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**RISK ESTIMATION TECHNOLOGY FOR ISCHEMIC HEART DISEASE AND
ESSENTIAL HYPERTENSION BASED ON CREATING A NON-INVASIVE AUTOMATED
DIAGNOSTICS COMPLEX OF A MICROCIRCULATION STATE**

The purpose of the project proposal is the development of monitoring technology and the formation of primary health examination algorithm for revealing persons with the raised risk of ischemic heart disease and essential hypertension based on the creation of a medical-technological complex for the non-invasive automated estimation of microcirculation component state of cardiovascular system.

The state of the art in the field of the diagnosis and monitoring of cardiovascular system diseases

Diseases of cardiovascular system, first of all ischemic heart disease (IHD) and essential hypertension (EH), are remaining one from principal causes of population death rate and disablement in the industrially developed states, that defines social and demographic losses in the majority of them. For example, about 500 thousand persons die from the above-mentioned cardiovascular diseases annually only in Northern America.

At present time despite of revealing numerous risk factors and significant successes in treatment of this kinds of a cardiovascular pathology, the high IHD and EH sick rate is kept. The tendency to increasing this parameter among persons of the most able-bodied age - from 35 till 50 years is marked especially as adverse by researchers of many countries. It causes a necessity to improve efficiency of existing diagnostics and treatment methods and development of new one, and, in particular, the primary preventive IHD and EH maintenance. The main condition of the prevention of development and progressing these diseases is the active revealing presymptomatic states, allowing to carry out necessary preventive or, in some cases, medical actions in time. From these positions the development of the diagnostic approach directed to an estimation of IHD and EH development risk degree on presymptomatic disease stage is a topical scientific and practical problem, the decision of which is being the project's basic purpose.

The main factors which role in IHD and EH pathogenesis now actively are studied occurs the pathogenetic parts. They are concerning the reasons and mechanisms of lipid disorders, functional and structural changes of arteries, rheological properties of blood, coagulation and anticoagulation systems, the genetic factor, a role of immune system, character of a meal and others. At the same time the results of some researches specify the important role of microcirculation disturbances in IHD and EH pathogenesis. The attention which has considerably increased to microcirculation by cardiologists' part for last years is connected to its special value in operating cardiovascular system which consists of providing an optimum microenvironment of any tissue working structures. Therefore now the characteristic of blood system circulation condition are not be able considered enough full without detailed studying a microcirculation system. Besides a microcirculation system sensitivity to influence of various factors determines the high importance its state in cardiovascular disorder diagnostics on presymptomatic stages and at asymptomatic diseases.

Among numerous clinical methods of microcirculation research the most perspective is the biomicroscopy of bulbar conjunctiva. The value of this method in clinical researches is caused its information completeness, availability, non-invasivity, nearness to natural conditions, an opportunity of supervision practically all parts microcirculatory network. So, the conjunctiva biomicroscopy allows to estimate a condition of microvessels (arterioles, capillaries, venules), perivascular spaces, structure of blood flow, kind and a degree of intravascular disorders of microcirculation. The modern level of digital and analog engineering development, computer methods gathering and storage of the videoinformation allows to receive on the personal computer qualitative microcirculatory network images and to carry out their automated processing that opens real opportunities for increase of diagnostic precision and information completeness of this method.

Now investigations of conjunctiva microcirculation with using computer added analytical systems are carried out in several research centers (Department of Medical Pathology and Internal Medicine at the Californian

University, USA; the National Cardiovascular Center, Osaka, Japan; Scientific Research Institute of Eye Illnesses of the RAMS, Moscow). Thus authors are carrying out a quantitative estimation separate characteristics of a microvascular network: diameter of vessels, their form, flow structure or velocity in one kind vessels (Komatsu R. et al., 1997; Homma S., et al., 1999; Podelinskaja L.V. etc., 1995; Cheung ATW et al., 2001). Such approach allows to receive the information about separate parts of microcirculatory net, but it does not give an opportunity to estimate a state of this system as a whole. It may be used in research of microcirculatory disorders at the established clinical forms of various diseases and an efficiency estimation of the influences directed to the correction of concrete abnormalities. Semiquantitative criteria used for studying the microcirculation of system is the reason of significant subjectivity and, frequently, incomparability of the results received by various researchers. Thus, a developing system of the criteria based on quantitative definition of parameters of the main phenomena, which are registered at biomicroscopic observation of microcirculatory network, is the topical task representing an interest from the point of view for international cooperation in the field of microcirculation research. Such system will allow to receive the objective information on a state of microcirculatory system as a whole and to create classification of normal and pathological conditions of conjunctival microcirculation, which are typical for early stages IHD and EH.

The establishment of interrelation between presence of major risk factors and IHD and EH diseases, and also morphological and functional abnormalities of microcirculation at various forms of this diseases is a result of a plenty of the researches which have been carried out to present time. Besides in a number of researches the interrelation of structural and functional disorders of microcirculation is shown at IHD and EH. However till now there is investigated insufficiently a character of changes of microcirculation, on the one hand in age aspect, with another - in interrelation with major risk factors of IHD and EH development for practically healthy persons. There is very important circumstance, that only at biomicroscopy in conditions of natural filling vessels by blood when the vascular tone is kept, it is possible to receive an objective estimation vascular and, that it is especially important, intravascular parameters of microcirculation. From these positions the investigations of laws of functioning microcirculation system have the big value in conditions both normal and modified plasma lipid composition, rheological properties and a structurally-functional state of blood cells for practically healthy persons of various age and for patients with early IHD and EH stage of the appropriate age groups. The establishment of dependence of conjunctival microcirculation disorders from a functional state of cells, plasma lipid composition and rheological properties of blood, and also interrelation between morphological and functional characteristics of microcirculation at practically healthy persons and at early stages of development cardiovascular pathology is a topical problem which decision will allow to reveal principal causes and consequences of microcirculatory network abnormalities in prepathological conditions. Results of such research will allow to define characteristic attributes of structural changes of microcirculation, diagnostically adverse from the point of view of development IHD and EH for persons of the most able-bodied age, to develop an algorithm of initial health examination of these persons and to determine ways of correction of revealed disorders. Taking a count the fact, that the problem "rejuvenation" of these diseases takes place in the majority of industrially developed countries, the decision of this problem has the international value.

