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NATIONAL RESEARCH NUCLEAR UNIVERSITY MEPHI
(MOSCOW ENGINEERING PHYSICS INSTITUTE)

The 5th International Symposium and International School for Young Scientists on “Physics, Engineering and Technologies for BioMedicine”

November 21-25, 2020

PROGRAMME
BOOK OF ABSTRACTS

MOSCOW

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The International Symposium and International School for Young Scientists on «Physics, Engineering and Technologies for BioMedicine» is held annuallyby the Institute PhysBio at MEPhI in Moscow (Russia). The Symposium and School aims at bringing together leading scientists, experts, young scientists and students to present their achievements in the format of the invited lectures and poster reports in nuclear medicine, biophysics, bio-photonics, and etc.

Abstracts are published in author's edition

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5th International Symposium and
International School for Young Scientists on
"Physics, Engineering and Technologies for Biomedicine"

The Symposium and School are organized by the Institute of Engineering Physics for Biomedicine (PhysBio) of the National Research Nuclear University MEPhI (Moscow Engineering Physics Institute) in close collaboration with the research centers of the Russian Academy of Sciences, Russian Ministry of Health, State Atomic Energy Corporation and the partner universities in Russia and abroad.

The Symposium aims at bringing together the leading researchers, high level engineers and experts in biophysics, bio-photonics, nuclear and nano-medicine to present their recent achievements and to take part in the following discussions. The School will be held in the format of lectures addressed to students, young scientists and specialists whose activities are related to the life sciences and medicine. The Symposium provides an opportunity to obtain knowledge in today and future biomedicine, to exchange opinions and establish professional contacts all over the world.

Conference topics

- Nanomaterials for biomedical applications
- Bio-photonics for diagnosis and therapy
- Plasma and laser technologies for biomedicine
- Advanced approaches in MRI and PET
- Novel contrast agents for radiation treatment of tumor
- Immuno-therapy
- Nuclear medicine
- Engineering in translational medicine
- Bioprinting

Official Language

The official language of the conference is English.

The format of the Symposium – invited lectures and poster sessions.

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PROGRAMME
5th International Symposium and International School for Young Scientists on "Physics, Engineering and Technologies for Biomedicine"

School for Young Scientists

November 21, Saturday

10.00 - 10.15	***OPENING CEREMONY, GREETING SPEECHES***
10.15 – 11.00	**Andrei Kabashin,** CNRS, Aix–Marseille University, France, MEPhI, Russia *Laser-ablative nanofabrication*
11.00 – 11.45	**Andrey Zviagin,** Macquarie University, Australia *Biodegradable containers for drug delivery to tumours*
11.45 – 12.30	**Anton Fojtik,** Czech Technical University in Prague, Czech Republic, MEPhI, Russia *Surface-modified nanoparticles and nanofibers for biotechnology/biomedical applications*
12.30 – 13.30	***LUNCH***
13.30 – 14.15	**Victor Timoshenko**, MSU, MEPhI, Russia *Porous silicon nanoparticles: formation, functionalization, and biomedical applications*
14.15 – 15.00	**Rudolf Steiner,** Ulm University, Germany PhysBio MEPhI, Russia *Some immunological aspects of Photodynamic Therapy and also in relation to covid-19*
15.00 – 15.45	**Moustafa Enas Mahmoud,** National centre for radiation research and Technology, Egypt *Withania somnifera modulates radiation-induced generation lung Cancer Stem Cell via restraining the Hedgehog signaling factors*
15.45 – 16.15	***COFFEE BREAK***

16.15 – 17.00	**Anderson Gomes,** Federal University of Pernambuco, Brazil PhysBio MEPhI, Russia *Optical Coherence Tomography: A Multipurpose 3D Real Time Imaging Technique*
17.00 – 17.45	**Paras Prasad,** University at Buffalo, USA, MEPhI, Russia *Nanomedicine : Impact on Global Healthcare*
17.45 – 18.30	**Denise Zezell,** IPEN Center for Laser and Applications (CLA), Brazil *Infrared thermography and thermographic analysis in Laser Dentistry and Orthopedics*

November 22, Sunday

10.00 - 10.15	***GENERAL INFORMATION***
10.15 – 11.00	**Vladimir Oleinikov,** Institute of bioorganic chemistry RAS, MEPhI, Russia *The effect of plasmon silver and exciton semiconductor nano-particles on the bacteriorhodopsin photocycle*
11.00 – 11.45	**Natalia Epstein,** MEPhI, Russia *How do the medicines are made?*
11.45 – 12.30	**Victoria Shipunova,** Institute of bioorganic chemistry RAS, Russia, MEPhI, Russia *Small but smart: plasmonic nanostructures for onco-theranostics*
12.30 – 13.30	***LUNCH***
13.30 – 14.15	**Vladimir Fomin**, Institute for Integrative Nanosciences, IFW Dresden, Germany, PhisBio MEPhI, Russia *Spin-Dependent Phenomena in Semiconductor Micro-and Nanoparticles — From Fundamentals to Applications*

14.15 – 15.00	**Tatiana Savelieva,** A.M. Prokhorov General Physics Institute of RAS, MEPhI, Russia *Possibilities of optical-spectral analysis in the diagnosis and treatment of intracranial tumors*
15.00 – 15.45	**Igor Meglinski,** Aston University, Birmingham, UK *The advancement of blood cell research by optical tweezers*
15.45 – 16.15	***COFFEE BREAK***
16.15 – 17.00	**Ahmed Al-Kattan,** Aix Marseille University *Novel nanoparticle-enhanced biomimetic platforms for medical and tissue engineering applications*
17.00 – 17.45	**Mikhail Shestakov,** PhysBio MEPhI, Enikolopov Institute of Synthetic Polymeric Materials, Russia *Organic semiconductor transistors as chemical and biological sensors*

International Symposium on "Physics, Engineering and Technologies for Biomedicine"

November 23, Monday

10.30 - 11.00	***OPENING CEREMONY, GREETING SPEECHES***
11.00 – 11.30	**Andrey Kaprin,** National Medical Research Radiological Centre of the Ministry of Health of the Russian Federation, General director
11.30 - 12.00	**Andrei Kabashin,** CNRS, Aix–Marseille University, France, MEPhI, Russia *Research Agenda in PhysBio MEPhI*
12.00 – 12.30	**Indrajit Roy,** University of Delhi, India *Functional nanomaterials in externally activated biomedical applications*
12.30 - 13.30	**PLENARY LECTURER** **Alexander Makarov,** Thermo Fischer Scientific, Germany *Mass spectrometry in modern medicine: perspectives and applications*
13.30 - 14.30	***LUNCH***
14.30 – 15.00	**Igor Nabiev,** Université de Reims Champagne-Ardenne, France PhysBio MEPhI, Russia *Polariton-assisted donor–acceptor role reversal in resonant energy transfer between organic dyes strongly coupled to electromagnetic modes of a tuneable microcavity*
15.00 – 15.30	**Subhasree Roy Choudhury,** Institute of Nano-Science and Technology, India *Nanotherapeutic intervention for epigenetic regulation of cancer*

15.30 – 16.00	**Anton Popov,** MEPhI, Russia *Laser-generated titanium nitride nanoparticles for applications from solar energy harvesting to biomedicine*
16.00 – 16.30	**Anton Fojtik,** Czech Technical University in Prague, Czech Republic, MEPhI *Nanotechnology against Viruses*
16.30 – 17.00	***COFFEE BREAK***
17.00 – 17.45	**KEYNOTE SPEAKER** **Paras Prasad,** University at Buffalo, USA, MEPhI, Russia *Biophotonics and Nanomedicine: Some Recent Developments*
17.45 – 18.15	**Anderson Gomes,** Federal University of Pernambuco, Brazil PhysBio MEPhI, Russia *Exploiting Photoacoustics for Nonlinear Absorption and Imaging in Laser-Synthesized Plasmonic Titanium Nitride Nanoparticles*
18.15 – 18.45	**Denise Zezell,** IPEN Center for Laser and Applications (CLA), Brazil *FTIR hyperspectral imaging for label-free histopathology*

November 24, Tuesday

10.30 - 11.00	***GENERAL INFORMATION***
11.00 – 11.30	**Victor Timoshenko,** MSU, MEPhI, Russia *Multifunctional Silicon Nanoparticles for Biomedicine*
11.30 - 12.00	**Amitava Patra,** Institute of Nano-Science and Technology, India *An overview of recent Activities of Nanotherapeutics*
12.00 – 12.30	**Irina Zavestovskaya,** MEPhI, Lebedev Physics Inst., Russia *Nuclear nanomedicine: today and tomorrow*

12.30 - 13.00	**Viktor Tsetlin,** Inst. of Bioorganic Chemistry of RAS, PhysBio MEPhI, Russia *Fluorescent proteins: from fundamental studies to medical applications*
13.00 - 14.00	***LUNCH***
14.00 – 14.30	**Pavel Varaksa,** N.N. Blokhin National Medical Research Center of Oncology, Russia, *Morphology of organs and tissues of mice after application of gold nanoparticles*
14.30 – 15.00	**Panda Jiban Jyoti,** Institute of Nano Science and Technology, India, *Peptide/Amino Acid Nanotherapeutics for Combating Neural Disorders*
15.00 – 15.30	**Gavdush Arsenii Alekseevich,** General Physics Institute of RAS, Russia *THz dielectric spectroscopy of human brain gliomas of different WHO grades*
15.30 – 16.00	**Ivan Zelepukin,** PhysBio MEPhI, Inst. of Bioorganic Chemistry of RAS, Russia *Cytoblockade of mononuclear phagocyte system for boosting nanoparticle efficiency*
16.00 – 16.30	**Igor Meglinskiy,** Aston Univestity, UK PhysBio MEPhI, Russia *Scattering and birefringence in phase retardation revealed by locus of Stokes vector on Poincare sphere*
16.30 – 17.00	***COFFEE BREAK***
17.00 – 18.30	**POSTER SESSION**

November 25, Wednesday

10.30 - 11.00	***GENERAL INFORMATION***
11.00 – 11.30	**Viktoria Tischenko,** National Medical Research Radiological Centre, PhysBio MEPhI, Russia *Preliminary biological evaluation of of chromium nanoparticles labelled with Re-188*
11.30 - 12.00	**Alexey Lipengolts,** PhysBio MEPhI, N.N. Blokhin National Medical Research Center of Oncology, Russia *MRI and CT enhanced imaging with bimodal nanoparticle contrast agent*
12.00 – 12.30	**Vladimir Morozov,** Institute of Biochemical Physics, RAS *The high-Z nanoradiosensitizers for superficial radiotherapy*
12.30 - 13.00	**Alexey Trukhin,** PhysBio MEPhI, National Medical Research Center of Endocrinology of the Ministry of Health of Russia *Technology of personalized radioiodine treatment of thyrotoxicosis*
13.00 - 14.00	***LUNCH***
14.00 – 14.30	**Deepika Sharma,** Institute of nano science and Technology, India *Evolution of Magnetic Hyperthermia for Cancer Therapy: Past, Present and Future Outlook*
14.30 – 15.00	**Ekaterina Barmina,** General Physics Institute of RAS, Russia *Laser micro- and nanotechnologies, fundamental results and trends of their applications*
15.00 – 15.30	**Dminry Ivanov,** University of Kassel, Germany, PhysBio MEPhI *Molecular Dynamics Modeling of NPs Generation Processes for Bio-medical Applications*

15.30 – 16.00	**Mikhail Povarnitsyn,** Joint Institute for High Temperatures, RAS, PhysBio MEPhI, Russia *Raman spectroscopy insight into surface modes of silicon nanoparticles: molecular dynamics simulation*
16.00 – 16.30	**Martin Garcia,** University of Kassel, Germany *Simulating the manipulation and damage of biological systems via external fields: from small proteins up to SARS-CoV-2*
16.30 – 17.00	***COFFEE BREAK***
17.00 – 18.30	**POSTER SESSION**
18.30	**DISCUSSIONS AND CLOSING CEREMONY**

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5th International Symposium and
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INVITED LECTURES

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5th International Symposium and School for Young Scientists on "Physics, Engineering and Technologies for Bio-Medicine"

INVITED LECTURES

NANOMEDICINE: IMPACT ON GLOBAL HEALTHCARE

Paras N. Prasad
Institute for Lasers, Photonics, and Biophotonics and Department of Chemistry, University at Buffalo, State University of New York, Buffalo, New York 14260, United States

This talk will discuss how physics, engineering, Chemistry and biomedicine can be integrated with nanotechnology to open up Nanomedicine using multifunctional nanomaterials for new generation targeted medical imaging and therapies. It will present examples of multidisciplinary research in principles, designs and functions of nanoformulations for Nanomedicine, specifically applied to cancer, Infectious diseases and brain diseases.

1. P.N. Prasad "Biophotonics" John Wiley & Sons, New York (2003).
2. P.N. Prasad "Nanophotonics", John Wiley & Sons, New York (2004).
3. P.N. Prasad "Introduction to Nanomedicine and Nanobioengineering" Wiley (2012)

BIOPHOTONICS AND NANOMEDICINE: SOME RECENT DEVELOPMENTS

Paras N. Prasad
Institute for Lasers, Photonics, and Biophotonics and Department of Chemistry, University at Buffalo, State University of New York, Buffalo, New York 14260, United States

The talk will present our current multidisciplinary research in Biophotonics and Nanomedicine, specifically applied to cancer, Infectious diseases and brain diseases. In biophtonics, we use IR light for enhanced tissue penetration and are developing the concept of smart PDT using stimuli responsive nanoformulation which show strong photodynamic action only under the tumor acidic environment. For nanomedicine, our program is developing new generation IR -photoresponsive nanoformulations for externally controlled therapy activation, and laser ablation to produce nanoparticles of multiple drugs for combination therapy, an example being for Covide-19 and HIV. Our brain research is developing neurophotonics.

NOVEL NANOPARTICLE-ENHANCED BIOMIMETIC PLATFORMS FOR MEDICAL AND TISSUE ENGINEERING APPLICATIONS

Ahmed Al-Kattan
Aix Marseille University

The presentation will review novel biomimetic platforms for biomedical applications with particular emphasis on tissue engineering. In particular, it will review platforms based on calcium phosphate apatite as one of most promising materials, as well as present nanoparticles prepared by laser ablation in liquids as a promising functional element for tissue engineering platforms

LASER MICRO- AND NANOTECHNOLOGIES, FUNDAMENTAL RESULTS AND TRENDS OF THEIR APPLICATIONS

Prof. G.A. Shafeev and Dr. Habil. Ekaterina Barmina
A. M. Prokhorov General Physics Institute RAS(GPI RAS)
barminaev@gmail.com

In this presentation we would like to familiarize our colleagues with current investigations of the development of nanomaterials with unique properties by laser irradiation of solids. Such nanosurfaces found applications in tribology, sport games, LED technologies also as SERS sensors, black absorbers for satellite equipment and photovoltaics.

NANOTECHNOLOGY AGAINST VIRUSES

Anton Fojtik
Czech Technical University in Prague, Czech Republic
PhysBio MEPhI, Russia

We started to open this way already at 2007, and we published first attempt at 2008.

At that time target was against HIV virus. Virus is very small, much less then bacteria or mould. Virus could be very clever conceal and hidden; we must also use such a clever unusually smart technology to attack him.

I shall speak about the way, how we proceeded. Nanotechnology is not biological tool. We must find the way, with success, even a little, effective, but possible. We have done some tests at "Czech Laboratory against HIV virus" at that time. Try to tie up on this way, as possible, to defense and protection, in this way to use Nano fibers, fibers with big surface and his modifications possibilities.

How to do, explain technology and possible practical applications for the biological using I would like to speak.

We work not for obtain vaccine; we try to get possibilities for defense and protection against virus at the way, using Nanotechnology.

Defense and protection, that's our way.

I like bring a small drop, for this afford. Maybe should be useful.

SURFACE-MODIFIED NANOPARTICLES AND NANOFIBERS, FOR BIOTECHNOLOGY/BIOMEDICAL APPLICATIONS

Anton Fojtik
Czech Technical University in Prague, Czech Republic
PhysBio MEPhI, Russia

Nanotechnology is getting still more attention and is becoming emerging topic of recent days. Its biological and medical approaches and applications are opening novel, unpredicted and efficient ways of solving health issues that is why the extraordinary field of bionanotechnology is shaping into one of the leading sciences of the 21st century…

Goal of the project is to functionalize Fe3O4 magnetic nanoparticles, which according to chemical groups attached at the surface, are able to bond to special pathogens (bacteria or virus) and being easily manipulated by magnetic field, they can be removed from the system taking the pathogens with them as well.

Nanoparticles are produced by 'wet' chemical way under special conditions. Final product is tens of nanometers in diameter and possesses special superparamagnetic properties, which give it ability to be manipulated while working in complex biological systems such as human body. Shape and size of nanoparticles are evaluated using AFM, magnetic properties measured by Mössbauer Spectroscopy and Superconducting Quantum Interference Device (SQUID). Surface of the particles is stabilized and treated, so that they maintain their unique properties and remain stable and separated. Certain chemical groups, proteins or residues are attached onto the surface to functionalize it. Particles are then ready to play a key role in recognition of the pathogens bonding to the surface of nanoparticles and following applied magnetic field to get out of the system.

Magnetic nanoparticles offer many attractive possibilities in the fields of biology and medicine.

1. Alexandro Tocchio (2008): diploma thesis entitled "Surface-modified magnetic nanoparticles for biotechnology/biomedical applications".

2. Magnetic poly(glycidyl methacrylate) particles prepared in the presence of surface-modified γ-Fe2O3: Alexandro Tocchio, Anton Fojtík, and others. Journal of Polymer Science, Part A, Polymer chemistry, Volume 47, issue 19, 1 October, 2009.

3. Magnetic and Metallic Nanoparticles for Biomedical Application, A. Fojtik, D. Horák, K. Piksová, Tran Quang Trung and T. Škereň, Proc. NANOCON 2009, No. 90, ps. 1-8, ISBN: 978-80-87294-12-3

4. Metallic and Magnetic Nanoparticles for Enviromental and Biomedical Aplication, A. Fojtik, K. Piksova, P. Kovacik, T. Skeren, poster, Proc. EuroNanoForum 2009, Prague, June 2-5, 2009.

EXPLOITING PHOTOACOUSTIC FOR NONLINEAR ABSORPTION AND IMAGING IN LASER-SYNTHESIZED PLASMONIC TITANIUM NITRIDE NANOPARTICLES

Anderson S. L. Gomes[1,2]
[1]*Department of Physics, University Federal of Pernambuco, Recife, PE, BRAZIL*
[2]*MEPhI*

Photoacoustic (PA) deals with the interaction of optical waves generating acoustic waves in an absorptive medium. In this talk, I shall describe recent results of the exploitation of PA to characterize the nonlinear absorption (NLA) and to generate PA images in 40nm diameter Titanium Nitrite (TiN) nanoparticles (NP) prepared by femtosecond laser ablation in water suspension. Using a combination of optical and acoustic Z-Scan, the NLA properties of the TiN NP were studied in the first biological window (600nm-800nm) and the origin of the nonlinearity will be discussed based on combined NLA, nonlinear scattering, and bubble generation triggered by NPs-mediated light absorption. As an application, we will demonstrate the generation of images using the TiN NP as contrast agent for the photoacoustic image. Further applications of TiN in biomedicine will be highlighted.

OPTICAL COHERENCE TOMOGRAPHY: A MULTIPURPOSE 3D REAL TIME IMAGING TECHNIQUE

Anderson S. L. Gomes[1,2]
[1]*Department of Physics, University Federal of Pernambuco, Recife, PE, BRAZIL*
[2]*MEPhI*

Optical Coherence Tomography (OCT) is one of the most powerful optical imaging technique, providing a high spatial resolution (sub-micrometer) with few millimeters penetration depth, depending upon the material or biomaterial.

In this lecture, I will initially describe how the OCT technique works, and then will take you through a journey of OCT applications in the biomedical world, with pre-clinical (laboratory) and clinical examples. To conclude the talk, a live demonstration of OCT in dermatology and dentistry will be given.

MOLECULAR DYNAMICS MODELING OF NPS GENERATION PROCESSES FOR BIO-MEDICAL APPLICATIONS

Dminry Ivanov
University of Kassel, Germany
PhysBio MEPhI

Serving as acceptors of drugs and their targeted delivery, NPs of different materials and their oxides have found a number of applications in bio-medicine, specifically in biosensing and cancer tumor therapy [1]. The NPs with demanded morphological, magnetic, and optical properties are among those that highly utilized, and could be obtained in predesigned technological processes of NPs generation: chemical, biological, mechanical, and laser ablation [2]. The latter, due to relatively low cost and high level of reproduction is intensively studied in Pulsed Laser Ablation in Liquid (PLAL) experiments [3]. It is important to obtain a better understanding of complex, transient, and interrelated processes involved into generation of NPs in PLAL. In this presentation, these processes are simulated with a combined atomistic-continuum numerical approached and investigated at atomic level. In the frames of a single computational approach fast laser-induced phase transitions are described with Molecular Dynamics (MD) method, whereas the effect of laser-excited free carriers is accounted for via Two Temperature Model (TTM) [4]. The combined MD-TTM model is applied for investigation of the formation of Au NPs due to a short laser pulse ablation of metal target in water. We describe the numerical procedure in general and present few peculiarities modeling of laser ablation in water. The results of modeling assumes that by means of laser irradiation parameters manipulation it is possible to generate colloidal liquids with NPs of predesigned properties with controlled mean size and size distribution [5].

1. K. McNamara and S.A.M. Tofail, "Nanosystems: the Use of Nanoalloys, Metallic, Bimetallic, and Magnetic Nanoparticles in Bio-

medical Applications", Phys. Chem. Chem. Phys. 17, 27981-27995 (12015).

