Ministry of Science and Higher Education of the Russian Federation
NATIONAL RESEARCH
TOMSK STATE UNIVERTSITY (NR TSU)
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«17» 06 2019

MASTER'S THESIS

PHYSICAL AND MATHEMATICAL MODELING OF ELECTRICAL AND MECHANICAL ACTIVITY OF THE HEART

within the Basic Educational Programme of Master's Degree
subject area 03.04.02 – Physics

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«14» 06 2019

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Tomsk – 2019

ABSTRACT

An important problem of modern medicine is the creation of effective methods of treatment and prevention of cardiovascular diseases. Cardiovascular system distributes blood with oxygen and many others of vital substances and therefore is the most important part of human body. Knowledge about cardiovascular system allows us to treat some heart diseases, but it also helps us to learn about its disfunctionality.

An increasing role in their development is played by mathematical modeling and numerical calculations of blood flow in a network of vessels with pathologies. They allow you to predict surgery, optimize the shape of implants, explore their effects on hemodynamics. Numerical simulation of cardiovascular system has also become a useful tool of surgeon who diagnoses cardiovascular diseases and recommends the way of their medical treatment.

Currently, invasive measurement of fractional blood flow reserve (PRK) is one of the main methods used to detect induced myocardial ischemia. The specificity of invasive PRK <0.75 is 100%, and the sensitivity of PRK> 0.80 is more than 90%. Modern advances in computational fluid dynamics and computational modeling allow us to calculate non-invasive PRK based on computed tomography data - an angiography of the coronary arteries, performed according to a standard protocol, at rest, without increasing radiation load.

As a result of the work done, a method of individualized numerical modeling of blood flow in the coronary vessels was developed, which makes it possible to isolate the personal characteristics of the patient’s coronary blood flow and can later be used to assess the regional reserve of blood flow in a particular patient.

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LIST OF ABBREVIATIONS

AIF – acquisition related factors
ATP – adenosine triphosphate
ACFR – absolute coronary flow reserve
AP – angina pectoris
ARHL – age related hearing loss
ASL – arterial Spin Labelling
ATT – arterial transit time
AP – arterial pressure
AH – arterial hypertension
BSD – Berkeley software distribution license
BSD – berkeley Software Distribution license
CASL – continuous Arterial Spin labeling
CA – coronary arteries
CB CT – cone beam computed tomography
CG – cardiogram
CVD – cardiovascular diseases
CVS – cardiovascular system
CBF – coronary blood flow
CHD – coronary heart disease
CT – computed tomography
DTI – diffusion tractography processing
EMF – electromotive force
ECG – electrocardiography
EchoCG – echocardiography
fMRI – functional magnetic resonance imaging
FSE – Fast Spin Echo

FFR – fractional flow reserve

GPU – graphics processing unit

HR – heart rate

HCVS – human cardiovascular system

IR – inversion recovery

IHD – ischemic heart disease

LV – left ventricle

MB – microcirculatory bed

MRI – magnetic resonance imaging

NIH – national institutes of health

PET – positron emission tomography

RF – radiofrequency

SCD – sudden heart death

TE – echo time

TOF – time – of – flight

VCAQ – vein of the cochlear aqueduct

VSBM – vessel of the basilar membrane

VSTL – vessel of the tympanic lip

INTRODUCTION

In recent decades, the incidents of sudden manifestations of circulatory-system diseases that are life-threatening, often developing in people of working age, have become more frequent. So, in Russia, among the causes of mortality, diseases of the circulatory system rank first (54%). Every third death from circulatory diseases among the male population is registered at working age.

The human cardiovascular system (CVS) is among the main systems of the body, and a complete study of the peculiarities of how it functions has not yet been achieved. Diseases of the circulatory system are widespread and is the leading cause of death. In this regard, the study of the cardiovascular system is one of the most important problems of modern fundamental medicine.

Hemodynamic analysis, based on the theory of viscous fluid flow, provides an opportunity to obtain important objective data on the state of the heart and blood vessels, including an assessment of the ability of an individual's cardiovascular system (CVS) to adapt whilst exercising.

In this regard, it is necessary to develop methods and means of assessing the parameters of the state of the cardiovascular system, which are applicable for widespread use in order to detect pre-pathological conditions within an appropriate timeframe. This is primarily relevant for the regular and mass screening of workers in hazardous occupations and for athletes through the use of fast, cost-effective and non-invasive diagnostic techniques.

The closed circulatory system was described by W. Garvey in the 17th century, and already in the 18th-19th centuries the first attempts were made to describe it mathematically: L. Euler, D. Bernoulli and J. Poiseuil discovered some fundamental patterns in blood flow through vessels. The first mathematical model of blood circulation in a closed cardiovascular system was developed much later: at the beginning of the 20th century, O. Frank suggested describing the circulatory system through an analogy of electrical circuits. This model was subsequently developed along with other models of blood flow [1, 2].

In recent years, in connection with the development of numerical methods for solving problems of hemodynamics and a significant increase in the performance of computing technology, mathematical modeling has begun to play an important role in studying the circulatory system [1]. It allows doctors to obtain information about the qualitative and quantitative characteristics of blood flow in health and disease, to identify patterns in how the circulatory system functions, and to predict the consequences of surgical interventions and various diseases. All this determines the theoretical and practical value of mathematical modeling.

Relevance of this work: the main causes of death in industrialized countries are diseases of the cardiovascular system, in particular, coronary heart disease (CHD) is the cause of mortality in approximately 7.3 million people every year (World Report on Noncommunicable Diseases, 2010 Geneva, WHO; Global atlas on cardiovascular disease, Geneva: World Health Organization; 2011). The mortality rate, the extent of disability and temporary disability in CHD in general and coronary artery diseases in particular, which are characterized by impaired myocardial blood supply, are not only an important medical, but also a serious socio-economic problem, since it primarily relates to the youngest, most highly skilled and most creatively active segment of the population.

In order to create recommendations on the choice of the optimal method of coronary bypass surgery, it is necessary to build an appropriate biomechanical model and study the mechanics of the vessel in terms of the hemodynamic theory of atherogenesis [32]. The biomechanical model of the coronary arteries provides an opportunity to assess the hemodynamics of the arteries at the stage of the patient’s preoperative examination, predict the natural course of the disease, and develop recommendations for choosing a rational method of surgical intervention on the coronary arteries.

In this regard, developing an adequate biomechanical model of the coronary arteries which takes into account the patient’s physiological characteristic, is relevant.

The mechanisms behind the functioning of the circulatory system, one of the main systems of the human body, are very difficult to study. Thanks to the efforts of specialists from various scientific fields, extensive knowledge has been accumulated about the structure and functions of the vascular system, its connections with other life support systems of the body, and blood circulation regulation [13–15]. Nevertheless, there is still much that is not understood about many of the patterns in how the cardiovascular system operates.

The modeling of a biological object has its own particular characteristics: each organism is unique in terms of the geometry of the vascular network, the composition of the blood, and it has its own reactions to psychophysiological exercise. When creating basic models, researchers strive for the most complete and detailed description of how the blood vessel system functions, trying to take into account all aspects of the interaction between blood and blood vessels, as well as between blood vessels and surrounding biological tissues. However, when creating models for practical use, it is necessary to identify and describe the most essential properties of an object.

The mechanism of regulation of blood circulation includes the following functions:

– self-regulation of major and precapillary vessels which depend on oxygen deficiency in tissues and other biochemical parameters (acidity level, adrenaline content, etc.) and muscular regulation of blood flow;

– central regulation (change in the period of contraction of the heart, the reflex effect of baroreceptors on peripheral resistance, the effect of blood pressure on the vascular tone);

– vegetative regulation and hormonal regulation.

In order to understand the mechanisms of regulation of blood circulation and develop a model of the HCVS, it is necessary to solve the problem of formalizing all hemodynamic processes, taking into account the individuality of the subject [13]. From the point of view of system theory, modeling the hemodynamics of the human cardiovascular system is a difficult task due to its inherent features:

– the ability to adapt by moving the system to different states when the external environment changes;

– the presence of a complexly organized decision-making algorithm and the transfer of control actions between the components;

– the need for an individual representation of the system, despite the typical nature of the behavior of its components and composition;

– the difficulty of measuring parameters in real conditions for analyzing the situation and formalizing processes due to complex and difficult-to-separate connections, and the lack of the necessary recording devices.

One of the most important conditions for an adequate description of hemodynamics is the choice of a heart model. The heart provides blood to the system and has a significant effect on the pattern of blood flow. Thus, the work of the heart and the characteristics of hemodynamics are functionally dependent and self-consistent subsystems of the entire human cardiovascular system. Consequently, disorders of the heart are the cause and at the same time the result of hemodynamic disorders. This relationship is of particular importance in modeling the hemodynamics of coronary arteries, since impaired blood flow in the coronary arteries can serve as the basis for the diagnosis of heart disease.

Therefore, the purpose of this work is to develop a systematic approach to the diagnosis of heart problems and the study of its disorders based on a self-consistent model of the human cardiovascular system.

To achieve this aim, the following tasks need to be addressed:

1) to study the electro-mechanical characteristics of the heart, the structure and dynamics of its electrical and contractile impulses;

2) to master the method of reconstructing 3D images of the cardiovascular system using CT and MRI images;

3) to develop a mathematical model of coronary blood flow;

4) to develop an approach to the noninvasive diagnosis of the heart and the development of its diseases based on mathematical modeling of coronary blood flow.

Practical significance: the developed biomechanical model of the human coronary arteries can be used to study the normal and pathological physiology of the coronary bed, which allows a more reasonable assessment of the risk of coronary heart disease, as well as developing a biomechanical basis for choosing rational surgical intervention to restore myocardial blood supply. When the data correlates to real conditions, it can be adapted to a virtual operation.

In modern medical practice, a timely diagnosis plays an essential role in the treatment of the disease, the invasiveness of which should be minimized. With regards to diagnosing of stenosis, an ultrasound, following the Doppler method, is most often used. However, it is often impossible to clearly see the vessel walls without coronary angiography, but this method is invasive. [4,5] In order to minimize the impact on the patient this paper proposes diagnosing stenosis based on modeling the fractional reserve of blood flow in the coronary arteries.

Scientific novelty of research: a mathematical model of intravascular research has been developed as a non-invasive diagnostic method that facilitates the work of a cardiologist and helps in deciding whether surgical intervention is necessary.

The structure and scope of the thesis: the dissertation work consists of an introduction, three chapters, a conclusion, and a list of references. The thesis is presented on 74 pages, contains 29 figures, 4 tables and 38 items in the list of references.

1 Methods diagnose a human cardiovascular system

Cardiovascular diseases (CVD) are the leading cause of death worldwide. Every year more than 17 million people die from this type of disease [1]. In the Russian Federation in 2014, more than 32 million people turned to the country's medical institutions for CVD [2].

All existing diagnostic methods are aimed at displaying the processes occurring in the human body. The most common is electrocardiography (ECG), since this technique is very easy to use and has been largely studied. However, every year non-invasive visual diagnostic methods play an increasing role in diagnosis. For example, such methods are ultrasound, magnetic resonance (MR) diagnostic methods and others. Almost all such medical equipment is stationary and is located in medical institutions. But the main problem of CVD are outside hospitals and clinics.

Among all causes of death occurring outside medical institutions, the share of Sudden Heart Death (SCD) is about 40% [3]. At the same time, due to SCD, people die in 95% of cases either at home or on the street. Every third death occurs without witnesses [3]. Most often, BCC is associated with Ischemic Heart Disease.

Another common cause are various kinds of arrhythmias. They can be divided into life-threatening and non-life-threatening. The first type requires immediate intervention in the patient's condition, with the second person can live for many years without any suspicion. The most common variant of arrhythmia is atrial fibrillation (AI), belonging to the group of non-dangerous arrhythmias. The prevalence of this type of arrhythmia in the general population is about 2% [4, 5]. At the same time, “silent”, asymptomatic AI develops in approximately 0.4% of the total world population [6]. AI leads to a twofold increase in the risk of mortality, in particular, due to a significant increase in the likelihood of complications. One of the most serious complications is pulmonary embolism (PE), which requires immediate medical attention. Every year, more than 800 thousand people die from PE all over the world [7].

Due to the presence of asymptomatic types of cardiac abnormalities, as well as taking into account a significant increase in the likelihood of repeated life-threatening seizures (for example, strokes or heart attacks), it is necessary to investigate the condition of the cardiovascular system (CVS) of each person during examinations and, especially, in the development of a disease. Additional information about the patient's CVS status may allow for more accurate selection of an individual treatment method, which will ensure higher treatment efficacy [35].

To assess the condition of a person's cardiovascular system, the heart itself is investigated first. The phase structure of the activity of the heart is the generally accepted basis of all methods of cardiac diagnosis. Traditionally, when analyzing cardioactivity, the electrical, mechanical, and electromechanical phases of the work of the heart are considered. It is the latter that make it possible to characterize numerically the causal events in the activity of the heart. It is especially important to obtain the phase structure of electromechanical activity in the monitor mode. This requires simultaneous non-invasive measurements of the parameters of the electrical and mechanical activity of the heart.

The lack of reliable non-invasive methods for analyzing the phase structure of the heart departments, as well as the difficulty of monitoring hemodynamic parameters in the monitor mode, in some cases can lead to late detection of disorders in lung activity, the development of various types of emboli, cardiac arrhythmias and other serious diseases.

Diagnostics of the human cardiovascular system is one of the most important tasks of cardiology.

Known methods for diagnosing the cardiovascular system (ultrasound diagnostics, radionuclide methods, X-ray contrast studies, etc.) [1–3] are intended to reveal pathologies such as the formation of a blood clot on the inner surface of a blood vessel, the sclerotization of its wall, the local narrowing of the vessel's passage section as well as a number of factors that cause not only the "mechanical" anomaly of the structure of the vascular system and the heart muscle, but also a disturbance of the physiological rhythms of their work. The desynchronization mode of the heart [1, 4] is among the problems faced by practical cardiology.

Most methods can be classified into the following groups: active methods involving the effects on the body of fields and substances, and methods of passive diagnostics, based on the registration of acoustic fields generated by the organism itself. Such a classification is widely used in solving technical problems of diagnostics of various kinds of materials, products and entire structures. These are methods of non-destructive testing known in the art [5].

1.1 Methods of radiation diagnostics: computed tomography and magnetic resonance imaging

One of the most pressing issues of modern biomechanics is the creation of realistic three-dimensional geometric models of biological objects based on data from medical diagnostic equipment (magnetic resonance imaging (MRI) and computed tomography (CT)). Such objects include elements of the cardiovascular system (heart, arteries), elements of the musculoskeletal system (bones, joints, vertebrae, etc.), etc.

Biomechanical modeling is one of the stages of preoperative planning reconstructive surgical interventions and allows you to choose one or another version of the operation and justify it. To perform biomechanical modeling, it is necessary to create a patient-oriented three-dimensional solid-state geometric model of the object under study. This problem can be solved with the help of computer data processing computer (CT) or magnetic resonance (MRI) tomography. However, the manual procedure for processing CT or MRI studies is quite lengthy and time consuming. Therefore, there is the task of automating the stage of processing these data in order to speed up the process of building models and increase their accuracy and quality. This problem remains unresolved today. For semi-automatic processing of CT or MRI data, various image segmentation methods are used.

The computed tomography (CT) method is based on the use of thin X-ray beams for imaging in different planes. In the process of removing the tomogram, the X-ray tube rotates around the body of the subject and the beams of rays are partially absorbed by the tissues. Unabsorbed radiation is captured by detectors that transmit information to the computer that forms the image. Usually the study is carried out with a contrast that allows differentiation of vessels and myocardium. The method allows to clearly visualize aortic dissection, aneurysm, myocardial anomalies, blood clots.

Computed tomography is commonly used to diagnose damage to the body's hard tissues. However, even with the use of the simplest radiological equipment of this type, it is possible to obtain data on the location and size of the heart.

Modern technology of multispiral CT allows to investigate in detail the state of the coronary vessels and the work of the heart chambers. Such systems in automatic mode are able to determine the main hemodynamic parameters of the activity of the heart muscle and even create three-dimensional models that visualize the processes occurring in the patient's body (Figure 1).

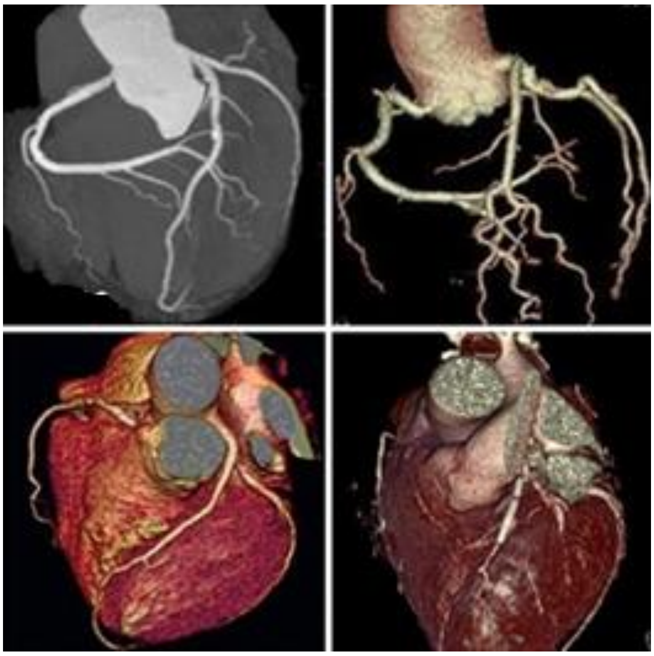

Figure 1 – The reconstructed image of the heart based on CT images

However, CT requires a specially equipped room, as well as a high level of qualification of medical workers.

