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NATIONAL RESEARCH NUCLEAR UNIVERSITY MEPHI
(MOSCOW ENGINEERING PHYSICS INSTITUTE)

# The 7-th International Symposium and School for Young Scientists on Physics, Engineering and Technologies for Biomedicine

November 19-24, 2022

PROGRAMME
BOOK OF ABSTRACTS

MOSCOW

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**Physics, Engineering and Technologies for Biomedicine.** The 7-th International Symposium and School for Young Scientists November 19-24, 2022: Programme. Book of Abstracts. Moscow MEPhI, 2022.– 216 p.

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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**The 7-th International Symposium and School for Young Scientists on Physics, Engineering and Technologies for Biomedicine**

The Institute of Engineering Physics for Biomedicine of the National Research Nuclear University (PhysBio MEPhI) announces the International Symposium and School for young scientists and students organized in collaboration with the research centers of the Russian Academy of Sciences, of the Russian Ministry of Health, the State Atomic Energy Corporation and 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 for young scientists, scheduled within the Symposium, is addressed to students, young scientists and specialists whose activities are related to the life sciences and medicine.

The Symposium and School provide an opportunity to obtain knowledge in the latest advances in biomedicine, to exchange opinions and establish professional contacts all over the world. Invited, Oral and Poster presentation are planned within the event.

**The presentations and lectures embrace the following topics:**

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

**Important information**

- The Symposium and School are held in-person (with the option of remote connection)
- The official language is English
- Registration is free of charge

- Zoom connection will be provided to the registered participants
- Registration and abstract deadline is November 14, 2022
- Detailed information is available on https://physbio-conf.mephi.ru/symp22/
- Questions can be addressed to Organizers by physbiosymp@mephi.ru

**Key Speakers (Tentative)**

***Valery Tuchin***
Saratov State University, Saratov, Russia

***Paras N. Prasad***
University of Buffalo, New York, USA

***Anton Fojtik***
Czech Technical University in Prague, MEPhI, Moscow, Russia

***Irina N. Zavestovskaya***
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The Symposium webpage: https://physbio-conf.mephi.ru/symp22/
The Symposium e-mail: PhysBioSymp@mephi.ru

# PROGRAMME
# The 7th International Symposium and School for Young Scientists on Physics, Engineering and Technologies for Biomedicine

## *School*
## *"Physics Engineering and Technologies for Biomedicine"*

### *November 19, Saturday*

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|---|---|
| ***09.30*** | ***Opening of the School*** |
| ***10.00*** | *Anton Fojtik*<br>*Czech Technical University in Prague (Czech Republic),*<br>*MEPhI (Russia)*<br>***Embryonic and prenatal stage of nanostructures*** |
| ***10.30*** | *Victor Timoshenko*<br>*MSU (Russia), MEPhI (Russia)*<br>***Nanocontainers for drug delivery*** |
| ***11.00*** | *Ekaterina Blinova*<br>*Sechenov University (Russia), MEPhI (Russia)*<br>***Biophotonics in surgery: advances and prospects*** |
| ***11.30*** | *Vladimir Oleinikov*<br>*Institute of Bioorganic Chemistry of RAS (Russia), MEPhI (Russia)*<br>***Modern trends in correlation microscopy*** |
| ***12.00*** | *Elizaveta Kudan*<br>*NUST MISIS (Russia), MEPhI (Russia)*<br>***Tissue spheroids: fabrication, characterization and applications*** |
| ***12.30*** | *Anton Popov*<br>*MEPhI (Russia)*<br>***Clean colloids for biomedicine by laser ablation*** |
| ***13.00-14.00*** | **Lunch** |

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|---|---|
| ***14.00*** | *Maria Kolyvanova*<br>*FMBC FMBA (Russia)*<br>***Machine learning for reconstruction of the spectrum of a medical photon source from dose distributions*** |
| ***14.30*** | *Nikita Lavrukhin, Alla Savchenko*<br>*Lupin Limited LLC (India), MEPhI (Russia), Kaluga Pharmaceutical Cluster (Russia)*<br>***Clue steps to registration of medical products*** |
| ***15.00*** | *Tatiana Savelieva*<br>*Prokhorov General Physics Institute (Russia), MEPhI (Russia)*<br>***Methods for determining the optical properties of biological tissues by means of optical spectroscopy*** |
| ***15.30*** | *Julia Finogenova, Alexey Lipengolz*<br>*National Medical Research Center of Oncology N.N. Blokhin (Russia), MEPhI (Russia)*<br>***Effect of size and coating on biodistribution of gold nanoparticles*** |
| ***16.00*** | *Victoria Shipunova*<br>*Moscow Institute of Physics and Technology (Russia)*<br>***Flow cytometry: basics and applications*** |
| ***16.30*** | *Alexey Kopylov*<br>*MEPhI (Russia), Moscow Institute of Physics and Technology (Russia)*<br>***Cartilage tissue engineering*** |
| ***17.00*** | ***Debriefing, discussions, closing of the School*** |

## *Symposium*
## *"Physics Engineering and Technologies for Biomedicine"*

### *November 21, Monday*

***10.00*** *Sergey Klimentov, Alexander Garmash*
*MEPhI (Russia)*
***Greetings from organizers***
***Research Agenda in PhysBio MEPhI***

***10.20*** ***PLENARY LECTURER***
*Valery Tuchin*
*Saratov State University (Russia)*
***Tissue photonics: towards multimodal tissue imaging and therapy through optical clearing***

***11.05*** ***KEYNOTE SPEAKER***
*Anton Fojtik*
*Czech Technical University in Prague (Czech Republic), MEPhI (Russia)*
***Nanotechnologies against viruses***

***11.45*** ***KEYNOTE SPEAKER***
*Irina Zavestovskaya*
*Lebedev Physics Inst. of RAS (Russia), MEPhI (Russia)*
***Advanced nuclear-physics and nano-technologies for radiation theranostics***

***12.25*** *Irina Selezneva*
*Institute of Theoretical and Experimental Biophysics of RAS (Russia)*
***Research Agenda of the Institute of Theoretical and Experimental Biophysics of RAS***

***13.00-14.00*** ***Lunch***

***14.00*** *Ekaterina Blinova*
*Sechenov University (Russia), MEPhI (Russia)*
***Novel approaches to innovative drug development***

***14.30***

*Alexander Shemyakov*
*Lebedev Physics Inst. of RAS (Russia), Protom Ltd. (Russia)*
***Status of radiobiological research at proton therapy facility "Prometheus"***

***15.00***

*Alexander Pryanichnikov*
*Lebedev Phycs Inst. of RAS (Russia), P-Cure Ltd. (Israel)*
***Development of proton imaging at synchrotron based facilities***

***15.30***

***Coffee break***

***16.00***

*Indrajit Roy*
*University of Delhi (India)*
***Engineered nanoscale photonics for enhanced bacterial sterilization and infectious wound healing***

***16.30***

*Victoriya Tishchenko*
*A.Tsyb Medical Radiological Research Centre (Russia)*
***Preclinical investigations of 99mTs-PSMA – a new radiopharmaceutical for spect imaging of prostate cancer***

***17.00***

***HONORARY KEYNOTE SPEAKER***
*Paras Prasad*
*University at Buffalo (USA), MEPhI (Russia)*
***Biophotonics and Nanomedicine to meet current challenges in Healthcare***

***17.45***

*Maria Kolyvanova*
*FMBC FMBA (Russia)*
***Possible applications of artificial intelligence in nuclear medicine and radiotherapy***

## *November 22, Tuesday*

***10.00*** *Victor Timoshenko*
*MSU (Russia), MEPhI (Russia)*
***Pure and composite nanoparticles for photo-hyperthermia applications***

***10.30*** *Anton Popov*
*Institute of Theoretical and Experimental Biophysics of RAS (Russia)*
***Gadolinium-based nanotheranostics for radiotherapy and cell tracking***

***11.00*** *Ivan Zelepukin*
*Inst. of Bioorganic Chemistry of RAS (Russia)*
***Disassembling metal-organic frameworks for drug delivery***

***11.30*** *Gleb Tselikov*
*Center for Photonics and 2D Materials, Moscow Inst. of Physics and Technology (Russia)*
***Laser-fabricated $MoS_2$ nanoparticles with tunable optical properties for biomedical theranostics applications***

***12.00*** *Olga Gryaznova*
*Institute of Bioorganic Chemistry RAS, Skoltech, NRNU MEPhI (Russia)*
***Hybrid Fe-Au nanoparticles as sensitizers for photothermal therapy and MRI/CT visualization***

***12.20*** *Gleb Tikhonowski*
*MEPhI (Russia)*
***Laser synthesis of hybrid nanomaterials for biomedical applications***

***12.40*** *Mikhail Konoplyannikov*
*Federal Research Clinical Center, FMBA (Russia)*
***Salinomycin-loaded mesoporous silicon nanoparticles for cancer therapy***

***13.00-14.00*** ***Lunch***

***14.00*** *Pavel Samokhvalov, Alyona Sukhanova, Igor Nabiev*
*MEPhI (Russia),Université de Reims Champagne-Ardenne (France)*
***Diagnostic nanomaterials: from chemical engineering to nanomedicine***

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|---|---|
| ***14.30*** | *Vsevolod Skribitsky*<br>*MEPhI (Russia), National Medical Research Center of Oncology (Russia)*<br>***Distribution and retention patterns of gold nanoparticles in animal tumor models*** |
| ***14.50*** | *Pavel Subochev*<br>*Institute of Applied Physics of the RAS (Russia)*<br>***Optical-acoustic angiography using ultra-wideband ultrasonic antennas*** |
| ***15.10*** | *Danil Zarezin*<br>*MEPhI (Russia)*<br>***Optimization of the InP nanocrystals synthesis using tris-aminophosphines as a phosphorus precursor*** |
| ***15.30*** | ***Coffee break*** |
| ***16.00*** | *Dayana Gulevich*<br>*MEPhI (Russia)*<br>***Artificial intelligence guided synthesis of colloidal nanomaterials*** |
| ***16.20*** | *Irina Kriukova*<br>*MEPhI (Russia), Université de Reims Champagne-Ardenne (France)*<br>***Hybrid systems based on porous silicon photonic crystals, liquid crystals and quantum dots*** |
| ***16.40*** | *Daria Kalenichenko*<br>*MEPhI (Russia), Université de Reims Champagne-Ardenne (France)*<br>***Multilayered polymer capsules for targeted delivery of antitumor compounds*** |
| ***17.00*** | *Evgenia Gerasimovich*<br>*MEPhI (Russia)*<br>***Interaction of human serum and plasma proteins with polyelectrolyte microcapsules of different structures*** |
| ***17.20*** | *Anatoly Grigoriev*<br>*Financial university under the government of the Russian Federation (Russia)*<br>***Prospects for the use of quantum dots and quantum sensors in the therapy and treatment of COVID-19*** |

## *November 24, Thursday*

***10.00*** *Victor Loschenov*
*Prokhorov General Physics Institute of the RAS (Russia), MEPhI (Russia)*
***New technologies in fluorescent diagnostics and photodynamic therapy***

***10.30*** *Polina Kotelnikova, Sergey Deev*
*Inst. of Bioorganic Chemistry of RAS (Russia)*
***Multifunctional nanoagents for targeted therapy and imaging***

***11.00*** *Tatiana Savelieva*
*Prokhorov General Physics Institute of the RAS (Russia), MEPhI (Russia)*
***Different approaches to analysis of optical spectral data in neurooncology for perioperative decision support***

***11.30*** *Dmitry Ivanov*
*University of Kassel (Germany), MEPhI (Russia)*
***Modeling of Laser-Induced Surface Structures Generation due to Surface Plasmon-Polariton Excitation***

***12.00*** *Georgy Ermolaev*
*Moscow Institute of Physics and Technology (Russia)*
***Topological darkness in atomically thin materials for biosensing***

***12.20*** *Artem Iliasov*
*MEPhI (Russia), NUST MISIS (Russia)*
***Si-particles with the thermopolymer shell for controlled drug release***

***12.40*** *Anna Krivetskaya*
*Prokhorov General Physics Institute of the RAS (Russia), MEPhI (Russia)*
***Investigation of the algorithms for assessing the degree of tissue saturation of mammary gland***

***13.00-14.00*** ***Lunch***

***14.00*** *Alexander Dymnikov*
*RUDN University (Russia)*
***Engineering of surface morphology of dental implants: modern trends and commercial products***

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|---|---|
| ***14.20*** | *Kristina Shpakova*<br>*N.N.Blokhin National Medical Research Center of Oncology (Russia), MEPhI (Russia)*<br>***Preclinical PET/SPECT/CT in Biomedical Research*** |
| ***14.40*** | *Ruslan Rytov*<br>*IZMIRAN (Russia), NUST MISiS (Russia)*<br>***Specific absorption rate of randomly oriented magnetic nanoparticles in a static magnetic field*** |
| ***15.00*** | *Almaz Manaev*<br>*MEPhI (Russia)*<br>***Signs of thyroid nodules malignancy on ultrasound images*** |
| ***15.20-16.00*** | ***Coffee break*** |
| ***16.00*** | ***Poster session*** |
| ***18.00*** | ***Discussions and Closing ceremony*** |

## Abstracts contents

***The 7th International Symposium and School for Young Scientists on Physics, Engineering and Technologies for Biomedicine***

### *INVITED LECTURES*

Book's contents

Book's contents

Book's contents

***POSTER REPORTS***

Book's contents

Book's contents

Book's contents

Book's contents

# *The 7th International Symposium and School for Young Scientists on Physics, Engineering and Technologies for Biomedicine*

## *INVITED LECTURES*

# BIOPHOTONICS AND NANOMEDICINE TO MEET CURRENT CHALLENGES IN HEALTHCARE

**Paras N. Prasad**
*Institute for Lasers, Photonics and Biophotonics*
*Department of Chemistry, Physics, Electrical Engineering and Medicine*
*State University of New York at Buffalo, Buffalo, New York 14260, USA*
*Presenting author e-mail address: pnprasad@buffalo.edu*

Major breakthroughs needed to meet 21st Century technical challenges across areas of top global priority, including alternative energy, healthcare, environmental monitoring, information technology, and world security, will be achieved through convergence of science. This talk will provide examples of how our institute is conducting multidisciplinary convergent research linking light-based photonics technology with biomedical science, materials science with nanotechnology to create multiscale modeling guided new generation multifunctional hybrid materials for applications to health care.

Biophotonics is a multidisciplinary field that utilizes various light activated physical and chemical processes for biomedical imaging and sensing as well as for light initiated therapies, enabling image guided therapies for Theranostics (combined therapy and diagnostic). We have a global vision to produce breakthrough approaches for meeting healthcare challenges in areas such as cancer, neurological disorders, infectious diseases, age-related diseases such as Alzheimer's, drug addiction, chronic pain and depression.1-3We have developed an integrated Biophotonics Platform that combines optical imaging modalities with quantitative Raman spectrometry for real-time bimolecular cell diagnostics. Our approach of Ramanomics using biomolecular analysis coupled with localized, confocal quantitative Raman microspectrometry provides cellular site-specific molecular concentrations and their changes as a function of cellular processes or drug-cell interactions. This talk will give new directions of bioimaging such as 3-D IR optical imaging of deep tissues using photon-converting nanomaterials. Example of light initiated therapies smart photodynamic therapy (PDT) using our photo-

sensitizer, which generates toxic reactive oxygen species upon light absorption only at tumor site to destroy tumor.

For nanomedicine, our program is developing multiscale modeling guided nanostructures for functioning as nanoemitters for optical imaging, nanoheaters for PTT and photoacoustic imaging, and Nanotheranostic agents for image guided therapy. Examples of nanoemitters are rare-earth ion doped upconversion nanoparticles (optical nanotransformers) which transform a Near IR (NIR) light from an external source by sequential single photon absorption, in situ and on demand, to a needed wavelength. An exciting direction is the use of femtosecond ablation to produce nanoparticles of multiple drugs for combination therapy, an example being for Covide-19 and influenza. A major direction in brain research, pursued in our lab, is neurophotonics, where we apply photoresponsive materials for functional mapping of the brain using optical and photoacoustic imaging. We also use nanoformulations of natural drugs such as ginseng and curcumin to treat Alzheimer, traumatic brain injury and brain cancer as well as optogenetic stimulation and microglia activation to enhance brain function.

This talk will end by presenting multidisciplinary opportunities.

[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).

# MACHINE LEARNING FOR RECONSTRUCTION OF THE SPECTRUM OF A MEDICAL PHOTON SOURCE FROM DOSE DISTRIBUTIONS

**A.V. Belousov[1], A.Yu. Kharin[2], G.A. Krusanov[1], M.A. Kolyvanova[1,3]**
*[1] Burnazyan Federal Medical Biophysical Center, Federal Medical Biological Agency of the Russian Federation, Moscow, Russia*
*[2] National Research Nuclear University MEPhI, Moscow, Russia*
*[3] Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, Moscow, Russia*
*Presenting author e-mail address: kolyvanova@physics.msu.ru*

Nuclear medicine and radiation therapy are one of the classic methods for diagnosis and treatment of oncological diseases. Radiation medicine uses in its arsenal high-tech equipment associated with the use of ionizing radiation sources. For this reason, digital platforms are most actively used in radiation medicine to help carry out image reconstruction, calculation and analysis of dose distributions in the patient's body. Every year there are programs using artificial intelligence technology that optimize the radiologists work, helping in the organs contouring and their characterization; assessment of the treatment plan and the consequences of post-radiation complications, etc. Another promising direction for radiotherapy in the field of modeling the interaction of ionization radiation with matter is the use of neural networks and machine learning techniques to speed up the calculations of the absorbed dose performed by the Monte Carlo method, which will subsequently speed up transition to a new technique of online adaptive treatment of patients [1].

In the present work, a study has begun on the possibilities of using artificial intelligence to improve computer simulation by the Monte Carlo method using medical sources of ionizing radiation. At the first stage, a study was made of the possibilities for reconstraction the spectral composition of X-ray radiation from a known dose distribution in the medium using a neural network approach. To solve this problem, an adaptive gradient algorithm [2] and a cascade of convolutional neural

networks were used to reconstruct the spectrum of the X-ray source. This approach showed high efficiency and calculation speed.

*Funding:* The study was carried out as part of the scientific program of the National Center for Physics and Mathematics (direction "Artificial Intelligence and Big Data in Technical, Industrial, Natural and Social Systems").

[1] V.T. Taasti, P. Klages, K. Parodi, L.P. Muren. Developments in Deep Learning Based Corrections of Cone Beam Computed Tomography to Enable Dose Calculations for Adaptive Radiotherapy, Phys Imaging Radiat Oncol, vol. 15, pp. 77–9, (2020).

[2] J. Duchi, Hazan, Y. Singer, Adaptive subgradient methods for online learning and stochastic optimization, Journal of machine learning research, vol. 12, pp. 7, (2011).

# INTERACTION OF HUMAN SERUM AND PLASMA PROTEINS WITH POLYELECTROLYTE MICROCAPSULES OF DIFFERENT STRUCTURES

**E. Gerasimovich[1], G. Nifontova[2], I. Nabiev[1, 2], A. Sukhanova[2]**
*[1] Laboratory of Nano-Bioengineering, National Research Nuclear University MEPhI, 115409 Moscow, Russia*
*[2] Laboratoire de Recherche en Nanosciences, LRN-EA4682, Université de Reims Champagne-Ardenne, 51100 Reims, France*
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Polyelectrolyte microcapsules obtained by the layer-by-layer technique with the use of calcium carbonate templates are useful for many applications in biomedicine [1]. However, interaction of biomolecules with the surface of microcapsules occurring in biological media leads to the formation of an additional layer on their surface and changes their properties [2]. This study was aimed at analyzing the interplay between serum or plasma proteins and core/shell microparticles and hollow polyelectrolyte microcapsules.

To obtain small calcium carbonate cores, we used a polyvinyl alcohol/methylcellulose solution in ultrapure water as a thickening agent. The resulting microparticles had a spherical shape and an average size of 1.6 μm, as estimated by dynamic light scattering. Using calcium carbonate templates, we applied oppositely charged polyelectrolytes as described earlier [3] to obtain a polyelectrolyte shell of the following structure: $(PAH/PSS)_4/PAH/PAA$. The resulting microparticles had a strong negative surface charge, as determined by Doppler microelectrophoresis. For dissolving the cores, the obtained microparticles were incubated in excess of EDTA. Then, the core/shell microparticles and hollow polyelectrolyte microcapsules were incubated with human serum or plasma for 24 h at 37°C. Proteins adsorbed on the surface of the microparticles and microcapsules were eluted using Laemmli sample buffer and separated by SDS-PAGE. In addition, proteins were identified in the bands cut out from gels using MALDI-TOF mass spectrometry.

Mass spectrometry analysis demonstrated clear differences in the composition of the protein layer formed on the surface of the core/shell microparticles and hollow polyelectrolyte microcapsules during incubation in serum or plasma of healthy donors. In addition, it was shown that the relative amounts of some proteins adsorbed on the surface of microstructures depended on the type of blood derivatives used for incubation. We suppose that the results of our study can be used for improving the design of drug delivery systems based on polyelectrolyte microcapsules.

This study was supported by the Russian Science Foundation (grant no. 22-75-10103).

[1] A. S. Vikulina, J. Campbell, Biopolymer-based multilayer capsules and beads made via templating: Advantages, hurdles and perspectives, Nanomaterials, 11(10), 2502, (2021).
[2] Q. Dai, Y. Yan, C.S. Ang, K. Kempe, M.M. Kamphuis, S.J. Dodds, F. Caruso, Monoclonal antibody-functionalized multilayered particles: Targeting cancer cells in the presence of protein coronas, ACS Nano, 9(3), 2876–2885, (2015).
[3] D. Kalenichenko, G. Nifontova, A. Karaulov, A. Sukhanova, I. Nabiev, Designing functionalized polyelectrolyte microcapsules for cancer treatment, Nanomaterials (Basel), 11(11), 3055, (2021).

# ENGINEERING OF SURFACE MORPHOLOGY OF DENTAL IMPLANTS: MODERN TRENDS AND COMMERCIAL PRODUCTS

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One of the most important characteristics for modern biomaterials used in dentistry, orthopedics and reconstructive surgery is the study of the formation of chemical bonds between the implant surface and bone tissue. The primary task of chemical materials science is to form the surfaces of dental implants, which are able to create the necessary conditions for contact osteogenesis - the formation and further development of bone tissues. This mechanism is considered the most optimal for the formation of organotypic bone substance on the surface of implants. According to studies [1-3], the main role in the formation of young bone cells - osteoblasts is played by the primary stability of the implant, which depends on the elemental composition and surface topography, which also affects the increase in their osteocompatibility.

Most dental implant companies develop products with unique competitive characteristics. At the same time, there are still no real standards for determining the surface quality and safety of commercial implants. In fact, there is not even a standard according to which the performance of dental implant surfaces should be evaluated. As a result, many companies use statements in the advertising campaign that do not correspond to reality, but attract the attention of buyers, such as nanomaterials, nanomodification, nanostructuring, although the products do not have these characteristics. At the same time, some products on the mar-

ket do not meet minimum sanitary standards and are potentially dangerous for patients to use. [4].

This work is devoted to the study and evaluation of the quality of 17 dental implant systems available on the Russian market. The control and study of the morphological features of dental implants was carried out using a scanning electron microscope (SEM). The seed was taken under a microscope. Jeol JSM-6458LW at an accelerating voltage of 30 kV and a working length of 17 mm in the secondary electron detection mode. The obtained information allows to prepare about the parameters of the surface layer, its homogeneity, structure and biocompatibility. Sample Study Results for an Implantable System XIVE is shown in Figure 1.

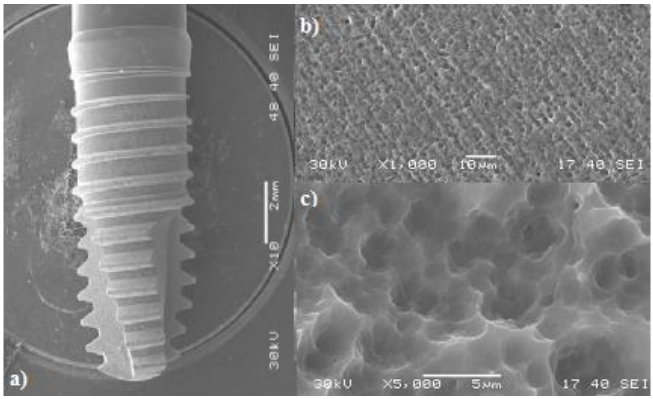


Fig.1. SEM image of XIVE dental implant, a) general view, b) surface at 1000x magnification, c) surface at 5000x magnification

The surface of the implant is homogeneous throughout the sample, has microroughness with locus sizes within 5 μm. The composition of the material from which the implant is made was studied using X-ray fluorescence analysis (XRF). The results are presented in Table 1. The analysis was performed on a Thermo scientific ARL perform'x spectrometer.

The implant is made of an alloy similar in composition to the VT6 alloy, Si, Fe, Na andmgmay be background for titanium production. The presence of Pt may be associated with the process of electrochemical

processing of the product to form a developed surface, in which these elements were used as the electrode material.

Table 1. XRF analysis of a dental implant XIVE

| element | wt% | Est. error |
|---|---|---|
| Ti | 92.17 | 0.14 |
| Al | 2.86 | 0.08 |
| V | 1.52 | 0.06 |
| Na | 1.25 | 0.10 |
| Fe | 0.334 | 0.032 |
| Pt | 0.330 | 0.045 |
| Si | 0.276 | 0.018 |
| Mg | 0.270 | 0.023 |

As a result of the study, many implant models revealed quite significant deviations associated with poor-quality washing and the presence of contaminants on the surface after the surface modification process. Characteristically, the presence of contamination does not depend on the method of obtaining the implant surface and its type. With regard to surface morphology, manufacturers do not have a unified approach and a preferred method for processing implants, however, most of the studied models have a micro-rough surface structure with high homogeneity.

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# HYBRID Fe-Au NANOPARTICLES AS SENSITIZERS FOR PHOTOTHERMAL THERAPY AND MRI/CT VISUALIZATION

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Laser synthesized nanoparticles possess chemically pure surface without any contamination. Thus, such nanoparticles are attractive for biomedical application, as potentially they will have lower toxicity comparing to conventional nanoparticles.

Hybrid multimodal nanoparticles, applicable to the simultaneous noninvasive imaging and treatment, are highly demanded for clinical use. We studied Fe-Au core-satellite nanoparticles prepared by the method of pulsed laser ablation in liquids as sensitizers for dual magnetic resonance imaging (MRI) and computed tomography (CT) and as sensitizers for laser-induced hyperthermia of cancer cells. [1] Surface coating of Fe-Au nanoparticles by polyacrylic acid provided excellent colloidal stability of nanoparticles with highly negative ζ-potential in water and retained hydrodynamic size in a physiological environment, thus greatly improving NPs' biocompatibility

The ferromagnetic iron cores offered contrast in MRI images with at 1 T, while Au satellites showed X-ray attenuation in CT. The intravenous injection of nanoparticles enabled clear tumor border visualization in mice. Plasmonic peak in the Fe-Au hybrids had a tail in the near-infrared region (NIR), allowing them to cause hyperthermia under 808 nm laser exposure. Under NIR irradiation Fe-Au particles provided significant heating and an $IC_{50}$ value below 35 μg/mL for three different cancer cell lines.

Taken together, these results show that laser synthesized Fe-Au core-satellite nanoparticles are excellent theranostic agents with multimodal imaging and photothermal capabilities.

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# ARTIFICIAL INTELLIGENCE GUIDED SYNTHESIS OF COLLOIDAL NANOMATERIALS

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The use of artificial intelligence, and in particular the machine learning methods, significantly increases the efficiency of industrial processes and scientific research, making the treatment of accumulated experimental data faster and easier, saving one of the most important resources – the time. In past decades the application of mathematical methods and algorithms in chemistry has considerably grown. The most widespread and active application of machine learning is observed in the areas of new materials and drug design, spectra prediction and analysis, and microscopy images recognition. However, a chemical reaction is a much more complex, multiparametric process. Colloidal, hydrothermal synthesis, chemical reduction, synthesis in flow are example of the most important methods for obtaining phase-, size- and morphology controlled colloid nanomaterials used in optoelectronics, catalysis, visualization and sensors applications. These parameters are influenced by many factors, such as the temperature and time of synthesis, the chemical nature and ratio of precursors and stabilizers. Thus, the determination of the key factors affecting the colloidal synthesis process and selection the optimal conditions for obtaining materials with specified physicochemical properties is the important task that can be solved by machine learning methods. The aim of this review is to analyze the current progress in this field.

The report will review a brief history of the development of machine learning methods and the stages of their integration into the research work of the chemical industry. The use of artificial intelligence to optimize the parameters of the synthesis of colloidal nanomaterials will be

considered using the example of obtaining perovskite nanocrystals and $A^{II}B^{VI}$ quantum dots by hot-injection method, hydro- and solvothermal synthesis of semiconductor metal oxides, and obtaining metal nanoparticles by chemical reduction. The examples of successful integration of AI in areas adjacent to the synthesis of colloidal nanomaterials, which intensificate the research and development at all stages of optoelectronic devices production will also be provided.

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# Si-PARTICLES WITH THERMOPOLYMER SHELL FOR CONTROLLED DRUG RELEASE

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Controlled drug release is a longtime dream of researchers.

In this work, we studied the possibility of releasing the drug Mitomycin C from porous silicon particles. They were coated with a thermosensitive polymer. The heating was carried out by laser radiation at a wavelength of 830 nm. Cytotoxicity was assessed on the device X in terms of A.

