Biotechnical System for Endovascular Treatment of Cerebral Aneurysms Using Mathematical Modeling of Hemodynamics and Endoscopic Optical Coherence Tomography

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Abstract: - In this study we present a design of biotechnical system for endovascular treatment of aneurysms using mathematical modeling of hemodynamics and endoscopic optical coherence tomography. The approaches for obtaining patient-specific mechanical properties of the vessel wall and individualized mathematical modeling of the cerebral blood flow are described in detail. The proposed biotechnical system takes into account the individual biomechanical properties of the cerebral artery wall measured in vivo and has a potential to be used in clinical practice for improved patient-specific evaluation of hemodynamics in the cerebral artery with an aneurysm before and after the endovascular treatment.

Key-Words: - biotechnical system, intracranial aneurysms, vessel wall, compression elastography, flow-diverter stents, non-Newtonian fluid

1 Introduction

The progress of medicine and health care requires continuous improvement and development of the high quality medical equipment. Modern medical systems are characterized by wide application of methods for integrating technical and biological objects. Research and development of interaction methods between technical and biological objects is especially relevant for operating rooms and neurocomputer interface systems, neuroprosthetics, artificial circulation, respiration, hemodialysis, perinatal dialysis, maternal and child support, computer control of drug delivery, pacemakers, defibrillators, ventricular assist devices, cardiomonitors, electrostimulants of the gastrointestinal tract, brain, bladder etc. For the development of theoretical foundations, applied research and development, implementation and practical use of such systems in 1975, Prof. V.M. Ahutin first introduced into scientific terminology the term "Biotechnical Systems" (BTS) to describe "a special class of large systems that are a set of biological and technical elements connected together in a single control loop" [1].

One of the topical medical tasks which require a complex interaction between biological and technical elements is an endovascular treatment of cerebral aneurysms with flow diverter stents. Such BTS system should take into account individual parameters of the patient, such as patient-specific hemodynamics of the cerebral artery harboring aneurysm as well as mechanical properties of the aneurysm wall. In this study we present a design of biotechnical system (BTS-M) for endovascular treatment of aneurysms using mathematical modeling of hemodynamics and endoscopic optical coherence tomography.

2 Theoretical foundations

The development of the BTS theory is discussed in Refs. [2-3]. According to the definition, the BTS includes not only medical systems, but also a wide class of systems in which biological and technical objects are connected in a single control loop. The examples of BTS are human life support systems in a closed space, control and management of a human's state while performing various professional functions. In Ref. [2] two human states are shown in the BTS. It could be a human-operator (controller) providing control of a technical system, or a human-patient (an object for diagnosis and treatment) in the medical system. In these systems, a human is connected by technical links to a single system forming a BTS.

Let us consider the first state of human as a human-operator, operating automated control systems, based on software-hardware complexes (SHC). The price of the human error is constantly increasing, as the level and reliability of technical equipment grows, while capabilities of the human-operator remain at a same constant level. Therefore, fundamentally new approaches are required to the design of modern SHCs, in which the role of the human error should be reduced.

Design and development of technical systems, in which, along with technical components, biological objects are included, e.g., a human-operator, requires an understanding of the processes occurring during interaction between technical means and a living organism within the BTS framework. Systems, in which a human performs the role of a controller of complex technical systems, have been called BTS of ergatic type - BTS-E [3]. The human-operator is included in the BTS-E structure as a controlling element, and the system performs certain tasks with external technical objects [2]. BTS-E is represented as "a combination of biological and technical elements, united in a single functional system of purposeful behavior" [3]. In ergatic systems, the human-operator performs its functions as one of the elements of BTS-E. The human-operator should analyze information about the progress of the processes in the system controlled by him and make adequate decisions and execute them, or give orders for their execution [2].

The problem of harmonizing the characteristics of biological and technical elements included in a single system is the main one in the theory of BTS synthesis. In such human-machine systems, the biological element is represented by the human operator, performing various functions in a closed control loop of the technical system. Fig. 1 uses a generalized structure of BTS-E to demonstrate the place and role of SHC for various purposes that are part of BTS-E (Fig. 1).