2. S. Lal Pal, U. Jana, P. K. Manna, G. P. Mohanta, and R. Manavalan," Nanoparticle: An Overview of Preparation and Characterization", Journal of Applied Pharmaceutical Science 01 (06), 228-234 (2011).

3. A.V. Kabashin, M. Meunier, C. Kingston, and J.H.T. Luong, "Fabrication and Characterization of Gold Nanoparticles by Femtosecond Laser Ablation in an Aqueous Solution of Cyclodextrins", J. Phys. Chem. B 107, 4527-4531 (2003).

4. D.S. Ivanov and L.V. Zhigilei, "Combined Atomistic-Continuum Modelling of Short-Pulse Laser Melting and Disintegration of Metal Films", Phys. Rev. B 68, 064114 (2003) also in Virtual Journal of Ultrafast Science, September (2003).

5. D.S. Ivanov, Th. Izgin, A.N. Mayorov, V.P. Veiko, B. Rethfeld, Y.I. Dombrovska, M.E. Garcia, I.N. Zavestovskaya, S.M. Klimentov, and A.V. Kabashin, "Numerical Investigation of Ultrashort Laser-Ablative Synthesis of Metal Nanoparticles in Liquids Using Atomistic-Continuum Model", Molecules 25, 67 (2020)

MRI AND CT ENHANCED IMAGING WITH BIMODAL NANOPARTICLE CONTRAST AGENT

A. Lipengolts[1,2], Yu. Finogenova, V. Skribitsky, M. Abakumov, P. Varaksa, A. Smirnova, R. Popovtzer, E. Grigorieva

[1] N.N. Blokhin National Medical Research Center of Oncology, Moscow Russia
[2] National Research Nuclear University MEPhI, Moscow Russia
[3] A.I. Burnazyan Federal Medical Biophysical Center, Moscow, Russia
[4] Bar-Ilan University, Ramat-Gan, Israel
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MRI and CT are imaging modalities widely used both in clinic and experimental scientific studies. CT provides better bones and air visualization with better spatial resolution while MRI is more suitable for soft tissue imaging. To gain advantage of both these two modalities bimodal nanoparticles based contrast media for MRI and CT were developed [1].

Nanoparticles with iron oxide core and surrounding gold shell coated with PEG-glucose (Fe-Au-NPs) were synthesized and studied as bimodal contrast agent for CT and MRI. The studied Fe-Au-NPs had overall core size of 27 nm with hydrodynamic diameter about 140 nm.

In vivo imaging of Fe-Au-NPs in mice C57Bl/6 with transplanted subcutaneous mammary adenocarcinoma Ca755 was made. Animals' CT imaging was performed with IVIS Spectrum CT imaging system and MRI was made with Bruker ClinScan 7T scanner. Mice under isoflurane gas anesthesia were injected intravenously via tail vein with 180 uL of Fe-Au-NPs solution containing 0.45 mg of iron. T_2^{star} weighted MRI images of the mice were acquired using Gradient Echo sequence with following parameters: TR= 400 ms, TE = 3,5 ms, flip angle = 30, FOV = 27x35 mm, base resolution = 200x256, slice thickness = 0.69 mm. Each mouse underwent CT and MRI imaging before Fe-Au-NPs injection and after the injection at several time points.

Contrast enhancement of main blood vessels, liver, spleen and tumor was observed both in MRI and CT images. Fe-Au-NPs uptake by the

tumor was clearly seen (fig 1). Spatial correspondence of the enhanced areas at MRI and CT images was observed.

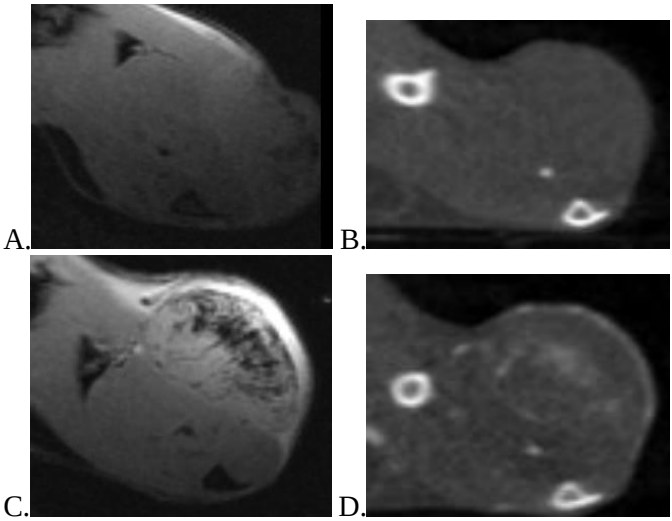

Fig.1. MRI (A,C) and CT (B,C) images of subcutaneous tumor Ca755 before (A,B) and 90 min (C,D) after bimodal iron gold nanoparticles (Fe-Au-NPs) intravenous injection

In this study feasibility of contrast enhancement both in MRI and CT imaging with a single contrast agent in the same living object was shown. Obtained results are of great practical value for studying of nanoparticles behavior in a living organism allowing more reliable and precise identification and quantification of nanoparticles presence in different organs and tissues. Bimodal CT/MRI contrast agents can also be useful for contrast enhanced radiotherapy (CERT) [2]. Treatment planning of CERT with bimodal nanoparticles as dose enhancing agent can be made more reliably.

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A JOURNEY TO THE WORLD OF HIGH RESOLUTION

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Starting from a brief introduction to mass spectrometry, this talk focuses on techniques for high-resolution accurate mass (HR/AM) analysis, especially Orbitrap mass spectrometry as the leading technique in this field. Basic principles of this technology are presented against a backdrop of its brief but colorful historic development. Its 15-year history as a commercial technique has witnessed introduction of four major families of Orbitrap-based instruments, with numerous new modes of operation enabled by parallelization of detection and ion processing, and intricate coordination of multiple ion-optical devices.

It is shown that Orbitrap-based mass spectrometry possesses compelling potential as an (ultra-) high resolution platform not only for high-end proteomic applications but also for screening, trace and targeted analysis by LC/ and GC/MS.

THE ADVANCEMENT OF BLOOD CELL RESEARCH BY OPTICAL TWEEZERS

Igor Meglinskiy
Aston Univestity, UK
PhysBio MEPhI, Russia

In the framework of novel medical paradigm the red blood cells (RBCs) have a great potential to be used as drug delivery carriers. This approach requires an ultimate understanding of the peculiarities of mutual interaction of RBC influenced by nano-materials composed the drugs. Optical tweezers (OT) is widely used to explore mechanisms of cells' interaction with the ability to trap non-invasively, manipulate and displace living cells with a notably high accuracy. In the current presentation, the mutual interaction of RBC with various nano-particles is investigated utilizing a two-channel OT system and microscopy.

SCATTERING AND BIREFRINGENCE IN PHASE RETARDATION REVEALED BY LOCUS OF STOKES VECTOR ON POINCARE SPHERE

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Biological tissues are typically characterized by highly anisotropic scattering of light and may also exhibit linear form birefringence. Both scattering and birefringence bias the phase shift between transverse electric field components of polarized light. In fact, the majority of polarization-based techniques are not able to distinguish the nature of the phase shift between transverse electric field components induced by birefringence or scattering of light. We explore the distinct contributions of scattering and birefringence in the phase retardation of circularly polarized light propagated in turbid tissue-like scattering medium.

POLARITON-ASSISTED DONOR–ACCEPTOR ROLE REVERSAL IN RESONANT ENERGY TRANSFER BETWEEN ORGANIC DYES STRONGLY COUPLED TO ELECTROMAGNETIC MODES OF A TUNEABLE MICRORESONATOR

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Resonant interaction between excitonic transitions of molecules and localized electromagnetic field allows the formation of hybrid light–matter polaritonic states. This hybridization of the light and the matter states has been shown to be able to significantly alter the intrinsic properties of molecular ensembles placed inside the optical cavity. Here, we have achieved strong coupling between the excitonic transition in typical oligonucleotide-based molecular beacons labelled with a pair of organic dye molecules, demonstrating an efficient donor-to-acceptor resonance energy transfer, and the tuneable open-access cavity mode. The photoluminescence of this hybrid system under non-resonant laser excitation and the dependence of the relative population of light–matter hybrid states on cavity detuning have been characterized. Furthermore, by analysing the dependence of the relaxation pathways between energy states in this system, we have demonstrated that predominant strong coupling of the cavity photon to the exciton transition in the donor dye molecule can lead to such a large an energy shift that the energy transfer from the acceptor exciton reservoir to the mainly donor lower polaritonic state can be achieved, thus yielding the chromophores' donor–acceptor role reversal or "carnival effect". Our experimental data confirm the theoretically predicted possibility for confined electromagnetic fields to control and mediate polariton-assisted remote energy transfer

thus paving the way to new approaches to remote-controlled chemistry, energy harvesting, energy transfer and sensing.

THE EFFECT OF PLASMON SILVER AND EXITON SEMI-CONDUCTOR NANOPARTICLES ON THE BACTERIORHO-DOPSIN PHOTOCYCLE

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Bacteriorhodopsin (bR) belongs to the class of light-sensitive proteins. The natural function of bR is the light-dependent transfer of a proton across the cell membrane. The chromophore of bR is retinal. Upon absorption of a quantum of light, retinal is isomerized, initiating the bR photocycle. The photocycle is characterized by a consistent change of the optical properties of bR. The discreteness of the optical properties of bR each intermediate makes it possible to use the Ferster resonant energy transfer (FRET) to act on the certain intermediate form of the bR. The most attractive candidate for the role of a donor is quantum dots (QDs), which have a broad absorption/excitation band in the UV/blue region and a narrow, tunable emission peak in the absorption region of any bR's intermediates [1].

It was shown that FRET from QDs to bR makes it possible to expand the spectral range of the natural function bR and increase the efficiency of proton transfer [2].

In our investigations we used the flash photolysis method to study the kinetics of the photocycle. It was shown that QDs with fluorescence $\lambda = 570$ nm are weak influenced on the kinetics of the bR photocycle [3, 4]. Our analysis shows that due to the insufficiently long fluorescence lifetime of QDs (5-20 ns) the last could act only on the initial steps of photocycle. Recently, we shown that the use of QDs with fluorescence $\lambda = 620$ nm permits us to induce direct transfer from the K-intermediate to the ground state of the bR.

In order to interfere in the bR photocycle at a later stage, in particular, at the moment close to the time of the reprotonation of retinal and change the path of the photocycle for formation of P- and Q-intermediates, it could be use the nanoparticles with a sufficient fluorescence lifetime. A promising candidate is nanophosphors, in particular $NaYF_4:Yb^{3+}$, excited in the IR region and fluorescent at λ = 540 nm and λ = 650 nm [5]. These hybrids are promising for the creation of information storage systems.

In this work, we also consider hybrid bR with the silver nanoparticles (AgNP) [6, 7]. The possibility of fixing the bR state localized in hot spots near the surface of AgNPs, in which the effect of SERS is realized, is shown. The possibility of using near-field microscopy to create devices based on single bR molecules is discussed.

This work was supported by the RSF (project 19-14-00171).

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AN OVERVIEW OF RECENT ACTIVITIES OF NANOTHERAPEUTICS @ INST

Prof. Amitava Patra
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Scientists at Institute of Nano Science and Technology (INST), India are working on various areas including Agricultural and Food technology, Nanotherapeutics and Nanotoxicology, NanoTheranostics, smart nanobiomaterials for tissue regeneration, Biomechanics for understanding human diseases. Cancer nanotherapy is one of the major areas of interest, where Protein nanoparticles based delivery of drug and siRNA to regulate epigenetic machinery. Combinatorial nanoplatform for photodynamic and magnetic hyperthermia therapy, and carrier free transcatheter delivery of the pure drug for therapy are some of the approaches taken to beat the cancers. Dynamic mucus penetrating microspheres for efficient pulmonary delivery of anti TB drug and lipid based hybrid nanostructured materials for drug delivery for the treatment of leishmaniasis were developed under nanotherapeutics for infectious diseases. This nanotherapeutics will have future translational potential for novel applications in nanomedicine.

LASER-GENERATED TITANIUM NITRIDE NANOPARTICLES FOR APPLICATIONS FROM SOLAR ENERGY HARVESTING TO BIOMEDICINE

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Owing to a red-shifted absorption/scattering feature compared to conventional plasmonic metals, titanium nitride nanoparticles (TiN NPs) constitute a very promising candidate for plethora of different applications, among which solar energy harvesting and nanomedicine looks as the most exciting. However, the applications of TiN NPs are still underexplored despite the presence of extensive data for conventional plasmonic counterparts. This is mostly due to difficulties of synthesis of colloidally stable and "clean" colloidal solutions of TiN NPs. Recently emerged laser-ablative synthesis opens up opportunities to produce stable pure colloids of "bare" TiN NPs at relatively large scale [1]. Here, we provide results of elaboration of laser-ablative synthesis of TiN NPs in liquids [2], demonstrate some of their unique properties [3], their performance for solar energy harvesting and assessment of their biocompatibility [4].

We present the first comprehensive assessment of their toxicity, biodistribution and pharmacokinetics. Tests in vitro using 8 cell lines from different tissues evidenced safety of TiN NPs. Systemic administration in mice did not cause any sign of toxicity or organ damage up to concentration of 6 mg kg^{-1}. The TiN NPs covered by PEG demonstrated efficient passive accumulation in EMT6/P mammary tumor. The obtained results evidence high safety of laser-synthesized TiN NPs for biological systems, which promises a major advancement of phototheranostic modalities on their basis.

A nonlinear photoacoustic response from solutions of 40 nm TiN NPs synthesized by laser ablation in acetone is reported. Using a photo-

acoustic Z-scan with 5 ns pumping pulses, values of effective nonlinear absorption coefficients $\beta_{PA,eff}$ were measured and found to be $3.27 \pm 0.17\times10^{-8}$, $6.41 \pm 0.17\times10^{-8}$, and $3.22 \pm 0.17\times10^{-8}$ cm/W for 600, 700, and 800 nm pumping wavelengths, respectively.

Solar weighted absorption coefficient of nanofluids based on 30 nm TiN NPs reach 99% at very low volume fractions (2.0×10^{-5}), which is 50% higher than that of Au NPs of similar size. The thermal efficiency of a direct absorbance solar collector (DASC) using TiN working fluid was up to 80% higher compared to Au spherical NPs. The recorded high photothermal efficiency and excellent colloidal stability of TiN NPs-based nanofluids give a promise for the major advancement of DASC technology, while the flexibility of laser-ablative synthesis promises easy scalability and relative cost-efficiency necessary for the implementation of systems for solar energy harvesting.

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POSSIBILITIES OF OPTICAL-SPECTRAL ANALYSIS IN THE DIAGNOSIS AND TREATMENT OF INTRACRANIAL TUMORS

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Now, there are a number of complications in the treatment of intracranial tumors due to the peculiarities of their growth. Fluorescent markers are used to accurately remove tissue affected by tumor cells. However, not in all cases, tumor cells accumulate such a dye. In this regard, other approaches can be used to demarcate tumor boundaries, including other optical-spectral methods. For example, Raman spectroscopy, which allows analysis of molecular composition. The possibilities of differentiation of tumor and healthy tissues by the contribution of lipids, proteins, and DNA to the Raman spectrum were shown. The combined approach was proposed which allows tissue analysis using both fluorescence spectroscopy and elastic and inelastic scattering analysis.

This report presents the results of machine learning techniques to classify fluorescence, diffuse reflectance and Raman spectra of human intracranial tumors. As a result, differences were found in the principal component space, corresponding to tissue samples with microcystic components, extensive areas of necrosis, and foci of fresh hemorrhages. It is shown that this approach can serve as the basis for constructing a system for automatic intraoperative tissue classification based on the

analysis of Raman spectra. As a result, differences were found in the principal component space, corresponding to tissue samples with microcystic components, extensive areas of necrosis, and foci of fresh hemorrhages. It is shown that this approach can serve as the basis for constructing a system for automatic intraoperative tissue classification based on the analysis of Raman spectra.

The reported study was funded by RFBR according to the research project № 18-29-01062

ORGANIC SEMICONDUCTOR TRANSISTORS AS CHEMICAL AND BIOLOGICAL SENSORS

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Organic semiconductor transistors have recently become promising and perspective for applications as biological and chemical sensors. In this lecture, the principles and architecture of transistor-based sensors will be highlighted. Also, there will be discussed a few types of organic semiconductors potentially promising as active layers in the sensors. Finally, there will be shown some examples of organic semiconductor transistors based chemical and biological sensors.

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SMALL BUT SMART: PLASMONIC NANOSTRUCTURES FOR ONCOTHERANOSTICS

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Nanomaterials exhibit many valuable characteristics unavailable for bulk samples and are expected to provide effective solutions for ongoing problems in modern biomedicine. Organic and inorganic nanoparticles of different nature are the most effective tools for the development of targeted drug delivery systems possessing both therapeutic and diagnostic properties [1-10].

Here we describe the development of effective theranostics agents based on silver nanoparticles directed toward HER2 receptor on cancer cell surface. HER2 is tyrosine kinase receptor and belongs to the EGFR receptor family. HER2 is a clinically relevant oncomarker which is overexpressed in 20-30% of human breast tumors. Its overexpression predicts a high risk of disease recurrence, high metastatic tumor potential, resistance to chemotherapy and reduced overall survival of patients. However, this receptor normally presented on healthy cells in a much lesser extent. So, the precise and quantitative detection of this oncomarker has important clinical implications.

These nanoparticles possess surface plasmon resonance property and can be inductively hated by an external light source leading to cancel cell hyperthermia. To selectively deliver these particles to HER2-overexpressing cancer cells, particle surface was modified with anti-HER2 scaffold protein – affibody ZHER2:342 through intermediate modification with PEG.

He show both in vitro and in vivo that such HER2-directed silver plasmonic nanoparticles can spesifically eliminate cancer cells leading to full remission in vivo using mouse xenograft tumor model with HER2-overexpression.

This study is a step towards the creation of new generation of theranostic agents, which are capable of affecting only certain cell types under specific conditions and act as a therapeutic agent when it necessary.

The research was supported in part by Russian Science Foundation grant (project No. 17-74-20146, nanoparticle synthesis, *in vivo* studies) and Russian Foundation for Basic Research (project No. 19-29-04012, cell culture and No. 20-34-70136, plasmonic particle characterization).

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MULTIFUNCTIONAL SILICON NANOPARTICLES FOR BIOMEDICINE

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Nanoparticles (NPs) of pure silicon (Si) are known to be biocompatible, biodegradable and promising for various biomedical applications as bioimaging, drug delivery, photodynamic therapy and photothermal treatment (hyperthermia), and ultrasound-assisted (sonodynamic) therapy of cancer. Si NPs can be efficiently heated by radio-frequency radiation to realize a hyperthermia regime for destruction of tumors. Recently, Si NPs and those with iron impurities have been explored as contrast agents (CAs) for MRI. Measurements of the proton magnetization lifetime and MRI experiments with phantoms show maximal CA properties for transversal time mode that is explained by enhanced proton relaxation in water molecules due to the interaction with silicon dangling bonds of Si NPs. Porous Si NPs are explored as containers for positron-emitting radionuclides as 68Ga in high quantities (up to 95%). 68Ga-labeled PSi NPs exhibit high stability in vitro. In vivo studies of the pharmacokinetic proper-ties of PSi NPs with incorporated 68Ga after intratumoral administration to animals with experimental cholangioma RS-1 show that more than 50% of the labeled PSi NPs were retained by tumor tissue for 5 h. The intravenous administration resulted in gradual accumulation of labeled nanoparticles in the tumor. The highest levels of the radioactivity during intravenous administration were observed in the organs of the reticuloendothelial system. The obtained results show high prospects for creating new porous silicon-based radiopharmaceuticals for the positron emission tomography (PET), as well as novel theranostic agents for the PET-guided treatment of malignant tumors. In vivo and in vivo studies confirm outstanding properties of PSi NPs for mild therapy applications. PSi NPs produced by mechanical grinding of porous silicon were explored as antiviral agents for sup-pression of the

infections induced by human immunodeficiency virus (HIV) and respiratory syncytial virus (RSV) in vitro. A suppression of the viral activity was observed for the SiNP concentration, which were significantly lower than the corresponding cytotoxic concentrations. The observed effect is related to an efficient binding of the viruses with PSi NPs.The obtained results indicate new prospective area of biomedical applications of PSi in both therapy and diagnostics (theranostics) of cancer and inflectional diseases.

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PRELIMINARY BIOLOGICAL EVALUATION OF CHROMIUM NANOPARTICLES LABELED WITH RE-188

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Cancer therapy using β-emitting radionuclides is an effective approach of cancer treatment. Nanoparticles (NPs) can be engineered as radionuclide delivery platform to target cancer cells. NPs possess unique characteristics that distinguish them from bulk material and make them suitable devices to deliver high radiation dose to the tumor. Rhenium-188 has appropriate nuclear and physical properties ($T_{1/2}$ = 16.9 h, $E_{\beta max}$ = 2.12 MeV, E_{γ} = 155 keV). It also can be obtained from $^{188}W/^{188}Re$ generator up to 6–8 months. In this work chromium NPs were labeled with ^{188}Re and their biodistribution were studied.

^{188}Re-chromium NPs was synthesized with high radiochemical yield. Radiochemical purity was obtained more than 95 %. All biodistribution studies were performed in BALB/c mice with subcutaneously inoculated colon adenocarcinoma. 10 days after tumor transplantation the animals were injected with 0.37 MBq in a volume 0.1 ml of ^{188}Re-chromium NPs. Animals were sacrificed at 5 min, 1, 3, 24, and 48 h post-injection (p.i.), the samples of different organs and tissues were collected. The radioactivity was measured by gamma counter. The uptake was expressed as percentage of injected dose per gram of tissue (%ID/g).