The size of particles obtained by electrochemical etching of silicon wafers with their further grinding to a microsize were assessed. The average particle size with the drug is up to 5 μm. Particles successfully were loaded with the drug, as evidenced by the small amount of Mitomycin C in the supernatant after centrifugation. Laser heating affects the structure of the polymer, facilitating the release of the drug. According to studies on the SKOV3 cell line, the cytotoxicity of the particles with the drug was revealed, comparable to the toxic effect of pure Mitomycin C not loaded into the particles. Silicon particles with a residual amount of the drug showed a weaker toxic effect on cells.

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# MODELING OF LASER-INDUCED SURFACE STRUCTURES GENERATION DUE TO SURFACE PLASMON-POLARITON EXCITATION

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Ultrashort laser pulses, focused on metal surfaces, can produce Laser-Induced Periodic Surface Structures (LIPSS), which have found a lot of applications in IT- and Bio- technologies. During the laser energy deposition Surface Plasmon Polaritons (SPP) [1] can be excited on a rough material surface. The interference of the plasmons wave and the incoming pulse leads to the redistribution of the laser intensity across the material's surface and the subsequent formation of LIPSS. In this work we propose a combined atomistic-continuum Molecular Dynamics based numerical approach for investigation of LIPSS formation mechanism on metals in super-large simulations [2]. We introduce the corresponding source term description due to SPP in the combined model [3]. The simulation results are directly compared with the experimental data, generated on the same temporal and spatial scales, and analyzed. This allowed to extract the main mechanisms of LIPSS formation. The performed research allows for a possibility for the structures generation with predesigned topological, morphological, and optical properties.

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# MULTILAYERED POLYMER CAPSULES FOR TARGETED DELIVERY OF ANTITUMOR COMPOUNDS

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Development of systems for cancer treatment and monitoring of the treatment efficacy is an important strategy in modern anticancer therapy. Multilayered polymer capsules (MPCs) have been shown to be promising microcarriers (MCs) that can be adapted for delivery of various agents to cancer cells [1]. The preparation of MPCs via layer-by-layer (LbL) adsorption of oppositely charged polyelectrolytes onto templates makes it possible to encapsulate various compounds, e.g., drugs, metal, or fluorescent semiconductor nanoparticles (quantum dots, QDs) [2]. Biofunctionalization of the MPC surface with biomolecules can enhance the selectivity of interaction with cancer cells to ensure their targeted delivery [1, 3, 4].

Here, we present the results of (1) engineering of MCs with different structures; (2) encapsulation of an anticancer agent (doxorubicin, DOX) and fluorescent nanoprobes (QDs) into the MCs; (3) efficient biofunctionalization of the MCs with antibodies via their oriented conjugation.

Initially, calcium carbonate cores were synthesized and characterized. MCs with the core/shell and shell structures were obtained by the LbL method using PAH/PSS polyelectrolytes deposited onto the calcium carbonate templates. The prepared MCs were characterized using light scattering analysis, scanning electron and fluorescence microscopies, and laser Doppler microelectrophoresis. DOX was encapsulated into the MCs by coprecipitation or spontaneous loading. Water-soluble QDs were incorporated into the polymer shell of the MCs during the assembly of the polyelectrolyte shell as described earlier [5]. To modify the surface of the MCs with capture molecules to ensure targeted inter-

action with cancer cells, the MC surface was activated using a heterobifunctional crosslinker and modified with specific antibodies.

The synthesized MCs with the core, core/shell, and shell structures had a narrow size distribution (2.5±0.7 μm) and a spherical shape. The DOX encapsulation efficiency per single MC was no less than 70%. The resulting MCs, optically encoded with QDs, were clearly identifiable by fluorescence detection methods. The optimal conditions for activating the surface of MPCs and its biofunctionalization were determined. The obtained results show that fluorescently encoded MCs containing anticancer drugs, particularly DOX, and conjugated to biomolecules for targeted delivery represent a promising platform for the development of theranostic agents for fluorescent tracking and targeted drug delivery to cancer cells.

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# SALINOMYCIN-LOADED MESOPOROUS SILICON NANOPARTICLES FOR CANCER THERAPY

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Mesoporous silicon nanoparticles loaded with salinomycin, a promising anticancer drug, were investigated as potential nanocontainers for cancer therapy. The drug loading and release were studied by means of the infrared spectroscopy, which revealed a gradual release of the drug with rate dependent on the mass ratio between the nanoparticles and salinomycin. In vitro studies revealed that the prepared nanoparticles loaded with salinomycin resulted in a notable cytotoxic effect on human glioblastoma cells, MCF-7 breast cancer cells and multidrug resistant MCF-7/MDR1 cells. In vivo experiments showed a strong suppression of the Lewis lung carcinoma tumor growth for 10–30 days after intraperitoneal administration of the nanocontainers. The obtained results indicate that salinomycin-loaded mesoporous silicon nanoparticles are prospective for mild chemotherapy of both primary cancer tumors and metastasis. The revealed efficiency against chemotherapy-resistant cancer stem cells and possibility of the intraperitoneal administration are very promising for further clinical applications of the prepared nanocontainers.

# MULTIFUNCTIONAL NANOAGENTS FOR TARGETED THERAPY AND IMAGING

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Cancer develops when cells start to divide and spread out of control. Some types of malignant cells tend to move to other parts of the body with the blood or lymph where they begin to grow, forming metastases. Surgery and radiation therapy cannot be used in the treatment of metastatic cancer. Chemotherapy drugs injected into the blood can overtake tumors in any part of the body, however, they inevitably affect healthy cells, especially rapidly dividing ones. Targeted medicine is based on the idea of recognizing the characteristic features of cancer cells and aims to specifically target only malignant cells and reduce harmful effects to healthy tissues.

Nanomedicine allows to combine targeting, therapeutic and imaging agents with the unique physical properties of nanoparticles (e.g. plasmonic or magnetic ones) providing a theranostic platform. This report focuses on the nanoagent developement usuing scaffold proteins such as DARPins and Affibodies [1]. Outstanding stability, time- and cost-efficient production and small size make them convenient biotechnological tools. Furthermore, scaffold proteins can surpass the binding affinity of antibodies and help avoid unwanted immunogenicity effects. The report includes examples of the successful use of such nanoagents *in vitro* and *in vivo* [2, 3].

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# HYBRID SYSTEMS BASED ON POROUS SILICON PHOTONIC CRYSTALS, LIQUID CRYSTALS AND QUANTUM DOTS

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Porous silicon (pSi) photonic crystals are of much interest for basic and applied research. Embedding of luminophores into these structures allows the control of their emissive properties, which is promising for the use in lasers and displays and for studies on light–matter interaction. At the same time, the development of photonic crystals in which the spectral position of the photonic band gap can be shifted by external stimuli offers prospects for the development of new photonic and optoelectronic materials. In particular, external light irradiation as a non-contact method for modification of physical and chemical properties of the hybrid systems is one of the most effective and promising approaches.

Here we propose a technology for the fabrication of hybrid systems based on CdSe/CdS/ZnS quantum dots (QDs) and a mixture of photochromic nematic liquid crystals containing an azobenzene-based dopant [1] embedded into pSi microcavities (MCs) obtained by electrochemical etching. The photoluminescence (PL) spectrum of QDs is narrowed upon their embedding into the MCs, which is due to the Purcell effect [2, 3]. This indicates the regime of weak coupling between exciton transitions in the QDs and the eigenmode of the MC. The mixture of nematic liquid crystals, also embedded into the pSi MCs, undergoes an isothermal transition to the isotropic phase under UV irradiation. This leads to a change in the effective refractive index of the hybrid system, to a long-wavelength shift of the photonic bandgap of the MC, and, consequently, to a shift of the emission spectrum of the hybrid system (Fig. 1). The transition back to the nematic phase occurs very slowly, with a charac-

teristic time of about 20 days [1]. At the same time, exposure to visible (blue) light leads to rapid recovery of the nematic phase and back shift. Thus, the demonstrated photo-optical response under visible and UV irradiations can be used to control the PL properties of the hybrid systems and to design, on their basis, new photonic, optoelectronic, and sensing devices.

This study was supported by the Russian Science Foundation, grant nos. 21-79-30048 (synthesis of nanomaterials) and 22-13-00055 (liquid crystals engineering).

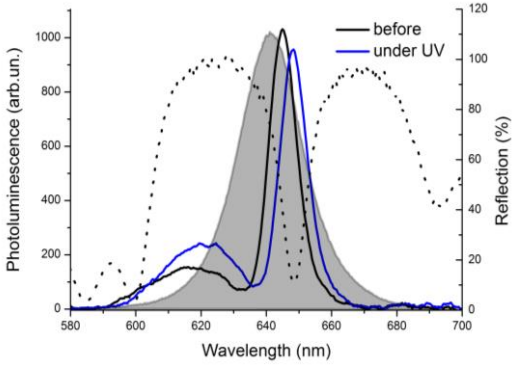


Fig.1. Shift of the emission spectrum of the hybrid system under UV irradiation. The photoluminescence spectrum of the solution of QDs is shown as a grey area; the reflection spectrum of the microcavity is shown as a dashed line.

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# INVESTIGATION OF THE ALGORITHMS FOR ASSESSING THE DEGREE OF TISSUE SATURATION OF MAMMARY GLAND

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Introduction: This study is conducted to determine the degree of tissue saturation of multilayer biological objects on breast tissues by methods of optical spectroscopy. The level of saturation can be a quantitative value of the state of the tissue. It can be used to select further actions in the treatment of the patient when stitching any biological structures together and be a control method in the postoperative period.

Goal: The purpose of the study is to select measurement parameters to determine saturation value of biological tissues and to assess the degree of tissue saturation of mammary glands in clinical conditions.

Materials and methods: To determine the sensitivity of the developed technique several experiments with optical phantoms simulating breast tissue were conducted with the use of spectrometric measuring equipment which includes light source, spectrometer, optical fibers and PC with a special program. The phantoms were made on the basis of hemoglobin, fat emulsion and pig skin. To achieve the saturation degree backscattering spectra were recorded and processed using the developed algorithm [1].

Results: During the experiments, the optimal parameters for the saturation assessment were determined. The characteristic depth of tissue

probing was also defined at the distance between the receiving and lighting fibers, which was determined to be optimal. Also, the investigated method of measuring tissue saturation was used in clinical measurements of mammary glands in patients with breast cancer, during which the applicability of this technique for practical clinical use was verified and confirmed. In addition, there has been conducted statistical analysis of data samples for each research day. The assessment of the degree of tissue saturation of mammary glands after surgery can be used to estimate the blood supply in the postoperative period and be a quantitative parameter to determine the state of the investigated tissue [2].

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# SIGNS OF THYROID NODULES MALIGNANCY ON ULTRASOUND IMAGES

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Thyroid nodules are common thyroid disease, prevalence is 19–68% with the use of high-resolution ultrasonography (US) [1]. Malignancy occurs in 7–15% of detected thyroid nodules - differentiating malignancy is an important clinical process, depending on various risk factors [2].

The interpretation of ultrasound images is often subject to significant interobserver variabilities, particularly for junior radiologists at nonacademic centres, with reported variability in sensitivity from 40.3% to 100% and in specificity from 50% to 100% radiologists [3].

Overall, assistance with decision support system might reduce the number of fine needle aspirations by 26.7% and the number of missed malignancies by 1.9% [4].

The study is conducted within the framework of the RSF grant № 221500135. All patients gave necessary informed consents.

**Objective**. The current study dedicated to investigations of different image signs either visible or invisible to the human eye that might be useful for detection of thyroid nodule malignancy.

**Materials and methods.** Study group included 135 cases of thyroid nodules, that was surgically removed. US European Thyroid Imaging Reporting and Data System (EU TI-RADS) was used to categories all cases: TR2 – 16 cases, TR3 – 41 cases, TR4 – 31 cases, TR5 – 47 cases. Pathomorphological analysis shows 0%, 22%, 45%, 87% malignant cases in TR2, TR3, TR4, and TR5 categories. Most common was papillary thyroid carcinoma 82.8% of all cases, then goes medullar thyroid carcinoma 7.8%, follicular thyroid carcinoma observed in 6.3 %, the rest 3.1 % was other types of thyroid cancer.

The statistical analysis shows significant prognostic odd-ratio of linear size of thyroid nodule L, mm (OR = 1.15, CI = 1.09-1.22), presence of anechogenity (AN: 1 - yes, 0 - no) (OR = 6.11, CI = 1.16-32.18) and micro calcification (MC: 1 - yes, 0 - no) (OR = 0.07, CI = 0.04-0.13)

Statistical texture features of ultrasound thyroid nodule images, energy E, entropy S, moment of inertia MI, local uniformity LU, maximum probability MP, were obtained by spatial adjacency matrix and average value AV were investigated.

**Results.** Developed logistic regression model {0,246+0,016*L+2,602*AN-2.646*MC} with 0,84 cut-off shows 95% accuracy in malignancy detection. Around 85% of nodules sorted by model as benign were true benign. Using texture features{-2,538-1,396*LRM-0,697*Ln(AV)} with 0.165 cut-off shows a specificity and sensitivity value of 67% for binary classification of TR 2 and TR 5. LRM is stand for a logistic regression model {11.143-0.400*Ln(E)-7.585*Ln(S)-0.049*Ln(MI)-1.656*Ln(LU)+0.747*Ln(MP)} with 0.17 cut-off.

**Conclusions.** Thus, it is possible to assess the status of thyroid nodule using linear size of thyroid nodule, presence of anechogenity, micro calcification and some texture features of ultrasound images. The practical effect of developed models implementation might be 10-20% decrease assignation of fine needle aspiration.

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# MOLECULAR DIAGNOSTICS WITH QUANTUM SENSORS

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Nonspecific (e.g., nitrogen-vacancy centers in diamonds) and specific (e.g., conjugates of quantum dot photonic labels with capture molecules) quantum sensors have recently demonstrated their potential in breakthrough applications for molecular studies (drug transport across membranes), physiological monitoring (neurotransmission), analysis of the state of individual cells (temperature variation), ultrasensitive imaging (including MRT, optical, AFM, and NMR), and highly sensitive diagnosis (detection and monitoring of disease markers).

The ideal specific quantum sensor should combine:

- the best quantum material, e.g., quantum dots with a quantum yield close to 100%, high level of crystallinity, maximal shelf life, and minimal toxicity;
- an optimal solubilization procedure ensuring the smallest sensor size, highest stability in biological fluids, maximal signal after solubilization, and quantitative control of surface charges and surface functionalities;
- the best capture molecules with the smallest size and highest affinity; and
- the best conjugation protocol ensuring that the recognition sites of the sensors are not perturbed.

The performance of specific quantum sensors based on quantum dots conjugated with conventional and single-domain antibodies in an oriented manner has been demonstrated in emerging applications such as diagnosis of autoimmune diseases and cancer, where they have proved to have clear comparative advantages over the current gold standards of optical diagnostic assays.

# GADOLINIUM-BASED NANOTHERANOSTICS FOR RADIOTHERAPY AND CELL TRACKING

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The use of non-invasive methods for tracking stem cells in the body is very important for analyzing their distribution in tissues and organs, as well as for ensuring control of their lifetime after injection. Recently, human mesenchymal stem cells (hMSc) attracted a great deal of attention as a potential therapeutic agent in the treatment of various socially significant diseases. The ability of hMSc to invade tumor tissues and specifically locate in them, affecting tumor cells, suggests their potential use as a delivery vehicle for various anticancer agents, and *in vivo* hMSc imaging methods will be required to control the effectiveness of such therapy.

Here, we synthesized of a new type of gadolinium-doped cerium oxide nanoparticles ($Ce_{0.8}Gd_{0.2}O_{2-x}$) as an MRI contrast agent for tracking hMSc and presented a comprehensive study of their cytotoxicity and processing. We synthesized the citrate-stabilized gadolinium doped ceria nanoparticles via different modification of hydrothermal method. $Ce_{0.8}Gd_{0.2}O_{2-x}$ nanoparticles have not shown any cytotoxic effects in all the range of concentrations (0.3–5 mg/mL) for mesenchymal stem cells. No reliable effect of citrate-stabilized nanoparticles on the intracellular ROS level was observed. Thus, $Ce_{0.8}Gd_{0.2}O_{2-x}$ nanoparticles can be considered as a safe theranostic agent for monitoring human MSCs.

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# ENGINEERED NANOSCALE PHOTONICS FOR ENHANCED BACTERIAL STERILIZATION AND INFECTIOUS WOUND HEALING

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The noticeable augment of cutaneous wound infection with drug-resistant bacteria underlines the dire need for novel disinfection methods in vivo. The advent of nanotechnology has facilitated several novel antibacterial strategies, which offer a better alternative to antibiotics, particularly in treating drug-resistant strains. Prussian blue nanoparticles are extremely promising candidates for antibacterial therapy owing to their inherent enzyme-like behavior and photothermal property. Moreover, these nanoparticles can be loaded with drugs/antibiotics for additional therapeutic gain. Herein, we have formulated chitosan coated Prussian blue nanoparticles to load photosensitizer (FITC-dextran) and confirmed their ability to photogenerate singlet oxygen, which is further mitigated by the catalase-like behavior of the core nanoparticles, demonstrating a pronounced cytoprotective effect. This photosensitizer loaded Prussian blue (CHPB-FD) nanoparticles were used for dual phototherapy in bacterial cells, namely blue-light activated photodynamic therapy (PDT) and red-light activated photothermal therapy (PTT). This developed exogenous antibacterial agent is able to kill methicillin-resistant Staphylococcus aureus and Pseudomonas aeruginosa in vitro and in a rat model of cutaneous wound infection. The local hyperthermia and photogenerated singlet oxygen accelerates amendment in intracellular metabolic pathways and bacteria killing without eliciting systemic toxicity. On the other hand, the catalse-like behavior attenuates the levels of ROS at the wound site. The beneficial effect of topically applied CHPB-FD nanoparticle treatment on infection-mimicking cutaneous wound model was evident compared to the control and lead to up regulation of genes involved in tissue remodeling, promotes collagen

deposition and enhances wound repair. Finally, robust antibacterial combination phototherapy was also demonstrated using a single, commonly available white-light excitation source. This multimodal nanoformulation utilizes few dosages, low laser flux or readily accessible white light excitation source, making it an alternative platform to current antibiotic therapies against bacterial wound infections.

# SPECIFIC ABSORPTION RATE OF RANDOMLY ORIENTED MAGNETIC NANOPARTICLES IN A STATIC MAGNETIC FIELD

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Magnetic nanoparticles, mainly iron oxides, are promising materials for the diagnosis and therapy of oncological diseases [1]. The main applications of magnetic nanoparticles in biomedicine are magnetic particle imaging (MPI) and magnetic hyperthermia (MH). MPI is a minimally invasive technique for spatial detection of magnetic nanoparticles in-vivo [2].

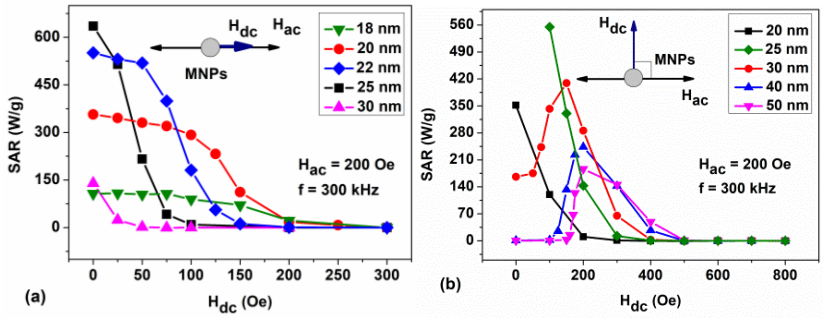


Fig. 1. Dependence of specific absorption rate (SAR) on an external static field $H_{dc}$ applied parallel (a) and perpendicular (b) to an external alternating field $H_{ac}$ for a randomly oriented assembly of nanoparticles in a solid matrix

Together with MH, the technique will make it possible to localize heating by controlling the value of the SAR of particles by a strong constant magnetic field [3].

Using numerical simulation of the stochastic Landau-Lifshitz equation, the dynamics of the magnetization of assemblies of magnetite nanoparticles with a uniaxial type of magnetic anisotropy, which are simultaneously in an alternating and static magnetic field, was studied.

The amplitude and frequency of the external alternating magnetic field were taken equal to $H_{ac}$ = 200 Oe and $f$ = 300 kHz, which are typical for use in magnetic hyperthermia. Static field strength, $H_{dc}$ = 0 – 800 Oe. Special cases of parallel and perpendicular arrangement of a static, $H_{dc}$, magnetic field with respect to an alternating, $H_{ac}$, magnetic field were considered.

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# PRECLINICAL INVESTIGATIONS OF $^{99m}$Tc-PSMA – A NEW RADIOPHARMACEUTICAL FOR SPECT IMAGING OF PROSTATE CANCER

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High morbidity and mortality associated with prostate cancer (PCa) requires the early visualization of the primary tumor as well as metastasis or recurrence. It is important for the subsequent treatment strategy, as it can reduce the risk of complications and improve prognosis.

Prostate-specific membrane antigen (PSMA), a type II integral membrane glycoprotein overexpressed in 95% of advanced PCa, is a promising molecular target for the imaging and radionuclide therapy of PCa using specific radiopharmaceuticals [1]. Low-molecular-weight PSMA inhibitors (peptidomimetics) are of particular interest. They have appropriate biodistribution profile: high tumor uptake and rapid elimination from the blood and non-target tissues via the renal route provide high contrast of SPECT or PET images.

Among the radionuclides currently in use, technetium-99m ($^{99m}$Tc) has become the "workhorse" of diagnostic nuclear medicine [1]. The wide use of $^{99m}$Tc can be explained by its nuclear properties ($T_{1/2}$ = 6.01 h, Eγ = 140.5 keV) and the convenience of its production using commercially available $^{99}$W/$^{99m}$Tc generator. In addition, the greater availability of gamma cameras compared to PET scanners, as well as their significant improvements with cadmium zinc telluride solid-state photon detectors, have led to renascence of interest for $^{99m}$Tc SPECT imaging [1].

In National Medical Research Radiological Centre a new radiopharmaceutical targeting PSMA ($^{99m}$Tc-PSMA) has been developed. Currently, preclinical investigations of $^{99m}$Tc-PSMA are being performed. Biodistribution, acute toxicity and local irritant effect has been studied. All studies were carried out in agreement with the ethical standards, Russian animal protection laws and guidelines for scientific animal trials [2].

Biodistribution studies were performed *ex vivo* on BALB/c nu/nu (nude) mice with 22Rv1 human prostate carcinoma xenografts by measuring radioactivity with gamma counter. Tumor uptake of $^{99\ m}$Tc-PSMA was 1.81-3.91 % of injected dose per gram (% ID/g). The highest uptake was observed in kidneys (up to 140.11 % ID/g. Rapid clearance from other organs and tissues led to high tumor/organs ratios.

The acute toxicity of $^{99m}$Tc-PSMA was studied in healthy mice F1 (CBAxC57Bl/6) and Wistar rats and estimated using the next doses: equivalent dose (ED), ED2 and ED4. $^{99m}$Tc-PSMA was administered intravenously. There was no mortality from toxicity. No pathological changes of organs (brain, heart, lungs, liver, kidneys, thymus, spleen, adrenal glands, testes, prostate and ovaries) were detected.

Local irritant effect was studied using chinchilla rabbits after intravenous injection of $^{99m}$Tc-PSMA in ED. No pathological local tissue reactions in all animals in area of $^{99m}$Tc-PSMA injection were observed.

In conclusion, $^{99m}$Tc-PSMA has favorable biodistribution profile without acute toxicity and local irritant effect.

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# $^{99m}$Tc-METALLOTHIONEIN AS RADIONUCLIDE-BINDING AGENT FOR RADIOPHARMACEUTICALS DEVELOPMENT

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Metallothioneins (MTs) belong to a family of intracellular low molecular weight proteins (6-8 kDa). They were first described in 1957 by Margoshes and Wallee. The main feature of MT is the extremely high cysteine, a sulphur-containing amino acid, content. They are involved in regulating of the homeostasis of elements, particularly Zn and Cu, and serve as antioxidants and protect the cells and tissues against damage caused by oxidation and apoptosis [1, 2].

The ability of MTs of binding different metals allows them to be considered as a component of radionuclide delivery systems. Technetium-99m (99mTc, $T_{1/2}$ = 6.01 h, Eγ = 140.5 keV) is still the most used radionuclide in diagnostic nuclear medicine. $^{99m}$Tc-MT conjugate can be used for further synthesis of radiopharmaceuticals, especially of labeled antibodies or their fragments.

The aim of this work was to investigate the biodistribution of $^{99m}$Tc-MT-metallothionein ($^{99m}$Tc-MT) in comparison with $Na^{99m}TcO_4$.

Metallothionein was derived from rat liver. Rats were previously injected with $KdCl_2$. Extracted liver was washed with saline and homogenized in 0.1 M tris-HCl buffer solution (pH 7.4). Obtained mixture was centrifuged at 1000 g for 20 min at 4 °C. Subsequent purification of metallothionein was carried out by ion-exchange chromatography in column with DEAE-sepharose.

Animal studies were performed in intact outbred mice. Mice were divided into 2 equal groups (n = 16 for each group). Mice were injected intravenously with 0.37 MBq of $^{99m}$Tc-MT or $Na^{99m}TcO_4$ in a volume of 0.1 ml. At 5 min, 1, 3 and 24 h postinjection (p.i.) animals were sacrificed, organs and tissues were excised, placed in plastic tubes, weighed,

and the radioactivity was measured using gamma counter. The values were expressed as percentage of injected dose per gram of tissue (% ID/g).

It was shown that biodistribution of $^{99m}$Tc-MT differed significantly from $Na^{99m}TcO_4$. The highest uptake of $^{99m}$Tc-MT was observed in kidneys (up to 299.5 ± 69.9 % ID/g at 1 h p.i.). In contrast, kidneys uptake of $Na^{99m}TcO_4$ did not exceed 30.0 ± 2.18 % ID/g at 5 min p.i. But thyroid gland uptake of $Na^{99m}TcO_4$ was as high as 267.2 ± 59.0 % ID/g at 1 h p.i., whereas the uptake of $^{99m}$Tc-MT was significantly lower (0.79-1.20 % ID/g). The highest blood uptake of $^{99m}$Tc-MT was registered in blood 3.10 ± 0.16 % ID/g at 5 min p.i., which decreased to 0.21 ± 0.02 % ID/g by 24 h p.i. The concentration of $^{99m}$Tc-MT in liver remained 1.61-2.98 % ID/g throughout the study. In other organs uptake of $^{99m}$Tc-MT was lower than 2 % ID/g.

In conclusion, metallothionein can form stable conjugate with $^{99m}$Tc. The biodistribution of $^{99m}$Tc-MT-metallothionein had more favorable profile as compared with $Na^{99m}TcO_4$.

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# LASER-FABRICATED $MoS_2$ NANOPARTICLES WITH TUNABLE OPTICAL PROPERTIES FOR BIOMEDICAL THERANOSTICS APPLICATIONS

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Two-dimensional (2D) layered transition metal dichalcogenides (TMDCs) have attracted tremendous research interests due to their unique properties for developing new-generation electronic and optoelectronic devices [1]. TMDCs exhibit a strong excitonic response, ensuring non-trivial optical phenomena enabled by strong light-matter interactions: exciton-polariton transport, enhanced second and third harmonic generation, high refractive index and giant optical anisotropy [2]. Thus, nanostructures made from TMDCs represent unique platform for realization of light-matter interaction at the nanoscale. The manuscript addresses an important topic of laser engineering of spherical resonant Mie-excitonic nanoantenna from layered materials, particularly transition metal dichalcogenides (TMDC), with tunable optical response. The proposed approach leverages femtosecond laser ablation and fragmentation in liquids for the fabrication of colloidal ultra-stable spherical $MoS_2$ nanoparticles (NPs) of variable size (10 – 100 nm) and controllable oxidation level. Such nanoparticles demonstrate very exciting optical and electronic properties due to laser-induced transformation of its crystalline structure, which is followed by the conversion of Mie resonances in high refractive index $MoS_2$ NPs into excitonic resonances in $MoS_2Ox$ suboxide NPs, making possible a strong concentration of electromagnetic field in nanoparticles.

For the production of colloidal solution of $MoS_2$ NPs in water and ethanol from bulk crystal we adopted the methods of femtosecond

pulsed laser ablation in liquids (PLAL) [3]. It was found that for all the NPs its structure is formed by polycrystalline inner part covered by fullerene-like outer shell. Preserved crystalline structure of 2H-phase $MoS_2$ provided pronounced Mie-excitonic response of synthesized NPs. Further modification of $MoS_2$ NPs size distribution, composition and crystalline structure was done by laser fragmentation approach. It was demonstrated that laser fragmentation of produced colloidal solutions of $MoS_2$ nanoparticles leads its oxidation accompanied by evolution of its optical response. Such partially oxidized $MoS_2Ox$ NPs provide efficient absorption of near-infrared radiation and pronounced photothermal response. for the case of laser fragmented $MoS_2$ NPs in ethanol the photothermal response of fabricated $MoS_2O_x$ NPs in the optical transparency window of biological tissue is 6 times higher than one for conventional dielectric nanoresonators based on Si. Being in a mobile colloidal state and exhibiting superior optical properties compared to other dielectric resonant structures, the oxidized TMDC nanospheres with tunable optical properties are ideal candidates for developing the next-generation nanophotonic and nanotheranostic platforms, including photothermal therapy and multimodal bioimaging.

