Whole blood clotting time assessment by method of laser-speckle correlation

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***Abstract*— The paper presents the results of study of the coagulation process of the whole blood with anticoagulant using the method of laser speckle correlation. The clotting time dependence curves of the correlation coefficient have been presented and discussed. Analyzing the changing trend of these curves is possible to assess the clotting time, which prove the capability of using the method of laser speckle correlation for determining the diseases of blood coagulation.**

Keywords—optical coagulometer, blood, clotting time, speckle

I. INTRODUCTION

As an important adjustable function, the mechanism of blood coagulation plays a key role in protection of biological organs from accidental injuries [1]. The diseases of blood coagulation bring much significant risk to normal life. Severe patients need to take medication regularly to maintain normal mechanism of blood coagulation. More than that, the capability of coagulation mechanism is also a routine indicator of blood tests in clinical practice. Therefore, a faster and more accurate detection of coagulation mechanisms remains an urgent task.

Until now, the most effective method for study the mechanisms of blood coagulation is to measure the clotting time of blood. The coagulation factors that complete the coagulation mechanism are present in the plasma [2]. In this connection, the method of measuring the clotting time requires the plasma extracted from the blood in clinics. Modern coagulometers do not allow to make a quick assessment of blood clotting time. This method is slow and need a large amount of blood for centrifugation to produce plasma. For the analysis carried out using laboratory coagulometers, it is necessary to separate the blood cells from the plasma, place non-magnetic balls. These processes are time consuming. In addition, the device is in contact with the sample, it is necessary to place a non-magnetic ball in the sample that is in sample during the entire study and may make to add any changes in the formation of a fibrin clot. Therefore, researchers started to develop the means of measuring the clotting time using the whole blood for determining the disease of blood coagulation.

The method of laser speckle correlation is a new optical method that can observe or measure many sorts of changes of objects, such as the displacements [3, 4], distorts and the velocity of liquid flow [5], mechanical tension [6], by analyzing the laser speckle patterns. In biomedical flied methods of laser speckle techniques are well applied for measuring the heartbeat pulse [7], the velocity of microvascular blood flow [8], bacteria activity [9].

The correlation coefficient reflects the ratio of two speckle patterns, as a result, reflects velocity of change of two speckle patterns. The higher the rate of change of the image, the less optically dense is the object under study. In the process of blood coagulation, the rate of light scattering changes, corresponding to the rate of formation of a fibrin clot. The laser-speckle methods allow to analyze biological fluids without contacting with the sample. Due to this, non-contact optical analysis of clotting time of whole blood is possible. The blood coagulation process proceeds independently, without prior intervention in the sample under study [10-12].

In [11, 12] we tested the method of laser-speckle correlation using the control plasma. The aim of this work is to test this method with citrate whole blood of the laboratory animals.

II. EXPERIMENTAL DETAILS

In this paper, we used whole blood of test systems (rats) for the analysis of prothrombin time and Techplastin reagent. "Techplastin" is thromboplastin-calcium mixture from the rabbit brain. For the preparation of the regents, 5 ml of distilled water was added to Techplastin. Then the mixture was mixed and left for 20 minutes at a temperature of +37 °C. According to the instructions [13] for analysis, whole blood and Techplastin reagent were used in a 1:2 ratio.

Blood was taken from the aorta of animal. To prevent a premature start of the coagulation process, blood was placed in a tube with sodium citrate immediately after collection. Sodium citrate blocks the blood coagulation system allowing

Figure 1 shows the scheme of the experiment. A He-Ne laser with a wavelength of 650 nm and a power of 5 mW illuminated the container into which the test sample with a volume of 50 μl was placed. The resulting image was recorded with USB digital camera ELP-USBFHD01M-MFV with a Canon Macro Lens EF 100 mm lens. During the process of coagulation a chaotic movement of suspended particles, formed elements, proteins occur in the blood. When the blood is illuminated by coherent radiation, multiple reflections of the beam from moving particles mix and form a speckle pattern. In the proposed method, changes in speckle patterns are

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recorded using a camera and then processed in the Matlab software. Images were being recorded during 6 minutes.

Fig. 1. The scheme of the experiments with lens.

Figure 2 shows the experimental setup without lens. In contrast to the experiments presented in [11, 12], in this case we removed the objective keeping the position of the camera approximately the same. Registration of speckle patterns was carried out with 30 fps speed. To determine the blood coagulation time, the calculation of the correlation coefficient during the entire coagulation process were conducted. The correlation coefficient reflects the ratio of two speckle patterns. The closer this value is to 1, the less they differ and the less changes occurs in the blood sample. For the calculation, the formula for the correlation coefficient, given in [14], was used.