Positive aspects of multispiral CT:

– high quality of the obtained images;

- ability to determine any dimensions and volumetric parameters of interest;
- high measurement accuracy;
- the opportunity to see the structure of the internal tissues of the body;
- large data set for analysis;
- the ability to detail the processes occurring in the body.

Negative sides of multispiral CT:

- the complexity of the procedure;
- the need to use special solutions to prepare the patient;
- the requirement of a low patient heart rate (HR);
- significant patient exposure;
- high cost of equipment and, accordingly, procedures;
- high complexity of work on the equipment;
- the inability to monitor the parameters of the heart.

Modern visualization methods allow to view the condition of the heart, coronary arteries and cardiovascular system as a whole from all sides. However, for the most part, each procedure requires a great knowledge of doctors in the use of medical equipment, as well as high qualification for the correct interpretation of the images obtained using technical means of visualization.

CT, like MRI, can provide an opportunity to analyze the work of the heart valves only in case of an increase in the frequency of image acquisition. But it is not always possible for doctors, since not every installation has such functionality.

Magnetic resonance imaging (MRI) is a modern non-invasive technique that allows you to visualize the internal structures of the body. The method is based on the use of a powerful magnetic field to obtain a detailed image of the internal structures. Ionizing radiation source is not required, the contrast, as a rule, also. The method is based on the effect of nuclear magnetic resonance, makes it possible to obtain a three-dimensional image of any tissue of the human body. The method is widely used in various fields of medicine: gastroenterology, pulmonology, cardiology, neurology, otolaryngology, mammology, gynecology, etc. Due to its high informational content, safety and reasonable price, MRI takes leading positions in the diagnosis of diseases and pathological conditions of various organs and systems.

The method clearly visualizes blood, fluid, adipose tissue, myocardium, and other soft tissues. The method is highly informative in the diagnosis of tumors, thrombosis, aneurysms, aortic dissection.

MRI of the heart - the procedure for scanning the heart in sync with the cardiogram to obtain a clear image in the form of layer-by-layer images in different planes of the working organ. This is necessary to assess the structure (morphology) of the myocardium, heart valves, papillary muscles, cavity size, the effects of heart attacks, degenerative changes, tumors and functions - prolapses or stenoses of the heart valves, contractility of the heart muscle and its perfusion (Figure 2).

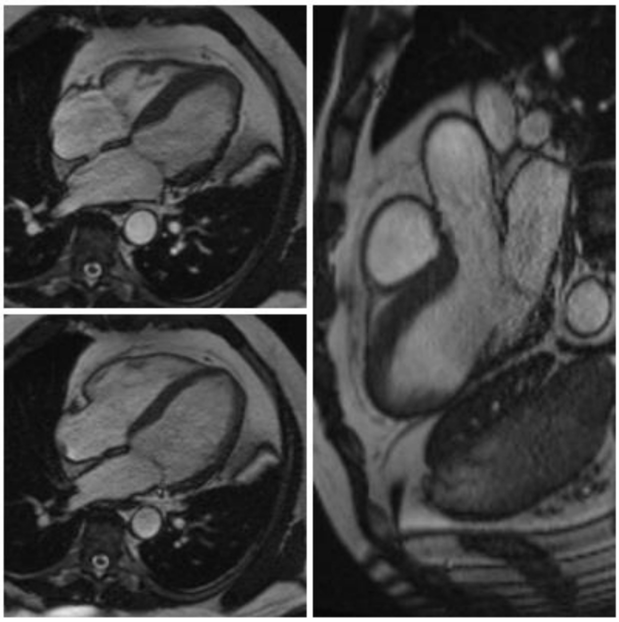

Figure 2 – MRI - a picture of the heart

To imagine how to build a 3D model, for example, of the brain, from 2D DICOM files, you need to understand how images are represented in medicine. To begin with, all modern tomographs (MRI, CT, PET) do not produce ready-made images. Instead, a file is created in a special DICOM format, which contains information about the patient, the study, as well as information for drawing the image. In fact, each file represents a slice of an arbitrary part of the body, in a plane, most often in a horizontal one. So each such DICOM file contains information about the intensity or density of tissues in a particular slice, on the basis of which the final image is built. In fact, intensity and density are different concepts. Computed tomography saves files x-ray density, which depends on the physical density of tissues. Bones have greater physical density, less blood, etc. A magnetic resonance imager retains the intensity of the reverse signal. We will use the term density, thus summarizing the concepts described above.

The density information in a DICOM file can be represented as a regular image, which has a resolution, pixel size, format, and other data. Only instead of information about the color in the pixel stored information about the density of tissues.

The diagnostic station produces not one file, but several at once for one study. These files have a logical structure. Files are combined in a series and represent a set of consecutive sections of an organ. Series unite in stages. The stage defines the entire study. The sequence of the series in the stage is determined by the study protocol.

The voxel model from the inside consists of voxels. A voxel is an element of a three-dimensional image containing the value of an element in three-dimensional space. In general, anything can be a voxel value, including color. In our case, the density represents the value of the voxel. With regard to the shape of the voxel, in general, voxels can be cubic, or can be a parallelepiped. We have voxels in the form of cubes for simplicity and ease of operation. The coordinates of the voxels are not stored, they are calculated from the relative location of the voxel.

In fact, a voxel is a complete analogue of a pixel in 3D. Pixel (English picture element) - an element of the image, Voxel (English volume element) - an element of volume. Almost all the characteristics of the pixel are transferred to the voxel, so you can safely draw analogies, given the dimension. Thus, voxels are used to represent three-dimensional objects.

The input for the voxel render is the DICOM series, i.e. several images representing any area of the body. If images of one series are superimposed on each other in the sequence and in the plane in which they were made, you can get a 3D model. This can be represented somehow (Figure 3):

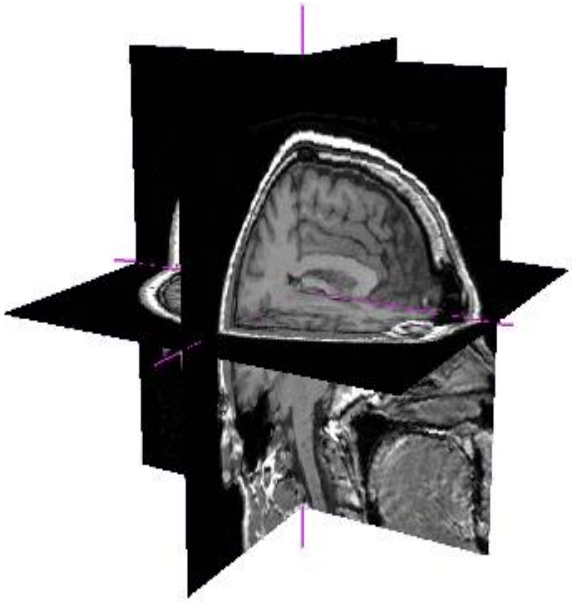

Figure 3 – 3D-model of the skull presented in different planes

Since the DICOM protocol does not clearly declare in which tag the value of the distance between images in the series is stored, it is necessary to calculate the distance between images using other data. So, each image has space coordinates and orientation. This data is sufficient to determine the distance between the images. Thus, having the image resolution and the distance between them in a series, you can determine the size of the voxel. Image resolution in X and Y, as a rule, is the same, i.e. The pixel is square. But the distance between the images may differ from this value. Therefore, the voxel may be in the form of an arbitrary parallelepiped.

1.1.1 Reconstruction of biological tissues: 3D Slicer

Medicine constantly opens up new possibilities of medical treatment, therefore, it is possible to see the improvement of technologies and techniques. The treatment is becoming more and more complex and requires accuracy that can only be satisfied through lethal planning or even modeling. Diagnostics, planning and modeling rely on the medical image of the individual patient. However, it can be very difficult to interpret complex three-dimensional structures, as well as spatial relationships in a series of two-dimensional image slices. Since the scan data is initially three-dimensional, it is best to use all three dimensions to display and interact with the data.

The use of 3D modeling in medicine is not yet very widespread in Russia, although today it is an indispensable assistant in the practice of doctors. 3D modeling is a safe procedure that does not harm the patient's health, with the help of which it will be possible to make operations more accurate and predictable, since three-dimensional models of organs give a three-dimensional, realistic picture.

In connection with the foregoing, it seems relevant to use software based on three-dimensional models for planning surgical operations. The work is based on the analysis of medical images for planning an operation based on three-dimensional models on clinical data. The data represent a series of images obtained in the study of patients with CT and MRI. The software included in the tomograph, allows you to export them to DICOM files (Digital Imaging and Communications in Medicine). The DICOM format is an industry standard for creating, storing, transmitting and visualizing medical images with a tag organization. DICOM files are the basis for further processing, data analysis.

One of the effective methods of 3D visualization is the 3D Slicer reconstruction method. 3D Slicer 4 is a free, open-source, cross-platform program for viewing CT scan in medicine. Created over nearly two decades by grants from the National Institutes of Health (NIH), 3D Slicer4 is a powerful tool for medical image processing, visualization and data analysis.

3D visualization and analysis of data technology have improved significantly in recent years and software has become readily available. To establish a diagnosis, a doctor can visually analyze images of individual tomographic sections of an object, however, for some clinical tasks like surgical planning, it is necessary to understand the 3D structure in all its complexity, see defects, and even more important to see nerve fibers around the pathological area, because each bundle is some kind of heart function. And if during the operation the area is damaged, the corresponding function will be lost.

3D Slicer is free open source (license), and is a flexible, modular platform for image analysis and visualization. 3D Slicer can be easily extended for the development of interactive and batch processing tools for various applications.

3D Slicer provides image registration, DTI processing (diffusion tractography), an interface for external devices, a GPU (graphics processing unit) with volume support, among other features. 3D Slicer has a modular organization that allows you to easily add new functionality and provides a number of common features not available in competing tools.

3D Slicer's interactive visualization capabilities include the ability to display arbitrarily oriented image slices, surface creation, and high volume rendering performance. 3D Slicer also supports a wide range of annotations. Slicer is designed for use on various platforms, including Windows, Linux and Mac OS X (Figure 4).

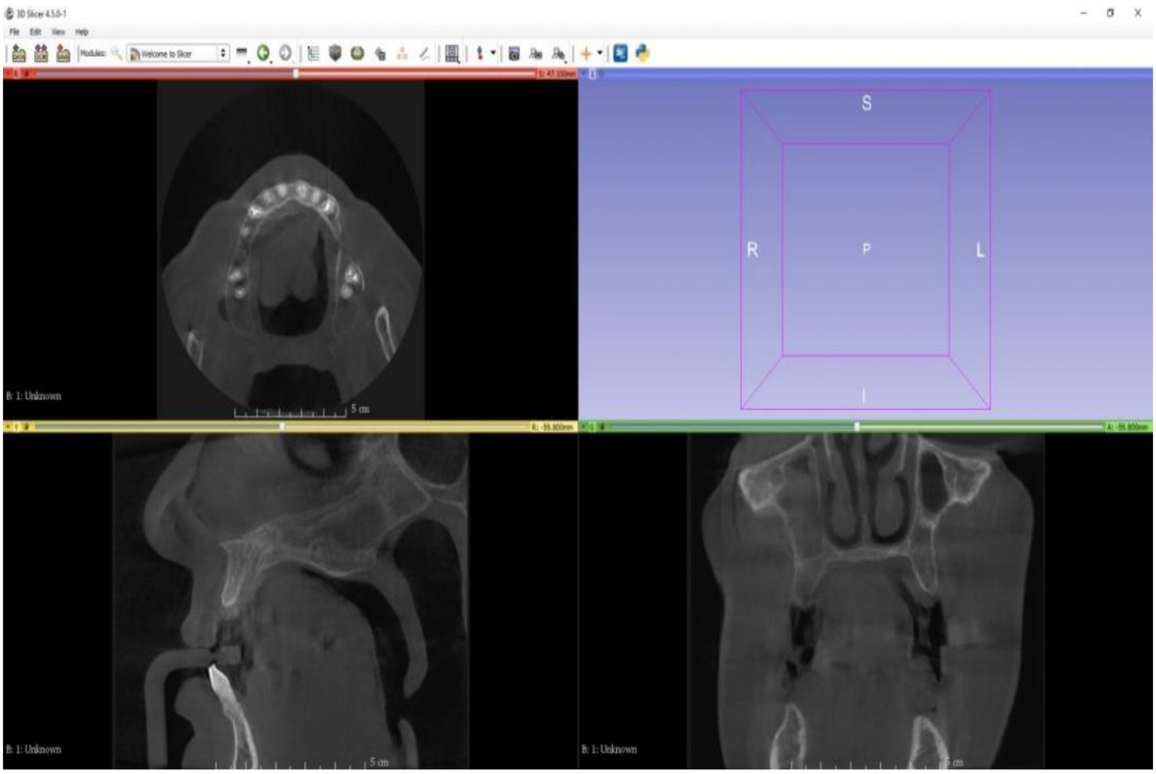

Figure 4 – Interface of the program 3D-Slicer

To carry out numerical modeling, computerized (CT) or magnetic resonance (MRI) tomography data is used to determine the geometry of the problem. An example of data on the geometry of the arteries is presented in Figure 5 [33].

Figure 5 – Three–dimensional reconstruction of the coronary arteries in the case of normal

1.2 Ultrasound diagnosis

Ultrasound (EchoCG) EchoCG is one of the most commonly used methods for diagnosing a person's heart. Ultrasound systems allow you to evaluate the structure of heart tissue, the size of the heart, the speed of blood flow and much more. However, due to the peculiarities of the energy used in the method for analyzing the state of the heart muscle, it is necessary to position the sensor between the ribs. Restrictions in the localization of the sensor in combination with the anatomical features of the location of the organ in the human chest does not allow us to examine the heart from all sides.

The positive aspects of ultrasound are the following:

– the ability to see in real time the movement of the internal structures of human organs;

– can assess the state of tissue structures;

– you can quantify the size of internal cavities and tissues;

– Doppler measurement methods allow to estimate the speed of blood movement;

– the ability to non-invasively determine the hemodynamic parameters of cardiac activity.

Negative side of echocardiography:

– limited review;
– low clarity of tissue boundaries;
– very high requirements for the experience and skills of the doctor;
– high cost of equipment;
– the need for multiple sensors with different parameters;
– the inability to monitor hemodynamic parameters of the heart.

The measurement error of hemodynamic parameters for EchoCG is up to 15%. But in case of low quality of the obtained images, unsuccessful selection of the measurement plane and low level of possession of the ultrasound equipment by the doctor, measurement errors can reach 40-50% of the real values.

Echocardiography in most cases is used to analyze the left heart chambers. One of the reasons for less attention to the right areas is the increased difficulty of obtaining correct images of the tissues of the right heart (Figure 6) [34].

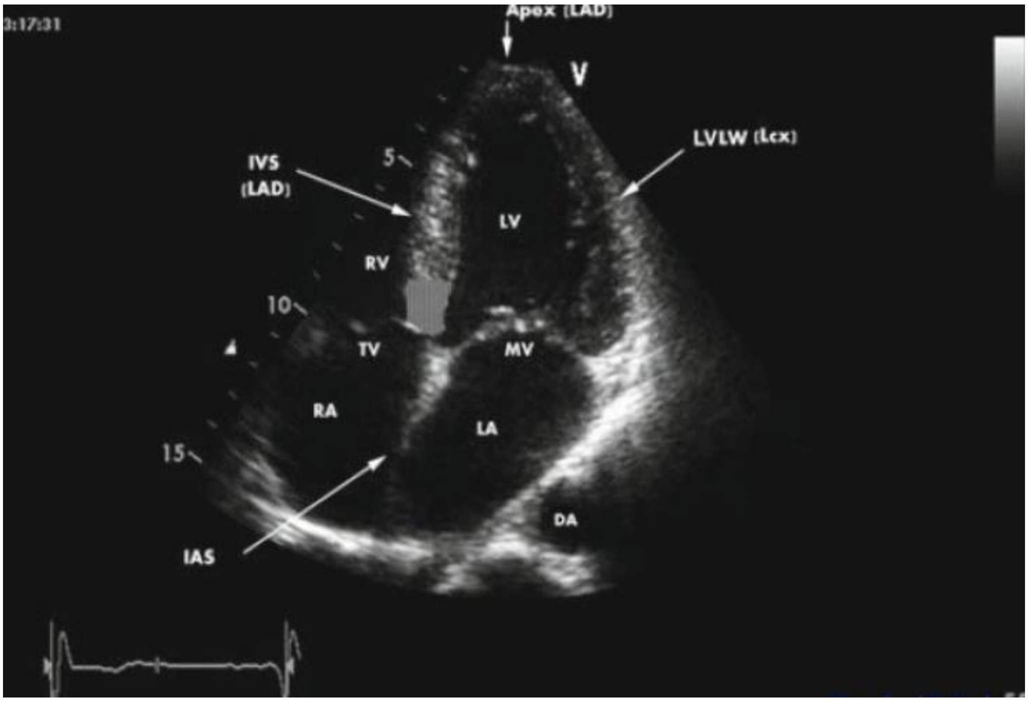

Figure 6 – Echocardiographic picture of the heart

EchoCG allows you to select atrial and ventricular systoles. However, for a detailed analysis of the phase structure of the activities of the heart departments, information obtained via the ECG channel is necessary. Only a small amount of ultrasound equipment has the ability to synchronously record ultrasound and ECG data. In most cases, especially in the clinic, doctors do not use the ability to synchronize ultrasound and ECG.

