2nd International Symposium on “Physics, Engineering and Technologies for Biomedicine”

October 10-14, 2017

BOOK OF ABSTRACTS

MOSCOW

MINISTY OF EDUCATION AND SCIENCE OF RUSSIAN FEDERATION

MINISTY OF HEALTH OF RUSSIAN FEDERATION

STATE ATOMIC ENERGY CORPORATION ROSATOM

NATIONAL RESEARCH NUCLEAR UNIVERSITY MEPhI
(MOSCOW ENGINEERING PHYSICS INSTITUTE)

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2nd International Symposium on

"Physics, Engineering and Technologies for Biomedicine"

The 2st International Symposium on "Physics, Engineering and Technologies for Biomedicine" is organized following the successful 1st International Symposium on "Physics, Engineering and Technologies for Biomedicine", held in Moscow at the occasion of the foundation of the new Institute PhysBio at MEPhI (Russia).

The conference is dedicated to the 75th anniversary of the National Research Nuclear University "MEPhI"

Under the auspices of the Russian Ministry of Science and Education, the Ministry of Health and the State Company Rosatom, the 2nd Symposium is again organized by the Institute of Engineering Physics for Biomedicine (PhysBio) of the National Research Nuclear University MEPhI (Moscow Engineering Physics Institute) in close collaboration with non-profit partnership «Kaluga pharmaceutical cluster».

Conference topics

The Symposium aims at bringing together leading scientists and experts in nuclear medicine, biophysics, bio-photonics, and emerging fields to present their works and having invited lectures on the following topics:

- Advanced materials and methods for MRI and PET
- Bioimaging technologies and materials
- Bio-photonics for diagnosis and therapy
- Bioprinting
- Brachy-, Proton and Ion therapy methods
- Diagnosis methods, today and in the future
- Immuno-therapy
- Isotopes for medical purpose
- Medical-biological aspects of radiation effects
- Nanomaterials for biomedical applications
- Plasma and laser technologies for biomedicine
- Translational medicine

The Symposium provides a unique opportunity for fruitful scientific discussions and for establishing contacts with scientists all over the world.

Official Language
The official language of the conference is English.

The 2nd International school for young scientists "Physics, Engineering and Technologies for Biomedicine" will be held in the framework of the 2nd International Symposium on the 8-9th of October 2017 in Moscow, Russia.

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2nd International School for young scientists "Physics, Engineering and Technologies for Biomedicine"

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INVITED LECTURES

MAGNETIC RESONANCE IMAGING IN BIOMEDICAL RESEARCH. MODERN PROBLEMS AND METHODS

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Magnetic resonance imaging in modern form originated in just 40 years ago and was marked in the 2003 year by Nobel Prize in medicine, the winners were Paul Lauterbur (University of Stony Brook, New York, United States) and Peter Mansfield (University of Nottingham, United Kingdom). In fact the first proposal on the use of NMR phenomena for MRI visualization was made for 13 years before Nobel laureates by a young officer of the Soviet Army Vladislav A. Ivanov. Unfortunately, in the beginning the Ivanov’s patent was rejected by our Patent Institute and approved only in 1986, when MRI scanners appeared already in most multidisciplinary clinics throughout the world. Now, any serious diagnosis does not be put by doctors without passing MRI Diagnostics. The method is exclusively informative, particularly for the diagnosis of soft tissue of living organisms. However, the level of NMR signals that form the MRI image, usually small and to improve the signal-to-noise ratio is necessary to apply special methods of accumulation of NMR response and mathematical processing of images with significant temporary costs.

The signal value is determined by the difference in population of basic and excited by resonant radiofrequency exposure levels at which are allocated nuclei of magnetized ensemble. At room temperature, the difference of the populations, which determines the polarization of the ensemble, is extremely small. However, polarization with the help of special hyperpolarized techniques and together with it the NMR signal may be increased to 5-6 orders that leads to dramatic improvements in MRI signal characteristics – reducing analysis time, increasing spatial resolution and contrast of received images. For the first time, this technique was developed at the University of Nottingham in MRI Center named Sir Peter Mansfield.

It has allowed to solve one crucial, before unrealized task of monitoring the lungs, which contain very small number of protons, on the Larmor frequency of which all regular medical scanners are adjusted. It was developed a methodology of the laser polarization for noble gas nuclei of helium, xenon, krypton, inhalation of which provides a vivid response when you configure the imager on the Larmor frequency of hyperpolarized gas. Later was established a task to detect areas where injected to a body medicene molecules containing, for example, carbon C13 or silicon-29 atoms. This was a method of dynamic polarization of nuclei (DPN) at very low (sub-helium) temperatures when microwave EPR (electron paramagnetic resonance) pumping electronic ensemble with the subsequent transferring magnetization of electrons to nuclei polarization.

It is very expensive procedure connecting with a rapid loss of hyperpolarized state during defrosting preparation and its injection into the body. However, the signal from the nuclei even in some depolarized state, has a value so much more regular levels, that bright and clear images of tissues containing hyperpolarized substances are obtained in a very short times in tens of seconds. Consequently, the difficulties of the DNP method forming the hyperpolarized conditions may be quite justified, if substances beeing in such state provide visualization not realized by conventional ways.

This methodology is evolving and in recent years has got serious, truly breakthrough nature continuation: silicon-29 microparticles, covered with polymer shell being subjected to effects of the DPN procedures could keep hyperpolarized state at room temperature from tens of minutes to half an hour. Now, when you use the hyperpolarized particles of Silicon-29 either as independent medication or as bio-container it is possible to confidently record their location in the body. The physical nature of slow relaxating hyperpolarized state of the Si-29 particles is in action of multistage processes of magnetized state diffusion from surface layers into internal parts of microparticles when the magnetization and reverse of the same kind stage depolarization diffusion after their defrosting have place.

In this process, there are 3 main stages. When siting the microparticles in the magnetic field with intensity 1-2 T and irradiation of microwaves at a frequency 80-90 Ghz have place, quasi-free electrons on silicon surface defects under polymer liner are polarized due to the EPR effect and transfer then its magnetization to upper layers of Si-29 nuclei by electron-nuclear Overhauser effect. In turn, magnetization from hyperpolarized surface layers of Silicon nuclei is transferred to the deeper layers under acting nuclei-nuclear Overhauser effect, etc., until full hyperpolarized state. Such diffusion process of magnetization transfer from the outer layers of silicon particles up to the root takes 10-20 hours, whereas inverse diffusion of demagnetization from the external layers to the root goes much faster – about half an hour, what, however, is quite enough for medical procedures.

But hyperpolarized technologies are enough expensive and labour-intensive, requiring for their implementation the availability of cryogenic infrastructure in combination with a special microwave or laser installations. In this regard, searching other, alternative ways to improve MRI imaging not related with hyperpolarized procedures is as well actual. One such method is the use of fluorinated drugs, giving sufficiently intense signal on the Larmor frequency of fluorine-19. Work of MRI scanner at a frequency of fluorine is functionally similar to the proton NMR imaging – Larmor frequency of fluorine nuclei is different only on 5% from proton one and allows restructuring standard transmitter-receiver coils of medical scanners onto the frequency of fluorine-19, a natural contain of which is 100%, i.e. even better than for hydrogen.

A special advantage of medical diagnostics for fluorine nuclei is the almost complete absence of these nuclei in human and animal tissues – NMR signal from the fluorine-19 nuclei will be observed, thus, as the zero signal on a background of tissues which are free of injected into the body fluorine-containing drug. Most clearly the dignity of fluorine MRI techniques in comparison with hyperpolarization is manifested for diagnosing hollow areas, such as the lungs or gastrointestinal tract. So, filling the lungs fluorine gases gives a clear picture of the internal structure of the respiratory system and helps to identify pathological forms on the walls of the lung tissues. Injection of specially synthesized fluorine fluids can also significantly improve contrast MRI images.

Investigations on the fluorine-19 nuclei were performed on the equipment of the Collective Using Center "Biospectrotomografy" and supported by RFBR grant No. 17-02-00465-A.