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# PURE AND COMPOSITE NANOPARTICLES FOR PHOTO-HYPERTHERMIA APPLICATIONS

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Nanoparticles (NPs) based on different inorganic and organic materials can be used to prepare efficient sensitizers of local photoinduced heating in living systems that is required for realization of localized and targeted photo-hyperthermia (PHT) to treat cancer tumors and cells. Pure semiconductor and plasmonic NPs exhibit interesting physical properties, which can be used in PHT [1]. Silicon (Si) NPs are promising for HT because they are biodegradable and can be easily prepared by different methods [1,2]. Si-NPs act as an efficient absorber of light in the visible and near-infrared spectral regions as it confirmed by experiments *in vitro* [3]. Recently, pure germanium (Ge) NPs, which were prepared by laser ablation of Ge-target in inert gas atmosphere followed by ultrasonic treatment in liquid, were demonstrated as an efficient light absorber in a window of the maximal transparency of bio-tissue [4].

Aluminosilicate halloysite nanotubes with immobilized gold NPs can localize the photo-HT under laser excitation with photon energy close to the plasmonic resonance [5]. These physical properties of semiconductor and plasmonic NPs and different composite ones are promising for mild therapy of cancer.

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# NANOCONTAINERS FOR DRUG DELIVERY

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In recent years, nanotechnological approaches have been widely used in biomedicine, including antibacterial and antiviral treatments as well chemotherapy of cancer. One of the most promising areas in biomedical applications of nanotechnology is the use of nanoparticles (NPs) as nanocontainers (NCs) for drug delivery. There are several principles underlying the potential of NP-based drug delivery systems [1-3], e.g. (i) passive accumulation of NPs based on the enhanced permeability and retention (EPR) effect; (ii) active accumulation of NPs and NCs conjugated with specific bioactive substances vectors; (iii) activation of controlled drug release from NCs under certain stimulus and conditions. The latter systems are usually based on temperature-sensitive polymeric NPs, changes in pH-level and other physical and chemical parameters [4]. Despite medical advances in the treatment of different diseases, many drugs even in forms of pure polymeric of liposomal NCs have a serious disadvantage because of their low stability and residual toxic effect.

Biodegradable porous silicon (PSi) NPs appear to be extremely promising for biomedicine, that was confirmed by their numerous preclinical studies for both diagnostics and therapy [4-7]. PSi NPs with various surface modifications can penetrate inside living cells with practically no cytotoxic effect, while various functional modalities for biomedical diagnostics can be realized [6-8]. The porous structure of PSi NP allows a high degree of loading and provides time-distributed yield of various peptides [9], hydrophilic and hydrophobic drugs [10].

Immobilization of drug in NCs and NPs can be used for increasing the bioavailability of the former, improving solubility, and ensuring overcoming various barriers, for example, the blood-brain barrier, re-

ducing the effect on the body as a whole, targeting the damaged area. An important additional advantage is the possibility of creating drugs with prolonged action.

Beside PSi NPs nonporous Si ones, which are synthesized by femtosecond laser ablation followed by PEGylation, can be also considered as efficient carriers of therapeutic radionuclides for cancer theranostic applications [11].

Thus, drugs and radionuclides immobilized in NCs and NPs open up new perspectives for effective treatment of various pathological processes.

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# OPTIMIZATION OF THE InP NANOCRYSTALS SYNTHESIS USING tris-AMINOPHOSPHINES AS A PHOSPHORUS PRECURSOR

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The new-generation of nanomaterials, colloidal quantum dots (QDs) have exhibited attractive characteristics, such as their unique size-, shape-, and composition-dependent optical properties. A spectrally narrow and tunable emission line of QDs allows them to be applied in photoluminescent color converters and electroluminescent displays, lighting, energy applications, photocatalysis and bioimaging technologies. Among the different classes of QDs, cadmium chalcogenide-based materials have received most attention and are widely used. However, the high toxicity of Cd severely limits the practical application of Cd-based QDs. Among different Cd-free nanocrystals, QDs based on indium phosphide (InP QDs) are the most promising alternative materials. However, the synthesis of high-quality InP QDs is still challenging and more complicated in comparison with Cd-based QDs. Also, InP QDs demonstrate relatively low photoluminescence quantum yields and broad emission bandwidths. Many studies have been devoted to the preparation of InP QDs but the overall properties of InP QDs are still worse than those of Cd-based QDs. Thus, the development of new effective approaches to the synthesis of InP QDs is one of the most important goals in chemistry of nanomaterials [1-3].

Here, we report on the optimization of the synthetic procedures used for fabrication of indium phosphide quantum dots using $InCl_3$, tris(dimethylamino)phosphine ($P(NMe_2)_3$), and oleylamine as a starting materials. The size of the InP QDs was controlled by varying the reaction parameters such as the reaction time and temperature, the type of indium precursors and other reaction parameters. We have optimized the

reaction conditions including the ones for shell growth (ZnS/ZnSe). Our approach has the potential for synthesis of highly-emissive InP-based QDs both from a practical and fundamental points of view.

This work was supported by the Russian Science Foundation (grant no. 18-19-00588-П).


Fig.1. Photographs of the colloidal solutions of InP QDs under UV illumination

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# ADVANCED NUCLEAR-PHYSICS AND NANO-THECHNOLOGIES FOR RADIATION THERANOSTICS

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The results of the work obtained in the Laboratory of Radiation Biophysics and Biomedical Technologies of LPI of RAS, conducted jointly with the Laboratory of Bionanophotonics of MEPhI, are presented.

The aim is in solving new fundamental problems in the field of binary nuclear-physics methods for creating new technologies for diagnostics and radiation therapy using proton and ion beams to solve the problem of current interest – the treatment of socially significant diseases.

Methods of binary nuclear-physical technologies are aiming at the development of targeted proton therapy technologies using promising nanoparticles and their-based systems as sensitizers of therapy and active agents for diagnostics.

This area involves a significant development of the field of modern nuclear medicine through integration with nanomedicine, which uses unique properties of nanoparticles for cancer diagnosis and therapy. These properties include passive/active delivery, high load capacity, large cross-section of interaction with biological tissues, unique surface properties of nanomaterials, giving them many functional capabilities and combining many capabilities within a single nanoformulation.

The work will be carried out using the infrastructure of high-tech Russian-made accelerator. The proton therapy complexes (PTC) “Prometheus” with a scanning beam and energy from 30 to 250 (330) MeV based on research proton synchrotron in LPI Protvino branch.

The Prometheus PTC is a unique development. It is a compact (outer diameter is 5 m, weight is 15 tons) synchrotron for protons with low energy consumption (up to 100 kW). Currently, such proton synchrotrons of Russian production by ZAO «PROTOM» are being put into operation for use in the treatment of patient in Tsyb Medical Radiology

Center in Obninsk, Russia and several places in Europe and the United States. Combining rapid acceleration (<300 ms to maximum energy) with an extraction cycle of up to a few seconds, a high duty cycle of the Prometheus PTC is achieved. PTC «Prometheus» can operate in a special proton beam extraction mode, in which single protons are released for each revolution, that allows such facilities to work effectively in tomographic mode.

On CPT «Prometheus» a fast formation of rectangular fields with high dose uniformity is realized for targets irradiated by a monoenergetic proton beam. There were carried out the experiments with irradiation of cell cultures with nanoparticles by protons

Experiments on irradiation with protons of various energies of cells with boron 11 nanoparticles obtained by laser ablation methods have shown that the presence of boron nanoparticles leads to increased cell culture death. Different types of cells were investigated: MFC7, MNNG/Hos, MSK human.

It was carried out also the investigation in boron neutron capture therapy technologies. Irradiation was carried out at the accelerator-based neutron source at Budker Institute of Nuclear Physics of RAS in Novosibirsk experiments on irradiation with thermal neutrons of cells with boron 10 nanoparticles obtained in MEPhI by laser ablation methods have shown that the presence of boron nanoparticles leads to strong increased cell culture death. Human tumor cell lines U87 (glioblastoma) and SW-620 (colorectal adenocarcinoma) were obtained from the 'Center for Genetic Resources of Laboratory Animals' of the Institute of Cytology and Genetics of the RAS in Novosibirsk.

The results obtained now and in future in the development of binary radiation technologies will allow us to prepare recommendations on the use of new technologies for diagnostics and therapy based on proton and ion beams for the medical community of the Russian Federation.

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# DISASSEMBLING METAL-ORGANIC FRAMEWORKS FOR DRUG DELIVERY

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Here we present novel concept in drug delivery, based on the rapid accumulation of the nanoparticles in the tumour-surrounding vessels, following by rapid dissolution of nanoparticles.[1] Elevated intracapillary drug concentration drives drug diffusion through endothelial walls to the surrounding tissue with ensuing therapeutic effects. This concept differs from other commonly used, which are based on the "enhanced permeability and retention" effect.

This concept was justified by theoretical modelling and validated experimentally using rationally designed MIL-101 metal organic frameworks. We described rapid 15-min dissolution of MIL-101 nanoparticles and investigated the mechanism behind this process. In the blood serum phosphate and hydroxide ions attack the iron clusters and effectively displace the 2-aminoterephthalic acid, while the iron core remains in the particle structure. It leads to the pore collapse in nanoparticle structure and to formation of the amorphous iron phosphate species. As a result, almost all the drug loaded into the nanoparticles pores can be released to the environment.

Then we show that after administration to the bloodstream the nanoparticles release their cargo even before the cells can uptake them. It was confirmed in a series of *in vitro* experiments, including direct observation of nanoparticle endocytosis via transmission electron microscopy.

Finally, we performed an animal study. About 60% of the injected dose were trapped in the lung capillaries after intravenous injection. We

developed two models of highly aggressive metastatic melanoma in the lungs: simulated early and late-stage metastases. We found that the developed nanoparticles loaded with doxorubicin released drug in a burst manner, leading to the surprisingly effective tumour treatment in comparison with the free drug injection. Novel drug delivery mode led not only to a decrease in the quantity of the observed metastases but also size reduction of the remaining ones. These two processes resulted in a significant improvement in the mean animals' survival from 30 days to 43 days.

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# *POSTER REPORTS*

# EFFECT OF LOW-TEMPERATURE ATMOSPHERIC PRESSURE PLASMA ON CELLULAR MODEL OF PARAMECIUM CAUDATUM IN THE STUDY OF THE ANTIOXIDANT PROPERTIES OF MEXIDOL

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It is known that the effect of low-temperature plasma obtained using relative but compact sources of high-frequency or arc discharges - plasma torches, capable of activate oxidative stress in cells and one nocellular organisms, which leads to their death. The search for the best animal model in the study of drugs that can remove the oxidative effects of this plasma, taking into account modern bioethical norms, led us to the decision to use the unicellular eukaryotic organism *Paramecium caudatum* as a model object [1]. This study has practical interest for biomedicine, since it allows conducting toxicological studies of new drugs on a large sample in a short time.

**Objective**. Consider the effect of low-temperature atmospheric pressure plasma on the *Paramecium caudatum* cell model in the study of the antioxidant properties of pharmacological preparations.

**Methods**. In our work, a pure culture of *Paramecium caudatum* was used. The cell culture was kept in the Lozin-Lozinsky solution at a temperature of 21 $^{o}$C. Cells were counted daily for 120 h after exposure using the ImageJ program (Fiji) with the "counting cell" plugin [2]. The cytoproct effect of antioxidant drugs was studied on the example of mexidol (ethylmethylhydroxypyridine succinate) taken at a concentration of $3^{\times}10^{-7}$ mol/ml. In our study, two series of experiments were carried out: in the 1st series, **He** plasma was used, in the 2nd series, **Ar** plasma was used. Plasma exposure was carried out using a two-

electrode plasma torch (cold plasma generator), the air flow was obtained by the power of the Metabo Power oil-free compressor 180-5W (Metabo, Germany). Plasma arc was formed in a gas flow with a flow rate of 3 l/min. The experiment was carried out for 5 minutes.

According to the results of the study, it was revealed that under the influence of **Ar**-plasma and **He**-plasma, the pH of the medium changes towards lower values.

The cell death after plasma exposure to *Paramecium caudatum* culture was 63% and 81%for **He**-plasma and **Ar**-plasma, respectively.

The presence of mexidol in the medium prior to the plasma exposure had a cytoprotective effect on the cells, almost completely neutralizing the oxidative effect of **He** and **Ar** plasmas [3].

The use of low-temperature plasma has shown its effectiveness for studying the antioxidant properties of pharmacological preparations. This method of using plasma is a promising area of interdisciplinary research in plasma medicine.

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# ANTIBIOTIC RESISTANCE OF HELICOBACTER PYLORI

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About 80% of the population of the Russian Federation suffer from some form of chronic gastritis. Currently, the main cause of gastritis is considered to be infection with a gram-negative bacterium - Helicobacter pylori. According to Russian clinical guidelines: "Eradication of H. pylori contributes to the cure of chronic gastritis and the elimination of its morphological manifestations regardless of the continuation of antisecretory therapy." Accordingly, the use of antibacterial agents in the treatment of chronic gastritis is extremely common, based on high efficiency. Unfortunately, the effectiveness of H. pylori eradication decreases annually; the emergence of clarithromycin-resistant strains has been declared a global threat by the World Health Organization [1]

According to Russian clinical guidelines, H. pylori, detected in various regions of Russia over the past 10 years, to clarithromycin was 8.3%, to metronidazole — 35.8%. These indicators indicate a low level of H. pylori resistance to clarithromycin and metronidazole in most regions of Russia. The prevalence of H. pylori strains with double resistance to clarithromycin and metronidazole is low — on average 3.3%.

The data of foreign authors [2] based on a meta-analysis of articles from 2009 to 2019 is much higher. In general, H. pylori were resistant to clarithromycin in 83.1% (95% CI = 80.7–85.2), metronidazole in 66.7% (95% CI = 63.8–69.5) and levofloxacin in 47.2% (95% CI = 44.2–50.2) of cases. This is probably due to the fact that the levels of antibiotic resistance are unknown in most regions of Russia.

There are several fundamentally different strains of H. pylori: CagA, vacAs1/2m1/2/. Karbalaei M [3] found that CagA-positive strains are resistant to metronidazole, the vacA s1m1 genotype significantly in-

creases resistance to metronidazole, while vacA s1m2 reduces resistance to clarithromycin and metronidazole, while while VACA s2 m1 reduces resistance only to clarithromycin, vacA s2m2 reduces resistance to all five antibiotics (clarithromycin, metronidazole, amoxicillin, tetracycline and levofloxacin)

Thus, we found out that the antibiotic resistance of H. Pylori is steadily growing. Therefore, we must be guided by all the rules of rational antibiotic therapy.

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# METHODS FOR OVERCOMING THE IMMUNOSUPPRESSIVE ENVIRONMENT OF THE TUMORS IN THE TREATMENT WITH CAR-CELLS

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CAR-T-cell therapy is an innovative method of treating certain types of blood cancers, in which the patient's own leukocytes are genetically programmed to destroy tumor cells. In addition, on the basis of studies on the production of CAR-T cells, the production of modified chimeric antigen CAR-NK cells is widely developing. These technologies are widely used for the treatment of hematological tumors. In the treatment of solid tumors, they have been ineffective for a long time due to the presence of an immunosuppressive tumor microenvironment (TME). To overcome these obstacles, new CAR-T cell engineering strategies have been developed to enhance tumor recognition, infiltration, and anti-cancer activity in a hostile TME.

A sufficient number of ways to overcome TME have been developed and proposed. The most obvious solution seems to be to inject CAR cells not intravenously, but locally - into the tumor or into the area from which the tumor was surgically removed. Indeed, some papers have demonstrated the advantages of this approach. [1]

The next problem is the inconsistency in the chemokines secreted by the tumor and the receptors for chemokines on CAR cells. It is possible to ensure the migration of effective CAR-T cells to the tumor by expressing receptors for chemokines secreted by tumors in them. In two studies, the authors expressed CCR-2b, a subunit of the CCR-2 receptor synthesized by many tumors, on CAR cells. In one study, the efficiency of CAR-T cell homing towards neuroblastoma increased [2].

Further, the scientists faced the problem of suppressing the anti-tumor activity of T-lymphocytes in TMA with the help of suppressor factors such as Tregs, MDSC, tumor-associated macrophages, cytokines and soluble factors associated with immunosuppression (TGF-β and IL-10). The solution to this problem was to target those cells that produce these inhibitory cytokines and the inhibitory cells themselves. Most often, such cells were tumor-associated macrophages (TAMs). To date, various therapeutic strategies targeting TAMS have already been tested in preclinical studies and clinical trials. [3] Immunotherapeutic strategies focused on macrophages are aimed at either depletion or repolarization of TAMs.

So, we found out that modern science has theoretically found many ways to overcome TME. Of course, this direction is only developing, and, fortunately, there are already the first clinical results.

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# LASER-INDUCED FLUORESCENT NAVIGATION FOR ASSESSING THE DEPTH OF PHOTODYNAMIC EXPOSURE IN BIOLOGICAL TISSUES

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The study aimed to develop a non-invasive method for determining the depth of laser-induced photodynamic exposure with a variable energy density and laser spot diameter in biological tissues, which will improve the efficiency of photodynamic exposure by providing a therapeutic effect throughout the entire depth of tumor tissue invasion without superficial thermal damage and excessive tissue necrotization.

**Material and methods.** The depth of the photodynamic exposure was estimated by spectral-fluorescence methods on models of biological tissues using a laser with a wavelength of 632.8 nm. Photodynamic exposure was carried out with a laser radiation wavelength of 660 ± 5 nm on biological tissues containing a photosensitizer of the chlorine series, at the same power density of 0.15 W/cm$^2$ with a change in spot diameter from 5 to 15 mm and radiation energy density from 100 to 300 J/cm$^2$. The simulation of the influence of the laser spot diameter on the relative radiation fluence rate in the near-surface layer of biological tissue was carried out using the Monte Carlo method.

**Results.** An experimental setup has been developed to study the depth of laser-induced photodynamic exposure on biological tissues. The distributions of the fluorescence intensities of the photosensitizer normalized to the intensity of backscattered laser radiation, as well as the depth distributions of the degree of hemoglobin oxygenation in a biological tissue with optical parameters characteristic of the mucous membrane of various organs, are obtained. The dependence of the pho-

tobleaching of the photosensitizer on the energy density is established at the same power density and different spot diameters of laser radiation. The results of numerical simulation of the propagation of laser radiation with different spot diameters in biological tissue showed that the laser radiation fluence rate in the near-surface layer of biological tissue with optical parameters of cervical tissue, increased relative to the incident radiation fluence rate with increasing spot diameter in the range from 0.2 to 15 mm. The deviation of the results of the experimental study from the results of numerical simulation was 2%. The energy parameters of tumor tissue irradiation obtained during the study were tested on patients with dysplasia and cervical cancer [1, 2].

**Conclusion.**

The developed methods of fluorescent navigation for non-invasive assessment of the depth of laser-induced photodynamic exposure with different energy density and laser radiation spot diameter in biological tissues will improve the efficiency of photodynamic exposure by providing a therapeutic effect throughout the entire depth of pathology invasion without superficial thermal damage and excessive tissue necrosis, and , thus minimizing side effects on the one hand and preventing possible continued growth and recurrence of the disease on the other hand.

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# INVESTIGATION OF PHYSICO-CHEMICAL PROPERTIES OF A NANOCOMPOSITE BASED ON CERIUM DIOXIDE STABILIZED BY TRIETHYLENE GLYCOL

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Nanocrystalline cerium dioxide ($CeO_2$) is a well-known antioxidant. In addition, it has radioprotective properties, is able to block inflammatory reactions, accelerate proliferation and regeneration and have an antimicrobial effect [1-3]. The listed properties of $CeO_2$ nanoparticles make them a promising object for use as a prevention and treatment of radiation-induced skin damage.

We have proposed the synthesis of a nanocomposite based on $CeO_2$ nanoparticles from cerium (III) chloride heptahydrate salts stabilized with triethylene glycol (TEG). The use of TEG in synthesis is due to the fact that the size of TEG-stabilized nanoparticles does not exceed 10 nm, and glycol groups on the surface of $CeO_2$ nanoparticles facilitate the passage of nanoparticles through the stratum corneum of the skin. In addition, glycols have anti-inflammatory activity and exhibit a disinfectant effect, which is extremely important in the development of an agent for the prevention and treatment of radiation-induced skin damage.

The hydrodynamic radius and polydispersity index of the synthesized nanocomposite were studied by dynamic light scattering using the Zetasizer Nano ZS nanoparticle characterization system. The shape and size of the nanoparticles in the nanocomposite were determined by transmission electron microscopy on a Leo912 AB Omega electron microscope at an accelerating voltage of 100 kV.

It is shown that the size of synthesized $CeO_2$ nanoparticles in the nanocomposite does not exceed 7 nm, which, according to the literature data, may indicate their non-toxicity and bioavailability [4].

The synthesized nanocomposite based on $CeO_2$ had a pH of 8.7. At this pH value, the average size of the nanoparticles was 6 nm. Insignificant agglomerations of nanoparticles from submicron to micron sizes were observed, which did not exceed 10% of the total number of nanoparticles.

For the application of this nanocomposite with radiation-induced skin damage, the pH value was shifted to a value close to the skin pH by adding 2M HCl (pH 5.9). Analysis of the size distribution of nanoparticles at pH 5.9 showed that 93% of $CeO_2$ nanoparticles in the nanocomposite at this pH value had an average size of 6 nm, and the remaining 7% of nanoparticles did not exceed 26 nm.

Thus, a nanocomposite based on ultra-small $CeO_2$ nanoparticles, stable at 5.9 – 8.7 pH, suitable for biomedical applications, including for the prevention and treatment of radiation-induced skin damage, was obtained.

This research was funded by Russian Science Foundation (№22-63-00082).

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# EFFECT OF GAMMA RADIATION ON MORFOMETRIC AND CYTOGENETIC PARAMETERS IN BARLEY

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It remains unclear which biological processes are involved in the formation of the effect of radiation hormesis. In this regard, the aim of our study was to investigate possible changes in the mitotic activity in root meristem of barley plants after γ-irradiation of seeds in a wide range of doses (2–50 Gy). Increase in cell division is the most obvious answer to question how hormesis stimulating effect is formed. Changes in mitotic activity are considered important stages in the formation of a plant's response to stress factors [1].

The main goal of the work was estimation of gamma radiation effects in the dose range from 2 to 50 Gy on mitotic activity and frequency of chromosomal aberrations in the root meristem of germinated seeds of barley (Hordeum sativum). In our experiment we choose 3 varieties of barley: Vytyaz, Ladny, Badioryi. The batches of seeds were irradiated by 2, 15, 17, 20 and 50 Gy, with dose rate 58 Gy/h. The irradiation of seeds was performed at the γ-facility "GUR-120" ($^{60}$Co, RIRAE). 3 samples contained 30 seeds for each cultivar and dose in a papper bag 5x5 cm were irradiated. Non-irradiated seeds were used as control.

Irradiated and control seeds were sown on paper rolls soaked in distilled water immediately after irradiation. Each paper roll contained 30 seeds. For each variety, 360 irradiated seeds were used. Paper rolls were placed in the thermostat where seedlings grew for five days at the constant temperature 23 ◦C, in the dark. In first day of cultivation, roots (5-10 mm) of five seeds for each dose and each cultivar were sampled for standard test [2]. In second day of cultivation, roots were preserved in a mixture of 96% ethyl alcohol and glacial acetic acid (3:1) and stored in a refrigerator at 4°C. In seven day, lengths of roots and shoots were measured. The results showed that after irradiation of seeds of three va-

rieties (Vityaz, Ladny, Badyoriy) at a dose of 2 Gy, there is no change in the length of the seedling compared with control. A dose of 50 Gy has a depressing effect. At 15, 17 and 20 Gy doses seedlings increase in the length of both roots and shoots.

In this study, it was not possible to identify significant differences from the control, the exception is the dose of gamma irradiation of 50 Gy, which reduces mitotic activity in three varieties of barley (Fig.1).

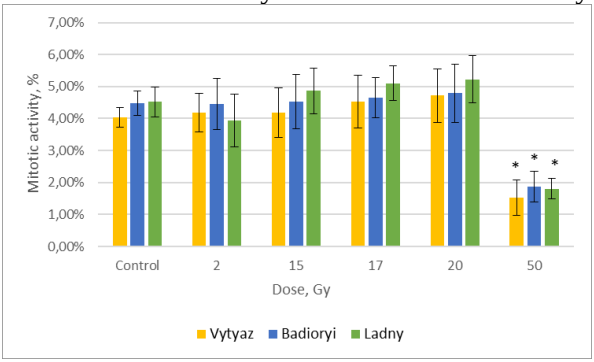


Fig. 1 The effect gamma irradiation ($^{60}$Co) of seeds on mitotic activity in seedling's shoots * The effect is statistically significant comparing to non-irradiated plants, $p<0.05$ (t-test)

Another possible explanation for visible stimulating effect in seedlings is acknowledged to be growth through cell wall modification. Obtained in this study data can serve as evidence of acid-growth hypothesis as possible part of complex radiobiologic response.

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# CHANGES IN CYTOGENETIC PARAMETERS OF HORDEUM VULGARE L. WITH COMBINATION OF RADIATION AND HEAVY METALS

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Heavy metals and gamma radiation have a significant impact on plant life. It can manifest itself in several ways. The presence of stress agents may not have consequences. However, in some cases, it is external factors that cause a toxic effect, or stimulation of the growth characteristics of plant organisms, as, for example, in radiation hormesis [1]. Some heavy metals, such as zinc, take part in metabolic processes [2].

Fluctuations in the natural background of such stressors are mostly insignificant. Most of them are directly dependent on the anthropogenic load on the biota. In real conditions, the combined effect of various pollutants is also often observed, which affects the final effect - it can differ significantly from the effect of the separate presence of metal in the environment [3]. The study of both separate and multicomponent effects of the mentioned physical factors is relevant, since it is directly related to the productivity of agricultural crops.

The purpose of this work is to study the effect of reducing the toxic effect of aluminum through its combined action with zinc ions and γ-irradiation.

The significance of the study lies in the possible prevention of the accumulation of the element in the tissues of the body, as well as reducing the effect of its toxicity on the growth characteristics of plants.

The variations of the combination of aluminum ions with other physical factors presented in the work indicate the possibility of reducing its toxicity to plants through the effects of hormesis and antagonism.

The result of the content of aluminum ions in the solution for germinating barley seeds was an increase in the number of aberrant cells by 7.4 times and a decrease in the mitotic index by 11.9% on average for

varieties compared to the control. In the experiment with zinc, the advantages of a combination of factors over the individual presence of $Al^{3+}$ are clearly recorded. This is expressed in a decrease in the proportion of aberrant cells by 1.3 times and an increase in the mitotic index by 1.1 times on average for varieties. In the presence of presowing gamma irradiation of barley, the rate of aberrant cell output decreases by 4 and 7 times for the Gris and Erema varieties, respectively, the mitotic index increases by 1.9 times.

The percentage of the frequency of chromosomal aberrations caused by mobile forms of aluminum completely overlaps only in the case of gamma irradiation, however, a significant decrease in the index is also recorded with $Zn^{2+}$ ions at a concentration of 5.0 mg/l.

In the presented cases, the leveling of the adverse effect is possibly carried out through detoxification and excretion of $Al^{3+}$, as well as the exclusion of its entry into the cell through the release of metal-chelating ligands. These resistance mechanisms of the organism are likely to be activated in response to the activity of radiation and zinc ions.

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# STUDY OF CYTOTOXIC EFFECTS OF $LAB_6$ NANOPARTICLES WITH LASER HEATING AND WITHOUT *IN VITRO*

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Lanthanum hexaboride refers to materials with surface plasmon resonance. This allows LaB6 nanoparticles to be heated by electromagnetic irradiation in the wavelength range from 700 to 1000 nm. The frequency range at which plasmon resonance is observed coincides with the window of optical transparency for tissues and organs, which opens new possibilities in the use of LaB6-based nanoparticles in medicine. This property has been used for a long time, for example, in solar panels, and is promising for the treatment of cancerous tumors using photothermy. The use of this method for the treatment of tumors is possible due to apoptotic mechanisms activation when cells are heated to 45-60 ℃.

In this investigation, LaB6 nanoparticles were synthesized by laser ablation. They had hydrodynamic size of 1200 nm and zeta potential of 24 mV in a phosphate buffer solution. A colloidal solution of these nanoparticles was heated in various modes using an 808 nm laser. Cytotoxicity was tested on several cell cultures without heating and after laser heating up to 60 ℃. CHO and A549 cell cultures were selected, and their viability was assessed using the MTT test. An attempt was made to coat the nanoparticles with a PEG-silane-COOH polymer to increase their stability. PEGylation was carried out in various polymer ratios:nanoparticles from 10:1 to 1:10 according to our previous successful technique used for TiN nanoparticles.

An increase in the concentration of nanoparticles in 10 times contributed to a decrease in the heating time. LaB6 nanoparticles with concentration 450 mg/mL show a significant toxic effect, causing the death of about 50 % of cells. After heating with an 808 nm laser, the cytotoxic

effect increased, 150 mg/mL concentration became critical, decreasing by 3 times compared to that without heating. PEG coating of LaB6 nanoparticles did not lead to the expected results. All samples showed instability in the phosphate buffer solution, which makes their use impossible in biological systems.

Acknowledgement

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# PHOTOTHERMIA-BASED APPROACH TO SYNTHESIS OF HYBRID NANOPARTICLES FOR BIOMEDICINE

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Nanotechnology is believed to revolutionize the field of drug development by introducing nanoparticles versatile clinical use. Common design of such particles is core-shell structures, where each component has its unique functionality. Multiple strategies for obtaining shell-layers have been proposed by chemical and physical techniques [1]; however, they are often compromised by low yield and challenging separation.