1.3 Angiography

Some violations of the cardiovascular system can be identified using special radiation (radiological) diagnostic methods. It is possible to assess the state of the vessels with the help of modern x-ray techniques:

Angiocardiography – diagnosis of large vessels with the use of a special contrast agent. The method is almost indispensable in detecting congenital heart defects;

Angiography - x-ray of blood vessels, which is performed using a substance that contrasts blood vessels. The types of this study include coronary angiography, arteriography and phlebography.

The essence of these techniques is the introduction of a contrast agent into the vessel, the main component of which is iodine, and a one-time X-ray examination. Such radiation methods have some contraindications, but they are highly informative and can detect serious diseases of the cardiovascular system (Figure 7) [35].

Figure 7 – Coronarogram obtained using a contrast agent - iodine

Contrast angiography. The method is based on the introduction of contrast material during catheterization to visualize various areas of the cardiovascular system. The catheter is inserted into the vessel and moves under x-ray control to the place where the contrast will be introduced. Then X-rays are taken and the vascular permeability is evaluated. The most common variant of this study is coronary arterial angiography.

Indications for:

1) identification of lesions of the coronary arteries, when the diagnosis of coronary artery disease cannot be established according to non-invasive tests;

2) determination of the possibility of myocardial revascularization (endovascular treatment or coronary artery bypass grafting) in patients with a known diagnosis of coronary artery disease;

3) evaluation of the long-term results of revascularization surgery or the results of drug treatment (progression / regression of coronary atherosclerosis).

The technique allows:

1) determine the type of myocardial blood supply and variants of the discharge of the coronary arteries;

2) to determine the presence, location, extent, degree and nature of atherosclerotic lesions of the coronary bed;

3) to detect signs of complicated lesion (thrombosis, ulceration, calcification, etc.);

4) identify coronary artery spasm;

5) evaluate collateral blood flow;

6) detect abnormal anatomy of the coronary arteries.

1.4 Electrocardiography

Electrocardiography is designed to study the electrical activity of the heart. This diagnostic method is used as the main method of researching the patient's heart activity. It allows you to perform single measurements, as well as monitor the condition of the heart in the monitor mode. It serves primarily for the qualitative and quantitative assessment of the propagation of an electrical impulse through the tissues of the heart. Allows you to determine the rhythm of the heart and arrhythmias.

The positive aspects of this method of measurement are:

- ease of measurement;
- ability to monitor the state of the heart in real time;
- identification of any types of arrhythmias, including life-threatening;
- the possibility of localization of areas of myocardial ischemia.

Negatives are:

- does not provide data on the volume parameters of the activity of the heart;
- does not allow to explicitly determine the mechanical problems in the work of the heart;
- does not allow to detect local changes in the structures of the heart;
- there is no possibility to assess the total hemodynamics of the heart;
- the accuracy of determining the localization of myocardial ischemia is very low.

ECG diagnostics is common due to the relatively low cost of the equipment while providing the doctor with a large amount of accurate information.

A separate direction of ECG diagnostics is Holter monitoring. The Holter system is as automated as possible and allows you to identify most of the abnormalities in the heart’s work in the normal way of life for the patient.

In order to obtain a more complete picture of the patient's CVS condition, an ECG study is necessary to measure blood pressure.

With the help of electrocardiography, you can determine in which areas there is a violation of the conduction of an electrical impulse by the tissues. However, this approach does not allow to evaluate changes in the hemodynamics of the heart.

Figure 8 shows the typical structure of an electrical heart rate diagram (ECG).

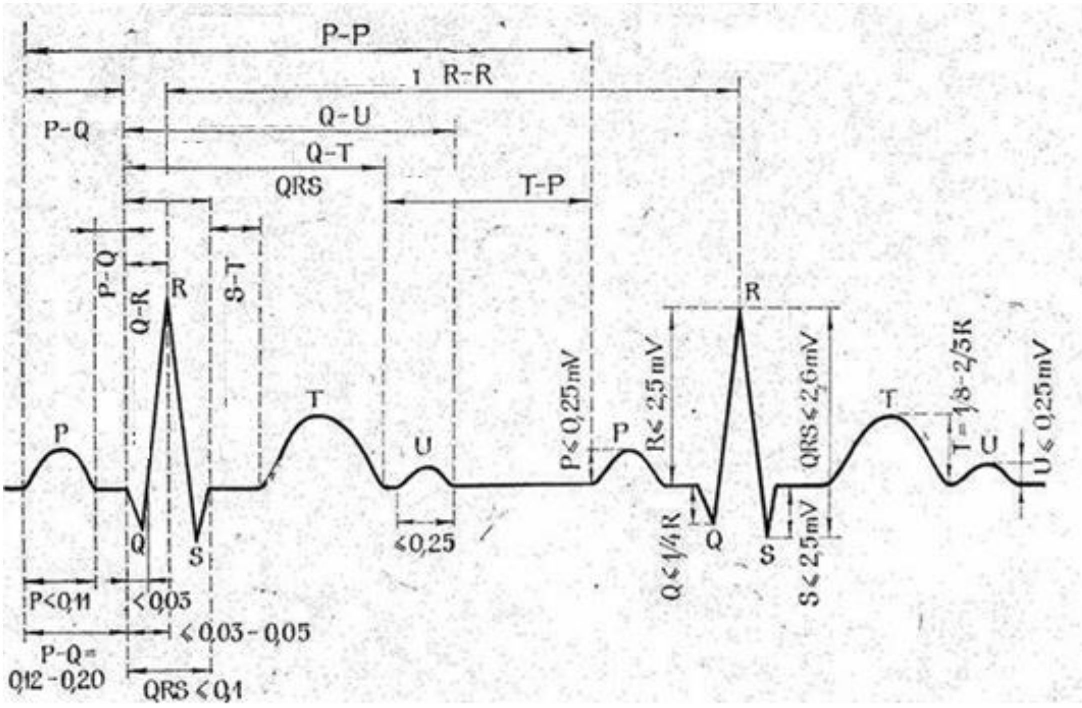

Figure 8 – Time intervals of the electrocardiogram and their typical values in seconds

When describing the ECG, as a rule, indicate the heart rate (HR). The norm is from 60 to 90 (for adults), for children (see table.) The following indicates the different intervals and teeth with Latin designations. (ECG with decoding see. Figure 8)

PQ – (0.12–0.2 s) is the time of atrioventricular conductivity. Most often lengthened against the background of AV blockades. It is shortened in CLC and WPW syndromes.

P – (0.1s) height 0.25–2.5 mm describes atrial contraction. Can talk about their hypertrophy.

QRS – (0.06–0.1 s) -ventricular complex

QT – (no more than 0.45 s) is prolonged with oxygen starvation (myocardial ischemia. Infarction) and the threat of rhythm disturbances.

RR – the distance between the tops of the ventricular complexes reflects the regularity of the heartbeat and makes it possible to calculate the heart rate.

Analysis of the heart rhythm includes determining the frequency and heart rate, the source of excitation, as well as the assessment of the conduction function.

Heart rate regularity is assessed by comparing the duration of R–R intervals between successively recorded cardiac cycles.

On the ECG curve, there are teeth: P, Q, R, S, T, sometimes U, segments: PQ, ST, and TR connecting the electrocardiogram teeth. The segments together with the teeth form intervals: PQ, QT, RR, PP. The prong P reflects the coverage of the excitation of the muscles of the Atria. The PQ interval corresponds to the time of passage of the pulse from the onset of atrial excitation to the onset of ventricular excitation. The QRS interval reflects the process of the spread of excitation through the ventricles. The Q wave reflects the electromotive force (EMF) of the interventricular septum and partially the apex of the right ventricle. The R-wave reflects the electromotive force (EMF) of the myocardium of the free walls of the left and right ventricle, V - excitation of the basal regions of the heart. The BT segment corresponds to the early repolarization period. The T wave is the process of rapid repolarization of the ventricles, the end of their excitation. The QT interval reflects the electrical systole of the heart: depolarization and repolarization of the ventricles. Genesis prong and not exactly known. Furbetto et al associate its origin with delayed repolarization of the papillary muscles, but there are other hypotheses. The tooth and appears after 0.01–0.03 seconds after the T wave.

The characteristics of the cardiac rhythm corresponding to various disorders in the work of the heart, which are correlated with disorders in the general cardiovascular system of a person [17]. Diagnosis of these disorders is made on the basis of an electrocardiogram analysis (Table 4).

2 Modeling of hemodynamics in coronary arteries

Coronary circulation is blood circulation through the vessels of the myocardium to supply the tissues of the heart with oxygen and nutrients [18].

The outflow, depleted in oxygen (venous) blood, is carried out on 2/3 of a large vein, medium and small, which are woven into a single extensive vessel - the coronary sinus. The remainder of the blood is inferred by the anterior and tebesian veins.

During ventricular contraction, the aortic valve valves block the coronary arteries inlets and almost completely stop blood flow through them, and when the ventricles relax, the semilunar valves return blood flow through the aorta and the blood from the aorta does not return to the left ventricle. At the same time, the aortic sinuses are filled with blood, the inlets of the coronary arteries are fully opened.

Coronary arteries are the only possible source of blood for the myocardium, therefore any violation of their integrity or mechanism of work is very dangerous. The coronary arteries originate in the aortic mouth, the left blood supply to the left ventricle and left atrium, partially the interventricular septum, the right right atrium and right ventricle, part of the interventricular septum and the posterior wall of the left ventricle. At the apex of the heart, branches of different arteries penetrate inside and supply blood to the inner layers of the myocardium and papillary muscles; collaterals between the branches of the right and left coronary arteries are poorly developed. Venous blood from the pool of the left coronary artery flows into the venous sinus (80-85% of the blood), and then into the right atrium; 10-15% of venous blood enters through the veins of Thebesia into the right ventricle. Blood from the pool of the right coronary artery flows through the anterior heart veins into the right atrium. At rest, 200-250 ml of blood per minute flows through the human coronary arteries, which is about 4-6% of a minute cardiac output.

Myocardial blood supply depends on the phase of the cardiac cycle, and two factors influence the blood flow: the myocardial tension, which squeezes the arterial vessels, and the blood pressure in the aorta, which creates the driving force of the coronary blood flow. At the beginning of systole (during the stress period), the blood flow in the left coronary artery is completely stopped as a result of mechanical obstructions (branches of the artery are pressed by the contracting muscle), and in the expulsion phase, the blood flow is partially restored due to the high blood pressure in the aorta, which is opposed to mechanical force. In the right ventricle, the blood flow in the phase of tension suffers slightly. In diastole and rest, coronary blood flow increases in proportion to the work done in the systole to move blood volume against pressure forces; This contributes to the good distensibility of the coronary arteries. The increase in blood flow leads to the accumulation of energy reserves (adenosine triphosphate (ATP) and creatine phosphate) and the deposition of oxygen by myoglobin; these reserves are used during systole when oxygen supply is limited.

The density of the capillary network of the myocardium is 3-4 times greater than in skeletal muscle, and is equal to 3500-4000 capillaries in 1 mm3, and the total area of the diffusion surface of capillaries here is 20 m2. This creates good conditions for the transport of oxygen to myocytes. The heart consumes alone 25-30 ml of oxygen per minute, which is about 10% of the total oxygen consumption of the body. At rest, half the diffusion area of the capillaries of the heart is used (this is more than in other tissues), 50% of the capillaries are not functioning, and are in reserve. Coronary blood flow alone is a quarter of the maximum, i.e. There is a reserve for increasing blood flow by 4 times. This increase occurs not only due to the use of reserve capillaries, but also due to an increase in the linear velocity of blood flow.

Arteries lying on the surface of the heart are called epicardial. They are rather large vessels capable of self-regulation. Blood flow in the epicardial arteries with certain assumptions can be described by the Navier-Stokes equations [18]. Coronary arteries, which are located deep in the myocardium, are called subendocardial. They are smaller than the epicardial and are strongly affected by the tissues of the heart.

Coronary blood flow is justified is of great importance for the whole organism. After all, arteries of this kind are responsible for the blood supply to the main organ of a person - the heart.

Therefore, the damage of these vessels, the development of abnormal processes in them leads to the occurrence of myocardial infarction or ischemic disease.

The blood flow may be impaired due to blockage of blood vessels by plaques or blood clots.

Insufficient blood flow to the left ventricle can result in disability and even death. Due to vasoconstriction, stenosis may also develop. The stenosis of the coronary heart vessels leads to the fact that the myocardium cannot fully reduce the heart. The doctor usually uses shunting to restore blood flow.

It is advisable to undergo periodic diagnosis in order to prevent the appearance of stenosis, as well as timely treat atherosclerosis. Coronary artery types provide the blood supply to the main organ in the human body. If the coronary vessels do not cope with the task, lose elasticity, then the heart is deficient in vital elements. This can provoke various diseases of the “motor” of the human body and even lead to an attack.

Ischemic heart disease (IHD), also referred to as coronary heart disease (CHD), refers to any disease associated with a sharp deterioration in the blood supply to the heart, due to insufficient coronary system activity.

Most often it is manifested against the background of atherosclerosis of arteries, arising from the general thinning or violation of the integrity of the vessel. A plaque forms at the site of injury, which gradually increases in size, narrows the lumen and thereby prevents normal blood flow.

The list of coronary diseases includes:

– angina pectoris;
– arrhythmia;
– embolism;
– heart failure;
– arteritis;
– stenosis;
– cardiac infarction;
– distortion of the coronary arteries.

For many years, blood circulation in the circulatory system has been the object of close scrutiny from both theoretical and practical points of view.

Thanks to numerous and promising applications, the study and development of mathematical and numerical models of biological processes occurring in the human body has increased significantly, which allowed mathematical modeling, thanks to the accumulation of knowledge and experience, to become an attractive tool for analyzing the processes occurring, including circulatory system.

All existing work in the field of hemodynamics, in addition to the construction and development of the models themselves, require some effort to create numerical methods for solving relevant problems, and are also associated with the problem of implementing the developed techniques on a computer.

A special place is occupied by the preparation of a computational experiment and the processing of its results. The key problem of mathematical modeling of hemodynamic problems is to obtain reliable numerical values of the physiological parameters of the elements of the cardiovascular system, which is a separate and rather complex and time-consuming work.

It should be noted that due to the requirement of acceptable accuracy of calculations and the complexity of the computational domain, many authors use the finite element method on very detailed grids, for example, in [13-15, 22, 24-27, 31-34].

A large place in mathematical models of hemodynamics is the mathematical description of the work of the heart, as an essential element of the cardiovascular system. In this area, a large number of models have been built and used - from imitation and simplest one-dimensional (representing the heart as an ordinary piston) to the most complex three-dimensional. The problem of building such full-size models consists both in the difficulty of calculating three-dimensional hydrodynamic processes in a complex, changing region (corresponding to the ventricles or atria of the heart), and the need to take into account and reproduce the properties of the heart muscles, their particular structure, function, regulation system, etc. (see [1, 2, 3, 33-35]). When constructing multidimensional models of the heart, modeling of the contractile activity of the heart muscle plays an important role. In many works, Starling's law is the basis for heart models [3, 30-33]. Of course, this law describes only one of the many regulatory features of the work of the heart muscle.

The authors of mathematical models of the integral cardiovascular system use different mathematical approaches and types of models. Historically, the first attempt to reproduce the work of the cardiovascular system as a whole, apparently, was the work of O. Frank (28), who proposed to compare its analogue in terms of an electrical circuit to the cardiovascular system. Later on, this approach was developed (see, for example, [27–32]) and is used to study a wide variety of phenomena.

2.1 Principles of mathematical modeling of the human cardiovascular systems

The task of mathematical modeling of internal fluid flow through a system of elastic tubes has a wide area of scientific and practical application, including the modeling of blood flow through the cardiovascular system.

The foundations of the modern physiology of the blood flow and its mathematical description are associated with the name of an English doctor and scientist W. Harvey [2] and later Euler, D. Bernoulli, Poiseuille. It should be noted that the task of building a general mathematical model of the cardiovascular system and computer methods for studying it has not been solved at the moment. First of all, this is due to the extreme complexity of the biological system under consideration, the functioning of which depends on a huge number of factors, on virtually every element of a living organism, and these dependencies are largely not formalized even at a physiologically descriptive level.

The key problem of mathematical modeling of hemodynamic problems is to obtain reliable numerical values of the physiological parameters of the elements of the cardiovascular system, which is a separate and rather complex and time-consuming work.

There are many practically important medical and physiological problems that require accurate and accurate calculations of multidimensional flows in a vessel. Suffice it to mention the study of blood flow in stenotic and thrombosed vessels, blood flow modeling in the presence of stents, shunts and filters, flows in the bifurcation of blood vessels and aneurysms.

A series of studies on the formation and evolution of blood clots in a multidimensional formulation was carried out, for example, in [3-6] and other works of these authors. In these works, a thrombogenesis model is proposed, and the flow in a large thrombosed vessel is modeled using a specially developed numerical method.

Symptoms of a number of circulatory system diseases are disorders in the propagation of a pressure wave (in biomechanics it is called a pulse wave). These disorders can be diverse in nature - from a weakening of the amplitude of the pulse wave and its delay in a number of peripheral arteries to an increase in the amplitude of the pulse pressure and an increase in the velocity of propagation of the pulse wave [11].

Simulation algorithm:

The basis for modeling biological – organs (living organisms) by the method of physical technical analogy. The essence of this method is as follows [10]:

1. The morphology and interrelations between the morphological units of the organ being modeled during its functioning are thoroughly studied (structure).

2. Physical-technical objects are selected that perform functions similar to the functions of selected morphological units.