The control system (CS) is the basis for the SHC, which by means of control signals, generated in accordance with the specified control objective, acts on the control object, providing the required operation mode. The control object could be a technical system, a technological process, a power supply system, a transport rail system, an air or pipeline transport system, etc. The CS includes technical means for information display and control tools (TMDC) and decision support system (DSS). DSS develops recommendations to the human-operator for the control on the basis of gathered information from the control object. By means of technical diagnostic tools (TDT), information about the state of the control object transfers to the CS, which generates control signals for the control object (based on the operator's decisions or using a local control system (LCS) operating in automatic mode) by technical means of influence (TMI). LCS is controlled by CS or human-operator. Due to a possible change in environmental conditions, the technical control system of the environment (TCSE), where the human-operator and the SHC are located, is of high importance. This system should control various characteristics of the environment recommended for the human-operator and SHC, for example, temperature, humidity, pressure, etc. Such systems should not only evaluate the parameters of the environment, but also contain technical means for changing these parameters according to the applied control algorithm.

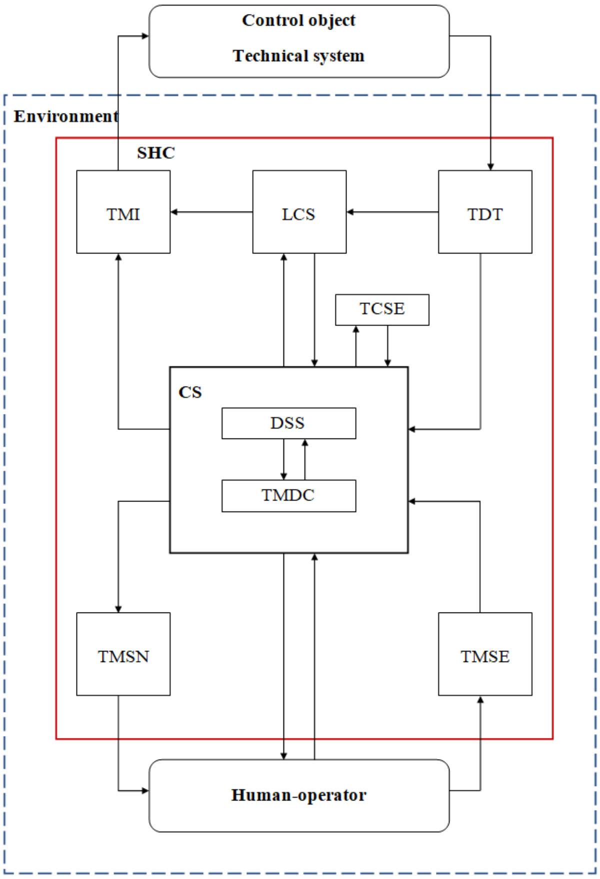

Fig. 1. Generalized structure of BTS-E.

Increasing the speed of processes that cause an increase in the intensity of information flows with increased requirements for control accuracy, as well as an increase in the complexity of systems controlled by a human-operator radically changed the very nature of the human-operator's work. So now, increased requirements should be applied to the reliability of both the entire system as a whole and to the human-operator. Therefore, the human-operator becomes an element, which state is monitored and controlled by special technical means of state estimation (TMSE) and state normalization (TMSN).

The analysis of the BTS-E structure showed that the development of such systems is a time-consuming and ambiguous task requiring use of various methods, including numerical simulation and experimental methods.

Let us consider the second state of a person as a human-patient (Fig. 2). BTS, which is used for medical purposes is abbreviated as BTS-M [3]. In BTS-M, the human-patient acts as the control object, and the human-doctor is an element of the patient state control.

Similarly as in BTS-E, in the BTS-M the CS includes TCSE and clinical DSS. DSS on the basis of the gathered information from the control object (human-patient) develops recommendations for the doctor on management of the human-patient state. With the assistance of the TDT, information about the state of the human-patient transfers to the medical SHC, which, on the basis of the doctor's decisions or in automatic mode, generates control signals to the human-patient using LCS and TMI. Control over the work of the LCS is performed by a doctor. LCS could be elements that perform the control of pacemakers, apparatus of artificial circulation, infusion pumps, anesthesia and respiratory equipment, etc.

To monitor and control the state of the environment, where the medical SHC and the doctor are located, similarly, as in BTS-E, TCSE are used. The characteristics of the environment recommended for SHC, the patient, and the doctor are determined and maintained by special technical means on the basis of control algorithms. Likewise, as in BTS-E, in BTS-M, the doctor's state is monitored and controlled by TMSE and TMSN.