FORMATION, PROPERTIES AND BIOMEDICAL APPLICATIONS OF SILICON NANOCRYSTALS

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Silicon nanocrystals (SiNCs) exhibit unique physical properties for applications both in optoelectronics and in biomedicine. SiNCs with sizes from 2 to 100 nm can be prepared by laser ablation of crystalline Si (c-Si) targets in gaseous and liquid ambiences. Arrays of crystalline silicon nanowires (SiNWs) can be formed by metal-assisted chemical etching of c-Si wafer in a hydrofluoric acid solution. Layers of SiNWs possess an extremely low reflection in the ultraviolet, visible and near-infrared spectral ranges due to the strong light scattering accompanied by absorption. The strong light absorption and low thermal conductivity result in efficient photoinduced heating of SiNWs. SiNCs with sizes of 5-100 nm can be easily formed from porous silicon (PSi) layers and SiNWs by their mechanical fragmentation (ball-milling, ultrasonic grinding, etc). SiNCs formed from microporous PSi exhibit efficient photoluminescence due to the radiative recombination of excitons in small Si nanocrystals.

SiNCs are extensively explored as agents for the optical diagnostics and phototherapy of cancer as well for applications in different therapy modalities, e.g. drug delivery, sonodynamic therapy and radiofrequency induced hyperthermia. The obtained results demonstrate that SiNCs are promising for applications in both medical diagnostics and therapy, i.e. theranostics.

This work was supported by the state project 16.2969.2017/4.6.

METHODOLOGICAL APPROACHES TO IMMUNOTHERAPY OF CANCER USING CULTURED NATURAL KILLERS (NK CELLS)

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Key words: adoptive immunotherapy, lymphocyte culture, IL-2, IL-15, activated lymphocytes in vitro, NK cells, cancer.

Increasingly important in the treatment of various types of cancer are integrated approaches using methods of adoptive immunotherapy based on cultured cells in vitro. Activated lymphocytes can open a new window, which is of great interest for this direction. Immunotherapy of patients using natural killer (NK) cells is one of the most promising methods for treating many types of cancer. New immunotherapy focuses on the detection of biologically active substances (cytokines) that can enhance the cytotoxic antitumor activity of NK cells. In recent years, several cytokines have been extensively studied as potential therapeutic agents for manipulating the immune response against malignant cells. Among these cytokines, tested in different conditions in vitro and in vivo, most important are interleukin (IL) -2 and IL-15.

The lecture tells about the nature of natural killer cells, the ways of their cultivation (in vitro), the effect on their activity of special biologically active substances - cytokines, the joint antitumor effect of NK cells with activated lymphocytes.

NANO – SMART NANOSTRUCTURES AND CLEVER NANOTECHNOLOGY APPLICATIONS AND POSSIBILITIES

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Contemporary science reached the level which makes possible to peep into very tiny pieces of matter to observe natural processes taking place inside. On top of that the modern technology allows interfering with these internal processes and working upon them. Very important are characteristics and properties, which such form of matter manages, as well as processes that take place on nanometers scale.

Nanostructures represent the new forms of matter, which science and technology have been eagerly investigating in recent years. Problems of nanostructures is an inter-disciplinary field of research, where chemistry, physics, biology and mathematics, and perhaps some other branches of science as well, overlap in creating possibility to describe, study and employ these directions.

Nanophysics, nanochemistry, nanobiology, and particle nanostructures are categories of current nanoscience which describes and studies these processes and characteristics. Today’s technology already achieved the levels that makes possible to observe and copy the process of formation tiny structures and to imitate these structures in „nanosize" scale, or to find the ways how to prepare them. As these structures exhibit unique characteristics, unknown in the macro-world, it can be said that from the point of view of utilization of these structures for practical applications, doors are becoming wide open to undreamt-of development of science and technology. This area has received the name **nanotechnology**, or new as **Nanology** !

Thanks to their extraordinary properties nanoparticles offer a wide and important applications in *biomedicine* and *medicine*.

Among them a very specific position belongs to the *carriers* (nanoparticles properly *functionalized* to attach and carry a specific load). Material of the nanoparticles should be biologically compatible, i. e. the nanoparticles can be introduced into the organism (bloodstream) without any damage or side effects. Nanoparticles can be used either as support for drugs or as an active medium.

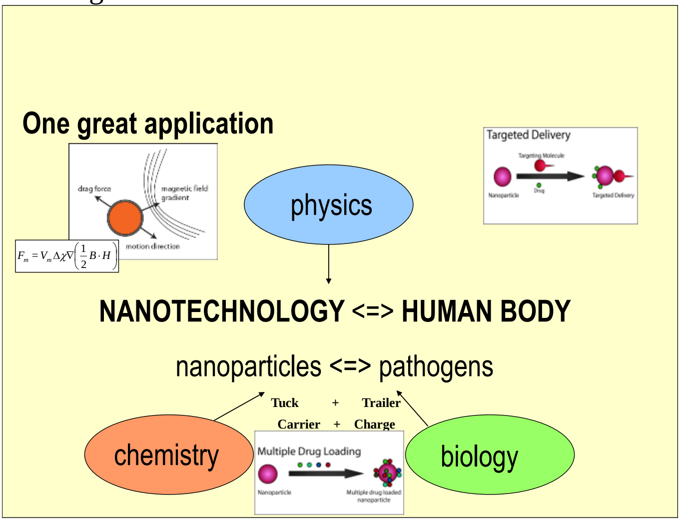

Fig. 1. Application in biomedicine

Nanoparticles of some metals and their oxides (Fe_3O_4) have significant magnetic properties. They are an ideal candidate for the *carrier* purpose. Their magnetic properties enable for direct manipulation, targeting within or removing from the organism by means of an external magnetic field. This can be used to *necrotise tumor* (and after relief of magnetic field let the blood circulate again). Another possibility is the use of *thermal cancer ablation*. Functional samples of such nanoparticles were already prepared.

Alternatively they could be used in an opposite manner. By surface modification "encapsulation" (i.e. enclosing the nanoparticle in chemicaly and biologicaly impervious shell) and by further surface modifications can use those nanoparticles as a *selective seekers of* *choosen patogenes* (f.e.HIV virus). This is followed by subsequent magnetic *extraction* (as easy as possible) of such nanoparticles from the bloodstream, thus cleaning the organism.

Another brilliant example is using of noble metal particles and some metal oxides (Ag, MgO...) for their antiseptic purposes – they are harmless for the human organism but lethal for the bacteria.

Application of metal and semiconductor nanoparticles for **electronics** and **Environmental sensors.**

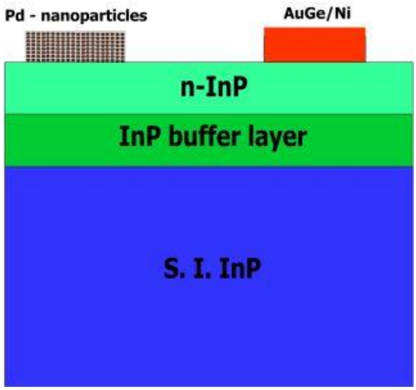

Fig. 2. Technology for Environmental sensors

BIOFUNCTIONAL PHOTOLUMINESCENT NANOCOMPLEXES FOR VISUALISATION OF MOLECULAR TRAFFICKING, DIAGNOSTICS AND THERAPY

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Development of new approaches for diagnosis and therapy of tumours (taken together, termed theranostics) - one of the most dynamic areas of the life sciences, where new nanomaterials afford new opportunities. This paper reports on multifunctional theranostics agents based on a new-generation biofunctional photoluminescent nanoparticles with unique optical properties – fluorescent nanodiamonds[1], nanorubies[2] and upconversion nanoparticles (UCNP)[3]. These nanoparticle biocomplexes, such as nanoruby-(opioid ligand) or UCNP-(designed ankyrin repeat antibodies) are pieced together to form biohybrid nanocomplexes capable for targeted delivery. We demonstrated binding of functional biomolecules by flexible design using solid surface peptide binding technology[4]. The attachment of therapeutic vectors for photodynamic therapy, such as Killer Red, Rose Bengal[4], bacterial exotoxin PE40 and radioactive beta-emitter ^{90}Y were developed and demonstrated, where a super-additive effect of PE40 and ^{90}Y was pronounced. UCNPs of unparalleled 2%-efficiency of conversion deeply-penetrating excitation at 975 nm to ultraviolet-blue power were purpose-designed to photosensitise Riboflavin (Rf), aka Vitamin B2, and kill human breast adenocarcinoma cells. Ablation of adenocarcinoma xenograft in mice treated with UCNP-Rf+975-nm was observed for 50 days.