3. From the selected technical units, a computational scheme is drawn up, which shows the links between morphological units and the functioning of the modeled organ.

4. On the basis of the computed calculation scheme, a system of differential and algebraic equations used in engineering and physics, reflecting the functioning of the simulated organ, is compiled.

5. The digital values of the coefficients are determined and calculated from the accumulated biophysical knowledge of the functioning of the organ being modeled.

6. A language environment is selected to draw up a program for the numerical solution of the composed system of equations.

7. The compiled system of equations is solved step by step, at each step substituting new parameter values used to solve the next step.

8. The decision is accompanied by the construction of graphs of the change in time of all the parameters reflected by the equations connecting the morphological units into the system, the functioning of the modeled organ.

9. The obtained graphs of changes in the simulated parameters of a biological organ in time are compared with the parameters available in the biology of the simulated organ. Based on this comparison, we judge the accuracy of the model obtained.

10. Analyzes the differences of the results with physiological data and make a correction of the calculation scheme or the numerical coefficients of the equations.

11. After obtaining the results reflecting the functioning of the modeled body in norm, with permissible accuracy, one can proceed to the modeling of its pathologies.

12. To model pathologies, it is necessary to change the design scheme, add equations reflecting the change in the design scheme from the normal state model by introducing new dependencies or changing the coefficients of the equations.

13. A new program for solving equations that reflect the corresponding pathology is being prepared.

14. Build comparative graphs, taking into account the norms and new parameters, reflecting the simulated pathology.

2.2 Existing models of human cardiovascular system

There are modern approaches to hemodynamic modeling. Due to the complexity of the hydrodynamic problem under consideration, the use of existing models is usually limited to the description of a fragment or certain conditions for its functioning [16], [17]. Hybrid base models are being developed that describe the various components of the system using 3–D and 2–D simulations, 1–D simulations (averaging multidimensional models in the transverse direction) and 0–D simulations with lumped parameters (performed averaging over the length of the vessel) [18], [19], [20], [16], [21], [22].

With three-dimensional (3D) hemodynamic modeling, a numerical solution of the unsteady Navier-Stokes equations for a viscous incompressible fluid is required together with the equations of the dynamics of elastic shells of complex and time-varying geometry (the free boundary problem). Since this decision is associated with huge computational costs, multidimensional models for describing the cardiovascular system are mainly used for a detailed study of hemodynamics in a local area, for example, in the area of implantation of prostheses, bifurcation or stenosis of arteries, etc.

As noted above, 3–D modeling is used for a detailed description of blood flow in local areas [19], allowing you to correctly estimate the change in pressures and blood flow rates at a specific point in time. However, within the framework of these models, the laws of rapid changes in physiologically significant parameters cannot yet be formalized. Detailed consideration of the complex system of arterial vessels also presents significant difficulties.

Modeling even local parts of the cardiovascular system of a specific person requires the use of expensive preoperative examination with the use of special diagnostic equipment (angiographs, ultrasound devices, etc.) and software for numerical hydrodynamic analysis.

This confirms the need for informed choice of the set of essential components of the model.

2.2.1 Dual–chamber model of the human cardiovascular system

A two-chamber model of the human cardiovascular system is described in [30, p. 28–31].

When modeling the circulatory system as a whole, it is necessary to properly describe the work of the heart. A complete mathematical description of the work of the heart, taking into account all possible factors, is a separate and extremely complex task. In this paper, we restrict ourselves to the consideration of simplified models that reproduce the basic functions of the heart and allow us to obtain physiologically reasonable flows in the vascular system.

To do this, consider the following scheme for the functioning of the heart [1, 7–9, 10, 12] (Figure 9). The movement of blood in the body is provided by the heart, which can be considered as two hollow muscular organs - the "left" heart and the "right" heart, each of which consists of the atrium and the ventricle. Blood from the organs and tissues of the body goes to the right heart, pushing it to the lungs, where it is saturated with oxygen, returns to the left heart (in a small circle) from which it goes back to the organs, from where it returns to the right heart (in a large circle). The injection function of the heart is based on the alternation (cardiac cycle) of relaxation (diastole) and contraction (systole) of the ventricles. During diastole, the ventricles fill with blood, and during systole, they throw it into the large arteries (aorta and pulmonary trunk). Before filling the ventricles, blood accumulates in the atria.

Thus, the work of the heart is normally of a quasi-periodic nature and consists of cardiac cycles. In turn, systole and diastole are divided into several periods. Systole is subdivided into the period of isovolumetric contraction and the period of exile, and diastole is divided into the period of isovolumetric relaxation and the period of filling. The duration of isovolumetric contraction and relaxation is approximately 50–60 ms, whereas the duration of systole and diastole is 0.3–0.5 s, and therefore when building models we will consider systole as the period of expelling blood from the heart, and diastole as the period of filling.

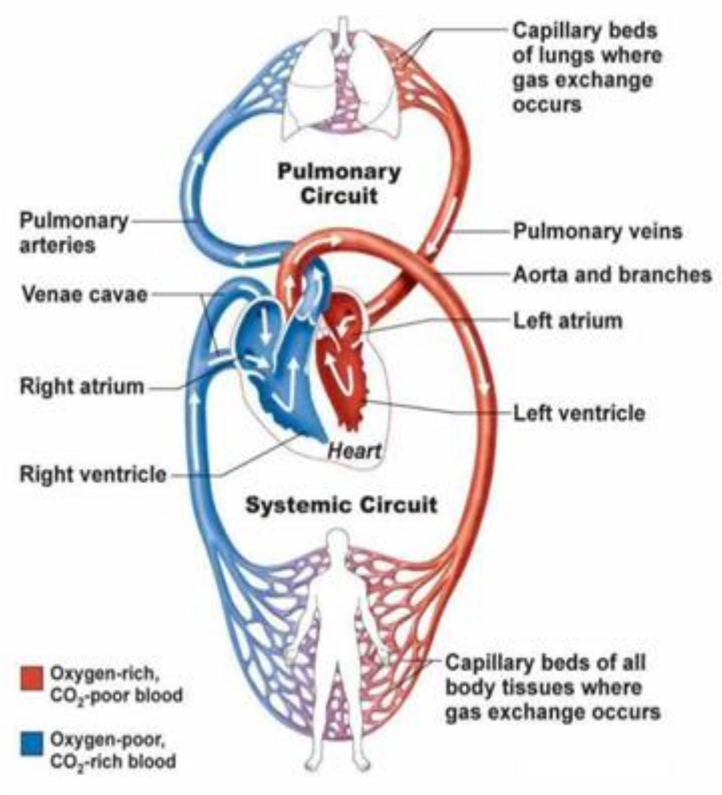

Figure 9 – Scheme of the functioning of the heart

When the pressure in the left ventricle becomes higher than the diastolic pressure in the aorta (on average, approximately 80 mm Hg), the ventricular valves open and a period of expulsion of the blood begins. First, the intraventricular pressure continues to rise, reaching about 130 mm Hg, and at the end of systole it falls again. At rest, the stroke volume of the ventricle, i.e. the amount of blood released in one cycle is about half of the end-diastolic volume, equal to about 130 ml. Thus, at the end of the expulsion period, about 70 ml of blood remains in the heart, this is the so-called finite systolic, or reserve volume.

During the period of filling with blood, the pressure in the ventricle changes slightly (7-9) (Figure 10), and the volume increases — at first very quickly (fast filling phase), then slower (diastasis phase). With a high frequency of contractions, diastole is shortened to a greater extent than systole (Figure 10, [7]). All the above refers to the left heart, however, the same periods are observed in the cycle of contraction of the right heart. The right heart is distinguished by the fact that the systolic pressure it develops must be significantly lower than in the left heart (this is due to the lower resistance of the pulmonary vessels). The impact volume in both ventricles is about the same. The cycle periods of the two halves of the heart do not quite coincide, however, the phase shifts are small (about 10-30 ms) and, as a first approximation, have practically no effect on hemodynamics as a whole.

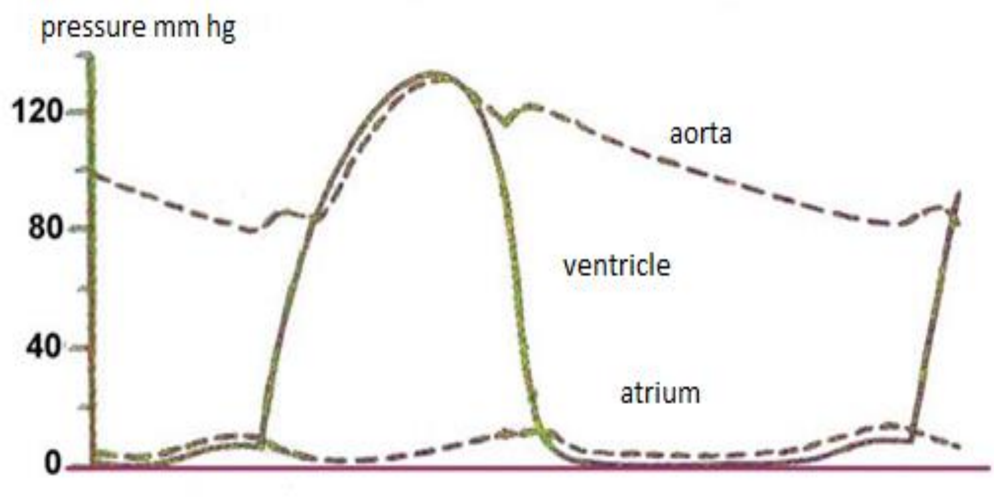

Figure 10 – The distribution of pressure in different parts of the heart

Thus, in principle, the four-chamber heart model is represented as the union of two two-chamber models, perhaps with different parameters (Figure 11 a and b).

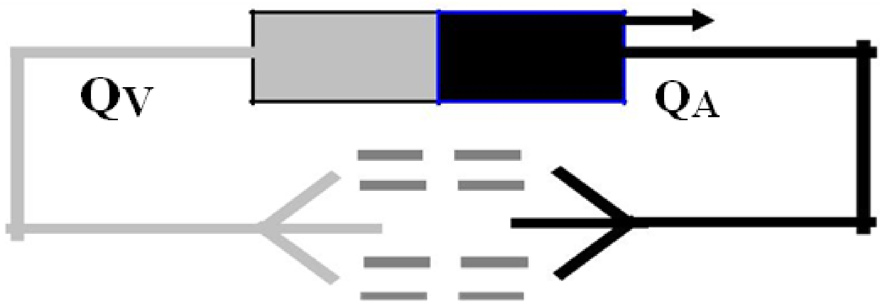

Figure 11 a – Two-chamber model of the heart

Here QV, QA – venous and arterial flows, respectively.

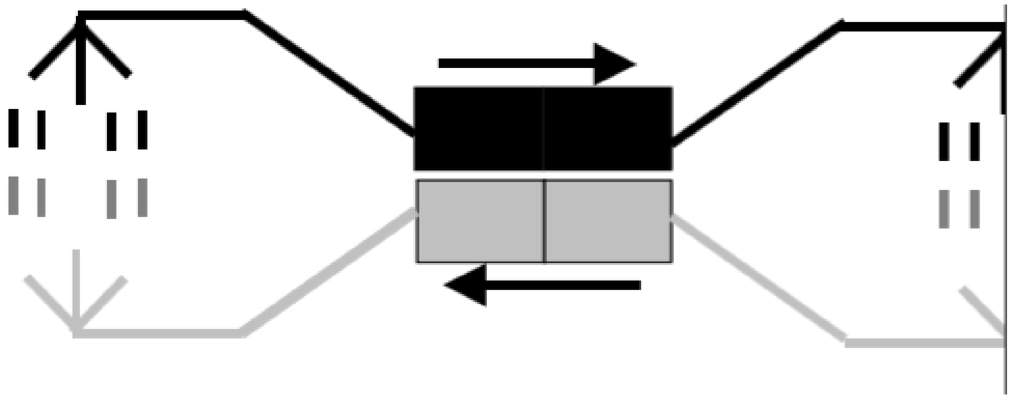

Figure 11 b. Four–chamber model as a combination of two-chamber models hearts

In this regard, we will further consider precisely the two-chamber heart model, with the help of which it is possible to simulate both circles of blood circulation.

2.2.2 Four-chamber model of the human cardiovascular system

A four-chamber model of the human cardiovascular system is described in [31, p. 51-60].

A mathematical description of a four-chamber model of the cardiovascular system with a pulsating heart is presented. The cardiovascular system has the appearance of four connected elastic chambers (Figure 12).

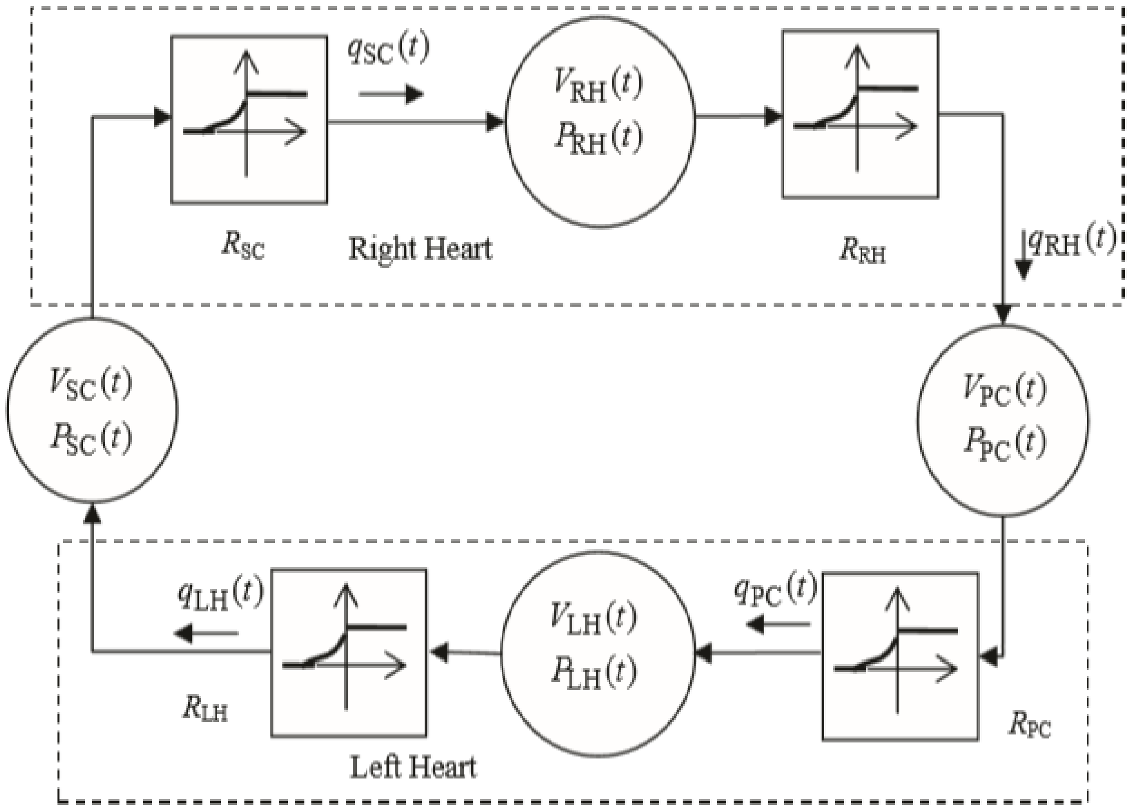

Figure 12 – Chamber structure of the blood circulation model

A mathematical model of the CVS is proposed, consisting of four elements connected in series: LH - Left Heart; SC - systemic circulation (Systemic Circulation); RH - Right Heart; PC is the pulmonary circuit (Figure 12). The elements of the CVS includes serially connected chambers and valves.

The designations used in the formulas: C - elasticity of the chamber, $\text{см}^3/_{\text{torr}}$; E^{SE}, E^{PE}– coefficients characterizing the elastic properties of parallel and sequential elements of the myocardium, respectively, Torr; G is a geometric constant; h is the average wall thickness of the heart chamber, cm; K^{SE}, K^{PE}– dimensionless coefficients characterizing the elastic properties of the elements of the myocardium; k - pump coefficient; L– inertia of blood flow, $\text{torr} \cdot \text{см}^2/_{\text{см}^3}$; l is the length of the element, cm; P– pressure in the chamber, torr; q– volumetric blood flow, $\text{см}^3/_{\text{торр}}$; r is the radius of the camera, cm; R is the hydraulic resistance, torr ·c/cm; s – the proportion of contractile filaments in the cross-sectional area of the myocardium; T is the period of heart contractions, s; T_{sys}– – systole duration, s; t - time, with; U is a non-stressed volume, cm^3; u is the systolic tone of the heart chamber, cm^3; V is the volume of the i-th camera, cm^3; $V^{ed}$is the final diastolic volume, cm^3; V^{SV}– shock volume, cm^3; β is a constant characterizing the conductivity of the heart valve during regurgitation, cm^{-3}; Δ is the volume of regurgitation, cm^3; η – coefficient characterizing the viscosity of the myocardium, torr·s; ε – relative linear deformation; ρ is conductivity, cm/(torr · c); σ^{PE}, σ^{SE}– stresses in a parallel and sequential elastic element, respectively, Torr; χ is the contraction coefficient, c^{-1}; i – camera model.

In the CVS model, each i-th camera (Figure 13). characterized, respectively, by the functions of volumetric blood flow, volume, pressure: q_i (t), V_i (t), P_i (t), i∈ {LH, SC, RH, PC}.