The aim of this study was to explore the applicability of laser-induced photothermal heating for controllable synthesis of core-shell nanoparticles. Nanoparticles possessing bands of enhanced light absorbance, namely TiN NPs [2], acted as a photoactivatable core material. Cu-BTC metal-organic frameworks (MOF) were selected as a shell material to provide high specific surface for drug encapsulation. To the best of our knowledge, photothermal excitation have not been used for coating nanoparticles before.

The pre-liminary results demonstrate that heating ability of nanoparticle is sufficient to rapidly start MOF nucleation. The obtained colloid had magnitudes of physicochemical properties (size, $\zeta$ – potential) in between those of TiN NPs and Cu-BTC and demonstrated patterns of crystal structures of both.

Further studies will be dedicated to morphological characterization of the obtained hybrid nanostructures and to testing of their drug loading and phototherapeutic properties.

This work was supported by the grant of the Russian Foundation for Basic Research, project No. 19-29-04012.

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# RESEARCH OF LOCALIZATION OF MICROVESICLES IN A CELL BY SCANNING FLUORESCENCE MICROSPECTROCOPY

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Fluorescence microscopy is an imaging technique that uses luminescence of excited atoms and molecules of a sample. A variety of molecules possess fluorescence and a number of factors and processes affect the spectral properties of fluorophores, making fluorescence microscopy a useful method for studying biological objects and allowing to obtain information about the structure of organized molecular systems.

The method of fluorescence microscopy [1] was used to study the interaction of cellular microvesicles (MV) with a cell [2]. The aim of this work was to obtain fluorescence spectra, by the intensity of which it is possible to determine how MV interact with the cell, whether they are on the cell surface or inside. To do this, the interaction of EA.hy 926 cells (obtained from the human umbilical vein) with the MV of the same cells was studied; Cy3-CMG2-DOPE lipid (a synthetic lipid containing carboxymethylglycyl spacer (CMG(2)) and a DOPE lipid residue (1,2-O-dioleoyl-sn-glycero-3-phosphoethanolamine) was previously embedded in the MV.

The fluorescence spectra were measured at the Renishaw inVia Qontor Raman microscope sensor at an excitation wavelength of 532 nm and an exciting radiation power of 2.3 mW on the sample.

Shown: 1) the fluorescence spectrum of individual microvesicles corresponds to the fluorescence spectrum of the lipid itself; 2) the intensity profile of the maximum peak of fluorescence (the value of the fluorescence intensity at a wavelength of 569 nm) was constructed with the

focal plane moving in height, the distance between two adjacent points at which the measurement was carried out was 3.125 μm. A total of 100 points were taken (the accumulation time for each measurement was 1 s). On the resulting graph (fig.1), two maxima were detected at a distance of 12.5 μm from each other. The size of the studied cells is 15-20 μm, taking into account the deformation in the vertical direction in connection with the preparation of the sample, it can be argued that microvesicles with an embedded lipid are localized mainly on the surface of the cell membrane.

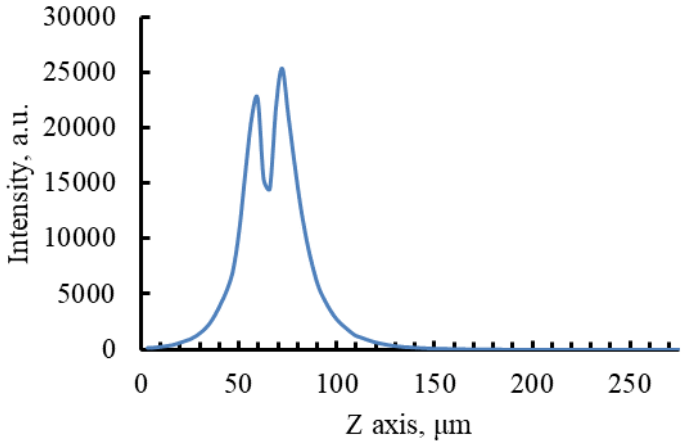


Fig.1. The intensity profile of the maximum peak of fluorescence

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# STUDY OF POLYMORPHISM OF OBESITY GENES IN STUDENTS

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According to the World Health Organization, in 2016, about 41 million children under the age of 5 were overweight or obese. Overweight and obesity, previously considered characteristic of high-income countries, are now becoming more common in low- and middle-income countries, especially in cities [1].

Obesity is increasingly being designated as a socially significant disease. Therefore, early detection of obesity and hereditary predisposition to it is important for the health of every person.

To identify a possible polymorphism associated with genes associated with FTO, PPARG, ADRB2, ADRB3 fat mass, 95 students of IATE MEPhI were examined.

Before the analysis, medical and genetic information was collected from all the examined persons, anthropometric measurements were carried out to calculate the body mass index (BMI). To clarify the value of BMI in all subjects, the type of fat distribution in the human body was determined.

According to the results of the survey, we assumed a genetic predisposition to obesity in 56% of students. For all the examined individuals, we conducted a real-time PCR analysis to determine the genotype by the FTO, PPARG, ADRB2, ADRB3 genes responsible for the genetic predisposition to obesity.

According to the results of PCR analysis, it was possible to determine: a normal variant of gene polymorphism (there is no mutation), a mutation in a heterozygous form (in one of the paired genes), a mutation

in a homozygous form (in both paired genes). The results are presented in Tables 1.

Table 1. Distribution of genetic variants

| | FTO (rs9939609) | PPARG (rs1801282) | ADRB2 (rs1042713) | ADRB3 (rs4994) |
|---|---|---|---|---|
| Homozygote for allele 1 (no mutation) | 33% | 69% | 8% | 92% |
| Heterozygote | 49% | 28% | 44% | 8% |
| Homozygote for allele 2 | 18% | 3% | 48% | 0% |

From the data presented, it can be seen that the largest number of students surveyed have mutations in the FTO and ADRB2 genes. This indicates that these students have a genetic predisposition to the development of obesity.

The results of the study indicate the prospects of the chosen direction. Since early detection of a genetic predisposition, in this case to obesity, as well as to other types of diseases, will allow timely measures to prevent the development of pathological conditions, correct the change in condition in time, which will allow you to lead a healthy lifestyle for many years.

Early diagnosis of genetic predisposition to obesity will help people to be more attentive to their health, prevent the development of certain diseases and avoid debilitating diets.

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# NANOPARTICLES OF SILICON AND SILICON-IRON AS PROSPECTIVE AGENTS FOR PHOTOHYPERTHERMIA OF PRIMARY HYPERPARATHYROIDISM REGION

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Primary hyperparathyroidism (PHPT) is one of the most widespread diseases of parathyroid glands (PGs) [1]. The disease is characterized by excessive secretion of parathyroid hormone and negative influence to bone, kidney and the cardiovascular system. There are two conventional ways to treat the phenomena: surgical and application medicines. Moreover, surgery is a single radical method to remove abnormal PGs, which possess some disadvantages: high risk of surgical complications, hospitalization, anesthesia, cosmetic problems and recovery period. Nowadays, laser ablation of abnormal PGs is a new method to treat of PHPT. There are some advantages in comparison with surgery: minimal invasiveness, local anesthesia, shorter period of rehabilitation. The method is based on phenomena of photoinduced heating of biotissue [2]. Moreover, positive effect from laser ablation can be if we use photoheating agent with a high absorbance ability. Nanoparticles (NPs) can become such agents.

Our work is dedicated to exploring the photoheating property of Si-Fe and Si NPs for potential application in photohyperthermia.

Si-Fe NPs were obtained using method of laser ablation of pressed microcrystalline Si-Fe targets in acetone followed by redispersing in water and Si NPs were obtained by the same laser ablation of Si target in water. A UV752P spectrophotometer (Wincom Ltd., Hunan, China) was used to measure extinction spectra of Si-Fe NPs (0.1 mg/mL) in the range from 350 to 1000 nm. To study the photothermal property of Si-Fe and Si NPs their aqueous suspensions (1 mL, 1 mg/mL) were irradiated by a semiconductor laser at 808 nm with power of 0.2-0.4 W. The

laser spot diameter was 2 mm. The measurements were carried out in cuvette having 10 mm optical path length. A platinum thermometer was used to measure heating of aqueous suspension of Si-Fe and Si NPs (characteristics of thermometer: an accuracy of 0.01°C and 15 Hz rate). Spatially homogeneous heating was achieved by stirring the solution with a magnetic stirrer (frequency of 110 rpm). The photothermal conversion efficiency was estimated according to Ref. [3].

The extinction of Si-Fe NPs in the infrared range is approximately 2 times higher than that for Si NPs. The spectra of Si-Fe and Si NPs exhibit maxima near 400 nm and 540 nm, respectively, which can indicate dielectric Mie resonances in those NPs. Also, we have received curves of heating and cooling of the NPs suspensions under laser irradiation. The samples retained their photothermal properties after repeated switching on/off the laser beam. The heating rate Si-Fe and Si NPs was 1.0 K/min and 0.3 K/min, respectively. The cooling curves of the NPs was fitted by exponential function (time decay near 0.3 $min^{-1}$). The values of photothermal conversion efficiency were 46±2% and 25±3% for Si-Fe and Si NPs, respectively.

Thus, Si-Fe NPs are more efficient for photohyperthermia than Si ones. Relationships between the efficiency of photothermal conversion and physical properties (sizes, composition) of Si-Fe NPs are required further investigations.

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# ERYTHROCYTE BLOCKADE OF PHAGOCYTES TO IMPROVE THE PHARMACOKINETICS OF NANOPARTICLES

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Nanomedicines due to their unique physical and chemical characteristics are finding new clinical applications for the treatment and diagnosis of various diseases. However, despite the demonstrated high efficiency in *in vitro* models, *in vivo* translation faces a number of problems. One of the key reasons limiting the pharmacological effect of nanocarriers is associated with the recognition of nanoagents by the immune system and their subsequent rapid elimination from the bloodstream and uptake by professional phagocytes. To solve this problem, we are developing a method of reversible phagocyte blockade to prolong the circulation of nanoparticles in the bloodstream and enhance their accumulation in the tumor.

Old erythrocytes that have lost the flexibility of their membrane do not pass well through narrow blood capillaries and are uptaken by phagocytes of the liver and spleen with subsequent degradation. Intravenous administration of artificially aged red blood cells labeled with radionuclides is a highly biocompatible method used in humans to visualize these organs [1]. Therefore, red blood cells denatured by mild heat treatment are an excellent candidate for temporary blockade of Kupfer cells in the liver or macrophages in the spleen (fig.1).

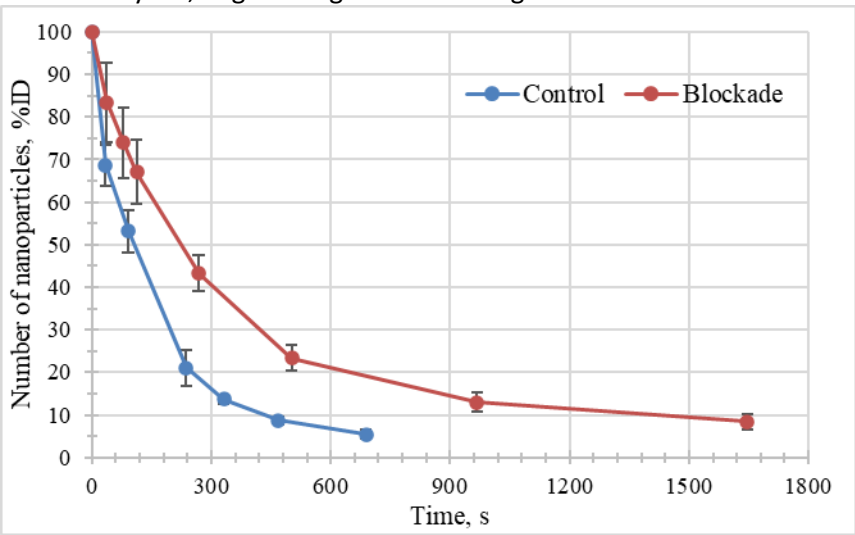


Fig.1. Nanoparticle circulation in the bloodstream

In this work, the blockade with erythrocytes allowed to significantly prolong the circulation of nanoagents in the bloodstream and change their bio-distribution in the body, reducing uptake in the liver. This biocompatible method can be used not only to increase the delivery efficiency of nanoagents for therapeutic purposes, but also to reduce side toxicity to the liver.

Acknowledgments: The reported study was funded by RFBR, project number 20-34-90052.

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# THE DEVELOPMENT OF $CeO_2$ – CURCUMIN NANOCOMPOSITE FOR BIOMEDICAL APPLICATIONS

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Cerium dioxide nanoparticles are one of the most promising agents for biomedical applications. This material is a nanozyme capable of mimicking the activity of various intracellular enzymes, showing anti- or prooxidant properties. The mechanism of biological activity of $CeO_2$ nanoparticles is based on the presence of both cerium in various valence states ($Ce^{3+}/Ce^{4+}$) and oxygen vacancies in their crystal lattice, which cause redox reactions on the surface of nanoparticles with the participation of reactive oxygen species (ROS) [1]. It was previously shown that $CeO_2$ has antitumor, antiinflammatory and immunomodulatory effects [2,3]. There is a technical possibility to vary the biological activity of cerium dioxide nanoparticles by modifying their surface with organic ligands. Curcumin, whose photosensitizing and anti-inflammatory activities have previously been demonstrated in various experimental models, can act as such a ligand [4,5]. Thermodynamic calculations show that the physical interaction of curcumin with the surface of $CeO_2$ nanoparticles is energetically beneficial and leads to the formation of an organo-inorganic nanocomposite. Meanwhile, ROS (for example, hydrogen peroxide) have an increased affinity to the surface of $CeO_2$ nanoparticles, which causes the release of curcumin from the surface of the nanocomposite when it interacts with ROS. Such feature of the nanocomposite can be used for its targeted delivery to an area with an increased level of oxidative stress.

We have developed a multi–stage scheme for the synthesis of the $CeO_2$ – curcumin nanocomposite, which includes the synthesis and stabilization of cerium dioxide nanoparticles with their subsequent binding

to molecular curcumin. The physicochemical parameters and cytotoxicity of the resulting nanocomposite were analyzed in a wide range of its concentrations. The optimal molar ratio of the nanocomposite components has been experimentally selected, at which their exhaustive binding is achieved, which, in turn, provides a high level of biocompatibility of the nanocomposite with respect to normal human cells.

We assume that the $CeO_2$ – curcumin nanocomposite developed by us will have a pronounced biological activity due to the synergism of its components and in the future can be used in photodynamic and radiation therapy of tumors.

The work was supported by the Russian Science Foundation grant No.22-63-00082.

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# PROSPECTS FOR THE USE OF QUANTUM DOTS AND QUANTUM SENSORES IN THE THERAPY AND THREATMENT OF COVID-19

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At the end of 2019, a pandemic of acute respiratory disease COVID-19 began. As of November 11, 2022, there were 630,832,131 confirmed cases of COVID-19 worldwide, including 6,584,104 deaths, according to WHO [1].

In this paper, an attempt was made to analyze the current literature on the use of quantum technologies, namely quantum dots and quantum sensors in the therapy and treatment of this disease.

Promising methods for the development of sensitive and economical methods for the quantitative determination of antiviral drugs (eg, molnupiravir) in real plasma samples and pharmaceutical tablets using CT will be considered [2]. The properties of AS-derived quantum carbon dots (AS-CD), which may have the potential to reduce the expression of pro-inflammatory cytokines and return immunological aberrations to normal in the case of COVID-19, are considered [3]. It has been shown that, in some cases, SARS-CoV-2 capsid proteins and nucleic acid can be targets for photodynamic therapy [4]. Quantum dots and quantum sensors can also be used to recognize SARS-CoV-2 RNA. For example, in [5], a nanobiosensor CdTe QDs-DNA for rapid recognition of SARS-CoV-2 RNA is presented. In [6], a Quantum sensor based on nitrogen vacancy centers in diamond is presented for the detection of the SARS-CoV-2 virus with a low number of false negative results.

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# STUDY OF SELF-ASSEMBLY OF PHOSPHOLIPID DERIVATIVES OF CYCLODEXTRINS BY THE METHOD OF MOLECULAR DYNAMICS

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Glycolipids based on cyclodextrins have amphiphilic properties and can self-organize into stable nanostructures, which can be used in drug delivery system. It is necessary to resolve the structure of nanoparticles with atomic accuracy which can be performed using the method of molecular dynamics [1].

In this paper, we created all-atom (AA) and coarse-grained (CG) models for three synthetic glycolipids based on $\alpha-, \beta-,$ and $\gamma-$ cyclodextrins (Fig. 1a,b). AA models are assembled in the Avogadro program, and CG models are obtained using the PyCGTOOL package.

The study of self-assembling of the molecules was carried out under two different initial conditions. The first starting structure was modeled as a cubic cell with a side of 20 nm, filled with water, NaCl ions at a concentration of 0.15 mol/l and the molecules in the amount of 100 pieces. The second simulated initial structure was the bilayers. Bilayers consisting of 98 molecules have been created for each three compounds. The bilayers with intermolecular distances: 1.5 nm, 2.0 nm and 3.0 nm were investigated. Both structures were created in GROMACS software After minimizing the energy, formation of nanoparticles was observed in both structure (Fig. 1c) [2].

We also obtained the full-atomic structure of micelle-like particles for each starting structure (Fig. 1d,e,f). The structures consisting of an average of 5 to 18 molecules are formed from based on $\alpha$ -cyclodextrins glycolipids. For β-CD-Ad-DOPE (Ad is –(CO)-$(CH_2)_4$-(CO)-, DOPE is

1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), these numbers are 8-18 molecules. And for γ -cyclodextrin glycolipids, the particles consist of 8-12 molecules. It can be concluded that the size of nanoparticles is affected both by what molecules it consists of and the initial conditions from which it was obtained. The size of micelle-like nanoparticles varies from 35 to 65 angstroms, while the size of a single molecule is about 30-35 angstroms. From this it can be concluded that the molecules in the micelle are not arranged in their linear conformations but have a different shape.

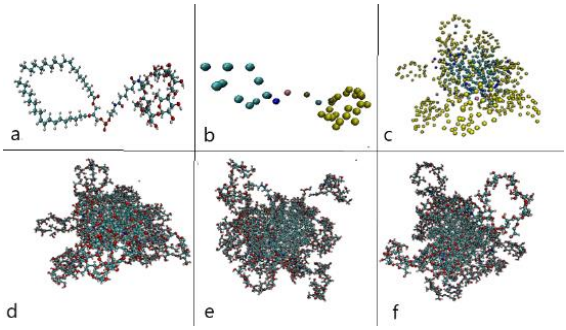


Fig. 1. (a) AA of α −CD-Ad-DOPE, (b) CG models of α − CD-Ad-DOPE, (c) CG models of micelle-like nanostructure consisting of α − CD-Ad-DOPE, (d) AA models of micelle-like nanostructure consisting of α − CD-Ad-DOPE, (e) AA models of micelle-like nanostructure consisting of β − CD-Ad-DOPE, (f) AA models of micelle-like nanostructure consisting of γ − CD-Ad-DOPE

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# NEAR-INFRARED PHOTOTHERANOSTICS OF TUMORS WITH PROTOPORPHYRIN IX AND CHLORIN E6 PHOTOSENSITIZERS

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The study is aimed to develop a method for tumor phototheranostics using protoporphyrin IX and (PpIX) and chlorin e6 (Ce6) photosensitizers (PSs), which includes spectral fluorescence diagnostics in the near infrared range (NIR) during photodynamic therapy (PDT) using one source of laser radiation. The implementation of tumor phototheranostics into clinical practice will make it possible to control the process of photodynamic exposure on deep-lying tumor tissues.

**Material and methods.** Spectral fluorescence diagnostics was carried out using a LESA-01-BIOSPEC spectrometer (Moscow, Russia) (Fig. 1). The spectral signal was registered in the range from 600 to 900 nm, which includes backscattered laser and fluorescent radiation.

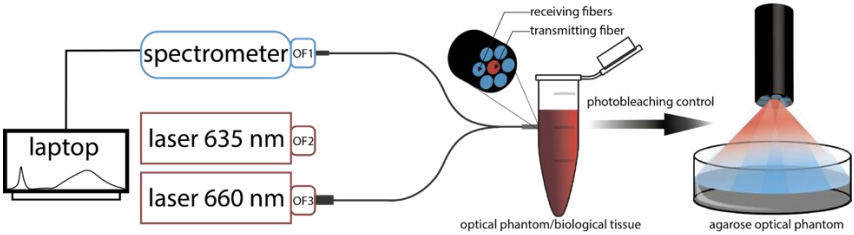


Fig. 1. Scheme of phototheranostics

An optical filter was installed in front of the spectrometer, attenuating therapeutic laser radiation exciting PSs fluorescence (635/660±5nm), which makes it possible to register backscattered laser radiation and PSs fluorescence in the same dynamic range. The studies were carried out on optical phantoms that simulate the scattering and absorbing properties of biological tissues. The developed method was tried on patients with basal cell carcinoma of the skin and leukoplakia of the oral cavity.

**Results.** Spectral fluorescence diagnostics of optical phantoms in the NIR range containing different concentrations of PpIX and Ce6 with alternating excitation of fluorescence by laser radiation sources 635±5 and 660±5 nm made it possible to register intense fluorescence in the wavelength range 725-780 nm. The presented method of phototeranostics made it possible to control the photobleaching of PpIX and Ce6 in the process of photodynamic exposure. In the process of clinical approbation of the method, a method for assessing the degree of thrombosis of the tumor vascular system the during PDT was revealed.

**Conclusion.** The developed method of phototeranostics makes it possible to personalize the time of light exposure to tumor tissues for different parts of the body individually for each patient, which will increase PDT efficiency.

# THE RESEARCH OF SPECTROSCOPIC PROPERTIES OF INDOCYANINE GREEN COLLOIDAL SOLUTION

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Indocyanine green (ICG) is clinically approved photosensitizer with absorption peak in near infrared range [1]. In certain conditions molecules of ICG can form J-aggregates (ICG NPs) with brickwork type and narrow intense absorption peak at 897 nm. The ICG aqueous solution consists of monomers and H-type dimers with two absorption peaks at 780 and 715 nm, respectively. According to the information, ICG NPs could be prospective for fluorescent diagnosis of various kinds of malignant neoplasms. However, the size of nanoparticles is an important value for diagnostics due to large particles provoking vascular thrombosis and embolism. Contrariwise, small particles cannot eliminate from organisms and enable to penetrate to health cells.

The investigation of ICG NPs applicability for fluorescence diagnosis of tumor has shown the promising outlook for the reason that J-aggregate assembling enhances circulation time in the organism from 30 minutes to 2 days [2]. After intravenous injection, ICG NPs save the free form in comparison with ICG molecular solution, which binds with plasma proteins [3]. Consequently, the study of behavior and spectroscopic properties of ICG NPs has a significant influence for revealing tumor boundaries and prediction of pathways of metastasis.

The research demonstrates the dependence of spectroscopic properties of ICG NPs and its concentration, but at the same time, absorption coefficient decreases. The phenomenon occurs due to decrease in the specific surface area with an increase in the size of the ICG NPs colloidal solution. Additionally, the increase of ICG NPs concentration promotes to appendance of ICG molecules with enhancement of sheet-like morphology of ICG NPs. According to the data, the behavior model of nanoparticles under laser radiation is presented in the research. The upper and lower molecules located on the domain are able to move from para-position to ortho-position, demonstrating fluorescent properties with a greatly increased oscillator strength, which is associated with an increase in the radiation velocity.

The reported study was funded by RFBR according to the research project No. 21-52-15025 and partly by IEA (International Emerging Action) CNRS grant 00534.

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# USE OF IODINE-125 SEED FOR INTRAOPERATIVE LOCALIZATION OF IMPALPABLE BREAST LESIONS: TECHNICAL SCIENTIFIC REPORT

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Lesions diagnosed in early stages that are impalpable require a localization method to guide the surgeon to identify and excise the exact lesion site in breast-conserving surgery. Among the intraoperative localization techniques are Wire Guided Localization (WGL), Radio-guided Occult Lesion Localization (ROLL), and Radioactive Seed Localization (RSL).

The aim is to develop a scientific technical report to support the decision-making on the RSL technology incorporation, through the analysis of clinical trials and economic studies on the outcomes of efficacy, safety, and organization of services. A systematic search was performed in the databases ClinialTrials.gov, Cochrane library, CRD database, EMBASE, HTA database, LILACS, PubMed, SciELO, Trip database, and Web of Science, through a search strategy with the terms: impalpable breast cancer, breast surgery, radioactive seed localization, wire localization, radio-guided occult lesion localization. The selected studies underwent a standard form for data extraction and risk of bias analysis according to the standard tool for study design. The collected data were grouped in a meta-analysis by the assessed outcome.

In the comparison RSL x ROLL, the results found by the outcome were: positive surgical margins (RR 0.83, 95% CI 0.50 – 1.39, I2 39%; 763 patients), reoperation (RR 1.14, 95 % CI 0.75 – 1.74, I2 17%; 1550 patients), and recurrence (RR 0.50, 95% CI 0.29 – 0.87, I2 0; 939 patients).

In the comparison RSL x ROLL, the results found by the outcome were: positive surgical margins (RR 0.78, 95% CI 0.70 – 0.88, I2 37%;

15095 patients), reoperation (RR 0.71, 95% CI 0.61 – 0.84; I2 61%; 13884 patients), recurrence (RR 0.41, 95% CI 0.19 – 0.86; I2 0%; 1525 patients), failure to identify the lymph node biopsy sentinel (RR 1.00, 95% CI 0.35 – 2.87, I2 0%; 1318 patients), implant complications (RR 1.05, 95% CI 0.61 – 1.78, I2 58%; 9107 patients), postoperative complications (RR 1.17, 95% CI 0.90 – 1.52, I2 0%; 5010 patients).

The results demonstrated that RSL is superior to WGL in surgical efficiency in the impalpable breast lesions intraoperative localization and is, at a minimum, equivalent to ROLL. This is important because the breast-conserving surgery success depends on the complete removal of the tumor. So, completion of surgery with negative surgical margins reduces reoperation rates and the disease recurrence risk. RSL also presented promising results regarding the organization of services, proving to be superior to WGL and ROLL technologies, because a longer time between the lesion localization and the surgery allows greater flexibility in the scheduling of the radiology and surgery sectors, in addition to the possibility of the seed placement procedure taking place before neoadjuvant chemotherapy.

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# TITANIUM CARBIDE NANOPARTICLES FOR PHOTOTHERMAL THERAPY

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Plasmonic nanoparticles represent one of the most promising classes of materials for nanomedicine and nanobioengineering. In this study, titanium carbide ($Ti_3C_2$) nanoparticles obtained by laser ablation were studied. Since titanium carbide particles have plasmon absorption within the biological transparency window, these nanoparticles can potentially surpass their gold counterparts in phototeranostic applications [1-2]. Fine spherical $Ti_3C_2$ nanoparticles are capable of generating a strong phototherapeutic effect at 750-800 nm excitation. In this study, the first toxicity assessment was presented and the biocompatibility of nanoparticles on human ovarian adenocarcinoma cell lines, cervix and basal epithelial cells of the alveolar layer was evaluated.

Titanium carbide nanoparticles are hydrophobic, so the first task was to achieve solubility of nanoparticles in aqueous solutions. To do this, the nanoparticles were coated with a hydrophilic shell consisting of ions of sodium oleate dissolved in water.

The next step was to study the thermal stability of nanoparticles. To do this, several experiments were conducted to identify the dependence of particle heating on laser power, the change in their temperature over time at constant power, and their thermal stability was measured by repeated sequential heating and spontaneous cooling of nanoparticles.

Next, colorimetric tests were performed to assess the metabolic activity of cells on SKOV-3, HeLa, A549 cell lines. The particles proved to be safe for cells in the absence of laser heating, which indicates high biocompatibility. Also, according to the test results, the minimum re-

quired concentrations of nanoparticles were calculated for effective action on cells.

The results of this work show that titanium carbide nanoparticles have prospects as preparations for photothermy. Further tasks are to study their pharmacokinetics and experiments on the treatment of mice using $Ti_3C_2$ nanoparticles.

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# CONSTRUCTION OF A MICRORESONATOR BASED ON BORON NITRIDE AND RHODAMINE

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Fabry-Perot microcavities are a type of microresonators that consist of two opposing reflecting surfaces. The reflecting surfaces help to concentrate optical waves at the center of the microcavity and produce resonant modes. The light-matter interaction allows excited molecules to exchange energy with an electromagnetic mode of the microcavity and gives the possibility of tuning the energy levels of the molecules, thus enabling control over chemical reactions. The unique properties of such hybrid systems may be exploited for the development of novel devices such as next-generation lasers [1]. In this work, we present the construction of an advanced Fabry-Perot microresonator with its cavity filled with boron nitride and fluorescent dye Rhodamine 6G. The diagram of the system under study is presented in Fig 1.

