**Ministry of Education and Science of the Russian Federation**
Federal Independent Educational Institution
**«NATIONAL RESEARCH TOMSK POLYTECHNIC UNIVERSITY»**

Research School of Chemical and Biomedical Technologies
Direction of training 12.04.04 «Biotechnical systems and technologies»

**MASTER'S THESIS**

| **Topic of the work** |
|---|
| **A device for rapid assessment of blood clotting**<br>**Прибор для экспресс-оценки свертываемости крови** |

UDC 615.47:616-072.85:616.151.5

Student

| **Group** | **Full name** | **Signature** | **Date** |
|---|---|---|---|
| 9DM8I | Iuliia D. Liushnevskaya | | |

Scientific Supervisor and Technical Advisor

| **Position** | **Full name** | **Academic degree, rank** | **Signature** | **Date** |
|---|---|---|---|---|
| Associate professor | Fedor A. Gubarev | PhD in Physics | | |

**ADVISORS:**

Section «Financial Management, Resource Efficiency and Resource Saving»

| **Position** | **Full name** | **Academic degree, rank** | **Signature** | **Date** |
|---|---|---|---|---|
| Associate professor | Ekaterina V. Menshikova | PhD in Philosophy | | |

Section «Social Responsibility»

| **Position** | **Full name** | **Academic degree, rank** | **Signature** | **Date** |
|---|---|---|---|---|
| Associate professor | Michael V. Gorbenko | PhD in Egeneering | | |

**ADMIT TO DEFENSE:**

| **Program supervisor** | **Full name** | **Academic degree, rank** | **Signature** | **Date** |
|---|---|---|---|---|
| Associate professor | Fedor A. Gubarev | PhD in Physics | | |

Tomsk – 2020

# Planned program learning outcomes

| Код результата | Результат обучения (выпускник должен быть готов) | Требования ФГОС, критериев и/или заинтересованных сторон |
|---|---|---|
| Профессиональные компетенции | | |
| P1 | Применять глубокие специальные естественнонаучные, математические, социально-экономические и профессиональные знания в инновационной инженерной деятельности при разработке, производстве, исследовании, эксплуатации, обслуживании и ремонте современной биомедицинской и экологической техники | Требования ФГОС (ОК-2, ОПК-2), Критерий 5 АИОР (п. 5.2.1), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P2 | Ставить и решать инновационные задачи инженерного анализа и синтеза с использованием специальных знаний, современных аналитических методов и моделей | Требования ФГОС (ОПК-1, 3; ПК- 1 – 4), Критерий 5 АИОР (п. 5.2.2), согласованный с требованиями международных стандартов EUR-ACE и FEANI |
| P3 | Выбирать и использовать необходимое оборудование, инструменты и технологии для ведения инновационной практической инженерной деятельности с учетом экономических, экологических, социальных и иных ограничений | Требования ФГОС (ОК-9, ПК-10, 14, 18). Критерий 5 АИОР (пп. 5.2.3, 5.2.5), согласованный с требованиями международных стандартов EUR-ACE и FEANI |
| P4 | Выполнять комплексные инженерные проекты по разработке высокоэффективной биомедицинской и экологической техники конкурентоспособной на мировом рынке | Требования ФГОС (ОК-2, 3; ПК-5 – 11, 14), Критерий 5 АИОР (пп. 5.2.3, 5.2.5), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P5 | Проводить комплексные инженерные исследования, включая поиск необходимой информации, эксперимент, анализ и интерпретацию данных с применением глубоких специальных знаний и современных методов для достижения требуемых результатов в сложных и неопределенных условиях | Требования ФГОС (ОК-2, 3; ОПК-5, ПК-1 – 4). Критерий 5 АИОР (пп. 5.2.2, 5.2.4), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P6 | Внедрять, эксплуатировать и обслуживать современное высокотехнологичное оборудование в предметной сфере биотехнических систем и технологий, обеспечивать его высокую эффективность, соблюдать правила охраны здоровья и безопасности труда, выполнять требования по защите окружающей среды | Требования ФГОС (ОПК-1, 2), Критерий 5 АИОР (пп. 5.2.5, 5.2.6), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| *Универсальные компетенции* | | |
| P7 | Использовать глубокие знания в области проектного менеджмента для ведения инновационной инженерной деятельности с учетом юридических аспектов защиты интеллектуальной собственности | Требования ФГОС (ОПК-2; ПК-14, 15). Критерий 5 АИОР (п. 5.3.1), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P8 | Владеть иностранным языком на уровне, позволяющем активно осуществлять коммуникации в профессиональной среде и в обществе, разрабатывать документацию, презентовать и защищать результаты инновационной инженерной деятельности | Требования ФГОС (ОК-1), Критерий 5 АИОР (п. 5.3.2), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P9 | Эффективно работать индивидуально и в качестве члена и руководителя команды, состоящей из специалистов различных направлений и квалификаций, с делением ответственности и полномочий при решении инновационных инженерных задач | Требования ФГОС (ОК-3, ОПК-3; ПК-3, 12, 13), Критерий 5 АИОР (п. 5.3.3), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P10 | Демонстрировать личную ответственность, приверженность и готовность следовать профессиональной этике и нормам ведения инновационной инженерной деятельности | Критерий 5 АИОР (п. 5.3.4), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P11 | Демонстрировать глубокие знание правовых социальных, экологических и культурных аспектов инновационной инженерной деятельности, компетентность в вопросах охраны здоровья и безопасности жизнедеятельности | Критерий 5 АИОР (п. 5.3.5), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |
| P12 | Самостоятельно учиться и непрерывно повышать квалификацию в течение всего периода профессиональной деятельности | Требования ФГОС (ОК-2, 4; ОПК-4), Критерий 5 АИОР (п.5.3.6), согласованный с требованиями международных стандартов *EUR-ACE* и *FEANI* |

**TASK FOR SECTION**
**«FINANCIAL MANAGEMENT, RESOURCE EFFICIENCY AND RESOURCE SAVING»**

To the student:

| Group | Full name |
|---|---|
| 9DM8I | I.D. Liushnevskaya |

| | | | |
|---|---|---|---|
| **School** | RSCBT | **Division** | |
| **Degree** | Master | **Educational Program** | 12.04.04 Biotechnical systems and technologies |

| **Input data to the section «Financial management, resource efficiency and resource saving»:** | |
|---|---|
| 1. *Resource cost of scientific and technical research (STR): material and technical, energetic, financial and human* | – Salary costs – 97785 rub;<br>– STR budget – 458730.7; |
| 2. *Expenditure rates and expenditure standards for resources* | – Electricity costs – 5,8 rub per 1 kW; |
| 3. *Current tax system, tax rates, charges rates, discounting rates and interest rates* | – Labor tax – 27,1 %;<br>– Overhead costs – 30%; |
| **The list of subjects to study, design and develop:** | |
| 1. *Assessment of commercial and innovative potential of STR* | – comparative analysis with other researches in this field; |
| 2. *Development of charter for scientific-research project* | – SWOT-analysis; |
| 3. *Scheduling of STR management process: structure and timeline, budget, risk management* | – calculation of working hours for project;<br>– creation of the time schedule of the project;<br>– calculation of scientific and technical research budget; |
| 4. *Resource efficiency* | – integral indicator of resource efficiency for the developed project. |
| **A list of graphic material** *(with list of mandatory blueprints):* | |
| 1. *Competitiveness analysis*<br>2. *SWOT- analysis*<br>3. *Gantt chart and budget of scientific research*<br>4. *Assessment of resource, financial and economic efficiency of STR*<br>5. *Potential risks* | |

| | |
|---|---|
| **Date of issue of the task for the section according to the schedule** | 03.02.2020 |

**Task issued by adviser:**

| Position | Full name | Scientific degree, rank | Signature | Date |
|---|---|---|---|---|
| Associate professor | Ekaterina V. Menshikova | PhD in Philosophy | | |

**The task was accepted by the student:**

| Group | Full name | Signature | Date |
|---|---|---|---|
| 9DM8I | I.D. Liushnevskaya | | |

**TASK FOR SECTION**
**« SOCIAL RESPONSIBILITY»**

To the student:

| Group | Full name |
|---|---|
| 9DM8I | I.D. Liushnevskaya |

| | | | |
|---|---|---|---|
| **School** | RSCBT | **Department** | |
| **Degree** | Master's degree | **Educational Program** | 12.04.04 Biotechnical systems and technologies |

Topic of the work

| **A device for rapid assessment of blood clotting** | |
|---|---|
| **Input data to the section «Social responsibility»:** | |
| 1. Characteristics of the object of study (substance, material, device, algorithm, method, working area) and its areas of application | The object of study is a prototype optical device for analyzing blood coagulation time. The device can be used to assess changes in the properties of biological fluids. |
| **The list of subjects to study, design and develop:** | |
| **1. Legal and organizational safety issues:**<br>1.1. Special legal norms of labor legislation<br>1.2. Organizational arrangements for the layout of the working area | 1. GOST 12.2.032-78 Occupational safety standards system (SSBT). Workplace while doing work while sitting. General ergonomic;<br>2. The Labor Code of the Russian Federation dated December 30, 2001 N 197;<br>3. GOST 31581-2012 Laser safety. General safety requirements for the development and operation of laser products;<br>4. GOST 31508-2012 Medical devices. Classification according to potential risk of use. General requirements;<br>5. GOST 12.2.049-80 Occupational safety standards system (SSBT). Industrial equipment. General ergonomic requirements. |
| **2. Industrial safety:**<br>2.1. Analysis of harmful and dangerous factors that can be created by object of study<br>2.3. Justification of measures to protect the researcher from the effects of hazardous and harmful factors. | 1. The increased gas contamination of the air of the working area;<br>2. Deviation of microclimate indicators;<br>3. Laser radiation;<br>4. Chemical active substances (plasma, whole blood);<br>5. Fire;<br>6. Electrical current. |
| **3. Environmental safety:** | Environmental pollutions:<br>1. Household waste;<br>2. Biological waste;<br>3. Medical waste.<br>The atmosphere is not polluted |
| **4. Safety in emergency situations:** | 1. Electricity<br>2. Fire safety |

| | |
|---|---|
| **Date of issue of the task for the section according to the schedule** | 03.02.2020 |

**Task issued by adviser:**

| Position | Full name | Scientific degree, rank | Signature | Date |
|---|---|---|---|---|
| Associate professor | Michael V. Gorbenko | PhD in Egeneering | | |

**The task was accepted by the student:**

| Group | Full name | Signature | Date |
|---|---|---|---|
| 9DM8I | I.D. Liushnevskaya | | |

**Ministry of Education and Science of the Russian Federation**
Federal Independent Educational Institution
**«NATIONAL RESEARCH TOMSK POLYTECHNIC UNIVERSITY»**

Research School of Chemical and Biomedical Technologies
Direction of training 12.04.04 «Biotechnical systems and technologies»

APPROVED BY
Program supervisor
_____ _____F.A. Gubarev
09.03.2020

**ASSIGNMENT**
**for the Master's Thesis completion**

In the form:

| **Master's Thesis** |
|---|

For a student:

| **Group** | **Full Name** |
|---|---|
| 9DM8I | Iuliia D. Liushnevskaya |

Topic of the work:

| **A device for rapid assessment of blood clotting**<br>**Прибор для экспресс-оценки свертываемости крови** | |
|---|---|
| Approved by the order of the Head (date, number) | |

| Deadline for completion of the Master's Thesis: | 03.06.2020 |
|---|---|

**TERMS OF REFERENCE:**

| | |
|---|---|
| **Initial data for work:**<br>*(the name of the object of research or design; performance or load; mode of operation (continuous, periodic, cyclic, etc.); type of raw material or material of the product; requirements for the product, product or process; special requirements to the features of the operation of the object or product in terms of operational safety, environmental impact, energy costs; economic analysis, etc.).* | The object of research is the method of correlation of digital speckle patterns for the analysis of blood coagulability.<br>The purpose of the work is to develop a laboratory prototype of an optical device for express analysis of blood coagulation time, which determines the coagulation time of whole blood by the non-contact optical method. |
| **List of the issues to be investigated, designed and developed**<br>*(analytical review of literary sources in order to elucidate the achievements of world science and technology in the field under consideration, the formulation of the problem of research, design, construction, the content of the procedure of the research, design, construction, discussion of the performed work results, the name of additional sections to be developed; work conclusion).* | 1. The working theory of digital speckle patterns correlation.<br>2. Estimation of the hemostatic system.<br>3. Schemes of experiments and procedure of the research.<br>4. Experimental data analyses.<br>5. Development of the laboratory prototype. |
| **List of graphic material**<br>*(with an exact indication of mandatory drawings)* | |

| **Advisors on the sections of the Master's Thesis** | |
|---|---|
| **Chapter** | **Advisor** |
| Section «Financial Management, Resource Efficiency and Resource Saving» | Ekaterina V. Menshikova |
| Section «Social Responsibility» | Michael V. Gorbenko |

| **Date of issuance of the assignment for Master's Thesis completion according to a line schedule** | 09.03.2020 |
|---|---|

**The task was issued by the Scientific Supervisor and Technical Advisor:**

| **Position** | **Full Name** | **Academic degree, rank** | **Signature** | **Date** |
|---|---|---|---|---|
| Associate professor | Fedor A. Gubarev | PhD in Physics | | 09.03.2020 |

**The assignment was accepted for execution by the student:**

| **Group** | **Full Name** | **Signature** | **Date** |
|---|---|---|---|
| 9DM8I | Iuliia D. Liushnevskaya | | 09.03.2020 |

**Abstract**

Master’s Thesis contains 83 pages, 14 figures, 25 tables, 46 references.

Keywords: blood coagulation, whole blood, optical coagulometer, coherent radiation, speckle pattern

The object of research is the method of correlation of digital speckle patterns for the analysis of blood coagulability.

The purpose of the work is to develop a laboratory prototype of an optical device for express analysis of blood coagulation time, which determines the coagulation time of whole blood by the non-contact optical method.