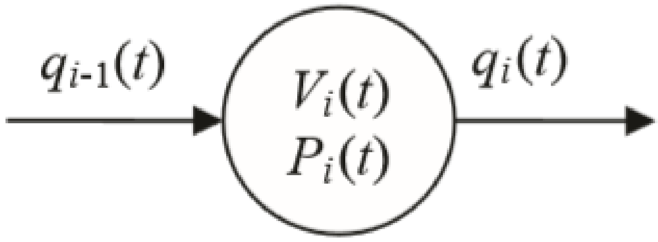

Figure 13 – Camera model CVS

In the pulsating heart model, the activity of the heart is considered as the alternation of contraction phases (systoles) and relaxation phases (diastoles). The characteristics of this process are: the period of cardiac contraction T and the duration of T_{sys}. The beginning of the cardiac cycle is the moment of diastole change to systole. In general, T and T_{sys} may be different for different cycles, then the moments of the end of systole $t_{es}(n)$ and end of diastole $t_{ed}(n)$ n-th cycle, n = 1, 2, 3, …, expressed by the formulas:

$$t_{es}(n) = \sum_{j=1}^{n-1} T(j) + Tsys(n) + t0;$$

(1)

$$t_{ed}(n) = \sum_{j=1}^{n} T(j) + t0.$$

A hypothesis is used to describe the phase of contraction of the heart [4]:

$$\frac{d\omega_i(t)}{dt} = \chi_i(\omega_i(t) - u_i) \; i \in \{LH, RH\}, \qquad (2)$$

where χ_i and u_i constants that are chosen so that Integral for the heart cycle is executed the law of Starling [5].

Throughout systole, the myocardium is subject to equation (2). The transition from systole to diastole occurs by changing the equations.

Thus, the closed system of equations determines the four-chamber model of human CVS, which, when solved, determines the volume functions V_i (t), pressures P_i (t) and volumetric flow q_i (t) in each i-th chamber, i∈ {LH, SC, RH , PC}.

3 Description of the local hemodynamic model

One of the main features of the coronary blood flow is its strong dependence on the phase of the cardiac cycle. In systole, interstitial myocardial pressure increases; opening of the aortic valve leads to overlapping of the orifices of the coronary arteries and reduces coronary blood flow to a minimum. Intramyocardial pressure (pressure in the thickness of the working cardiac muscle) reaches 150 mm Hg in systole and is practically absent in diastole [19]. On the other hand, the reduction of blood vessels leads to an increase in venous return [20]. The lumen of the small arteries in systole is reduced by an average of 60% [21]. The resistance of the peripheral region of the vascular bed increases several times. In some areas, the bloodstream turns in the opposite direction. All of these effects lead to the fact that a significant part of blood flow through the coronary arteries occurs in diastole.

There are two main coronary arteries - the right coronary artery and the left coronary artery (Figure 14). Both begin at the base of the aortic arch. The left coronary artery is divided into several large branches feeding the tissues of the left heart. The right coronary artery and its branches supply blood to the right heart. Intra myocardial pressure in the tissues surrounding the left ventricle is significantly higher than in the right heart. Therefore, all of the above effects are more pronounced in the branches of the left coronary artery.

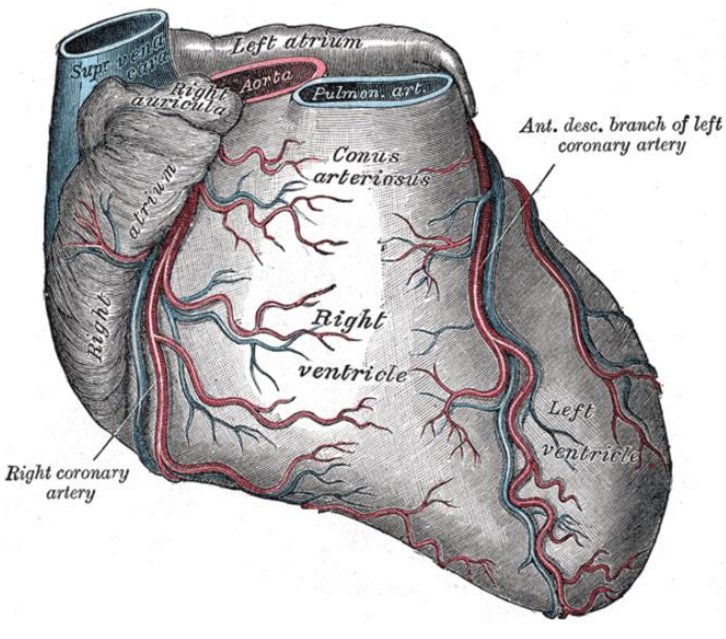

Figure 14 – Coronary arteries

Consideration of the above features of blood flow through the coronary vessels is an important condition for their simulation.

The main purpose of local hemodynamic modeling is to predict the behavior of blood pressure and blood flow in the arteries, depending on the influence of various factors. In addition to modeling the parameters of blood flow in the arteries, modeling of hemodynamics of the coronary arteries undergoing surgery with the imposition of shunts and stenting is of considerable interest. The use of mathematical models constructed based on the available data obtained on the basis of autopsy studies allows us to calculate the parameters of blood flow at any point in the vascular bed at any time and predict its change as a result of reconstructive surgery. Which in turn can serve as a basis for choosing one or another method of shunting, or decide whether surgical intervention is necessary, in particular, stenting for thrombosis [23].

The main indicators of local hemodynamics – blood pressure at the site of the vessel and blood flow velocity – are widely determined in the therapeutic clinic. The method of determining blood pressure is well known. To determine the speed of blood flow, there are many different methods. It is customary to distinguish the speed of blood flow in the large and small circles of blood circulation. The speed of blood flow in a small circle is determined by the time elapsed from the moment of the introduction of any substance into the vein until the appearance in the capillaries of the lungs, and in the large until the moment of appearance in the capillaries of the tissues. Depending on the methods and indicators used, the blood flow velocity varies significantly. Most often use such simple tools as calcium chloride. Being introduced into a vein and having completed a complete circuit, calcium chloride, getting into the capillaries, gives a sensation of heat. Apply and other means that give a feeling of bitterness in the mouth. Currently, they use the method of introducing isotopes. After injection into the vein, passing through the heart and lungs and getting back to the periphery, they can be marked with special devices - radiometers. Colorful samples are also used in which the paint changes the color of the mucous membrane while it passes through the capillaries. To determine the speed of blood flow in the pulmonary circulation, ether sampling is used when 5 ml of saline solution mixed with 1 ml of ether is administered intravenously and the time is noted when the patient smells the ether. The mixture must be prepared so that the air does not get into the air of the room. Normally, the blood flow velocity in the large circulation is from 12 to 15 seconds, in the small circle it is five to six seconds. In the presence of pathological messages between the atria or the ventricles, it is possible to obtain completely paradoxical changes in the speed of blood flow. This technique is used, for example, to diagnose Fallot's tetrad, when the blood flow velocity in the great circulation is drastically reduced. More complex studies of hemodynamics are made necessarily with the definition of the gas composition of the blood.

Characteristics of the heart rate corresponding to various disorders in the work of the heart, which are correlated with disorders in the general cardiovascular system of a person are shown in Table 4.

There are various ways to assess the blood flow reserve. With the development of technology, the transcatheter measurement of intracoronary pressure and blood flow velocity has become possible; In addition, non-invasive techniques for assessing myocardial perfusion using positron emission tomography, single photon emission computed tomography, magnetic resonance imaging (MRI) have appeared. Using these techniques, it was found that the pathology of the MB often determines the functional significance of stenosis in patients with chronic coronary artery disease. In addition, the possibility of isolated pathology of the MB with normal coronary arteries (CA). In this connection, an integrated approach is often required in order to determine what caused a decrease in myocardial perfusion: the severity of stenosis or pathology of the MB. Three main methods are currently used to determine the coronary blood flow (CBF) reserve: absolute coronary flow reserve (ACFR), relative blood flow reserve and FFR (Figure 15). The figure shows the experimentally measured pressure difference before and after stenosis [36]

Absolute coronary flow reserve (ACFR) is the ratio of speed in maximally dilated spacecraft to speed at rest. Normally, this indicator should be 4–5. Blood flow velocity can be measured using an intravascular ultrasound transducer or by thermodilution; maximum vasodilation is achieved by administering adenosine, papaverine or dipyridamole. ACFR values below 2 are considered as clinically significant [9]. This method has many drawbacks, the most important of which is the dependence of the resulting value both on factors influencing the maximum CBF (HR, BP, severity of stenosis, microangiopathy) and on factors affecting the blood flow at rest (hemoglobin level, hemoglobin oxygenation and others).

The relative reserve of blood flow is the basis for the identification of hemodynamically significant coronary artery stenosis using radiological methods for assessing coronary perfusion. To determine this indicator, local perfusion (per 1 g of myocardium) is compared with maximum vasodilation or with a load in the ischemic zone with perfusion in normal areas. In connection with this method of calculation, there are significant limitations of this technique: for example, to calculate the indicator, an LV segment with normal perfusion is necessarily needed [9]. Thus, the use of the method for multivascular lesions of the coronary bed or for diffuse myocardial hypokinesia due to microangiopathy is impossible. In addition, to measure the indicator requires a significant difference in the reserve of blood flow between areas. Currently, there are no prospective studies that prove the prognostic significance of this indicator in patients with IHD.

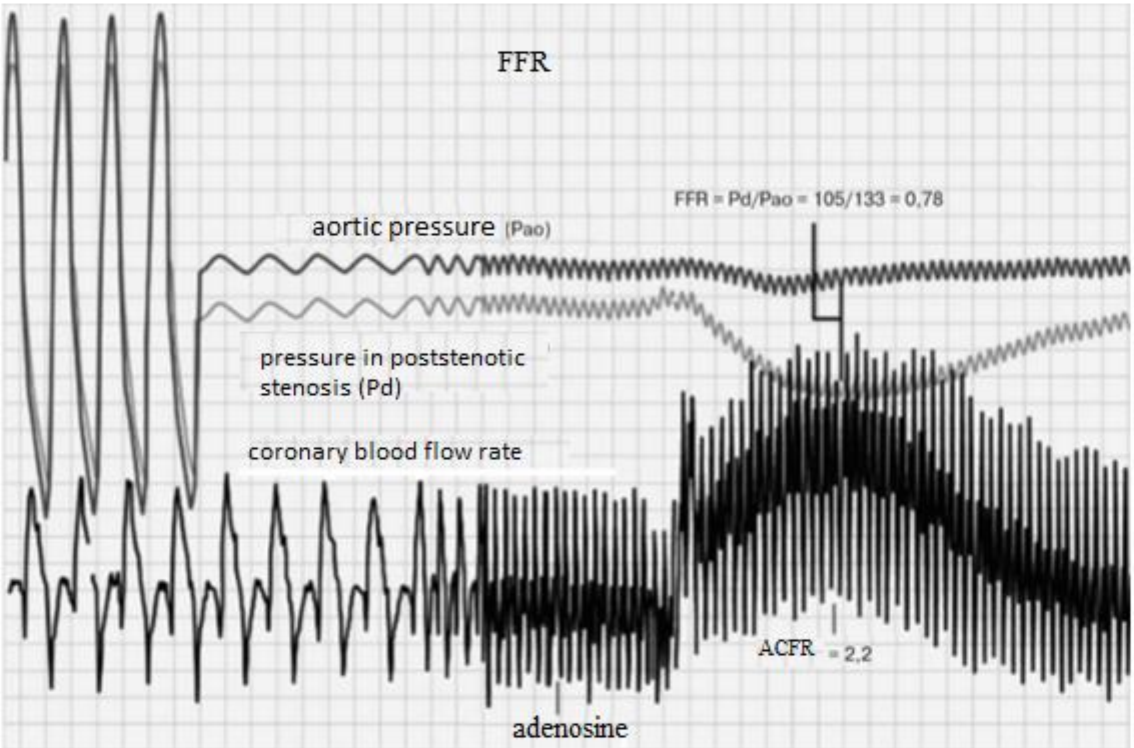

Figure 15 – Intracoronary pressure and blood flow rate in a patient with moderate stenosis

The “gold standard” of assessing the physiological significance of stenotic stenosis is the definition of FFR. FFR is defined as the ratio of the maximum blood flow in a narrowed artery to the maximum blood flow in the same vessel without stenosis. In other words, the maximum blood flow in a narrowed artery is considered as a fraction of the maximum blood flow in the same vessel without stenosis. For the first time, this indicator was proposed to be measured at the beginning of the 90s of the 20th century by N. Pijls and B. De Bruyne [10, 11]. Thus, FFR is the ratio of blood flow rates, which can also be expressed as a pressure ratio. FFR = Pd / Pa, where Pa is the pressure in the aorta, and Pd is the pressure in the poststenotic section, measured at maximum vasodilation. Normally, FFR should be equal to 1 in all patients and in all CA, does not depend on blood flow at rest or changes in hemodynamic parameters, takes into account the degree of perfusion and the presence of collaterals, has a clear threshold for determining the hemodynamic significance of stenosis - 0.75–0.80. In studies in humans, it has been shown that blood pressure and heart rate do not affect this indicator [12]. It is also proved that FFR has sufficient reproducibility. In addition, FFR unlike ACFR does not depend on gender and risk factors for cardiovascular diseases - CVD (arterial hypertension and diabetes mellitus). The threshold FFR degree of myocardial ischemia was determined in clinical studies when compared with non-invasive stress tests. FFR <0.75 was significantly associated with stress-induced myocardial ischemia (specificity 100%, diagnostic value of a positive test result 100%, diagnostic value of a negative test result 88%). However, with FFR > 0.80, most patients lack stress-induced ischemia (sensitivity 90%) [13]. At present, it is recommended that FFR <0.80 be used as a threshold value [2].

The specificity for detecting induced ischemia of FFR <0.75 is 100%, and the sensitivity of FFR > 0.80 is more than 90%. The study is invasive; it is performed at the same time as an x-ray operation with a diagnostic CG using a conductor with a pressure sensor at the end at the height of maximum hyperemia. Epicardial hyperemia is achieved by administering isosorbide dinitrate bolus, adenosine, adenosine 5'-triphosphate (ATP), papaverine is used to achieve microvascular hyperemia [1]. The indicator is calculated by the formula: FFR = Pd / Pa (Figure 16) [36]. This technique has a fairly high level of evidence and is widely used abroad.

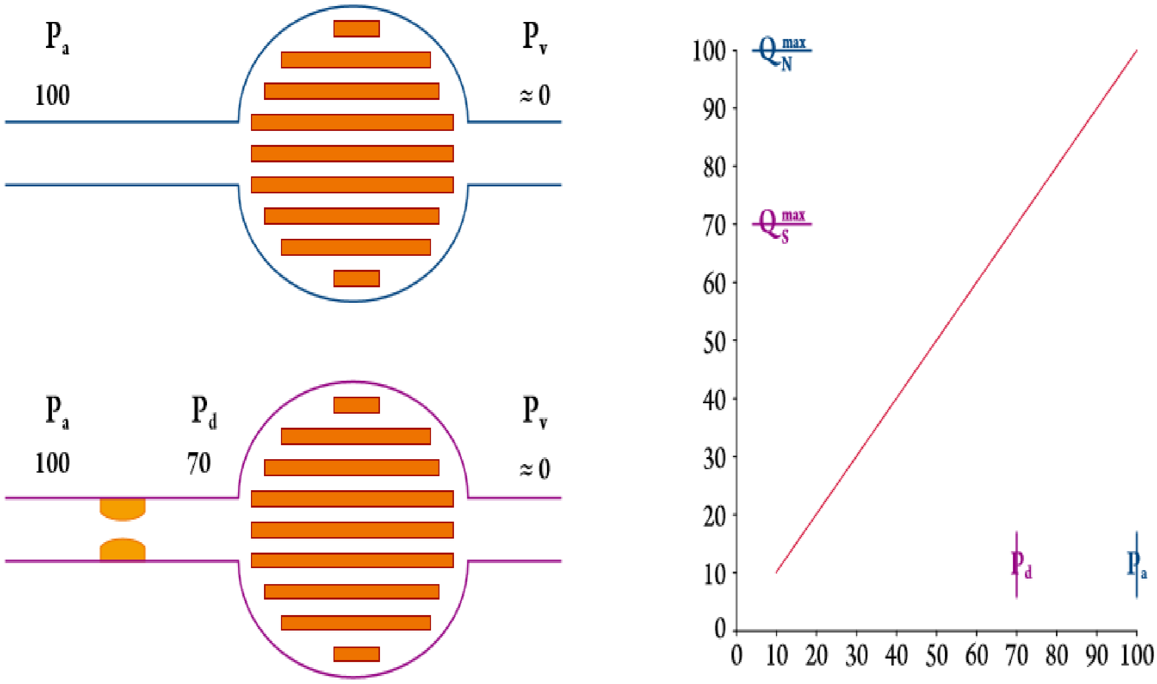

Figure 16 – The concept of an invasive measurement of a fractional reserve of blood flow. Pa - aortic pressure; Pd - pressure distal to stenosis; Pv - venous pressure; Qn max - the maximum blood flow is normal; Qs max - maximum blood flow in the presence of stenosis.

3.1 Hemodynamic Modeling: Comsol Multiphysics

The calculation of hemodynamics of coronary vessels was performed using the finite element method using the software package COMSOL Multiphysics.

COMSOL Multiphysics is a software platform for modeling and optimizing any physical system using advanced numerical methods, and creating your own applications for calculations.

COMSOL Multiphysics reads geometric files created by all major CAD packages. The graphical user interface supports consistent unit systems, and the moving-mesh feature allows you to simulate moving parts of a model and parametric geometries. The calculation algorithms process models with millions of degrees of freedom (Figure 17).

