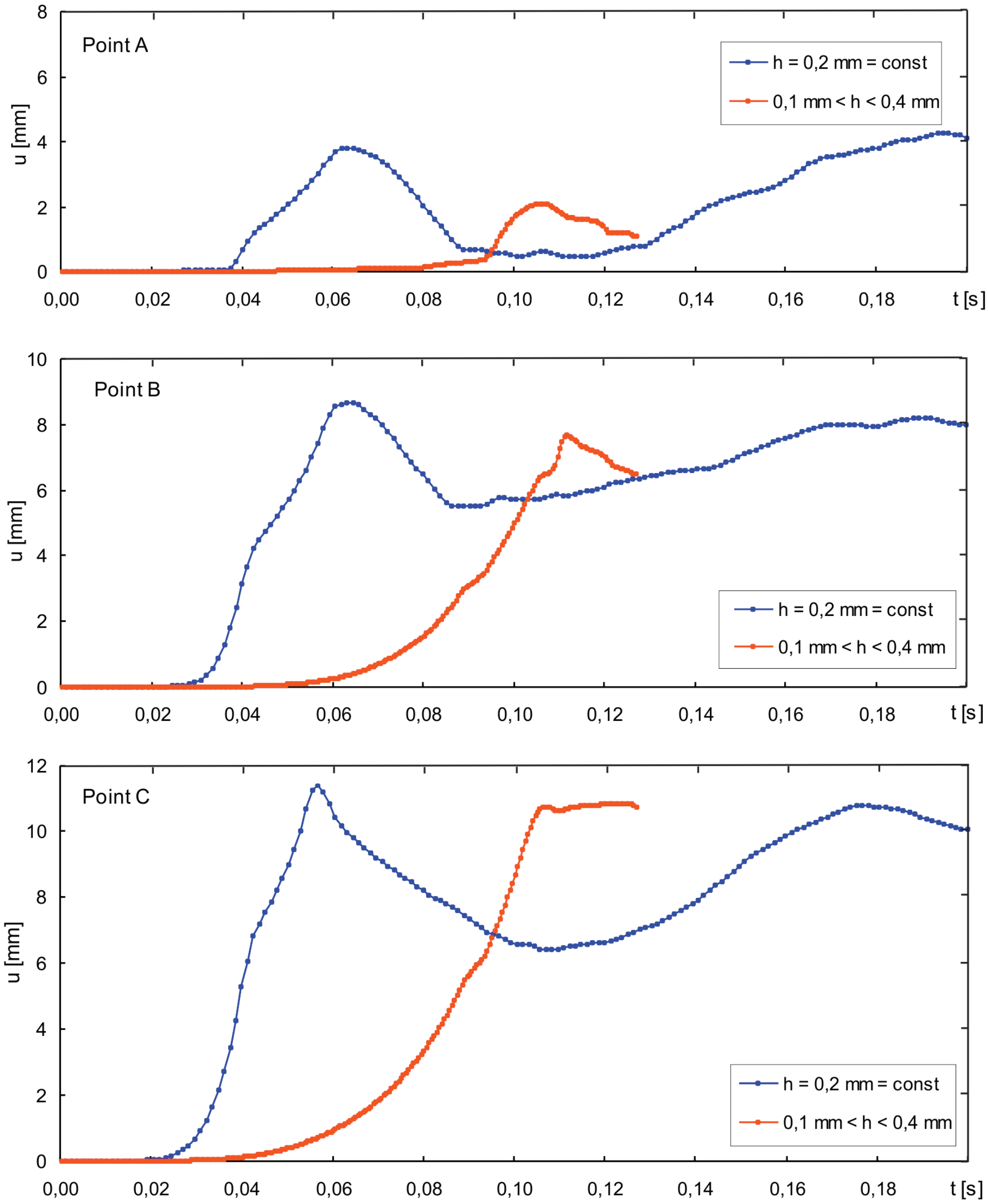

Fig. 7. Displacement of points as a function of time:
blue line for constant thickness, red line for optimized thickness

process was monitored at three nodal points located on the symmetry axis of the leaflet by reading the displacement which varies with time (Fig. 6). As a result of optimization, the time of valve opening was reduced by 50% (see Fig. 7).

Assessments were also made of the critical pressure required for the opening of the valve. The monitoring of this parameter at three nodal points on the symmetry axis of the leaflet has produced the following findings. In the case of the leaflet with a constant thickness, there was a local stability loss and a rapid pressure drop after the passage of the shell through the critical point. In the case of the leaflet with optimal parameters, the pressure required for the opening of the valve was higher, but the passage of the shell through the critical point was smooth (Fig. 8).