As a result of the study, the applicability of the method for the analysis of whole blood was practically confirmed, a data processing algorithm was developed that provides for automatic start-up of the device when a cell is detected in the measurement unit, a laboratory prototype design is developed.

**Contents**

## Introduction

The use of optical diagnostic methods in medicine to determine the main parameters and properties of an object is widely spread today due to the lack of physical contact of the device with the studied object and the harmlessness of low-intensity radiation for the body and biological fluids [1, 2]. The application of the digital correlation method for the analysis of speckle dynamics is widely used in materials science, medicine, chemistry, biology and other fields. Therefore, the development of new methods for the diagnosis of biological tissues using laser radiation is an urgent task for today. Changing the dynamics of speckles allows you to get information about the state of the medium and its optical properties [3-7].

If an object is illuminated by coherent radiation, then any changes in the structure of the object under observation will lead to a change in the speckles position. Therefore, the method of correlation of digital speckle patterns can be used to analyze the state of liquid biological media. Liquid media with low optical density is of particular interest, because they transmit optical radiation very well [7]. Blood is one of such medium.

Total coagulation time is an important parameter for assessing the patient's health status. The deviation of coagulation time from the norm may indicate the presence of diseases in humans. Particular attention should be paid to monitoring of the whole blood coagulation time during surgical interventions, after operations on the organs of the cardiovascular and central nervous system, organ transplantation, implantation, use of angioprotectors, antiplatelet agents, anticoagulants and fibrinolysis inhibitors [8]. An increase in blood viscosity can lead to thrombosis and a life threat to the patient. And an increase in coagulation time will lead to severe bleeding. Therefore, the development of a new optical device for continuous monitoring of blood coagulation time, which allows assessing the state of blood viscosity over several hours, is an urgent task.

In [9], the authors used the method of speckle pattern correlation to analyze the viscoelastic modulus of whole blood using software and a coherent radiation source.

The possibility of using the proposed method for analyzing the whole coagulation time of test plasma with a known coagulation time was shown in [10, 11].

Today, thromboelastographs and coagulometers are the most popular medical devices for determining the coagulation time of blood. These devices have disadvantages for continuous monitoring of blood coagulation time. Existing thromboelastographs analyze both blood plasma and whole blood. The volume of the test sample is 1.5 ml. However, this type of medical device has electrodes that are placed in the sample for examination. The electrodes must be cleaned, which takes a certain time. In this case, time is an important parameter for continuous monitoring of blood coagulation. The service life of the electrodes is reduces due to frequent cleaning. It is a significant drawback. In addition, the electrodes act by current or ultrasound on the test sample. It affects the coagulation process, which in this case does not proceed independently.

Optical coagulometers analyze only blood plasma, which makes it impossible to use these devices for continuous monitoring of blood coagulation time. Blood must first be placed in tubes with a coagulation blocker for analysis, then the blood cells must be separated from the plasma in a centrifuge. After this, the plasma is placed in a cuvette for measurement, in which the coagulability activator is previously added. In addition, a non-magnetic ball is placed in the sample for study; its motion is detected by the optical system. The movement of the ball can also affect the coagulation process, which means that the result will be relative. The optical coagulometer has a calibrated optical system that requires verification. And the optical elements wear out quickly, which is a drawback of the coagulometer.

The development of a new device for the analysis of prothrombin time of whole blood will help to carry out the analysis throughout the operation. To do this, the doctor must turn on the device, put blood in the tube, insert the tube into the device to analyze and display the result on the screen. Thus, the doctor will be able to receive operational information about blood coagulation throughout the operation. One analysis will take only 3 minutes, while the analysis with the help of widely used thromboelastographs takes from 20 to 40 minutes.

## 1. The working theory of digital speckle patterns correlation, obtaining and processing information

Digital pattern correlation is an optical method that allows non-contact measurements of the materials and substances deformations. The method is based on measuring the displacement of the speckle structure and the shape created on the surface of the material. When coherent radiation illuminates a rough surface, glare, scattered from the object mix and form a speckle pattern. If an object under observation moves, changes in the spatial picture occur accordingly. When measuring these changes, it is possible to determine the displacement of the object. In addition, the proposed method can be used to analyze the state of liquid biological media. Liquid media with low optical density are particular interest, because they transmit optical radiation well [12].

The method of correlation of laser speckle patterns is an optical method by which to study the dynamics of processes is possible: such as displacement [13, 14] structural changes and speed [15], mechanical tension [16]. In biomedicine, speckle methods have found application for heart rate measuring [17], microvascular blood flow velocity [18], bacterial growth activity [19], and other tasks. The advantage of the methods is the lack of contact with the test sample.

Correlation coefficient is used as a characterizing speckle changes parameter, which reflects the ratio of two speckle patterns at the first and second moment of time. The Pearson correlation coefficient given in Formula 1 is usually used.

$$C=\frac{\left\{\sum_{i=1}^{n}\sum_{j=1}^{m}[f(x_i,y_i)-\bar{f}]*[g(x_i,y_i)-\bar{g}]\right\}^2}{\sum_{i=1}^{n}\sum_{j=1}^{m}[f(x_i,y_i)-\bar{f}]^2*\sum_{i=1}^{n}\sum_{j=1}^{m}[g(x_i,y_i)-\bar{g}]^2} \quad (1)$$

where $\bar{f}$ – average intensity (initial) of speckle pattern;

$f(x_i, y_i)$ – speckle intensity with coordinates $x_i, y_i$;

$\bar{g}$ – average intensity obtained after moving;

$g(x_i, y_i)$ – speckle intensity after moving.

The main requirements for calculating the correlation coefficient formula are reliability, noise immunity, and calculation speed. It should be noted that the location

of the maximum correlation coefficient is detected with an accuracy of ± 0.5 pixels. Correlation coefficients are selected the maximum value to perform their interpolation in increments of 0.01 pixel. Thus, a more accurate location of the maximum correlation coefficient is found.

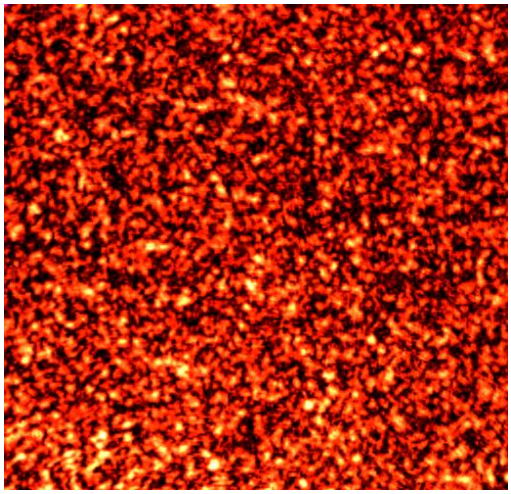


Figure 1 – Digital laser speckle pattern

When a laser illuminates a rough surface, light is scattered at every point on the surface. Therefore, the scattered light from different points on the object is received at all points in space. The amplitude and phase of coherent light are different, and their distribution is irregular. The complex amplitudes of the main light waves from elements of a small area on a rough surface are superimposed on each other, forming a certain statistical distribution. Due to the sufficiently large scattering of the transparent object, the contrast of the laser speckle is high, and the size of the speckle is determined in accordance with the nature of the optical path. The speckle field can be divided into two types according to the optical path: formed by propagation in free space (also called objective speckle), and by forming lenses (also called subjective speckle).

When monochromatic laser radiation passes through a glass plate with a rough surface, at a certain distance it can be seen that large and small bright spots are distributed on an almost total dark background on the observation plane. If the observation plane moves in the direction of the optical path, the spot size will change. If you change the spot area of the laser radiation on the glass surface, the speckle size

will also change. The size of these speckles is different, it refers to its statistical average and its change can be described by the correlation function.

## 2. Application of the method of digital speckle patterns correlation in biology and medicine

### 2.1 Analysis of bacterial growth

In [20], the authors use dynamic speckle estimation to analyze the growth rate of the bacteria colony. The experimental setup was used for experiments, which consists of a sample illuminated by a laser diode, the camera that records speckle patterns and transfers it to a computer for processing. As a result of the experiments, data were obtained on various degrees of activity of bacteria growing. Thus, a possible assessment of the bacteria growth rate has been shown. Published results can be used to control the quality of possible contaminated samples.

In [21], the authors show the possibility of using the method of correlation of digital speckle patterns for the detection of bacteria in food. Different variations of the correlation coefficient reflect a different number of bacteria. The threshold value of the correlation coefficient has been established, which corresponds to the minimum number of bacteria that can be detected. Thus, the proposed method can be used to control the quality of canned products. In this case, for the control of food products does not require microscopic analysis in the laboratory.

The authors of [22] used a changing of the speckle pattern intensity to estimate the rate and intensity of bacterial growth. As a result of the growth of bacterial colonies on the surface, the speckle pattern and the behavior of the resulting image will change. The time function is measured in order to detect and evaluate changes in the number of bacterial colonies. Thus, the rate of bacterial activity can be detected much earlier than using the standard method. It is shown that with an increase in the number of bacteria, the detected signal increases. In addition, the presence of bacteria can be detected after 2 hours. The authors propose using the method for express quality control of food products and for assessing the quality of the effect of antibiotics on bacterial colonies.

### 2.2 Blood flow assessment

The authors of [23] say that blood microcirculation disorders play an important role in the pathogenesis of various diseases. Thus, the registration of microcirculation disorders can provide grounds for determining the disease. Diseases of central hemodynamics are accompanied by changes in the blood microcirculation system. Thus, early detection of changes in the vessels allows predicting deviations in the general physical condition and human health. The experimental sensor for measurement consists of a semiconductor laser with a wavelength of 650 nm, a diaphragm and a collecting lens. The resulting scattered signal is transmitted through a multimode fiber to a computer. The developed setup allows daily monitoring and determination of blood flow velocity in the vascular bed.

The authors of [24] use the laser speckle pattern method to determine the external and internal diameter of the vessel of the rat cerebral cortex. For experiments, a white rat under anesthesia was used. The abdominal cavity was illuminated by a laser diode with a wavelength in the near infrared range. Scattered speckle structures were recorded using a CMOS camera. The obtained pictures were processed, the diameter of the vessel was calculated, and the obtained measurement errors were smoothed out. When assessing the diameter of the vessel, it was found that when measuring the thickness of the vessels, the number of speckle structures formed affects the estimation of blood flow velocity. Thus, it is recommended to evaluate on vessels of the same diameter. Blood flow velocity depends on whether the diameter of the channel changes or is it constant. The dependence of the flow velocity on the density of speckle structures has not been established.

In [25], the possibility of using the laser speckle-fluorography method to assess the speed and quality of the eye blood vessels was shown. The authors of [26] showed that using the method of correlation of laser speckle patterns, it is possible to estimate the diameter of the eye vessels. However, for the study, drugs were used to expand the pupil for better visualization. In addition, the authors show that this method allows to determine the speed of blood flow in the vessel and suggest the presence of diseases of the circulatory system.

### 2.3 Blood coagulation test

Effective blood coagulation is a key physiological process for maintaining hemostasis and preventing uncontrolled blood loss after injury. Disorders of coagulation with improper treatment can cause excessive hemorrhage, leading to organ failure, and increase the risk of mortality by five times in hospitalized patients. On the other hand, excessive clotting can lead to life-threatening thrombotic conditions, such as deep vein thrombosis, pulmonary embolism, myocardial infarction or stroke. Based on a coagulation defect, clinical management protocols include blood transfusions to manage impaired coagulation and prevent dangerous blood loss, or the introduction of anticoagulants to prevent thrombotic conditions. To determine the correct transfusion strategy or to allow effective dosing of the anticoagulant, an accurate assessment of the patient's coagulation state is crucial.

In [27] the authors developed a handheld LSR sensor to quantify the patient's prothrombin time by analyzing laser speckle patterns arising from a sample drop. of blood mixed with thromboplastin reagent shown in Figure 2. The LSR sensor measured the viscoelastic modulus G of a blood clot at a frequency of 5 Hz based on temporary changes in the intensity of speckle structures trapped during blood coagulation. Figure 3 shows the change in G (t) measured with LSR after adding thromboplastin reagent in two patient samples: a patient with prothrombin time within the normal range (blue solid line) and a patient on coumadin therapy with an increased prothrombin time (red dotted line). For a normal patient, a constant low G value observed during the early phase of coagulation (t <12 s), followed by a rapid increase in G, observed from 12 to 34 seconds, due to the conversion of soluble fibrinogen to fibrin and the initiation of a fibrin-platelet clot. In the plateau phase of the G (t) curve (> 34 s), no significant change in G was observed, which indicates the completion of the clot formation process. The prothrombin time measured for a normal patient was 12 s. On the other hand, for a blood sample obtained from one patient receiving coumadin therapy, G remained at a constant low level for ~ 47 seconds after activation of the tissue factor and stabilized to a higher G value by ~ 90 seconds. The prothrombin time measured by curve G for a patient treated with

coumadin was 51 s. The delay in increasing G for a patient receiving coumadin therapy can be explained by a delay in converting fibrinogen to fibrin, since coumadin is well known to inhibit the synthesis of the active form of vitamin K-dependent procoagulation factors, such as factors II, VII, IX, and X, which are necessary for fibrin catalysis. In addition, we observed that the modulus value of the plateau of the G (t) curve was significantly lower in the patient treated with coumadin compared to the normal patient, which can also be attributed to the inhibited formation and polymerization of fibrin, which, in turn, probably reduces the reflected bunch stiffness.