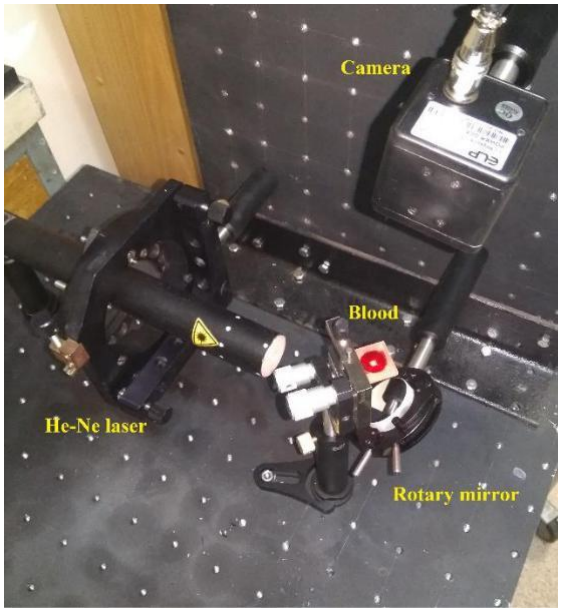

Fig. 2. The scheme of the experiments without lens.

III. Results

Figure 3 shows the time dependence of the correlation coefficient for six control experiments conducted on a laboratory setup with a lens shown in Figure 1. Experiments were conducted on whole citrate blood of test systems. To activate the process of clotting in the sample was added reagent Tehplastin. Experiments were carried out to test the applicability of the digital speckle pattern correlation method for analyzing the clotting time of whole blood. In this case, the time of blood clotting is determined by the coagulant Tehplastin. Analyzing the data, we can say that the clotting time in this case is 40-150 s for a series of experiments. The increase in clotting time depends on the concentration of sodium citrate in the sample.

Figure 4 shows a series of experiments conducted on the setup shown in Figure 2. The conditions of the experiments and the ratio of the volumes of the sample-Technical were the same as in the first series of experiments. In this case, we can to see the time of sample activation with Techplastin reagent. This time between 10 and 40 s. from the start of the experiment. Active growth of the fibrin clot is between 40 and 118 s. Thus, the generalized growth time of a fibrin clot for a series of experiments was 78 s.

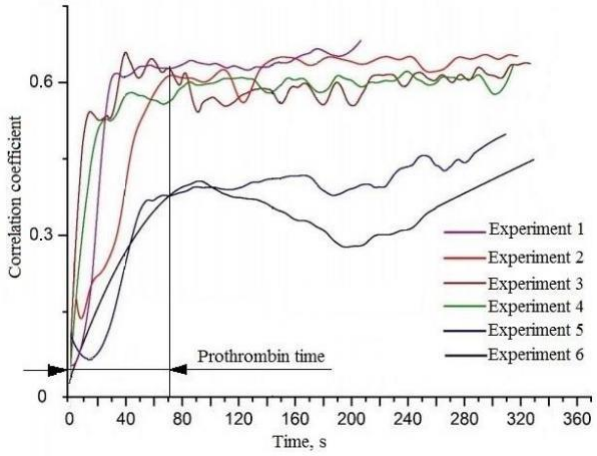

Fig. 3. The curves of correlation coefficient dependence on blood clotting time, obtained by recording with a camera with a lens.

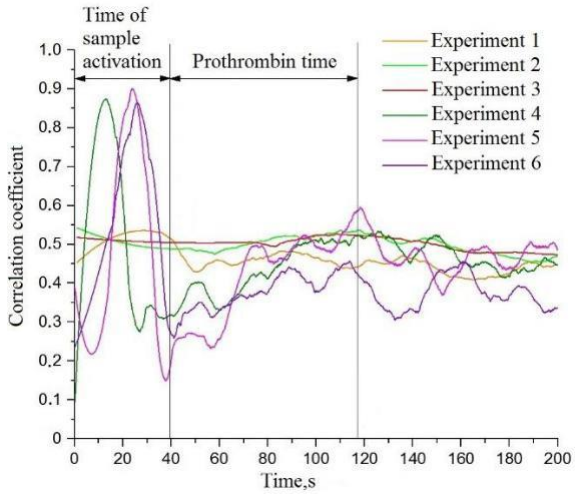

Fig. 4. The curves of correlation coefficient dependence on blood clotting time, obtained by recording without a camera with a lens.

IV. CONCLUSION

In this paper, we demonstrated the possibility of using the method of correlation of speckle patterns for analyzing the clotting time of citrated blood of laboratory animals (rats). The results of analyzes carried out on whole blood placed in a tube with sodium citrate are presented. The analysis was carried out on two installations. An objective lens was added to the camera in the first one, and in the second one, it was missing. We can conclude that method of laser-speckle correlation works both with objective and without objective. Due to this fact, we can construct more compact portable device by abandoning the optical elements.

Obtaining the prompt information about the clotting time, the doctor will be able to take the necessary measures immediately to optimize the composition of the patient's blood to avoid thrombosis of the lower veins or large blood losses.

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