According to the design of the Fabry-Perot microcavity, an aluminum coated coverslip was used as the bottom reflecting surface. A solution of boron nitride and Rhodamine 6G was prepared and casted as a thin film on its surface. To do this, the mixed solution was combined with different concentrations of the polymer polyvinylpyrrolidone (PVP, 55K). Hexagonal boron nitride – rhodamine - polymer polyvinylpyrrolidone 55K (hBN-R-PVP) layers were obtained by spin coating technique. We adjusted the thickness of the hBN-R-PVP layer by tuning the speed of spin coating process. The hBN-R-PVP film worked as the emitter host and rhodamine 6G as the fluorescence emitter. In addition, immersion oil was added on top of the composite to protect the sample while adjusting the convex mirror and for better mode visualization. Once the sample was placed on the stage, which consists of a Z-

piezopositioner and convex mirror placed above the sample. The microcavity length was determined by adjusting the Z-piezopositioner, and the convex mirror was placed as close as possible to the sample to find the resonant modes. Both Z-piezopositioner and mirror were adapted to the atomic force microscope [2]. The resonant modes were found in hBN-R-PVP thin films obtained with a small concentration of PVP (35 mg) that were created with a speed revolution at 2000 rpm for 30 s by spin coating technique. The nanometer length accuracy (in the range down to 10 μm) allows to achieve small mode volumes (as low as tens of (λ/n)^3) and consequently strong coupling of organic dye molecules and the localized resonant electromagnetic field at room temperature. The fluorescence spectrum of rhodamine 6G was found in the range [530-620 nm]. These results demonstrate the strong coupling conditions for materials with low dipole moments, broad absorption and luminescence spectra.

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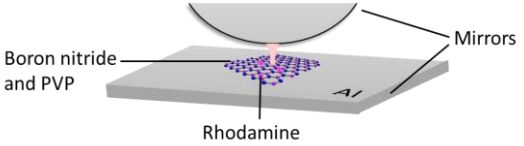


Fig.1. Diagram of a Frabry-Perot microcavity consisting of plane and convex mirrors and a sample prepared with boron nitride, rhodamine and polymer polyvinylpyrrolidone 55K

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# STRUCTURAL CHANGES OF Al- AND Cr- BASED METAL-ORGANIC FRAMEWORKS IN PHYSIOLOGICAL MEDIA

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Metal-organic frameworks (MOFs) are compounds with extremely high surface porosity, consisting of atoms of polyvalent metals or their clusters, ordered and interconnected by organic molecules. The properties of MOX, such as high surface area and adjustable pore structure, make them one of the most promising materials for potential applications, including drug delivery and cell imaging.

Nanoparticles (NPs) of metal–organic framework structures with crystal lattice consisting of trivalent Cr or Al and amino terephthalic acid, are promising due to their mesoporous structure, high surface area, and good hydrothermal stability. However, there are not many studies on the kinetics and mechanism of their degradation of NPs under physiological conditions. While these processes determine the biological fate of NPs after their intravenous administration. On the one hand, NPs must have sufficient stability during circulation in the bloodstream to deliver the drug to the target without allowing early release of the load. On the other hand, they must be degraded in the physiological environment in order to release the drug.

Recent study shows that nanoparticles of MIL-101 (Fe) metal-organic frameworks are rapidly transforming into amorphous iron in physiological media with release of drug load, thus enhancing therapy of B16-F1 melanoma metastasized in lungs. [1]

In this regard, when using nanoparticles of metal-organic framework based on trivalent Cr or Al for drug delivery and cell imaging, it is nec-

essary to maintain a balance between stability and biodegradation. This approach requires a deep understanding of the mechanisms that are involved in the degradation of MOFs.

In this work, Cr and Al MOFs were obtained by hydrothermal synthesis. The degradation kinetics of these nanoparticles was studied *in vitro* in isotonic sodium phosphate buffer pH 7.4 for three weeks.

The work was supported by the Russian Science Foundation under grant no. 21-74-10058.

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# MODELING RADIOFREQUENCY HEATING OF NANOPARTICLES FOR BIOMEDICAL APPLICATIONS

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In modern conditions, new methods of treating oncological diseases are needed. One of these methods is local tumor hyperthermia by Joule heating of electromagnetic radiation in the radio frequency range using nanoparticles as sensitizers [1].

To develop this technique, a mathematical model was built that describes the physical processes that occur during the interaction of a solid-state nanoparticle with radio emission in the environment of the human body. In this model, the contribution of a nanoparticle to the total heat release $q_p$ has the form:

$$q_p = \frac{1}{2}\varepsilon_{el} \cdot \omega \cdot Im(\vec{E}_0^* \vec{P}) + \frac{2\pi}{3}\sigma_{el} \cdot Re(\vec{E}_0^* \vec{P}) \quad (1)$$

Where $\omega$ external field frequency, $\vec{E}_0^*$ field strength in the medium, $\vec{P}$ induced dipole moment, $\varepsilon_{el}$ dielectric constant of the electrolyte, $\sigma_{el}$ conductivity of the electrolyte.

Based on the proposed model, the dependence of heat release on the frequency of the external field and the material of nanoparticles was obtained (Fig. 1), which was calculated for the following input parameters: size nanoparticle 10 nm, medium conductivity 1 S/m, which corresponds to the conductivity of the intracellular cytoplasm [2], zeta potential nanoparticle -20 mV.

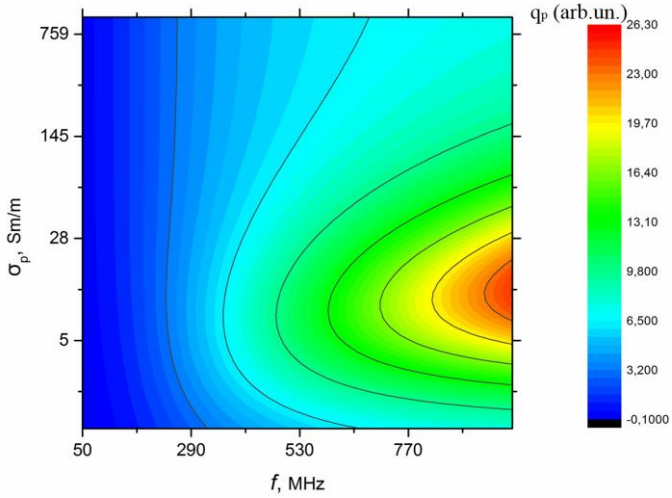


Fig.1. Dependence of heat release on the frequency of the HF field and the electrical conductivity of the material silicon NP

The proposed model can be further used to select the optimal parameters of nanoparticles and radiofrequency electromagnetic radiation for the treatment of malignant tumors. Acknowledgments: The reported study was funded by RFBR, project number 20-02-00861.

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# VERIFICATION OF THE INTRA-FRACTIONAL QUALITY ASSURANCE SYSTEM OF DOSIMETRIC PLANS

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Quality assurance of dosimetric plans is an integral part of the routine practice of the radiotherapy department. The main goal of quality assurance is to ensure the identity of the dose characteristics obtained in the treatment planning system (TPS) used in the department and the dose characteristics during the radiation therapy session directly in the patient [1]. To achieve this goal, dosimetric plans are usually checked before the patient is treated using various dosimetric systems (phantoms, ionization chambers, semiconductor detectors, detector arrays, etc.). However, these checks cannot exclude uncertainties that arise during the radiation therapy fraction. Such uncertainties may include changes in the patient's anatomy (breathing, digestion and heartbeat), random errors associated with the patient's laying and mechanical errors of the radiation delivery system.

A much racer type of quality assurance is QA in vivo, which allows you to track the dose directly during a radiation therapy session [2]. This type of quality assurance is possible thanks to detectors located on the patient's body or using an electronic portal imaging device (EPID). In comparison with the electronic portal imaging device (EPID), QA using detectors on the patient's body has difficulties in implementation – starting with the localization of the detector, ending with taking into account the contribution of the detector to the radiation field.

To date, the market offers in vivo dosimetric monitoring systems; one of such systems is SunCHECK/PerFRACTION, Sun Nuclear Corporation. When such systems are put into operation, the question of validation and analysis of the data obtained arises [3]. This paper will present methods of verification of such systems based on collecting statistics of log files recorded and analyzed by the SunCHECK platform, and dose verification using measurements of an ionization chamber in an anthropomorphic CIRS IMRT-phantom.

About 300 plans of different clinical cases were analyzed to verify the calculated model. At the first stage, only data based on accelerator log files were taken for analysis, with the help of which the SunCHECK platform calculates a number of parameters, such as dose at the isocenter point, PTV gamma, PTV mean, PTV D90 and PTV D95. In this work, the above data were compared with the data calculated in TPS. In addition, a series of absolute dose measurements was made using the SNC125c ionization chamber and an anthropomorphic CIRS IMRT-phantom. The anthropomorphic phantom allows measurements to be made both in a homogeneous environment and in a heterogeneous one, since it simulates the human chest, including the lungs and spine.

The results of the analysis revealed a discrepancy in the dose values at the isocenter point, PTV gamma, PTV mean, PTV D90 and PTV D95 for energies 6XFFF and 10XFFF and a deviation of doses calculated in SunCHECK/PerFRACTION and measured by an ionization chamber by more than 2% for cases with heterogeneity of the medium.

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# INVESTIGATION THE NATURE OF ENDOGENOUS AUTOFLUORESCENCE OF BIOLOGICAL TISSUES IN THE VISIBLE SPECTRAL REGION FOR BIOMEDICAL AND DIAGNOSTIC RESEARCH

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The autofluorescence (AF) signal of biological tissues in visible (VIS) and near-infrared (NIR) spectral region is actively used in biomedical applications. At the same time, in some cases, the molecular origin of intrinsic fluorescence has not been completely explored; a number of works describe an autofluorescence signal from an unknown type of biofluorophores, which, however, has practical significance, for example, the appearance of an intrinsic signal of amyloid fibers in the VIS/NIR range within brains of living aged mice with Alzheimer's disease [1].

Several works have shown that the appearance of AF in the VIS/NIR region can be accompanied by aggregation [1,2]. Other works attribute the appearance of this signal to chemical modifications occurring in the system, which may also be accompanied by the formation of a heterogeneous system of aggregates [3]. To better understand the nature of AF signal in such systems, it is necessary to investigate the optical properties of individual macromolecules of the heterogeneous system and the dependence of these properties on the size of aggregates [4].

In our work, we are interested in studying the mechanism of autofluorescence signal formation of amino acids and proteins using the example of an aqueous solution of tryptophan during photooxidation. We

report the analysis of the relationship between the optical properties of tryptophan photooxidation products and the heterogeneity of the system.

Using light sheet microscopy (LSM) and dynamic light scattering (DLS) methods, it was shown that photooxidation results in the formation of a heterogeneous mixture of aggregates with an average size of about 100 nm. For a detailed study of the heterogeneity of the solution, an experiment with sequential filtering through filters with pore sizes (1.3 - 450 nm) was carried out. The optical characteristics of the fractions were determined using absorption and fluorescent spectroscopy. We demonstrated that there is strong relation between aggregates sizes and their optical properties: the small aggregates (less than 3 nm) have a small spectral absorption slope ($\Lambda$) and a high fluorescence quantum yield value, in contrast to large aggregates (more than 3 nm) which have large values of $\Lambda$ and low fluorescence quantum yield. In addition, using fluorescence up-conversion method, we observed the presence of ultrafast picosecond component in the fluorescence decay kinetic for large aggregates, while this component was absent in the fluorescence anisotropy kinetics on the picosecond scale. These results provide further understanding of photophysical mechanisms of fluorescence signal formation in various biological systems, and are important for biophysical and biomedical applications.

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# INFLUENCE OF MICRO- AND NANOPOROUS SILICON LAYERS WITH DIFFERENT DEPTH AND PORE MORPHOLOGY ON CONTACT ANGLE, ADHESION AND VIABILITY OF CELLS

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The use of structured silicon substrates as model scaffolds is promising for the systematic study of the role of micro/nanomorphology in cell adhesion and growth.

In this study we created nano- and microstructured porous layers on silicon plates using electrochemical etching. Then we investigated the effect of pore depth and size on silicon plate's contact angle, cell adhesion, and viability.

We found that different porosity promotes different cell adhesion. Cells adhere more strongly to plates in the case of nanopores and weaker to micropores. Nanoporous layers were much more hydrophilic compared to the microporous ones.

Plates have great potential for modification. In the future, it is of interest to study plates on which there will be two layers simultaneously: microporous and nanoporous.

Acknowledgement

The study was supported by the Russian Science Foundation grant No. 19-72-30012.

# STUDY OF POLYMORPHISM OF OBESITY GENES PPARG, ApoB IN STUDENTS

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Nowadays, obesity is one of the most common diseases. According to the latest WHO estimates, more than 1 billion people in the world are overweight. This problem is relevant regardless of social and professional affiliation, area of residence, age and gender. In economically developed countries, almost 50% of the population is overweight, of which 30% are obese [1]. It has been established that body weight and tendency to obesity are caused not only by the influence of the environment and lifestyle, but also by genetic factors affecting the change in body mass index (BMI) in the range of 65-80%. Early detection of obesity and hereditary predisposition to it is important for the health of every person.

To identify possible polymorphism associated with genes associated with fat mass PPARG, ApoB 73 students of IATE MEPhI were examined.

Before the analysis, medical and genetic information was collected from all the examined persons, anthropometric measurements were carried out to calculate BMI. To clarify the value of BMI in all subjects, the type of fat distribution in the human body was determined.

According to the survey results, we assumed a genetic predisposition to obesity in 47% of students. For all the examined individuals, we conducted a real-time PCR analysis to determine the genotype by the PPARG, ApoB genes responsible for the genetic predisposition to obesity.

According to the data obtained as a result of PCR analysis, it was possible to determine: a normal variant of the polymorphism of the gene (there is no mutation), a mutation in the heterozygous form (in one of

the paired genes), a mutation in the homozygous form (in both paired genes). The results are presented in Table 1.

Table 1. Distribution of genetic variants

| | PPARG (rs3856806) | ApoB (rs5742904) |
|---|---|---|
| Homozygote for allele 1 (no mutation) | 36.5% | 78.6% |
| Heterozygote | 51.3% | 21.4% |
| Homozygote for allele 2 | 12.2% | 0% |

The presence of a mutation in these genes suggests that these people have a genetic predisposition to obesity.

This area is of great practical interest, because early diagnosis of a genetic predisposition to obesity can help people prevent the development of certain diseases and avoid debilitating diets.

It is of interest to further study the association of candidate genes for the development of obesity and the cluster of metabolic parameters in different ethnic groups of Russia.

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# DEVELOPMENT OF A TECHNIQUE FOR THE SELECTION OF SILICON NANOPARTICLES OBTAINED BY PYROLYSIS OF SILANE

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Nanotechnology is one of the most promising areas in biomedicine. Because of their specificity, silicon nanoparticles are one of the least toxic. There are various methods and Nanotechnology is one of the most promising areas in biomedicine. Because of their specificity, silicon nanoparticles are one of the least toxic. There are a lot of ways to obtain them [1-2], for example, ablation or the microwave method, however, when nanoparticles are obtained by the above methods, small concentrations of material are obtained, and with prolonged production, the life of the equipment is significantly reduced.

There is a method for producing silicon nanoparticles by pyrolysis of gases. This project uses silane gas, which, when exposed to a carbon dioxide laser, releases excited silicon (1), which subsequently forms an energetically advantageous shape of spheroids.

$$SiH_4 \rightarrow Si^* + 2H_2 \quad (1)$$

Their size directly depends on the pressure in the chamber where the reaction takes place. One of the significant advantages of these nanoparticles is their use in hyperthermia, the surface of nanoparticles is excellent for coating with gold, such composite nanomaterials are in great demand in this field, However, when they enter the oxygen atmosphere after pyrolysis, an oxide film forming agglomerates appears.

The aim of this project is to develop a methodology for size selection of nanoparticles obtained by pyrolysis of silane. To achieve it, the following tasks were solved: etching of silicon oxide and passivation of the particle surface separation and method of fixing the results of the nanoparticle technique

Etching took place using hydrofluoric acid ions, into ammonium fluoride compounds, this salt, when it got into an acidic ph medium, formed fluoride ions that reacted with silicon oxide. A centrifuge was used to separate the base material from the pyrolysis error products. Due to the hydrodynamic properties, at certain revolutions, larger nanoparticles settled when smaller ones remained in the supernatant, the result of centrifugation was recorded using a spectrophotometer, the resonance of the initial sample was 300 nm, when at a size of 100 nm of silicon particles, the resonance of the mi is 545 nm. After the technique developed in this project, the mi resonance was 550 nm.

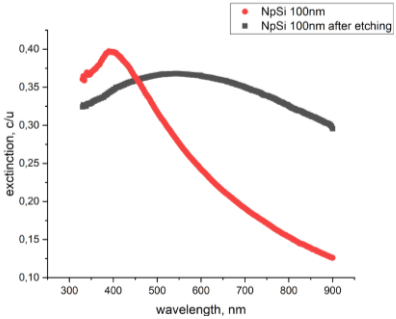


Fig.1. Graph of extinction dependence on wavelength after the technique

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# PLGA NANOPARTICLES LOADED WITH COBALT 1,2-DICARBOLLIDE FOR BORON NEUTRON CAPTURE THERAPY

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Boron-neutron capture therapy (BNCT) is a binary radiotherapy method based on the nuclear absorption reaction of the stable isotope $^{10}B$ by a neutron to form $^{7}Li$ and an alpha particle with high energy and a short lesion radius corresponding to the size of a mammalian cell, which allows you to target only tumor cells without affecting healthy tissue [1]. It is suggested that BNCT can be used in the treatment of various types of cancer. Clinical trials have shown positive results in the treatment of glioblastoma, melanoma, neck tumor, meningioma, pleural mesothelioma and hepatocellular carcinoma [2]. However, for successful therapy, the concentration of boron per gram of tumor should be ~20 μg. Nanoscale delivery systems, the synthesis of which is currently a promising field, can help to achieve the necessary concentration of the isotope in tumor cells. In this work, the conditions for production of PLGA nanoparticles with 1,2-dicarbollide cobalt with a maximum theoretical total drug content of 1.3 wt. % and minimum mean diameter of 59 nm were determined using Box-Benken plans and experiments were carried out to optimize the selected conditions.

Cobalt 1,2-dicarbollide [8,8′-I-3,3′-Co(1,2-$C_2B_9H_{10})_2$] was chosen as the drug for incorporation into nanoparticles because of its large number of boron atoms and hydrophilic properties. Three parameters were varied for the Box-Benken matrix in relation to the constant drug load: the amount of PLGA polymer, the amount of organic phase-chloroform and the amount of emulsion stabilizer - polyvinyl alcohol (PVA).

Box-Benken plans to plot drug loading (DL) and average nanoparticle diameter at different parameters were used.

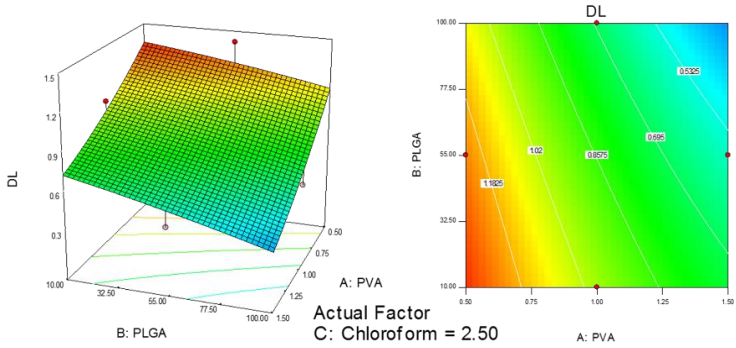


Fig.1. Two and three dimensional DL response surface diagram

Analysis of the diagram based on a series of experiments made it possible to determine the optimal conditions for obtaining nanoparticles with a maximum total content of the active substance - 1.3 wt. % and the smallest average diameter is 59 nm.

The obtained parameters of nanoparticles are optimal for effective BNCT, and further experiments on *in vitro* and *in vivo* will make it possible to choose drug administration regimens and doses.

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# STUDY OF THE OPTICAL PROPERTIES OF COMPOSITE MATERIALS BASED ON PEROVSKITE $CsPbBr_3$ NANOCRYSTALS FOR APPLICATION IN X-RAY DIAGNOSTIC STUDIES

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Perovskite semiconductor nanocrystals (PNCs), such as $CsPbBr_3$, represent a new class of materials that can be used in optoelectronic devices due to their high optical absorption coefficients and high fluorescence (FL) quantum yield (QY). PNCs can fluoresce in any region of the visible and near-IR spectrum by modifying their composition by varying the precursors during their synthesis. [1] The widespread use of PNCs in applied areas is limited due to their internal structural instability and deterioration of photophysical properties when exposed to moisture, light, and air. [2] PNCs $CsPbBr_3$ are of particular interest for use in new types of light-emitting diodes (LEDs) and photodetectors. [3] Scintillators based on PNCs $CsPbBr_3$ are a promising new imaging tool for X-ray radiography. PNCs $CsPbBr_3$ as a scintillator have better energy resolution (E ~ 1.4%) and faster scintillation decay times than NaI(Tl) which is used in most detectors. [4] The characteristic average lifetime of the luminescence kinetics ($\tau$) for $CsPbBr_3$ PNCs is about 5÷30 ns, while for NaI(Tl), which is used in most detectors, this value is around 230 ns. To use PNCs $CsPbBr_3$ as a detector scintillation layer, it is necessary to achieve uniform coverage of the PNCs layer.

In this work, PNCs $CsPbBr_3$ were synthesized as a material for fabricating the scintillation layer of the detector. The stability of the material

used was evaluated by measuring the dynamics of τ and QY values of thin films (TF) of PNCs with characteristic thicknesses of the order of 20–40 nm. Perovskite TFs were created on a glass substrate using the spin – coating method. In addition to thin films, samples with characteristic thicknesses of about 2 mm were also prepared and studied, for which PNCs was encapsulated in a polydimethylsiloxane matrix. The obtained samples have a stable value of τ over time. The advantage of these samples is the absence of contact between PNCs and the external environment, which eliminates the influence of factors such as moisture and oxygen. Finally, so that more effectively eliminate the influence of the environment, it was decided to encapsulate the PNCs in polystyrene through the radical polymerization of styrene. The produce samples have characteristic dimensions of the order of 0.5÷2.0 cm and have a stable QY FL value. For the latest, the amplitude characteristics of scintillation were studied in order to isolate samples (manufacturing technologies) with the maximum light output.

The fabricated bulk composite PNCs samples can be considered the most promising for use as a scintillation coating for X-ray and gamma-ray detectors.

This work was supported by the Ministry of Science and Higher Education of the Russian Federation through grant № 075-15-2021-1413.

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# PROBLEMS OF RESCANNING IN PROTON THERAPY: A SHORT REVIEW

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Organ motion is one of the major obstacles in charged particle therapy. It causes dose distribution disturbances due to interplay and blurring effects. Furthermore, motion can result in target dose miss and unwanted dose to healthy structures around the target 0. Rescanning is such an approach, where the interplay effect between tumour motion and treatment delivery is statistically smeared out 0. It consists of multiple repeated irradiations of the entire volume or individual iso-energy layers with the dose that is a multiple of the prescribed dose. As a result, the dose is averaged which leads to an increase in the homogeneity of the dose field. Several publications have compared different techniques of rescanning for plan parameters (number of fields, field directions, number of re-scans) as well as in respect to different motion parameters (motion amplitude, motion starting phase) 00. Based on the acquired motion information adequate plan parameters should be chosen. In this review, we investigate the limitations and possibilities of rescanning.

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# COMPOSITE SILICON-GOLD NANOPARTICLES WITH MIE-RESONANCES FOR PHOTOHYPERTHERMIA APPLICATIONS

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We present an approach for obtaining resonant silicon nanoparticles decorated with gold nanoparticles to enhance absorption in the transparency region of biological tissues. Highly selected spherical silicon nanoparticles with average diameters of 120 and 160 nm were prepared by femtosecond laser ablation of crystalline Silicon targets in water followed with centrifugation [1]. These nanoparticles were used to form nanocomposite particles consisting of initial silicon cores and gold nanoparticles (Fig.1-b) by using wet chemical synthesis. A twofold increase in the extinction of nanocomposite particles in the near-IR region was achieved compared to pure silicon nanospheres (Fig.1-c). An increase in extinction in the long-wavelength region with the deposition of gold NPs can be associated with the appearance of coupled plasmon-dielectric resonances [2].

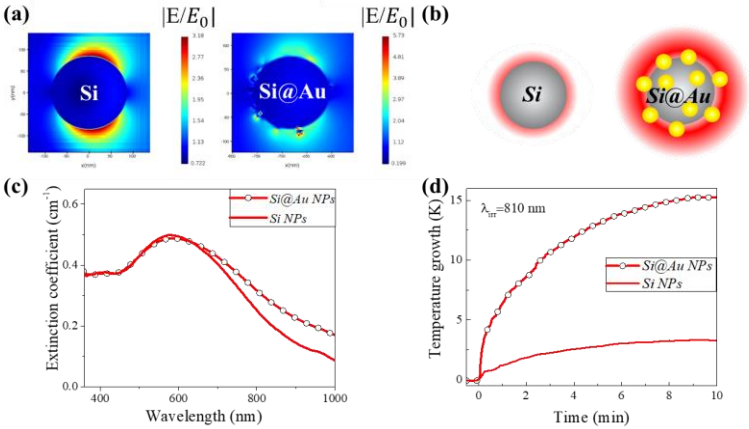


Fig.1. Electric field simulation (a) and schematic illustration of the nanoparticles (b), experimental exctinction spectra (c) and temperature growth curves under irradiation with laser with wavelengths of 810 nm (d)

Numerical simulations of the optical absorption, scattering and spatial distribution of electric fields in an ensemble of pure silicon and composite nanoparticles dispersed in water are carried out (Fig.1-a). Finite difference modeling is in good agreement with the experimental results.

The effect of Mie resonances in silicon nanoparticles and combined plasmon-dielectric resonances in composite ones for enhanced localized photoheating is demonstrated (Fig.1-d). An aqueous solution of silicon nanoparticles (0.05 g/l) with deposited gold was heated by 15 K when irradiated with a laser at a wavelength of 810 nm and an intensity of 200 mW. The obtained results are promising for use in biophotonics and photohyperthermia of biological tissues.

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# ARCHITECTURE OF THE ULTRASOUND PHYSICIAN ASSISTANT PROGRAM

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Digital transformation always involves the use of one or another digital platform to create applications and services. In this work, we are developing the architecture of a software application for diagnosing thyroid diseases using ultrasound images of the Healthcare domain of the Gostech platform, approved by the Government of the Russian Federation as the basis for all state information systems (GIS). Diagnosis of ultrasound images is an extremely difficult task for a doctor. There is a special classification of thyroid nodules - TI-RADS, with which you can determine whether there is a neoplasm in the picture or not and what its nature is. To simplify the definition of the TI-RADS class by a doctor, a system of an ultrasound diagnostics assistant for a doctor was developed.

This system is a web-based application in which doctors can upload ultrasound images in different formats and receive predictions using neural networks about the area in which the neoplasm is located and which TI-RADS class it belongs to. The software application can be installed in individual medical organizations, on the Gostech platform for general use or as planned on a separate gadget. The application collects information from each diagnostician. Further, the collected data and doctor's corrections can be used to retrain profile neural networks in order to improve the accuracy of their predictions.

Another important quality criterion is the time in which the application can predict the TI-RADS class and determine the areas of neoplasms. Due to the large number of matrix multiplications caused by the use of neural networks, the developed web application supports

graphics processing units (GPU) to reduce the processing time for ultrasound images.

We chose PostgreSQL as the database, because it is she who in the version of increased data security (Pangolin) is used on the Gostekh platform. Work with PostgreSQL is supported by many modern tools for developing services. This DBMS is built on an object-relational model, and is great for working with large amounts of data. Figure 1 shows the database attribute level diagram used in the web application.

The following libraries for the Python programming language were used to develop a web application:

- Djnago – web framework for creating web servers and ORM for working with a database;
- FastAPI – library for creating fast and lightweight servers. The application is used to create microservices on which predictions are made using neural networks;
- Pytorch – library for the development and operation of neural network models with support for computing on a video card;
- Celery – additional library for Django to work with deferred requests.

Also, to create a web server, ready-made open-source software systems used by the Gostech platform were used, namely:

- Redis – message broker for Django server and server communication with neural network models;
- Nginx – reverse proxy server;
- Docker – program for automatic deployment and application management.

Figure 2 shows a diagram of the relationship between the software used and the web server frameworks.