The detection limit was pushed to the single receptor visualisation and tracking of opioid receptors, as shown in Figure[2]. The transport and therapeutic action of nanodrugs were tested using biomimetic tissue engineering models.

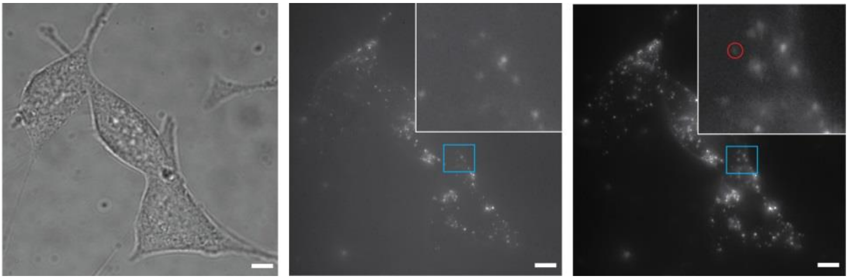

Fig.1. Microscopy images of AtT-20 cells incubated with nanorubies. (Left panel), (Middle panel) and (Right panel) show bright-field, epi-luminescence and time-gated, background-free images. Insets, zoomed-in images as framed by blue squares. A red circle marks the nanoruby indiscernible in Middle panel. Scale bars, 10 μm.

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WHAT DO WE NEED TO ANSWER THE QUESTIONS: WHAT IS CONSCIOUSNESS? WHAT PLACE DOES MAN HAVE IN THE COSMOS? ARE WE ALONE IN THE UNIVERSE?

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One of the most important current research trends is the study of the brain and consciousness. And whilst the number of laboratories researching the principles of brain science grows year by year, an answer to the question of what consciousness is and how it is linked to the function of the brain has, so far, yet to arrive. The basic working model used to described the functioning of the brain is the computational, information-processing model. However, a large number of authoritative researchers have confirmed that the brain in no way resembles a computer and that the metaphor of the computer does little to serve as an explanation. The persistence of this computer model stems from the fact that we traditionally view the world as an aggregate of material *bodies*. However in material *bodies* there is, in fact, no place for *the psychical* as the psychic is not a body or an object, it is immaterial. On the contrary it has a property that manifests itself in the 'object(ive)', physical world in a completely incomprehensible manner as *subjectivity*. There is a patent asymmetry between the external physical and internal psychic worlds: in distinction between the external world of objects, which simply *is*, there exists independently from us, 'in and by itself' a psyche that appears as an uninterrupted *current* of consciousness, feelings, emotions, that is continuous with us ourselves. It is the only original state which we know *without mediation*. Furthermore, if the physical body just *exists*, then consciousness is *intentionally*, always *directed* at something. It is the psyche's subjectivity and intentionality that lead to the principal theoretical and practical difficulties of its description and modelling.

It is possible to, in some sense, to include consciousness in the physical conception of the universe? Scientific thought in the Modern period creates a model of the world by introducing *quantitative values*. These take mathematical objects that do not exist in nature, namely *numbers*, and impose them on elements comprising the actual physical world. This imposition occurs in the process of realising acts of *measurement*, which is to say investigating the relations between one physical reality and another. Thus, objective science describes only a *projection* of the world onto devices of measurement. The resulting physical theories are *theories of relations* that are themselves open to meaningful *interpretation.*

Modern European science, as is today well-recognised, arose in the conceptual presentation of two complementary Books of the Creator: the Bible and the Book of Nature. Between them there is not, and cannot be, contradiction as they have both been written by the same Author. Resorting to the meaning of the theological context from which modern science emerged allows us to give a content-driven interpretation of the mathematically describable 'structured' understanding of the world and mankind. We may, then, fulfill object(ive) knowledge with subject(ive) content and establish a new conceptual language that is 'binary' and that has the ability to objectively describe the 'external' physical world as well as the subjective and intentional 'internal', psychical world [1].

In answer to the question 'What is the value of the exact sciences?', Edwin Schrödinger argued that they are there to serve mankind's self-knowledge. One of the aspects of this process of self-knowledge is conceptualising humanity's place in the cosmos. To the extent that physical theories are *theories of relativity*, open to meaningful *interpretation*, then their literary interpretation in the context of the biblical tradition allows them to 'speak' in the language of culture. In this case scientific theories that have been 'agents of influence' on the external world can become those through which the world – and in a particular sense the Creator himself – responds to us, acting on our internal world [2].

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2nd International Symposium on “Physics, Engineering and Technologies for Biomedicine”

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TOWARDS 1000 YEARS LONG HUMAN LIFETIME - FIGHTING THE ISOASPARTATE

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Human mortality curve exhibits a constant value of ca. 0.001 followed by an exponential increase. The mortality of 0.001 corresponds to an average lifespan of 1000 years, should such mortality remain constant throughout the whole life. The exact cause of the mortality increase after 30 is unknown; it is likely due to debris/damage accumulation in proteins. The main product of protein ageing is isoaspartate, resulting from deamidation of asparagine residues. Isoaspartate forms spontaneously and ubiquitously; it is toxic and accumulative. Isoaspartate accumulation causes protein aggregation that can initiate Alzheimer’s disease. We identified isoaspartate as a major factor limiting human lifetime, and are exploring ways of fighting it, including removal by proteases and antibodies, as well as its repair and possible reversal.

BIOPHOTONICS AND NANOMEDICINE FOR THERANOSTICS: CHALLENGES AND OPPORTUNITIES

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This talk will present our progress in biophotonics dealing with multimodal and multispectral imaging, combined with nanomedicine approach of image guided targeted delivery of therapy to produce an effective paradigm of combined diagnostics and therapy, now popularly referred to as Theranostics. A new approach involves nonlinear nanocrystals such as ZnO with which we can use four wave mixing, sum frequency generation and second harmonic generation to convert a deep tissue penetrating Near IR light at the targeted biological site to a desired shorter wavelength light suitable for bio imaging or activation of a therapy. Yet another direction for imaging, sensing and light controlled therapy is development of photon converting nanostructures that can enable imaging and sensing in the spectral regions called NIR window II (1,000 nm to 1,300nm) and NIR window III (1,600nm to 1,870nm) which provide deeper penetration through biological tissues. We introduce Ramanomics which is a new Omics disciplines using Micro Raman Spectrometry with Biomolecular Component Analysis for molecular profiling of biological structures . This provides a new biosensing tool to measure concentrations of proteins, DNA, RNA and lipids in the single organelles of live cells, leading to a new set of biomarkers to diagnose progression of diseases such as cancer.

In nanomedicine, our approach has been to develop nanoformulations that provide image guided and targeted delivery and as well as real time monitoring of therapeutic action. We also make sure that the nanostructures are biocompatible, causing no toxicity and can be bioeliminated. A major focus of our recent activities has been on nanodelivery of natural medicine. We have also focused on engaging nuclear physics in radiation-based diagnostics and therapy. An example presented is of our new formulation of boron nanoparticles for Neutron Capture Therapy. A major biomedical application area currently pursued in our lab is brain research in the emerging field of *Neurophotonics*, where we apply field responsive materials for functional mapping of the brain using optical and photoacoustic imaging. We have also demonstrated remote and noninvasive actuation of optogenetic stimulation of brain activity using near IR absorbing optical nanotransformers that can provide an effective intervention/augmentation strategy to treat many cognitive disorder and diseases, ranging from Alzheimer, to traumatic brain injury, to retardation.

This talk will conclude with a discussion of existing challenges and new opportunities.

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MICROFLUIDIC TECHNOLOGIES FOR DRUG SCREENING, POINT-OF-CARE ASSAYS, AND DISEASE MODELS

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Opportunities now exist to model disease processes such as the various step in the metastatic cascade using microfluidic technologies. This capability opens the door to personalized medicine scenarios in which a patient's own tumor is introduced to an external device and used to first determine optimal therapeutic approach, then follow the progression of the patient using a surrogate tumor model. Recently developed technologies that have facilitated this approach include the wide availability of patient-specific iPS cells, the ability to create organoids that replicate specific organ morphologies and functions, and a variety of lab-on-chip assays for a a variety of applications. Current capabilities to be discussed include models of metastasis and that contain a microvasculature perfusing a tumor spheroid with a natural complement of immune cells (monocytes, T cells, neutrophils) derived from patient blood. Such systemscan now be maintained for several weeks, with the prospect of extending their lifetime to months. Advantages include the need for small sample size, high resolution imaging, and low cost. Other applications in connection with neuromuscular and neurodegenerative diseases will also be discussed.