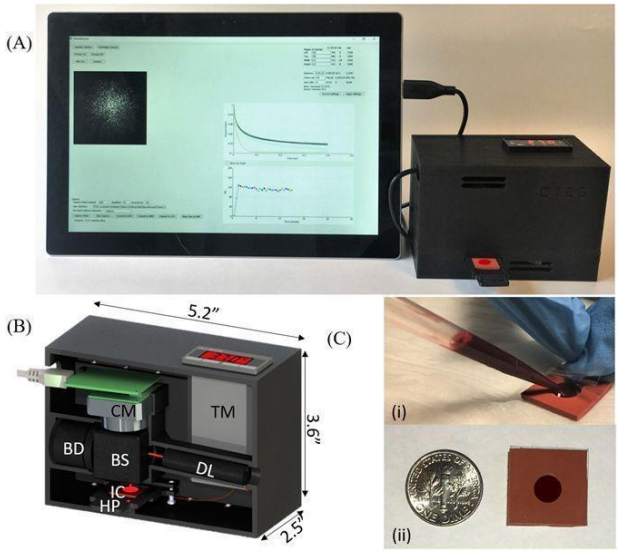



Figure 2 – Coagulation sensor based on LSR: (A) Photograph of the handheld sensor and compatible tablet interface with the window surface, (B) Computer circuit configuration of the optical and mechanical device.

Light from a 690 nm diode laser (DL) was focused (spot size 100 μm) with a lens on a disposable test cartridge (IC) containing 40 μl of whole blood, activated thromboplastin. Cross-polarized laser speckle images were obtained with a 180° backscattering geometry using a beam splitter (BS) using a USB CMOS camera (CM) equipped with an optical imaging system, consisting of a linear polarizer, aperture 500 microns and f 9 mm focusing lens. The beam retraction (BD) resets the laser beam passing through the beam splitter (BS). A miniature heating element (HP), temperature controller (TM) and a special pan for cartridges were embedded in the handheld sensor. The captured speckle patterns were transferred to the Microsoft

Surface TM tablet computer for further processing. (C) For the manufacture of whole blood droplets (40 μl), inexpensive test cartridges were made by laser cutting a silicone base with a transparent polycarbonate film

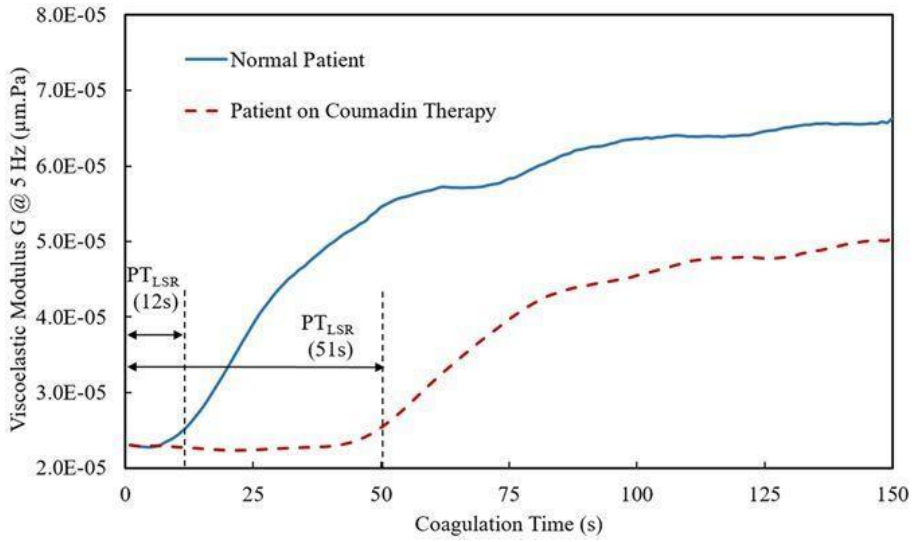



Figure 3 – The dependence of the viscoelastic modulus of time

In [28], the authors investigate the fractality of speckle patterns generated by blood in the process of coagulation under illumination by laser diodes with four wavelengths. The purpose of using laser diodes with several wavelengths is to study the optimal wavelength from which one can estimate the fractal size of speckle patterns with the greatest response to the progress of the coagulation process in the blood. Figure 4 shows the basic optical system used to detect incoherent transmission patterns and speckle patterns. Light from a white light source and LEDs with wavelengths of 450 nm, 532 nm, 650 nm and 780 nm, passes through two polarization filters (PF 1) and (PF 2), and then illuminates a layer of blood ~ 220 μm thick. The two polarizing filters is to control the intensity of light illuminating a layer of blood. All light sources used in this study are randomly polarized. Therefore, first linearly polarized light is extracted from randomly polarized light using PF 1, and then its intensity is adjusted using PF 2. In the work, the plane is not adjustable The polarization plane of the illuminating light is not regulated, but two polarization filters are used. The transmitted light from the blood layer passes through the camera lens, and then enters the microscope, which has an increase of 180. This increase was previously confirmed as the optimal increase for detecting the structure of platelet

aggregation and fibrin network. A personal computer (PC) is used to analyze image data and display the FD and AD cards of the subject.

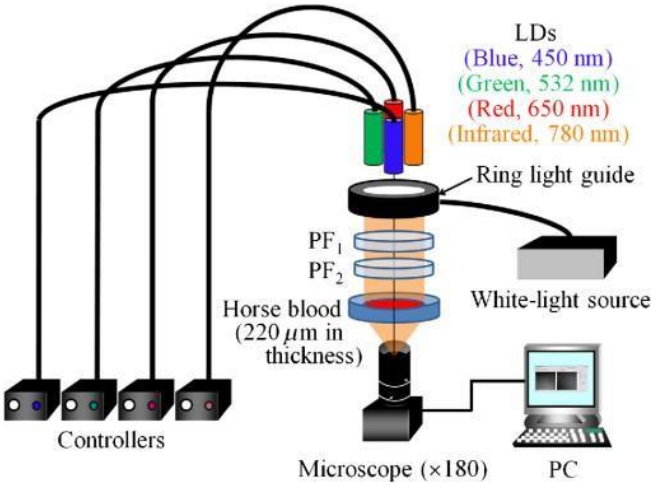



Figure 4 – Schematic diagram of the optical system for detecting non-coherent transmission models and speckle structures

Thus, the work investigated the fractality in combination with the dynamic characteristic of the speckle structure observed in the process of blood coagulation. First, FD patterns of speckles generated by a horse's blood layer were estimated by illuminating LD with four wavelengths, and it was shown that the speckle pattern fractality increases in accordance with platelet aggregation and fibrin network growth. This fact suggests that the fractality of the speckle pattern reproduces the process of blood coagulation as well as in the case of incoherent pictures. The disadvantage of FD is that it reduces the spatial resolution of the resulting blood coagulation map compared to the original picture. A possible solution to this problem is to use a high-resolution CCD camera. Then, the dynamic characteristic of movement in the blood layer during the coagulation process was investigated and it was confirmed that the blue and green LEDs reliably reflect the blood coagulation process. The most serious problem in evaluating AD was the influence of the noise included in the speckle pattern. This problem can be solved with a highly sensitive image sensor.

## 3. Estimation of the hemostatic system

### 3.1 Methods for the estimation of the hemostatic system

There is a method of assessing the parameters of blood coagulation using coagulation analyzers, most of which are measured optically or mechanically, or uses both methods. The purpose of both methods is to determine the end of the coagulation process. For example, the serially available coagulometer Minilab 70 in Figure 5. Using this device, it is possible to measure the clotting time of blood plasma. The device allows you to determine the speed of the returning of the nonmagnetic ball by the optical sensor. The mechanical coagulation analyzer is traditional optical analyzer which has following disadvantages: the device circuit is relatively complex, it is difficult to automate, low sensitivity, relatively many measurable indicators, etc. But due to the presence of possible anomalous optical properties of the sample, insufficient container cleanliness and other factors, the accuracy of the optical analyzer is worse than mechanical.


Figure 5 – Optical coagulometer «Minilab 701»

In addition to mechanical and optical methods for studying the process of blood coagulation, scientists use the method of determining changes in electrical conductivity. In [8], a method for assessing the functional state of the hemostasis system using electric current is proposed. Venous blood is collected by the method commonly used in coagulation, directly into a thermostated fluoroplastic cuvette heated to 37°C, electrodes are immersed in a cuvette and the electrical conductivity of an alternating current with a frequency of 200 Hz is measured, noting the time elapsed from the beginning of the blood sampling to the beginning of the study, a

continuous registration and recording of indicators (electrocoagulogram), using a printer or other recording device connected to the device. The recording duration varies from 15 to 100 minutes. The amplitude and chronometric indices characterizing the state of the hemostasis system are determined and analyzed according to the obtained graphic image. In this method, there is no mechanical effect on the object of study, which reduces sensitivity, but the method is a contact one.

One of the most widely accepted thromboelastographs is shown in Figure 6.

Figure 6 – Thrombelastograph

Comparing the presented methods, one can note the advantages and disadvantages of each of them. Firstly, the coagulometer analyzes the prothrombin time of only blood plasma. For analysis, it is necessary to separate the blood plasma from the formed elements in a centrifuge for 20 minutes. This not only increases the analysis time, but also requires a centrifuge in the laboratory to conduct the analysis. Secondly, for analysis, non-magnetic balls are placed in the sample cuvette. Thus, the coagulation process no longer proceeds on its own, which possibly affects the quality of the results. The optical system of the coagulometer requires regular adjustment. The sample volume for the study is 30 μl.

A thromboelastograph analyzes whole blood; this does not require a centrifuge in the laboratory. For analysis, electrodes are placed in a cuvette with blood. For the next study, they must be cleaned or replaced. This complicates the experiment and

increases its cost. The volume of the sample for study by elastography is 2 ml. The analysis is carried out within 20 minutes. Thus, thromboelastograph has consumables.

Analyzing the advantages and disadvantages of two popular methods used to analyze the coagulation system, we can say that both devices analyze the hemostasis system. However, thromboelastography can be used in surgery to analyze blood coagulation. While the coagulometer can only be used in the laboratory. This difference is very important, since the device developed in this work will be used for continuous monitoring of the hemostatic system.

Total coagulation time is an important parameter for assessing the patient's health status. Deviation of coagulation time from the norm may indicate the presence of diseases in humans. Particular attention should be paid to monitoring the total blood coagulation time during surgical interventions, after operations on the organs of the cardiovascular and central nervous system, organ transplantation, implant placement, the use of angioprotectors, antiplatelet agents, anticoagulants, fibrinolysis inhibitors [8]. An increase in blood viscosity can lead to thrombosis and a life threat to the patient. Therefore, the development of a new optical device for continuous monitoring of blood coagulation time, which allows assessing the state of blood viscosity for several hours, is an urgent task.

The method of low-frequency piezotromboelastography is based on recording changes in the resistance of the medium under investigation by the resonant oscillation of the resonator needle, which is mounted on the piezoelectric element. Native blood in a volume of 0.45 ml is placed in a cuvette for research, located in a thermostat, into which the resonator needle is lowered. A useful signal is the difference in the amplitudes of the oscillations of the needle in air and in a liquid. The electromechanical path is controlled by the measuring circuit of the recorder unit. All calculations, the output of graphs and research parameters, as well as the control of the operation of the device are performed by the processor. The processor uses a specialized computer program. The main measuring element is a precision piezoelectric sensor. The volume of the test blood is 0.45 ml, it is selected empirically and contains the minimum concentration of all factors involved in the studied process

of hemocoagulation and fibrinolysis. In this volume, their real ratio is maintained, reflecting that in vivo [8].

The method of low-frequency piezotromboelastography is implemented in the hardware-software complex for clinical diagnostic studies of the rheological properties of blood ARP-01M Mednord (piezoelectric thromboelastograph), which is shown in Figure 7. Today ARP-01M Mednord is the only Russian thromboelastograph competition to foreign devices.


Figure 7 – Piezoelectric thromboelastograph ARP-01M "Mednord"

ARP-01M "Mednord" allows you to conduct a comprehensive study of all components of the hemostatic system in real time directly at the patient's bedside. This device allows you to conduct research using native blood without the use of various reagents and reagents. This allows the specialist to receive useful information from the first second of the study and to avoid “lag-time”, as well as significantly reduce the cost of the study [8]. An example study is presented in Figure 8.

The method of low-frequency piezotromboelastography allows you to evaluate all stages of the fibrinogenesis process in native blood [8]:

- contact activation;
- adhesion, aggregation, sedimentation;
- thrombosis;
- gelation;
- lateral assembly of fibrin;

- stabilization;
- lysis.

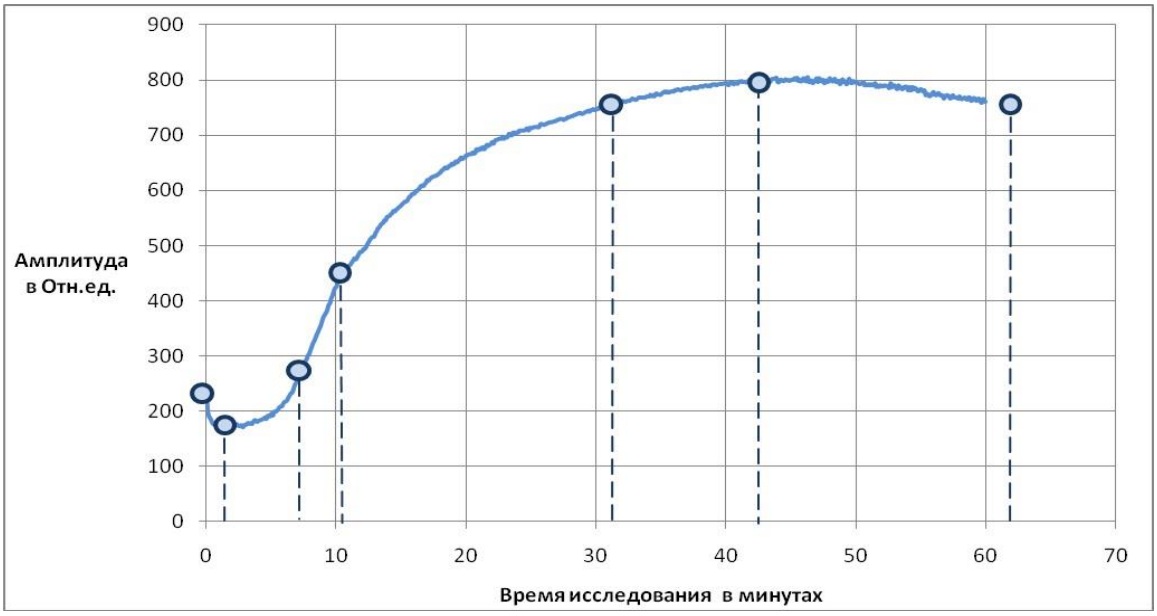



Figure 8 – Complete investigation example [29]

**3.2 The use of the method of digital speckle patterns correlation to assess the hemostatic system**

When an object is illuminated by coherent radiation, then any changes in the structure of the object that is under observation will lead to a change in the speckle pattern. Therefore, the method of correlation of digital speckle patterns is used to analyze liquid media. Liquid biological media with low optical density are of particular interest. Blood is one such medium.