Measurements performed prior to optimization disclosed high shear stress values in the regions of the two commissures, as well as in the middle part of the free edge of the leaflet. Equally high values of shear stresses were found to occur in the initiation region of the shell buckling induced by the flowing fluid. The optimization process produced a decrease of the average shear stress in the leaflet shell, as well as the unification of the stress field (Fig. 9).

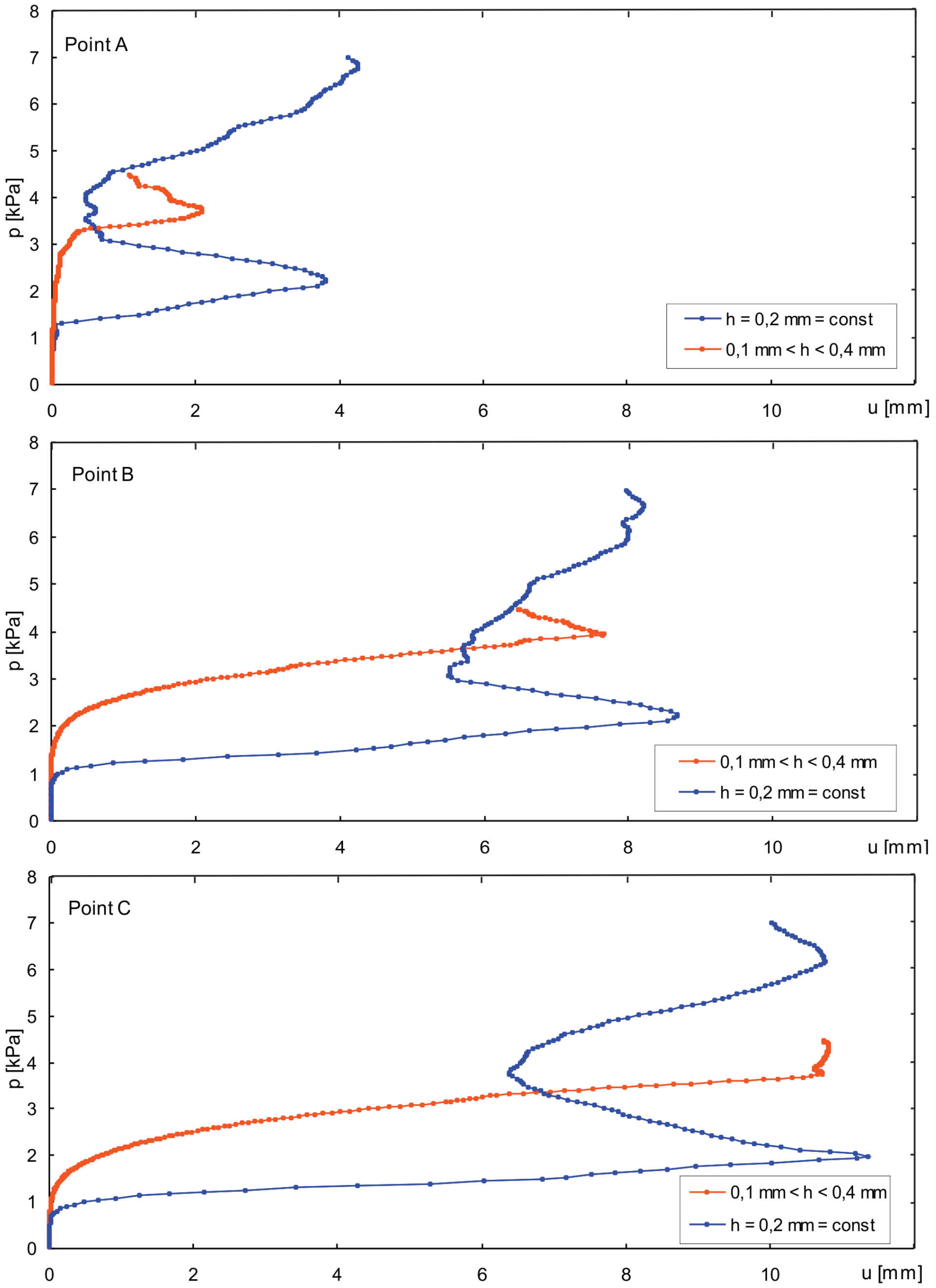

Fig. 8. Path equilibrium characteristics: blue line for constant thickness, red line for optimized thickness