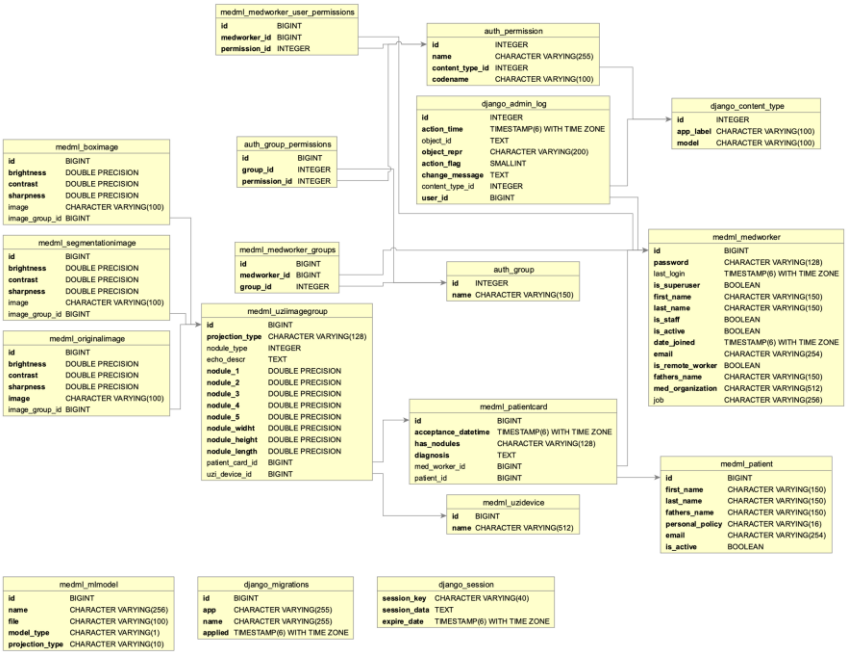


Fig. 1. Attribute level diagram

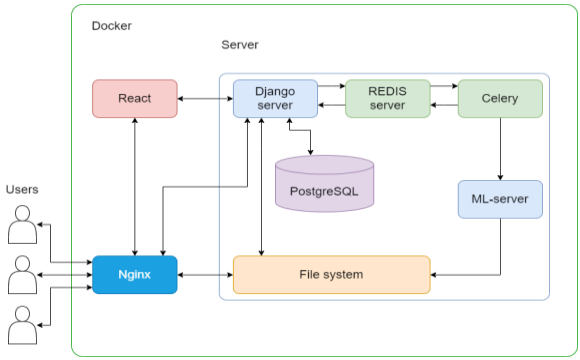


Fig. 2. Diagram of relationships between web server components

# USAGE OF BISMUTH-BASED NANOPARTICLES IN PROTON RADIOTHERAPY: REVIEW

**S.K. Korotkikh[1], A.E. Shemyakov[2], M.A. Belikhin[2], A.P. Chernyaev[1]**
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Nanoparticles (NPs) of high atomic number (Z) materials can act as radiosensitizers to enhance local radiation dose delivered to tumors. The types of nanoparticles and the energy of the ionizing radiation used are the most important factors that determine the optimum effects of nanoparticles radiosensitization.

The aim of this report is to overview the experimental data on application of bismuth-based nanoparticles in proton radiotherapy and provide theoretical explanation of their interaction mechanisms.

Studies [1-3] have shown that bismuth NPs cause maximum dose enhancement compared to gold NPs, platinum NPs and superparamagnetic iron oxide NPs. There are a number of advantages of using bismuth-based nanomaterials as radiosensitizers [2]:

1) Due to bismuth's larger atomic number (Z = 83) compared to gold (Z = 79), Bi-NPs enhance the effects of low-energy X-rays (Fig.1).
2) Bismuth and most of its compounds are considered harmless.
3) Bismuth-based NPs can be readily prepared in various well-defined shapes and sizes. Also, bismuth is the least expensive of the high atomic number (Z) elements.

As for protons' interaction mechanism, the majority of their energy is deposited at the end of proton range (Bragg Peak) in a targeted volume. Thus, the tissues beyond the tumor receive minimal dose. The inclusion of high Z metallic NPs in the target leads to the local increase of ionization energy loss. Coulomb collision of protons with nanoparticles causes ionization of the atomic electrons generating characteristic X-

rays and Auger electrons. Ionizing radiation interacts with water in which chemically active free radicals (reactive oxygen species, ROS) are formed that can react with biomolecules (phospholipids, proteins, RNA, DNA), thereby irreversibly damaging the cells.

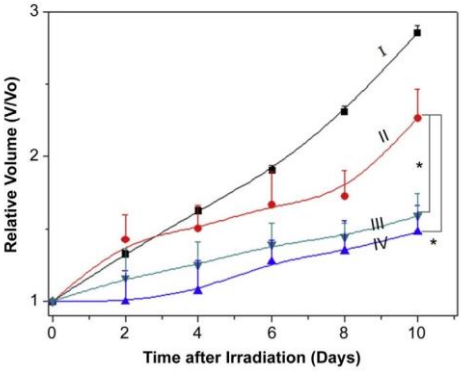


Fig.1. Tumor growth curve after different treatment in prostate tumor-bearing mice (I) NC; (II) RT only; (III) nanocapsules via intravenous injection; (IV) nanocapsules via intratumoral injection [4]

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# MODIFIED BISMUTH NANOPARTICLES FOR TARGETED DELIVERY TO HER2-POSITIVE CELLS

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Cancer is one of the leading causes of death worldwide, according to WHO, World Health Organization. Current cancer treatment methods, such as chemotherapy, radiation therapy and surgery, have severe limitations because of the toxicity, low selectivity and possible side effects on healthy tissues [1]. Therefore, the ability to precisely target the tumor plays a central role in safe and effective treatment. Many studies confirm that new tools based on nanotechnology can reduce side effects.

Bismuth nanoparticles (BiNPs) were chosen for their special physical properties. Bi as the heaviest non-radioactive element has a high absorption coefficient for a wide range of wavelengths. These NPs can be used as radiosensitizers to maximize the efficiency of radiation absorption [2]. To deliver bismuth to cancer cells, the surface of the nanostructure can be modified with targeting agents.

The main goal of the current work was to achieve specific binding to cancer cells. The HER2 receptor was chosen as a surface tumor marker. We used two human breast cancer cell lines with different HER2 expression level: BT-474 (HER2-positive) and MDA-MB-231 (normal HER2 expression). First of all, we coated BiNPs with Si-PEG-COOH. The coating stabilized the nanoparticles in water and phosphate-buffered saline (PBS) and prevented the oxidation of the BiNPs in water. In addition, this polymer promoted the attachment of the amino group of the targeting protein. DARPin scaffold protein and Trastuzumab antibody were selected for specific binding to HER2 receptor. Additionally, we obtained bovine serum albumin modified nanoparticles as non-targeted

control. Next, we conjugated the nanoparticles with FITC for imaging and determine binding specificity using flow cytometry.

As a result, we obtained polymer-stabilized bismuth nanoparticles and successfully modified them with the targeting agents. The obtained nanoagents specifically bind to cancer cells and can be used for oncotheranostics.

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# EXPERIMENTAL AND THEORETICAL INVESTIGATION OF LASER ABLATION THRESHOLD OF POROUS SILICON WITH DIFFERENT DEGREES OF POROSITY

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Porous nanosilicon is the basic element of a new trend, silicon nanotheranostics, whose technologies are actively used in methods of personalized diagnostics and therapy [1]. The unique optical properties of nanostructured silicon, as well as biocompatibility and biodegradability, make it a promising material for use as sensitizers for various therapeutic effects or as a vehicle for drug delivery to a cancerous tumor [2, 3].

In the present work, an experimental study and molecular dynamics simulation of laser ablation of a porous silicon target under irradiation with short laser pulses were carried out in order to determine the ablation threshold at different degrees of porosity of the initial target.

The laser ablation threshold was determined for porous silicon samples with a pore size of 8 nm and a porosity of 60, 66, and 70% at a wavelength of 1030 nm and a pulse duration of 270 fs. The experiment was carried out in a wide range of laser radiation flux densities - from 0.01 to 2 J/cm$^2$ with a variable step of 0.02-0.2 J/cm$^2$. To study the effect of target porosity on the ablation threshold, we performed ablation of a crystalline silicon target at the same laser radiation parameters.

A significant decrease in the ablation threshold for porous samples compared to crystalline ones was demonstrated, which can be explained by the large two-photon absorption coefficient of a porous target compared to a bulk material.

In addition, the laser ablation threshold decreases with increasing porosity to a porosity value of 60–65%, after which it starts to rise again. This effect can be associated with a decrease in the value of two-photon absorption at higher substrate porosities.

The calculated data on the thresholds of laser ablation of porous silicon targets obtained by the molecular dynamics method are in good agreement with the experimental data.

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# FUEL CELL: APPLICATION OF VARIOUS BACTERIA AND CREATION OF NEW SYSTEMS

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One of the most developing branches of alternative energy is bioenergy, through which people can receive energy from biological systems in the form of biofuels, hydrogen and other energy carriers. A particularly interesting section in this industry is biofuel elements (BFE). A distinctive feature of these fuel cells is the use of various microorganisms in them, which in turn are capable of producing all kinds of waste products. But so far, only 2 types of bacteria (methylotrophic and acetic acid) are most often used in this developing field.

This work is devoted to the study of the vital processes of bacteria, the number of protons produced by different types of bacteria and the conditions in which bacteria will be active and viable. In order to create a new type of fuel cell with high output characteristics, reliability and long operating time. In this work, various microorganisms were investigated: acetic acid bacteria (family Acetobacteraceae); methylotrophic bacteria (family Methylococcaceae); lactic acid bacteria (family Lactobacillaceae); butyric acid bacteria (family Bacillaceae); Bifidobacteria (family Bifidobacteriaceae); yeast cells. Different nutrient media were selected for each type of microorganisms. After analyzing the culture medium, the most effective ones for bacteria were selected. Further, various models of the biofuel element regarding the vital activity of bacteria were analyzed. Various studies have also been conducted on the activity of bacteria in nutrient media and their reaction to changes in the chemical composition of media. Methylotrophic and butyric acid bacteria were the most stable for changes in conditions. A study of the number of bacteria in the strains was carried out using the spectrometry

method, as a result, yeast cells and bifidobacteria had the largest number in the strain.

As a result, it can be said that for use in a biofuel element, the most promising can be considered oily bacteria and bifidobacteria, based on their characteristics and reaction to changes in the environment. Further studies will be conducted with the biofuel element itself and the results are summarized regarding the amount of hydrogen released and the efficiency of various models of the biofuel elements themselves.

# SYNTHESIS OF IRON-BASED MAGNETIC FLUIDS AND THEIR PROPERTIES

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In this paper, a variant of magnetic fluid synthesis is considered. The method of its preparation and the results of experiments on the study of properties are given. The liquid obtained during the experiment is characterized by high stability and magnetic susceptibility, a relatively low predisposition to oxidation and an acceptable range of operating temperatures.

In modern science, a special place is occupied by the study of methods for obtaining magnetic fluids and improving their quality, all this allows to increase the overall integrity of research. The direction of development of methods for obtaining ferrofluids allows us to achieve new results both in the production of various materials and products, and in related fields of science. There is a high potential for the use of such materials in biomedicine [1]. Magnetic fluids combine fluidity and the ability to interact with a magnetic field, which allows them to carry a high potential for practical application.

The main tasks in obtaining the magnetic fluid is the general reduction in price and simplification of the algorithm for obtaining the material. At the same time, it is important to preserve its quality. For the synthesis of magnetic particles, co-deposition methods [2] and a mechanochemical method [3] are usually used, they are characterized by simplicity of execution and availability of reagents.

The following reagents were used in the study: $FeSO_4$, $FeCl_3$, ammonia 10% aqueous solution ($NH_4OH$), distilled water, oleic acid, liquid glycerin, rheopolyglucine (10% colloidal solution of dextran (glucose polymer with a molecular weight of 30,000 - 40,000) with the addition of isotonic sodium chloride solution or 5% glucose solution), isopropanol, acetic acid, kerosene.

In the course of the study, various iron-based magnetic fluid were obtained (Fig. 1). The results of experiments on the repeated conversion of dried powder into magnetic fluid were obtained. During this transition, a low percentage of material losses was visually recorded. The study demonstrated sufficiently high indicators of the operating temperature range and resistance to oxidation of the resulting material. The magnetic properties of liquids practically did not change with the change of the carrier fluid (water, glycerin, kerosene), but depended on the concentration of the filler.

Fig.1. kerosene-based magnetic fluid

In the course of experiments on the study of heat resistance, with a short-term presence of magnetic fluid at temperatures up to 50 ° C, the material with a kerosene base remained the most stable. Heating was carried out in the ES-4620 drying oven. To study the powder, the magnetic fluid was completely dried. The average time of visually noticeable oxidation of particles turned out to be quite long, without observing special conditions (moisture, temperature, etc.), its signs began to manifest more than 8 days after synthesis. In the repeated conversion of the material from powder to liquid, the losses during one transition were no

more than 15% of the initial volume, three consecutive transformations were carried out.

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# SEMANTIC SEGMENTATION AND CLASSIFICATION OF THYROID ULTRASOUND IMAGES

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Machine learning methods are widely used in various fields of human activity, including medicine [1]. Thyroid nodules are one of the most commonly diagnosed nodules in humans. Ultrasound images allow you to localize the nodules and determine the class of the disease. To solve these problems, neural network approaches are mainly used today.

In this work, to solve the problem of semantic segmentation of images two networks DeeplabV3+ [2] and the EfficientNetB6 encoder were used, the classification problem was solved by the ResNet-18. The first segmentation network provided a "rough" localization of thyroid nodules [3]. The enlarged areas with localized nodules were inputs to the second segmentation network and the classification network.

The initial dataset consisted of longitudinal and transverse sections of the thyroid ultrasound images of 80 patients and labeled masks. Data preprocessing included converting cine loops from tif format to PNG images, removing text information and black irrelevant areas, normalizing images, converting images to grayscale, resizing images and masks for input to the appropriate networks.

The segmentation quality metrics IoU (Intersection over Union), the Dice coefficient (DC) and the classification metric accuracy were used.

To build well-generalizing models an experiment was conducted to select image augmentation methods [4]. The generated set, consisting of geometric and pixel-level transformations for the training set and test-time augmentation for the test set, diversified the initial data by improving the values of metrics. This can be observed in fig. 1.

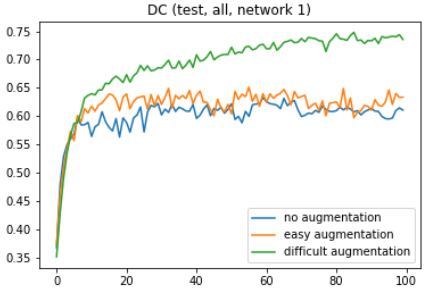


Fig.1. Graph of DC values on the test with different groups of augmentation

On the test set of images the best segmentation values were: $DC_{av.}$=83%, $IoU_{av.}$=75%, classification accuracy=85%.

Thus, models were trained to solve the problems of semantic segmentation and classification of thyroid ultrasound images, preprocessing of the dataset was implemented, and an experiment was conducted to select a variety of augmentation methods. Steps have been outlined to improve the quality indicators of the models: additional training of current models on new datasets, implementation of an approach for the localization of nodules, taking into account the sequence of images, study of other network architectures for solving these problems and assessment of the classification quality also by other metrics.

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# APPLICATION OF STATISTICAL METHODS FOR THE ANALYSIS OF RAMAN SPECTRA OF BRAIN GLIOMA

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Glioma is the most common type of brain tumors and today surgery is the main method of treatment. However, during the operation, the morphologist is forced to be guided only by visual data and his own experience. Also, due to the high invasiveness of gliomas, during surgery, the surgeon is forced to remove the preventive gap to minimize the risk of relapse. Excessive removal of healthy tissue of the patient can lead to changes in the functional work of the body due to the complexity of the human brain, and insufficient removal of tumor tissue entails a relapse of the disease, which poses a huge danger to human life, therefore, clarification and improvement of the quality of detection during surgery is an important aspect that needs to be constantly improved. Currently, a probe is being developed that uses Raman scattering of light to determine whether a tissue belongs to a tumor. To do this, it is necessary to develop a method that allows such estimates to be carried out with high accuracy. Such a probe will be indispensable for operations to remove a brain tumor.

Brain tissues were obtained during surgery to remove gliomas in patients with their voluntary informed consent after coordination of the research with the Ethics Committee of the Volga State Medical University of the Ministry of Health of the Russian Federation and the Lobachevsky National Research University (decision of the Ethics Committee of 25.06.2019, provided to the chief responsible researcher neurosurgeon MD Medyanik I.A.).

The Raman scattering method has a non-destructive effect and a sufficiently high resolution that allows the determination of tumor-affected

tissues with cellular accuracy, thus, Raman scattering is the optimal method. However, due to the extreme complexity of the spectra of cells and tissues, it is impossible to visually determine whether the spectrum is classified as tumor or healthy. Methods of statistical processing of spectra can be given for this task.

The spectra were collected using a Renishaw in Via Qontor confocal Raman microscope with an excitation wavelength of 633 nm and a sample power of 10 mW. The accumulation time for each sample was 2 seconds for each spectrum.

The method is based on studies that say that precancerous tissues contain both glioma cells and cells of healthy white matter [1]. The classification was selected for optimal separation of healthy tissues and tissues inside a dense tumor.

The spectrum under consideration was reduced to 100 $cm^{-1}$ from 2850 to 2950 $cm^{-1}$, where the highest differences between the spectra of tumor and healthy tissues are observed in the high-frequency part of the spectrum [2].

Normalization according to the min-max normalization was carried out for all spectra. Next, 2 classification models were trained: logistic regression and the support vector machine. 468 spectra of healthy tissue and 468 spectra of tissues inside a dense tumor were used for training, all spectra were taken from one patient. The accuracy for classification by logistic regression was 83,5% for healthy and 79,1% for cancer cells, and for the support vector method 89,7% and 81,3%. With the help of a trained model, it was already possible to predict the assignment of spectra b to the class of tumor and healthy. A threshold of 80% was chosen to predict the spectrum class, that is, the algorithm must be at least 80% sure of the prediction. For points that did not fall into any class, a third class was created - indefinite.

Further, maps were compiled for the spectra of precancerous tissue, predicting the assignment of each of the spectra to one of the classes. To obtain the final classification of the spectra, the predicted classes from both models that have passed the threshold we have chosen are taken.

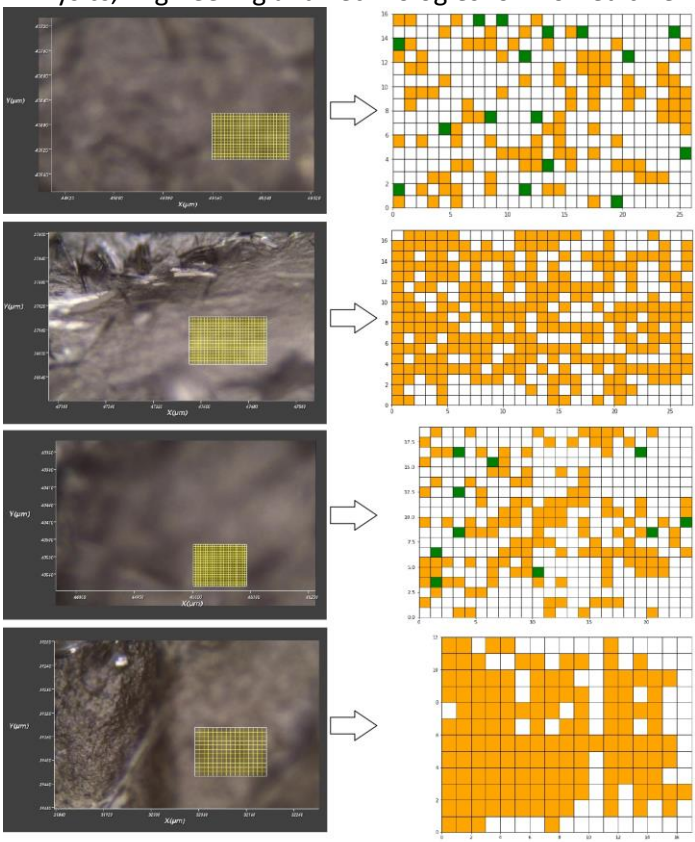

Fig.1. Maps of the precancerous area for 1 patient, taken at 4 different points. Orange points – cancer cells, green points – healthy cells and white points – indefinite cells

Then their correspondence with each other is checked, if the prediction does not match or is missing in one of the models, then the spectrum belongs to the indeterminate. As a result, only the spectra that were equally predicted by both models fall into the map of the region. The maps of the region were compiled by coordinates, which allows you to see the real display of the studied tissues. Such a map should predict the

presence and location of cancer cells in the tissues of precancerous areas.

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# STUDY OF THE COMBINED EFFECT OF FUMARIC ACID SALT AND IONIZING RADIATION ON FIBROBLASTS

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Irradiation of benign "normal" tissues during a course of therapeutic radiation can lead to a number of side effects, including acute toxicity, mild chronic symptoms, or severe organ dysfunction. [1] To reduce damage to normal tissues caused by radiation, chemotherapy is often used in combination with radiation as protection. Currently, the use of drugs with radioprotective properties is relevant.

In our work, we studied the possible radioprotective properties of the salt of fumaric acid. The evaluation of the radioprotective properties of the preparations was carried out on a culture of human fibroblasts. Cells were irradiated with Co-60 gamma rays at doses of 1 Gy, 4 Gy, 6 Gy (dose rate 0.9 Gy/min) in combination with the drug at doses of 0.05 mg/ml and 0.03 mg/ml and incubated for 10 days. After incubation, colony counts were made and survival was assessed.

The data obtained during the study are shown in Figure 1. It can be seen that with the combined effect of irradiation at a dose of 1 Gy and a fumaric acid salt at a dose of 0.05 mg/ml, their survival rate was 85%, which indicates the protective effect of this substance.

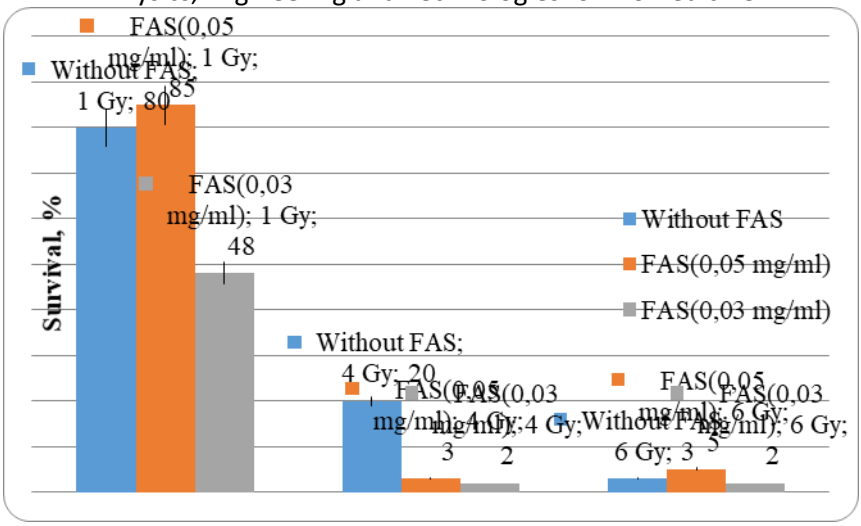


Fig.1. The effect of fumaric acid on the survival of fibroblasts, when exposed to fumaric acid salt at doses of 0.03 mg/ml and 0.05 mg/ml

The results obtained will allow further research to identify the mechanisms of action of the fumaric acid salt.

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# GADOLINIUM-DOPED CARBON DOTS FOR DUAL-MODALITY IMAGING

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Magnetic resonance imaging (MRI) is widely used for clinical diagnosis. In recent years, new MRI contrast agents with additional theranostic functionalities are widely investigated. While an optical contrast agent allows us to detect pathologies at the cellular or subcellular level, MRI contrast agents usually reveal physiological differences at the level of tissues and organs. Additional information and multimodal advantages can be obtained by using a combination of the luminescent imaging and MRI contrasting both for the diagnosis and therapy on the nanoscale, i.e. nanotheranostics.

In our work nanoparticles (NPs) based on carbon dots (CDs) and gadolinium (Gd) ions were synthesized and their properties were studied by using electron microscopy, energy dispersive X-ray spectroscopy and MRI relaxometry.

Three methods for obtaining CDs:Gd NPs were comparatively studied. In the first variant, a mixture of urea, citric acid, $GdCl_3$ was dissolved in distilled water, then conducted the synthesis in a microwave reactor (Anton Paar Monowave 450, Czech Republic) at temperature 180 $^0$C with stirring 1200 rpm for 15min (cosynthesis). In the second method, gadolinium chelate (Gd-DOTA) was used instead of gadolinium salt during cosynthesis. In the third variant, CDs were first synthesized from urea and citric acid, and then they were mixed with $GdCl_3$ and processed in the microwave reactor in the same conditions (post-modification).

Prior the structural and MRI studies the prepared NPs were cleaned by using dialysis (MWCO 500 Da) in deionized water. Then the yield kinetics were calculated and compared with the rate of Gd exit from the solution with an analogous concentration of $GdCl_3$.

The MRI relaxometry revealed an effect of the enhanced proton relaxation in aqueous solutions of CD:Gd NPs. The MRI contrast was observed for both the longitudinal (T1) and transverse (T2) relaxation times. The obtained MRI contrasting data are correlated with results on the electron microscopy, optical extinction and luminescence spectra of CD:Gd NPs.

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# LOW MOLECULAR WEIGHT SUBSTANCES DETECTION BY INTERFEROMETRIC BIOSENSORS

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In this work we optimized low molecular weight substances detection by label-free biosensor based on spectral correlation interferometry (SCI), which previously was used for autoimmune disease diagnostic [1].

As model agent of hapten for study was taken folic acid (FA). It is characterized by an artificially created analogue of natural vitamin B9 and plays an important role in fetal development and cell metabolism. The choice of this agent is a consequence of the lack of simple and convenient methods for detecting.

SCI is based on the method of using one surface of a thin plane-parallel glass chip as a reference. The changes of the optical thickness of the biolayer on the opposite surface is detected by low-coherence interferometry [2,3].

Significant abnormalities in folic acid levels in the body are known to cause a number of diseases, such as neural tube defects in newborns, cardiovascular disease, cognitive decline, depression, neuropathy, and even some types of cancer. However, folic acid levels are rarely measured in post-treatment patients with a previously identified deficiency. There is relatively sparse data on folic acid status and possible adverse effects in case of excessive folic acid intake [4]. The range of interest for measuring FA concentrations is in the range of 0.22 - 220 nmol/l relative to its physiological content.

Immediately prior to exceptional chemical modifications, microscope coverslips are washed with methanol and then treated with a mix-

ture of 30% hydrogen peroxide and 95% sulfuric acid (1:3) for 40 min at 70°C. After cooling, they are washed three times with distilled water and international methanol. Clean microscope coverslips were placed in a 3% solution of (3-aminopropyl)triethoxysilane (APTES) in methanol and left overnight at ambient temperature, washed three times with propanol-2, and dried. Cover slips with a covalently attached free aliphatic amino group are stored at temperature up to the limit of use. Cover slips with a covalently attached free aliphatic amino group were kept in 15 mmol of succinic anhydride in DMF for 2 h at ambient temperature, washed three times with DMF, dried, and stored at ambient temperature. before use.

The developed method for the design of glass biochips from large microscope coverslips with their subsequent implementation for the implementation of FA allows significant progress in methods for eliminating the content of FA both in pharmaceutical samples and significant in biological fluids. Sufficiency testing methods due to the state of natural equipment, consumables and labor-intensive technological operations.

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# CERIUM DIOXIDE NANOPARTICLES DOPING WITH RARE EARTH METAL IONS AS A WAY TO MODIFY THE BIOCATALYTIC ACTIVITY

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Nanobiotechnologies are developing actively nowadays. Nanocrystalline cerium dioxide is prospective from the biomedical applications' point of view. The crystal lattice of nanocrystalline ceria consists of oxygen vacancies and Ce3+ and Ce4+ mixed valence states. Such structure provides an ability to inactivate free radicals, namely: reactive oxygen and nitrogen species [1]. These radicals have a damaging effect on proteins, initiate lipid peroxidation, lead to the DNA damaging. Thus, organism is exposed to oxidative stress. It should be noted that in addition to studies where cerium dioxide nanoparticles exhibit antioxidant properties, there are papers where prooxidant effects are shown, also there are some papers where both these abilities are shown, namely: nanoceria can both generate and inactivate free radicals.

Doping with rare-earth metal ions leads to the oxidation degree modification and makes it possible to increase the oxygen vacancies concentration on the surface of nanoparticles [2]. Thus, doping can be considered as one of the ways to control the biocatalytic activity of nanoparticles. Many authors note that antioxidant potential increases for nanoparticles doped with different trivalent rare-earth ions, such as Europium, Erbium, Lanthanum, Samarium, Neodymium [2, 3]. At the same time there are papers indicating a decrease in antioxidant properties for nanoparticles doped with Samarium [4]. Some papers demonstrate that Samarium, Neodymium doped nanoparticles have high antibacterial activity [5]. Active oxygen vacancies of rare-earth doped nanoparticles could generate reactive oxygen species (ROS) and lead to oxidative stress and death of microorganisms.

Thus, there are fragmentary, sometimes contradictory data on the mechanism and results of doping in the literature. Therefore, this topic is significant today.

The purpose of the present work is to analyze literature data on the effect of nanoparticles' doping on their structure and multi-enzymatic activity and study peroxidase and oxidase-mimetic activity for pure samples and samples doped with trivalent rare earth elements, namely: Erbium (Er3+), Ytterbium (Yb3+), Samarium (Sm3+).

Study of doping mechanism, its effect on the different types of cerium dioxide nanoparticles activity, the dependence on the dopant ionic radius and its molar concentration will allow us to get a significant information about fine-tuning the structure of nanoparticles for a specific biomedical application.

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# GAS ANALYZER PHOTOSENSITIVITY IMPROVEMENT DUE TO DETECTOR OPTICAL AND ELECTRICAL CHARACTERISTICS LASER MODIFICATION

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Due to their high absorption in the near IR region of the spectrum and low electrical resistance, chalcogenide lead selenide films find applications in various developing fields of optics and optoelectronics [1]. The unique properties of such films also make it possible to use them for the photodetection of organic substances in the form of gases and liquids [2–4]. The study of the possibility of controlled modification of the optical and electrical characteristics of such materials is becoming increasingly popular for various applications, for example, in solar cells, photoelectric sensors, and photovoltaics [5].

Correction of the optical and electrical properties of PbSe films in most technological processes is carried out by heat treatment in an oven. This type of treatment activates the growth of a new oxide phase in the film, which leads to its clearing. It was shown that thermal sensitization in the temperature range 648–698 K can increase the photoresponse of PbSe films to IR radiation.