At the first time after the contact of the sample with air, the blood coagulation process begins. The growth of the fibrin plate begins in an arbitrary volume. The network increases with time and forms a fibrin clot. Blood viscosity increases with increasing clot volume. It is this feature of the hemostasis system that makes it possible to use the speckle pattern correlation method for analyzing blood coagulation time.

A series of experiments were carried out in the work using the developed laboratory setup; using the developed prototype of the device.

The general design for the experiments is shown in Figure 8 and consists of a camera recording changes in the picture with a frequency of 30 fps.

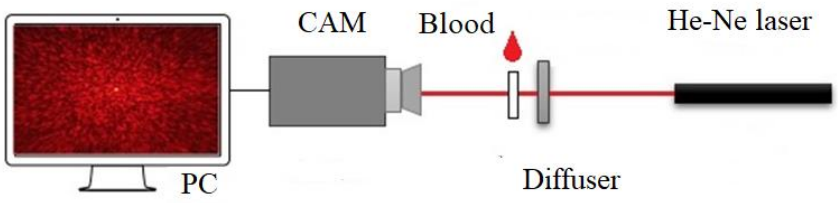



Figure 8 – The experimental setup

Data received from the camera is transmitted to a personal computer. The resulting speckle patterns are recorded during the coagulation process are written to the file. The correlation coefficient of digital speckle patterns is calculated using the MatLab software after recording. The ratio of the two speckle patterns reflects the correlation coefficient. The less speckle patterns differ, the closer the correlation coefficient to 1, the more dense the fibrin clot. In the work, the correlation formula (1) was used, which was selected on the basis of the data presented in [30].

The value of the correlation coefficient must be determined during the entire coagulation process. Thus, a series of speckle patterns is compared between the current and previous images to calculate the correlation coefficient.

In all experiments, the same sample volume was used, which is 50 μl. The test sample is placed in a cuvette, which is made of an optically relatively dense material that scatters coherent radiation. A source of coherent radiation illuminates the cuvette, in which case, the cuvette is also a diffuser. The cuvette is under camera surveillance. The coagulation process begins at the first moment after sampling. In this regard, the placement time of the taken sample was minimized to 20 seconds, which is significantly less than the average coagulation time.

The coagulation time is determined by the graph of the correlation coefficient versus time. The higher the optical density of the sample, the lower the dynamics of speckle structures. In the formed fibrin blood clot there is no movement of blood cells, therefore, the dynamics of speckle structures is minimal and the value of the correlation coefficient tends to 1.

## 4. The experimental part

### 4.1 The use of the method of digital speckle patterns correlation for the analysis of biological test models whole blood

The results of a series of experiments were published in [31].

For the experiments, we used the laboratory setup shown in Figure 9. In the present work, we used the whole blood of the control group of test systems (laboratory rats).

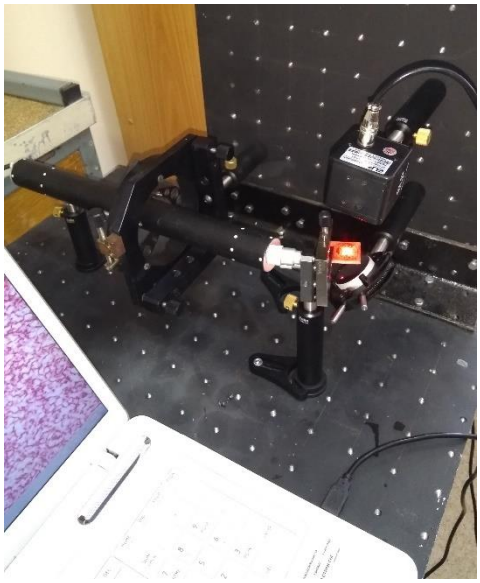


Figure 9 – A photo of experimental setup

A series of experiments was conducted to test the method of digital speckle patterns correlation to analyze the coagulation time of whole blood. The laboratory setup consists of the commercially available ELP-USBFHDO1M-MFV camera, a He-Ne laser, and a cuvette, created using additive technologies. In the present work, experiments were carried out to determine the coagulation time of venous blood of control test systems. The volume of the test sample in all experiments is the same and is 50 μl.

Figure 10 shows graphs of the correlation coefficient versus time. The dependences of the three control experiments to determine the coagulation time are given. Venous blood was drawn from different healthy test systems in each

experiment. The values of the correlation coefficient for 1000 s were calculated in each experiment.

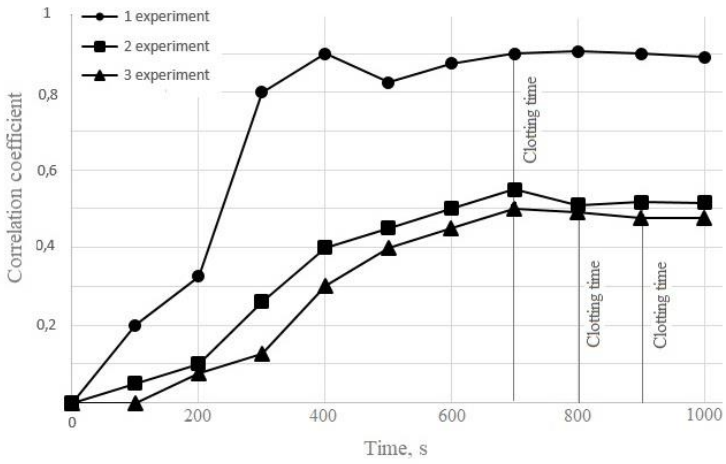



Figure 10 – Graphs of blood coagulation time dependence on the correlation coefficient of three control experiments

As mentioned earlier, the correlation coefficient characterizes the rate of change of the speckle position. The higher the optical density of the bunch, the lower the dynamics of speckle patterns. In a fibrin blood clot, the movement of the formed elements is almost absent. This leads to a decrease in the dynamics of speckles and the tendency of the correlation coefficient to 1.

The graphs shown in Figure 10 determine the total coagulation time. For example, in experiment 1, the active growth of a fibrin clot began at 350 s, and the total blood coagulation time was 700 s, and the correlation coefficient reached 0.9. In experiment 2, the total clotting time was 900 s; active clot growth began for 400 s. In some cases (experiments 2 and 3), the correlation coefficient reaches 0.5 and does not approach 1. In the 3rd experiment, the active growth of the fibrin clot started for 400 s, and the total blood coagulation time was 800 s, the correlation coefficient was the same as in 2 experiment reached 0.45. A large volume of blood plasma is formed on the surface of the clot, in which there is movement of suspended particles. In this regard, the movement of speckle structures does not stop, and the correlation coefficient does not reach 1.

Therefore, the formation time of a fibrin clot can be determined at the moment when the value of the correlation coefficient ceases to change significantly.

Thus, the possibility of applying the method of digital speckle patterns correlation to analyze the coagulation time of whole blood was shown.

### 4.2 Study the applicability of the proposed method for laboratory analysis of native blood coagulation time of biological test systems

To determine the efficiency of the developed device and its applicability for the analysis of whole blood coagulation time, it is necessary to evaluate the applicability of the method. For this, the previously developed laboratory facility was used, which is schematically presented in Figure 8.

The setup consists of a coherent light source – a He-Ne laser, a wavelength of 632 nm and a radiation power of 5 mW. The choice of wavelength is determined by the depth of radiation penetration into biological tissues. Thus, the red wavelength passes through the blood layer and forms a speckle pattern on its surface. A sample for research is placed in a cuvette with a diameter of 10 mm and a depth of 0.4 mm - whole blood or blood plasma. The camera is located on the same optical axis with the laser, registers changes in the position of the speckles and transmits the recorded information to a personal computer. The recorded speckle patterns are processed using the MatLab software, an area of 200x200 pixels is selected. Pictures are compared in turn at the first and second points in time. Then the value of the correlation coefficient is calculated. It reflects the ratio of two speckle patterns. When coherent radiation illuminates the surface of the blood, glare is scattered from the formed elements of the blood and the resulting fibrin threads. The rapid movement of blood elements begins when the coagulation process begins. The movement slows down at the end of the process and the fibrin filaments fill the entire space of the bunch. This process enables to use the method of correlation of digital speckle patterns, which is based on a comparison of speckle patterns. The faster the movement of the shaped elements, the more glare dissipates and the stronger the speckle patterns are differ from each other. When the movement stops, the speckle patterns become static and the value of the correlation coefficient tends to 1. Thus, the period of time from the beginning of the coagulation process to the moment when

the correlation coefficient tends to 1 is the prothrombin time or blood coagulation time.

In the first part of the work, 15 experiments were conducted to analyze the coagulation time of banked whole blood of the test systems. Whole blood is an optically dense medium, unlike blood plasma, so it is more difficult to analyze whole blood by the optical method. Figure 11 shows graphs of the correlation coefficient versus time for 5 test experiments.

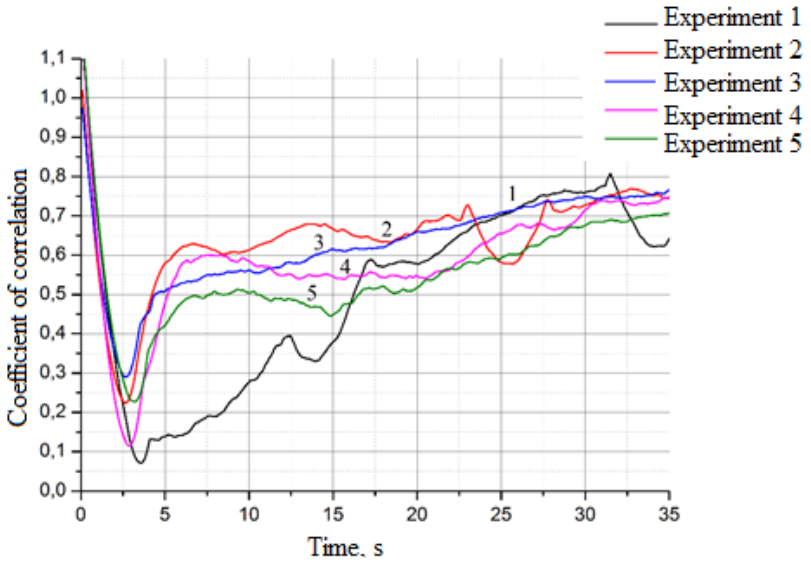



Figure 11 – Graphs of the dependence of the correlation coefficient on time for 5 test experiments

Whole native blood of the test systems was used in the experiments. It was placed in tubes with sodium citrate which block the coagulation process. 50 µl of blood and 100 µl of Tehplastin reagent manufactured by Technologiya standard were placed in a cuvette placed on the same optical axis as a coherent radiation source and a camera. The ratio of reagents 1:2 is recommended by manufacturers of reagent "Techplastin". All 15 experiments were performed using whole venous blood of 15 different test systems. This means that the coagulation time will be different in all experiments. All extraneous noise: sound, light and vibration was excluded during the experiment. External conditions were the same. The temperature of the samples was kept constant - 37˚C. From Figure 11, it can be seen that a time period of 0-3 s is the activation time of the test samples. This time period is not taken into account in the

analysis. The active growth of fibrin clot begins immediately after activation. The normalized prothrombin time is 25-30 s, according to the instructions for the reagents. The moment of a sharp change in the curve of the correlation coefficient is prothrombin time of whole blood. In case of whole blood, the correlation coefficient does not reach 1, because the liquid formed on the surface of the bunch continues to make speckle patterns. However, this does not preclude the analysis of the proposed whole blood method. The results of the analysis of whole blood prothrombin time of 15 experiments are shown in table 1.

Table 1 – Results of whole blood prothrombin time

| | Number of the Experiment | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| Time, s | 28 | 30 | 28 | 29 | 29 | 30 | 28 | 28 | 29 | 30 | 30 | 29 | 27 | 28 | 29 |

Analyzing the results, we can say that the method of correlation of digital speckle patterns can be used to analyze the coagulation time of whole blood. The average value of prothrombin time was 28.8 s, which falls into the time interval specified in the instructions for the reagents.

Thus, we can conclude that the method of correlation of digital speckle patterns can be successfully used to analyze the coagulation time of whole blood. We conducted fifteen experiments to determine the prothrombin time of whole blood, analyzed the research results and had made graphs of the correlation coefficient versus coagulation time.

### 4.3 Determination of the optimal wavelength for the analysis

The experiments were performed to analyze the prothrombin time using the setup presented schematically in Figure 12. Two laser beams from diode lasers operating at 635 and 650 nm with the nominal lasing power of 5 mW were turned on, using the lighting control program implemented on the STM 32F1 microcontroller (control unit in Figure 11). The program worked in such a way, that at one time there was only one laser emission, preventing the simultaneous operation of two lasers.

The lighting control program worked at a constant frequency of 30 Hz for each laser diode. The digital CMOS camera Phantom Miro C110 was operated at 60 frms/s rate and was synchronized with the operation of diode lasers. The camera was installed perpendicular to the illuminated sample and captures speckle patterns formed by both lasers.