PRECISION CANCER MEDICINE: ACHIEVEMENTS AND PROSPECTS

John Mendelsohn

The University of Texas MD Anderson Cancer Center

After briefly reviewing my early research developing Erbitux, one of the first cancer therapies targeting a growth factor receptor and a tyrosine kinase, I will describe experiences with initiating the precision cancer medicine program at the University of Texas MD Anderson Cancer Center. Over 20,000 patients have had their tumors sequenced, and an estimated 24% have been enrolled in clinical trials with genotype-matched experimental targeted therapies. This will be followed by a "dream list" of the next steps that could produce major advances with targeted therapies, and a description of the contributions of the WIN Consortium in personalized cancer medicine towards achieving this goal.

ORGAN PRINTING

Vladimir Mironov

3D Bioprinting Solutions, Moscow, Russia

Organ printing is a variant of rapidly emerging 3D bioprinting technologies which could be defined as a robotic additive biofabrication of functional 3D living tissues and organs from tissue spheroids as building blocks using digital model. Organ printing technology promises to solve a shortage of human organs for transplantation. Moreover, bioprinting could be used for biofabrication of 3D models of human diseases, in vitro models of normal human tissues and organs for drug testing and evaluation of their possible undesirable side effects and even for personalized medicine - the estimation of chemosensitivity of patient-specific bioprinted human tissues for personalised drug therapy. The world first functional and vascularized organ (mouse thyroid gland) have been successfully bioprinted in 2015 by Russian company 3D Bioprinting Solutions using original commercial 3D bioprinter Fabion-1. *In situ* 3D bioprinters for bioprinting of human hairs and teeths are also under development. It is becoming obvious that the next generation of 3D bioprinters or 3D bioassemblers will be based on combination of scaffold-free, label-free and nozzle-free magnetic and acoustic technology. First Russian magnetic 3D bioprinter for rapid magnetic levitational assembly of human tissues and organs in condition of microgravity for sensing space radiation will be presented. Recent trends and emerging business models in the ongoing commercialization of 3D bioprinting technology will be also discussed.

THE NEXT GENERATION SEQUENCING REVOLUTION AND HOW IT WILL TRANSFORM HOW WE TREAT CANCER PATIENTS

David Smith

Mayo Clinic, USA

The development of new sequencing strategies based upon massively parallel sequencing has completely transformed our ability to characterize genomes. While it used to cost billions of dollars to sequence a single genome, advances in next generation sequencing has now made it possible to completely sequence an entire genome for less than $1,000 and we are rapidly approaching this costing just $100. I will describe the technological revolutions that have occurred over the past 15 years and what are the best currently available technologies for genome sequencing. I will also describe what new technologies are currently being developed and what we have to look forward to, in just the next few years. Finally, I will describe how these high throughput technologies can completely transform how we characterize cancer genomes and the impact that this will have on the clinical treatment of patients with cancer.

DEVELOPMENT AND VALIDATION OF A NEW TECHNOLOGY AND BIOMARKER STRATEGY TO PREDICT THE EFFICACY OF COMBINATIONS OF TARGETED THERAPIES: THE MODEL OF LUNG CANCER

Vladimir Lazar

WIN Consortium, France

Position of the problem

To date only 10% of NSCLC patients are detected in stage I, at a stage when the disease is curable by surgery alone (90% of patients are alive at 5 years). Most of the patients, over 60 %, are unfortunately detected in late metastatic stage IV and remain incurable, with a median survival of 12 months, and less than 5% of patients alive at 5 years. The lecture will present WIN Consortium efforts to significantly improve the clinical outcome of lung cancer patients: A major component is international collaboration to improve molecular profiling and data management.

Combination of targeted therapies:

The key feature of future therapies in metastatic NSCLC, is switching from current monotherapies to combination of targeted therapies, as only way to fight against secondary resistance that occurs in all patients. This switch will need the identification and validation of new tools to match individually the patient's tumor biology profile to the most appropriate combination of therapies.

The main limitations of current companion diagnostics (Cdx) are:

a) multiplicity of drugs that require a large number of tests (and different technologies) to be performed on limited amount of biological samples,
b) inability to prioritize the best therapeutic options for each individual patient.

The lecture will present the Simplified Interventional Mapping System (SIMS), a Systems Biology based novel generation of multiplex combinatorial Cdx which provides biological support to prioritize and to select the classes of drugs that are predicted to be most effective at the individual patient level. The example used is metastatic Non Small Cell Lung Carcinoma (NSCLC), but the method applies to any solid tumor. SIMS is based on the use of dual biopsies in order to compare tumor with its histologically matched normal tissue from the same patients. SIMS algorithm integrates data of DNA sequencing, CNV, and the differential expression of mRNA and miRNA between tumor and matched normal tissue from 121 NSCLC patients. SIMS converts thousands of genomic and transcriptomic measurements into a simple and actionable result (a 1 to 10 score) that may be usable by physicians to select the optimal drug or drugs' combinations therapy. One of the most interesting hypothesis being the tri-therapy approaches, following the historical success in AIDS. Comparing tumor and normal tissue biopsies has proven feasible in the ongoing WINTHER trial (NCT01856296) SIMS outlines novel therapeutic possibilities by focusing on pertinent classes of targeted therapeutics to be used in combinations, and is a novel generation of combinatorial multiplex companion test enabling to match patients to drugs.

NOVEL APPROACHES FOR CANCER DIAGNOSIS AND TREATMENT

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The precise diagnostics of pathogenic cells and targeted delivery of certain compounds to the disease area should provide high selectivity of cancer treatment. A novel direction of biomedicine – theranostics (therapy + diagnostics) combines these two approaches on a single platform, and afford personified patients’ treatment with improved efficiency. A particular attention is directed towards investigating physiological characteristics of the designed agents in order to improve their tumour targeting, minimize the undesirable kidney, liver and spleen accumulation and increase circulation time in blood.

Different agents for targeted delivery of different compounds, tumour diagnostics and treatment have been designed and synthesised [1-9]. The developed approaches to such agents synthesis allow to design structures with desirable characteristics such as size, ζ-potential, hydrophobicity and optimize their behaviour in living organism. The obtained supramolecular multifunctional theranostic structures possess by a number of properties that are impossible to obtain using different components individually. This comprehensive effect on the tumor allows realizing the principle that the whole is greater than the sum of its constituent parts.

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FLUORESCENCE LIFETIME IMAGING AND ITS APPLICATIONS IN CELLULAR MICROENVIRONMENT MEASUREMENT AND AUXILIARY DIAGNOSIS

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Fluorescence lifetime imaging microscopy (FLIM) has been widely used in biomedical research. By labeling the biological sample with specific structure and spectral characteristics of fluorescent molecules, and measuring and mapping the fluorescence decay rates which reflect the interaction of the fluorescence probe and its microenvironment, we can quantitatively obtain various functional information of the sample, including cell refractive index, pH, viscosity and other physical/chemical parameters of the cellular microenvironment.

In this talk I will first introduce the basic principles of FLIM and different implementation methods, and then present our recent work on FLIM and its applications, including the measurement of intracellular viscosity, the analysis of cellular differentiation and apoptosis, the monitoring of macromolecule dynamic changes in the nucleus and the auxiliary diagnosis of H&Estained pathological sections.

OPTICAL COHERENCE TOMOGRAPHY: FROM BIOIMAGING ENHANCED BY NANOPARTICLES TO PATIENT EVALUATION IN DENTISTRY AND RHEUMATOLOGY

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Optical Coherence Tomography (OCT) is a well-known imaging diagnostic technique based on low coherence interferometry, widely used in Ophtalmology. In this talk, I shall briefly review the basics of OCT, and will describe its use in dental materials associated with nanoparticles, and*in vivo* applications in clinical environment performed by a multidisciplinary team involving physicists, dentists and rheumatologists. In dental materials, I shall describe how gold nanoparticles can be used as contrast agents for image enhancement [1], as well as the use of TiO_2 coated rare earth doped fluoride nanoparticles in multimodality imaging [2]. In a dental clinical environment, I will report on examples of OCT use to evaluation of periodontal diseases and veneers (laminates) placed by aesthetical reasons [3,4]. In rheumatology, I will describe how OCT can be used to evaluate*in-vivo*auto-immunediseases, evidenced by skin alterations, such as systemic sclerosis [5]. I will end the talk with some future view of OCT challenges and applications in health care.