Tumor uptake of radioactivity was 1.22 ± 0.11 % ID/g at 5 min p.i., increasing to 2.58 ± 0.20 % ID/g at 3 h. Then tumor uptake of ^{188}Re-chromium NPs declined to 1.74 ± 0.46 and 1.32 ± 0.41 % ID/g at 24 h and 48 h p.i., respectively. The highest level of activity was observed in

thyroid gland: up to 51.77 ± 13.14 % ID/g at 3 h p.i. High accumulation of activity was also observed in liver (up to 10.35 ± 0.75 % ID/g, kidneys (up to 11.75 ± 1.15 % ID/g) and spleen (8.79 ± 0.33 % ID/g).

In conclusion, it was the first attempt to label chromium NPs with ^{188}Re. ^{188}Re-chromium NPs could be applied as therapeutic tool for radiation therapy of cancer, but further investigations are necessary, especially in order to maximize their in vivo stability.

NUCLEAR NANOMEDICINE: TODAY AND TOMORROW

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The modern concept of nuclear nanomedicine as a synergy of nuclear and radiation medicine with nanomedicine is considered. Nanoparticles are actively used for the diagnosis and treatment of socially significant diseases, especially cancer [1,2].

The main advantages of nanoparticles are considered, such as an increased surface area-to-volume ratio, passive/active delivery, high loading capacity, large cross-section of interaction with biological tissues, and unique surface properties that allow a single nanostructure to obtain many functional capabilities.

The resulting nanoformulations can be targeted at the tumor for cancer therapy either with radionuclides or with non-radioactive materials that can be activated by various external sources of nuclear particles to produce radioactivity in situ. From a practical point of view, these properties of nanoradiopharmaceuticals can provide clear advantages in diagnostic and therapeutic effectiveness.

We review our results in testing laser senthesized nanoparticles as carries for promising radionuclides (Re-188, Ga-68) in nuclear medicine, as well as sensitizers in radiation therapy. Our tests on rat survival demonstrate excellent therapeutic effect (72% survival compared to 0% of the control group). Combined with a series of imaging and therapeutic functionalities based on unique intrinsic properties of Si*NPs, the proposed biodegradable complex promises a major advancement of nuclear nanomedicine.

We also apply methods of femtosecond laser ablation/fragmentation in deionized water to fabricate stable aqueous dispersion of152Sm-enriched samarium oxide nanoparticles, which can capture neutrons to

become153Sm beta-emitters for nuclear therapy. The final product presents dispersed solutions of samarium oxide NPs with relatively narrow size distribution, having spherical shape, a controlled mean size between 7 and 70 nm and high colloidal stability [3].

The combination of radiation therapy with the ability to activate nanomaterials in situ, as well as combination with other therapeutic methods using multifunctional nanoplatforms, opens an era of new technological and therapeutic achievements – the era of nuclear nanomedicine.

The research was carried out with the financial support of the Russian foundation for basic research (project 20-02-00861), and State Corporation "Rosatom" (agreement of September 05, 2019 № 313/1655-D).

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CYTOBLOCKADE OF MONONUCLEAR PHAGOCYTE SYSTEM FOR BOOSTING NANOPARTICLE EFFICIENCY

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Nanotechnology has potential to shift paradigm of cancer therapy and diagnostics. A lot of smart nanoparticles were designed for recognizing and targeting of cancer cells, controlled drug release in the tumor microenvironment, bright imaging, etc. But only few of them have been successful in vivo, because of rapid elimination from the bloodstream by the mononuclear phagocyte system (MPS) [1].

Here, we present a universal method for increasing the circulation half-life of nanoagents by MPS blockade with antibody-sensitized red blood cells (RBCs) [2]. For this aim we use 34-3C antibody, IgG2a subtype, derived from anemic mice. Administration of antibody induces erythrophagocytosis causes a temporary "MPS-cytoblockade," which increase nanoagent circulation more than in order. Method show higher efficiency than classical MPS blockade with solid nanoparticles. MPS cytoblockade potency was illustrated in several biomedical applications, including enhanced CD4+ blood cell targeting, improved magnetic guided delivery of nanoagents to tumor and their chemotherapy by nanocarriers. The proposed technology may allow to use in vivo various smart nanoagents, which previously have shown their efficiency on the cellular level.

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INFRARED THERMOGRAPHY AND THERMOGRAPHIC ANALYSIS IN LASER DENTISTRY AND ORTHOPEDICS

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Infrared thermography imaging has been used to diagnose a number of diseases where superficial temperature can indicate the presence of inflammation in underlying tissues or where blood flow is increased or decreased due to a clinical abnormality. Thermographic analysis can be used to determine the safe laser irradiation conditions when developing a new clinical procedure. In this talk, the basis of Infrared Thermography will be presented, and examples of measurements during laser treatment of myofascial back pain syndrome, temporomandibular disorders, dental cavity preparation with laser, caries prevention with lasers, laser in endodontics, periodontics, prosthodontics and implants will be presented.

FTIR HYPERSPECTRAL IMAGING FOR LABEL-FREE HISTOPATHOLOGY

Denise Zezell
IPEN Center for Laser and Applications (CLA), Brazil

FTIR hyperspectral pathology imaging of thin tissue slice samples are used to monitor the collagen during the healing process when evaluating burned skin, treated or not with femtosecond laser, in the diagnose and molecular differentiation between thyroid and goiter, skin squamous cell carcinoma, as well as for breast cancer cell subtypes.

BIODEGRADABLE CONTAINERS FOR DRUG DELIVERY TO TUMOURS

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Center of Biomedical Engineering, Sechenov University, Moscow, Russia

Laboratory of Cancer Nanotheranostics, Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences

Nanomedicine provides new hope for cancer treatment by enabling passive delivery of toxic anticancer pharmaceuticals to tumours sparing the healthy tissues. It was established that nanocarriers sized 10 - 100 nm alleviated unwanted accumulation of nanomedicine in the critical organs but appeared limiting for the growing demand for high-capacity delivery of multifunctional drug cargo. We introduce biodegradable sub-micron drug-loaded containers, which are accumulated in the tumour capillaries and swiftly release drug payload that permeate tumour and kill cancer cells.

POSTER REPORTS

REVEALING THE TOXIC EFFECT OF SILICON NANOPARTICLES ON *DAPHNIA MAGNA*

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Nanoparticles are increasingly used in many types of consumer products, in construction, catalysis, and pharmaceuticals [1]. The use of nanoparticles for medical and biological purposes is promising, since they are potential carriers of medicine directly to the site of injury. However, the growth in the production of nanomaterials and their successful implementation raise concerns about the increased likelihood of exposure and the manifestation of specific effects in living organisms. In this regard, the issue of the safety of using nanoparticles becomes urgent.

The objective of this work was to find out the toxic effect of silicon nanoparticles on living objects. We used micro-PSi silicon nanoparticles 5 nm in size, provided by V.Yu. Timoshenko, head of the laboratory "Nanoteranostika" of the IFIB NRNU MEPhI. The test object was the crustaceans *Daphnia magna*, which were cultivated according to the international protocol [2]. The MTT test was chosen as the cytotoxicity test. The optical density of the stained samples was measured on a StatFax 2100 plate immunoanalyzer (Awareness Technology, USA, VIS model).

There are data [3, 4], indicating that the toxic properties of materials do not always affect the decrease in the survival rate of crustaceans, especially in an acute experiment, but at the same time changes in the metabolic activity of animals are observed. Experiments were carried out to identify acute (7 days) and chronic (21 days) toxicity of nanoparticles at concentrations of 0,1 mg / ml and 0,05 mg/ml. When studying the acute effect of nanoparticles, a decrease in the metabolic activity of daphnia, cultivated in a medium with a concentration of

0,05 mg/ml nanoparticles by 20%, and in a medium with a concentration of 0,1 mg/ml, by 30% was observed.

Fig. 1 shows the analysis of the cytotoxicity of silicon nanoparticles at a concentration of 0,05 mg/ml and 0,1 mg/ml on *Daphnia magna* in a chronic experiment. A significant decrease in the metabolic activity of daphnia was established using the Mann-Whitney U test, cultivated in a medium with a concentration of microporous nanoparticles of 0,05 mg/ml by 30%, and in a medium with a concentration of 0,1 mg/ml by 40%.

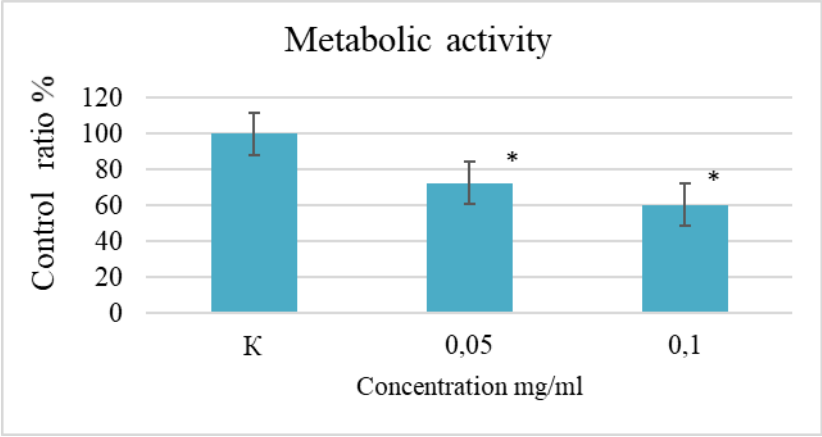

Figure 1 - Change in metabolic activity of *Daphnia magna* in a chronic experiment, cultivated in a medium with a concentration of silicon nanoparticles of 0,1 and 0,05 mg/ml by the 21st day of the experiment. * differences are significant at $p<0.05$

Thus, the toxic effect of silicon nanoparticles at concentrations of 0,1 and 0,05 mg/ml on the culture of crustaceans *Daphnia magna* was revealed, both in acute and chronic experiments.

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MATHEMATICAL MODEL OF ABNORMAL GLYCEMIC CONTROL IN HUMAN

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The correct work of the glycemic control system in humans is necessary to maintain stable blood glucose levels in both fasting and fed organism states. There are two major regulators – hormones insulin and glucagon. Their activity depends on the other's status and is regulated by pancreatic and liver cells [1-2]. Other tissues, like adipose and muscles, can uptake excessive glucose from blood under the influence of insulin.

We propose a mathematical model of glycemic control, using "the black-box" concept (see Fig.1), which allows us to describe the major-function of tissues without a detailed description of each one's work. This approach emphasizes the most critical factors contributing to the development of abnormalities in the complex biological system.

We modified our mathematical model [3] to include glucagon (***Gn***) as a major regulating hormone.

$$\frac{dG}{dt} = G_{in} - f_2(G(t)) - f_3(G(t)) \times f_4(i(t)) + f_5(i(t)) \times f_9(Gn(t))$$

$$\frac{dI}{dt} = f_1(g(t)) - d_i \times I$$

$$\frac{dg}{dt} = f_6(G(t)) - B_2 \times g$$

$$\frac{di}{dt} = f_7(I(t)) - D_2 \times i$$

$$\frac{dGn}{dt} = f_8(I(t)) + f_{10}(g(t)) - A_6 \times Gn$$

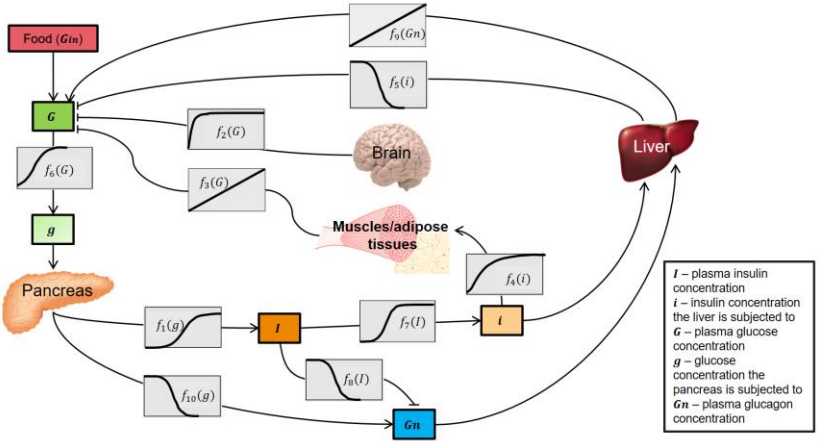

Fig.1. Model scheme.

Analysis of the model results shows that even a small delay in response of the key part of the biological system can lead to pathological blood glucose levels and further illness development.

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SYNTHESIS AND COMPARATIVE ANALYSIS OF THE SERS OF ENHANCING COLLOIDAL SILVER SOLUTIONS

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Raman spectroscopy is a promising method for optical vibrational spectroscopy. Nowadays, Raman spectroscopy finds many applications, in particular, in biological and medical diagnostics. Raman spectroscopy requires minimal sample preparation. If a substance in solution is present in a low concentration or its own spectrum is too weak, it can be improved using the method of Surface-enhanced Raman scattering, based on the effect of plasmon resonance on a nanostructured surface of noble metals, for which colloidal solutions are used.

In this work, three types of silver colloidal solutions were synthesized: borohydride, citrate and chloride. To check the enhancement factor of Surface-enhanced Raman scattering, an aqueous solution of phenylalanine at a concentration of 1 mM was used as sample (since when excited at a wavelength of 532 nm, it is peak at 1000 cm^{-1} can be effectively used to calculate the enhancing factor). A solution of cytochrome C in phosphate buffer at a concentration of 10^{-5} M was used as sample too (since it is a widespread available model substance with a much more complex structure).

Raman and Surface-enhanced Raman scattering spectra were obtained using the Renishaw inVia confocal Raman microscope at an excitation wavelength of 532 nm and a sample power of 3.15 mW with an accumulation time of 100 s. The Fig. 1 shows the Raman and Surface-enhanced Raman scattering spectra of phenylalanine and cytochrome C. The calculation and comparative analysis of the enhancement factors of various types of sols for two model substances was carried out. Borohydride, citrate, and chloride sols on phenylalanine gave an increase of

11.1, 160.9, and 8.5 times, respectively, and on cytochrome C 33.2, 162.6, and 22.5, respectively, which indicates that during the study of complex organic molecules by the Surface-enhanced Raman scattering method for analyzing the enhancement factor more effective use of cytochrome C.

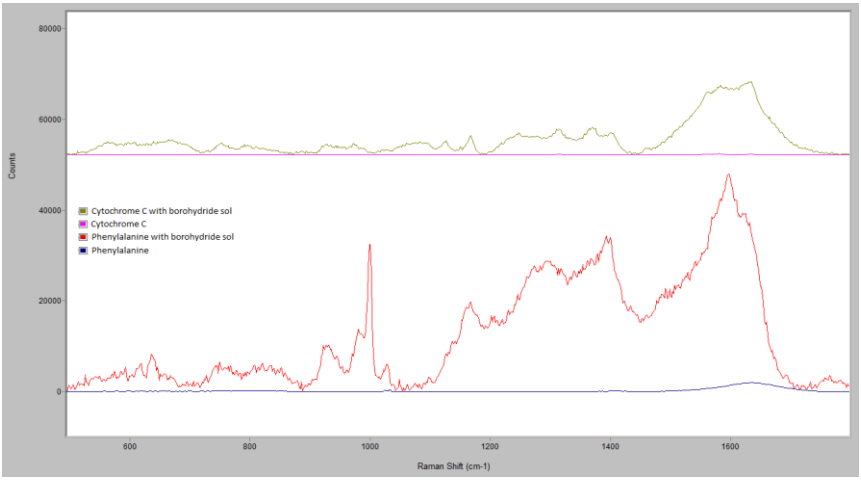

Fig. 1. Raman and SERS spectra of cytochrome C and phenylalanine

STUDY OF OBESITY GENE POLYMORPHISM IN IATE STUDENTS

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It was found that body weight and propensity to obesity are caused not only by environmental influences (level of physical activity, dietary habits, etc.), but also by genetic factors that affect the variation of BMI within 65-80%. To analyze the polymorphism of the genes associated with fat mass FTO, PPARG, PPARG **, 47 students of Obninsk Institute for Nuclear Power Engineering were examined [1].

Before the analysis, medical and genetic information was collected from all examined individuals and anthropometric measurements were taken to calculate the body mass index (BMI). According to the results of the survey, most of the examined persons - this is 72.3% of students - have a normal body weight. To clarify the BMI value, the type of fat distribution in the human body was determined in all the subjects.

Then the blood lipid profile was determined, which made it possible to determine the deviations in the body's lipid metabolism. The data obtained showed that 80.9% of students had normal levels of total cholesterol. One of these individuals has LDL values above the norm and one person has these indicators below the norm. In 21 people, HDL values are below normal. 100% of people have normal triglyceride levels [2].

To isolate DNA from whole blood, we used a commercial kit "DNA-EXTRAN-1". Human genomic DNA isolated from whole blood leukocytes is analyzed.

According to the results of anthropometry, 6 people were identified who have overweight and first degree obesity and lipid metabolism disorders. For all examined individuals, we performed real-time PCR analysis to determine the genotype for genes associated with fat mass FTO, PPARG, PPARG **, responsible for the genetic predisposition to obesity. The results are presented in table 1.

	A23525T polymorphism in the gene associated with fat mass FTO	Pro12Ala polymorphism in the PPARG gene	C1431T polymorphism in the PPARG ** gene
Homozygote for allele 1 (no mutation)	100%	100%	100%
Heterozygote	0%	0%	0%
Homozygote for allele 2	0%	0%	0%

According to the results of the analysis, all examined individuals have a normal variant of the gene polymorphism associated with fat mass FTO, PPARG, PRARG ** and no one has a hereditary predisposition to obesity. And all lipid metabolism disorders, overweight and first degree obesity can only be explained by an unbalanced diet, low level of physical activity or hormonal disorders.

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STUDY OF CHANGES IN SOME BIOCHEMICAL PARAMETERS OF THE CELL UNDER THE ACTION OF GAMMA RADIATION

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Ionizing radiation has a complex and multicomponent effect on living organisms. In addition to the direct effect, which is expressed in damage to the sensitive structures of cells, there is also an indirect effect of radiation associated with the formation of radiotoxins – charged ions, radicals, highly active substances of the peroxide type. With the accumulation of radiotoxins in cells, the permeability of the cell walls changes, the course of biochemical and physiological processes in the body shifts. When exposed to extreme environmental factors in plants, membrane structures are primarily damaged, and, as a consequence, an increase in the content of malondialdehyde (MDA), a lipid oxidation product, occurs, which is associated with the activation of free radical reactions in cells [1].

Proline is a heterocyclic amino acid that performs osmoprotective, antioxidant and signal-regulatory functions; therefore, the content of this amino acid increases many times under stress. Under the action of ionizing radiation, the accumulation of proline helps organisms to adapt to adverse conditions, protecting proteins, DNA, a number of enzymes and other cellular components from inactivation [2].

The aim of the work was to evaluate the effect of gamma radiation in the dose range from 2 to 50 Gy on the quantitative content of MDA and proline in germinated seeds of sowing barley (*Hordeum sativum*). Irradiation of two varieties of barley seeds (Vityaz and Ladny) was carried out at the Russian Institute of Radiology and Agroecology on the GUR-120 installation with a ^{60}Co radiation source. The investigated doses: 2 Gy, 5 Gy, 10 Gy, 15 Gy, 20 Gy, 25 Gy, 50 Gy, with a dose rate of 58 Gy/h. The study of the effect of gamma radiation on stress metabolites

of sowing barley was determined by the content of proline and MDA in the sprouts on the 10th day of germination.

In germinated seeds of the Vityaz variety, a statistically significant increase in the MDA level occurs at doses of gamma radiation of 2, 5, 10, 25, and 50 Gy. In the seeds of the Ladny variety, the process of lipid peroxidation is more intense under irradiation at doses of 2, 5, 10, 25, and 50 Gy. It can be assumed that at low doses, with an increase in the absorbed dose of ionizing radiation, the number of free radicals increases, which is not only a consequence of a violation of antioxidant-prooxidant homeostasis, but is an important component of phenotypic adaptation, since reactive oxygen species and MDA are signaling molecules during the development of stress reactions in plants [3]. Under gamma irradiation at doses of 15 Gy and 20 Gy, adaptive characteristics are formed: the antioxidant and phytohormonal systems are modulated, the intensity of the pentose phosphate pathway of glucose oxidation, which is involved in the protection of the cell from radiation-induced apoptosis, increases [4]. A further increase in the absorbed dose of ionizing radiation causes large-scale damage to membranes, disrupting their functions and increasing the MDA content.

In the present study, it can be noted that at practically all studied doses of gamma radiation, the proline content statistically significantly differs from the control. An exception is exposure at a dose of 15 Gy.

It was also noted that the higher the proline content in plant material, the higher the MDA (the correlation coefficient for the Vityaz variety was 0.871; for the Ladny variety – 0.892).

Thus, the formation of adaptive responses in response to low-dose irradiation depends on the combined work of the antioxidant system, phytohormones, and stress proteins. Further detailed study of the mechanisms will explain the effects of stimulation under the action of low-intensity stress factors.

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CALCULATION OF THE GAMMA INDEX ON RADIOCHROME FILMS

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In the course of this work, software was developed for reading intensities from a film, filtering out noise, comparing intensities with doses and calculating a gamma index.

The gamma index (γ) is one of the most commonly used indicators for verifying complex radiation therapy such as intensity modulated radiation therapy (IMRT) and volume modulated arc radiation therapy (VMAT) [1]. By combining dose differentiation and matching distance, γ provides a means for efficient analysis, which is especially important in a busy clinical environment [2], [3]. Schematically, the calculation of γ is presented in Figure 1.