Laser beams from two lasers were directed to one point in the center of the cuvette, in which the sample for examination was placed. Laser diodes were located at the distance of 10 cm from the object under study at the angle of 60° to the optical axis of the digital camera. The images from each source was recorded by the camera and transferred to the computer for displaying, storage and processing. The processing was carried out using MATLAB software. Pictures were used in size of 300×300 pixels. Two speckle patterns from 635 nm laser were compared at the first and second time instants during the entire coagulation process to calculate the correlation coefficient of digital speckle patterns. Speckle patterns obtained from the 650 nm laser were analyzed in a similar manner.

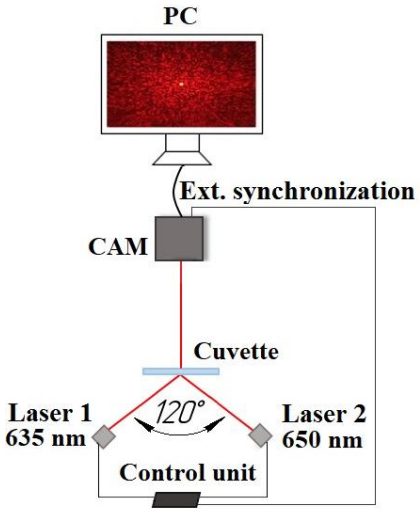



Figure 12 – Scheme of experimental setup

Reagents Techplastin and RNP plasma, produced by the company Technology Standard [32], were used for the prothrombin time analysis. The cuvette was made using 3D printer and transparent plastic. The volume of the cuvette was 200 µl; the bottom thickness was 2 mm. Plasma volume 50 µl and Tehplastin volume 100 µl were placed in the cuvette in each experiment. The ratio of reagents was 1:2,

recommended by the manufacturer for the analysis of prothrombin time. During the experiment, we tried to ensure the same reagent addition time, approximately equal to 3 seconds.

The coagulation process was initiated at the time of adding Techplastin to the plasma. When the laser beam illuminates the sample it is scattered by the formed elements of the blood mix and forms a speckle pattern. During the process of coagulation, the rapid movement of blood cells and an increase in the size of the fibrin network occurs in plasma. As a result of coagulation process, a rapid change in speckle patterns will begin when the process is activated by reagent and speckle patterns will cease to change only at the end of the process.

Characteristic graphics of the correlation coefficient versus coagulation time are shown in Figure 13. The curves presented do not tend to 1, as we observed earlier in [13], in which the laser beam was directed along the optical axis of the digital camera perpendicular to the cuvette. The correlation coefficient curve decreases after reaching a maximum. Since this feature is present in all experiments, we believe that at the time when the dependence of the correlation coefficient reaches a maximum, the process of formation of a fibrin clot is completed, and the recorded time to reach the maximum, indicated by a red dot, is prothrombin time. Analyzing the presented graphs, we can identify the activation time of the sample, which is 3 seconds from the start of the experiment. Active growth of the fibrin clot begins after 3 seconds and ends at 23-28 seconds for the presented samples.

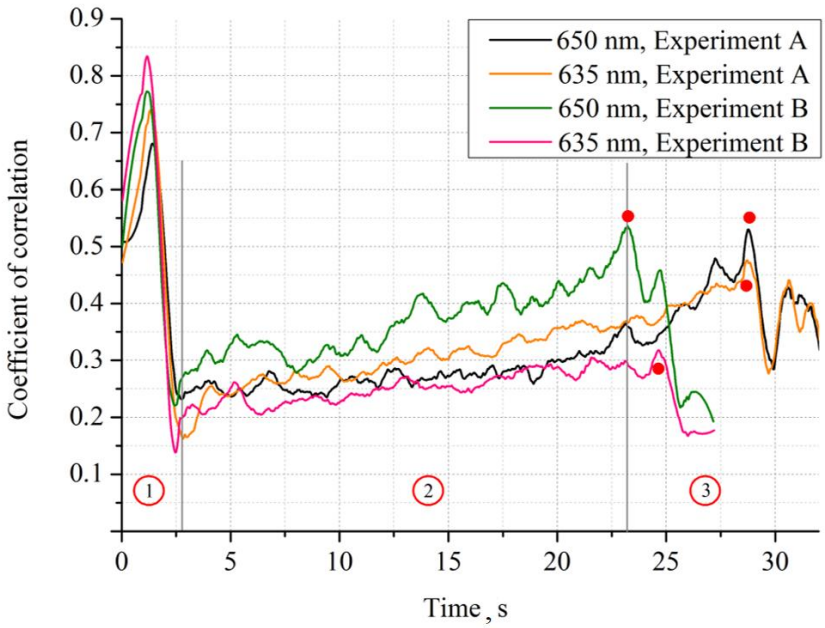



Figure 13 – The dependences of the coefficient of correlation from coagulation time for two experiments. (1) Activation time during Techplastin addition; (2) time of active growth of the fibrin clot; (3) end of clotting time. Prothrombin time is marked by red dots on the curves for each experiment

The obtained experimental results demonstrated that the method of correlation of digital speckle patterns can be used to analyze the prothrombin time of blood plasma, using commercially available diode lasers with different wavelengths in the red spectral range. Two lasers with different wavelengths, which operate alternately, can be used to reduce the random measurement error.

## 5. Development of the laboratory prototype

### 5.1 Development of the design of the laboratory prototype

The main view of the developed laboratory device for the analysis of blood coagulation time, shown in Figure 14.

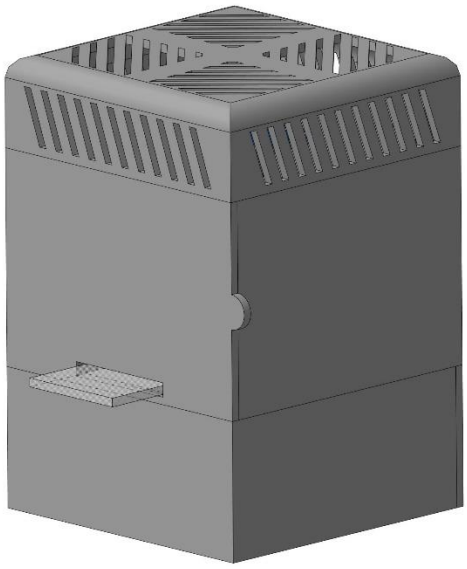


Figure 14 – The body of the developed laboratory prototype

The power on/off button and the power connector are provided in the developed device case. To turn on the laser diode, a voltage of 3.5 V is applied to it through the power adapter to the power connector. The connection unit and the diode holder are located at the bottom of the device. There is an opening for placing the cuvette and an opening front wall of the device for cleaning the inner surface. In addition, a USB camera holder and a ventilation unit are provided in the device case.

The design of the device will allow the operator to place the cuvette in the registration unit without additional manipulations. The detection of the cuvette will be carried out using an optocoupler. When the cuvette is placed in the block, the signal between the transmitter and the receiver of the optical signal disappears, the signal is sent to the microcomputer, which will start the process of analyzing the coagulation time.

The device body and sample cuvette will be manufactured using additive technologies. All walls of the developed laboratory prototype have a thickness of 0.5

mm. The diameter of the cuvette is 10 mm and the depth is 0.4 mm. The body of the laboratory prototype will be made of black ABS plastic. The choice of color is determined by the particular nature of optical systems. Black color absorbs light without reflection. The closed case of the device will reduce the amount of external interference during the research, and, therefore, increase the accuracy of the results. The cuvette will be made of transparent ABS plastic, because it is necessary to ensure the greatest passage of coherent healing through the cuvette.

### 5.2 Development of a data processing algorithm

To create a prototype of an optical device for the analysis of blood coagulation time, it is necessary to develop a data processing program for a microcomputer.

The main idea of the software is to reduce the number of manipulations performed by the operator before the analysis. Due to the fact that the coagulation process proceeds continuously, the operator must place the cuvette for the analysis in the unit of the device as quickly as possible.

The developed data processing algorithm involves the detection of a cell in a block which will be carried out using the built-in optocoupler. If the device is turned on and the cuvette is not detected in the camera, the program will be waiting. Then a new survey on the presence of the cuvette will be conducted. If the status is changed, the processor will start the shooting process; if it doesn’t, the device will turn itself off. In case when the cuvette is placed in the unit, the camera will start working, the laser LED will turn on and the recording program will start automatically. Then the image processing, calculation of the correlation coefficient over time, plotting dependencies and displaying information on the screen will begin. Then the camera and LED will be turned off sequentially. If the cuvette is removed from the device after the analysis, the second survey will be performed if there is a cuvette. If after analyzing, the cuvette is not removed, the device will turn itself off after the set time.

The developed algorithm will allow the operator to receive information without performing unnecessary actions, but only by placing the cuvette in the unit of the device. The prototype will do the rest automatically.

### 5.3 Experiments to determine the efficiency of the developed prototype device

In the experiment, the coagulation time of the blood plasma of one patient was studied. A total of 5 experiments were conducted.

According to the results of the analysis, the following results were obtained:

Table 2 – Results of the experiments

| | Results of the experiments | | | | |
|---|---|---|---|---|---|
| Coagulation time | 1 experiment | 2 experiment | 3 experiment | 4 experiment | 5 experiment |
| | 29 s | 25 s | 28 s | 29 s | 28,5 s |

The coagulation time of a patient's blood sample, measured by a laboratory instrument of the Research Institute of Cardiology, Tomsk, was 29 seconds, we consider this value as reference.

Thus, we can say that the average coagulation time of 5 experiments conducted using the prototype optical device was 27.9 seconds. The absolute measurement error was 1.1 seconds. The measurement error in this case is 3%. For medical research, the permissible measurement error is 20%. Analyzing the data obtained, today we can say that the prototype of the device allows you to determine the coagulation time of blood plasma with an accuracy of 97%.

For further work, it is necessary to conduct additional analyzes on the blood plasma and whole blood of other patients and compare them with the reference ones.

**Financial management, resource efficiency and resource saving**

The purpose of this section discusses the issues of competitiveness, resource efficiency and resource saving, as well as financial costs regarding the object of study of Master's thesis. Competitiveness analysis is carried out for this purpose. SWOT analysis helps to identify strengths, weaknesses, opportunities and threats associated with the project, and give an idea of working with them in each particular case. For the development of the project requires funds that go to the salaries of project participants and the necessary equipment, a complete list is given in the relevant section. The calculation of the resource efficiency indicator helps to make a final assessment of the technical decision on individual criteria and in general.

The aim of the work is to develop a prototype of optical device for analyzing the coagulation time of whole blood, which allows to do continuous monitoring of the coagulation system.

To date, the development of a device for determining the state of the coagulation system is an urgent task. During surgical interventions in the human body, especially when using a cardiopulmonary bypass, monitoring of the coagulation system is necessary. An increase in prothrombin time will lead to large blood loss for the patient, and a decrease will increase the probability of thrombosis.

Today, there are two popular methods for analyzing blood coagulation time - the thromboelastography method, which allows to analyze all parameters of blood coagulation. A coagulography method that analyzes blood plasma and allows to determine prothrombin time.

## 1. Competitiveness analysis of technical solutions

In order to find sources of financing for the project, it is necessary, first, to determine the commercial value of the work. Analysis of competitive technical solutions in terms of resource efficiency and resource saving allows to evaluate the comparative effectiveness of scientific development. This analysis is advisable to carry out using an evaluation card.

First of all, it is necessary to analyze possible technical solutions and choose the best one based on the considered technical and economic criteria.

Evaluation map analysis presented in Table 3. The position of your research and competitors is evaluated for each indicator by you on a five-point scale, where 1 is the weakest position and 5 is the strongest. The weights of indicators determined by you in the amount should be 1. Analysis of competitive technical solutions is determined by the formula:

$$C = \sum W_i * P_i \tag{2}$$

C – the competitiveness of research or a competitor;

Wi – criterion weight;

Pi – point of i-th criteria.

To compare competitiveness, several existing devices for blood coagulation analysis were used. As competitors, two devices: thromboelastograph ARP 01M Mednord ($C_{i1}$), optical coagulometer APG 2-02 Minilab 701 ($C_{i2}$).

The advantage of using the first two methods is ease of operation, accuracy of the results obtained, and application, minimal cost of financial resources. The advantage of the device under development is the minimum sample volume for research and the ability to conduct whole blood analysis. The device proposed in this work ($C_f$).

Table 3 – Evaluation card for comparison of competitive technical solutions

| **Evaluation criteria** | **Criterion weight** | **Points** | | | **Competitiveness** Taking into account weight coefficients | | |
|---|---|---|---|---|---|---|---|
| | | $P_f$ | $P_{i1}$ | $P_{i2}$ | $C_f$ | $C_{i1}$ | $C_{i2}$ |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| **Technical criteria for evaluating resource efficiency** | | | | | | | |
| 1. Energy efficiency | 0.1 | 5 | 5 | 5 | 0.5 | 0.5 | 0.5 |
| 2. Reliability | 0.15 | 4 | 3 | 3 | 0.6 | 0.45 | 0.45 |
| 3. Safety | 0.25 | 4 | 2 | 3 | 1 | 0.5 | 0.75 |
| 4. Functional capacity | 0.1 | 2 | 5 | 3 | 0.2 | 0.5 | 0.3 |
| **Economic criteria for performance evaluation** | | | | | | | |
| 1. Development cost | 0.1 | 5 | 2 | 4 | 0.5 | 0.2 | 0.4 |
| 2. Market penetration rate | 0.05 | 1 | 3 | 5 | 0.05 | 0.15 | 0.25 |
| 3. Expected lifecycle | 0.25 | 5 | 4 | 3 | 1.25 | 1 | 0.75 |
| **Total** | **1** | **26** | **24** | **26** | **4.1** | **3.3** | **3.4** |

Having calculated the competitiveness of the devices under consideration, the proposed device ($C_f$) has the highest competitiveness coefficient and is 4.1. The overall competitiveness coefficient of the thromboelastograph ($C_{i1}$) was 3.1, and the coefficient of the coagulometer ($C_{i2}$) was 3.4.