A feature of BTS-M is the presence of BTS-M of the lower hierarchy level, which includes a subset of TDT, TMI and LCS. BTS-M of the lower level can work in automatic mode. Implantable devices are examples of such systems: anesthesia breathing apparatus, pacemaker, drug dispenser, controlled bio-prosthesis, etc. BTS-M of the lower level can be considered as a classical automatic control system (Fig. 3) in which LCS implements the control algorithm. From the control object (human-patient) using the sensor (TDT), an output parameter y is transferred to the comparator. The difference between the reference y_r and the actual y passes to the input of the LCS, which generates a control signal x_c. Control action is implemented by TMI, the signal from which passes to control object (human-patient). Electrical pulses of given amplitude and a changing frequency of the electrostimulator could be an example of the control action.

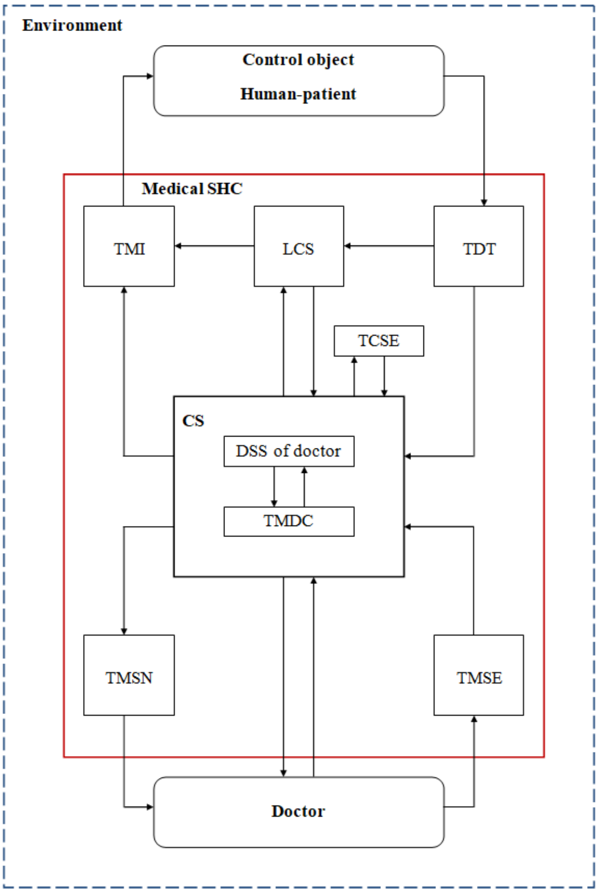

Fig. 2. Generalized structure of BTS-M.

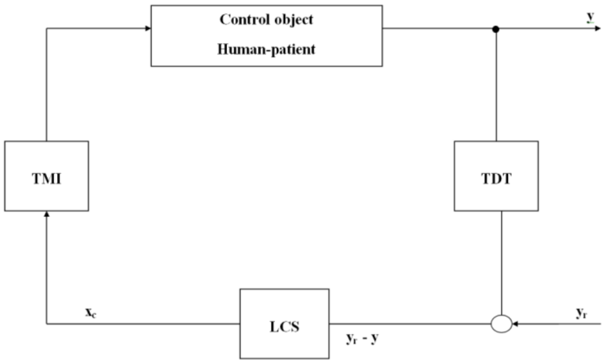

Fig. 3. BTS-M of the lower hierarchy level.

Since BTS-E and BTS-M are characterized by rapidly changing parameters in time, the topical task is to study the methods of mathematical modeling of dynamic processes in BTS-E, BTS-M and BTS-M of the lower level for the purposes of analysis, synthesis and generation of control actions.

3 Results and Discussion

In the proposed BTS design, the information about individual parameters of the patient is obtained using the following diagnostic tools, i.e. TDT: computed tomography or magnetic resonance imaging are used to acquire shape of the cerebral artery harboring an aneurysm, ultrasound Doppler is used to measure volumetric inlet flow rate at the inlet segment of the certain artery, a rotating viscosimeter is used for viscosity measurement of blood sample; endoscopic optical coherence tomography (OCT) is used to estimate an individual biomechanical properties of the aneurysm wall.

The obtained data is used by DSS and TMDC, i.e. control system, to evaluate the pre-operative condition of cerebral hemodynamics and assess the risk of further aneurysm growth and rupture. To evaluate the hemodynamics in the cerebral artery a numerical simulation is conducted, which takes into account the patient-specific shape of the artery, individual viscosity data and inlet flow rate.

According to estimated risk of rupture, provided by DSS, the doctor makes a decision about the treatment procedure, i.e. flow-diverter implantation to normalize intra-aneurysmal flow conditions.