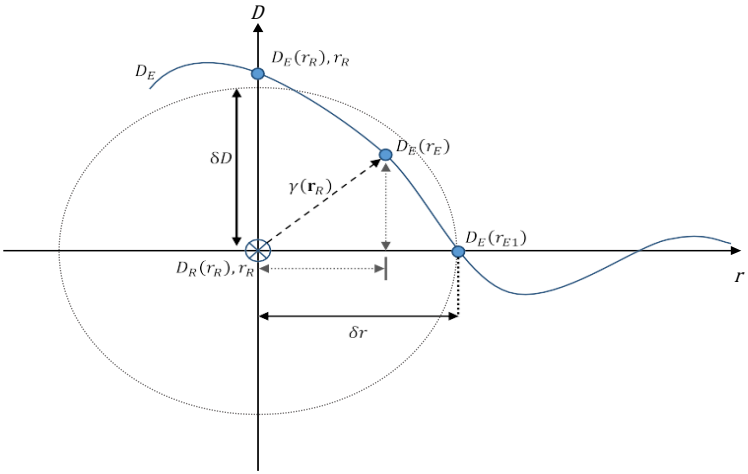

Fig.1. Schematic representation of the gamma index method in 1D

The ordinate is the dose, D, the abscissa is the distance r. The cross is the control point, and the blue line is the estimated dose distribution, and the solid circles are discrete points along the line. The δr and δD criteria create an ellipse around the control point. For the point $D_E(r_R)$,r_R relative to the considered point $D_R(r_R)$,r_R, γ will be greater than 1. For $D_E(r_E)$, γ <1. For $D_E(r_{E1})$, γ = 1.

To automate the calculation of γ, a program was written in the C programming language. The program interface is shown in Figure 2.

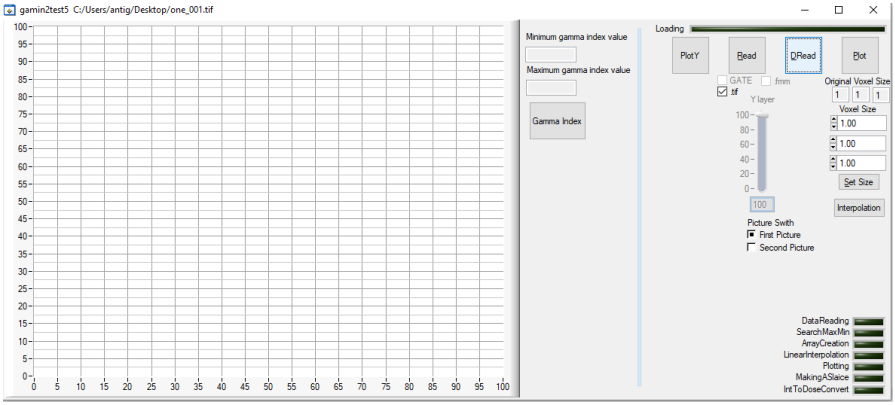

Fig.2. Program interface for reading doses from a film scan, removing noise, and calculating the gamma index

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GERMANIUM NANOPARTICLES BY FEMTOSECOND LASER ABLATION

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Germanium nanoparticles (Ge NPs) are of great interest to nanotechnology due to the semiconducting nature of their optical and electrical properties [1]. Moreover, Ge NPs are promising agents for biomedical application considering relatively low toxicity of germanium compounds [2].

We obtained a colloidal solution of germanium nanoparticles by femtosecond laser ablation of germanium wafer in acetone (Yb:KGW, 1030 nm, 270 fs, 30 μJ, 100 kHz). Average hydrodynamic size of particles is (100±25 nm). Nanoparticles have zeta-potential of (-40±5 mV). SEM images of particles were obtained along with the Raman spectrum, which showed peak at 299 cm^{-1}.

In order to investigate possible applications of Ge NPs we conducted an optoacoustic *in vitro* study. Nanoparticles show rather high light absorption ability in IR region with half-life of approximately 24 hours.

The work was supported by Russian Science Foundation (Project 19-72-30012).

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QUANTIFICATION OF GADOLINIUM CONTRAST AGENTS IN VIVO USING T1 RELAXOMETRY

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Gadolinium quantification in vivo is an important task for binary radiotherapy (BRT) methods such as neutron capture therapy (NCT) and contrast enhanced x-ray radiotherapy (CERT) [1]. In both of these methods absorbed dose in tumor is defined by dose enhancing agent (DAE) content and gadolinium can be used itself as DAE alone and in combination with other DAE as MR-marker for visualization and quantification. So proper gadolinium quantification in BRT defines efficacy of the treatment. So proper gadolinium quantification in BRT defines efficacy of the treatment

In this research T1 relaxometry in vivo was used to quantify gadolinium-based contrast agents Gadovist in mice with subcutaneous tumor. MR - images were obtained using gradient echo sequences (GRE) with short echo times (TE) compared to repetition times (TR), i.e.TR/TE = 16/2 ms. The series of images were divided into two groups: the first was taken before the injection of the CA, and the second - immediately after that. In addition, each group of pictures was obtained with two different angles of rotation: 3° and 16°. Two T1 maps were created by applying the DESPOT1 (Driven Equilibrium Single Pulse Observation of T1) algorithm to both groups of obtained images [2]. This algorithm was implemented mathematically in the Matlab software environment. Gadolinium concentrations' map was constructed from two calculated by DESPOT1 T1 maps. This method is possible due to the principle of longitudinal relaxation rates additivity that is given by the expression [3]:

(1)
$$\frac{1}{T_{1,withCA}} = \frac{1}{T_{1,withoutCA}} + r_1 * C_{Gd}$$

where $1/T_{1,withoutCA}$ and $1/T_{1,withCA}$ (1/c) are the longitudinal relaxation rates before and after the injection of CA, respectively, r_1 (L / mmol * s) is the relaxivity of gadolinium in the given substance, and C_{Gd} (mmol / L) is the concentration of gadolinium.

Thus, gadolinium concentration maps can be built to evaluate its distribution's dynamic and determine the areas of its maximum accumulation.

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MAGNETIC IRON OXIDE NANOPARTICLES OF DIFFERENT MORPHOLOGY FOR BIOMEDICAL APPLICATIONS: SYNTHESIS, CHARACTERIZATION

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Magnetic nanoparticles are one of the relevant and significantly developing directions of research in modern chemistry. The outstanding properties of magnetic nanoparticles determine their usage in various industries. One of the most demanded applications of magnetic nanoparticles is in biomedicine and in drug delivery direction in particular.

Magnetic nanoparticle could be manipulated using an external magnetic field. They also might be a basis for a "capsule" containing medication to be transferred to the required part in the body [1], for example, to the cancer cells cluster. As shown, heating nanoparticles near tumor was leading to its destruction without touching normal cells (cancer cells found to be more sensitive to the temperature than the healthy ones) [2].

To conduct our research, we carried out the two-step synthesis of iron oxide dopamine modified magnetic nanoparticles and studied their properties. Magnetic nanoparticles were obtained by reduction of precursor, akaganeite (that one was obtained according to [3]), with hydrazine-hydrate and oleylamine in microwave (MW) reactor.

We conducted the reduction of rod-like akageneite nanoparicles with oleylamine at 200°C for 4 hours. It resulted in a mixture of anisotropic nanoparticles with different morphology less than 90 nm in size: rod-

shaped, triangle-shaped with smoothed vertexes, or spherical. The majority of nanoparticles were rod-shaped.

At the next step, we investigated the ability of monodisperse iron oxide magnetic nanoparticles synthesis by the variation of precursor reduction time. It was shown that rod-shaped akageneite nanoparticles reduction by oleylamine at 200°C during one-hour was giving spherical nanoparticles less than 30 nm in diameter.

Thus, iron oxide anisotropic particles with different morphology were obtained which is quite important for the magnetic field study. Optimum conditions for spherical magnetic nanoparticles synthesis with less than 30 nm in diameter were found. Derived particles were characterized by X-ray phase analysis, transmission electron microscopy and nanoparticle tracking analysis (NTA)

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ASPECTS OF DECISION SUPPORT SYSTEMS BUILDING IN THE DIAGNOSIS OF ONCOLOGICAL DISEASES THAT REQUIRE SPECIAL ATTENTION

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Oncology stays one of the most important problems of modern society. According to the latest data from the Ministry of Health of Russia, the leading localizations in general (both sexes) structure of cancer incidence are the skin and the mammary gland. The percentage of oncological diseases for skin with melanoma is 14.4%, for breast - 11.5%. Early diagnosis is one of the key factors for effective treatment.

Decision support systems use artificial intelligence technologies. It contributes to achieve early diagnosis of cancer. One of the most important stages of building decision support systems is the choice of feature models. Feature can be qualitative or quantitative. Quantitative features have a numeric expression. For example, red colour has a numeric expression 255.0.0. in RGB model. Describing objects models that differ from the usual doctors' perception of these objects (for example, wavelet analysis), are difficult to understand the decision-making process, and thus they cause distrust of results. Qualitative signs make it possible to reproduce verbal description of objects, how a person sees the objects. Therefore, it is advisable to use qualitative features to present the results. The use of Qualitative and Quantitative features in creation of systemic decision making will be illustrated with the examples of Systems for the diagnosis of melanoma and breast diseases in this article.

But the greater efficiency of systems is reached by the use of both feature models. Such systems are useful for the recognition of malignant neoplasms as training and clinical systems. Systems can serve as a classifier, and also teach the associative perception of the features' appearance and their quantitative equivalent.

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THE EFFECT OF INTRA-CHAMBER IMPLANTATION OF POLYLACTIC ACID FILMS ON THE EYE STRUCTURE

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Polylactic acid is the most promising biodegradable polymer used in medicine as suture material, bone plates, abdominal meshes, stents, scaffolds, and also for drug delivery systems [1, 2]. The use of polylactic acid as a corneal implant is interesting for the treatment of bullous keratopathy.

The aim of this work is the effect of the intra-chamber implantation of thin films based on polylactic acid on the eye structures.

The original film samples were obtained by dissolving polylactic acid (Netherlands) in trichloromethane ($CHCl_3$) (Russia). After 48 hours the formed polymer films were removed from the Petri dish.

The intra-chamber implantation of polylactic acid films was performed on 6 rabbits of the Sylvilagus bachmani breed. The eye examination, photo registration, changes in intraocular pressure and optical coherence tomography (OCT) of the cornea were carried out. After 6 weeks from the beginning of the experiment, the material was taken, the eyeballs were enucleated for histological and electron microscopic examination. Sections were stained with hematoxylin and eosin, and according to the Van Gieson method. Second, unoperated eyes served as control. The ultrastructure was studied by transmission electron microscopy on a JEM-100 CXII electron microscope (JEOL, Japan). The calculation of the specific volume of the vessels was carried out using Avtandilov's eyepiece grid for 50 points (= 100%). The analysis of the obtained data was carried out using the "IBM SPSS Statistics 23".

It was revealed that the implantation of films based on polylactic acid into the anterior chamber of the eye of an experimental animal does not cause pronounced inflammation or an increase in intraocular pressure. It is accompanied by crimp collagen fibers of the cornea's own

substance and the formation of thin-walled vessels with a specific volume of no more than 5%.

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PULSED LASER DEPOSITION OF SILICON AND GERMANIUM FILMS WITH PHOTOLUMINESCENT PROPERTIES

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Among the various methods for producing nanocrystalline materials, the method of pulsed laser deposition PLD is distinguished. The main advantages of the laser ablation method are: the composition of the irradiated target is fully reflected in the composition of the resulting nanomaterials; no requirements for creating such difficult external conditions as high temperature, high pressure; high-speed performance; absence of contamination of the film by components of the materials of the camera and other devices, due to the small width of the laser beam. Laser ablation is a promising method for production nanomaterials for biomedical applications, where the purity of the resulting materials is important [1]. Laser nanostructuring of materials leads to a change in their properties, for example, to the appearance of intense luminescence, which can be used in the bioimaging [2].

The experimental results on the deposition of silicon and germanium films by pulsed laser deposition in a gaseous medium are presented in this paper. For deposition of the samples, the KrF laser with a wavelength of 248 nm and an output energy up to 300 mJ was used.

The samples were investigated for the presence of photoluminescent properties. Silicon films exhibit photoluminescence in a wide spectral range, the position of the maximum of which varies from red to blue. The photoluminescence of germanium films is predominantly located in the blue region of the spectrum. The luminescent properties of the films are determined by the preparation conditions and subsequent "aging".

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INFARED SPECTROSCOPY OF POROUS SILICON FOR BIOSENSORICS

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One of the promising biomedical nanomaterials for various applications is porous silicon, which is a system of nanocrystals of various sizes and shapes, as well as porous silicon nanocomposites with various biological and inorganic substances.

By means of a biosensor, each person will be able to monitor the presence of dangerous pathologies in his body by drop of blood. The cost of such an accurate analysis will be several times cheaper than current laboratory tests. Having these easy-to-use tools will make the personalized medicine much talked about today.

Advances in nanotechnology have made it possible to raise biosensorics to a qualitatively new level. New materials are still being investigated for use as a sensitive layer. It is important to solve such problems as high sensitivity of the material to the test object, selectivity, nontoxicity of the biomaterial, and biocompatibility. Porous silicon has become one of the promising nanomaterials for biosensorics [1].

The study of surfaces, chips, powders and colloidal solutions of porous silicon and PC + glucose nanocomposites by IR spectroscopy was carried out. The studies were carried out on an FSM 2201 using a diffuse reflection attachment.

For the analysis by the method of IR spectroscopy for the nanocomposite NaCl (9%) + glucose (various concentrations) and glucose (various concentrations) + Slezin, plates of textured surface were selected: K and P.

The figures show comparative IR spectra measured on an FSM-2201 spectrometer for glucose, a control plate sample, samples with 3%, 6% and 12% glucose solutions in a tear on porous silicon (Fig. 1).

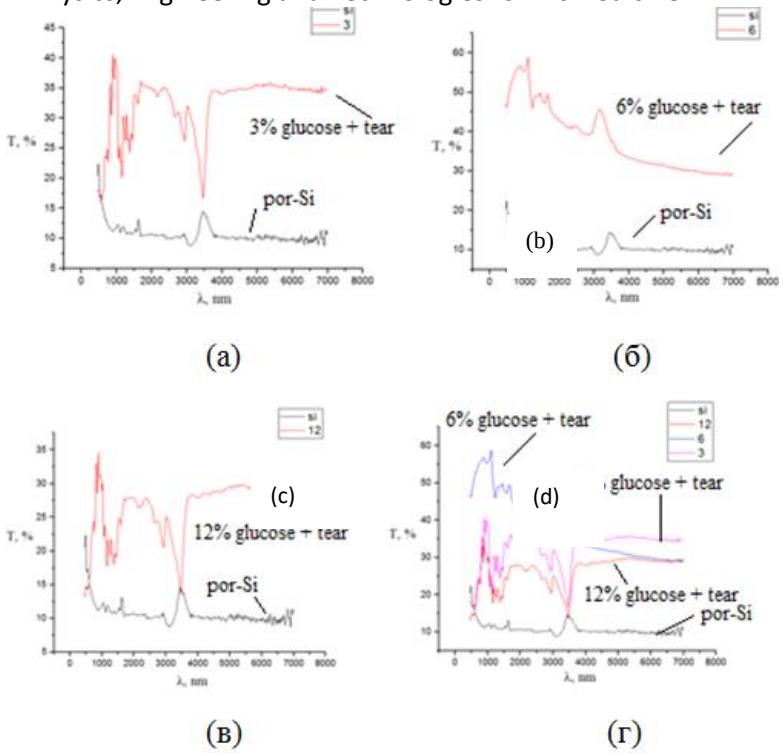

Figure 1. (a) IR spectra for a K-plate with a textured surface and for a plate with the addition of 3% glucose solution + tear; (b) IR spectra for a K-plate with a textured surface and for a plate with the addition of 6% glucose solution + tear; (c) IR spectra for a K-plate with a textured surface and for a plate with the addition of 12% glucose solution + tear; (d) IR spectra for a K-plate with a textured surface and for plates with added glucose of different concentrations + tear (general graph).

We decode the IR spectrum from 2500 nm to 4000 nm. The spectra in this region contain two strong peaks, reflecting two types of bonds between the hydrogen and carbon atoms, hydrogen and oxygen, in the form of stretching vibrations of the H – C and H – O atoms.

At 3500, organosilicon compounds Si-H are observed. The presence of CH bonds in the glucose spectrum is due to the presence of a bandwidth of 3085 nm. Bands responsible for the presence of OH stretching vibrations in glucose: 3085 nm, 3500 nm.

The IR spectroscopy study of PC + glucose nanocomposites shows that the presence of glucose in the pores noticeably changes the transmission spectra of the samples. Hence, we can conclude that porous silicon is a promising material for creating a biosensor.

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INVESTIGATION OF THE PHENOMENON OF PHOTOBLEACHING AND EVALUATION OF THE EFFECTIVENESS OF TREATMENT USING AN LED PHOTODYNAMIC THERAPY DEVICE ON OPTICAL PHANTOMS

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Aim. Evaluation of the efficiency of the PDT procedure using an experimental LED device for photodynamic therapy and fluorescence diagnostics of neoplasms by the level of photobleaching of the photosensitizer protoporphyrin IX (PPIX) in optical phantoms of the skin.

Material and equipment. All studies were carried out using two experimental installations of a LED illuminator for photodynamic therapy and fluorescence diagnostics. The first of the irradiators was designed for PDT with the photosensitizer protoporphyrin IX, which determined the technical characteristics and configuration of the irradiation system. The working part of the device is a matrix of 26 narrow-spectrum LEDs, of which 22 have a wavelength of a spectral maximum of 630 nm with a half-width of 25 nm and are intended directly for PDT, and 4 have a maximum radiation at a wavelength of 405 nm, a half-width of 30 nm and are used for conducting fluorescence control and diagnostics. The second installation of the LED irradiator was intended to be used together with the methylene blue photosensitizer as an experimental method of treating COVID-19, on the basis of which the parameters of the LED matrix were changed accordingly: it also consisted of 36 narrow-spectrum LEDs, but in this case with a radiation wavelength of 660 nm and half-width 22 nm. For testing the developed equipment, a tissue-like phantom was prepared to simulate the optical properties of the skin. In the process of creating a phantom, a 2% solution of Intralipid 10% in

distilled water was used. Next, a solution of protoporphyrin IX at a concentration of (1; 5; 10; 25 μM) was added to the phantom, after which the finished optical phantom with PS was poured into standard 15 ml Petriem dishes. Measurements of the spectral-fluorescent characteristics of LEDs, as well as the study of photobleaching at different assessments of PS were performed using the analysis of **LESA-01 "BIOSPEC"** ("Biospec", Russia).

Results. The results of spectral measurements showed that for LEDs with a nominal wavelength of 405 nm, the experimental value of the maximum radiation was 405 ± 2.5 nm with a half-width of radiation of 30 nm; for LEDs with nominal wavelengths of 630 and 660 nm, these values were found to be 630 ± 2 nm with a half-width of 25 nm and 660.2 ± 2 nm with a maximum half-width of 22.5 nm, respectively. Spectral fluorescence studies of the PPIX photobleaching process depending on the irradiation time, PS concentration, and parameters of the exciting radiation showed that the photobleaching relaxation time was 14.5 minutes upon excitation with 630 nm LEDs and was practically independent of the PPIX concentration in the optical phantom. When fluorescence was excited with 405 nm LEDs, which had a power density approximately 10 times lower, the photobleaching rate was significantly lower. To test the capabilities of the video system in the tasks of visualization and diagnostics, an experiment was carried out to register chlorophyll fluorescence in plant leaves when it is excited using the LED matrix of the irradiator. The results showed that when using the appropriate optical filters, the video system is able to effectively record fluorescent radiation from chlorophyll molecules. Also, a study of the dynamics of thermal processes on the surface of the subject's skin was carried out in order to determine the maximum allowable safe value of the power density, which does not cause moderate hyperthermia. We used two values of the power density of 300 and 80 mW/cm^2, while in the first case the temperature rose at a maximum to more than 42 ℃, which can cause hyperthermia, and in the second case, the temperature did not exceed 39 ℃, which is a safe enough safe temperature and such Therefore, for wide clinical use, it is the version of the LED illuminator with a power density of 80 mW/cm^2 that is recommended.

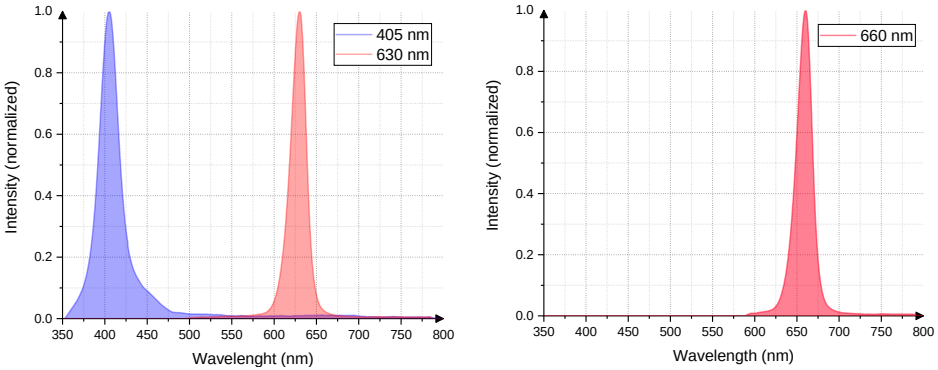

Figure 1. Emission spectra of LEDs for the first (a) and second (b) feed models. (a) The maximum emission for "blue" LEDs falls on a wavelength of 405 ± 2.5 nm, emission half-width of 30 nm; for "red" these values are 630 ± 2 nm and 25 nm, respectively. (b) The maximum emission for these LEDs is 660.2 ± 2 nm, FWHM 22.5 nm.