However, the proposed device has a clear drawback in comparison with competitors – functional capacity, since the developed device allows you to receive information about only one analyzed parameter – prothrombin time, while a thromboelastograph allows to get 8 parameters and a coagulometer – 4 analyzed parameters.

## 2. SWOT analysis

Complex analysis solution with the greatest competitiveness is carried out with the method of the SWOT analysis: Strengths, Weaknesses, Opportunities and Threats. The analysis has several stages. The first stage consists of describing the strengths and weaknesses of the project, identifying opportunities and threats to the project that have emerged or may appear in its external environment. The second stage consists of identifying the compatibility of the strengths and weaknesses of the project with the external environmental conditions. This compatibility or incompatibility should help to identify what strategic changes are needed.

Table 4 – SWOT analysis

| | **Strengths:**<br>S1. Relevance<br>S2. Minimum sample volume for research<br>S3. Quick analysis<br>S4. Ease of use<br>S5. Lack of supplies<br>S6. Lack of contact of the device with the sample<br>S7. Possibility of analysis of whole blood and blood plasma | **Weaknesses:**<br>W1. One measured parameter<br>W2. Lack of verification method<br>W3. Poor noise immunity<br>W4. The need for optical calibration<br>W5. Lack of device manufacturing |
|---|---|---|
| **Opportunities**:<br>O1. Continuous monitoring<br>O2. Lower demand for competitors<br>O3. Emergence of demand<br>O4. Use of the device in operating rooms and ambulances<br>O5. Examination of both blood plasma and whole blood | *Continuous monitoring of blood coagulation time will allow for quick analysis using a non-contact optical method. There is the possibility of using the device in operating rooms and ambulances, due to the ease of use and the lack of consumables* | *In order for there to be a demand for the developed device, it is necessary to find opportunities for the production of the device, and increase the noise immunity. A study of blood plasma and whole blood, which allows the device to create a new method, which must be registered by conducting indirect verification* |
| **Threats:**<br>T1. Competitive methods are traditional<br>T2. Clinical trial cost increase<br>T3 Inability to create software for a portable | *The relevance of the proposed development can be reduced due to the inability to create a portable device and the* | *The traditionality of competitive methods can lead to a lack of production and, consequently, to a lack of* |

| | | |
|---|---|---|
| device<br>T4. Inability to conduct continuous monitoring<br>T5. Lack of funding | *inability to conduct continuous monitoring* | *financing. And financing will help to increase noise immunity, which will make the device under development more competitive* |

## 3. Project initiation

The initiation process group consists of processes that are performed to define a new project or a new phase of an existing one. In the initiation processes, the initial purpose and content are determined and the initial financial resources are fixed. The internal and external stakeholders of the project who will interact and influence the overall result of the research project are determined.

Table 5 – Stakeholders of the project

| Project stakeholders | Stakeholder expectations |
|---|---|
| RSCBT TPU | Publication of articles in international journals with a high impact factor. Writing patents for an invention, obtaining grants for performing work. |
| Demutualized organization Semiconductor Research Institute | Development and sale of the device under development. Obtaining third-party and state funding for the project. Development output on the Russian and foreign market. |

Table 6 – Purpose and results of the project

| | |
|---|---|
| Purpose of project: | Development of a prototype device for the analysis of blood coagulation time, allowing for analysis by non-contact optical method |
| Expected results of the project: | The device under development allows both: the analysis of whole blood and blood plasma. The project is a new technical solution that has not been implemented by competitors before |
| Criteria for acceptance of the project result: | Results are verifiable, repeatable and easy to interpret |
| Requirements for the project result: | With increasing viscosity of the sample, the correlation coefficient increases and tends to 1 |
| | The results obtained confirm that the method under study allows the analysis of coagulation with an accuracy of at least 80% |
| | The results are discussed and published in scientific journals |
| | The project is prepared to create a control sample and conduct technical and toxicological tests |

The organizational structure of the project

It is necessary to solve the some questions: who will be part of the working group of this project, determine the role of each participant in this project, and prescribe the functions of the participants and their number of labor hours in the project.

Table 7 – Structure of the project

| № | Participant | Role in the project | Functions | Labor time, hours |
|---|---|---|---|---|
| 1 | Iuliia Dmitrievna Liushnevskaya | Master student / Engineer | Conducting and planning experiments<br>Results analysis<br>Design and construction of the device<br>Writing articles<br>Report writing | 468 |
| 2 | Fedor Aleksandrovich Gubarev | Researcher / Supervisor | Experiment control<br>Control of the design of the device<br>Checking articles and reports | 42 |

Project limitations

Project limitations are all factors that can be as a restriction on the degree of freedom of the project team members.

Table 8 – Project limitations

| Factors | Limitations / Assumptions |
|---|---|
| 3.1. Project's budget | 384455.66 rub |
| 3.1.1. Source of financing | RSCBT TPU |
| 3.2. Project timeline: | |
| 3.2.1. Date of approval of plan of project | 03.02.2020 |
| 3.2.2. Completion date | 26.02.2020 |

Project Schedule

As part of planning a science project, you need to build a project timeline and a Gantt Chart.

Table 9 – Project Schedule

| Job title | Duration, working days | Start date | Date of completion | Participants |
|---|---|---|---|---|
| Literature review | 5 | 03.02.20 | 07.02.20 | I.D. Liushnevskaya |
| Experiment planning | 2 | 10.02.20 | 11.02.20 | I.D. Liushnevskaya; F.A. Gubarev |
| Conducting experiments to study the coagulation time of blood plasma | 10 | 10.02.20 | 24.02.20 | I.D. Liushnevskaya |
| Conducting experiments to study the coagulation time of whole blood | 13 | 25.02.20 | 12.03.20 | I.D. Liushnevskaya |
| Verification of the coagulation time of blood plasma with the values of standard laboratory devices | 5 | 16.03.20 | 20.03.20 | I.D. Liushnevskaya |
| Results processing | 5 | 23.03.20 | 27.03.20 | I.D. Liushnevskaya |
| The discussion of the results | 5 | 30.03.20 | 03.04.20 | I.D. Liushnevskaya; F.A. Gubarev |
| Device design development | 15 | 06.04.20 | 23.04.20 | I.D. Liushnevskaya |
| Creating and debugging a device | 4 | 27.04.20 | 30.04.20 | I.D. Liushnevskaya |
| Conducting control tests using the developed device | 3 | 06.05.20 | 08.05.20 | I.D. Liushnevskaya |
| Report writing | 11 | 12.05.20 | 26.05.20 | I.D. Liushnevskaya |

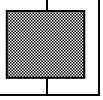
Total – 78 days

A Gantt chart, or harmonogram, is a type of bar chart that illustrates a project schedule. This chart lists the tasks to be performed on the vertical axis, and time

intervals on the horizontal axis. The width of the horizontal bars in the graph shows the duration of each activity.

Table 10 – A Gantt chart

| № | Activities | Participants | $T_c$, days | Duration of the project | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | February | | | March | | | April | | | May | | |
| | | | | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |
| 1 | Literature review | I.D. Liushnevskaya | 5 | | | | | | | | | | | | |
| 2 | Experiment planning | I.D. Liushnevskaya; F.A. Gubarev | 2 | | | | | | | | | | | | |
| 3 | Conducting experiments to study the coagulation time of blood plasma | I.D. Liushnevskaya | 10 | | | | | | | | | | | | |
| 4 | Conducting experiments to study the coagulation time of whole blood | I.D. Liushnevskaya | 13 | | | | | | | | | | | | |
| 5 | Verification of the coagulation time of blood plasma with the values of standard laboratory devices | I.D. Liushnevskaya | 5 | | | | | | | | | | | | |
| 6 | Results Processing | I.D. Liushnevskaya | 5 | | | | | | | | | | | | |
| 7 | The discussion of the results | I.D. Liushnevskaya; F.A. Gubarev | 5 | | | | | | | | | | | | |
| 8 | Device design development | I.D. Liushnevskaya | 15 | | | | | | | | | | | | |
| 9 | Creating and debugging a device | I.D. Liushnevskaya | 4 | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | Conducting control tests using the developed device | I.D. Liushnevskaya | 3 | | | | | | | | | | |  | | |
| 11 | Report writing | I.D. Liushnevskaya | 11 | | | | | | | | | | | |  | |

## 4. Scientific and technical research budget

The amount of costs associated with the implementation of this work is the basis for the formation of the project budget. This budget will be presented as the lower limit of project costs when forming a contract with the customer.

To form the final cost value, all calculated costs for individual items related to the manager and the student are summed.

In the process of budgeting, the following grouping of costs by items is used:

- Material costs of scientific and technical research;
- costs of special equipment for scientific work (Depreciation of equipment used for design);
- basic salary;
- additional salary;
- labor tax;
- overhead.

Calculation of material costs

The calculation of material costs is carried out according to the formula:

$$C_{mT} = (1 + k_i) * \sum_{i=1}^{m} P_i * N_{consi} \quad (3)$$

where $m$ – the number of types of material resources consumed in the performance of scientific research;

$N_{consi}$ – the amount of material resources of the i-th species planned to be used when performing scientific research (units, kg, m, $m^2$, etc.);

$P_i$ – the acquisition price of a unit of the i-th type of material resources consumed (rub./units, rub./kg, rub./m, rub./$m^2$, etc.);

$k_T$ – coefficient taking into account transportation costs.

Prices for material resources can be set according to data posted on relevant websites on the Internet by manufacturers (or supplier organizations).

Table 11 – Material costs

| Name | Unit | Amount | Price per unit, rub. | Material costs, rub. |
|---|---|---|---|---|
| Plastic | 500 g | 2 | 1000 | 2000 |
| Plasma and Techplastin | 5 g | 5 | 2000 | 10000 |
| Syringes | 5 ml | 25 | 8 | 200 |
| Gloves | items | 200 | 3 | 600 |
| Micropipettes | 500 mkl | 2 | 6000 | 12000 |
| Citrate tubes | 2 ml | 25 | 25 | 625 |
| Total | | | | 25425 |

**Costs of special equipment**

This point includes the costs associated with the acquirement of special equipment (instruments, stands, devices and mechanisms) necessary to carry out work on a specific topic.

Table 12 – Costs of special equipment and software

| № | Equipment identification | Quantity of equipment | Price per unit, rub. | Total cost of equipment, rub. |
|---|---|---|---|---|
| 1 | Minilab 701 | 1 | 90000 | 90000 |
| 2 | PC | 1 | 100000 | 100000 |
| Total | | | | 190000 |

Calculation of the depreciation

If you use available equipment, then you need to calculate depreciation:

$$A = \frac{C_{\text{перв}} * \text{Н}_\text{а}}{100} \quad (4)$$

$A$ – annual amount of depreciation;

$C_{перв}$ – initial cost of the equipment;

$\text{Н}_\text{а} = \frac{100}{\text{Т}_{\text{сл}}}$ – rate of depreciation;

$T_{сл}$ – life expectancy.

| № | Equipment identification | Quantity of equipment | Total cost of equipment, rub. | Life expectancy, year | Depreciation for the duration of the project, rub. |
|---|---|---|---|---|---|
| 1 | Minilab 701 | 1 | 90000 | 10 | 145 |
| 2 | PC | 1 | 100000 | 5 | 5000 |

Total cost – 5145 rub

**Basic salary**

This point includes the basic salary of participants directly involved in the implementation of work on this research. The value of salary costs is determined based on the labor intensity of the work performed and the current salary system

The basic salary ($S_b$) is calculated according to the formula:

$$S_{\text{b}} = S_a \cdot T_{\text{w}}, \quad (5)$$

where $S_b$ – basic salary per participant;

$T_w$ – the duration of the work performed by the scientific and technical worker, working days;

$S_d$ - the average daily salary of an participant, rub.

The average daily salary is calculated by the formula:

$$S_d = \frac{S_m \cdot M}{F_{\text{v}}} \quad (6)$$

where $S_m$ – monthly salary of an participant, rub.;

$M$ – the number of months of work without leave during the year:

at holiday in 48 days, M = 11.2 months, 5 day per week;

$F_v$ – valid annual fund of working time of scientific and technical personnel (244 days).

Table 13 – The valid annual fund of working time

| Working time indicators | |
|---|---|
| Calendar number of days | 365 |
| The number of non-working days<br>- weekend<br>- holidays | <br>104<br>14 |
| Loss of working time<br>- vacation<br>- isolation period<br>- sick absence | <br>24<br>7 |
| The valid annual fund of working time | 247 |

Monthly salary is calculated by formula:

$$S_{month} = S_{base} * \left(k_{premium} + k_{bonus}\right) * k_{reg} \quad (7)$$

where $S_{base}$ – base salary, rubles;

$k_{premium}$ – premium rate;

$k_{bonus}$ – bonus rate;

$k_{reg}$ – regional rate.

Table 14 – Calculation of the base salaries

| Performers | $S_{base}$, rubles | $k_{premium}$ | $k_{bonus}$ | $k_{reg}$ | $S_{month}$, rub. | $W_d$, rub. | $T_p$, work days | $W_{base}$, rub. |
|---|---|---|---|---|---|---|---|---|
| I.D. Liushnevskaya Engineer | 17890 | - | - | 1.3 | 23257 | 1055 | 78 | 82290 |
| F.A. Gubarev Assistant Professor | 35120 | | | | 45656 | 2070 | 7 | 14490 |
| Total | | | | | | | | 96780 |

**Additional salary**

This point includes the amount of payments stipulated by the legislation on labor, for example, payment of regular and additional holidays; payment of time associated with state and public duties; payment for work experience, etc.

Additional salaries are calculated on the basis of 10-15% of the base salary of workers:

$$W_{add} = k_{extra} * W_{base} \quad (8)$$

where $W_{add}$ – additional salary, rubles;

$k_{extra}$ – additional salary coefficient (10%);

$W_{base}$ – base salary, rubles.

$W_{add}(I.D.Liushnevskaya)$ =8229 rub;

$W_{add}(F.A.Gubarev)$ = 1449 rub.

Total – 9678 rub.