Using DSS and data collected by TDT, doctor could perform a series of numerical experiments for virtual implantation of different flow-diverter models to evaluate the hemodynamic performance of each one and select the stent model, which ensures the best flow reduction in the aneurysm sac.

Then using TMI doctor performs deployment of selected flow-diverter model to the treated cerebral artery. The patient state during the deployment is controlled by LCS, e.g. anesthesia breathing apparatus. The doctor state is controlled by TMSE and TMSN, while environmental conditions in operating room are controlled by TCSE.

After the treatment, the patient state is controlled periodically, normally every 6 months by TDT. DSS is used to evaluate the progress of the treatment and support the doctor in various adjustments of the treatment process during the follow-up period.

3.1 Mathematical modeling of hemodynamics

Conducting a patient-specific simulation of the cerebral circulation requires an individualization of a general mathematical model of hemodynamics, based on three-dimensional governing equations, by clinically available patient's data.

The individual geometry of a cerebral artery has a significant influence on distribution of hemodynamic parameters, especially velocity and wall shear stress (WSS), and should be taken into account in CFD studies. To obtain the individual geometry of the artery various medical imaging techniques could be used, such as magnetic resonance imaging (MRI) and computed tomography (CT), e.g., see Fig. 4. A surface, obtained by initial segmentation of available DICOM data, should be further post-processed to be used to generate a computational domain by smoothing, treating of irregular elements, etc.

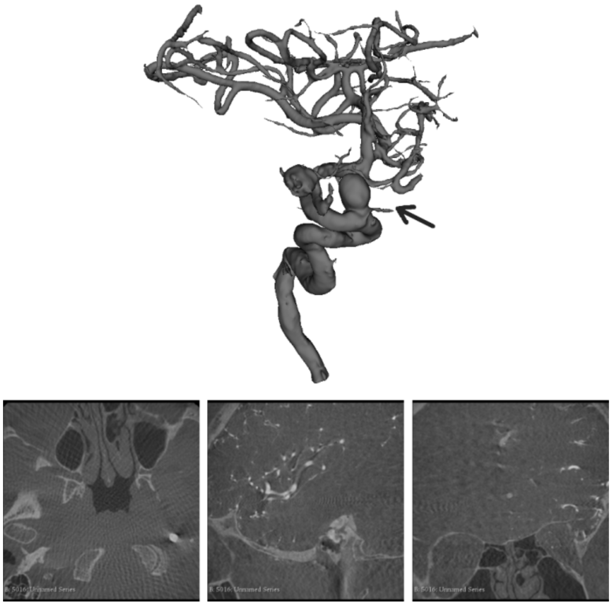

Fig. 4. An example of segmented cerebral vasculature (top) with aneurysm (arrow) and clinical visualization data (bottom)

A patient-specific flow rate curve for the studied cerebral artery could be measured by Doppler ultrasound and imposed as an inlet boundary condition. An outlet pressure curve is often not available and therefore a free outflow condition could be used for outlets [4].

The effect of blood rheology on distribution of hemodynamic parameters in cerebral arteries is comparably less than the effect of individual morphology; however, a presence of low shear rate zones and vortices in an aneurysm sac cause non-Newtonian fluid models to be used to represent blood [5, 6].

In contrast to a healthy artery wall with a three-layered structure, an aneurysm wall is generally composed of only intima and adventitia; media is often damaged. Such specific internal wall structure, causing an aneurysm to be less distensible than arteries, as well as limitations of in vivo measurement techniques, contribute to using a linear elastic model of a cerebral artery wall.

2.1 Compression elastography for evaluation of biomechanical properties of the vessel wall

Contrary to a traditional approach assuming a rigid vessel wall, we consider artery as a deformable region taking into account individual biomechanical properties of the wall, which are evaluated by the compression elastography method based OCT.

To evaluate biomechanical properties of the aneurysm wall a series of structural OCT images should be obtained for systolic and diastolic phases. After data filtering, a group of about one hundred control points are selected for comparison of B-scans. For each pair of control points (for systole and diastole) a displacement is calculated, i.e., local deformation of the vessel wall under a pulse wave. Thus, the Young's modulus E could be estimated as follows:

$$E = \frac{F_n}{S} \cdot \frac{l}{\Delta l}, \tag{1}$$

where F_n is a normal component of the deforming force F, which blood exerts on the vessel wall; S is an area under the force; l is longitudinal dimension of a deformed region; Δl is an averaged relative longitudinal deformation for local regions of the vessel wall. The following considerations could be taken into account to determine parameter values for Eq. 1. The force F could be evaluated by the difference between systolic and diastolic pressures. The length l could be assumed to be equal to the coherence probing depth, since it commensurates with an aneurysm wall thickness. For calculation of Δl only normal components of the deforming force F should be used.