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POROUS SILICON NANOPARTICLES FOR BIOMEDICAL APPLICATIONS

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Porous silicon (PSi) nanoparticles (NPs) are biodegradable and exhibit promising physical properties for biomedical applications [1]. It was found that PSi NPs could penetrate into living cells without any cytotoxic effect. In our work PSi NPs are analyzed as marker for visualization of cancer cells and tumors as well as sensitizer for photodynamic thera*py (PDT), sonodynamic therapy (SDT) and radio-frequency-assisted* hyperthermia of cancer. These properties are discussed in view of possible applications of PSi NPs in theranostics (therapy and diagnostics) of cancer [2]. PSi NPs can be fabricated by high-energy milling of PSi films in water by using a planetary-type mill as well by ultrasound-assisted fragmentation of Si nanowires in water [2]. PSi films are usually formed by the standard method of electrochemical etching of crystalline silicon wafers in hydrofluoric acid solutions. Typical sizes of as-prepared porous PSi NPs are in the range from 10 to 200 nm. It was revealed that aqueous suspensions of PSi NPs with concentration up to 2 g/L were non-toxic for normal cells in darkness [1,2].

In vitro fluorescent imaging was carried out with aqueous suspensions of PSi NPs introduced to cancer and normal cells. A comparison between the fluorescent images obtained under laser excitation and white light illumination showed that PSi NPs were localized into the cell cytoplasm. *In vitro* experiments showed that photoexcited PSi NPs suppressed the proliferation of cancer cells and it was explained by oxidizing properties of singlet oxygen sensitized by PSi NPs. These results demonstrate that PSi NPs can be considered as photosensitizer for the PDT of cancer and other tumors [1].

Aqueous suspensions of porous and nonporous (laser-ablated) Si NPs with relatively low concentrations below 1 mg/mL can be efficiently heated by radiofrequency electromagnetic radiation with intensities of 1–5 W/cm^2. The heating rate was linearly dependent on NP's concentration in the range from 0.01 to 1 mg/mL. The observed effect is explained by the Joule heating due to the generation of electrical currents at the NP/water interface. Profiting from the NP-based hyperthermia, we demonstrate efficient treatment of Lewis lung carcinoma *in vivo* [2]. Moreover, PSi NPs with a larger amount of electron spin centers have been found to exhibit properties of a contrast agent for magnetic resonance imaging (MRI) [3].

PSi NPs irradiated by therapeutic ultrasound are found to induce local hyperthermia and cavitation-induced damages of cancer cells *in vitro*. *In vivo* studies confirm that PSi NPs are efficient sensitizers for SDT of malignant tumors [2]. PSi NPs with hydrophilic-hydrophobic surface properties are also prospective contrast agents for ultrasonic diagnostics [4].

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QUANTUM DOT CONJUGATES IN FUNCTIONAL IMAGING AND HIGHLY SENSITIVE BIOCHEMICAL ASSAYS

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The existing photonic techniques of *in vitro* and *in vivo* diagnostics and imaging are mainly limited by the difficulties related to dye photobleaching and their detection in the optically noisy cellular and tissue environment [1,2]. As alternative tools, semiconductor quantum dots (QDs) have emerged for cellular labeling, biochemical sensing, probing biocatalyzed reactions, and drug delivery [1,2].

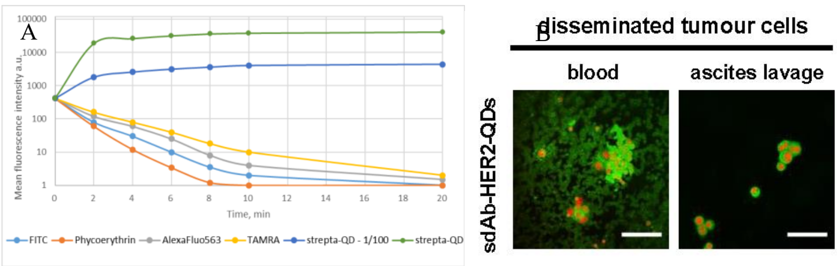

Fig. 1. Comparative advantages of semiconductor quantum dots (QDs) in *in vitro* (A) and *in vivo* (B) assays.
Panel A shows analysis of variations of fluorescent signals as a result of their accumulation for typical *in vitro* biochemical fluorogenic assays employing two concentrations of the fluorescent streptavidin-QD800 conjugate and the most popular organic dyes [3].
Panel B shows circulating tumor cells identified by fluorescent microscopy with the sdAb-QD conjugate specific for the HER2 antigen [4].

As seen from Fig. 1A, the fluorescent signal from the assay employing strepta-QD obtained in the course of signal accumulation is more than two orders of magnitude stronger than the maximal signals that may be obtained in fluorogenic assays employing the best organic dyes under optimal conditions [3]. This shows that the use of QD-based labels in fluorogenic assays is decisively advantageous.

Moreover, the QD-conjugates with single-domain antibodies (sdAbs) have proved to be an efficient tool to detect disseminated human tumor cells and micrometastases by binding HER2, an antigen overexpressed in metastatic breast tumor (Fig. 1B) [4]. Additionally, the better diffusibility of sdAb-QD nanoprobes through tissues facilitates the access to small metastases and complex structures, making them powerful tools for cancer diagnostic and therapeutic applications.

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NANO –FASCINATING PHENOMENON

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During the past several decades, “small-particle” research has become quite popular in various fields of physics and chemistry. By “small particles” are meant clusters of atoms or molecules of metals, semiconductors and others materials, ranging in size between single atoms or molecules and bulk materials.
In the very early stages of "Nano" science I had an opportunity to participate in the experimental shaping of this area. At the beginning, we stepped into nanostructure research, which was completely unexplored area, with a significant risk of failure and misunderstanding. This note presents the area of quantum nanoparticles from the perspective of one of the founders of the experimental study of nanotechnology and nanostructures as a completely new field of research, including subsequent unique applications.
At the beginning of the eighties, the team of prof. A. Henglein, (director of Hahn-Meitner Institute, HMI) in TU (West) Berlin, perform investigation of small colloidal particles.
Ambitious objective of project EUREKA (EU and Germany1980) was to end the domination of U.S. and Japan in the field of chip technology. To obtain chip units with a density record 10 ÷ 100 Mb/cm^2 was to ensure necessary material base. HMI in Berlin has become in the being a major centre for research and training materials for miniaturisation particles technology. We had an inconsiderable share in the preparation and study of metal and semiconductor colloidal materials. The work has gradually started to depend on the area of study super small particles, currently known as quantum nanostructures. The development of the nanostructural world and problem ignition began, when the systematic

research of small particles run in laboratories in Hahn-Meitner Institute in Berlin - prof. Henglein,[1,2], and at Bell Telephone Laboratories, NY USA - prof. L. E. Brus..The results of this research are dozens of original work in the field of training and study nanoparticles, nanostructures and nanotechnology[3]. We will try to illustrate the way, how the research and development in this area went. Practical and theoretical problems, which had to be faced on infancy of this new science industry, will be presented.

In this short note, we point out several key moments, which played in the development of this area decisive role.

The findings of the effect of space restrictions of colloidal particles(i)
The findings of absorption of exciton status in a normal temperature (ii)
Confirmation of the higher excited states on one particle (iii)
Surface and internal conditions of charge carriers in nanoparticles (iv)
The dimensional quantization effect, which caused unprecedented interest in the world in the research of this kind, appeared as a remarkable feature. Band structure of metals and semiconductors is also dependent on the number and arrangement of atoms in the crystalline grid, i.e. in quantum properties, there is considerable dimensional function of microcrystal when in semiconductors, or in metal occurs in the nanometre area a gradual transition from the macroscopic voluminous characteristics to quantum characteristics of molecules. Optical, photocatalytic and fotophysical characteristics of semiconductors are significantly changed and there were observed interesting electrochemical and physical effects.