The following results are expected to be achieved on the accomplishment of project:

- To create a medical-technological complex for the non-invasive automated estimation of a state of microcirculation component of cardiovascular system;
- To develop the uniform approach to an estimation of microcirculation condition, including international;
- To determine kind of age changes of microcirculation;
- To develop new information technology of monitoring and diagnostic algorithm of IHD and EH development risk definition;
- To determine the basic ways of primary prevention of these diseases on the basis of correction of microcirculation disturbances or their causing factors;
- To create the expert and educational electronic atlas of images of the basic variants of norm and pathological changes of microcirculation, characterized early IHD and EH stages.

The technical approach and methodology of the project fulfillment

For achievement of the purpose of the project proposal it is planned to investigate conjunctival microcirculation, characteristics of oxygen transport to tissue, blood flow in vessels of fine calibre, rheological properties, a functional state of cells and lipids composition of blood and a complex estimation of the investigated parameters with use the multifactorial analysis in the following groups:

- Healthy young age persons (29-35 years, 100 persons);

- Healthy middle age persons (36-50 years, 100 persons);
- Middle-aged persons with early stage of IHD developing (100 persons);
- Middle-aged persons with early stage EH (100 persons).

Such structure of surveyed persons will allow to carry out an differential estimation of age and pathological changes of microcirculation, characteristic for initial IHD and EH stages.

The present purpose will be realized by the decision of the following tasks:

1. To create expert system and medical-technological complex for the non-invasive automated estimation of a condition microcirculation.
2. To reveal typical intravascular abnormalities of microcirculation for early IHD and EH stages based on studying dependence of their kind and a degree of expressiveness from a functional condition of uniform elements (erythrocytes, platelets, neutrophils), lipids composition (lipids composition disorders of blood, activity of oxydative and antioxydative systems) and rheological properties of blood.
3. To reveal attributes of abnormalities of a microcirculatoru network state are typical for early IHD and EH stages based on studying interrelation between vascular characteristics of microcirculation and its functional parameters - exponents of oxygen transport and blood flow in vessels of small calibre.
4. To develop an algorithm of initial examination of practically healthy persons, including research of conjunctival microcirculation, revealing microcirculatory disorders, an establishment of their causing reasons, and definition of IHD and EH development risk degree and to develop the specialized software realizing this algorithm.
5. To develop information technology for monitoring a microcirculation condition with the aim of revealing persons with high-risk of ischemic heart disease and essential hypertension.
6. To create a database and the atlas of microcirculatory network images, including the basic variants of norm and IHD and EH early stages variants of abnormalities of vascular, perivascular and intravascular microcirculation components.

The Carl ZEIS slit lamp, the Pentium-IV-1000 personal computer, the 3-CCD color videocamera, the optical interface block, the jet color printer and the developed specialized software are included in medical-technological complex structure.

The purpose of the medical-technological complex is enter of the high-quality images, allowing to distinguish all details of a microvascular network and structure of microcirculatory blood flow. The purposes of the specialized software are automation of image processing and implementation of the diagnostic complex based on criteria system of state estimation of a microcirculatory network, including quantitative parameter definition of the basic phenomena which registered at biomicroscopic examination: vessel calibre (arterioles, venules, capillaries), arterio-venular ratio, a degree curvature of microvessels, extent change of their diameter, quantity of functioning capillaries and arterio-venular anastomosis on unit of the area, a perivascular space condition, kind and a degree of intravascular disorders, blood flow velocity in vessels of bringing, exchange and removing links of microcirculation, the integrated characteristic of this system and prognostic criteria of microcirculatory abnormalities.

The algorithms and the software of telediagnosics and teleconsultations system will be developed for support of the removed electronic consultations of regional cardiological clinics in Belarus and data exchange with the foreign medical centers with using Internet.

Also creation of corporate RRPCC WEB-server is planned for access of the foreign medical centers via Internet to a database of the expert and educational electronic image atlas of the basic variants of norm and pathological changes of microcirculation. The tools for publication of the electronic scientific papers prepared by RRPCC employees will be given also on the basis of a Web-server.

Application and the importance of expected results

Development of primary examination technology based on non-invasive automated estimation of a condition of conjunctival microcirculation will allow to increase medical and social-economic efficiency of primary diagnostic actions. It will be achieved due to revealing persons with high risk of IHD and EH development and differential choice for them methods of deeper examination. That will allow to avoid additional expenses at realization difficult and expensive invasive researches.

Creation of the medical-technological complex and examination algorithm will allow to carry out dynamic supervision with the purpose of the control of preventive actions efficiency. Availability, rather low cost and an opportunity of the dynamic condition control will allow widely to introduce this method in practice of various, first of all polyclinic level, treatment-and-prophylactic establishments that will allow considerably to increase an efficiency of primary prevention and, hence, to lower IHD and EH diseases.