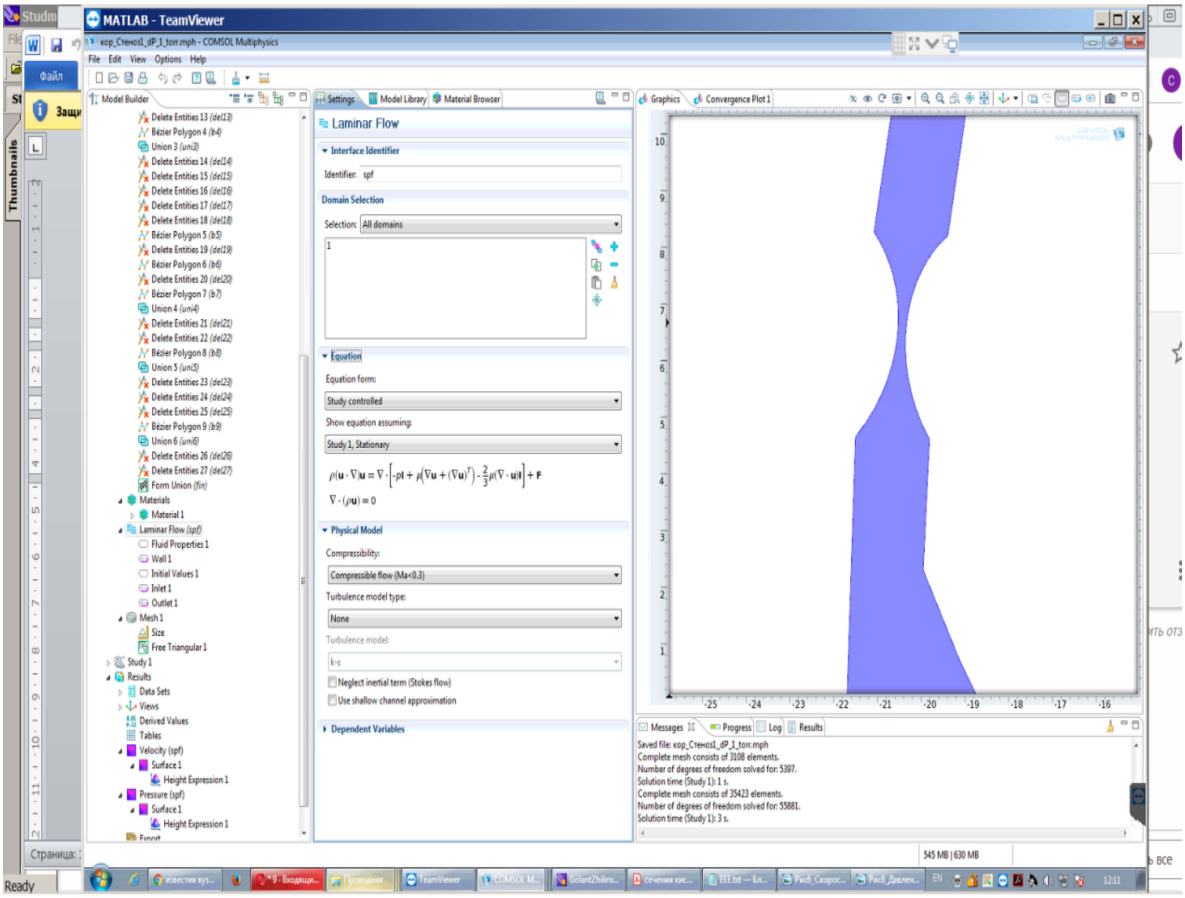

Figure 17 – Comsol Multiphysics program interface

The program COMSOL Script ** COMSOL Multiphysics is an interpreter language that includes more than 500 commands for numerical calculations and visualization in command line mode, and also allows you to create scripts (procedures written in text format). The COMSOL Multiphysics program is the only program that uses the finite element method to simulate the propagation of electromagnetic waves in a nonlinear medium (Figure 18).

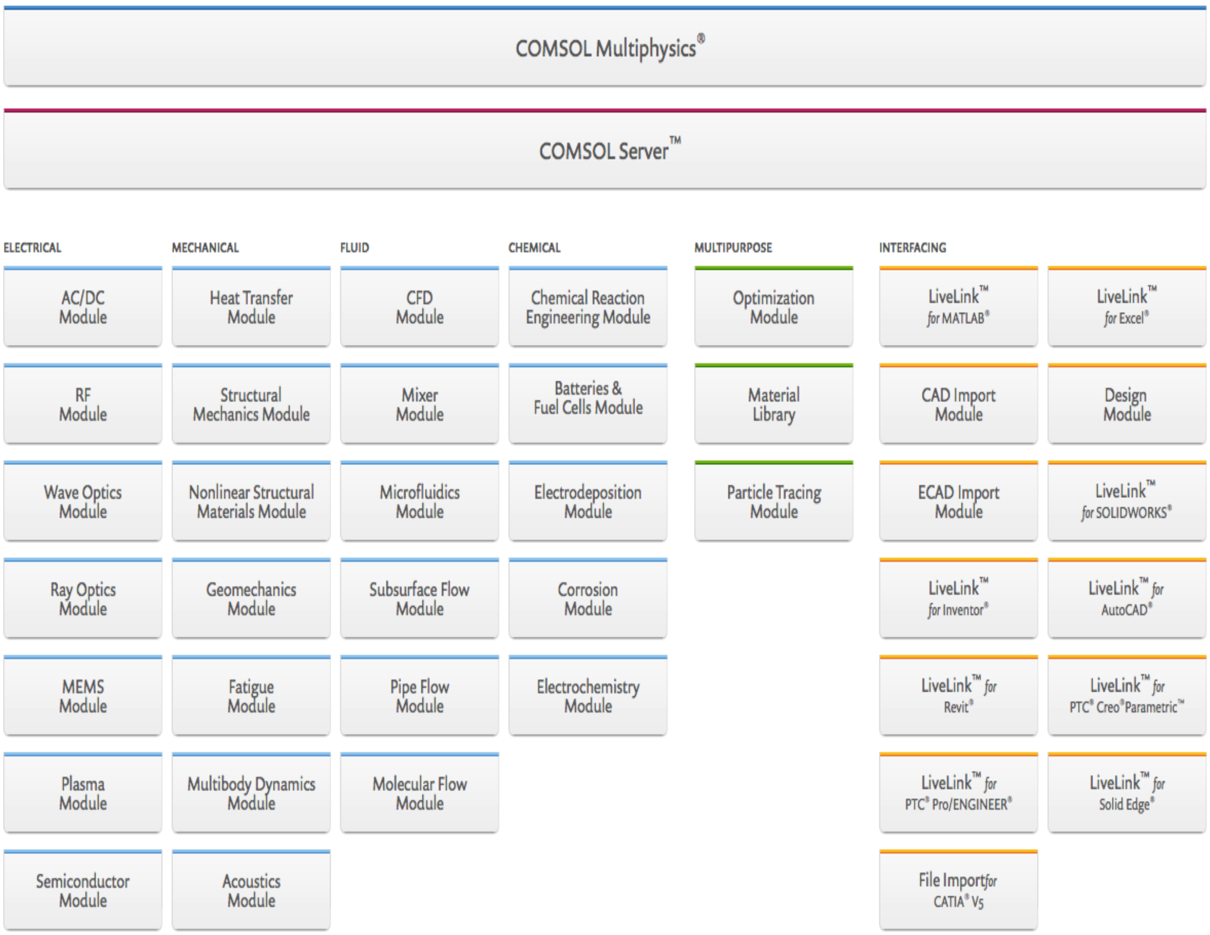

Figure 18 – Description of the modules of the program Comsol Multiphysics

The COMSOL Multiphysics package allows you to model problems from such areas as electrical engineering (low and high-frequency applications, geometric optics, plasma, semiconductors), mechanics (stress analysis, acoustics, thermal conductivity), hydrodynamics (laminar and turbulent flows, flows in porous media and for large numbers M), as well as chemistry (chemical reactors, corrosion, batteries and fuel cells).

3.2 Description of numerical experiments

To carry out numerical modeling, computerized (CT) or magnetic resonance (MRI) tomography data is used to determine the geometry of the problem.

We have carried out calculations of blood flow in the coronary arteries. Three cases of blood flow in a vessel without pathology and in a vessel with two types of blood clots were considered. Numerical calculation was performed using Comsol Multiphysics. For calculations, the method of finite difference elements was used. For calculating the dynamic characteristics of blood flow, the Navier – Stokes equations were used with a constant density and viscosity of the fluid (Newtonian fluid)[37]:

$$\rho \frac{\partial \vec{u}}{\partial t} + \rho(\vec{u} \cdot \vec{\nabla})\vec{u} = \vec{\nabla}[-pI + \tau] + \vec{f} \quad (3)$$

$$\frac{\partial \rho}{\partial t} - \left(\vec{\nabla} \cdot (\rho\vec{u})\right) = 0, \quad (4)$$

where ∇ is the operator nabla, ρ is the density (SI unit: , kg/m^3), p is pressure (SI unite: Pa), $\vec{u} = (u^1, \ldots u^n)$ is the velocity vector field (SI unit: m/s), τ – viscous stress tensor (SI unite: Pa), I – unit matrix, t – time (SI unit: s), $\vec{f}$ – volume force vector (SI unite: , H/m^3), in this model $\vec{f} = 0$.

Equation (4) is the continuity equation and represents the conservation of mass.

Equation (3) is a vector equation and represents the conservation of momentum.

$$\tau = \mu\,(\vec{\nabla}\vec{u} + \overrightarrow{(\nabla\vec{u})}^T) - \frac{2}{3}\mu\,(\vec{\nabla} \cdot \vec{u})I \quad (5)$$

where I is the unit matrix (tensor), S is the strain rate tensor, μ is the dynamic viscosity (SI unit: Pa · s), the last term in the expression for τ means volumetric expansion

In the two-dimensional approximation: $\vec{u}(\vec{r}, t) = \left(u_x, u_y\right), \vec{r}(x, y), p(x, y, t)$, for a viscous incompressible fluid, the problem is reduced to solving two-dimensional Navier-Stokes equations, which in the rectangular Cartesian coordinate system have the following form [37].

$$\frac{\partial u_x}{\partial t} + u_x \frac{\partial u_x}{\partial x} + u_y \frac{\partial u_x}{\partial y} = -\frac{1}{\rho}\frac{\partial p}{\partial x} + \nu \Delta u_x \quad (6)$$

$$\frac{\partial u_y}{\partial t} + u_x \frac{\partial u_y}{\partial x} + u_y \frac{\partial u_y}{\partial y} = -\frac{1}{\rho}\frac{\partial p}{\partial y} + \nu \Delta u_y \qquad (7)$$

$$div\vec{u} = 0 \qquad (8)$$

Here, $\Delta = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}, \nu = \frac{\eta}{\rho}$ −kinematic viscosity, $\rho - const.$

The initial condition for system (6)-(8) is the given velocity field $\vec{u}(t, \vec{r})$ of the fluid at t=0. The boundary condition is the condition of liquid sticking to the vessel walls $\vec{u}(t, \vec{r})_{\vec{r} \in L} = 0$. In addition, the velocity field at infinity must satisfy the boundary condition $\vec{u}(t, \vec{r})_{\vec{r} \to \pm\infty} = u_\infty$.

Equations (6) - (8) were used to find the velocity field (blood flow) with different geometry of the coronary vessels.

Figure 19 shows the structure of the coronary arteries of the heart.

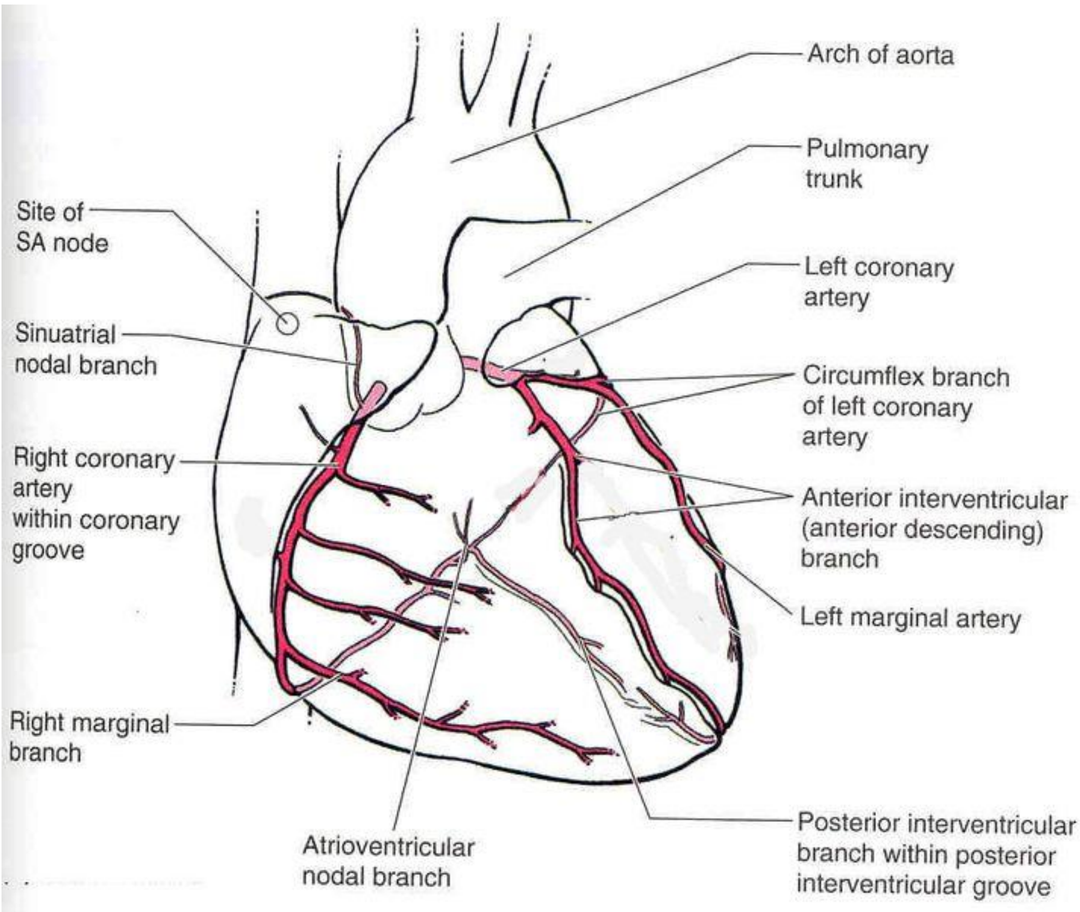

Figure 19 – Blood flow in the coronary arteries

Table 2 shows the typical geometric dimensions of the main myocardial arteries.

Table 2 – Diameter of the main subepicardial arteries

Name of the artery	Measurements on inanimate material, mm		Lifetime measurements, mm	
	Children	Adults	By M. Alpin (1975)	By A.A. Lillo-son (1978)
Trunk of the right coronary artery	0,8–2,5	2,2–6,8	2,3–4,5 3,2±0,6	2,7–6,0 3,3±0,07
The trunk of the left coronary artery	1,1–3,6	4,2–6,0	2,6–5,5 4,0±0,7	2,9–7,0 4,6±0,08
Trunk of the circumflex artery	0,7–1,3	0,5–3	1,7–4,4 3,9±0,7	2,0–5,5 4,6±0,08
Anterior interventricular artery	1,0–3,5	2,8–4,8	2,4–3,5 3,4±0,5	1,0–5,5 3,0±0,08
Posterior interventricular artery	0,7–1,3	1,0–3,0	n/d	1,0–3,0 1,9±0,04
Right marginal branch (in fig. A branch of a sharp edge)	n/d	n/d	0,8–2,7 1,7±0,6	1,0–3,0 1,8±0,05
Left marginal branch (in fig. Branch of blunt margin)	n/d	n/d	1,6–3,3 2,4±0,5	1,0–3,0 1,7±0,04
Diagonal branch (in Fig. 1st diagonal branch)	0,7–1,3	0,5–3,0	1,3–2,4 2,0±0,3	0,8–3,5 1,6±0,04

Both coronary arteries (left and right) originate at the mouth of the aorta.

More accurate metrics are given by A.A. Lilloson (1978). The metrics of vessels of cadaveric material are given for information and to confirm lifetime metrics.

The names of the arteries are given in accordance with the figure.

The table shows all the major myocardial arteries, to which a sensor can be inserted, and which are vital for feeding the heart muscle.

Blood flow, both in the heart and in the coronary arteries, can serve as a source of information for determining both their functional capabilities and their dysfunction. Below is an example of how the characteristics of blood flow can diagnose the presence of dysfunction of the simplest type - thrombus formation in the coronary arteries.

A detailed understanding of the laws of the ongoing processes gives a numerical simulation.

3.3 Results of numerical simulations of coronary hemodynamics

From the literary sources the right coronary artery without pathology was taken. Figure 20 shows the right coronary artery (RCA) and shows three segments of its main branch – R1 (proximal, upper, widest), R2 (medial, medium) and R3 (distal, terminal, narrowest).

We also took geometric data from Figure 20 and Table 3. We considered the element of the coronary artery 70 mm long and 2.7 mm in diameter.