The process of heat treatment in an oven is difficult to control; therefore, in recent years, laser radiation has been increasingly used to modify the film in order to correct its photosensitivity. As a result of laser exposure to femtosecond pulses of laser radiation with a wavelength of 800 nm, a decrease in the refractive index of GeSbSe films by 0.02–0.08 was observed. Laser technologies make it possible to significantly simplify the conditions for modifying chalcogenide films and correct their characteristics in a narrow range of values. This possibility opens up prospects for the creation of new photosensitive elements with a wider functionality in optoelectronics. After laser processing, a decrease in the

resistance of the films by several times was observed, which is especially important for LED technology and photovoltaics.

In the presented study, the modification of the structure and optical characteristics was carried out by nanosecond laser pulses of near-IR radiation (Fig.1).

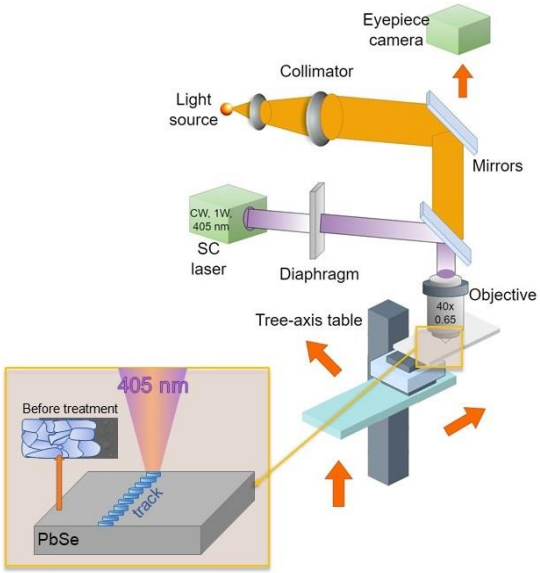


Fig. 1. Scheme of the experimental setup for laser modification of the structure of chalcogenide films

When studying the samples before and after laser exposure, an increase in absorption and a decrease in the band gap of the films were found. Further study of the mechanisms of laser modification of the structure and properties of chalcogenide films opens up possibilities for increasing the photosensitivity of sensors in devices for the analysis of organic liquids and gases.

**Acknowledgments**

The work was supported by Russian Science Foundation grant (project no. 19-79-10208).

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# RAMAN SPECTROSCOPY IN EX VIVO DIAGNOSTICS OF INTRACRANIAL TUMORS

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At the moment, there are a number of problems in neuro- that can be approached through the use of optical spectral techniques. One of these problems is the difficulty in determining the boundaries of tumors due to the peculiarities of their growth. Video-fluorescence navigation with protoporphyrin IX dye provides as high contrast between high-grade glioma and healthy tissue, but cannot detect malignant tissue in low-grade gliomas [1].

The purpose of this work was to study the differences in Raman spectra of brain tumors to determine differences in the chemical composition of tissues. The absence of the need for additional dyes is one of the advantages of this method.

The research was carried out in N.N. Burdenko Scientific and Research Center of Neurosurgery on tumor tissue samples taken during neurosurgical operations after removal.

Raman spectra of each sample were recorded in a series of 10 measurements with an exposure of 30 seconds. The background signal was measured before each series (a series of 20 measurements of 30 seconds each). The measurements were made in a darkened room.

Initial processing of Raman spectra was carried out. The spectra were averaged, smoothed with a Savitzky-Golay filter (moving window width 15 pixels, 3rd degree polynomial), background and fluorescent

signals were subtracted using the airPLS algorithm [2]. Figure 1 shows the averaged spectrum of 2 patients diagnosed with glioblastoma (WHO grade 4) and astrocytoma (WHO grade 3).

This work was supported by a Ministry of Science and Higher Education of the Russian Federation (agreement 075-15-2021-1343, October 4, 2021).

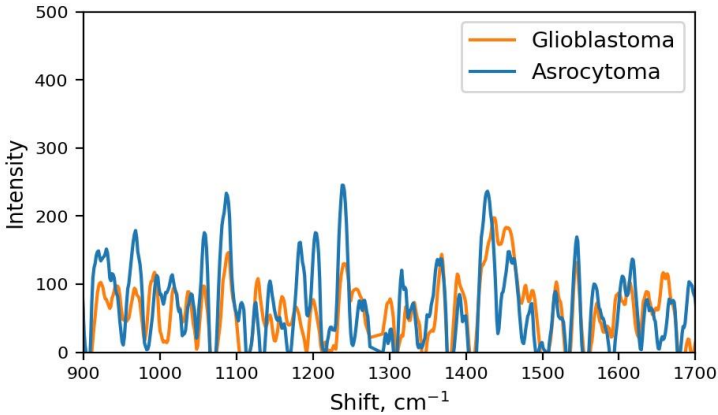


Fig. 1. Raman spectra of patients diagnosed with glioblastoma and astrocytoma

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# TEMPERATURE MONITORING OF SILICON NANOPARTICLES IN A LIQUID UNDER NANOSECOND PULSED PHOTOHEATING BY RAMAN SPECTROSCOPY

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Nanoscale forms of silicon (Si) are known to be biocompatible and biodegradable materials, so they have been studied for medical purposes including diagnostics and therapy [1]. Photoheating of silicon nanoparticles (SiNPs) was recently shown to be an efficient tool for the spatially localized hyperthermia in cancer therapy applications [2]. Our work is aimed to investigate the photoinduced heating of SiNP suspensions under cw and nanosecond pulsed laser excitation by means of the Raman spectroscopy (RS), which is highly sensitive for temperature monitoring of crystalline Si [3].

Temperature of a sample is calculated by according to the following equation:

$$\frac{I_S}{I_A} = A \exp\left(\frac{\hbar\Omega}{kT}\right), \quad (1)$$

where $I_S$ and $I_A$ are intensities of the Stokes and anti-Stokes RS lines, respectively; $A$ is a dimensionless experimentally accessible coefficient.

In our work nanocrystalline SiNPs of average size 30 nm dispersed in water/ethanol mixture were used as sample. Empirical values of $A$ were determined from RS measurements under cw laser excitation, when the heating of the sample can be controlled by direct measurements (Pt-thermometer). Then the nanosecond pulsed photoheating was studied (pulse duration ~ 20 ns). The results of suspension temperature measurements are shown in Figure 1.

With an increase in power of cw photoheating, the temperature of SiNPs rises more strongly than the temperature of ethanol, which indi-

cates that the radiation is absorbed mainly by nanoparticles and there is a dynamic equilibrium between such "absorption points" and the surrounding liquid.

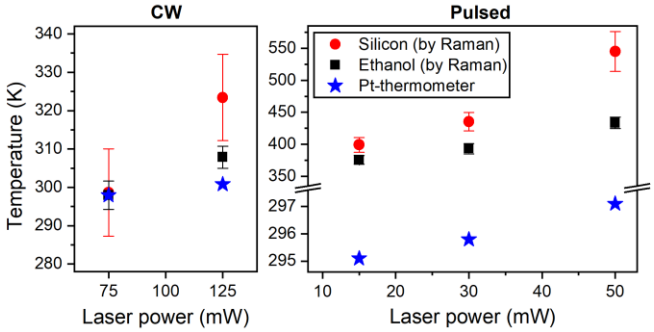


Fig.1. Temperature of SiNPs and ethanol from the Raman spectra under cw (left panel) and pulsed (right panel) excitation as well by Pt-thermometer

In the case of pulsed photoheating, SiNPs are heated to temperature significantly higher than the boiling point of the liquid in which they are located. Rapid transfer of heat from the particles to the liquid leads to short-time liquid overheating. However, the average suspension temperature measured by the thermometer (Figure 1, blue markers) turns out to be low under pulsed impact.

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# EFFECT OF UVA ON THE INFECTIVE PROPERTIES OF SARS-COV-2

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The worldwide spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first occurred in December 2019, has been recognized by the World Health Organization (WHO) as a global pandemic [1].

Like any other virus, SARS-CoV-2 is highly sensitive to UVC radiation ($\lambda < 290$ nm), since it is directly absorbed by nucleic acids (RNA, DNA) and amino acids. The bactericidal lamps such as low-pressure mercury lamps are most commonly used as sources for medical applications. Bactericidal lamps effectively disinfect surfaces, liquids and the atmosphere at $\lambda = 253$ nm. However, UVC radiation causes harm not only for pathogens but for human health as well. This is the reason why the UVC inactivation process must take place in a deserted room that is difficult to achieve in the red zone with a large number of patients.

Though nucleic and amino acids do not absorb UVB and UVA wavelengths, it is still possible to inactivate SARS-CoV-2 virions with these low-energy UV-photons if sufficiently high doses can be delivered. This fact may be explained by several photoreaction mechanisms leading to viral inactivation: strand breaks and dimers between adjacent

pyrimidine residues [2]. Thought there are few publications on UVA viral inactivation and it is still poorly understood, which mechanism is responsible for this process.

The inactivation spectra were obtained earlier [3] by irradiation of SARS-CoV-2 Delta variant (hCov-19/Russia/MOW-Moscow_PMVL-49/2021) with UVA LEDs ($\lambda$ = 385 nm). In this paper, we propose the measurements of irradiated spike and nucleocapsid proteins that has been carried out using Renishaw InVia confocal Raman microscope with wavelengths 633 nm and 785 nm. The aim of the current study is to determine whether inactivation occurs due to the structural proteins damage or RNA damage.

Understanding the fundamental causes of SARS-CoV-2 inactivation processes at UVA wavelengths will make it possible to develop new strategies for treating contaminated areas with UV radiation and visible light sources as a method for slowing the spread of SARS-CoV-2 and other pathogens.

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# CORRELATION OF METABOLIC SYNDROME MARKERS AND PARAMETERS OF UVA-INDUCED SKIN AUTOFLUORESCENCE IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

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**Relevance**: Today type 1 diabetes mellitus is one of the most common chronic diseases, and vascular complications of diabetes are among the most important medical and social problems of modern medicine. Currently, mainly invasive and expensive methods are used to assess carbohydrate metabolism in children with diabetes mellitus. Thus, clinicians need markers of carbohydrate metabolism compensation, which would allow to obtain new approaches to the diagnosis and monitoring of diabetes mellitus in children using non-invasive or minimally invasive examination methods.

**Objective**: Prediction of blood biochemical parameters by evaluating autofluorescence spectra of the forearm skin using an original compact spectrofluorimeter with UVA excitation generated by an LED (365 nm) in children with type 1 diabetes mellitus. The estimated parameters were such as age, gender, duration of disease (DD), skin phototype (PT), glycated hemoglobin (Hba1c), glucose variability (GLVAR), creatinine (CR), triglycerides (TG) and cholesterol (CL) levels in peripheral blood, urine microalbumin level (MA).

**Materials and methods**: The study focused on the assessment of autofluorescence spectra of the skin using an original compact spectrofluorimeter based on the microspectrometer STS-VIS OCEAN OPTICS © USA with UVA excitation generated by an LED (365 nm) in children aged 5-18 years with type 1 diabetes mellitus (n=50).

**Results and discussions**: Using simplified linear regression models, reference wavelengths were found that correspond to specific parameters of metabolism. (table 1) Then they were used to build regression models. The high accuracy achieved was due to the nonlinear dependence of the parameters on the fluorescence intensity up to the 5th order at these wavelengths. The best Pearson correlation coefficient r=0.96 was found for glycated hemoglobin, the lowest Pearson correlation coefficient r=0.74 was found for glucose variability, whereas in other cases, it was at least 0.8. However, due to the difference in the ratio of ranges to the average values of the parameters, the spread of the average relative prediction error varies from 4.4% (for glycated hemoglobin) up to 10% (for glucose variability). The accuracy of the model was 4.4% for glycated hemoglobin.

**Conclusions**: The approach used in this study reduces the frequency of invasive biochemical studies. The autofluorescence spectra of the forearm skin, which have been linearly standardized, demonstrate high stability of their shape. The average value of the relative variability of glycated hemoglobin was 4.4% within the specified range, whereas analytically significant changes usually occur in this range.

# STUDY OF THE COLLOIDAL STABILITY OF LASER-SYNTHESIZED GOLD NANOPARTICLES FOR BIOMEDICAL APPLICATIONS

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Capable of generating plasmonic and other effects, gold nanoparticles (AuNPs) are a promising material for biomedicine due to their biocompatibility and a favourable combination of physical and chemical properties [1]. One of unique features of the laser-synthesized NPs is high colloidal stability without using of any ligands [2]. Knowledge of the exact shelf lifetime is essential for successful application of the NPs.

In this work, the colloidal stability of laser-synthesized colloidal solutions of Au NPs obtained by pulsed laser ablation in liquids was studied in different storage conditions (temperature and external mechanical agitation). The solutions were put under following conditions: one group was kept in a thermostat at 25 °C ("heat"), another group was kept in a refrigerator at 4 °C ("cold"). Half of the samples were ultrasonicated before measurements ("shaken"), while the other half was handled very carefully ("still"). The optical extinction spectra of each solution were subsequently measured daily using the spectrophotometer for about two months. Total concertation of the metallic gold in the solution was evaluated by the value of optical extinction at 400 nm as shown in [3]. Kinetics of the size of the AuNPs was evaluated as a ratio of the optical extinction at the plasmonic peak to the optical extinction at 400 nm, as described in [4].

The results are shown in Figure 1. No significant difference was observed between "shaken" and "still" solutions. The size growth is observed in the first 5-10 days, then it stops both for "heat" and "cold" solutions. The difference in the sizes of AuNPs on the day of synthesis and after 5 days is approximately 10 nm both for "cold" and "heat" solutions (figure 1B). Also, the size of AuNPs in a colloidal solution grows only slightly more slowly at lower storage temperatures than at

room temperature (figure 1A). Therefore, we can conclude that the size of AuNPs does not depend on the storage temperature in studied range.

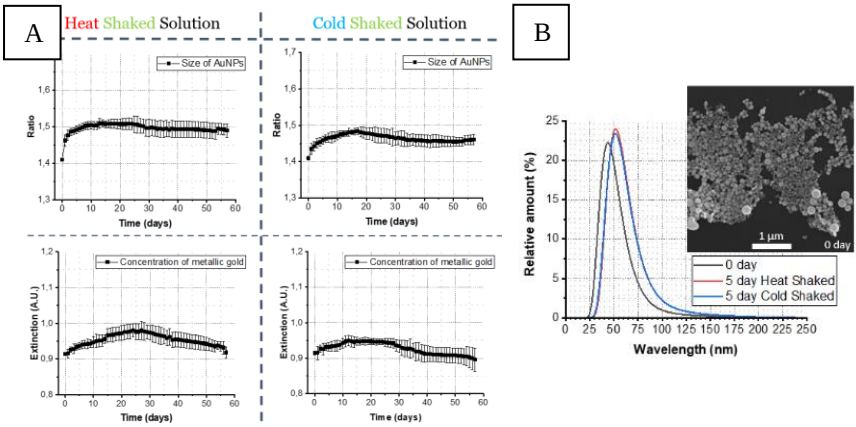


Fig.1. (A) Dependence of the size and concentration of AuNPs colloidal solutions on time; (B) Size distribution of AuNPs on the day of synthesis and after 5 days, and an insert SEM image of the AuNPs on the day of synthesis

Thus, for at least 60 days, the concentration of Au NPs does not decrease and their size remains stable within 5-6% and solutions of Au NPs keep their colloidal stability both at room and ~0°C temperature, which makes it possible to store them both ways.

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# DESIGN OF A HIGH-PERFORMANCE FLOW SYSTEM FOR THE SYNTHESIS OF TITANIUM NITRIDE NANOPARTICLES BY LASER ABLATION IN WATER

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Laser ablation in water is widely used for the synthesis of inorganic nanomaterials [1], which have found their wide application in biomedicine [2]. In a classical experimental setup, the target for laser ablation is immersed in a quartz cuvette with deionized water, but over time of synthesis the optical density of the colloidal solution increases, which reduces the efficiency of ablation due to energy dissipation both on nanoparticles and gas bubbles that formed on the target due to evaporation of water near the ablation site. Both negative factors can be minimized by applying a liquid flow and a continuous supply of clean water to the ablation zone, which can remove bubbles and reduce the concentration of nanoparticles near the ablation site.

Here we demonstrate the self-developed high-performance flow system for the synthesis of nanoparticles by femtosecond laser ablation in liquid. As a target, we selected the target of titanium nitride, a promising plasmonic nanomaterial [3] that might be used as a sensitizer in photothermal therapy of cancer. We also present the results of the synthesis productivity of titanium nitride nanoparticles in two configurations of the flow system: closed-loop and open-loop system.

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# OBTAINING SILICON OXIDE ON THE PDMS SURFACE USING FEMTOSECOND LASER ABLATION

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PDMS is one of the promising polymers used for invasive injection into the human body. An interesting task in materials science is to obtain a material conducting an electric current on the surface of PDMS, thereby creating a bioelectrode stimulating organs with current. One of the ways to obtain such a surface is the method of laser ablation, as a result of which a layer of SiC is formed.

The work consisted of research the properties of PDMS during femtosecond laser ablation in two environments were investigated: in water and in air. Pre-elastic PDMS was obtained by mixing PDMS and hardener in a mass ratio of 1: 10, after which polymerization took place at 90 ° C for an hour and a half. This ratio is optimal for creating the most flexible and durable structure of the substance. The resulting polymer was subjected to ablation using a Yb:KGW laser with a power of 108.4 MW, a frequency of 10 kHz and an ablation speed of 400 mm/s with a laser beam of 50 microns in size with a Gaussian distribution.

According to the results of the research, we established with the help of SEM that the PDMS surface contained more SiO2, which exhibits the properties of a dielectric. This compound was formed due to contact with substances in the external environment; therefore, an inert atmosphere must be used to obtain pure SiC.

So, this method can be used to create primary passivation on the surface of an already obtained semiconductor, which will make it possible to create a structure with the required semiconductor properties for creating a bioelectrode.

# DELIVERY OF NANOPARTICLES INTO THE CELL USING ISOLATED MITOCHONDRIA

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Nanoparticles are one of the promising means of theranostics of various diseases.

One of the difficulties hindering the introduction of nanomaterials into medical practice is the lack of ways to deliver them inside the cell. We have developed a new method for transporting nanoparticles inside cells using isolated mitochondria. The choice of mitochondria as a delivery tool was made due to their low immunotoxicity in vivo and their natural presence in the mammalian bloodstream.

Mitochondria were isolated from mouse liver by tissue homogenization and separation of organelles by centrifugation. All manipulations are carried out at a temperature of 4 ° C to avoid activation of phospholipases and proteases leading to organoid damage. [1]. The integrity of the isolated organelles was confirmed by scanning electron microscope.

Then the viability of isolated mitochondria was tested by measuring changes in the activity of membrane complexes of the respiratory chain. Organelles were stained with Rhodamine 123 dye, which is sensitive to changes in the membrane potential. A decrease in relative fluorescence was observed with the addition of substrates (ascorbic, glutamic, succinic, malic acids in the presence of adenosine diphosphate ADP) and an increase with the addition of membrane complex inhibitors (FCCP, rotenone) [2]. The above indicates the viability of isolated mitochondria and the absence of their significant damage during isolation.

Also, the possibility of delivering nanoparticles on the surface of mitochondria into cells in vitro was tested. The mitochondria were dyed with fluorescent nanoparticles, the excess of which was removed by centrifugation, and incubated with mouse epithelium cells and human tumor cells. Confocal microscopy in the dynamic showed the active penetration of the mitochondrial complex with nanoparticles into the cells.

The next step was the selection of nanoparticles to cover isolated mitochondria. Since the zeta potential of mitochondria is negative, the zeta potential of nanoparticles must be positive for better stability of the system. Nanoparticles from a copolymer of lactic and glycolic acids (PLGA) modified with chitosan were selected as particles. PLGA nanoparticles synthesized by the emulsion method.

Currently, work is underway to introduce fluorescent dyes inside the PLGA. By changing the intensity of blood plasma fluorescence, it is possible to judge the circulation in the bloodstream of mitochondria coated with nanoparticles, as well as their distribution to organs.

Thus, it has been shown that coating isolated mitochondria with nanoparticles is a novel tool for delivering nanomaterials inside cells. The presented method makes it possible to deliver the drug intracellularly, which significantly reduces the drug load on the body and the probability of side effects of the treatment.

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# OPTIMIZATION OF MAGNETIC IMMUNOASSAY FOR ULTRASENSITIVE DETECTION OF ZEARALENONE IN FOOD SAMPLES

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Currently, detection of xenoestrogens is a valuable problem in the food safety control. Zearalenone (ZEA) is a one of the major toxins with xenoestrogen activity, and it could be found in cereals and other common meals. Even despite the fact that there are some immunoassay platforms which were designed for ZEA detection, the problem of making both sensitive and rapid test is still needs to be solved. Here we show our approach to test system optimization for high-sensitive detection of zearalenone.

Xenoestrogen is a class of chemicals which have hormone-like properties and can induce the same response in human cells as sex hormones do. There are some evidences that zearalenone – mycotoxin with xenoestrogen activity, what can be found in food, especially in cereals, – can have an effect on hormone systems of animals and directly on humans [1]. For this reason, detection of zearalenone and its derivatives is a big problem in the food safety inspection. Here we show the process of optimization of high-sensitive immunoassay based on magnetic particles quantification method.

In this work commercially available spherical magnetic beads (size of about 200 nm) were used as the nanolabels of immunochemical reactions. The following steps were used for magnetic nanoparticle functionalization. Firstly, 3 μL of nanobeads were dispersed in 50 μL of MES buffer solution (pH = 5.0). 5 mg of EDC (Thermo Fisher, USA) were added to obtain a molar excess of carbodiimide over the amount of

nanoparticles present. After 1-hour incubation nanoparticles were washed 3 times with water. Solution of monoclonal antibodies against zearalenone was added to the nanoparticles. Within 3 hours of incubation nanoparticles were washed 3 times with water. After that, blocking buffer solution of BSA in PBS (3 μL, 10%) was added to the sample and was incubated for 1 hour in a horizontal shaker. Finally, nanoparticles were washed 3 times with water again. Prepared nanoparticles were used with samples containing known concentrations of zearalenone to construct a calibration plot. Detection of nanolabels was provided with a magnetic particles quantification method (MPQ) by registration of their nonlinear remagnetization at combinatorial frequencies [2].

Samples with different dilutions of antibodies to zearalenone were prepared for system optimization. Lateral flow assay strips with BSA-ZEA conjugate test-line were used to compare prepared nanolabels in terms of magnetic signal distribution.

Magnetic beads' surface was studied to investigate the optimal adsorption conditions by using two types of antibodies at one time. Magnetic nanoparticles were coated with two types of antibodies: anti-zearalenone antibodies and unspecific biomolecules (anti folic acid antibodies) were used to define the effects which orientation and dilution of antibodies to small molecules have on observed signal distribution. These two experimental series provided the basis of developed high-sensitive ZEA assay. The achieved limit of detection is one to two orders better than commercially available ELISA kits and the dynamic range of test system exceeds 3 orders of magnitude.

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# SPECIFIC ABSORPTION RATE OF ELONGATED MAGNETIC NANOPARTICLES CHAINS

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Magnetic nanoparticles are promising for using in biomedicine applications. Among them, magnetic hyperthermia is a promising direction for the treatment of cancer. This is a form of thermal therapy in which magnetic nanoparticles produce high temperatures in cancer centre in the presence of an alternating magnetic field [1].

The heating ability of magnetic nanoparticles assembly is characterized by the specific absorption rate (SAR). SAR depends on various magnetic and geometric parameters of nanoparticles assembly. Recent experimental data [2] have shown that elongated magnetic nanoparticles have high SAR values. Also found in nature are magnetotactic bacteria that grow chains of elongated nanoparticles inside themselves (Fig.1a) [3].

In this work, using numerical simulation of the stochastic Landau-Lifshitz equation, we studied the SAR dependence of chains of elongated magnetite nanoparticles on the geometric parameters of the chain, such as aspect ratio in particles, distance between particles in the chain, particle diameter.

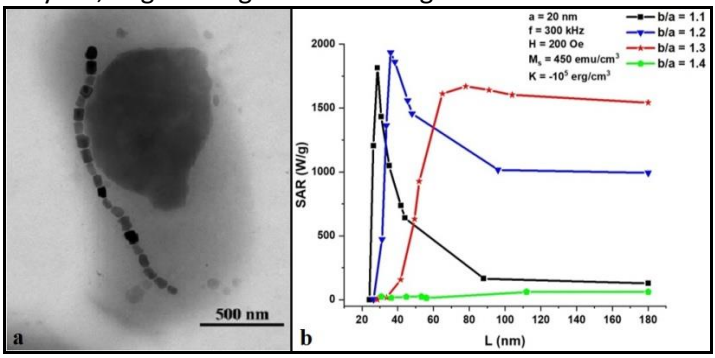


Fig.1 a) Cell of strain SS-5; b) SAR dependence of non-interacting assemblies of chains of elongated magnetite nanoparticles with a minor semiaxis $a$ = 20 nm on the distance between particles in the chain $L$ for various aspect ratios in particles: 1) $b/a$ = 1.1; 2) $b/a$ = 1.2; 3) $b/a$ = 1.3; 4) $b/a$ = 1.4

As shown in Fig. 1b for the case of aspect ratios $b/a$ = 1.1-1.3, a sharp increase of SAR on the distance between particles in a chain is seen with a pronounced maximum. For particles with an aspect ratio $b/a$ = 1.4, an increase in the distance between particles leads to a slow increase in SAR.

The study was supported by a grant from the Ministry of Science and Higher Education of the Russian Federation, topic number FSWU-2020-0035.

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# SIMULTANEOUS ENCAPSULATION OF DOXORUBICIN AND VORINOSTAT IN POLYMERIC NANOPARTICLES FOR THE BREAST CANCER THERAPY

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Breast cancer is a complex disease whose treatment is complicated by the emergence of multidrug resistance, which reduces the effectiveness of therapy. Choosing the most effective therapy and overcoming multidrug resistance is critical for the treatment of cancer, including breast cancer. To overcome resistance, combination therapy and drug delivery systems can be used. In phase I trial Munster et al. reported doxorubicin (DOX) and vorinostat (SAHA) can be safely combined and are promising in treatment of solid tumors [1]. Vorinostat is a histone deacetylase inhibitor (HDACi), an effective anticancer agent approved by the FDA for the treatment of T-cell lymphoma. The HDACi can increase the cytotoxicity of anthracycline-type topoisomerase II inhibitors such as doxorubicin [2]. Nanocarriers (e.g., PLGA nanoparticles) have the advantage of local drug release in tumors, which can overcome multidrug resistance, as well as significantly reduce effective doses, improve drugs bioavailability [3]. The goal of this work is developing a technology for producing PLGA nanoparticles containing SAHA and DOX for breast cancer therapy.

For further development of PLGA nanoparticles containing doxorubicin and vorinostat, PLGA nanoparticles containing vorinostat (SAHA-NP) were obtained by double emulsion using the Box-Behnken Design (BBD). To optimize the nanoformulation, a 12-run, three-factor, three-level BBD was employed. Factors investigated were the amount of PLGA (X1), the ratio of the aqueous and organic phases $W_1/O$ (X2) and the concentration of PVA (X3). The nanoparticles obtained using the

optimized method had a size of 253±33 nm and a drug loading of 0.56 %.

A high-performance liquid chromatography (HPLC) method was also developed for simultaneous determination vorinostat and doxorubicin encapsulated into polymeric nanoparticles using the Box-Behnken design. The separation was performed using a Nucleodur C-18 Gravity column (250 mm × 4.6 mm × 5 μm). Three independent variables were analyzed to determine the most optimal conditions: methanol concentration (0-20%), pH (2.5-4.5) and flow rate (0.8 -1.2 mL /min). The developed method is suitable for analysis nanoparticles containing doxorubicin and vorinostat, including the analysis of impurities.

Thus, SAHA-NP were synthesized, and a method for simultaneous determination of DOX and SAHA encapsulated into polymeric nanoparticles by HPLC was developed. The data obtained are significant and relevant for the development of PLGA nanoparticles containing DOX and SAHA for safe and promising breast cancer therapy.

This study was supported by the Russian Science Foundation research grant No. 22-25-00293, https://rscf.ru/project/22-25-00293/

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# POLYMER COATING METHOD DEVELOPMENT AND BIOLOGOCAL CHARACTERIZATION OF PROSPECTIVE LASER-ABLATED NANOPARTICLES

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Since the beginning of XXI century rapidly developing nanotechnologies have become widely applied in biomedicine as biosensors, contrast agents for computer tomography [1], target drug carriers for gastrointestinal diseases, bacterial and fungal infections therapies [2], for various cancer tumors, malaria, and schizophrenia treatment [3]. Nowadays one of most essential aim for nanotechnologists is to prolong circulation time of administered into the blood nanoparticles (NPs).

The main barrier for particles movement is mononuclear phagocytes system, which on the one hand provides a protective mechanism by filtering the bloodstream from foreign pathogens, but on the other hand eliminates therapeutic NPs. Modification of the particles surface properties can significantly increase the circulation time, provide controlled and sustained release, and affect the pharmacokinetics, stability, and functionality of nanoparticles in the medium. Biodegradable polymers are considered to be the most popular compounds for a given purpose. Choice of a particular polymer for coating determines the characteristics of the particles [4]. Successfully coated particles are used for in vivo and in vitro tests leading up to clinical trials [5].

