СЕКЦИЯ «ФИЗИОЛОГИЯ ЖИВОТНЫХ И БИОМЕДИЦИНА»

MODEL STUDIES OF HEMODYNAMICS OF CARDIOVASCULAR SYSTEM FOR RESEARCH OF CEREBRAL ANEURYSM GENESIS

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One of the most common disorders of circulation is a cerebral aneurysm. Damage of the vessel wall is caused by local hemodynamics disorders; therefore, the study of cerebral hemodynamics plays a key role in identifying the causes of the emergence and development of the aneurysm. The purpose of this work is to present an integrated approach with usage of both mathematical modeling and experimental method.

For the investigation of cerebral artery circulation it is proposed to use a multiscale mathematical model of hemodynamics, which is a set of mathematical models of circulation with different levels of detail. It is proposed to develop a 0D model to describe all major compartments of cardiovascular system and to describe heart in terms of physiology.

Developing the one-dimensional hemodynamics (1D model) model of arterial tree it is planned to describe upper body arteries as a set of quasi-one-dimensional vessels.

Using 3D model it is planned to describe the cerebral artery local hemodynamics. The researcher will receive information about a blood flow rate and blood pressure at any point of the artery. According to simulation results risk of developing an aneurysm of the cerebral artery can be predicted.

In the experimental setup the silicone rubber models used to provide transparent, true-to-scale replicas of human vessels. To obtain geometry data of patients, digital images from the MRI or CT are segmented. The vessel's model is mounted on an x-y-z-moving table so that velocities can be measured and recorded very precisely at each point of interest. To simulate the physiological human flow conditions we use a blood-like fluid developed in IFL laboratory.

Velocity, pressure and flow rate data obtained with the above described experimental set-up allow to correlate with the mathematical simulation in order to evaluate its reliability. The aim is to determine when there is a rupture of the aneurysm, and to provide criteria to avoid a rupture. This is done through the comparison and analysis of the experimental data with the data calculated by means of computer simulation in a multiscale mathematical model of hemodynamics.

DEVELOPMENT OF A MULTICELLULAR MAGNETIC 3D SPHEROIDS FROM DIFFERENT CELL LINES

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Multicellular spheroids are ordinary and widely used 3D cell culture systems. Between various approaches have been used to generate 3D spheroids nowadays we applied the method of hanging drops. This methodology could be applied in tissue engineering, drug screening and in nanomedicine as well. An important achievement is the use of various nanomaterials, mainly nanoparticles in medical research.

Three following human cell lines were used in our study: Human cervical carcinoma cells (HeLa), Human lung adenocarcinoma epithelial cells (A549), Human hepatocyte carcinoma cells (Hep3B) and mesenchymal stem cells (MSK). We find the ability of spheroids formation from all type of cells we used. We observed the evolution of spheroids within seven days formed from cells coated by magnetic nanoparticles. Magnetic nanoparticles were synthesized from iron oxide magnetic nanoparticles and stabilized with PAH (MNPs-PAH). Under the gravitation force in the hanging drops the cellular aggregates were formed after 24 hours and the compact spheroids were formed after 48 hours. Moreover we formed multicellular spheroids from A549 and Hela covered by MNPs.

Using different types of viability tests and images, obtained by light and fluorescent microscopy, we can conclude that MNPs-PAH do not adversely effect on the survival of cells and formation of spheroids from cell cultures. Spheroids formed from magnetic cells demonstrated the ability to move under the influence of a constant magnetic field.

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MAGNETIC RESONANCE SPECTROSCOPY OF THE ISCHEMIC BRAIN UNDER LITHIUM TREATMENT INDICATES CHANGES IN METABOLITES

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In the last two decades, a growing body of evidence has shown that lithium has several neuroprotective effects. Lithium is a classic drug for the treatment of bipolar disorder. Most neuroprotective effects of lithium were shown only with pretreatment and prolonged use, for example, protecting against glutamate-induced apoptosis and ischemia-induced brain damage. The major mechanism underlying lithium-induced neuroprotection is inhibition of glycogen synthase kinase-3β, however, the certain metabolic changes mediated by lithium is still unclear. At the same time, many studies indicate mitochondrial dysfunction in stroke. Along these lines, in vivo analysis of metabolites associated with mitochondrial function may provide the key to understanding the mechanisms of brain damage and neuroprotection by lithium.

In this study, 1H-MRS was employed to examine the metabolic changes in the cortex and thalamus during the acute phase of rat brain ischemia/reperfusion and those after lithium treatment.

1H-MRS used for detecting the ratios of Cho/Cr, Glu/Cr, Lac/Cr, mI/Cr, NAA/Cr and Lip0.9/Cr at 1, 2, 3 and 24 h after occlusion of the middle cerebral artery (MCAO) revealed that significant metabolic changes in the infarct area were obvious beginning at 1 h after MCAO for lactate, myo-inositol and N-acetyl aspartate. 1H-MR spectra showed significant elevation in the lactate and myo-inositol and a marked decrease in N-acetyl aspartate 24 h after MCAO. In a post-MCAo period we detected decreased spectra of two metabolites – at 2 and 3 h time points for glutamate and at only 2 h time point for choline. At 24 h after MCAO, the Lip0.9/Cr ratio in the vehicle group was significantly higher than that in the control group. Quantitative analysis of 1H-MRS in the group treated by lithium revealed a persistent decrease of lactate levels after the occlusion onset compared to vehicle group at every time point explored. In addition, in lithium-treated animals when compared with a vehicle group, N-acetyl aspartate levels in the damaged area were elevated starting from 2 h of a post-ischemic period and kept high until 24 h.

Therefore using this approach one can estimate the severity of brain damage and effectiveness of applied therapy. In that way we were able to show lithium-mediated neuroprotection, associated with preserving of mitochondrial function.

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EVALUATION OF TOXIC EFFECTS OF SILVER NANOPARTICLES

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Silver nanoparticles are one of the most promising types of metal nanoparticles. Their production and scope is constantly expanding, which can lead to a negative impact on human health and the environment, in connection with the evaluation of the toxic effect of nanoparticles of different chemical composition and structure is actual problem.

In this work we have investigated the toxicity of silver nanoparticles stabilized with polyallylamine hydrochloride (PAH). As target cells were selected human lung carcinoma cells A549.