Using similar considerations the Poisson's ratio μ could be found as follows:

$$\mu = \frac{\Delta d}{d} \cdot \frac{l}{\Delta l}, \tag{2}$$

where d is a transverse dimension of a deformed region (equals to the scan area size of the OCT system); Δd is an averaged relative transverse deformation of local regions of the vessel wall.

Fig. 5 shows structural OCT images of the cerebral artery before and after a deformation. Red and green areas mark displacements of dark and light regions of the OCT image respectively. The displacements were obtained by comparison of the structural OCT image at the systolic peak with the corresponding image at the diastolic end. The obtained average Young's modulus (1) and Poisson's ratio (2) were 1.03 MPa and 0.495 respectively.

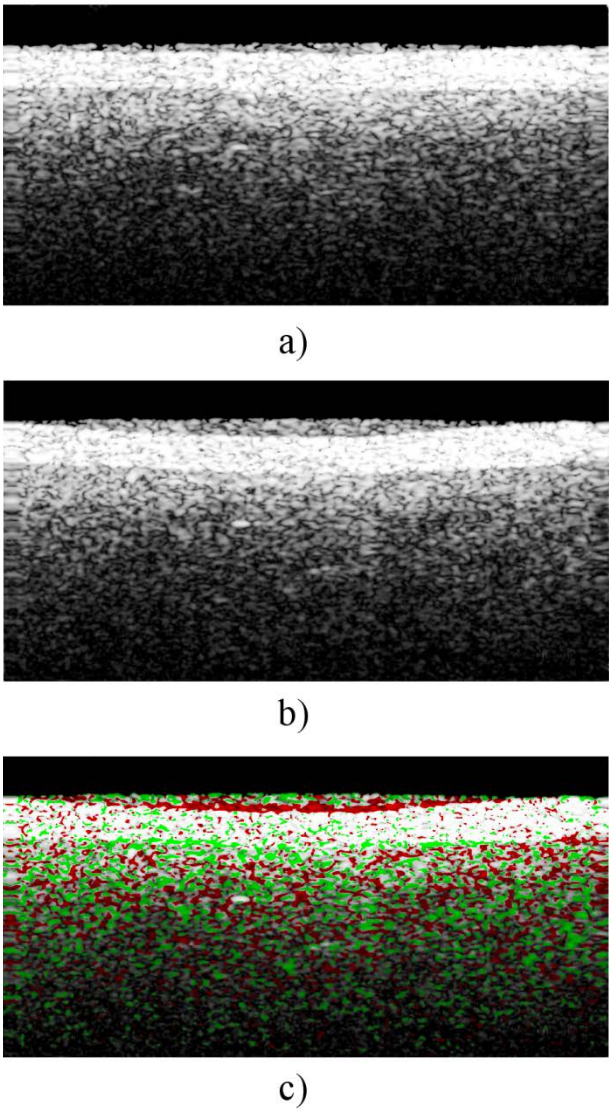

Fig. 5. Structural OCT images of the cerebral vessel phantom before (a) and after (b) deformation; deformed regions are marked by red and green (c). Image size is 2.2 x 1.1 mm

In the proposed BTS an individual geometry of the studied cerebral vessel along with individual biomechanical properties of the vessel wall are used for patient-specific evaluation of hemodynamic parameters in the cerebral artery (Fig. 6). The main steps of the workflow could be represented as follows:

(1) Acquiring diagnostic images of patient's vasculature using clinical visualization techniques; extraction of individual geometrical 3D model of the cerebral artery with an aneurysm.

(2) Reconstruction of structural images of the cerebral artery wall using endoscopic OCT.

(3) Evaluation of biomechanical properties of the vessel wall using compression elastography.

(4) Setting up the mathematical models by adjusting material's coefficients of the vessel wall and imposing patient-specific boundary conditions.
(5) Transient simulation of preoperative hemodynamics of the patient.
(6) Evaluation of three-dimensional distribution of velocity and pressure, computation of WSS and derived parameters (e.g., oscillatory shear index (OSI), time averaged wall shear stress (TAWSS), etc.).
(7) Analysis of obtained hemodynamic parameters in the cerebral artery.