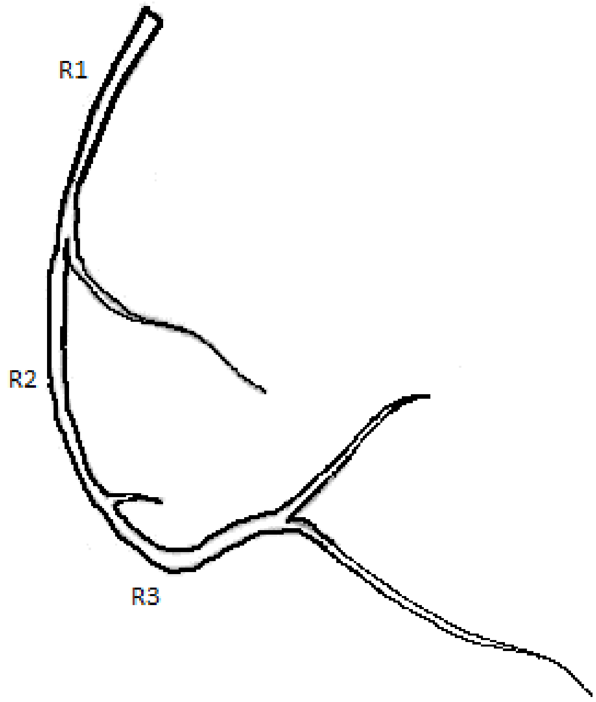

Figure 20 – Right Coronary Artery

Table 3 – The geometric dimensions of the coronary artery

	Right coronary artery		
	Proximal (proximal) part - R1	Medial (middle) part - R2	Distal (distant) part - R3
Average length, cm	2,7	3,6	2,9
Diameter, mm men / women	2,75±0,6 / 2,55±0,57	2,47±0,66 / 2,31±0,13	2,14±0,61/ 2,01±0,43

For the calculations, the triangular grid shown in Figure 21 was used.

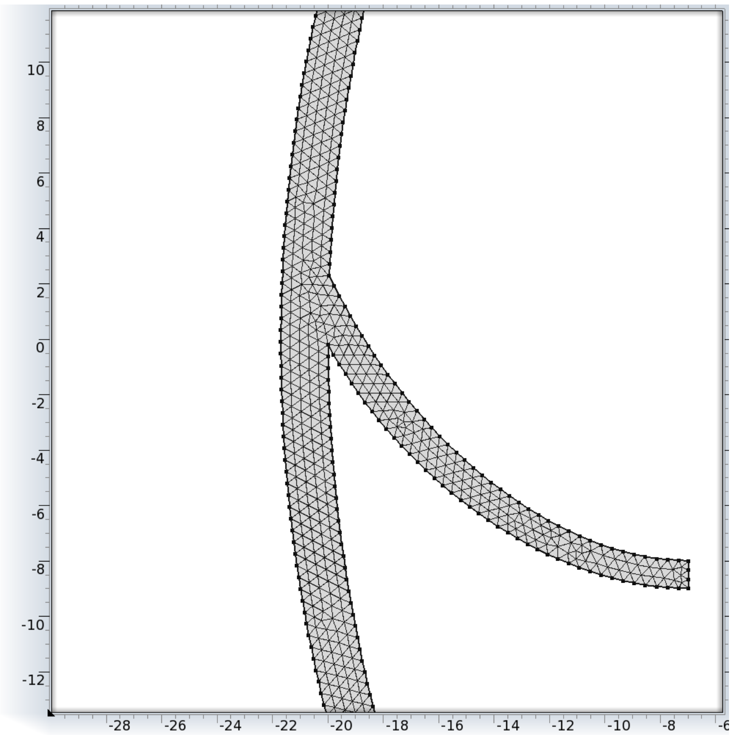

Figure 21 – View of a model of a plot of the coronary artery with a superimposed grid

The illustration shows the coronary artery with the outgoing vein. In Figure 21 are arranged horizontally - x, mm; vertically - y, mm. X, Y are the geometric dimensions of the artery, where x is the length, y is the width.

To solve the Navier – Stokes equation, we used boundary conditions for pressure in Torra, on the left border: P = 1 Torr. On the right border: P = 0 Torr. Selected pressure allows for the flow of blood with an amplitude of 10-20 cm / s which corresponds to the literature data

The pressure distribution along the selected area of the coronary artery without pathology for the time point corresponding to the maximum pressure at the left border is shown in Figure 22. From this figure it can be seen that the pressure monotonously drops from the left border to the right border.

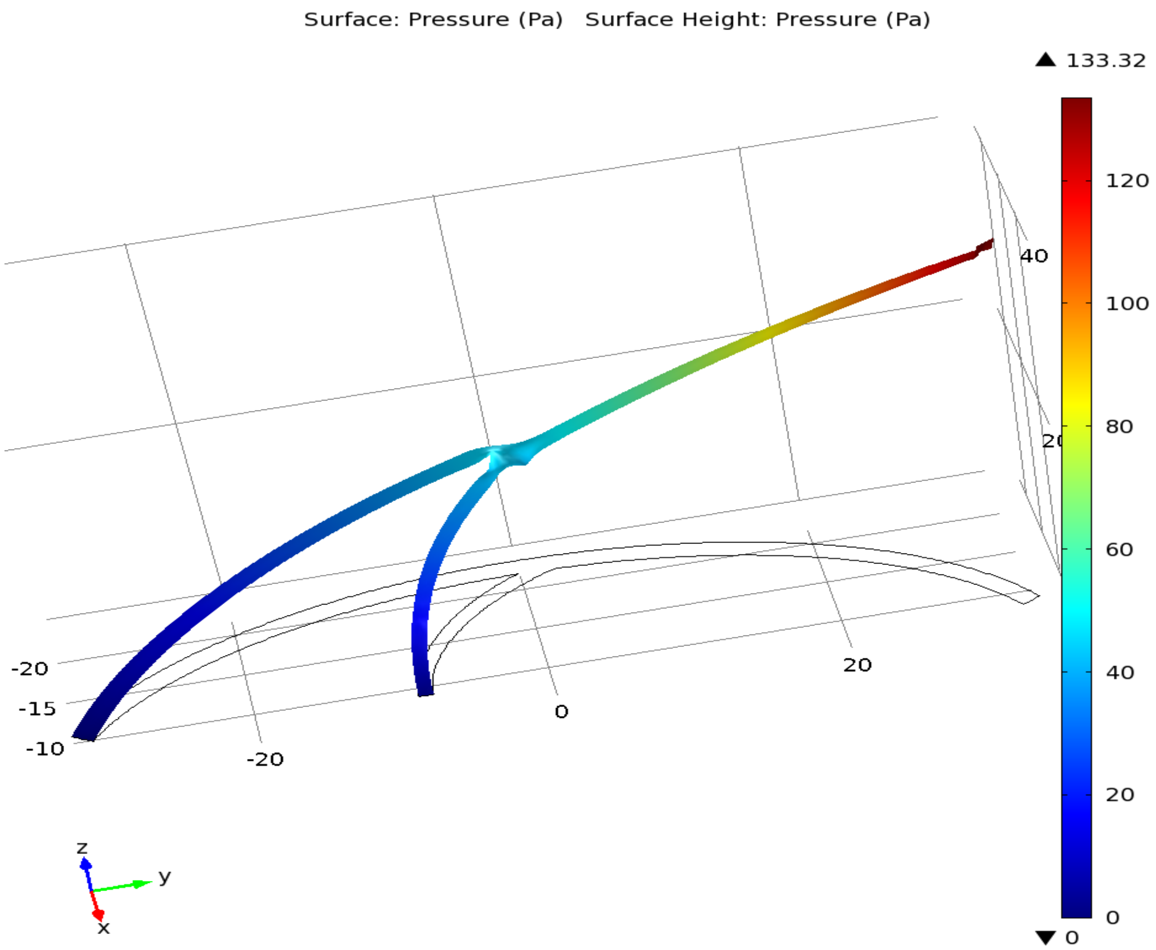

Figure 22 – The distribution of pressure at the site of the coronary artery

The axes (X, Y) of the coordinate system, reflecting the geometric dimensions of the co-trial (in mm), are shown in the lower left corner of the figure. The z axis shows the pressure in pascals.

The calculations, in this case, show that the ratio of pressure after stenosis to pressure before stenosis (FFR) is 0.99.

The change in the pattern of the rate of blood flow in the case of an artery without pathology is shown in Figure 23.

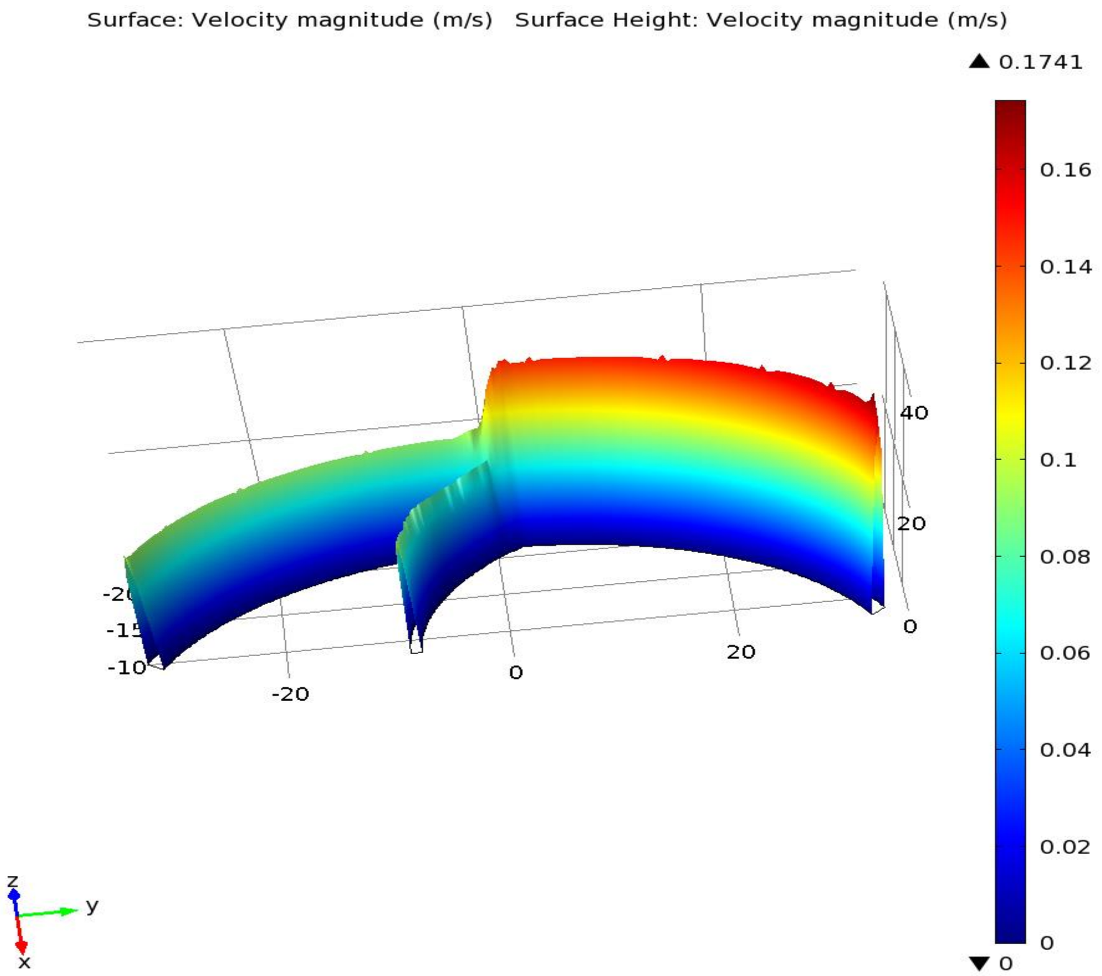

Figure 23 – Picture of the rate of blood flow in the artery in the case of normal

Similar calculations were performed for this part of the artery in the case of the presence of two different types of thrombus with a different lumen of the artery.

Coronary artery of the same parameters in the case of the first type of thrombus is shown in Figure 24.

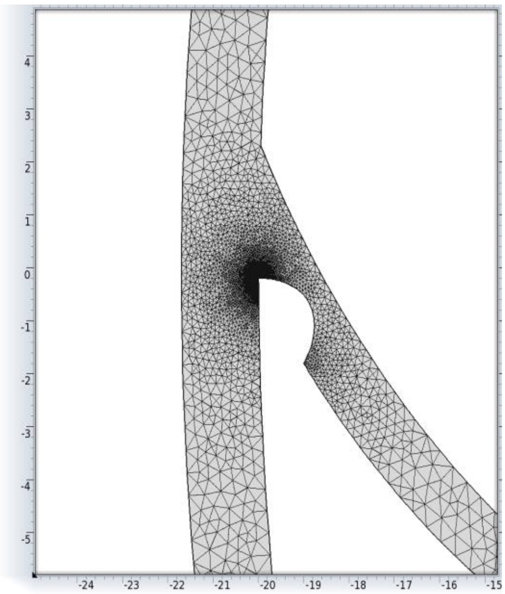

Figure 24 – View of a model of a coronary artery area in the case of the first type of thrombus.

The distribution of pressure on the artery site in the case of the presence of the first type of thrombus is shown in Figure 25.

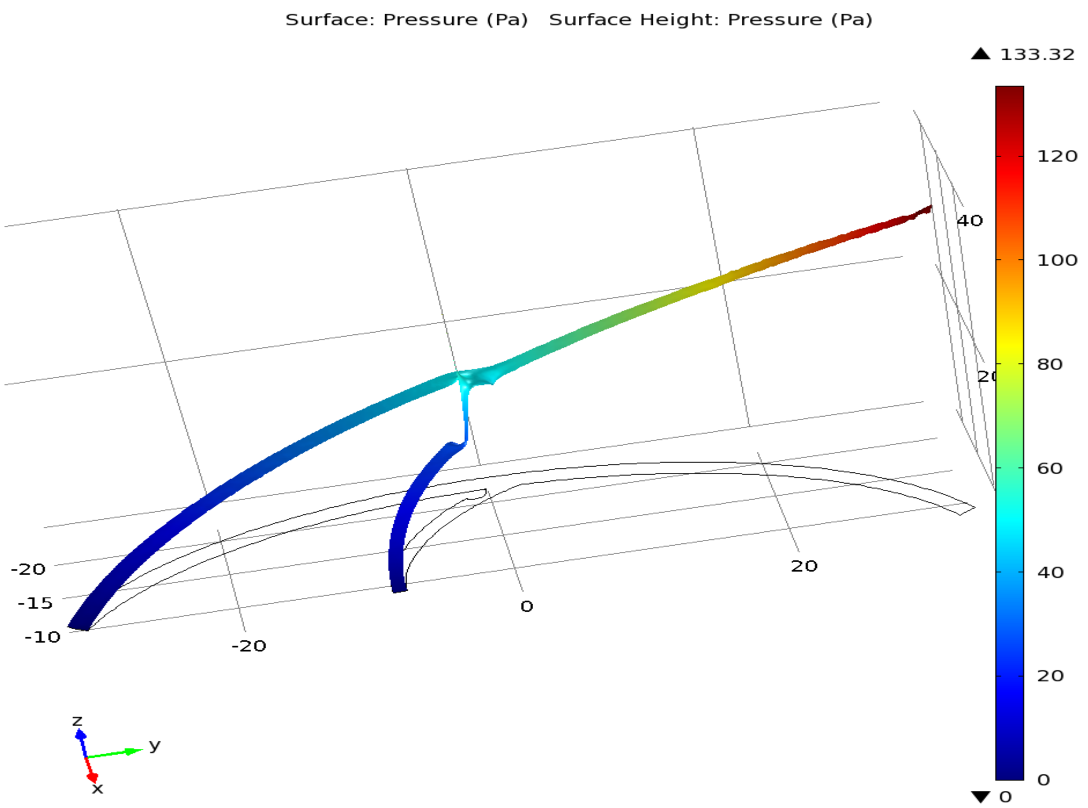

Figure 25 – The distribution of pressure in the area of the artery in the presence of the first type of thrombus

It can be seen from the figure that pressure before narrowing and after did not change much with respect to a case without pathology, but at the time of branching it decreased. The calculations, in this case, show that the ratio of pressure after stenosis to pressure before stenosis (FFR) is 0.90. Since this value is greater than 0.75, then surgical intervention to eliminate stenosis is not required.

The change in the pressure distribution in the arteries leads to a change in the pattern of the velocity of blood flow, which is shown for this point in time in Figure 26.

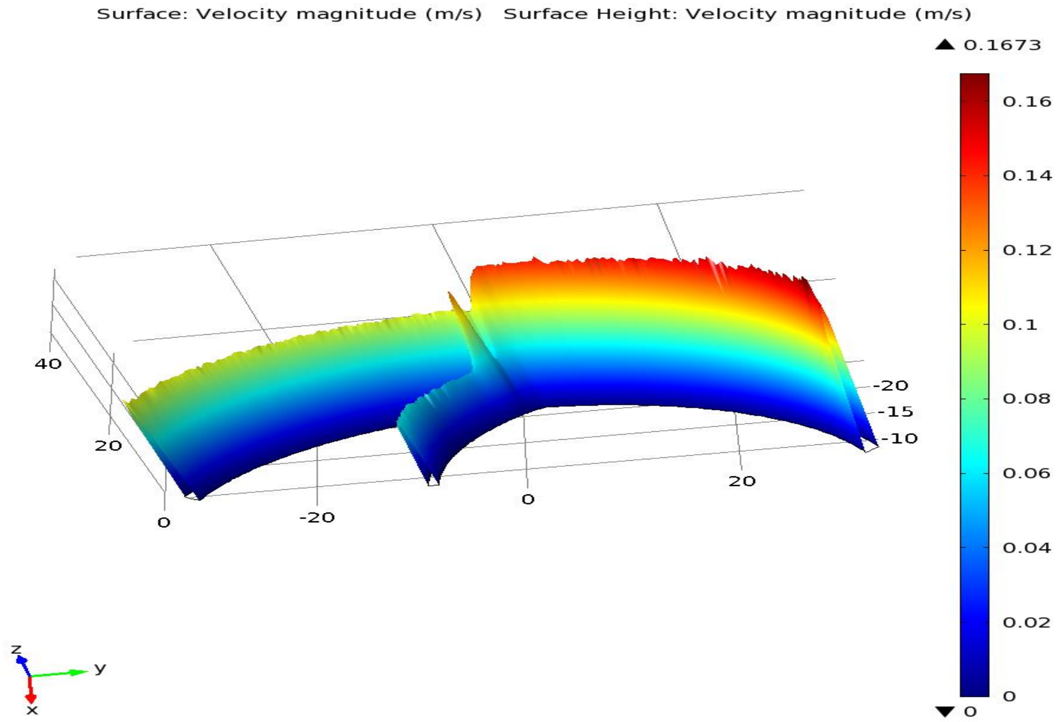

Figure 26 – Picture of the rate of blood flow in the artery in the presence of the first type of thrombus

As can be seen from the figure, the rate of blood flow increases at the site of arterial constriction. And before narrowing and after does not change relative to the norm.