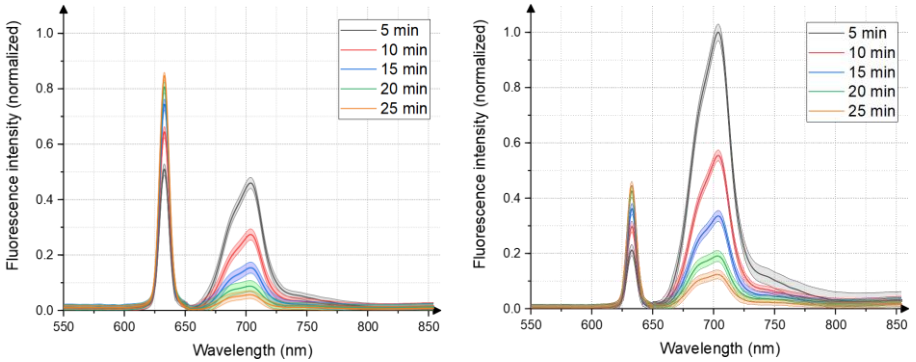

Figure 2. Fluorescence spectra of protoporphyrin IX in an optical phantom at different time intervals after the start of irradiation with LEDs with a wavelength of 630 nm (5, 10, 15, 20, 25 min.). PS concentration in the phantom: (a) 10 μM; (b) 25 μM. The power density of the exciting radiation in both cases was 380 mW/cm2.

Conclusion. Thus, thanks to the assessment of the effectiveness of PDT using an experimental LED device for photodynamic therapy and fluorescence diagnostics of neoplasms by the level of photobleaching of the photosensitizer protoporphyrin IX (PPIX) in optical phantoms of skin tissues, it is possible to significantly improve the quality of treatment of oncological diseases with superficial localization.

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PROSTATE GLAND 3D MODEL BASED ON SPECT/CT FOR 125-IODINE SEEDS APPLICATION

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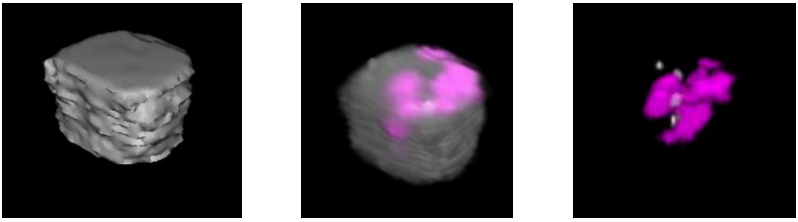
The treatment of prostate cancer (PC) is challenging due to the variable clinical and pathological conditions. Therefore, to increase efficacy, the focus of PC should be localized prior to therapeutic manipulation. It might be surgical removal, brachytherapy.

Current diagnoses of PC include the use of laboratory biomarkers, instrumental imaging with SPECT, PET, ultrasound, MRI, CT, and palpation. Although the results of the instrumental techniques are represented by a three-dimensional matrix, in practice the organ is visualized in three projections, which requires the spatial orientation skill of the doctor to determine its coordinates in different planes. To simplify intraoperative orientation a pre-therapeutic prostate model for brachytherapy or surgery should be created. For this reason, we investigated methods that resemble the anatomical structure of the prostate and those that show the functional activity of the organ.

First application of our new model is brachytherapy, when encapsulated radioactive sources are introduced into or near tumor tissue. The method allows a high cumulative dose of therapeutic radiation to be created within the tumor without causing lethal damage to surrounding healthy organs and tissues. The current implantation technology for radioactive sources is carried out under the control of computed tomography or ultrasound that allow guiding a long needle used for the injection of radioactive sources.

In the present work we will focus on the potential of combining SPECT technology and CT to implement the brachytherapy protocol for localized prostate tumors. For this, a reproducible method of image processing has been developed, as well as three-dimensional images in all

its dimensions, which add depth to the image allowing the immediate identification of the prostate, locating the functionally active site and implementing brachytherapy treatment with greater implantation precision (Fig. 1.). Thus improving the result of the therapy and reducing the cost of the procedure.



a) b) c)

Fig.1. Visualization of the 3D model of the prostate gland, a) volume surface, b) SPECT/CT, c) SPECT

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MIL-101 (Fe) AS TARGETED DRUG DELIVERY SYSTEM

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One of the challenges of modern medicine is the diagnosis and treatment of lung cancer. It is the most common cancer, and also ranks first among cancers in terms of the number of deaths per year. The drugs used in chemotherapy have an effect not only on cancer cells, but also on healthy tissues, which raises the question of creating and using means of targeted drug delivery to the lungs. One of the candidates for this role is nanoparticles (NPs) of metal-organic frameworks MIL-101 (Fe) due to their high sorption capacity, as well as biocompatibility, biodegradability, and low toxicity (1).

In this work, MIL-101 (Fe) NPs were obtained by the solvothermal method. It was shown that these particles are destroyed in an isotonic sodium phosphate buffer pH 7.4, due to the replacement of the linker in the crystal structure with a phosphate group with the release of linker into solution. It was shown that the kinetics of NPs degradation is affected by the presence of proteins in the buffer.

In vivo experiments on the biodistribution of MIL-101 (Fe) NPs showed that particles accumulate in the lungs. This fact, as well as their high sorption capacity, for example, of doxorubicin, proves that MIL-101 (Fe) NPs can be used to treat lung metastases. In a melanoma model, it has been shown that such treatment reduces the number of tumor nodules, as well as the size of cancers, compared with treatment with doxorubicin.

The research was supported by RSF (project No. 19-72-30012)

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NANOPARTICLES AS SENSITIZERS OF RADIO-FREQUENCY ELECTROMAGNETIC HYPERTHERMIA

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There is now a need for new cancer treatments. One of these methods is based on local hyperthermia as a result of Joule heating associated with local electric currents around nanoparticles [1]. To describe this physical process in the context of therapeutic application, it is necessary to build an adequate mathematical model.

In this paper, we propose a model for the interaction of a spherical nanoparticle in an electrolyte with an external radio-frequency electromagnetic field at various values of the electrolyte conductivity and frequency of the applied field. This model also takes into account the polarization of nanoparticles and electrolyte in an external electromagnetic field. On the basis of the proposed model, the dependences of the heat release around the nanoparticles on the zeta potential nanoparticle, the conductivity of the solution, and the frequency of the external field are obtained.

The proposed model can be further applied to calculate the optimal parameters of nanoparticles and radio-frequency electromagnetic radiation for applications in hyperthermia of malignant tumors.

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STUDY OF HOMOCARNOSINE LEVEL AND PH-VALUE IN RESPONSE TO VISUAL ACTIVATION

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Homocarnosine (Hc) is a dipeptide of Gamma-Aminbutyric Acid (GABA) and histidine. Homocarnosine acts as neurotransmitter in human brain and shows anticonvulsant effects. NMR signals of Hc and CABA are quite similar (because molecule of Hc contains molecule of GABA) and differ only with the presence in the homocarnosine's spectrum of imidazole protons resonance line in low-field range. We can receive Hc's signals by using pulse sequences MEGA_PRESS [1]. It is possible to measure pH-value due to Hc's signals [2]. Levels of homocarnosine and ph-value in response to visual stimulation are estimated in this study.

Methods

The study involved 17 healthy people. Scanning was performed on a Philips Achieva 3T scanner. At first, spectra in rest were accumulated, after that spectra during continuous 8 Hz flashing checkerboard stimulation (9 min 36 s each) also were accumulated. The MEGA-PRESS pulse sequence (TE=80ms, TR=2000ms, NSA=288) was used for spectrum accumulation.

Data from the scanner were processed in Matlab using FID-A packages and Gannet3.0. For this purpose, phase and frequency correction was performed using the Gannet3.0 package. As a result, the resonant lines of creatine protons N(CH)3 (δ = 3.027) in all the spectra

were reduced to 3ppm. After that, the spectra were averaged over the dynamics within each volunteer. Finally, the spectra were averaged among all participants of the experiment, as well as on and off series.

The intensity for the real part of the spectrum was determined as one of the approximation parameters in the range 6.85-7.15 ppm for the homocarnosine peak (δ = 7.0) and in the range 2.85-3.15 ppm for $N(CH)_3$ protons (δ = 3.027) of creatine using FID-A processing Tools.

Maximum value of the homocarnosine peaks have been found as well as their chemical shifts. The pH-values were calculated using the equation:

$$pH = pK_A + log\left(\frac{\delta - \delta_{AH}}{\delta_A - \delta}\right) \quad (1)$$

where pK_A=6,86 is the logarithm of the acid dissociation constant, δ_{AH}=7,27ppm is the chemical shift of homocarnosine acid, δ_A=6,92ppm is the chemical shift of homocarnosine's base [2].

Results

The studied homocarnosine peaks in the range of 6.8-7.15 ppm, in absolute values (to exclude the influence of phase signals), at the time of activation and at rest are shown in figure 1. The following results were obtained:

Table 1 The Results

	Peak, ppm	pH	S_{pH}	I_{Hc}	I_{Cr}
Act	7,0412	7,136	0,003	0,77569	5,6921
Rest	7,0317	7,189	0,003	0,83101	5,3119

For obtained pH-values, Welch's t-test was performed for $\alpha<0.05$, $p=0.006$. We can see from the test result that there is a statistically significant difference between pH levels in the presence of a visual stimulation and in its absence.

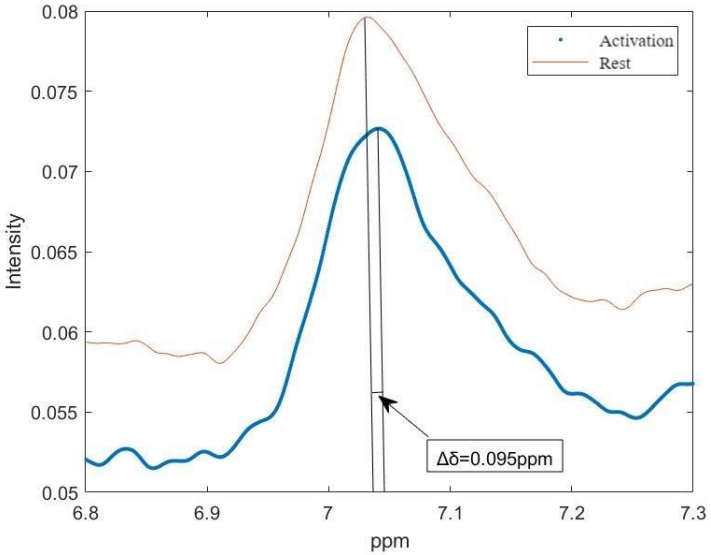

Fig. 1 Peak of homocarnosine in presence of visual activation and in the absence of it

Discussion

The decrease in pH during visual activation can be explained by an increase in the concentration of lactate. The existence of an inverse correlation between these values has been proved by various studies. [3-4] During prolonged visual stimulation an increase in the concentration of lactate in the human visual cortex is observed, which confirms our results [5].

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METHOD FOR NUMERICAL SIMULATION OF THE EFFECT OF INTRAFRACTION MOTION PARAMETERS ON THE DOSE DISTRIBUTION IN PROTON THERAPY WITH A SCANNING BEAM

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Such physiological processes as respiration, digestion, and heartbeat provoke the movement of organs and tissues. This physiological feature of the human body causes not only artifacts in the visualization of organs and tissues but also possible complications in the treatment of malignant diseases with various methods of radiation therapy. If in the first case the image quality is lost and, subsequently, leads to an incorrect diagnosis, in the second case it seriously affects the dose distribution in the target volume [1]. The latter is especially critical in the treatment of highly conformal methods such as IMRT/IGRT, SBRT/SRT, PBS. This work aimed to evaluate the effect of intrafraction motion and its parameters on the dose distribution during scanning beam irradiation in proton therapy.

To assess the effect of intrafraction motion on the dose distribution during irradiation with a scanning beam of protons (PBS), the TOPAS software package [2] implemented a model consisting of a target in the form of a 25×25×5 mm plate made of ABS plastic; a scanning beam of protons whose distribution is close to the Gauss distribution, a Sigma of 2.5 mm, and an angular divergence of $2.6*10^{-3}$ mrad. The target was located inside a 30×30×30 cm water phantom at a depth of 15 cm,

which corresponds to the path of a monoenergetic proton beam with an energy of 150 MeV.

The method included irradiation of a stationary target to obtain a uniform field on the plate, the maximum deviation from the average did not exceed ±3 %, as well as irradiation with the addition of target movement characteristic of the movement of tumors induced by the respiration process, after which the points of overexposure and underexposure were determined, in which the deviation from the average value obtained for the model without movement was calculated. In addition, the motion parameters, such as the amplitude and direction of motion relative to the beam direction, were consistently changed.

As a result of the calculation, when irradiating a target moving perpendicular to the beam along the 0X axis with an amplitude of 5 mm and 10 mm, a strong distortion of the dose distribution is observed, while the maximum deviation from the average value obtained for the model without movement was -40.8 % and 58.6%, respectively.

When irradiating a target moving with the same amplitude (5 mm) and different directions (0X, 0Y, and X0Y), the maximum deviation from the average value was observed when moving in the X0Y plane (the equation of motion $y = x$), in this type of motion, the plate was overdosed by 60.2% and the dose characteristics were strongly distorted.

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DELIVERY OF MAGNETIC NANOPARTICLES VIA THEIR TRANSPORTATION ON THE SURFACE OF MITOCHONDRIA

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A lot of nanoparticles are used in biomedicine nowadays for different purposes, such as therapy, diagnostic, drug delivery, etc. There are exist few ways to deliver nanoagents to target organs safely, and we proposed absolutely new method - transportation of nanoparticles on the surface of isolated mitochondria.

Standart protocol [1] was used to isolate mitochondria from mouse liver and then organells were incubated with commercial magnetic particles fluidMAG-Chitosan (100 nm) in various concentrations. Scanning electron microscopy was performed to prove particles binding to mitochondria surface.

Modified mitochondria were injected intravenously in mice and then animals were sucrificed and organs were collected. Time of circulation and biodistribution of nanoparticles were studied by MPQ-method[2]. We show that magnetic nanoparticles binding to mitochondria eliminated from the bloodstream and accamulated in lungs and liver within 30 min after injection whereas nanoparticles without mitochondria accamulated only in liver.

Considering applicability of mitochondria for transplantation in medical practice and results of our experiment, mitochondria are safely and perspective agents for nanoparticles delivery to target organs.

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PROPERTIES OF POLYCAPROLACTONE FILMS AFTER PLASMA MODIFICATION AND STERILIZATION

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Polycopraloctone materials are widely used in medicine as sutures, bone plates, abdominal meshes, stents, scaffolds, and also for drug delivery systems [1, 2]. The use of polycaprolactone as a corneal implant is interesting for the treatment of bullous keratopathy. One of the main requirements for a material is its wetted surface, which is achieved by exposing the polymer to a low-temperature plasma at atmospheric pressure. However, the acquired properties of the polymer after plasma can be lost after the sterilization procedure.

The aim is to study the surface properties of thin films based on polycaprolactone after the low-temperature plasma treatment and sterilization.

The original film samples were obtained by dissolving polycaprolactone (Netherlands) in trichloromethane ($CHCl_3$) (Russia). After 48 hours the formed polymer films were removed from the Petri dish.

The surface modification of the obtained films was carried out using an experimental setup for a low-temperature atmospheric pressure plasma. The plasma exposure time was 30 s. Sterilization was carried out with a source of ^{60}Co radionuclide. The exposure dose of γ-radiation was 1 kGy (Si, silicon).

Electron microscopy of the surface of the samples was performed on a Hitachi S3400N Type II microscope (Japan). The contact angle was measured by the sessile drop method at room temperature (25 ± 2) °C using a KRÜSS Easy Drop DSA 20 device (Germany).

Films based on polycaprolactone have topographically different sides of the surface. The outer surface is more relief. The inner surface is smooth. It is reflected in the roughness parameters.

The plasma treatment increases the roughness parameters of the inner side of the surface of films based on polycaprolactone by 1.5 times

as compared to the original films, while the differences in parameters between the sides are statistically insignificant ($p > 0.05$).

The study of wetting showed that the plasma treatment increases the hydrophilicity of the film, reducing the contact angle of wetting of the inner side by 9° - 10° (by (12 - 14)%), and also increases the surface energy values mainly due to the polar component to (20.6 ± 0.3) mJ/m^2. Statistical analysis showed that there were no significant differences in the contact angle of wetting, as well as in the surface energy between the sides of the material, $p > 0.05$.

Sterilization by γ-radiation does not contribute to a significant change in the roughness parameters: no statistically significant differences were found between the samples treated with plasma without sterilization and with sterilization, $p > 0.05$. The study of wetting showed that exposure to γ-rays reduces the wetting angle of the material after the plasma by 2º - 3º, which is statistically insignificant, $p > 0.05$.

Plasma surface modification increases (1.5 times) the roughness of the material. The plasma treatment increases the hydrophilicity of the material, reducing the contact angle by 9° - 10° (by 12% - 14%), and also increases the surface energy values to a greater extent due to the polar component. Sterilization by γ-radiation does not contribute to a significant change in the parameters of roughness and wettability of the polycaprolactone material after plasma modification.

The reported study was funded by RFBR, project number 20-08-00648.

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DYNAMIC 11C-METHIONINE AND 18F-FDG PET/CT IN DIFFERENTIAL DIAGNOSIS OF CEREBRAL GLIOMAS

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Brain gliomas are a heterogeneous group of neoplasms and account for 24% of all brain tumors in adults. Differential diagnosis of tumors is based on stereotactic biopsy, which is considered the "gold standard" in determining the histopathological diagnosis. But when using this method, there is a possibility of sampling error, and it cannot be carried out often due to its invasive nature.

Magnetic resonance imaging (MRI) is the main method of preoperative diagnostics of brain gliomas and a widely used method of structural imaging, providing significant detailing of anatomical structures with high spatial and contrast resolutions. However, according to MRI data, it is not always possible to accurately assess the boundaries and correctly classify the type of brain tumor. As a result, the use of radioisotope diagnostic methods, mainly positron emission tomography in combination with computed tomography (PET-CT), at the present stage of neuroimaging development occupies a leading position in the differential diagnosis of gliomas. The aim of this work is to study the metabolism of brain gliomas and to develop a non-invasive method for differential diagnostics using dynamic PET studies with 11C-methionine and 18F-FDG.

This study included 39 patients with primary glial brain tumors. All patients underwent the necessary diagnostic examinations, after which the pathological diagnosis was verified histologically by means of surgical intervention. In addition to the standard static parameters (SUV and T/N(tumor-to-normal ratio)), a new dynamic parameter was considered - "The first peak of maximum uptake" of tracer(Pmax), which is T/N at the point of the first maximum values of the metabolic activity of

the tumor, after which there was a decline in the distribution curve of tracer within the first minute of dynamic scanning.

According to the 11C-methionine PET/CT studies, only high-grade tumors (glioblastomas and anaplastic astrocytomas) in the area of the tumor core can be distinguished, while the infiltration zones and nearby intact brain tissues do not statistically differ in these parameters. In addition, when comparing the indicators of 18F-FDG accumulation in the area of a nearby intact substance and T/N in healthy brain tissue, statistical differences were obtained only in the glioblastoma group, which may mean the presence of tumor infiltration outside the FLAIR zone, which is characterized by a decrease in glucose consumption.

SENSITIZED ONCOLOGICAL HYPERTHERMIA WITH THERMAL TEMPERATURE CONTROL WITH FEEDBACK

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Recently, medical technologies that use nanoparticles have been widely discussed. It is assumed that new methods of therapy will be developed with the help of nanotechnology. One of these methods is sensitized oncological hyperthermia.

For oncological hyperthermia, cancer cells must be heated to a temperature of 41-45 degrees [1]. However, at the same temperature, healthy cells of the body also die. Therefore, it is necessary to use nanoparticles, which are delivered to the tumor in a targeted manner and are heated under the influence of the HF field. In this regard, nanoparticles are heated to temperatures above 41 degrees only cancer cells, without damaging the surrounding healthy ones.

As shown by the studies [2], for effective tumor therapy, a long-term maintenance of the temperature level in a given corridor of values is required, which is why the device has been improved. To create an HF field, a modified UHF therapy device is used.

Monitoring and control are carried out using a thermal imager and a board with an ATmega 8 microcontroller installed on it, connected to the control buttons of the UHF device [3].

The thermal imager measures the temperature of tissue heating, then the data goes to the computer, where the program checks if the temperature is within the required range (41-45 °C). If the temperature is below or above the specified threshold, the program sends a command to the controller, which in turn sends a signal to the buttons of the UHF device and returns the temperature readings to the specified limits (Figure 1.2).

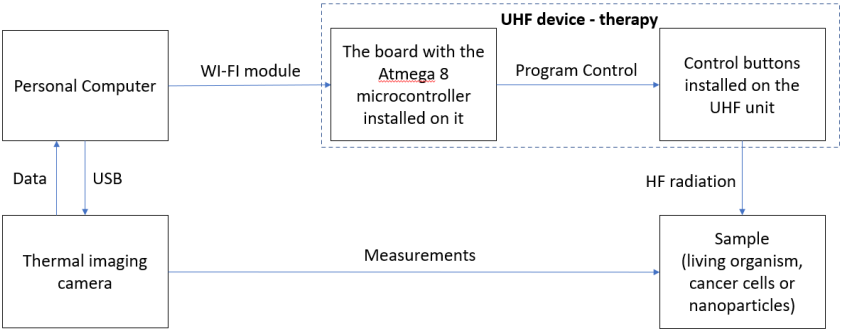

Figure 1 - Block diagram of the installation

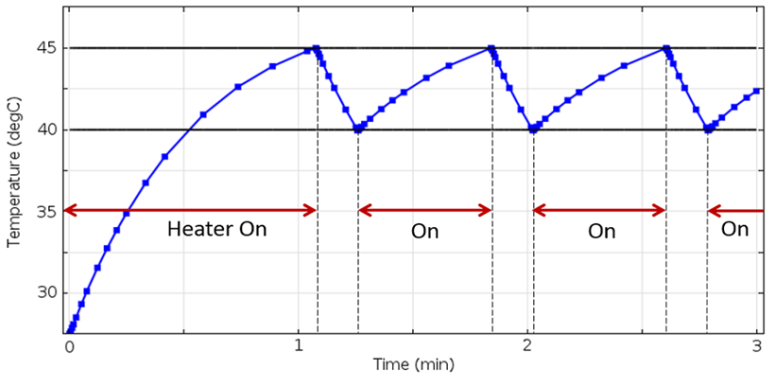

Figure 2 - Temperature of the model object

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PHOTODYNAMIC THERAPY OF MALIGNANT NEOPLASMS OF THE TONGUE USING THE PHOTOSENSITIZER CHLORIN E6

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The treatment of head and neck tumors is challenging, and treatment with standard methods is associated with high patient risks. During surgery or radiation treatment, the patient may lose the ability to chew, swallow, and speak. Also, the treatment may fail to complete, and the tumor will give a relapse, more dangerous than the primary tumor [1]. Head and neck tumors are very difficult to reach, and doctors need specialized equipment to diagnose and treat them.