**Labor tax**

Tax to extra-budgetary funds are compulsory according to the norms established by the legislation of the Russian Federation to the state social insurance (SIF), pension fund (PF) and medical insurance (FCMIF) from the costs of workers.

Payment to extra-budgetary funds is determined of the formula:

$$P_{social} = k_b * (W_{base} + W_{add}) \quad (9)$$

where $k_b$ – coefficient of deductions for labor tax.

In accordance with the Federal law of July 24, 2009 No. 212-FL, the amount of insurance contributions is set at 30%. Institutions conducting educational and scientific activities have rate – 27.1%.

Table 15 – Labor tax

| | Project leader | Engineer |
|---|---|---|
| Coefficient of deductions | 0.271 | |
| Salary (basic and additional), rubles | 15939 | 90519 |
| Labor tax, rubles | 4319 | 24531 |
| Total | | 28850 |

**Overhead costs**

Overhead costs include other management and maintenance costs that can be allocated directly to the project. In addition, this includes expenses for the maintenance, operation and repair of equipment, production tools and equipment, buildings, structures, etc.

Overhead costs account from 30% to 90% of the amount of base and additional salary of employees.

Overhead is calculated according to the formula:

$$C_{ov} = k_{ov} * (W_{base} + W_{add}) \quad (10)$$

where $k_{ov}$ – overhead rate.

Table 16 – Overhead

| | Project leader | Engineer |
|---|---|---|
| Overhead rate | 0.3 | |
| Salary, rubles | 15939 | 90519 |
| Overhead, rubles | 4782 | 27156 |
| Total | | 31938 |

**Other direct costs**

Energy costs for equipment are calculated by the formula:

$$C = P_{el} * P * F_{eq} \quad (11)$$

where $P_{el}$ – power rates (5.8 rubles per 1 kWh);

$P$ – power of equipment, kW;

$F_{eq}$ – equipment usage time, hours.

C (He-Ne laser) = 5.8*0.08*0.08*48= 1.78 rub;

C (Minilab 701) = 5.8*0.08*0.08*30= 1.12 rub;

C (PC) = 5.8*0.8*0.8*480= 1781.76 rub.

Total – 1784.66 rub.

**Formation of budget costs**

The calculated cost of research is the basis for budgeting project costs.

Determining the budget for the scientific research is given in the table 17.

Table 17 – Items expenses grouping

| Name | Cost, rubles |
|---|---|
| 1. Material costs | 25425 |
| 2. Equipment costs | 190000 |
| 3. Basic salary | 96780 |
| 4. Additional salary | 9678 |
| 5. Labor tax | 28850 |
| 6. Overhead | 31938 |
| 7. Other direct costs | 1784.66 |
| **Total planned costs** | **384455.66** |

## 5. Evaluation of the comparative effectiveness of the project

Determination of efficiency is based on the calculation of the integral indicator of the effectiveness of scientific research. Its finding is associated with the definition of two weighted average values: financial efficiency and resource efficiency.

The integral indicator of the financial efficiency of a scientific study is obtained in the course of estimating the budget for the costs of three (or more) variants of the execution of a scientific study. For this, the largest integral indicator of the implementation of the technical problem is taken as the calculation base (as the denominator), with which the financial values for all the options are correlated.

The integral financial measure of development is defined as:

$$I_f^d = \frac{C_i}{C_{max}}, \tag{12}$$

where $I_f^d$ – integral financial measure of development;

$C_i$ – the cost of the i-th version;

$C_{\max}$ – the maximum cost of execution of a research project (including analogues).

$$I_f^d = \frac{458730.7}{2000000} = 0.23;$$

The obtained value of the integral financial measure of development reflects the corresponding numerical increase in the budget of development costs in times (the value is greater than one), or the corresponding numerical reduction in the cost of development in times (the value is less than one, but greater than zero).

Since the development has one performance, then $I_f^d$ = 1.

The integral indicator of the resource efficiency of the variants of the research object can be determined as follows:

$$I_m^a = \sum_{i=1}^{n} a_i b_i^a \, ; I_m^p = \sum_{i=1}^{n} a_i b_i^p \tag{13}$$

where $I_m^a$ – integral indicator of resource efficiency for the i-th version of the development;

$a_i$– the weighting factor of the i-th version of the development;

$b_i^a$, $b_i^p$ – score rating of the i-th version of the development, is established by an expert on the selected rating scale;

$n$ – number of comparison parameters.

The calculation of the integral indicator of resource efficiency is presented in the form of table 18.

Table 18 – Evaluation of the performance of the project

| **Criteria** | **Weight criterion** | **Points** | **Minilab 701** |
|---|---|---|---|
| 1. Energy efficiency | 0.15 | 4 | 4 |
| 2. Reliability | 0.2 | 5 | 5 |
| 3. Safety | 0.1 | 5 | 5 |
| 4. Functional capacity | 0.05 | 2 | 3 |
| **Economic criteria for performance evaluation** | | | |
| 1. The cost of development | 0.2 | 3 | 5 |
| 2. Market penetration rate | 0.1 | 3 | 3 |
| 3. Expected life | 0.1 | 4 | 3 |
| 4. After-sales service | 0.1 | 4 | 3 |
| **Total** | 1 | 28 | 31 |

Integral indicator of resource efficiency:

$$I_m^p = 0.15 * 4 + 0.2 * 5 + 0.1 * 5 + 0.05 * 2 + 0.2 * 3 + 0.1 * 3 + 0.1 * 4 + 0.1 * 4 = 3.9;$$

$$I_{mMinilab}^p = 0.15 * 4 + 0.2 * 5 + 0.1 * 5 + 0.05 * 3 + 0.2 * 5 + 0.1 * 3 + 0.1 * 3 + 0.1 * 3 = 4.15.$$

The integral indicator of the development efficiency ($I_e^p$) is determined on the basis of the integral indicator of resource efficiency and the integral financial indicator using the formula:

$$I_e^p = \frac{I_m^p}{I_f^d}; I_e^a = \frac{I_m^a}{I_f^a} \text{ , and etc.} \quad (14)$$

$$I_e^p = \frac{3.9}{0.23} = 16.9; I_e^a = \frac{4.15}{0.23} = 18;$$

Comparison of the integral indicator of the current project efficiency and analogues will determine the comparative efficiency. Comparative effectiveness of the project:

$$E_c = \frac{I_e^p}{I_e^a} \quad (15)$$

$$E_c = \frac{16.9}{18} = 0.93$$

Thus, the effectiveness of the development is presented in table 19.

Table 19 – Efficiency of development

| № | Indicators | Points |
|---|---|---|
| 1 | Integral financial measure of development | 0.23 |
| 2 | Integral indicator of resource efficiency of development | 3.9 |
| 3 | Integral indicator of the development efficiency | 16.9 |

Comparison of the values of integral performance indicators allows us to understand and choose a more effective solution to the technical problem from the standpoint of financial and resource efficiency.

Thus, in this section was developed stages for design and create competitive development that meet the requirements in the field of resource efficiency and resource saving.

These stages includes:

- development of a common economic project idea, formation of a project concept;
- organization of work on a research project;
- identification of possible research alternatives;
- research planning;

- assessing the commercial potential and prospects of scientific research from the standpoint of resource efficiency and resource saving;
- determination of resource (resource saving), financial, budget, social and economic efficiency of the project.

The calculations allow us to analyze that the device under development has advantages over existing analogues: it allows the analysis of whole blood and blood plasma.

**Social responsibility**

A device for analyzing blood coagulation time is being developed in this work. A whole blood and plasma RNP experiments were performed. The correlation of digital speckle patterns is the basis of the using method.

A series of experiments to determine the coagulation time of blood plasma made in the course of work. The experiments, technical calculations, design and testing of the device were carried out in TPU laboratory, 16V building, 101 room. The purpose of this section is to analyze and evaluate harmful and hazardous labor factors that may affect project development personnel. The development of protective measures against these factors, the assessment of working conditions. Also in this section, issues related to safety, fire prevention and environmental protection, recommendations for creating optimal working conditions are considered.

During the development and operation of the designed solution, the following harmful factors should be taken into account: speckle patterns are obtained by illuminating the studied object with a He-Ne laser. This type of laser poses a danger when the eyes are exposed to direct or specularly reflected radiation. When conducting experiments, the studied objects are the RNP-plasma of the company "Technology Standard" and whole blood. Samples of human blood plasma and whole rat blood should be considered as potentially infected, capable of storing and transmitting HIV, hepatitis B virus or any other causative agent of viral infection for a long time.

Potential risk of using RNP plasma and whole blood - class 2a GOST 31508-2012.

When working with a laser, one should be guided by the following document: GOST 31581-2012 Laser safety. General safety requirements for the development and operation of laser products. According to the degree of danger, the He-Ne laser belongs to class II.

Collective protective equipment includes the use of a special room for research. Individual protective equipment includes: when working with a laser - avoid contact

with direct laser beams, use individual glasses that do not transmit laser wavelengths; when working with plasma and whole blood, use disposable rubber or plastic gloves.

## 1 Legal and institutional security issues

### 1.1 Special legal norms of labor legislation

In according to [33]

1. The normal duration of working time cannot exceed 40 hours per week;
2. During the working day, the employee should be given a break for rest and meals lasting no more than two hours and at least 30 minutes, which is not included in working hours;
3. All employees are given days off (weekly continuous rest). With a five-day working week, employees are given two days off per week; with a six-day working week, one day off;
4. Annual vacations with retention of the place of work and average wage should be paid to employees;
5. Annual paid leave is granted to employees lasting 28 calendar days, in accordance with [34].

In accordance with [35], persons over 18 years old, who don't have medical contraindications, who have undergone special training. Who training in the prescribed manner to work with a specific laser product and certification to the labor protection group during a work on electrical installations with the appropriate equipment are allowed to work with laser products voltage.

Workers involved in laser installations are required to:

1. A medical examination by a qualified professional after a suspected or obvious traumatic effect on the eyes. Such an inspection should be supplemented by a full investigation of the circumstances in which the accident occurred;
2. Preliminary and subsequent ophthalmological examination of workers. Verification of the visual function is required for each case;
3. Additional payments.

According to [36] involved in work with class 2a medical devices employees are required to:

1. Compulsory medical examination;

2. Additional payments.

### 1.2 Organizational measures in the layout of the working area

When performing research for this project, the work is doing by the operator in a sitting position. In accordance with [37]:

The workplace should ensure the performance of labor operations within the reach of the motor field. The performance of labor operations “often” and “very often” must be ensured within the zone of easy reach and the optimal zone of the motor field.

The design of production equipment and the workplace should ensure the optimal position of the worker, which is achieved by regulation:

1. Height of the working surface, seat and leg space;

2. The height of the seat and footrest (with unregulated height of the working surface).

The optimal working position for working man of lower growth is achieved by increasing the height of the working seat and footrest by an amount equal to the difference between the height of the working surface for a worker with a height of 1800 mm and the height of the working surface that is optimal for the growth of this worker. Requirements for the height of the workplace are shown in table 20.

Table 20 – A height of a workplace surface with various types of work

| Name of works | A height of a workplace surface, mm | | |
|---|---|---|---|
| | Women | Men | Women and men |
| Delicate work | 700 | 750 | 725 |
| Light work | 630 | 680 | 655 |

Workplaces should be organized in such a way as to exclude the possibility of laser radiation exposure to personnel. Laser products must be operated in specially designated areas that comply with fire safety requirements and have the necessary fire prevention and fire protection equipment [35].

## 2 Industrial safety

Harmful and dangerous factors are analyzed that may occur during the development or operation of the device under development in this section

GOST 12.0.003-201 is used to select factors. A list of hazardous and harmful factors is presented, which are typical for the designed production environment in the form of a table

Table 21 – Hazardous and harmful factors in the development of a method

| The source of the factor, the name of the type of work | List of factors (according to GOST 12.0.003-2015) | | Normative document |
|---|---|---|---|
| | Harmful | Dangerous | |
| 1. Work with the He-Ne laser;<br>2. Use of RNP plasma and blood. | 1. The increased gas contamination of the air of the working area;<br>2. Deviation of microclimate indicators;<br>3. Laser radiation;<br>4. Chemical active substances (plasma, whole blood). | 1. Fire;<br>2. Electrical current. | 1. GOST 31581-2013;<br>2. MU-287-113 (materials disinfection);<br>3. GOST 12.1.030-81;<br>4. GOST 12.1.005-88;<br>5. GN 2.1.6.3492-17;<br>6. SP 60.13330.2012. |

Identified harmful and dangerous factors are discussed in more detail below. Each factor is considered in sequence: the source of the factor; reduction of permissible norms with the required dimension; safety products (collective and individual) to minimize the impact of the factor.

### 2.1 Analysis of hazardous and harmful industrial factors

#### 2.1.1 Requirements for safe operation of laser systems

The following special rules must be observed when operating the laser system: systematically monitor and maintain all safety devices (screen, panels, doors, locks,

alarms) in good condition. The shutdown procedure must be strictly observed, at the end of which remove the key of the main switch from the lock.

The laser used is class 3A. Laser products are safe for observation with an unprotected eye. For laser products that generate radiation in the wavelength range from 400 to 700 nm, protection is provided by natural reactions, including the flashing reflex.

When detecting disorders in the operating mode of the laser system, immediately stop the flow of the optical head, coordinate table, and, if necessary, make an emergency shutdown of the system. In the event of an emergency failure of the optical element from zinc selenide (lens, exit window), turn off the emergency button, immediately leave the room and begin to replace this element no earlier than 30 minutes later.

When the laser system is attendanced, use only expendable materials (especially lubricants and cleaning agents), spare parts and replaceable components that are specified in the manufacturer's instructions [35].

### 2.1.2 Precautions measures during operations with RNP plasma and whole blood

The potential risk of using RNP plasma and whole blood is class 2a [36]. All reagents included in the RNP plasma kit and whole blood are used only for *in vitro* use.

All kit components in used concentrations are non-toxic and tested for hepatitis and HIV viruses.