Coronary artery of the same parameters in the case of the presence of the second type of thrombus is shown in Figure 27.

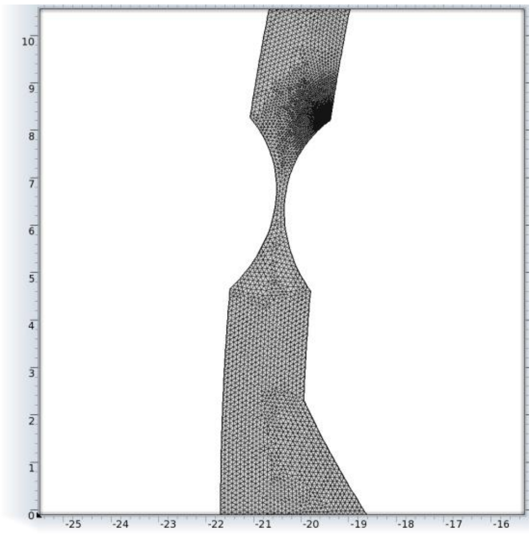

Figure 27 – View of a model of a coronary artery area in the case of a second type of thrombus with a superimposed grid

The distribution of pressure on the artery in the case of the presence of the second type of thrombus is shown in Figure 28.

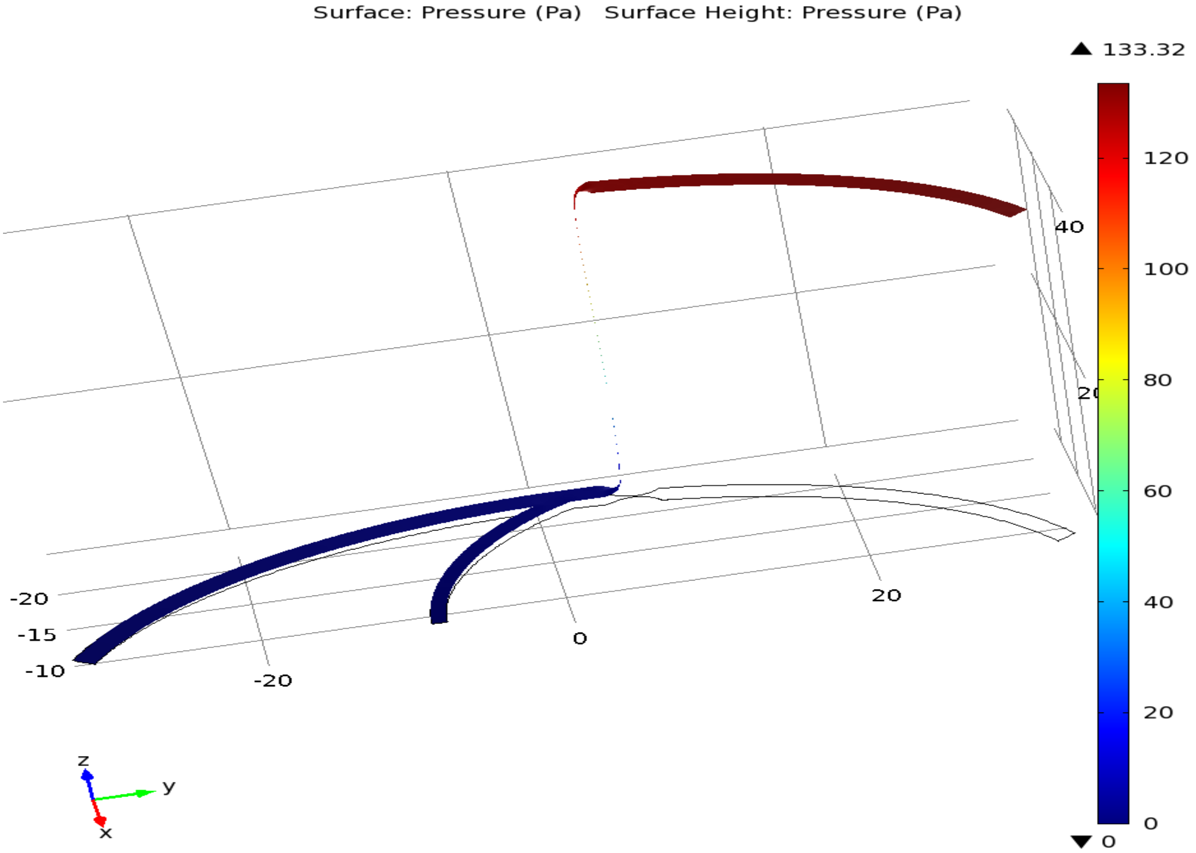

Figure 28 – Distribution of pressure in the area of the artery in the case of the presence of the second type of thrombus

It can be seen from the figure that, on the left side, the pressure before stenosis is increased relative to the case without pathology, and decreases at the site of stenosis and decreases after stenosis. The calculations, in this case, show that the ratio of pressure after stenosis to pressure before stenosis (FFR) is 0.65. Since this value is less than 0.75, surgical intervention is required to eliminate stenosis.

The change in pressure distribution in the artery leads to a change in the pattern of the velocity of blood flow, which is shown for this point in time in Figure 29.

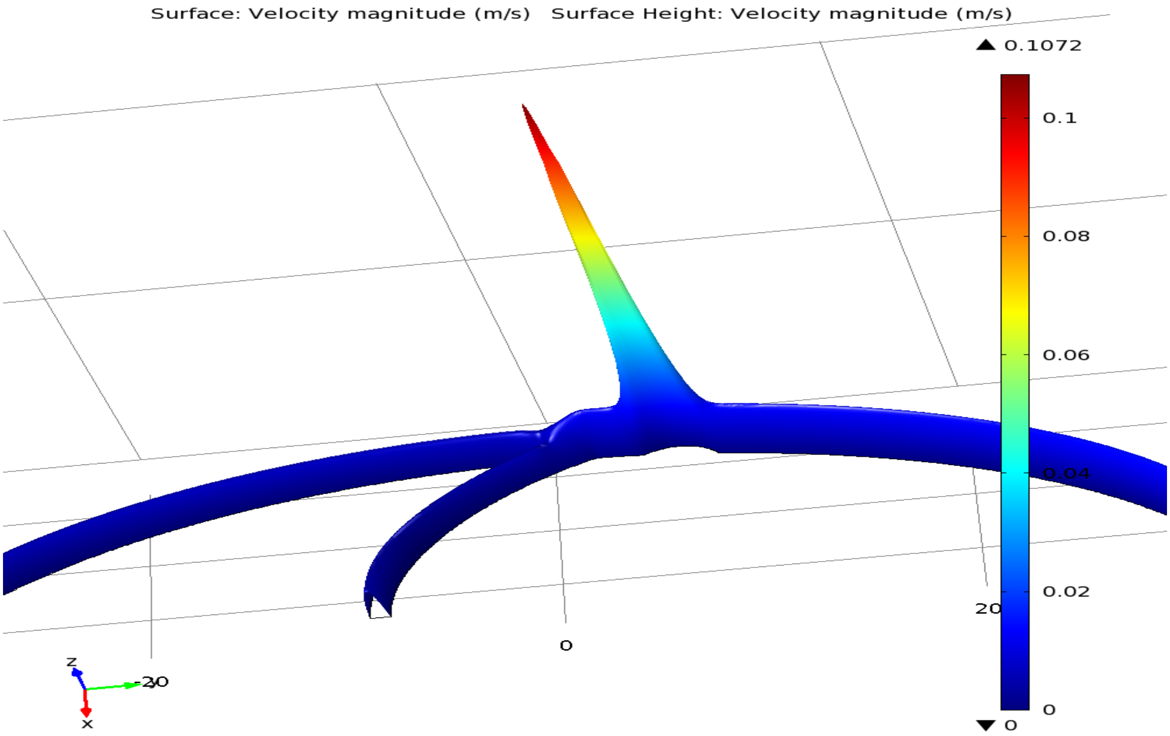

Figure 29 – Picture of the velocity of blood flow in the artery in the case of the presence of the second type of thrombus

As can be seen from the figure at the site of the artery narrowing, the rate of blood flow increases, and the rate of blood flow decreases before and after the narrowing.

We can calculate the pressure dependence in the coronary arteries before and after stenosis, the calculations used can be compared with experimental data and our calculated data. It is possible to draw conclusions about the need for surgical intervention in the presence of stenosis

CONCLUSION

The carried out goal of the research is particularly relevant today, when the number of cardiovascular diseases is steadily increasing. Furthermore, the fact that they frequently affect people of an increasingly younger age makes cardiovascular diseases the most important medico-social problem of public health. A mathematical computer simulation of blood flow in the coronary arteries of the heart and the modeling of hemodynamic processes of the affected vessels is an urgent scientific and practical task.

In accordance with the tasks assigned to this study:

– the electro-mechanical characteristics of the heart, the structure and dynamics of electrical and contractile impulses were studied;

– the method of reconstructing 3D images of the cardiovascular system from CT and MRI images was studied;

– a local mathematical model of coronary blood flow was developed;

– proposed an approach to a non-invasive diagnosis of pathology in the dynamics of the cardiac cycle based on the mathematical modeling of coronary blood flow was developed.

According to the obtained results, it can be concluded that the developed method of individualized numerical modeling of blood flow in the coronary arteries is quite satisfactory. It allows doctors to highlight the personal characteristics of the patient's coronary blood flow and can later be used to assess the indicator of regional blood flow reserve in a particular patient.

The results of the work are of great interest both for practical applications in physiology and medicine, and for theoretical studies, including the further development of the model and its integration with models of other systems of the human body.

The calculations performed are consistent with the data obtained during the direct measurement of the pressure difference in the arteries. The developed model of local hemodynamics of coronary arteries can later be used as a method for a non-invasive diagnosis of pathology in the dynamics of the cardiac cycle based on mathematical modeling of coronary blood flow

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APPENDIX A

Characteristics of heart rate

Table 4 – Characteristics of heart rate, corresponding to various disorders in the heart

Norm / pathology	Cardiac output - stroke volume (systolic discharge)	Electrocardiogram
Norm	60–70 ml of blood with a heart rate of 70–75 beats per minute	The heart rate is 60-100 / min. The normal index of the electrical axis of the heart is 40-70º. A tooth P – positive (is directed up), negative only in assignment of aVR. The width (duration of excitation) is 0.7–0.11 s, the vertical size is 0.5–2.0 mm. The PQ interval is the horizontal distance of 0.12–0.20 s. Q tooth - negative (below the contour). duration 0.03 s, negative height value 0.36–0.61 mm (equal to ¼ of the vertical size of the R-wave). R tooth - positive. The value has its height – 5.5–11.5 mm. S tooth – negative height 1.5–1.7 mm. QRS complex - horizontal distance 0.6–0.12 s, total amplitude 0–3 mm. T tooth – asymmetrical. Positive height 1.2–3.0 mm (equal to 1 / 8–2 / 3 teeth R, negative in aVR–lead), duration 0.12–0.18 s (longer than the duration of the QRS complex). ST segment – runs at the level of the isoline, length 0.5–1.0 s. U wave – height indicator 2.5 mm, duration 0.25 s.

Coronary heart disease (angina)	There may be some reduction in cardiac output.	Essential electrocardiographic signs of myocardial ischemia are various changes in the shape and polarity of the T wave. A high T–wave in the chest leads indicates either subendocardial ischemia of the anterior wall, or subepicardial, transmural, or intramural ischemia of the posterior wall of the left ventricle (although even normal, especially in young people, there is often a high positive T wave in the chest leads). Negative coronary T wave in the chest leads to the presence of subepicardial, transmural or intramural ischemia of the anterior wall of the left ventricle. Two-phase T waves are usually detected at the border of the ischemic zone and intact myocardium. Ischemic damage. The main electrocardiographic sign of ischemic myocardial damage is the displacement of the ST segment above or below the isoline. An elevation of the S–T segment in the chest leads to the presence of subepi-cardial or transmural damage to the anterior wall of the left ventricle. Depression of the S–T segment in the chest leads to the presence of ischemic damage in the subendocardial regions of the anterior wall or transmural damage to the posterior wall of the left ventricle.
Myocardial infarction	Varies within wide limits (decrease in	The main electrocardiographic sign of necrosis of the heart muscle is a

	minute volume), depending on the degree and place of necrosis.	pathological Q wave (with non-transmural necrosis) or a QS complex (with transmural heart attack). The appearance of these pathological signs in the thoracic leads of V1-V6 and (less often) in leads I and aVL indicate necrosis of the anterior wall of the left ventricle. The appearance of abnormal Q wave or QS complex in leads III, aVF and (less often) II is characteristic of myocardial infarction, posterior diaphragm (lower) sections of the left ventricle. Abnormal Q wave or QS complex in additional thoracic leads V7–V9 indicates necrosis of the posterior basal or posterolateral regions of the left-ventricle. An enlarged R–wave in V1, V2 may be a sign of posterior necrosis.
Valvular defects (stenosis, prolapse, insufficiency)	Varies widely (reduced minute volume), depending on the extent of the disease	With a slightly and moderately severe ECG defect, it may remain unchanged. In more severe cases, signs of left atrial hypertrophy are observed: – the appearance of a double-vertex P-wave in leads I, aVL, V4–V6, with the second vertex reflecting the excitation of the left atrium, exceeds the first, due to the excitation of the right atrium; – in lead V1 sharply increases in duration and amplitude of the second (negative) phase of the P wave; – as the degree of hypertrophy increases, the P–wave lengthens and exceeds 0.10 s.

		Signs of left ventricular hypertrophy: – an increase in the amplitude of the R-wave in leads V4–V6 and the S-wave in lines V –V; – in leads V4-V6, less often in V1 and aVL, the ST segment decreases, and the T wave changes its shape (its amplitude decreases, then it becomes isoelectric and, finally, two-phase and negative). With the development of severe pulmonary hypertension on the ECG, signs of right ventricular hypertrophy appear in the form of an increase in the R-wave amplitude in leads V1–V2, and the ECG becomes characteristic of both ventricular hypertrophy.
Cardiomyopathy	Reduced stroke volume in severe stages of the disease	Often in patients with hypertrophic cardiomyopathy, an abnormal Q wave can be detected on an ECG, which can imitate signs of myocardial infarction. In obstructive cardiomyopathy (subaortic muscular stenosis), ECG changes are in many ways similar to those in non-structural form. Signs of left ventricular hypertrophy are typical. Pathologically deep Q wave can be detected, usually in leads V4 – V6, I, aVL, less often - in leads III and aVF. The origin of this tooth in this disease is often associated with interventricular septal hypertrophy. A high R-wave and a deep Q-wave are not only in the left, but also in the right chest leads, which are also referred to as signs of septal hypertrophy. Very often, with this pathology, changes in the ST segment are revealed, it is

		either raised or lowered, as well as changes in the T wave, which can be inverted, deep. Pathological Q wave, changes in the ST segment and T wave are often forced to make a differential diagnosis of this disease with myocardial infarction. An example of infarct–like changes in this disease can be the patient K., 50 years old, presented in the ECG picture with a diagnosis of idiopathic hypertrophic subaortic stenosis, confirmed echocardiographically. On this ECG, one can see signs of left ventricular hypertrophy, in particular, an unusual (up to 35–40 mm) increase in the height of the R wave in leads V4 – V6 and marked changes in the myocardium, manifested in ST elevation in lead V2 and its depression in leads II, III , aVF, V4 - V6, as well as in the deep inversion of the T wave in leads I, II, aVL, V4 - V6. The deep Q wave in the aVL lead also attracts attention. These changes are very similar to the picture of myocardial infarction, but the absence of clinical manifestations and ECG dynamics over several months allowed them to be attributed to chronic changes in the hypertrophied left ventricle. For dilated myocardiopathy, a decrease in ECG teeth voltage, T wave inversion, pronounced Q wave, signs of atrial and ventricular myocardial hypertrophy, and various cardiac rhythm and conduction disturbances are considered typical.
Hypertension	60–70 ml of blood with a heart rate of 70–75 beats per minute	KG changes arising from arterial hypertension are the result of an increase in the left ventricle. In the early stages, left ventricular hypertrophy can occur

	There may be some reduction in cardiac output.	mainly in the septal area; in this case, the QRS loop will probably be oriented to 0 ° in the horizontal plane. From the point of view of the clinic, it should be emphasized that the ECG is associated with the severity of hypertension, the voltage of the QRS complex increases accordingly, the T wave becomes more negative and the segment depression. ST is more noticeable as the disease progresses..

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