A progress has been made in improving the properties of particles by surface modification[4,5,6] and by the preparation of composite structures ("sandwiches"), in which the particle consist of two semiconductor components[7,].

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ENCAPSULATED BIO-SENSORS FOR NON-INVASIVE STRESS ASSESSMENT OF AQUATIC ANIMALS FOR ENVIRONMENTAL MONITORING

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The development of *in vivo* bio-sensors for non-destructive, rapid quantification and analysis of various chemical compounds and parameters of mammalians and other living organisms is a major challenge in medical, biological, and ecological express tests. The most of recently developed sensors detect changes of electrical properties that occur on the probe surface after exposure to analytes. We develop a new type of bio-sensor that is based on screening of optical response occurred in the array of fluorescent dyes placed in biological medium. The performance of the approach is based on the analysis of spectrum of the selected fluorescent dyes with the operational principle similar to electronic nose and electronic tongue systems. Encapsulation of the array permits targeted delivery of sensor in tissue. The capsules shell performed as a membrane is impermeable for florescence dyes suspended within the capsules and is permeable for the external environment. Thus, the direct contact of fluorescence dyes with the surrounding medium is excluded and the issues associated with the toxicity of fluorescence dyes can be omitted. We demonstrate that micro-/nano- capsules are circulating in tissues without restraint, including brain and trunk, with no blood flow disruptions or any other deleterious effect on its cardiac function. The developed approach has a great potential to use of encapsulated biomarkers as a diagnostic tool in vascular biology and medicine, as well as for monitoring of aquatic pollution and ecological risk assessment in eco-toxicological studies.

SILICON AS PHOTOELECTRIC SCREEN FOR CELL IMAGING

Vladimir Lysenko

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A new cell imaging approach based on photoelectric measurements on bulk silicon wafers will be presented. Main photo-induced electronic mechanisms involved in such cell imaging technique will be reported. Application of gold nanoparticles as contrast agents will be particularly highlighted.

“LIQUID BIOPSY” AS A NEW BIOMEDICAL APPROACH IN CANCER DIAGNOSTICS: BENEFITS AND PITFALLS

Irina Nazarenko

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Introduction of “liquid biopsy” made a revolution is cancer diagnostics. Meantime for a number of tests blood or other body fluids, e.g. urine, tumor ascites or pleural effusion can be used instead of, or additionally to a conventional tissue biopsy for diagnostic purposes. We focus on identification of new liquid biopsy-based biomarkers for monitoring of therapy response and prediction of cancer therapy resistance. Specifically, we are interested in extracellular vesicles (exosomes, microvesicles, oncosomes) in blood or urine, transporting activated oncogenes decisive for sensitivity of tumor cells to certain drugs. Thereby detection of low amounts of tumor-derived nano-, or micro-sized vesicles harboring biomarkers of interest in complex solutions such as blood, remains the main challenges for implementation of this approach in the clinic. Using our know-how in vesicle biology and high throughput approaches, we search for new biomarkers, e.g. proteins, miRNAs, RNA or DNA. In collaboration with physicist and engineers, we develop new technologies allowing highly specific and ultrasensitive biomarker detection. In my talk, I will introduce our findings in early detection of prostate carcinoma and breast cancer prognosis based on highly sensitive spectral analysis and resonance measurements.

MULTIMODAL NANOSYSTEMS FOR THERANOSTICS

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The principles of translational medicine are based on collaboration of clinicians, biologists, chemists and physicists. This cooperation should accelerate the development and incorporation of new high-technology methods of diagnostics and therapy in clinics that improve human health life. The emergence of hybrid nanostructures with unique properties and functionality can significantly improve theranostics and helps to realize translational medicine ideas. The development of multimodal nanosystems that can be used for theranostics of the cardiovascular diseases, in oncology, and as antibacterial agents is the modern trend of nanotechnology [1].

Traditionally, nanosystems for theranostics contain fluorophores such as organic phosphors, nanoparticles doped with rare earth ions, or quantum dots, QDs. The fluorophores are utilized for imaging and controlling nanosystems distribution in the biological media; they can also be used as energy donors. By contrast with other fluorophores, the optical properties of QDs depend not only on their chemical composition, but also on their core size. This specific feature of QDs enables researchers to tune properties of the nanosystems based on QDs easily. In the last decade our group has developed nanosystems based on QDs and tetrapyrroles for Photodynamic Therapy (PDT) that often demonstrate a complex behavior in biological media due to appearance of new nonradiative channels of excitonic relaxation in these systems [2]. At the same time, we have shown that by careful tuning of nanosystems composition and architecture, the efficiency of energy transfer from QDs to tetrapyrrole up to 90% [3] and a doubled PDT effect in live cancer cells as compared to PDT medicine alone [4] can be achieved. These nanosystems can become a prototype of new theranostic medicine for

PDT if their active targeting into a tumor and their biodegradation and/or excretion from a body will be provided.

Passive targeted drug delivery with nanoparticles is well known nowadays. For a lot of nanoparticle types it has been shown that their size, shape and surface charge dictate the distribution of nanosystems in the organs. For realization of active target drug delivery the surface of nanoparticles can be passivated with target molecules, or with avidin for specific avidin/biotin interaction [5]. Including magnetic nanoparticles (MNPs) into nanosystems also gives opportunity to realize active targeting of nanosystems into tumor and at the same time improves their multimodality: nanosystems with MNPs can act as MRI agents and provide magnetic hyperthermia.

The toxicity of nanostructured materials is a complex problem that depends on nanoparticles size, chemical composition and their tendency to aggregate in biological media. Therefore, we believe that using Cd-free QDs or alloyed QDs with thick shell in the stable multimodal nanosystems could minimize their toxic effect on the life systems, and these nanosystems can be considered as medicines for theranostics.

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ORGANIC-INORGANIC HYBRID NANOSYSTEMS FOR PHOTODYNAMIC THERAPY

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Photodynamic (PD) therapy takes advantages of light absorption by light-sensitive photosensitizers and the generation of photochemical species such as singlet oxygen ($^1O_2$) or other reactive oxygen species (ROS) linked to apoptosis or necrosis of cancerous cells.[1] One of the necessary conditions for the efficient generation of ROS is wavelength matching of excitation wavelength to optical absorption of a photosensitizer.[2]

Upon last decades, there have been a lot of research activities directed toward the development of PD complexes based on different nanomaterials which are able to expand the excitation spectral region beyond the absorption of a photosensitizer and to enhance the efficiency of ROS generation.[3] Among others, semiconductor quantum dots (QDs) are highly attractive for PD therapy applications. QDs benefit from an extended absorption spectrum and high extinction coefficient both of which make them perfect as highly efficient light harvesting energy donors in complexes with PD molecules.[4,5]

In this report we focus on recent investigations into the enhancement of photodynamic properties of a photosensitiser using colloidal QDs. As a photosensitizer we used organic dye methylene blue (MB) that has been extensively used for a variety of photochemical and medical applications, including PD therapy. Highly absorptive and luminescent CdTe QDs were utilized as an inorganic constituent of formed hybrid nanosystem.

Absorption spectroscopy, photoluminescence spectroscopy, and fluorescence lifetime imaging of this system revealed an efficient energy transfer between nanocrystals and the MB dye.

Near-infrared photoluminescence measurements provided direct evidence for an increased efficiency of a singlet oxygen production by the organic-inorganic hybrid nanosystem.

Moreover, in vitro studies on the growth and viability of HepG2 and HeLa cancerous cells incubated in MB/QDs-containing mixtures of various concentrations were also performed. These studies point toward an improvement in the cell kill efficiency for the developed organic-inorganic hybrid nanosystem.

All these results suggest the possibility of improving the efficiency of any generic photosensitizer utilizing colloidal semiconductor QDs as light-harvesting nanoantenna. The broad absorption bands of QDs imply that the necessity of the expensive monochromatic light sources for PD therapy can be reduced.

