Measuring blood flow velocity with a magnetic label

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Abstract. The article describes the method of measuring blood flow velocity by a non-invasive method of magnetizing blood with a magnetic pulse and detecting a magnetized substance using a magnetolectric magnetic field sensor. The influence of the magnetic field on the parameters of blood and blood flow is considered. The methods of measuring blood flow velocity are considered, the distinguishing features of each method are given. The use of a magnetolectric composite structure of bidomain lithium niobate\nickel\\textit{metglas} is proposed as a sensitive element for detecting blood flow velocity.

1. Introduction

Currently, there are a number of methods for studying the microvasculature. Microscopic techniques are distinguished among them, in particular, ophthalmoscopy, computed TV microscopy of the vessels of the conjunctiva of the eyeball, nail bed, and vessels of the skin. They make it possible to evaluate the structure and diameter of microvessels and the state of their tone, and to identify various vascular changes inside and outside (slowing down blood flow, stasis, lipid inclusions, etc.). A number of methods allow you determining the linear velocity of blood flow. However, these research methods do not allow evaluating tissue blood flow in general and to identify the features of its regulation. There are methods for evaluating tissue blood flow, including occlusive plethysmography, leaching of radioactive isotopes, fluorescence microangiography, introduction of labeled microspheres, etc. However, some of them found application only in experimental medicine because of the complexity of human use; others are associated with the need to use expensive equipment. In addition, the above methods for the study of microcirculation allow evaluating the features of the regulation of peripheral hemodynamics only indirectly.

Measurement of blood flow velocity in the main arteries and veins is of great diagnostic value, since the leading cause of death in Russia and the rest of the world are diseases of the cardiovascular system; in Russia this number makes 56.4%, in the world 21.9% (figure 1), and also indirectly indicates a pathological change in the geometry of the vessel and the elastic properties of the vessel wall.

In this regard, in clinical practice, methods for registering blood flow in large vessels and heart structures are widely used.

The possibility of a non-invasive, objective and dynamic assessment of blood flow through small-caliber vessels remains one of the urgent tasks of modern angiology and related specialties. The success of the early diagnosis of diseases such as obliterating endarteritis, diabetic microangiopathy, Raynaud’s syndrome and disease depends on its solution.
2. The effect of a magnetic field on blood parameters and blood flow

A magnetic field affects many blood flow parameters. The ability of blood to respond to external magnetic fields is determined by the complex interaction between hemoglobin inside the erythrocyte and erythrocyte membrane, as well as the electrical conductivity of blood plasma. Red blood cells exhibit diamagnetic and paramagnetic properties depending on oxygen saturation [1], being oriented parallel to the lines of the external magnetic field [1–5]. Direct measurements of the magnetic susceptibility of blood obtained values of $3.5 \times 10^{-6}$ and $-6.6 \times 10^{-7}$ rel. units for venous and arterial blood respectively [6–8]. Blood is a magnetically saturated medium, since the iron atoms of hemoglobin have a magnetic moment. Each red blood cell erythrocyte contains millions of hemoglobin molecules, in the center of which are an iron atom. The bulk of the iron in the human body is concentrated in the hemoglobin of blood, that is 2.2–3 g, about 75%. As carriers of magnetism, iron atoms embedded in complex organic molecules can record, store and transmit information in the form of signals in the direction of the magnetic field and its intensity [9].

The effect of a magnetic field on blood has been studied by many scientists using methods such as nuclear magnetic resonance and magnetic tomography. Data were obtained on the diamagnetic susceptibility of oxyhemoglobin (oxygen-enriched arterial blood) and paramagnetic susceptibility of deoxyhemoglobin (venous blood poor in oxygen). The effect of a magnetic field on blood viscosity was also studied and that the flow of blood slows down in the presence of a field. Microscopic examination revealed the formation of “coin columns” of 3 to 6 red blood cells under the action of the field. Sometime after magnetization, the columns disintegrated, and the viscosity decreased to control values.

The orientation of normal red blood cells in a strong constant magnetic field was researched. It was found that in the presence of an external field, red blood cells are oriented in such a way that the plane of their disk is parallel to the direction of the applied field, that is, domains consisting of iron atoms are oriented along the field, increasing the magnetization to a certain limit, and when the field strength decreases, the magnetization decreases along the curve hysteresis, i.e. with residual magnetization.