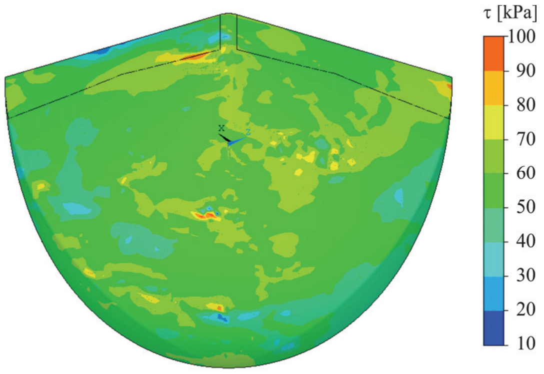

Fig. 9. Distribution of the shear stress in the optimized leaflet

4. Discussion

The heart is one of those organs that have adapted their structures to the ambient environment as a result of evolution. The system of fibre nets that has developed during evolution is regarded as the mechanism underlying a smooth and long-term function of the aortic valve. The loading induced by the fluid flowing through the valve causes its leaflets to lose stability, and they begin to act as non-return valves. Aortic valves become dysfunctional due to the impact of different factors, both external and internal. What significantly affects the life of bioprostheses is the concentration of shear stresses in the shell structure. Those impacts reduce the durability of the bioprostheses that are designed as substitutes for natural valves.

The remodelling model proposed in our present study involves the criterion of minimum shear stresses in the leaflet shell. The distribution of the thickness field obtained corroborates the findings of the study reported by Driessen et al. [4], who developed a similar optimization criterion, where mechanical factors induce the process of leaflet structure remodelling. In both studies, the results substantiate the occurrence of a material of enhanced rigidity (dense fibre nets, enhanced thickness) in the region of leaflet attachment to the wall of the aorta, as well as in the commissures, i.e. at places where a leaflet joins another (neighbouring) leaflet of the valve. These results are justified from the viewpoint of the strength and functioning of the valve.

Upon termination of the remodelling process the valve leaflet model was made subject to dynamic liquid loading. The leaflet shell was tested during the systole phase and analyzed for the pressure of stability loss and for displacements. The values obtained for the two parameters indicate that the resistance of the leaflet decreased, and that the process being modelled proceeded at a faster rate. As a result of optimization, the entire process of leaflet buckling took a stable course and no sudden increment in displacements was detected. The slight reduction in the orifice area during the systole phase, observed during fluid flow through the valve, is of no significance from the viewpoint of hemodynamics.

Our study on the remodelling of the valve leaflet entailed the application of the stress criterion, which visibly upgraded the functioning of the valve by improving its mechanical and hemodynamic parameters. The stress fields obtained for the leaflet prior to optimization show a number of potential concentrations of values for this parameter. The results of numerical analysis are consistent with the results of the in vitro tests reported by Deiwick et al. [2]. In their laboratory experiment they observed that the concentration of stresses in the leaflet accounted for the calcification, i.e., dysfunction, of the bioprosthesis.

Upon optimization, unified average shear stress fields were obtained using the algorithm of leaflet mass redistribution. The significantly increased thickness of the shell in the commissures implies that those regions are characterized by the occurrence of high stresses. Other contributory factors in those high stresses may be the elements of the free edges of the neighbouring leaflets, which join there. During each cycle of valve functioning, under conditions of full opening, leaflet compression was found to occur in this region.

5. Conclusions

It is essential to note that in the region on the symmetry axis, above the reinforcement region, a reduction was observed in the shell thickness. In view of the results obtained in our previous studies, this region can be identified as the area where the process of leaflet shell deformation initiates. The changes in this area had a direct influence on the reduction of the valve opening time.

In our previous research into remodelling, consideration was given to the energy criterion, the objective function being the minimum of the average density of the leaflet's internal energy, $F(b) = U_s$. The objective function defined *via* the above route had an obvious physical interpretation: the structure of the valve leaflet should display a minimal resistance during the cyclic opening of the valve, and preserve the required rigidity after the closure of the valve. The thickness distributions obtained upon optimization revealed the following: the shell displayed the highest rigidity at the points of contact between neighbouring leaflets; over a major part of the shell surfaces, rigidity showed a tendency to decrease, which might have contributed to the loss of the shell's load-bearing capacity. In general, this method failed to produce the expected results.

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