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BIOCOMPATIBLE FILMS AND NANOFIBERS FOR BIOENGINEERING, MULTIMODAL BIOIMAGING AND SENSORS

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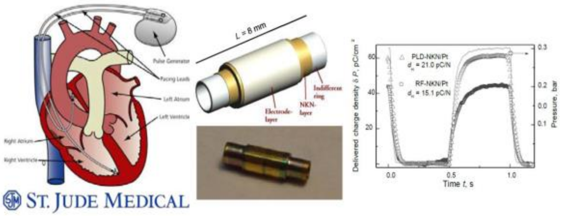
I survey our results on nanoengineered sodium-potassium niobate ceramics [$(Na,K)NbO_3$, hereinafter NKN] FDA-approved (U.S. Food and Drug Administration) as a biocompatible material for implants. The story of NKN had been started in 1949 by Matthias who grew in Bell Labs perovskite NKN single crystals, discovered piezoelectricity, birefringence, dielectric hysteresis loop, and polymorphic phase transition below their Curie points. [1] The next five decades works on NKN were mainly dedicated to the refinement of a phase diagram of continuous solid solution $NaxK1\text{-}xNbO_3$, proof of ferroelectricity and achievement of piezoelectric constant d33 as high as 160 pC/N at morphotropic phase boundary x = 0.5 (see references in Ref. [2]). The next important step in exploration of NKN occurred in 1998. Thorough toxicology tests showed that there were no any bacterial products (endotoxin) appear as well as viability of human monocytes was not negatively affected by the presence of NKN ceramics. Ferroelectric NKN ceramics was FDA-approved and patented as a biocompatible material for implants. [3] In late 1990s, we had grown high performance NKN films by pulsed laser deposition (PLD) technique. [4,5] Conformal coated self-assembling highly crystalline NKN films were grown on slightly textured and even amorphous substrates due to simultaneous stoichiometric material transfer and re-sputtering of unproperly oriented crystallites by laser plasma. [4] For St. Jude Medical, we fabricated and tested biocompatible NKN pressure sensor placed on the tubular Pt electrodes at the ends of two pacemaker's catheters (see Figures and Ref. [5]).



Changing the ambient oxygen pressure, PLD-grown NKN films were tailored from superparaelectric to strongly ferroelectric state. [6] Later on, we found high voltage tunability of dielectric permittivity and optical refractive index in epitaxial RF-sputtered NKN films. Combination of high performance multifunctional properties were exploited to fabricate and test various NKN devices: microwave varactors [7], surface acoustic wave transducer and acoustoelectric delay line [8] as well as to demonstrate electro-optic effect and waveguiding phenomenon for integrated optics [9]. Since 2000, number of papers, especially on Li and Ta substituted NKN, grows exponentially.

Recently, we added highly crystalline NKN nanofibers to the portfolio of lead-free biocompatible strongly ferroelectric materials. [2, 10] Dense homogeneous NKN nanofiber mat was sintered by sol-gel calcination assisted electrospinning technique. The process requiring neither catalysts nor templates yields continuous bead-free NKN nanofibers 100 μm long and 50-200 nm in diameter. High resolution electron microscopy and X-ray diffraction revealed preferential cube-on-cube fibers' growth in [001] direction. [2]

Raman spectroscopy and hysteresis *P*-*E* polarization tests ascertained all features characteristic to electrically spontaneously poled (ferroelectric) orthorhombic phase. Piezoelectric force microscopy revealed properties of individual NKN nanofibers which withstand without breakdown of electric field as high as 0.3 MV/cm. [10] Piezoelectric coefficient $d33$ was found to be strongly anisotropic varying from 75.8 to 18.3 pm/V in out-of-axis and on-axis oriented ferroelectric domains, correspondingly. Hysteresis *P*-*E* loop yields: coercive field $E\mathrm{c}$ = 31 kV/cm, remnant $P\mathrm{r}$ = 6.2 $\mu C/cm^2$, and the maximum achieved polarization $P\mathrm{max}$ = 21.2 $\mu C/cm^2$. [10] Intense room-temperature photoluminescence was achieved in Er-doped NKN fibers, bipolar resistance switching and strong rectification effect in nanoporous sandwich Au/Er:NKN/Pt capacitive cell were verified in electrical and impedance spectroscopy tests. [11] Photoexcited luminescence, enhanced piezoelectric and strong electrostriction effects promise great potential of NKN fibers as tensile and torsion sensors, electrically polarizable scaffolds for engineering, repair, and regeneration of damaged tissue as well as for energy harvesting biocompatible nanogenerators.

Further investigations of electrospun ceramic nanofibers we direct towards the engineering of biocompatible multifunctional sensors and multimodal bioimaging markers. We sintered bead-free *C*-type cubic gadolinium oxide (Gd_2O_3) nanofibers. Fibers with a giant length-to-diameter aspect ratio possess superparamagnetic behavior: they are magnetized twice stronger than Gd_2O_3 powder. Fabricated Gd_2O_3 *d*i*e*thylene*g*lycol coated (Gd_2O_3-DEG) nanofibers were compared with the Magnevist® (Gd_2O_3 gadopentetic acid, Gd-DTPA, *d*iethylene*t*riamine*p*ent*a*cetate) that had been administered in 1988 as magnetic resonance imaging (MRI) contrast agent to millions of patients worldwide. Our Gd_2O_3-DEG fibers show high $1/T_1$ and $1/T_2$ proton relaxivities. Intense room temperature photoluminescence, high NMR relaxivity and the record high neutron scattering cross-section of 157Gd nucleus promise to integrate Gd_2O_3 fibers for multimodal bioimaging and neutron capture therapy. [12]

We explore synthesis and comprehensive characterization of biocompatible core-shell ferromagnetic/ferroelectric nanofibers. The goal is to combine broad-band ferromagnetic resonance (FMR) properties already observed in highly crystalline core $Y_3Fe_5O_{12}$ nanofibers [13] with highly piezoelectric properties of NKN shell to achieve solid heterogeneously integrated multiferroic fibers. They can serve as agents for magnetic hypothermia, multifunctional 3D magnetic field/tensile sensors and energy harvesting nanogenerators. Novel micro- and nanoelectronic applications for biocompatible implants emerge from the non-volatile voltage switchable resistance memory found in Nb_2O_5 and NKN nanofibers.[14,11]

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METAL-CARBON NANOCLUSTERS FOR SERS

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The creation of new hybrid and composite materials based on carbon structures and metal nanoparticles is the most prospective area of nanotechnology. Carbon quantum dots demonstrate a variation of optical properties depending on the degree of crystallization, size and shape. The amplification of the observed phenomena can be realized by the addition of the noble metal nanoparticles having a plasmon resonant peaks in the visible region of the spectra. The linear carbon chain (carbyne) is the promising carbon material for the creation of the hybrid and composite materials.

The strategy to incorporate metal nanoparticles in a carbon matrix is a great method to integrate the different properties to various materials, enabling to realize multifunctional composites. Such materials may be used in advanced applications like nanobiotecnology, optoelectronics, etc. In particular, a widely used approach is given by the combination of linear carbon chains and metals. In effect, linear carbon chain is the one of the most attractive materials because its unique physicochemical properties and wide potential applications in nanophotonics. The possibility to obtain composites with large visible photoluminescence spectra for optoelectronic devices becomes especially interesting.

In this work we present the investigation of metal-carbyne clusters formation under the laser radiation of colloidal systems [1]. Colloidal solutions were consisted of carbon [2] and noble metals nanoparticles [3]. As a result, there was shown that clusters are forming during the irradiation process. The Raman spectra of those systems depends on the concentration of the particles in the solution and on the laser radiation conditions.

The SERS research by deposited films was performed using Senterra spectrometer (Bruker), with the pump laser wavelength of 532 nm, the power of 0.1 mW and the focal spot diameter of 2 microns (Center for laser and optical materials research, SPbSU).

The standard due Rhodamine 6G and DCM was used as a test molecule. The due solution in ethanol (10^{-5}-10^{-7}M) was placed on a metal-carbon structures using a micropipette. The metal-carbon surfaces are formed on an oxide glass substrates with different composition of metal nanoparticle. The use of films as a substrate of metal-carbon nanostructures under the same measurement conditions allow to detect and identify the dye on the Raman spectra with sureness.

The reported study was also supported by the Ministry of Education and Science of the Russian Federation (state project no. 16.5592.2017/VU), RFBR grants # 16-42-330531r_a, #16-32-00759mol_a and by the grant of president of Russian Federation by project MK-3053.2017.2.