Disposable rubber or plastic gloves should be worn during work with the kit, as human plasma samples should be considered as potentially infected, capable of storing and transmitting HIV, hepatitis B virus or another causative agent of a viral infection for a long time.

Disinfect all used materials in accordance with the requirements [38].

## 2.2 Analysis of harmful and dangerous factors that may arise in the laboratory during research

### 2.2.1 Increased air pollution

Local exhaust ventilation must be used if the emission of hazardous levels of airborne contaminants is observed during laser operation, for example:

1. Evaporation of target materials and reagents when working with a laser installation;

2. Gases from laser systems using a fluid gas, or by-products of laser reactions (fluorine, bromine, chlorine, hydrogen cyanide) [39];

3. Gases or vapors from cryogenic coolers [35].

Table 22 – The value of maximum permissible concentration of emitted gases

| Material name | MPC level, $mg/m^3$ | State of aggregation in production | Hazard class | Features of the action on the body |
|---|---|---|---|---|
| Fluorine | 1 | Aerosol | II | |
| Bromine | 0,5 | Steam/Gas | II | Substance with a highly directed mechanism of action |
| Chlorine | 1 | Steam/Gas | II | Substance with a highly directed mechanism of action |

### 2.2.2 Climate deviation

Favorable conditions for the workplace microclimate must be created while working in the laboratory. Prolonged exposure of a person to adverse weather conditions can dramatically worsen his well-being, reduce labor productivity and lead to diseases. The microclimate is determined by combinations of temperature, humidity, air velocity and thermal radiation acting on the human body. High air temperature contributes to the rapid fatigue of the worker, and can lead to overheating of the body, cause a violation of thermoregulation, impairment of well-being, decreased attention, heat stroke, increased stress on the heart. Low air temperature

can cause local or general hypothermia, cause colds, and lead to diseases of the peripheral nervous system (radiculitis, bronchitis, rheumatism). Low humidity can cause the mucous membranes of the respiratory tract to dry out. Air mobility effectively contributes to the heat transfer of the human body and is positively manifested at high temperatures and negatively at low. optimal and permissible microclimate indicators of industrial premises are given according to [40].

Table 23 – Optimum microclimate indicators at workplaces of industrial premises

| Period of the year | Category of work on the level of energy consumption, W | Air temperature, ℃ | Relative humidity, % | Air velocity, m/s |
|---|---|---|---|---|
| Cold | IIa(175-232) | 19-21 | 60-40 | 0.2 |
| Warm | IIa(175-232) | 20-22 | 60-40 | 0.2 |

Table 24 – Permissible microclimate indicators

| Period of the year | Air temperature, ℃ | | Relative humidity, % | Air velocity, m/s | |
|---|---|---|---|---|---|
| | Upper bound | Lower bound | | Upper bound | Lower bound |
| Cold | 23-24 | 15-17 | 40-60 | 0.1 | 0.2 |
| Warm | 27-29 | 17-18 | 40-60 | 0.1 | 0.3 |

### 2.2.3 Electrical safety

Electrical safety is a system of organizational and technical measures aimed at protecting people from the harmful and dangerous effects of electric current.

There is a danger of electric shock in all cases where electrical installations and equipment are used. Electrical installations are classified by voltage - with a rated voltage of up to 1000 V (rooms without increased danger), up to 1000 V with the presence of an aggressive environment (rooms with increased danger) and over 1000 V (rooms especially dangerous) (according to the Rules for the Installation of Electrical Installations).

To ensure safe operation, it is necessary to exclude possible sources of electric shock:

1. Accidental contact with live parts under voltage;

2. The appearance of voltage on the mechanical parts of electrical equipment (cases, covers, etc.) due to insulation damage or other reasons;

3. The occurrence of stress on the ground or supporting surface.

According to the degree of danger of electric shock, this laboratory belongs to rooms without increased danger, it is a dry room without increased dusting, the air temperature is normal, the floor is covered with insulating material. All electrical equipment and devices are in place and have protective grounding with a resistance of not more than 4 Ohms [41]. All employees undergo initial electrical safety training.

It is necessary to check the serviceability of conductive wires before starting work. It is forbidden to use wires with damaged insulation or without insulation, as well as wires that are not equipped with plugs or soldered terminals, to connect electrical appliances.

Instruments must be kept clean. It is necessary to disconnect the equipment from the network at the end of work.

Electric shock may occur because of careless operations with connecting wires. In addition, a short circuit can occur when current-carrying parts close on the device about absence of nulling or grounding and cause the electric shock.

Table 25 – Permissible levels of effective touch voltage and currents

| Mode | Current type | | | | | |
|---|---|---|---|---|---|---|
| | AC, 50 Hz | | | DC | | |
| | U, V | I, mA | Duration, min | U, V | I, mA | Duration, min |
| Normal | 2 | 0,3 | <10 | 8 | 1 | <10 |

First aid to the victim should consist in immediately disconnecting the current that caused the injury, disconnecting (in rubber gloves) the victim from the leads and calling the doctor. If the victim is conscious, but before that he was swooning or has been under current for a long time, he needs to ensure peace before the doctor arrives. If the victim lost consciousness, but breathing persists, it is necessary to put it comfortably, evenly, unfasten tight clothing, create an influx of fresh air, remove unnecessary people from the room, breathe ammonia, spray with water, rub and warm the body. It is necessary to apply artificial respiration with convulsive and rare

breathing. In the absence of signs of life (lack of pulse and breathing), the victim cannot be considered dead. It is necessary immediately, without wasting time, before the arrival of the doctor to do artificial respiration.

### 2.2.4 Room illumination

Light sources with a color temperature of 2400 to 6800 K should be used for general and local lighting of rooms. The intensity of ultraviolet radiation in the wavelength range of 320-400 nm should not exceed 0.03 W/m [42].

The presence in the radiation spectrum of wavelengths less than 320 nm is not allowed.

For artificial lighting, energy-efficient light sources should be used, giving preference to equal power sources of light with the highest light output and service life, taking into account the requirements for color differentiation.

## 2.3 Justification of measures to reduce the impact of hazardous factors on the researcher

### 2.3.1 Fire safety

The laboratory room where the work was carried out belongs to category B [43].

The causes of the fire may be:

1. Short circuit currents;

2. Malfunction of electric networks;

3. Ignorance of fire safety rules or negligence of staff;

4. Smoking in the wrong places.

In this regard the following fire safety standards must be met in the laboratory:

1. It is forbidden to include additional non-intended consumers to protect the network from congestion;

2. Carry out work in the laboratory only when the equipment and electrical wiring are in good condition;

3. To extinguish a fire (fire extinguisher);

4. Have a plan of evacuation of people, which should hang in a conspicuous place;

5. Place the equipment so that there is sufficient passage to the exit.

The TPU building in which the laboratory is located complies with fire safety requirements.

### 2.3.2 Determination of air exchange in laboratory

Air exchange in public buildings is necessary to clean the air of harmful substances: to remove harmful substances (emitted harmful gases, vapors and dust), to remove water vapor and excess heat.

In residential and public buildings, carbon dioxide ($CO_2$) exhaled by people is a constant harmful emission. The required air exchange is determined by the amount of carbon dioxide exhaled by a person and by its permissible concentration. The amount of carbon dioxide, depending on the age of the person and the work performed, as well as the permissible concentration of carbon dioxide for different rooms. The carbon dioxide content in the air can be determined by the chemical composition of the air. However, given the increased carbon dioxide content in the atmosphere of settlements, the $CO_2$ content should be taken into account when calculating:

- for large cities (over 300 thousand inhabitants)– 0.5 l/m$^3$.

Determine the required rate of air exchange in a laboratory for three people, if the volume of the room is V=72 m$^3$. The amount of carbon dioxide exhaled by an adult with light work in an institution is 23 l/h. The maximum permissible concentration of carbon dioxide for institutions is 1.25 l/m$^3$. The required air exchange in the laboratory is determined by the formula 16:

$$L = \frac{G * P}{\mathrm{x}_v - \mathrm{x}_n}, \tag{16}$$

where L – air exchange required, m$^3$/h;

G – the amount of harmful substances released into the room air, g/h;

P – number of people working in the laboratory;

$x_v$ – maximum permissible concentration of harmfulness in the air of the working area of the room [39], mg/m$^3$;

$x_n$ – the maximum possible concentration of the same harmfulness in the air of populated areas [44], mg/m$^3$.

The rate of air exchange (n), which shows how many times in one hour the air is completely replaced in the room, which is determined by the formula 17.

$$n = \frac{L}{V_n}, h^{-1} \quad (17)$$

where $V_n$ is the internal volume of the room, m$^3$.

According to [45], the permissible air exchange rate should be in the range from 3 to 10 h$^{-1}$.

Required air exchange in the laboratory, according to 16:

$$L = \frac{23 * 3}{1.25 - 0.5} = 92 \frac{\text{m}^3}{\text{h}},$$

The required air exchange rate is:

$$n = \frac{92}{72} = 1.27 \text{ h}^{-1}$$

Thus, the calculated consumed air exchange in the laboratory should be 92 m$^3$/h.

### 2.3.3 Laser safety

The laser product must have protective devices to prevent unauthorized exposure to laser radiation personnel, as well as protective interlocks to ensure safety during maintenance and operation.

Protective interlocks must include shutting off the supply of hazardous electrical voltage to the laser product or its component parts. The possibility of generating laser radiation in the event of accidental disconnection of locks should be excluded.

Screens should be used as laser protection for class 3A, 3B, and 4 lasers. Screens should be made of fire-resistant and impervious to laser radiation material and to close the area of interaction of the laser beam with the target.

If the level of laser radiation does not exceed the permissible level for class 3A: "Do not look into the beam and do not observe directly using optical instruments."

## 3 Environmental safety

### Analysis of the impact of the object of research on the environment

This subsection considers the environmental impact of the laboratory facility. The alleged sources of environmental pollution resulting from the implementation of the solutions proposed in the are identified.

During operation of the facility, the main types of impacts of the designed facility are established:

– household waste;

– biological waste;

– medical waste.

Measures to reduce the intensity of environmental pollution is the creation of obstacles to the distribution and treatment of waste by various methods.

Utilization of household, biological and medical waste is the Main Event. Glass, metal waste, waste paper, as well as plastics are processed into secondary raw materials.

Class B biological wastes (blood plasma, whole blood) are collected in yellow disposable soft or hard packaging or yellow labeled. The choice of packaging depends on the morphological composition of the waste.

To collect organic, liquid waste of class B, disposable, non-punctureable, moisture-resistant containers with a lid (containers) must be used to ensure their sealing and exclude the possibility of spontaneous opening.

After filling the bag by no more than 3/4, the person responsible for the collection of waste in this medical unit fastens the bag or closes it using tag tags or other devices that prevent the discharge of Class B waste. Solid containers are closed with lids. Class B waste disposal outside the unit in open containers is not permitted.

At the final packaging of class B waste to remove it from the unit (organization), disposable containers with class B waste are marked with the

inscription "Waste. Class B" with the name of the organization, unit, date and name of the person responsible for collecting the waste.

Class B medical waste (gloves and containers) from units in closed disposable containers is placed in containers. Then they are moved to a waste management site or a temporary storage room for medical waste until the next transport of specialized organizations to the place of disinfection. Access by unauthorized persons to the temporary storage of medical waste is prohibited.

When organizing medical waste disinfection sites using hardware methods, the collection, temporary storage, and transportation of Class B medical waste without prior disinfection at the places of formation are permitted, provided that the necessary epidemiological safety requirements are met.

In this case, the organization engaged in medical and/or pharmaceutical activities should be provided with all necessary expendables, including disposable packaging [46].

During operation, the atmosphere is not polluted.

## 4 Safety in emergency situation

**Analysis of probable emergencies that may occur in the laboratory during research**

In case of emergency, you must immediately call the fire department at number “01” from your business phone or “101” from your mobile phone.

The notification of civil defense alerts in the event of an emergency to the personnel of the facilities is carried out using voice information via broadcasting channels, radio broadcast networks and communication networks. On the territory of TPU they do not use, do not produce, do not process, do not store radioactive, fire hazardous, as well as explosive substances that create a real threat of an emergency source. As the most probable technological emergencies, the project considers:

- fire in the facility.

Fire hazards for humans include toxic combustion products, low oxygen concentration, open flames, smoke, and high air temperatures.

The following measures must be observed to prevent fire:

1. Reducing the determining size of the combustible medium;

2. Prevention of the formation of a combustible medium.

In case of overheating, short circuits, etc. possible ignition of electrical installations, wiring. To extinguish the fire, it is necessary to use special means, it is impossible to use water and other conductive substances. Therefore, the premises should be equipped with means for extinguishing electrical installations and electrical wiring under voltage.

The analysis and evaluation of harmful and hazardous labor factors that may affect the personnel involved in the development of the project. The development of protective measures against these factors, the assessment of working conditions. Also in this section, issues related to safety, fire prevention and environmental protection, recommendations for creating optimal working conditions are considered.

## Conclusion

The paper considers the method of digital speckle patterns correlation for the analysis of blood coagulation time. The relevance of this method is considered. The proposed method is compared with existing hemostasis system analyzers.

The work shows experiments confirming the applicability of the method of digital speckle patterns correlation for the analysis of the whole blood coagulation time. Analyzing the results obtained, we can say that the proposed method can be used to analyze blood coagulation time. Laboratory experiments were conducted comparing the data, obtained by the method of speckle patterns correlation, by the method of thromboelastography “ARP Mednord”, and using an optical coagulometer “Minilab 701”. Thus, it was found that the accuracy of the results was 97%.

A prototype of an optical device for blood coagulation time analyzing has been developed and tested. The error in the data obtained was 3%. Such accuracy is applicable for a medical device, since the error of medical measurements can be up to 20%.

In further work, it is necessary to conduct a series of experiments to confirm the operability of the developed device. Create software for the microcomputer Raspberry Pi3, which will run the study and display the result on the microcomputer screen. Develop a device enclosure for toxicological and clinical trials.

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