A promising method for the treatment of head and neck tumors is a combination of fluorescence diagnostics (FD) with photodynamic therapy (PDT) [2]. Fluorescence diagnostics makes it possible to determine in real time the accumulation of a photosensitizer in a tumor, to accurately determine the tumor boundaries and the effectiveness of photodynamic therapy by the level of photosensitizer photobleaching. The therapy is carried out with the same photosensitizer, but using more intense laser radiation, which makes it possible to transfer oxygen to an active state.

A video system with a specialized endoscope was developed for real-time fluorescence diagnostics. This system makes it possible to assess the accumulation of the photosensitizer and to quantitatively record the

fluorescence signal. In this work, fluorescence diagnostics and photodynamic therapy of malignant neoplasms of the root of the tongue were carried out using the photosensitizer Photoditazin (Veta-Grand, LLC) based on Chlorin e6 (Ce6). Diagnostics was carried out before and after PDT. During the therapy, the radiation dose of the tumor tissue was 100 J / cm2, the laser radiation power was 1.5 W.

As a result, the fluorescence signal after PDT was quantitatively reduced by several times, which indicates the photobleaching of chlorin e6 during therapy and its effectiveness.

The research was carried out within the state assignment of goverment-commissioned research for 2019-2021 (theme"New phenomena in the in-teraction of laser radiation, plasma, corpuscular and radiation fluxes with condensed media as a basis for innovative technologies" № 0723-2020-0035).

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DIAGNOSTIC MELANOME USING A LASER RANGE METER

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The work is devoted to solving a common human problem of the 21st century – to counteract cancer, the work considers a possible solution to the problem of early diagnosis of such a disease as melanoma.

The main topic of this study is the early diagnosis and detection of malignant tumors, namely melanomas. The importance of work seems to be deplorable statistics of this disease and its rate of spread of the disease among other cancers in the modern world. According to statistics from the Republican Cancer Research Center OGII

and Medical Radiology H.H. Aleksandrov's melanoma occurs about 10 times less frequently than skin cancer and accounts for 1–4% in the total structure of human malignant neoplasms. This tumor is one of the most malignant and is characterized by rapid growth and early rapid lymphogenous and hematogenous metastasis.

Purpose of work: development of a method for measuring, staging and diagnosing melanomas by laser measurement of the tumor, detecting melanomas.

At the moment, the statistics, geometric and color characteristics of melanomas are known. In view of the spread of oncological diseases and their immediate danger at the moment and in the nearest foreseeable future, an expansion of the human arsenal is required to protect against the threat that has arisen.

This device, when creating a prototype, finalizing and properly debugging, may become one of the most popular tools for an oncologist. The main advantages of this medical device should be simplicity, speed and availability in operation,

the project is at the stage of development and the development of theoretical knowledge and information, both about this disease and the

effect of possible radiation on it, and requires further attention and immersion in the topic.

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INVESTIGATION THE KINETICS LUMINESCENCE OF CUINS$_2$/ZNS QUANTUM DOTS

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$CuInS_2$/ZnS quantum dots are luminescent nanocrystals used in various fields of analysis, in production of solar cells [1], LEDs [2], in bioimaging applications [3]. $CuInS_2$/ZnS quantum dots have a number of attractive characteristics [4], such as high photostability, broad absorption band, as well as their tunable band gap. Also, $CuInS_2$/ZnS have a high optical absorption coefficient and a high probability of radiative recombination, which make QDs attractive to researchers and developers.

$CuInS_2$/ZnS quantum dots are emerging as a promising alternative material for research due to their low toxicity and high absorption coefficient [5], unlike the highly toxic CdSe QDs. In this contribution, we propose a study of the luminescence decay spectra, as well as the time-resolved luminescence spectra, which will make it possible to study the influence of external conditions on the probability of luminescence of quantum dots from defect states. The most probable mechanism of QD photoluminescence is radiative recombination of a free electron with a hole captured by a deep defect (impurity copper cation).

This study is of practical importance, since not much of data on the nature of the luminescence process of $CuInS_2$/ZnS quantum dots based on the time-resolved luminescence spectra have been presented earlier. We choose the method based on time-resolved luminescence spectra, since it allows to separately monitor radiative transitions. Understanding the physical processes occurring in quantum dots will help more accurately select the application areas of $CuInS_2$/ZnS.

As a result of the work, it is expected to obtain data that will allow more accurate understanding of the features of photoluminescence in quantum dots $CuInS_2$/ZnS.

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COMPOSITE POLYMER MATERIAL FOR MEDICAL AND BIOLOGICAL PURPOSES

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In modern human life, there is a need for polymer materials with a short service life. Recently, the world has seen an increase in the production of polymers for medicine and other areas of the national economy.

The current topic is the use of biodegradable polymer materials with a fixed service life and the ability to maintain operational properties during the period of their use, with subsequent destruction without the formation of toxic substances. Biomedical polymers are used to create medical implants, suture materials for surgery, fasteners for traumatology and orthopedics, systems for targeted delivery and prolonged release of drugs.

The aim of this work is to evaluate the biological degradation of polymer composite materials from nanostructured composite material using a layered natural mineral from the class of metasilicates.

A biodegradable composite polymer material is a mixed multicomponent system that ensures the biodegradability of the entire system [1].

The objects of research were a biodegradable binder of 2-hydroxypropanoic (lactic) acid and a micro-reinforcing filler of a natural mineral from the class of metasilicates.

The presence of an alkaline pH in the filler of natural origin causes no harmful effects on human health and the environment as a whole [2].

In nanostructured polymer materials, particles of inorganic or organic fillers of nanometric size are distributed as uniformly as possible, which can be classified by their shape as needle-like or tubular structures (carbon nanotubes), two-dimensional plate structures (layered silicates) [3].

Due to the biocompatibility, as well as the possibility of regulating the physical and mechanical properties and terms of biodegradation, polymer materials from a thermoplastic matrix of 2-hydroxypropanoic (lactic) acid are used in various areas of biomedicine.

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MONONUCLEAR PHAGOCYTE SYSTEM BLOCKADE BY NANOAGENTS IN VARIOUS *IN VIVO* MODELS

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Various nanoparticles are widely used in biomedical research for the diagnosis and therapy of malignant tumors. Some have been approved for use in the clinic. However, many smart nanomaterials under development are rapidly cleared from the bloodstream due to intense nonselective uptake by cells of the mononuclear phagocyte system (MPS), mainly by macrophages of the liver and spleen [1]. To extend the circulation of functional nanoagents in the bloodstream and enhance their accumulation in the target tissues, we are studying the MPS blockade technique. It involves the temporary inhibition of macrophages ability to phagocytosis due to the uptake of low-toxic non-functional agents (blockers). This phenomenon allows to significantly extend the circulation of therapeutic nanoparticles in blood and improve their efficiency [2]

Here, using a library of synthesized magnetic nanoparticles coated with silicon dioxide, we studied the effectiveness of the MPS blockade technique for prolonging the circulation of 50, 100, and 200 nm particles in the bloodstream. The efficacy of the method was also tested in various immune states - in a model of a chronic pathological condition caused by the development of a grafted tumor (melanoma B16-F1, breast cancer EMT6/P), as well as in a model of acute inflammation caused by the administration of E. coli lipopolysaccharide.

MPS blockade was carried out *in vivo* with 500 nm silica particles used as blockers. The concentration of magnetic nanoparticles in the bloodstream of a mouse was measured non-invasively in real time using the MPQ-technology [3].

Thus, the results of the work prove the effectiveness of the MPS blockade technique in both healthy and pathological states of the body, demonstrate the versatility of the method for prolonging particles of various sizes, and show the practical significance of this technology for nanomedicine.

The work was supported by the grant of the Russian Foundation for Basic Research 17-74-20146.

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DEVELOPMENT OF A VIDEO FLUORESCENCE REGISTRATION SYSTEM FOR AN LED EMITTER

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Aim. Photodynamic therapy (PDT) is widely implemented in clinical practice. This contributes to the development of new devices for fluorescence diagnostics (FD) and PDT. One of the key parameters for new devices is the ability to conduct an FD during PDT and evaluate the fluorescence signal. Most PDT devices do not have the ability to perform PD and register the fluorescent signal, which is important for monitoring the quality of treatment. Development of a video system based on a digital camera for recording a fluorescent signal when using an led emitter for photodynamic therapy or fluorescent diagnostics. Development of a hardware component for a video system that registers a fluorescent signal during photodynamic therapy or fluorescent diagnostics. Development of software for a video system that registers a fluorescent signal during photodynamic therapy or fluorescent diagnostics. Application of a video system and registration of fluorescence on model samples during photodynamic therapy or fluorescence diagnostics

Results. In the course of photodynamic therapy, an important component is the possibility of conducting fluorescent diagnostics. With the help of this software and hardware, you could see the fluorescent signal. It was written in SOFTWARE. There are snapshot and settings buttons. The main part is an image from a video camera. By clicking the snapshot button, the photo is saved to a folder. Clicking the settings button opens a win

Figure 1. Chlorophyll fluorescence in the leaves of the lemon with the optical filter.

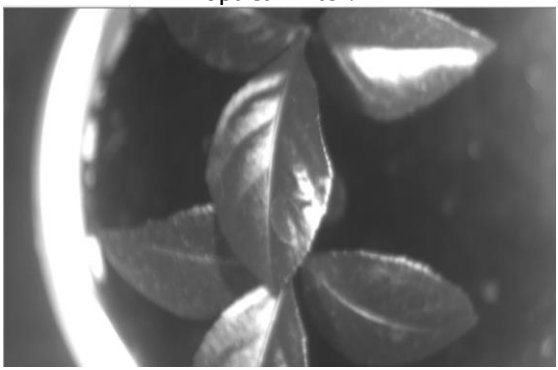

Figure 2. An image taken from the camera without using an optical filter.

Conclusions. The hardware part of the video system has been developed, which consists of a Point Grey FL3-GE-12S2M-C camera that registers fluorescence during FD, as well as an optical filter of the Longpass BLP01-633R-25 type, which in turn does not pass radiation from the emitter, but only a fluorescent signal. Software for the video system has been developed, based on the freely distributed software package Flycapture, which registers the fluorescent signal during FD.

This SOFTWARE has a simple and user-friendly interface. This video system was used for registering a fluorescent signal from the excitation of chlorophyll in lemon leaves, but it is potentially applicable for medical and biological research, including the diagnosis of human neoplasms

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MODELING AND SIMULATION OF TISSUE SPHEROIDS FUSION USING FUNCTION REPRESENTATION (FREP) APPROACH

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Considering 3D bioprinting as a research field, it is a part of the significant research field "3D printing in medicine." 3D bioprinting could be considered as upgraded 3D printing with adaptation for living cells, tissues, and construct. Bioprinters could be considered as one of the varieties of medical 3D printers. Even the 3D printing industry requires digital models and mathematical prediction, 3D bioprinting, as the field of living materials, require it not less. The most critical issues in 3D bioprinting are heterogeneous tissue creation and complex organ development [1].

Considering that the basis of 3D bioprinting process is the natural phenomenon of tissue spheroids fusion, errors in this point could lead to a not desirable result of the experiment and even for non-viability of the bioprinted construct. Besides, tissue spheroids fusion becomes more complicated when we consider widespread now problem in reaching a compromise between the task of making fusion more effective with the help of increasing tissue spheroid radius and avoiding necrotic processes that could arise in the tissue spheroid center when it is getting bigger. Such a complex task is not convenient to be solved with the usual modeling of STL files in CAD software tools, as it is often solved in 3D printing. Therefore, a possible solution is to model this situation with the Function Representation (FRep) approach, considering all critical moments with mathematical functions [2, 3].

To develop model of the biggest tissue spheroid without any necrotic processes, the diffusion-reaction task had been solved with the help of FRep approach. The concentration of oxygen in cells was considered

depends on the time interval and coordinate to realize what diameter of the tissue spheroid is maximum without any necrotic processes arise in the center. Consumption of cells was considered as a source member in the equation, named by OCR (oxygen consumption rate), and depends on the properties of the chosen cellular matrix and chosen cells. Due to the fact that approbation and validation of the model were provided on bovine chondroblasts in cellular culture DMEM, the OCR was taken as 2.47*10-16g/cell/s [4] divided on cell volume. Calculations were produced in the Wolfram Mathematica software toolkit. Due to modeling results, the maximum diameter of tissue spheroid from bovine chondroblasts in cellular culture DMEM without any necrotic processes in the center equals 285 mcm. The validation of the model was provided at 3D Bioprinting Solutions on tissue spheroids on the third day after seeding. Tissue spheroids were seeded in concentrations of 29000 cells/ml and 16000 cells/ml. Half of the tissue spheroids from both two groups were painted by CellTox Green during seeding, and another half was painted by Live/Dead on the third day. Considering experimental results in comparison with modeling results, both have the same trend of concentration decreasing after 250 mcm, and in experiment results, the first necrotic processes start at 285 mcm. Therefore, the model passed the validation and requires further upgrading with cells compacity considering to simulate more complex bioconstructs.

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FLUORESCENCE DIAGNOSTICS AND PHOTODYNAMIC THERAPY OF CERVICAL NEOPLASMS

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Aim. To evaluate the methods of spectral- and video-fluorescence diagnostics of cervical neoplasia (CIN) associated with 16 and 18 HPV types, and to evaluate the effectiveness of photodynamic therapy (PDT) via photobleaching of the photosensitizer chlorin e6 ("Photolon").

Materials and equipment. Spectral-fluorescence diagnostics and PDT were carried out using a single laser with wavelength of 660 nm, which became possible with a Y-shaped optical fiber equipped two fibers with diameters of 200 (for delivering fluorescent and backscattered laser radiation to the spectrometer) and 400 μm (for delivering laser radiation to tissues for PD and PDT). The fiber spectrometer LESA-01-BIOSPEC was used for PD. The two-channel video-system [1] was employed to obtain fluorescent images of the studied normal and pathological tissues. Patient aged 52 years with cervical dysplasia (D26.0), associated with 16, 18 HPV types, was included in the study. Chlorin e6 (Photolon) at a dose of 1.2 mg/kg was used as a photosensitizer (PS).

Results. Morphological examination of a cervical biopsy taken from this patient 3 months after PDT with chlorin e6 confirmed successful treatment and complete regression of pathological tissues. Previously identified HPV types and signs of CIN were not observed.

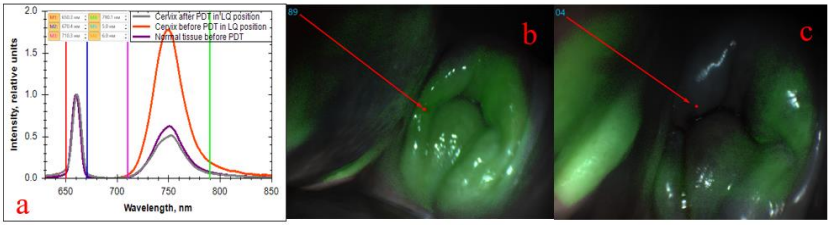

Fig.1. Fluorescence spectra of cervix in Left Quadrant position before and after PDT and normal tissue before PDT (a), video-fluorescence diagnostics before PDT (b) and after PDT (c).

Table 1. Fluorescence index (relative units) in normal tissue and different positions of cervix before and after PDT

Position / Investigated zone	Left Quadrant	Right Quadrant	Upper Quadrant	Lower Quadrant	Cervical canal
Pathological tissue before PDT	6.329	2.867	3.419	2.938	3.200
Pathological tissue after PDT	1.858	1.185	1.760	1.308	4.329
Normal tissue before PDT	2.154	2.154	2.154	2.154	2.154

Conclusions. The combined use of video- and spectral-fluorescent diagnostics for cervical neoplasms allows controlling the PDT process at all stages of the procedure. The study demonstrated the possibility of simultaneous spectral-fluorescent diagnostics and PDT using a laser source with a wavelength of 660 nm.

The research was carried out within the state assignment of goverment-commissioned research for 2019-2021 (theme"New phenomena in the interaction of laser radiation, plasma, corpuscular and radiation fluxes with condensed media as a basis for innovative technologies" № 0723-2020-0035).

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DNA DETECTOR

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Polymerase chain reaction is a modern method of multiple copying of certain regions of DNA, which is widely used for DNA diagnostics of biological materials [1]. The advantages of this method are: high accuracy, the ability to work with minimal amounts of test material. The disadvantage of the polymerase chain reaction method is the duration of the study, which in some cases reaches 12 hours. Nanoantennas are nanostructures that are widely used for receiving and transmitting electromagnetic waves [2]. These elements are very promising for use as photoelectric converters and sensors. The advantage of these structures, from the point of view of diagnostics, is the possibility of resonant tuning to a specific wavelength range and high sensitivity. Modern research in this area is focused on the analysis of the parameters of the entire material, rather than individual molecules. It is advisable to use the high sensitivity and selectivity of nanoantenna structures for the detection of specific DNA.

The aim of the work is a theoretical calculation of the proposed nanostructure for DNA detection.

The proposed DNA detector consists of a monopole nanoantenna (a parallelepiped with dimensions a - length; b - width; l – height); primer - a short fragment of a nucleotide sequence complementary to the detected DNA region, which binds to the detected DNA sequence, conventionally indicated in the figure by a cylinder with height d.

The DNA detector works as follows. Geometrical dimensions, type of material, dielectric elements surrounding a monopole nanoantenna affect its resonance frequency - the frequency of absorption of an incident electromagnetic wave. In the initial state, the primer is not connected to the DNA strand, while a small primer with the corresponding value of the relative permittivity insignificantly changes the resonance fre-

quency of the monopole nanoantenna. When denatured DNA strands are applied to the surface covered with the described nanoantennas, each primer captures a specific complementary DNA strand, attracting it to the nanoantenna surface. In this case, the sizes of DNA chains are much larger than the sizes of primers, which leads to a noticeable change in the resonance frequency of the nanoantenna. So, the surface covered with nanoantennas, without introducing a DNA sample, absorbs an electromagnetic wave with one length, and when DNA is introduced and its complementary correspondence to the selected primers, the absorbed wavelength changes, which can be observed directly, even without the use of instruments.

From the theory of antennas it is known that the maximum efficiency of the receiving antenna is achieved when the imaginary part of the impedance is equal to zero. In fig. 1 shows the graphs of the dependence of the imaginary part of the impedance of the monopole nanoantenna on the wavelength of the incident radiation with and without a DNA segment.

From fig. 1 it can be seen that the presence of a DNA segment significantly changes the resonance wavelength of the nanostructure: by more than 100 nm, which can be established even without the use of instruments.

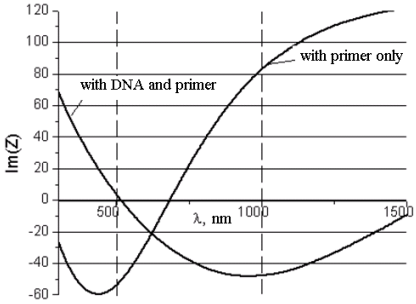

Fig.1. Experimental scheme of a dye laser with semiconductor pumping

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TECHNIQUE FOR QUANTIFYING ELECTRON DENSITY DISTRIBUTION OF MICELLES BASED ON FUNCTIONAL LIPIDS WITH SPACER GROUP BY SMALL ANGLE X-RAY SCATTERING METHOD

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Small angle x-ray scattering (SAXS) is a structural method which allows to study objects of various physical nature and aggregate state in native conditions, including biological and polymeric macromolecules in solution. A quantitative evaluation of the electron density distribution pattern reconstructed from small angle x-ray scattering data will provide more detailed information about the structure of biological objects. Modern software and methods of SAXS data interpretation allow to extract from the intensity spectrum geometric and weight characteristics of scattering objects, called invariants, and restore the qualitative pattern of electron density distribution. However, qualitative pattern does not provide complete structural information of the object.

In this paper, we propose a contrast variation method characterized by the addition of "electron-dense" substances to the solvent to quantify reconstructed structural models. The effective scattering capacity of a substance is determined by the difference (contrast) between the averaged electron density of the solvent ρ_s in which the scattering particle is located and the electron density of the particle itself: $\Delta\rho = \rho - \rho_s$. Thus, when the electron density of the solvent ρ_s changes, the final picture of the object`s electron density distribution will become different, too.

The SAXS experiment was performed for a Function-Spacer-Lipid (FSL) construct biot-CMG(2)-Ad-DOPE [1] in a pure phosphate buffer (PB) and in PB with the addition of various mass concentrations of glucose: from 92.7 mg / ml to 321.9 mg / ml. 3D structures of the electron density distribution were obtained for each sample (Fig.1).

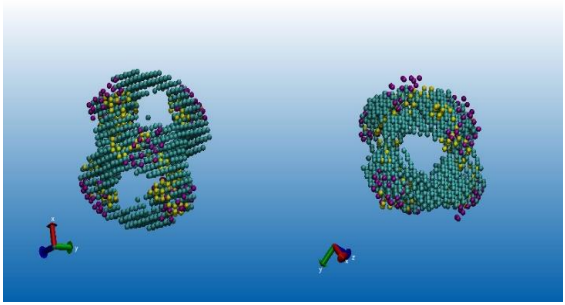

Fig.1. Restored structures
Stereo image of a structural models reconstructed by ab initio modeling of biot-CMG(2)-Ad-DOPE in pure PB (blue color), in PB with a mass concentration of glucose 92,7 mg/ml (yellow) and 180,2 mg/ml (purple).