Based on the foregoing, it can be assumed that the magnetic moment of blood is stored for a certain period of time, which allows determining the speed of blood flow using the “magnetic label” method; the essence of the method is described below. This assumption gives life to a method of measuring blood flow velocity in vessels based on the principle of magnetic marking of blood in vessels.
3. Comparison of methods for measuring blood flow velocity

It is customary to use instruments and devices that are based on the Doppler effect, which is used both with ultrasound and with laser radiation to measure the speed and direction of blood flow in medicine. Ultrasonic (US) Doppler methods are an effective means of non-invasive study of the characteristics of tissue movement in the human body and are widely used in cardiology and vascular diagnostics.

3.1. Doppler methods for measuring blood flow velocity

The following classification of Doppler methods depending on the methods of obtaining and displaying information can be introduced:

1. Method for assessing the change in time of blood flow velocity in the cross section of a vessel or part of a section of the heart or vessel.
2. Method for assessing heart rate using the Doppler effect.
3. Spectral Doppler echography, or briefly spectral Doppler (D-mode, or spectral Doppler) is an assessment of the spectrum of blood flow velocities in the heart and blood vessels in the process of its change over time.
4. Methods of color Doppler ultrasonography, which primarily include color Doppler mapping of blood flow (CFM mode - colorflowmapping) is a two-dimensional image of biological structures in which the speed of individual elements is displayed using colors of various shades.

When measuring low blood flow velocities, a number of difficulties arise, one of which arises in connection with the need to filter powerful low-frequency components in the spectrum of the received ultrasound signal, appearing from the reflection of the emitted signal from the walls of the vessels that oscillate with the heart rate. Therefore, it is advisable to use the highest possible ultrasonic frequencies. However, as the frequency increases, the attenuation coefficient of ultrasound in the tissues of the human body rapidly increases in proportion to the oscillation frequency. Thus, the attenuation in soft tissues is on average 0.7 dB/cm at 1 MHz, so, at a frequency of 20 MHz in the study of the vessel it will be about 30 dB, i.e. the amplitude of the received signal will be significantly less. In addition, with increasing frequency, the proportion of ultrasound reflected by the blood flow increases, since in the case of Rayleigh scattering (the size of the scatterer - erythrocyte is 7.2-2.2 microns is much less than the length of the scattered wave), the power of the scattered wave is proportional to the fourth power of the frequency.

The main disadvantage of a blood flow meter with continuous ultrasound is the lack of range resolution. Any moving target falling within the area of the radiation pattern of the ultrasonic sensor will contribute to the final Doppler output signal. As a result, during the clinical use of such devices, it is not always possible to isolate blood flows in neighboring vessels. And range selectivity can sometimes be the main requirement in Doppler studies.

The disadvantages of echo pulse Doppler devices include:

- long-range speed limits;
- large deviation of the maximum radiated power (intensity) from average.

Since the average intensity strictly determines the sensitivity of the system and there is evidence that high-intensity ultrasound can have a certain effect on human tissue, the signal-to-noise characteristic, and therefore the sensitivity of a pulsed Doppler system, is strictly limited by the patient’s safety conditions.

Limitations when using continuous radiation:

1) echo signal is emitted from all the depth within the sensitivity zone, therefore, it is impossible to separate the signals from different vessels falling into the sensitivity zone of the device, and it is also impossible to estimate the diameter of the vessel;
2) the minimum possible measured Doppler speed is limited by a high-pass filter, which is used to suppress powerful signals from slowly moving vessel walls; insufficient suppression of these signals leads to the overload of the receiving path;
3) dependence of the accuracy of the estimation of the velocity spectrum, and sometimes the very possibility of estimating the spectrum on the angle between the axis of the ultrasound beam and the direction of blood flow;
4) with established standards for a patient safe radiation power, the bone is an insurmountable obstacle to the propagation of ultrasound, which makes it impossible to conduct transcranial studies;
5) complication of the doctor’s work due to the need to manipulate the sensor and its orientation so that only one observed vessel can enter the ultrasonic beam of the sensor and the desired viewing angle can be selected.