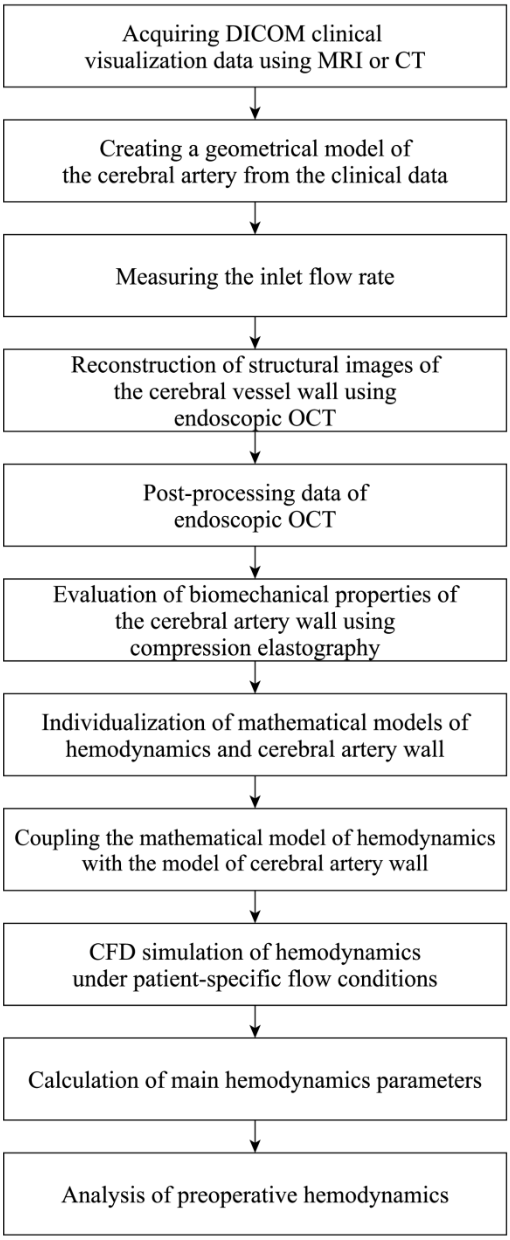

Fig. 6. A workflow for patient-specific modeling of hemodynamics taking into account individual biomechanical properties of the cerebral artery

Information about mechanical properties of the cerebral artery wall provides physician a valuable support in assessment of various cerebral disorders and further treatment planning; however, in vivo evaluation of mechanical properties is challenging due to the limitations of available clinical visualization techniques.

Wittek et al. [7] proposed an approach for identification of artery material properties using time resolved 3D ultrasound. Despite of advances in identification of material properties of aortic walls, an application of the method for cerebral arteries is limited by low spatial resolution of an ultrasound device and visualization problems for structures within the skull.

Alternatively, in our study we propose using of minimally invasive endoscopic OCT method, providing a sufficient resolution for imaging of internal wall structures, for evaluation of cerebral artery material properties and further patient-specific numerical studies of cerebral circulation. It should be noted that, in vivo evaluation of the deforming force F is a complicated task and requires some workaround. The difference between systolic and diastolic pressures in the proposed approach could be estimated either by numerical simulation of blood flow in the artery with rigid walls or by direct measurement of blood pressure using an intravascular pressure sensor, e.g., dual-sensor guidewire ComboWire XT (Philips, Amsterdam, Netherlands). A detailed description of measurement procedure was reported by Schneiders et al. [8].

The proposed approach has some limitations. First, an aneurysm size should be at least two times larger than a diameter of forward-imaging OCT probe, which means that the approach is applicable only for cerebral aneurysms larger than 4 mm. Second, a construction of endoscopic OCT probe should be improved to allow an easy access to the studied segment of the cerebral circulation. Third, a cerebral artery wall is considered as a homogeneous material, assuming constant thickness, Young's modulus and Poisson's ratio along the vessel wall. Forth, a representation of a cerebral artery wall by a linear elastic model could lead to overestimation of vessel deformations during CFD simulations compared to non-linear models [9].

Presented BTS, methods and workflow are the results of ongoing study and further investigations should be done to address the listed limitations and prepare the proposed BTS design to be used in clinical practice for endovascular treatment of cerebral circulation disorders.

4 Conclusion

The proposed biotechnical system takes into account the individual biomechanical properties of the cerebral artery wall measured in vivo and has a potential to be used in clinical practice for improved patient-specific evaluation of hemodynamics in the cerebral artery with an aneurysm before and after the endovascular treatment.

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