These structures were compared with the calculated electron densities of each buffer. As we expected, an increase in the electron density of the buffer led to the selection of the most "electron-dense" sections of the sample and the disappearance of those sections which electron density was less or equal to the buffer density. It was obtained that the most "electron-dense" sections of the sample, corresponding to the buffer electron density of 353.8 e/nm^3, are located near the mycelium surface, and less "electron-dense" sections, corresponding to the buffer electron density of 334.4 e/nm^3, are located near the mycelium center. The obtained result confirmed the effectiveness of the contrast variation method for quantifying the electron density distribution patterns reconstructed from the SAXS data.

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VISUALIZATION OF RADIOTRACERS FOR SPECT IMAGING USING A TIMEPIX DETECTOR WITH A CODED APERTURE

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Single-photon emission computed tomography (SPECT) is a well known imaging method of nuclear medicine, which allows obtaining tomographic images of the biodistribution of radiolabeled compounds, both throughout the patient's body and in separate organs. At the same time, a small animal SPECT is currently a key tool in the development of new radiopharmaceuticals and to seek for methods for their targeted delivery[1]. However, in studies of small animals, the region of interest typically has a small size and a high spatial resolution is necessary to get a good image.

A system based on the coded aperture[2] and the hybrid pixel Timepix detector[3] with the CdTe sensor is developed as a possible imaging solution for the small animal SPECT[4]. Characterization of the system using an X-ray source and various radioactive gamma emitters, including Tc-99m and I-125, is made. The spatial resolution is shown to be of 0.9 mm at the field of view of 3 cm x 3 cm for the energy range typical for SPECT(Table 1). The experimental data, supported by the simulation, confirm that a 1 mm thick tungsten coded aperture is sufficient to obtain an image of the distributed radioactive sources with the energy of gamma rays at least up to 180 keV without significant reconstruction artifacts[5]. The reconstructed tomographic images of a SPECT phantom are presented.

Table 1. The calculated data obtained for the gamma emitters most commonly used in SPECT.

Isotope	Energy [keV]	Spatial resolution [mm]	Registration efficiency, % (with collimator)		SNR
			CdTe 1 mm	CdTe 2 mm	
^{125}I	30	0.88	40	40	96
^{67}Ga	93.3	0.89	28	36	90
^{177}Lu	113	0.89	23	31	88
^{201}Tl	140.5	0.89	16	27	87
^{99m}Tc	158.6	0.9	15	23	87
^{117m}Sn	158.6	0.9	11	20	86
^{123}I	159	0.9	11	20	85
^{201}Tl	167	0.9	10	18	84
^{111}In	171.3	0.9	10	17	83
^{67}Ga	184.6	0.91	8	16	83
^{177}Lu	210	0.91	7	12	81
^{111}In	245.4	0.91	5	10	78
^{67}Ga	300	0.92	4	7	74
^{133}Xe	350	0.92	3	6	69

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Acknowledgments
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REGULARITIES OF THE ACTION OF THE ANTITUMOR DRUG DOXORU-BICIN TOGETHER WITH SILICON NANOPARTICLES ON MESENCHYMAL STEM CELLS

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It is well known that stem cells are the basis for maintaining the body's regenerative potential [1]. The greatest loss of stem cells is associated with severe and long-term diseases. One of such diseases are cancers. Among the existing methods of cancer treatment, one of the main ones is chemotherapy. Cytostatic drugs kill cells, and moreover the most active ones, there are not only cancer cells, but cells of the mucous membranes, blood, bone marrow, and gonads as well. Because of chemotherapy very often develop different side effects such as vomiting, damage to the mucous membranes of the gastro-intestinal tract (stomatitis and diarrhea), and death of some bone marrow cells. [2]. One of the methods for solving these problems is the targeted delivery of chemotherapy drugs directly to tumor cells. Nanoparticles of various origins are used as carriers in modern pharmacology. Porous silica materials are the most demanded in this area.

The aim of the work was to studying the pattern of the action of the anticancer drug doxorubicin together with silicon nanoparticles on mesenchymal stem cells (MSC) of the human bone marrow, which make up the regenerative potential of the adult body.

The MSC culture was grown from human bone marrow at a concentration of $2x10^5$ cells per ml of growth medium. The growth medium was pumped out from the mattresses, and the medium with the drug doxorubicin at concentrations of 0.001 mg / ml and 0.002 mg / ml was added, both separately and together with nanoparticles at concentrations of 0.25 mg / ml and 0.5 mg / ml. The cells were incubated with chemotherapy drugs for a day, cells with nanoparticles separately and in a

combination of chemotherapy drugs with nanoparticles were incubated for 7 hours. Then the survival rate of cell cultures was assessed. About 1500 colonies were counted for each point.

Based on the obtained results, it was found that doxorubicin at a concentration of 0.001 mg / ml after 2 hours of incubation reduces cell survival to 85%, while when the drug at a concentration of 0.002 mg / ml, the survival rate was 46 ± 2%. Under the action of the drug in the studied concentrations with microporous nanoparticles at a concentration of 0.25 mg / ml, no decrease in the survival of mesenchymal stem cells was revealed. Another picture was observed with the combined action of the drug with nanoparticles at a concentration of 0.5 mg / ml, cell survival after 7 hours of incubation is 22% ± 2.75. These data indicate that the nanoparticles-transporters of the drug penetrate into cells, which leads to decrease in MSC survival.

As a result of the study, it was revealed that microporous nanoparticles can be used as a delivery of chemotherapy drugs into cells. The cytotoxic effect of silicon nanoparticles on mesenchymal stem cells of the bone marrow was not revealed.

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INTERACTION BETWEEN PLASMINOGEN AND MODIFIED MAGNETIC NANOPARTICLES

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In the last decade, in connection with the intensive development of quantitative instrumental methods for analyzing the blood of patients in acute pathological conditions or with the development of chronic diseases, it is necessary to carry out rapid procedures for the extraction of protein markers-analytes from the blood. One of these markers may be plasminogen, a precursor protein for plasmin, which plays a major role in the fibrinolytic system. The aim of this work is to study the interaction of plasminogen with the surface of magnetic particles modified with silicon dioxide and amino groups [1] and particles modified with human serum albumin (HSA) [2]. We have proven the binding, on average, of about 0.22 and 0.33 mg of plasminogen per 1 mg of particles modified with silicon dioxide and amino groups, and particles modified by HSA, respectively. With the help of commercially available kits for determining the activity of plasminogen NPO "Renam" (Russia), the preservation of up to 30% of the fibrinolytic activity of the protein was confirmed. Based on quantitative estimates of the binding and elution of plasminogen, data on the preservation of functional abilities by plasminogen on the surface of particles, the proven possibility of effective desorption of plasminogen and reuse of particles, as well as literature data on sufficient hydrophilicity and inertness in biological fluids of particles with similar coatings in composition, we assume the possibility of using the particles created by us for the transport of plasminogen, as

well as for its extraction from solution. Our data on the nonspecific binding of plasminogen are of great importance due to the widespread use of works on the modification of the surface of magnetic particles with silicon dioxide with various functional groups, as well as serum albumin, which is traditionally used to reduce nonspecific sorption when working with blood and plasma.

The study was carried out with the financial support of the Russian Science Foundation, project No. 18-73-00350.

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"Physics, Engineering and Technologies for Biomedicine"

CORRECTION FACTORS FOR THE OUTPUT OF MICRO-IONIZATION CHAMBERS FOR DOSIMETRY OF SMALL FIELDS

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When ionization chambers are used in small fields in dosimetry, problems arise associated with the absence of electronic equilibrium in small fields, the perturbation introduced into the field by the presence of the detector, and the effect of the finiteness of the detector size on its readings. In this work, the correction factors of detectors are determined for a number of small ionization chambers intended for dosimetry of small fields.

Key words: small fields, output correction factors, micro-ionization chambers, bremsstrahlung, Monte Carlo method

The correction factors were determined for the 18 MV spectrum bremsstrahlung beams generated by medical accelerators of the Varian type, using calculations by the Monte Carlo method and experimentally at the Trilogy accelerator. The EGSnrc code was used for calculations. At the first stage, using the Beamnrc subprogram, phase space files were formed for different transverse sizes of square fields, including for a reference field of 10x10 cm^2. An EBT3 dosimetric film was taken as a reference detector. Radiochromic film EBT3 has the closest to unity values of correction factors $k_{Q_{clin},Q_{ref}}^{f_{clin},f_{ref}}$ in the smallest fields of all the considered detectors. This is due to the proximity of the effective atomic number and density of the active layer of the film to water. According to [1] Zeff = 7.46 for the active layer EBT3, while for water Zeff = 7.42. The values of the correction coefficient of the output for a specific detector, on the assumption that its readings are proportional to the ab-

sorbed dose in the sensitive volume of the detector, were determined from calculations by the Monte Carlo method using the formula:

$$k_{Q_{clin},Q_{ref}}^{f_{clin},f_{ref}} = \frac{D_{w,Q_{clin}}^{f_{clin}} / M_{Q_{clin}}^{f_{clin}}}{D_{w,Q_{ref}}^{f_{ref}} / M_{Q_{ref}}^{f_{ref}}} \approx \frac{D_{w,Q_{clin}}^{f_{clin}} / D_{\det,Q_{clin}}^{f_{clin}}}{D_{w,Q_{clin}}^{f_{ref}} / D_{\det,Q_{ref}}^{f_{ref}}}, \quad (1)$$

where $D_{w,Q_{clin}}^{f_{clin}}$ and $D_{w,Q_{ref}}^{f_{ref}}$ – doses in a small volunme of water;

$M_{Q_{clin}}^{f_{clin}}$ and $M_{Q_{ref}}^{f_{ref}}$ – detector readings in water;

$D_{\det,Q_{clin}}^{f_{clin}}$ and $D_{\det,Q_{ref}}^{f_{ref}}$ – doses in the sensitive volume of the detector for the clinical and reference fields at the reference depth in the water phantom [2].

Conclusion

In this work, we obtained specific values of the correction factors for the output for micro-ionization chambers PTW31010, PTW31015 and PTW31016 for bremsstrahlung beams of the 18 MV spectrum. The results of calculations and experiments are consistent with each other.

The results obtained will improve the accuracy of dosimetry of small fields in the region of high-energy bremsstrahlung radiation. This work was carried out with the financial support of the Russian Foundation for Basic Research and SITMA within the framework of research project No. 18-52-3408.

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TESTING THE CAPABILITIES OF THE DESIGNED PHANTOM AT INTRAFRACTIONAL MOTION ON THE DOSE DISTRIBUTION IN PROTON THERAPY-SCANNING BEAM

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Proton therapy provides a highly uniform dose distribution relative to the target, which is an advantage over photon radiation therapy. The beginning of clinical practice of proton therapy was limited to the treatment of tumors of the eye, the base of the skull and inoperable sarcomas, these types of diseases have a high radioresistance in relation to photon radiation therapy. Due to this, it has become considered as a promising treatment method due to the reduction of undesirable side effects by reducing the dose to normal tissues [1].

However, during a proton therapy session, high accuracy in positioning patients and stability in the location of the tumor when the target position changes relative to other organs, due to physiological processes such as respiration, heartbeat, and digestion [2]. The purpose of this work is to test the capabilities of the developed phantom for intrafractive motion on the dose distribution during proton beam scanning.

Previously, a single-coordinate dynamic water phantom was developed [3], optimized for working with the proton therapy complex "Prometheus", LPI Physico-technical Centre. The volume of the phantom made of plexiglass is 300x150x200 mm^3. The target is made of PLA-plastic with a size of 60x60x60 mm, optimized for working with PTWTM PinPoint 3D Chamber 31022 ionization cameras and GAFCHROMICTM EBT3 dosimetric films. The movement model simulates

a breathing cycle consisting of the phases of inhalation, exhalation, and pause, described by linear functions.

The experiment was divided into 3 stages with different movement parameters. In the first stage, the target was static and no movement parameters were set. In the second stage, the following parameters were set: duration of inhalation 1500 ms, exhalation 1500 ms, pause 500 ms, with an amplitude of 5 mm. And in the third stage, the following movement parameters were set: the duration of inhalation is 1500 ms, exhalation is 1500 ms, pause is 500 ms, with an amplitude of 10 mm.

Thus, the first experiment was conducted with the developed phantom, which is a development of the previously proposed method [3]. In the first stage, the maximum deviation from the average dose distribution was 1.7% and -1.9%, in the second 4.1% and -6.6%, and in the third 4.0% and -13.7%. That shows that interfraction motion considerably influences dose distribution. And the developed phantom can be used in further experiments.

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HAFNIUM-BASED COMPLEX AS CONTRAST AGENT FOR RADIOLOGY

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Nowadays only iodine-based X-ray contrast agents are in clinical use [1]. From a physical point of view, all elements that have a serial number in the periodic table greater than iodine have a better ability to absorb X-rays. Thus, if the drug is developed on the basis of element with $Z > 53$, tissue contrast can be increased. One of such elements is hafnium. It has a higher absorption capacity than iodine [2-4].

In this work, a study of a substance based on a hafnium complex was performed. An acute toxicity study was carried out in female C57Bl/6 mice 20–22 g body weight for intravenous route of administration.

The study of biodistribution was carried out in female C57Bl/6 mice with transplanted murine mammary adenocarcinoma Ca755. The biodistribution study was carried out for the intravenous route of administration using microCT in vivo. MicroCT of mice was performed using an IVIS Spectrum CT imaging system (Perkin Elmer Inc).

As a result of this work, a half-lethal dose was established for the hafnium complex. The possibility of contrasting tissues in vivo was also shown in mouse model. After administration of hafnium complex, contrast enhancement of heart chambers was observed in 2 min (fig. 1) and kidneys – in 27 min (fig. 2). Thus, hafnium-based compounds are potential x-ray contrast media.

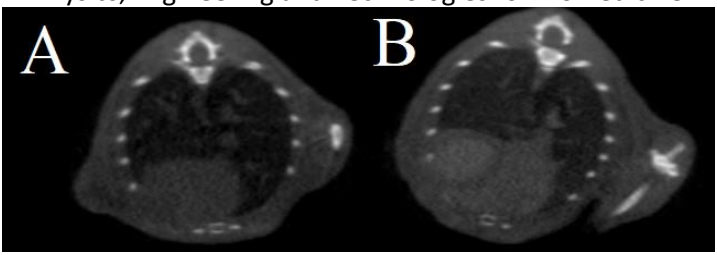

Fig.1. Axial microCT images of heart before (A) and in 5 min after (B) intravenous injection of a substance based on a hafnium complex .

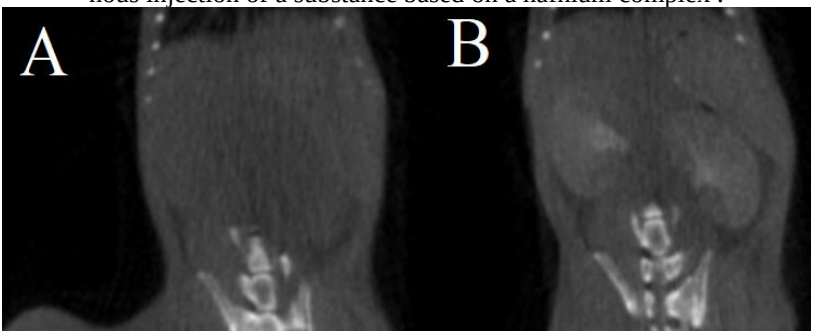

Fig.2. Coronal microCT images of the kidneys before (A) and in 27 min after (B) intravenous injection of a substance based on a hafnium complex.

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INFERRING NETWORK STRUCTURE FROM ITS DYNAMICS

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The interaction topology of complex networks strongly impact their collective dynamics and thus the function of entire system. For many networks the dynamics of individual units becomes more and more accessible whereas their intricate web of interactions remains uncertain [1]. The described model of a neural network consists of nodes and connections between them, representing neurons and synapses.

In this work, it will be discussed how to describe networks by systems of ordinary equations using an adjacency matrix for a network topology and reviewed several techniques for inferring network connectivity, in particular Granger Causality and the Dynamic Bayesian Network. The combinations of multiple methods may result in better reconstruction.

Reconstructing the structure of interaction networks from only the collection of local data has the potential of recovering the functional organization in brains at multiple levels and of designing a network system for a specific function.

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BIOTECHNOLOGICAL BASIS FOR SYNTHESIS OF PROTEIN-LINKED ANTIBIOTICS FROM THE *BACILLUS* BACTERIA

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Abstract

Nowadays the problem of resistance of microorganisms to antibiotic is quite urgent. Using of antibiotics lead to the development of multi-resistant forms of microbes and cause hospital infections, have a pollution effect to the environment, destroy the microbiota of biocenoses, suppress the immune system and have a number of side effects. One of the options for solving this challenge is the development and introduction of natural antibiotics of bacterial origin - bacteriocines. Various methods of obtaining them have been tested and successfully implemented. In particular, more than 30 different antibacterial agents were obtained on the basis of bacteria of the genus Bacillus. However, in practice, their synthesis is rather complicated and requires serious financial investments and special equipment. The main objectives of this study were to determine the antibacterial properties of the strains *Bacillus Cereus* ATCC 14579 and *Bacillus Subtilis* ATCC 6633 and, therefore, their ability to secrete bacteriocins, as well as to develop the method for obtaining bacteriocines from that strains.is presented below.

Key words: bacteria, bacteriocine, Bacillus cereus, Bacillus subtilis, syntheses, antibiotic, biotechnology

Introduction

The purpose of the study was developing of methods for the extraction of bacteriocines from bacteria of the genus Bacillus, or rather two strains of this genus - *Bacillus subtilis* ATCC6633 and *Bacillus cereus* ATCC 14579.For study of the antibacterial properties of the *Bacillus subtilis* ATCC6633 and the *Bacillus cereus* ATCC 14579 strains, we

have developed special methods, based on co-cultivation of these strains with Gram+ bacteria *Staphylococcus Aureus* (ATCC 29213), *Staphylococcus epidermidis* (ATCC 122286), *Streptococcus aqalactia* (ATCC 13813), *Streptococcus pneumonia* (ATCC 49619), *Streptococcus pyogenes* (ATCC 19615) and Gram - bacteria *Escherichia coli* (ATCC 15922), *Pseudomonos aerogenosa* (ATCC 27853), *Salmonella typhimurium* (ATCC 14028), *Proteus mirabilis* (ATCC 25933). It was found, that *Bacillus subtilis* ATCC6633 inhibited growth of these bacterial strains *Staphylococcus epidermidis*, *Streptococcus pyogenes*, and *Streptococcus agalactia*, while *Bacillus cereus* ATCC 14579 inhibited the growth of the corresponding bacterial strains of *Staphylococcus epidermidis*, *Streptococcus pyogenes*, *Streptococcus agalactia, Escherichia coli* and *Pseudomonos aeruginosa.*

To obtain a new bacteriocine, especially freeing of bacterial suspension from bacterial cells, various methods were tested: centrifugation, filtration, precipitation, and others. As a result of the research, the antibacterial properties of the strains *Bacillus subtilis* ATCC6633 and Bacillus cereus ATCC 14579 were confirmed and new peptides were synthesized. These proteins inhibited the growth of mainly Gram-positive bacteria - staphylococci and streptococci. It was observed, that from the methods, selected for cleaning of bacteriocine solution from alive bacterial cells (filtration, pasteurization and centrifuge sedimentation) most suitable method is centrifuge sedimentation. Accidentally was observed one very rare described phenomenon[1,2] of aging of the bacteria and morphological differentiation of Bacillus bacteria in fresh and old culture. Continue scientific work to identify the synthesized substances and study their physicochemical, biological and antibiotic indicators is expected. Scientific investigation in this direction is to be continued and the results are quite promising for intended purpose.

Conclusion

Developing of technological methods for syntheses of natural antibacterial bacteriocins is very important for microbiology and biotechnology sciences. This research will allow providing medicine, veterinary and agriculture with safe, effective and affordable antibacterial sub-

stances in alternative to classic antibiotics. Usage of bacteria of Bacillus genus opens wide perspectives for this type of researches.