Limitations when using pulsed radiation:
1) the smallest measured Doppler frequency is determined by the characteristic of the high-pass filter used to suppress powerful signals from slowly moving vessel walls;
2) the maximum measured speed is determined by the pulse repetition rate;
3) when using short signals, a much lower accuracy of measuring the Doppler frequency shift is obtained than with long signals due to the presence of a lower energy level, and, therefore, the always present noise and interference make it more difficult to measure the frequency shift;
4) with decreasing signal duration, the corresponding spectrum of frequencies expands, while it is difficult to measure small Doppler frequency shifts, the magnitude of which is less than the width of the frequency spectrum of the signal.

If the velocity of the blood element exceeds a certain boundary value determined by the repetition frequency of the probe pulses, then due to the superposition of the frequencies, the corresponding Doppler shift will be transferred to the low-frequency region, which corresponds to a low velocity. In other words, ambiguity arises when measuring blood flow velocity.

3.2. Using the function of anastomoses to measure blood flow velocity using the Doppler method
The main idea is to use the function of direct extra-intracranial anastomosis at the level of the branches of the orbital artery with the branches of the external carotid artery in the projection of the superior medial angle of the orbit, nasal dorsum and forehead. By measuring the speed and direction of blood flow in the right and left anastomoses and further comparing the results with each other and the patient’s norm, the patient’s condition is determined relative to the presence of signs of cerebral ischemia. The method of measuring the speed and direction of blood flow is carried out due to a portable device operating on the Doppler effect for long-term wear by the patient and long-term monitoring of his cerebral blood flow in various physical and psycho-emotional states, which provides measurement outside the hospital [10].

3.3. The method of magnetic label
A promising method for measuring blood flow velocity is the magnetic label method. A certain volume of blood that has a magnetic moment as a result of exposure to an external magnetic pulse is meant by a magnetic label is meant. The essence of the method is to mark blood particles with a magnetic pulse, which affects the magnetization of blood gems. Further, due to the conservation of the magnetic moment of blood over time, blood particles with a magnetic label move through the bloodstream towards the magnetic induction sensor. Then the magnetic tag is read by the sensor and thus the blood flow velocity is determined [11]. Devices have been developed for measuring blood flow velocity, working on the principle of magnetic labels [12–14]. The main principle of the device’s operation is to generate a magnetic pulse, which is transmitted to the amplifier, then filter the signal from disturbance, noise, and interference using a band-pass filter that selects the fundamental frequency harmonic of the magnetic tag generator and then the signal from the channels is subtracted on the amplifier and formed into a rectangular and transmitted to the comparator. A significant drawback of such devices is their low sensitivity due to the receiving sensor, which uses Hall sensors. Increasing the sensitivity of the receiving sensor can significantly improve the performance of the device as a whole. Finding a new sensor for this device is an urgent task for scientific research.
4. The use of magnetoelectric composite structures for devices for measuring blood flow velocity

Recently, there has been a great demand for sensitive magnetic sensors for biomedical applications as measuring instruments for the magnetic fields of humans and living things; for measuring magnetobiological reactions; electrical signals of the heart; search for ferromagnetic inclusions; skeletal muscle signals; eye; background and induced brain activity; fiber of the eye, and it is also possible to use sensors for magnetic tomography, since it requires the detection of very weak magnetic fields, less than 10 nT.

The generation of weak magnetic fields can be caused by direct currents or magnetic particles, which are very effectively used in biomedicine, therapy and diagnostics of a number of serious diseases, such as coronary heart disease, cerebral ischemia, brain tumor, epilepsy, diseases of the gastrointestinal tract, which makes the measurement and diagnosis of biological magnetic fields very relevant for the study.

The magnetoelectric effect (ME) underlying the operation of magnetoelectric devices is promising for study in medical diagnostics [15]. The direct ME effect consists in the appearance in the material of electric polarization $\delta E$ under the action of an external magnetic field $\delta H$; the ME voltage coefficient $\alpha_E = \delta E/\delta H$ characterizes the magnitude of the ME effect.

It is more promising to use the magnetic tag method using ME materials to improve the accuracy of blood flow velocity measurements. This will eliminate the problems of known devices for measuring blood flow velocity using the magnetic label method based on Hall effect sensors, such as low sensitivity and high noise level. Due to the high sensitivity of the ME element, achieved due to the large ME coefficient and low level of intrinsic noise [16], it is possible to achieve an acceptable result of the detection of weak blood magnetization.