This paper presents the results of laser-ablated [6] TiN nanoparticles coating with a Poly(acrylic acid), Mw = 5100 and Mw = 2100; Poly(styrene sulfonic acid), Mw = 300 000; Poly(sodium 4-styrenesulfonate), Mw = 70 000; Poly(vinyl pyrrolidone), Mw = 1 300 000; Poly(vinyl pyrrolidone), Mw = 58; Poly(ethylene gly-

col), Mw = 4000; mPEG-Silane, Mw = 5000 и mPEG-SH Mw = 5000 and Ta nanoparticles coating with mPEG-Silane, Mw = 5000. TiN and Ta targets were ablated by Yb:KGW laser (TETA 10, wavelength 1030 nm, pulse duration 270 fs, Avesta, Russia) focused via plane-field (F-theta) objective. Samples characterization was carried on Zetasizer ZS, (Malvern Instruments, France), spectrophotometer ML 122 (SOL Instruments, Belarus) and scanning electron microscope MAIA 3 (Tescan, Czechia). The stability of the coatings in biological media was compared with Au NPs coatings, for which a universal protocol of PEGylation and method for estimating the size and concentration of particles by the spectrophotometry were developed [7].

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# INVESTIGATION OF THE POSSIBILITY OF FRACTAL TEXTURE FEATURES APPLICATION FOR CLASSIFICATION OF BONE MARROW CELLS

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One of the key stages in the diagnosis of acute leukemia is morphological research of bone marrow cell preparations using light microscopy. At this stage, the ratio of cells in various stages of hematopoiesis, which differ in many parameters, including shape and texture of the nucleus, is evaluated. Due to this difference, textural analysis capabilities can be applied to classify cells of different types. Currently, there are a significant number of approaches for texture features calculation: statistical methods, and methods based on image transformations. But not all of the available methods are used in the diagnosis of acute leukemia. The most common are texture features based on the image histogram, co-occurrence matrix, run length matrix and wavelet decomposition [1]. Among the promising methods that have not yet been used to classify cells of various stages of hematopoiesis are fractal textural features.

The purpose of the work is to estimate the possibility of fractal texture features application for the classification of bone marrow cells.

One of the fast and efficient algorithms of fractal texture features extraction is described in the articles [2] and [3]. The first stage is binary decomposition, then the border finding and, at the final stage, the fractal dimension calculation using the box counting algorithm. Many different methods are used for binarization. For example, in the article [2] the usual binarization with one threshold was used, and in the article [3] the two-threshold binarization was used. In the article [4], the fractal dimension of the chromatin of the cell nucleus was calculated by several methods: the fractal dimension of the pseudo-three-dimensional image of the cell was calculated, and the Otsu algorithm was used for binariza-

tion of the two-dimensional one. This approach allows to calculate only a few features, so it will not give efficient results in machine learning classification methods.

The proposed approach to fractal features extraction is the same as in the articles [2-3], but using several different binarization algorithms: two-threshold binarization and adaptive mean and Gaussian threshold binarization. According to the results of experimental studies, it has been shown that two-threshold binarization is the least effective for separating cells of various types.

The texture and shape of the nucleus of cells of different types vary greatly. Cells in earlier stages have a rounded nucleus and a fine texture, whereas more differentiated cells have a more complex typical shape and a coarser texture with large elements. Based on this assumption, it is possible to obtain a set of images containing elements of different scales by choosing a suitable binarization method. Consequently, due to the fact that the fractal dimension reflects the complexity of the boundaries, the proposed method makes it possible to classify cells with different texture scales.

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# ANTIBACTERIAL EFFECT OF ACOUSTIC CAVITATION PROMOTED BY MESOPOSOUS SILICON NANOPARTICLES

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Several types of nanoparticles ($TiO_2$, ZnO, Au, Ag) have been investigated as antibacterial agents [1]. They can cause oxidative stress, electrostatic interaction, and disruption of membrane integrity. Biocompatible and biodegradable mesoporous silicon nanoparticles (m-PSi NPs) can provide bright photoluminesce and generate ROS under UV excitation [2]. Ultrasound (US) being low-invasive and high-penetrative is widely used in medicine and could stand as an external trigger for the activation of m-PSi NPs [3]. The observed sonosensitizing effect manifests in the form of enhanced absorption of US energy followed by local heating and acoustic cavitation leading to high-energy bubble collapse [4]. The above phenomena of combined action of m-PSi NPs and US were studied both *in vitro* and *in vivo* for the inhibition of cancer cell proliferation and tumor growth [5]. In the current research the sonosensitizing properties of m-PSi NPs were applied against the colony-forming ability of bacteria.

M-PSi NPs with mean size 100–200 nm and concentration 0.5–1.5 g/L were synthesized by the process of electrochemical etching of crystalline silicon and subsequent high-energy ball milling of PSi layers in water. The pores on m-PSi NPs' surface entrap nanoscale air nuclei, which grow up to submicron bubbles of resonant sizes when irradiated with ultrasound of frequency 0.88 MHz and intensity 1–4 W/cm$^2$. An original acoustic setup recorded the dynamics of f/2 subharmonic magnitude in samples, the squared temporal integral of which is a measure of cavitation energy released in the system. Such cavitation index appeared to be 2–5 times higher for the suspensions of m-PSi NPs at various concentrations as compared to pure water (Fig. 1a). The detected

thresholds of US intensity necessary for the cavitation inception appeared to be lowered in the suspensions as well. The antibacterial effect of combined action of US and m-PSi NPs caused by enhanced cavitation was observed as a dramatic decrease of bacterial viability down to 5–30 % after 20 min of irradiation. At a microscale, this effect is due to sonoporation from jets produced by collapsing air bubbles in the vicinity of bacteria membranes (Fig. 1b), which turns off the ability of bacteria to form new colonies.

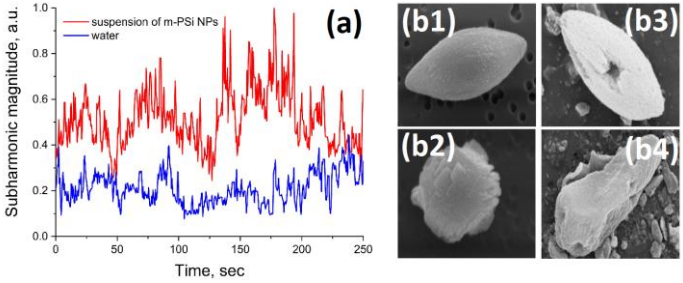


Fig.1. f/2 subharmonic magnitude in water and a 1 g/L suspension of m-PSi NPs vs. time of exposure to the ultrasound (a). Microscopic images of *Lactobacillus casei*: as-grown (b1), after exposure to ultrasound (b2), after exposure to ultrasound in the presence of m-PSi NPs (b3-4).

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# LASER SYNTHESIS OF COLLOIDAL TITANIUM CARBIDE NANOPARTICLES FOR BIOMEDICAL APPLICATIONS

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Laser ablation in a liquid is a relatively simple physical method for the synthesis of colloidal solutions of nanoparticles (NPs), offering a unique level of purity of the obtained nanomaterials. This method originated in the last decade of the 20th century and is currently used to synthesize a wide range of nanomaterials used in various applications, including biomedicine.

Hyperthermia, as a method of thermal damage to biological tissues, has been known since ancient times, however, with the advent of laser systems and the development of nanotechnology, it has received a new development. During hyperthermia, the tissue is heated to a temperature 41-47 °C. Nanoparticles are used to improve the process of laser hyperthermia. Nanoparticles selectively accumulate in the pathological focus, including tumors, absorb laser radiation and thereby enhance laser heating. [1]

This poster presents a scheme for the synthesis of titanium carbide ($Ti_3C_2$) particles. This complex of nanoparticles has also been studied in detail. Figure 1 demonstrates the heating trend of nanoparticles.

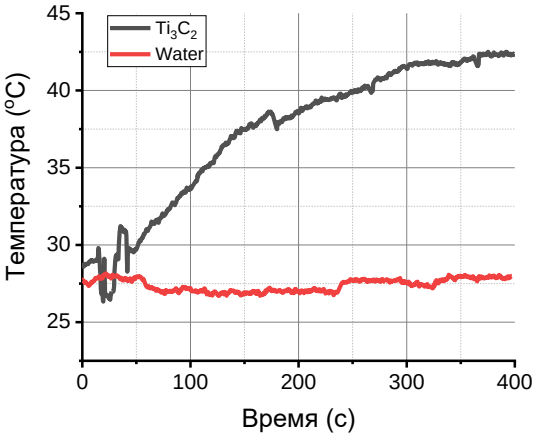


Fig.1. Heating of $Ti_3C_2$ nanoparticles for 6 minutes.
Concentration 0.2 g/l

It can be seen from the picture that the nanoparticles are heated from 26 to 43 °C, what is the temperature of protein denaturation.

Studies were also conducted to test the cytotoxicity of the material. This experiment showed very good characteristics of the material as biocompatible, since titanium carbide practically did not cause cell death. When heated, these particles caused intense cell death.

Summarizing all the above, the complex of titanium carbide nanoparticles, which presented in the work, is excellently heated in the biological transparency window and does not cause cell death by itself. From this way we can conclude that titanium carbide is a promising agent for oncology hyperthermia.

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# DEPENDENCE OF THE PERFORMANCE QUALITY OF NEURAL NETWORKS ON THE CHARACTERISTICS OF TRAINING DATA WHEN WORKING WITH THYROID ULTRASOUND IMAGES

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In recent years, deep neural network architectures have provided unique opportunities and significant breakthroughs in solving problems in various fields [1]. In clinical medicine, computer diagnostic systems based on deep learning have been shown to provide competitive and sometimes even superior diagnostic accuracy and efficiency compared to experienced clinicians [2], [3], [4], [5].

One of the important problems in the application of deep architectures in medicine is the selection of significant volumes of training datasets. Since most clinics have limited data sets, the impact of different sampling approaches needs to be analyzed.

The paper investigates the effectiveness of various training sample manipulations using deep neural network architectures for image segmentation and object detection in medical imaging on the example YOLOv5 and DeepLabV3 architectures.

**Network training process**

For the experiments, 261 video loops of 166 patients' thyroid ultrasound examinations were used. These video loops were recorded on LogiqE and GE Voluson E8 ultrasound machines.

During the experiment, YOLOv5 and DeepLabV3 network models were trained on the images provided.

Fifteen datasets were used to train YOLOv5. Datasets were divided into 3 main categories: cross-sectional images, longitudinal images, and all images. There were 5 sets of each category using different number of

images. For DeepLabV3 training, 6 sets of images were compiled by number of images in each.

**Results**

Based on the results shown in the graphs (Fig. 1 and Fig. 2), the number of shots does not affect the learning outcomes. Differences in metrics are less than 10%. At the same time, the best result was shown by networks when training on transverse projections of ultrasound of the thyroid gland. At the same time, when training on every 32nd snapshot, Loss metric starts to converge more slowly during testing. However, due to the small amount of data during training, the model retrains faster.

Based on the results obtained during model validation and testing, as well as metrics analysis during training, it was found that the quality of learning is almost unaffected by the over-abundance of uniform data. When training such deep architectures, it is necessary to have a large amount of unique and qualitative data. To summarize, it can be concluded that similar images (images of the same projection of the same patient) cannot be used as independent data. To improve the quality performance of deep architectures, it is necessary to expand the sample by increasing the number of patients.

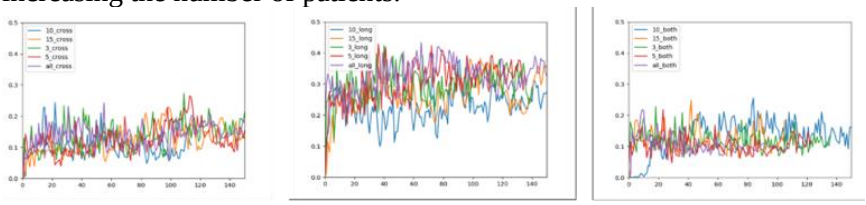


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Fig. 1. Diagrams of the mAP-0.5 metric in the process of model training: a) models with training on longitudinal images; b) models with training on cross-sectional images; c) models with training on all images

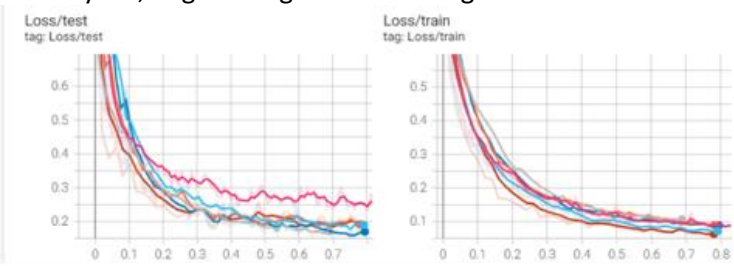


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Fig. 2. Diagrams of the Loss metric during training and when testing models: a) Loss when testing models; b) Loss when training models

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# PROPERTIES OF SILICON AND GERMANIUM NANOPARTICLES SYNTHETIZED IN GAS

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The paper compares research data on silicon and germanium. Nanoparticles were synthesized by pulsed laser deposition in a gaseous medium in the form of films on a silicon substrate. We evacuated air from the chamber up to $10^{-7}$ Torr and let in buffer gases. Various proportions of gases were provided during deposition. The sputtered target was rotated to reduce the impact of laser radiation on the same point and irradiated in the experiments. The material was deposited on a substrate located 2 cm from the target. During the action of thousands of laser pulses in the process of pulsed laser ablation, nanostructured films with a thickness of ~1 μm were formed.

Scanning electron microscopy, X-ray analysis, and Ramon spectroscopy were also used to determine the structural, elemental, and phase composition of the films. The content of germanium crystals in the film samples was revealed from the obtained data. The results, which were obtained by Raman spectroscopy, indicate that germanium nanograins are formed by crystals, and also that the particles have a less structured shape and a greater tendency to conglomerate and their size is 1 micron. It can be seen that silicon obtained in this way differs in its structure from germanium nanoparticles. The particles have a more structured shape and are less prone to agglomeration. For all Ge samples on the Si substrate, a broad photoluminescence excited at 350 nm was observed. It can be seen from the spectra that the gas pressure does not affect the photoluminescence wavelength of the samples, but does affect the emission intensity. All samples have a pronounced emission peak centered at

430 nm. There is a tendency for the intensity to increase with increasing helium pressure in the gaseous medium. When nitrogen is added, the intensity drops. Silicon nanoparticles obtained under similar conditions have a more significant spread in the spectra associated with the deposition conditions, which is explained by nitrogen passivation of silicon nanocrystals and is associated with radiative transitions between electronic states in amorphous silicon oxynitride, which is formed on the surface of silicon nanocrystals. The spectra are presented under the same gas evacuation conditions. The comparison clearly shows the differences in fluorescence. Germanium has a more intense PL line, with a peak in the blue spectrum, while silicon has a peak in the red zone.

After that, the particles were dissolved in a suspension, which was obtained as follows: the film was mechanically scraped off, placed in a test tube filled with 96% ethanol, and sonicated for half an hour. Suspensions were examined for structural, elemental and phase composition using methods such as scanning electron microscopy (SEM), X-ray diffraction analysis, Raman spectroscopy, with special attention paid to photo luminescent properties. The luminescence spectra of suspension samples are presented. The difficulty with the measurements was that the suspension quickly spread and dried on a metal substrate, and a sufficient number of particles was achieved by repeating the process many times. At the same time, there were still critically few of them for measuring optical properties. The result was obtained in the course of long attempts to aim a laser beam at a cluster of particles. A comparative analysis of the results obtained for silicon and germanium is carried out.

This scientific work was experimental in nature. The comparison of germanium and silicon particles was of great importance.

# BIOMEDICAL APPLICATIONS OF CERAMIC-BASED SOLID-STATE LASERS

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Currently, various technical problems can be solved with the help of laser technology. The most interesting and difficult object to which lasers are applicable are biological objects. Biotechnologies with the use of laser technology and laser systems directly relate to the solution of a large number of global problems on the planet Earth, such as environmental protection, cancer, human immunodeficiency virus and others. Within the framework of biotechnology with the use of laser technologies and laser systems, a large number of issues are dealt with, but three main ones can be distinguished:

- Laser diagnostics,
- Laser surgery and destruction of biological tissues,
- Laser therapy.

Solid state lasers find their application in various kinds of applications such as micromachining in the semiconductor industry, heavy and metal industries, and medicine. Today, ceramic lasers are among the fastest growing research and development areas for solid state lasers. Polycrystalline ceramics includes many single-crystal grains ranging in size from 10 to 100 microns, separated by thin boundaries. To date, samples made on the basis of ceramics make it possible to obtain an output power of a solid-state laser of more than 100 kW in a quasi-continuous mode with semiconductor diode pumping [1]. At the present time, there is great interest in obtaining highly transparent ceramics of yttrium oxide and yttrium aluminum garnet doped with Nd3+ or Yb3+ ions. The mechanism of action of laser radiation on biological determines the wavelength of laser radiation. Dermatology, for example, is in dire need of safe treatments that do not cause allergies and side effects.

The laser is therefore attractive in this scientific field of application. As an example, physicians use 1.064 μm laser radiation to remove pigmentation on the skin, and 0.532 μm laser radiation removes pigmentation on the epidermis. That is why it is very important to create and study solid-state lasers in this region of the spectrum with a long service life and stable characteristics.

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# ENZYMATIC BIOFUEL CELL OPERATED IN BLOOD MIMICKING SOLUTION

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Implantable medical devices (IMDs) could replace some functions of the organism in nonfunctioning parts of body. Active IMDs convert the energy of a power supply into a work of insulin pumps, pacemakers, neurostimulators, and so on. [1] The problem of traditional energy supplies is connected with their tendency to discharge. Also, they are bulky and non-biocompatible. In contrast, enzymatic biofuel cells (EBFCs) have large resources of fuel produced by the organism itself and also provide high efficiency of energy transmission. The functioning of EBFC is based on the principle of converting chemical energy directly into electrical energy using biocatalysts such as enzymes. [2] We have elaborated a micro-sized EBFC which used glucose oxidase (GOx) as a catalyst. Carbon fibers were chosen as an electrodes material. It has high electrical conductivity, chemical stability, biocompatibility, and a highly specific surface. [3] That's why carbon commonly uses in biofuel cells to immobilize additional linking components to increase power. A composite bioanode was covered by layers of multi-walled carbon nanotubes (MWCNTs), insoluble mediators, GOx, and linking chemicals. The coverage of MWCNTs provided an increase in the contact area between the substrate and the enzyme, which influenced the total power density. Insoluble mediators facilitated the transfer of electrons from the solution to the electrode. [4] Linking chemicals made the bioanode more stable. A highly efficient cathode was produced with Pt nanoparticles and electroconductive polymer (PEDOT:PSS) as a catalyst. The already made micro-EBFC was dipped in blood-mimicking buffer (BMB) to demonstrate the device's operation in near-physiological conditions of

blood plasma (Figure 1). The open circuit voltage of micro-EBFC in BMB was 0.12 V. The power generated by one cell was ~ 0,6 μW.

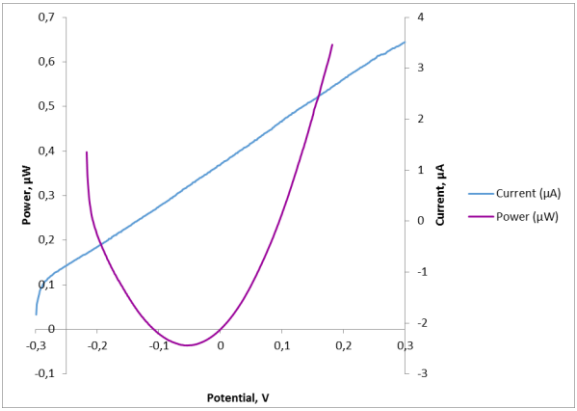


Fig.1. Linear polarization and power generated by EBFC in the presence of 5 mM glucose in blood mimicking buffer at a scan rate of 1 mV/s with OCV=0,12 V

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# CHONDROMALACIA PATELLA DIAGNOSTICS AFTER LATERAL PATELLAR DISLOCATION USING T2 MAPPING

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**Purpose.** Chondromalacia is a pathology of the patella cartilage that often occurs after lateral patellar dislocation (LPD). The aim of the study is to examine short-term consequences of the first-time LPD on patellar cartilage condition in teenagers using T2 mapping.

**Materials and Methods**. The study includes 77 patients (15.1 ± 1.8 years) with different stages of chondromalacia caused by first time LPD and 48 healthy volunteers (14.7 ± 2.2 years). All research participants underwent MRI including T2 mapping (TSE, 6 TE from 13 to 78ms, voxel size 0.4×0.4×3 mm). T2 values were calculated in manually segmented cartilage area via averaging over three middle level slices in 6 cartilage regions: deep, intermediate, superficial layers and medial, lateral parts (Fig.1).

**Results.** In the lateral part of the cartilage, an increase in T2 values was found for both the mild and severe chondromalacia group in the deep and intermediate layers compared to the control group. In the medial part, an increase in T2 values is observed only for the severe group in the deep layer, while T2 in the mild chondromalacia group either doesn't change (deep and intermediate layers) or decreases (superficial layer).

**Conclusion.** The study showed a principal difference in T2 changes between medial and lateral cartilage facet. Although the medial part

usually suffers first after LPD, the absence of T2 changes for the mild group may indicate completed reparative processes, while the decrease in T2 indicates that the reparation is still ongoing [1]. Elevated T2 in the lateral part are a sign of metabolic problems [2] and increased load due to medial patellofemoral ligament injury [3].

This work is supported by RSF 21-75-00068 grant.

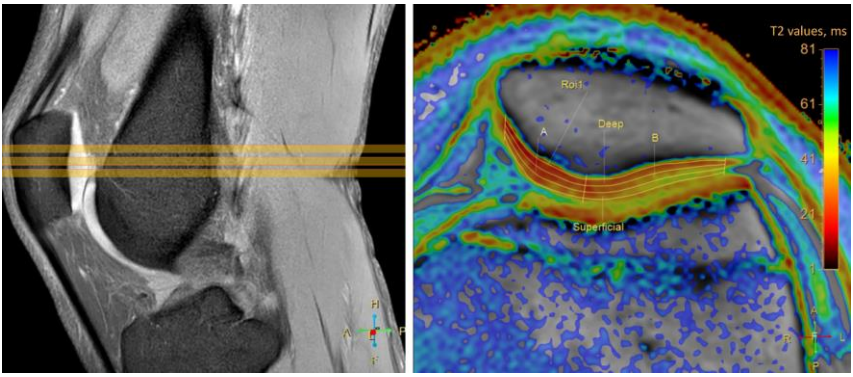


Fig. 1. Position of the three axial slices in the middle level of the patellar cartilage (left); An example of a T2 map of the patella cartilage (right)

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# STUDY OF THE CYTOTOXIC EFFECT OF THE DRUG «DALARGIN» ON NORMAL HUMAN CELLS USING THE MTT TEST

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There is a slow but steady growth of oncological diseases in the world. Among modern technologies for the treatment of tumors, radiation therapy occupies one of the leading places in oncology. The success of using radiation treatment methods depends not only on the level of technical equipment of oncological institutions, but also on the ability to preserve the anatomical and functional ability of irradiated normal tissues, since ionizing radiation has a damaging effect not only on tumor cells, but also on healthy ones located near the tumor [1]. In this regard, a promising direction of modern radiobiology is the development of new ways to increase the radioresistance of healthy tissues to the action of ionizing radiation during radiation therapy of oncological diseases.

A promising compound that can act as a radioprotector is «Dalargin». This substance is able to activate repair processes in cells and has antioxidant properties.

Thus, the aim of the work is to study the cytotoxic effect of the drug «Dalargin» on normal human cells using an MTT-test.

The human fibroblast cell culture (hTERT) was chosen as the object of the study. Cultivation was carried out according to the standard method. Cell survival was assessed using the standard MTT-test method. Various concentrations of «Dalargin» were added to the hTERT cell culture by by titration (100, 50, 25, 12.5, 6.25, 3.12 and 1.56 micromole).

The survival rate of fibroblast cells in the lowest concentration of «Dalargin» (1.56 micromoles) is 91%, and in the highest concentration (1000 micromoles) – 36%. In the interval between the highest and lowest concentrations, there is a gradual decrease in cell survival with an increase in the concentration of «Dalargin».

Thus, it has been shown that the drug «Dalargin» in the concentration range of 1.56–25 micromoles do not have a toxic effect on human fibroblast cells. In high concentrations (50-1000 micromoles), «Dalargin» has a negative effect on fibroblast cells. The first stage of the study of a compound that could potentially have radioprotective properties was performed. This provides the basis for the next stage of research to study the possible radioprotective properties of «Dalargin» in the concentration range of 1.56–25 micromoles.

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# THE STUDY OF THE OPTICAL PROPERTIES OF NANOCOMPLEXES BASED ON $AgInS_2$/ZnS QUANTUM DOTS AND ALUMINUM PHTHALOCYANINE PHOTOSENSITIZER

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The development of new photosensitizers is one of the most important tasks to improve the efficiency of both laser-induced diagnostics and therapy. In addition, one of the most interesting areas is the use of QDs either as the main marker in bioimaging or as an energy donor [1]. In our investigation, we conjugated PS with AIS/ZnS triple quantum dots. It was shown that in the complexes of PS with QDs does not change the PS fluorescence lifetime, which is a marker of the preservation photophysical properties of PS. In particular, efficient resonant Förster energy transfer from QDs to PS molecules in the complexes increases the PS luminescence response (Figure 1). The FRET from QD to PS molecules with different ratios of donor and acceptors are shown. It has been demonstrated that the average efficiency of FRET depends on the ratio of PS and QD and reaches a maximum value of 80% at a ratio of 6 PS molecules per 1 QD molecule (Table 1). Thus, these studies could help to contribute to the development of new complexes based on QD and PS to improve the efficiency of phototheranostics.

Table 1. Values of theoretical and experimental FRET depending on the ratio of donor and acceptors in the samples.

| Sample | QD Size, nm | QD : AlPc ratio | $Q_{theor.}$, % | $Q_{exp.}$, % |
|---|---|---|---|---|
| Conjugate 1 | 16 | 1:6 | 97 | 81 |
| Conjugate 2 | 20 | 1:3 | 92 | 48 |
| Conjugate 3 | 20 | 1:6 | 96 | 80 |

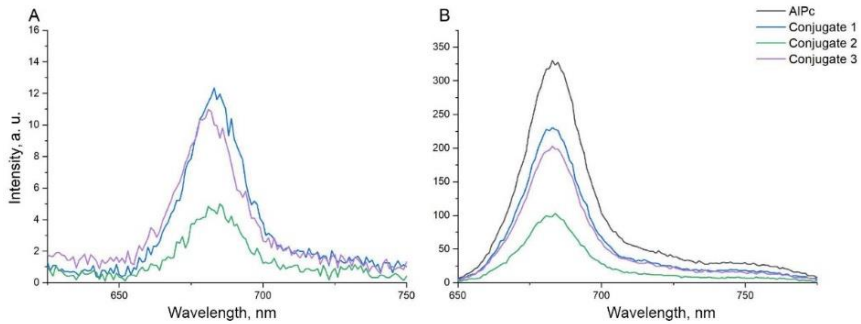


Fig.1. (A) Fluorescence spectrum of samples (λex= 485 nm), (B) Fluorescence spectrum of samples (λex = 600 nm)

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# DOXORUBICIN LOADED SILICA NANOPARTICLES AS POTENTIAL COMPONENTS OF THERANOSTIC SYSTEMS

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Anthracycline antibiotics with antitumor activity have been recognized as an essential component of cancer therapy for many decades. Despite the fact that anthracycline drugs such as doxorubicin are valuable elements of antitumor therapy, problems associated with resistance and cardiotoxicity limit their use in clinical practice [1].

Recent studies show that mesoporous silica nanoparticles (MSNPs) are one of the most promising nanocarriers for drug delivery due to their structural properties in overcoming multidrug resistance and limiting the chance of developing acute side effects [2]. The surface of MSNPs can be functionalized with stimulus responsive agents or target ligands to provide controlled release as well as active targeted drug delivery.

In this work, we selected the optimal conditions for the MSNPs synthesis by the Stober method. The physicochemical characteristics of nanoparticles were studied using the Zetasizer Nano ZS nanoparticle characterization system (Malvern Panalytical, UK). We have shown that the synthesized nanoparticles were 165 nm in size and had a zeta potential of -45 mV.

To study the cytotoxicity of nanoparticles using the MTT assay, human osteosarcoma cell culture (MNNG/HOS) was used. The studies were carried out in the concentration range of doxorubicin loaded silica nanoparticles ($SiO_2$ + DOX) and free doxorubicin from 10 μg/ml to 1 mg/ml.

24 hours after incubation with free doxorubicin, the dehydrogenase activity of MNNG/HOS was comparable to control values, while in the case of incubation with $SiO_2$ + DOX nanoparticles at concentrations

from 50 μg/mL to 1 mg/mL, a decrease in dehydrogenase activity to 75% is observed. Subsequently, during incubation for 48 hours with free doxorubicin, no significant differences were observed with the control. When MNNG/HOS is incubated with nanoparticles in the concentration range from 100 μg/ml to 1 mg/ml, a decrease in activity is observed to values of 55%. When the cell culture is incubated for 72 hours with free doxorubicin, an increase in the dehydrogenase activity of cells is observed compared to the control by 75%. In the case of incubation with $SiO_2$ + DOX nanoparticles, these values drop to 35%. Thus, the MNNG/HOS cell culture, despite the initial decrease in dehydrogenase activity, showed resistance to free doxorubicin over time. On the contrary, doxorubicin present in the composition of MSNPs had an inhibitory activity on the MNNG/HOS culture for three days. The obtained data should be used to develop a theranostic system based on the obtained nanoparticles with the possibility of real-time visualization.

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