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LASER-ABLATIVE SYNTHESIS OF ELEMENTAL BI AND SM OXIDE NANOPARTICLES FOR RADIATION NANOMEDICINE

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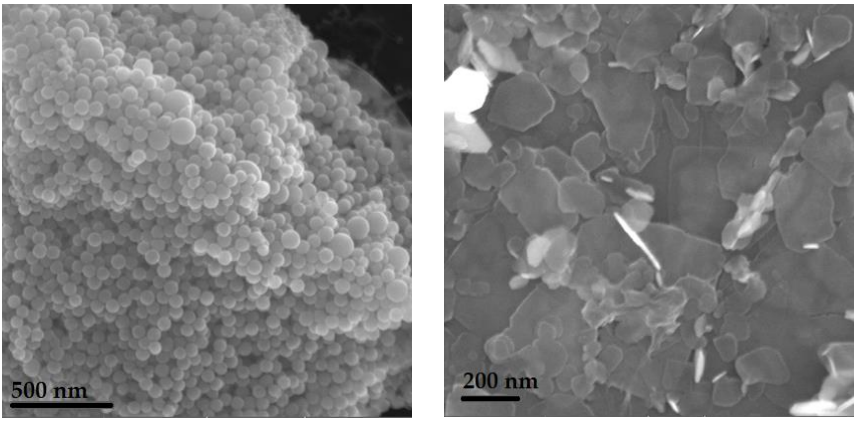
Radiation nanomedicine is an emerging field, which utilizes nanoformulations of high-Z elements [1,2] and nuclear agents to increase their local concentration at targeted sites to improve therapeutic outcome and to reduce radiation dosage [3]. This field lacks methods for controlled fabrication of biocompatible, non-toxic nanoformulations with low polydispersity and high colloidal stability, which are required for efficient targeted cancer treatment. Here, we present application of methods of femtosecond (fs) laser ablation in water and organic solvents to fabricate stable aqueous colloidal solutions of ultrapure elemental Bi and isotope-enriched samarium oxide nanoparticles (NPs) and their characterization by a variety of techniques, including TEM, SEM, XRD, FTIR, Raman, and optical spectroscopy [4,5]. We demonstrate that fs laser ablation of Bi target leads to the formation of spherical elemental Bi NPs with 20–50 nm mean size and a low size-dispersion. The NPs prepared in water experience fast conversion into 400–500 nm flake-like

nanosheets, composed of bismuth subcarbonates, while the NPs prepared in acetone demonstrated high stability (**Fig. 1**). Stable aqueous solution of elemental Bi NPs suitable for biomedical applications can be obtained by coating NPs with Pluronic® F68. We also show that elemental Bi NPs, due to their vanishing band gap, exhibit remarkable absorption in the window of maximal optical transparency in biological media (NIR-IR range), which can be used for the activation of photothermal therapy. At the same time, we show that methods of fs laser ablation of a 152 Sm-enriched samarium oxide target can be applied to prepare solutions of samarium oxide NPs with relatively narrow size distribution, having spherical shape fraction with controlled mean size between 7 and 70 nm and high colloidal stability (**Fig. 2**). Exempt of any toxic synthetic by-products, laser-ablated elemental Bi and Sm oxide NPs present a novel appealing nanoplatform for combination image-guided photo and nuclear radiotherapies.



a) **b)**

Fig.1. SEM images of Bi NPs produced from fs-laser ablation **(a)** in water and re-dispersed in acetone immediately after the synthesis, **(b)** in water without re-dispersion in acetone.

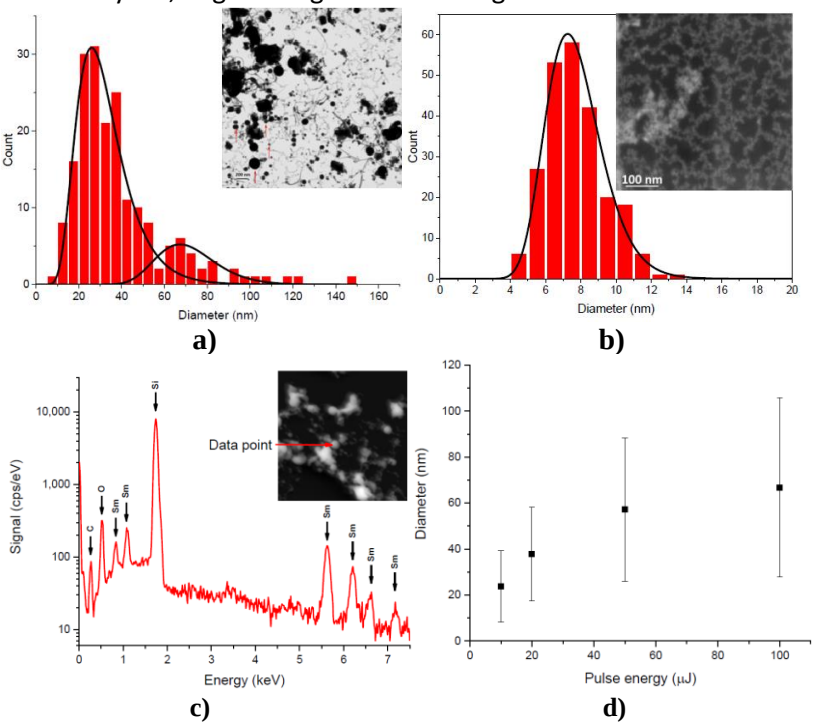


Fig.2. SEM images and size distributions of Sm oxide NPs produced from fs-laser ablation **(a)** immediately after ablation, **(b)** after 5 hours of laser fragmentation. **(c)** Energy-dispersive X-ray spectroscopy (EDS) spectrum of synthesized NPs. **(d)** Diameter of spherical Sm oxide NPs obtained by laser ablation at different pulse energies.

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MATHEMATICAL MODELING OF CALCIUM-DEPENDENT INSULIN SIGNALING IN HEPATOCYTES

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Proper insulin signaling in hepatocytes provides the organism with metabolic flexibility by keeping blood glucose concentration stable in both the organism's fasting and postprandial state. The shift between the states is regulated by a switch from glucagon to insulin signaling and occurs in a calcium-dependent manner on the intracellular level.

There are three major factors in intracellular calcium signaling, including, among others, the sensitivity of IP_3-receptors, the endoplasmic reticulum stress, and the mitochondria-associated membranes (MAMs) (see Fig.1). However, it is still unclear which factor is more or the most important than others.

Our model describes all involved players and allows us to study the individual contribution of each of the assumed factors to the development of hepatocyte insulin resistance. It is assembled from combination of well-established models of IP_3-receptor dynamics and of mitochondrial impact on cytosolic Ca^{2+} signaling [1]-[2].

Its results are in good agreement with available experimental data [3].

We consider both normal and dysfunctional cells. Analysis of modeling results shows that miscommunication between the mitochondria and the ER only is not able to noticeably increase the level of Ca^{2+} in the cytosol. Far greater impact on the level of cytosolic Ca^{2+} has the modulation of IP_3-receptors, both by itself and accompanied by MAMs dysfunction. That factor is quite efficient in terms of insulin inhibition of Ca^{2+} signaling during the postprandial state, likely leading to hepatocytes insulin resistance.

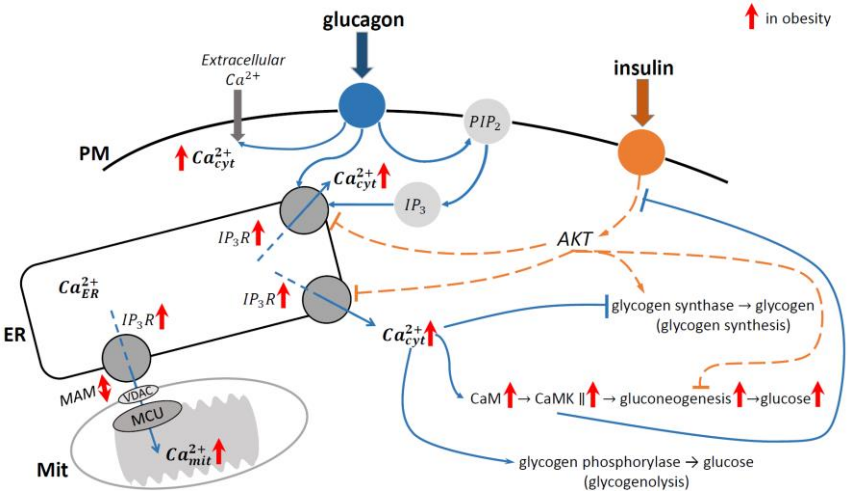

Fig.1. Model scheme.

Thus, the model allows us not only to reproduce available experimental data but also to analyze the role of various factors in the development of hepatocyte insulin resistance, suggesting the hypothesis about the dominant role of the modulation of IP_3-receptors. The modeling results suggest that both the MAMs dysfunction and IP_3-receptors dysregulation combined can lead to improper insulin signaling and together could cause hepatocyte insulin resistance.

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INVESTIGATION OF THE CONCENTRATION DEPENDENCE OF MICELLES OF NEOGLYCOLIPIDE A (TYPE 2) SP-AD-DE BY THE SMALL ANGLE X-RAYS SCATTERING METHOD

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One of the most actual tasks in the section of biocompatible structures is to obtain a micellar structure with a low critical micelle concentration that stably retains its shape and size. In this regard, the neoglycolipid A(Type2)-sp-Ad-DE, which is a synthetic analogue of natural glycolipids, was considered. Structural studies were carried out by small-angle X-ray scattering method.

In this work, a sample A(Type2)-sp-Ad-DE was measured at varying concentrations ranging from 0.6 to 3.35 mg / ml. The study of the biocompatible structure was aimed at determining the ability of this structure to maintain a stable shape and size with decreasing concentration. The functional part of the molecule (A Type2) is a "lipoid antigen" containing complex carbohydrates that carry certain blood groups A or B, which cannot be extracted by water directly from the tissue, in contrast to antigens associated with mucins. The Type 2 chain in erythrocytes is often present as a polymeric form of N-acetyllactosamine bound to a membrane protein. Blood group A antigens are most widely expressed in endoderm epithelial cells, where most human cancers arise. Therefore, changes in these blood groups or related antigens constitute the main tumor-associated changes in glycosylation, and many of these lead to the formation of tumor-associated carbohydrate antigens. Knowing that blood group antigens are localized in erythrocyte membranes, the study of the properties and behavior of A(type2)-sp-Ad-DE in isotonic

solutions (analogs of human blood) becomes an actual task for determining the size and shape of micelles with a change in concentration.

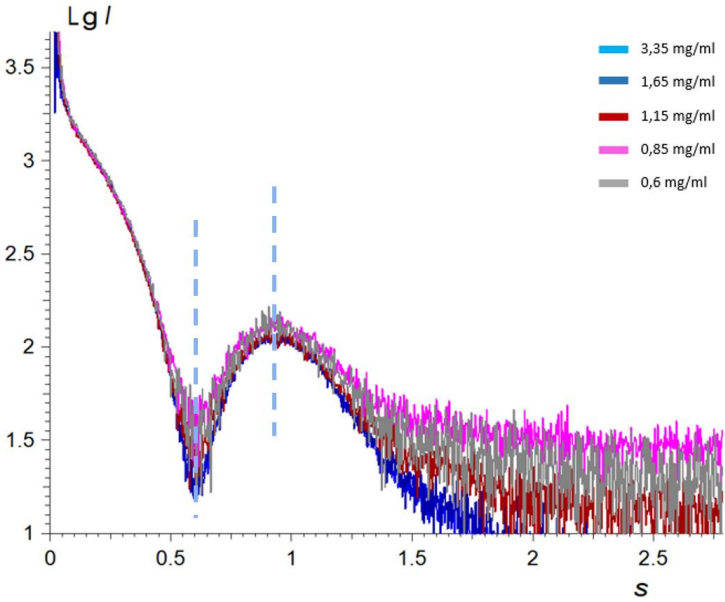

Fig 1. The intensity curves of A (Type 2) sp-Ad DE in different concentrations.

Analysis of intensity curves (Fig.1), distance distribution functions and 3D-models of the sample obtained on their basis showed that the resulting micelles do not change their shape and size with varying concentration, which makes them successful candidates in the field of targeted drug delivery, including anticancer antibiotics.

EVALUATION OF THE CYTOTOXICITY OF RESVERATROL OF THE CYTOTOXICITY OF RESVERATROL ANALOG PREPARATIONS BY THE MTT TEST

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Resveratrol is a naturally occurring polyphenol capable of causing the death of various types of tumor cells. Its use in clinical practice is limited by its low bioavailability and rapid metabolism [1]. In a number of studies, the antitumor effect of resveratrol derivatives has already been established, which served as a stimulus for research [2].

The aim of the study was to study the cytotoxicity of some resveratrol analogs.

We used the HEK-293 cell culture, a human embryonic kidney cell line, and the MCF-7 cell line, an epithelial line of human breast duct tumor cells.

To conduct a study on the cytotoxicity of anticancer drugs were used:

1. Resveratrol as a control.
2. An analogue of resveratrol with code number 2
3 . An analogue of resveratrol with code number 3
4. An analogue of resveratrol under the code number 4
5. . An analogue of resveratrol with code number 2

The study showed that the effect of the drug-analogue №. 2 in all studied concentrations, characterizing the cytotoxic effect of the drug, is significantly higher compared to resveratrol. This indicates that this drug has no destructive effect on tumor cells. The optical density (OD) values of cells under the influence of analogs № 3 and № 4 do not significantly differ from each other, but significantly differ from the values of the cell OD after the action of resveratrol, while the cytotoxic effect

of these drugs is lower than that of resveratrol. In addition, it can be seen that the drugs have the greatest toxic effect at concentrations of 3.12; 6.25 and 800 mg / ml. The most effective concentration is 6.25 mg / ml.The effect of the drug-analogue № 5 is twofold. At low concentrations, the OD values are higher than the OD values of the samples in the presence of resveratrol exposure. In the concentration range from 100 to 400 μM, the OD values of analog No. 5 dropped below the OD values of resveratrol. Effective concentrations are 100-400 μM.. On average, resveratrol has a pronounced cytotoxic effect in all concentrations in comparison with analogues. At the same time, analogs under codes 2 and 3 differ insignificantly from each other, and in most cases have OD similar to resveratrol. The study showed that, against the background of exposure to analogue 4 at each concentration, the OD value significantly increased compared to resveratrol. Apparently analogue № 4 is the least toxic for this type of cells. The OD of analogue № 5 compared to resveratrol was significantly higher at low concentrations, but decreased with increasing concentration. It can be assumed that analogue № 5 in low concentrations does not have a cytotoxic effect, and in the concentration range of 50-800 μM it reduces metabolic activity, like the natural prototype.

It was revealed that the greatest toxic effect on tumor cells of analogue preparations № 3 and № 4 was observed at concentrations of 3.12; 6.25 and 800 mg/ml. The most effective concentration is 6.25 mg/ml.

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INVESTIGATION OF SELF-ORGANIZING SUPROMERS BASED ON AMPHIPHILIC MOLECULES WITH A CYCLODEXTRIN GROUP BY ATOMIC FORCE MICROSCOPY METHOD

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Neoglycolipids are synthetic analogues of glycolipids, which are molecules that include polar "heads" consisting of carbohydrates and non-polar "tails", which are fatty acid residues. The presence of hydrophobic and hydrophilic parts in neoglycolipids allows them to self-organize into micelles, which makes them attractive for biotechnological purposes, such as changing the properties of cell membranes and development of target drug delivery systems based on self-assembly of amphiphilic molecules. Cyclodextrins (CDs), which are the polar part of the investigated supromers, helps to improve the solubility and stability of drugs in water, help to increase their bioavailability and reduce toxicity [1].

Micelles formed by α-CD-Ad-DOPE in an aqueous buffer were deposited on mica substrates as a test sample. In this work to study the the structural properties of these micelles, which include shape and size, the method of semicontact atomic force microscopy was chosen. Samples were prepared at the atomically smooth mica at different concentrations. In the course of varying the concentrations from 0.1 μM to 50 μM, the optimal value of 50 μM was revealed. At such concentration separately located micelles were obtained on the mica surface.

Obtained data led to the conclusion that such constructs in water solution form ellipsoidal micelles ranging in size from 10 to 12 nm

(Fig.1), which allows them to be used as containers for target drug delivery.

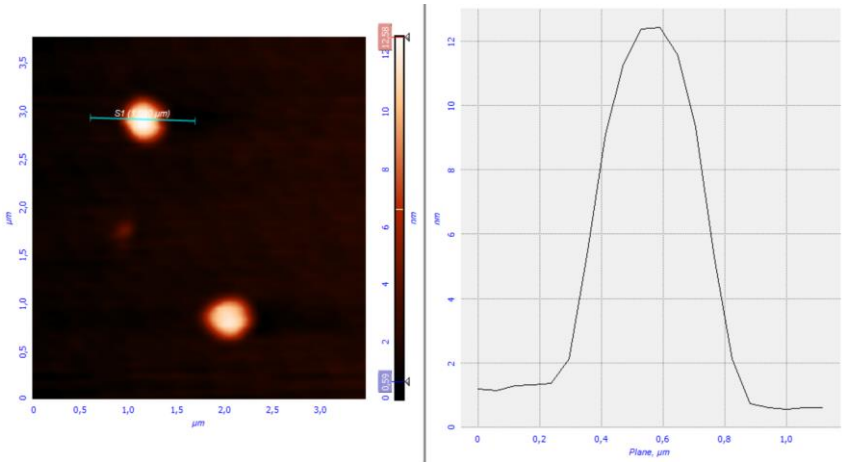

Figure 1. Image of individual α-CD-AD-DOPE micelles and the cross-section along the lined one.

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3D IMAGE PROCESSING: AUTOMATIC SELECTION OF THE LEFT ATRIAL FRAGMENT FROM RCT HUMAN RIB CAGE

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Key words: Automation, Three-dimensional image processing, Atrial fibrillation treatment, RCT, Hounsfield Density.

Description of the research: The main idea of the project is isolation of the left atrium from the results taken on a computed tomography with the injection of contrast medium. During the research, the results of groups of patients were analyzed, statistical results were obtained, programs for working with histograms and their approximation were written, programs for detecting concentration contrast regions in different places of rib cage were written to obtain clear 3D model of the left atrium, programs implemented in medical institutions and approved by cardiac surgeons

Relevance: Atrial Fibrillation becomes a dangerous pathology if not detected and eliminated the sources of origin in time. It can lead to heart attack and stroke in case of untimely treatment. The surgeon treats a heart by catheter ablation to prevent these serious pathologies.

The problem often occurs during surgery. Surgeons need to quickly and accurately obtain a true left atrial model with CT for favorable cardiac surgery. Previously, this was done manually and took tens of minutes. With the help of the developed program, this time will be reduced to seconds.

Research methodology: Based on CT scan results of tens of patients, a statistical range of contrast media densities was found on the Hounsfield scale. An approximation by cubic splines was performed on this range. After examining the function, the program automatically selects the contrast medium range and displays the resulting 3D model. It then uses an algorithm to explore areas with zero contrast and obtain a

contrast mask. Such a contrast distribution of non-zero voxels makes it possible to automatically cut off previously adjacent areas of the atrium and obtain a clean left atrium.

The results: The result of the work is a set of algorithms:

- For processing the obtained histograms
- For image processing in order to isolate the left atrium from them.

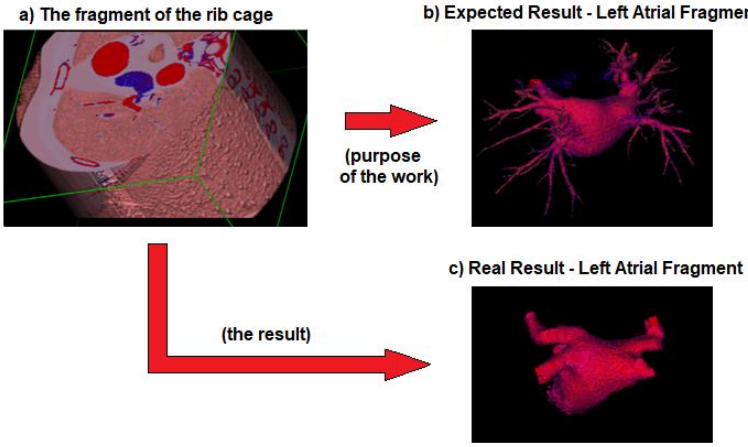

Fig.1. The purpose and the result of the research.

Practical application of research results: The developed programs and algorithms are used in the software of equipment intended for the treatment of atrial fibrillation in A.V. Vishnevsky Institute of Surgery and National Research Centre for Therapy and Preventive Medicine.

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INVESTIGATION OF 2-ETHYL-6-METHYL-3-HYDROXYPYRIDINE NICOTINATE EFFECT ON CLOT FORMATION TIME IN VITRO AND BLEEDING TIME IN VIVO

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Recent studies have shown that the key role for the many side effects of chemotherapeutics and X-ray therapy plays the hyperproduction of reactive oxygen species. The benefits of supportive antioxidant therapy of cancer have been shown in several studies [1]. In this regard, it is of interest to study 3-hydroxypyridine derivatives, which demonstrated hepatoprotective and cardioprotective effects, including protective effects against toxic damage caused by cytostatic drugs [2, 3, 4]. Because of the increased risk of thrombosis in the presence of malignant neoplasms [5], it is important to study the potential effect of new candidates for supportive antioxidant therapy on coagulation and bleeding time.

The purpose of the study was to investigate of the effect 2-ethyl-6-methyl-3-hydroxypyridine nicotinate (EMHN) on the clot formation time in vitro and capillary bleeding time in vivo.

Materials and methods. For all experiments, we used healthy Chinchilla rabbits of both sexes, weighing 4.5-5 kg, reached maturity, kept in a vivarium on a standard diet. Experiment 1 was carried out in vitro using blood taken from 5 animals. Two series of investigations were carried out: a control series (with the adding of 5 μL of 0,9% NaCl) and an intervention series (5 μL of 0,9% NaCl containing EMHN at various concentrations 5 μg/ml, 10 μg/ml, 50 μg/ml or 200 μg/ml). A modified method for examination of clot formation time according to Lee White was used. Experiment 2 was carried out on 5 rabbits. A liposomal form of EMHN was applied for 2 h onto the prepared area of the skin of the right ear of to the skin surface. The left ears of the same animals was

used as control. Than the standard test on capillary bleeding time was carried out. Experiments were carried out in compliance with the relevant laws and institution guidelines. Statistical processing of the obtained results was carried out using the Excel software package with the determination of the Student's t-test, the differences were considered significant at $p < 0.05$.

Results and conclusions. The average control clot formation time was 356 ± 20 s versus those with addition of EMHN at a concentration of 5 μg/ml - 331 ± 21 s ($p > 0.05$), 10 μg/ml - 345 ± 18 s ($p > 0.05$), 50 μg/ml - 331 ± 16 s ($p > 0.05$), 200 μg/ml - 315 ± 16 s ($p < 0.05$). The average time of capillary bleeding in the control group was 157 ± 12 s, in the intervention group - 152 ± 12 s ($p > 0.05$). Thus, a shortening of the clotting time of rabbit venous blood in vitro was established only for the highest concentration of EMHN - 200 μg/ml (by 11% vs control values), without any effect in lower concentrations. The results of the experiment 2 provide the view that liposomal form of EMHN do not affect the capillary bleeding time when applied topically on to the skin.

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