It is proposed to use the magnetoelectric composite structure of the bidomain LiNb/ Ni/Metglas, which has a high sensitivity sufficient to detect the magnetic label to implement the magnetic label method [17]. The use of ME materials in medical diagnostics will reduce the time of measuring blood flow velocity, as well as increase the accuracy of the results, therefore ME sensors have great prospects for use as reading magnetic labels and determining blood flow velocity.

5. Conclusion

In this paper, we propose the use of magnetoelectric composite structures for measuring blood flow velocity using the magnetic label method. The influence of magnetic field on blood parameters and blood flow is considered. Since the magnetic moment of blood is stored for a certain period of time, this makes it possible to read the magnetic label and determine the speed of blood flow. Other methods for determining blood flow velocity, such as pulsed and continuous Doppler, are also considered. The proposed ME LiNb/Ni/Metglas composite structure can be used as a highly sensitive element for reading the magnetic moment of blood. The use of ME materials will make it possible to increase the sensitivity of the magnetic label method and use it in practical applications as well as apply them in medical diagnostics. It is also possible to use this method in other areas, such as automotive, spacecraft, archaeological research, robotics and measuring equipment.

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References

[1] Higashi T, Yamagishi A, Takeuchi T, Kawaguchi N, Sagawa S, Onishi S and Date M 1993 Orientation of erythrocytes in a strong static magnetic field J. Blood Vol 82 1328–1338
[2] Gasparovic C, Matweiyoff N A 1992 The magnetic properties and water dynamics of the red blood cell Magn. Reson. Med. Vol 26 274–287
[3] Shaylgin N, Norina S B and Kondorsky E I 1983 Behaviour of erythrocytes in high gradient magnetic field J. Magn. Magn. Mater. Vol 31 555–561
[4] Takeuchi T, Mizuno T, Yamagishi A, Higashi T and Date M 1995 Orientation of red blood cells in high magnetic field J. Magn. Magn. Mater. Vol 140-144 1462–1470
[5] Higashi T, Ashida N and Takeuchi T 1997 Orientation of blood cells in static magnetic field *Physica B* Vol 237–238 616–621
[6] Haik Y, Pai V and Chen C J 1999 Biomagnetic fluid dynamics *Fluid Dynamics at Interfaces* ed W Shyy and R Narayana (Cambridge University Press, Cambridge) 439–452
[7] Motta M, Haik Y, Gandhari A and Chen C J 1998 High magnetic field effects on human deoxygenated hemoglobin light absorption *Bioelectrochem. Bioenerg.* Vol 47 297–307
[8] Bartoszek M and Drzazga Z 1999 A study of magnetic anisotropy of blood cells *J. Magn. Magn. Mater.* Vol 196-197 573–582
[9] Semenova K V 2012 Method for measuring blood flow velocity using the magnetic properties of blood *Materials of the All-Russian Youth Conference Methods of computer diagnostics in biology and medicine* 192–193
[10] Lobekin V N, Petrov R V, Bichurin M I, Rebinok A V and Sulimanov R A 2018 Study of capabilities of making detection device for cerebral ischemic state *Medical Research and Innovations* Vol 2 1–5
[11] Belsky A M and Belskaya T A 2016 Analysis of the error of the magnetometer measuring device for blood flow velocity *Kazan National Research Technical University named after A.N. Tupolev* 4
[12] Belsky A M and Berdnikov A B 2010 Device for measuring blood flow velocity *Utility Model Patent №102481*
[13] Belsky A M and Berdnikov A B 2014 Device for measuring blood flow velocity. *Utility Model Patent №149843*
[14] Belsky A M, Berdnikov A B and Savelyeva V N 2016 Device for measuring blood flow velocity. *Utility Model Patent №166193*
[15] Petrov R V and Leoniev V S 2014 Magnetolectric magnetometer *Vestnik NovSU Ser.: Engineering* 75 1 29–32
[16] Yaojin Wang, David Gray, David Berry et al 2011 An Extremely Low Equivalent Magnetic Noise Magnetoelectric Sensor *Adv. Mater.* Vol 23 4111–4114 doi: 10.1002/adma.201100773
[17] Bichurin M, Sokolov O, Leontiev V, Petrov R, Tatarenko A, Semenov G, Ivanov S, Turutin A, Kubasov I, Kislyuk A, Malinkovich M, Parkhomenko Y, Kholkin A and Sobolev N 2019 Magnetolectric effect in a gradient structure LiNbO3/Ni/Metglas *Proceedings of IWAMO* (Aveiro, Portugal) 15–17