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RESEARCH ON MEDICAL RADIOISOTOPES AT ELI-NP: DAY-ONE STUDIES AND PROSPECTIVE SOCIETAL BENEFITS*

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At the Extreme Light Infrastructure – Nuclear Physics facility (ELI-NP), a high-power laser system (HPLS) and a high-brilliance gamma beam system (GBS) are the main research tools. The status of the project will be reported. Selected topics of the emerging experimental program production of new medical radioisotopes at the ELI-NP GBS and HPLS will be presented. The expected performance of the related instruments, which are under construction for the realization of this research program,will be discussed, too.

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CURRENT STATUS OF NEUTRON CAPTURE THERAPY IN THE WORLD AND IN RUSSIA

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Neutron Capture Therapy (NCT) is a method of binary radiotherapy for curing malignancies. NCT is based on a physical phenomenon of neutron capture, which results in triggering a nuclear reaction inside a tumor, which in turn provides secondary radiation emission at its site. NCT combines properties of two radiation therapy modalities in one technology. Firstly, it is a beam radiotherapy like conventional radiotherapy, which uses external sources of radiation. Secondly, similarly to brachytherapy and radionuclide therapy, NCT uses radionuclide sources of short range high-LET radiation for killing tumor cells. Those radionuclides are produced as the result of the neutron capture phenomenon. A unique property of NCT, which attracts scientists and physicians all over the world, is its tumor selectivity. The use of isotopes capable of absorbing external neutrons much more efficiently than elements comprising biological soft tissue in conjunction with tumor-specific pharmaceutical substances could lead to complete tumor destruction with no damage to surrounding healthy tissues. The most widely used type of NCT is boron NCT (BNCT) utilizing neutron capture reaction on the stable isotope ^{10}B – $^{10}B(n,\alpha)^{7}Li$. ^{10}B has the probability to capture thermal neutron of ~1000 times higher than that of elements of a tumor (H,N,C,O etc.). Also, as the result of the nuclear reaction, an α-particle and ^{7}Li-nucleus are emitted with a range in water less than 10 μm and total energy of 2.31 MeV. Such properties of secondary radiation in BNCT excel any isotope used in brachytherapy or radionuclide therapy. However, despite the NCT unique therapeutic abilities and quite a long history (over 80 years since it was suggested by Locher in 1936), NCT is still not a standard treating modality in curing cancer. Different explanations of such a situation of NCT can be found elsewhere [1,2]. So, what is the prospect of NCT in the near future? For the average man, the answer can be found in two conflicting values, i.e. for the last 15 years, the number of centers in the world, which treat patients with NCT, has been decreasing (from 12 to 5), but the total annual number of NCT-treated patients has been increasing (Fig.1). The variety of tumor types treated with NCT is also increasing. At the beginning of the NCT-era, only brain tumors and skin melanoma were considered as indications for NCT, but for now NCT is applied for about 12 types of tumors. Fear of nuclear reactors caused in people by the Chernobyl and Fukushima disasters leads to decommissioning of operating research nuclear reactors, which for now are the only sources of neutrons for NCT. But success of physicians in Japan, Finland and Argentina in application of NCT for curing different types of tumor leads to annual increase of patients treated with NCT (about 50-60 cases per year in Japan). Decommissioning of nuclear reactors, on the one hand, and the need for neutron source for NCT from the medical society, on the other hand, stimulate development and production of accelerator-based neutron sources all around the world. Currently, at least 9 neutron generators for NCT are being installed in Japan, USA, Finland, Italy and Argentina. Two Phase I Clinical Trials of NCT with accelerator-based neutron generator are being held in Japan.

In Russia, NCT is being developed in Obninsk (A. Tsyb MRRC and SC "SSC RF – IPPE") and Moscow (MEPhI together with N.N. Blokhin NMRCO , A.I. Burnazyan FMBC). Most significant results were obtained at MEPhI in curing spontaneous oral cavity melanoma in dogs. Unique data were obtained on the efficacy of BPA-mediated NCT as a monotherapy in treating melanoma. 13 dogs with spontaneous oral cavity melanoma were treated with NCT as a first method of choice, and over 30 dogs were treated with NCT in combination with other methods. Complete tumor regression was observed in 92% of animals, no recurrence of tumor within 1.5 year in 61%, and survival median was 16 months.

A new moderator was designed and installed on the horizontal channel HEC-1 of the MEPhI Reactor to produce epithermal neutron beam for clinical application of NCT. Currently, the Research Reactor at NRNU MEPhI is being relicensed, and upon operating authorization, NCT studies at NRNU MEPhI will be continued.

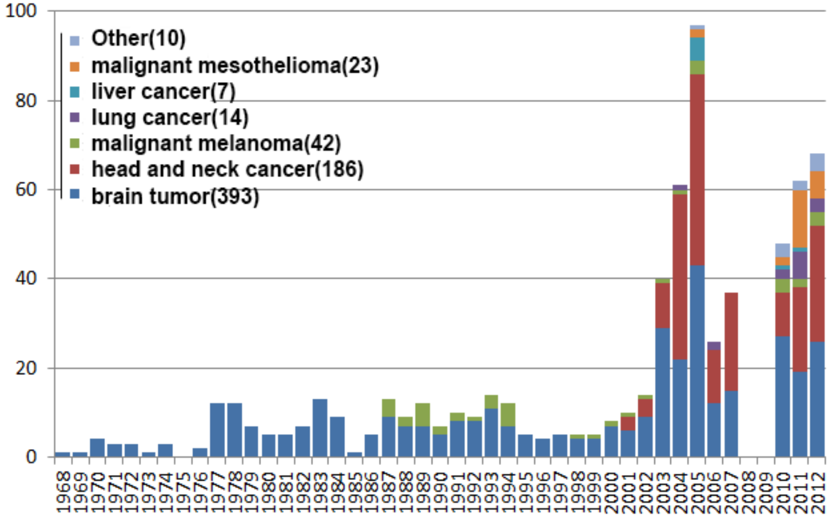

Fig.1. Number of patients treated with NCT in Japan by year [4]

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OPPORTUNITIES IN THE PROTON THERAPY: BRIEF ANALYSIS OF ONE YEAR EXPERIENCE AT RUSSIAN PROTON SCANNING BEAM FACILITY

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Introduction. Modern achievements in the early diagnosis and treatment of both oncological and non-oncological diseases are deeply connected with the hi-tech radiation-based technologies, which allow~~s~~ the most effective treatment techniques to be chosen concerning the proper diagnosis. The currently existing treatment practice suggests the wide variety of different methods and their combinations which ultimately lead~~s~~ to the patients' quality of life and after-treatment life expectancy increase.

The main issue of radiation therapy is to optimize the balance between delivering a high and conformal dose to the tumour and limiting the doses to healthy tissues. To achieve that various radiation kinds (X-rays, charged particles) with different energy spectra can be successfully used, depending on their penetration depths and local dose deposition features, to targetly irradiate the tumour sparing the adjacent normal tissues. The proton therapy has a highly accurate dose deposition profile (i.e. the Bragg peak), which can be spread out in three dimensions to match the target volume with a highly uniform dose distribution inside the tumour region. The proton beam can be focused precisely only to tumour sites what is highly important because of risk minimization for critical structures (ROIs) or in the presence of highly radiosensitive tissues.

The Russian therapeutic proton scanning beam facility developed by CJSC "Protom" (Protvino, Russia) has been specifically designed as highly accurate stereotactic radiotherapy tool and meets the existing common requirements and gold standards as medical technology to treat the different tumour localization. A vertical patient alignment and immobilization in a rotating armchair (360 deg with 1 deg step) coupled with scanning beam allows to achieve the notably lower dose in healthy tissues due to targeting the radiation beam from multiple directions. The main technical parameters of the facility meet all the clinical requirements while some features are exceeding the currently existing analogues. The synchrotron diameter is 5 meters, power consumption is 50 kW, scanning beam flux density is 10^9 particles/s, proton energy range is 30-250 MeV.

The clinical application of the proton therapeutic proton scanning beam facility implies–the beam quality assurance trials, the dosimetric and radiobiological parameters evaluation, and the radiation treatment quality assurance confirmation.

Methodology. A new methodology and technique development for dynamic volumetric-conformal treatment planning with scanning proton beam are essentials of the treatment efficiency and accuracy optimization. The absorbed dose value, its uniformity and accuracy has been measured with ionization chambers (flat IBA® PPC40 and cylindrical PTW® TM30010), and radiochromic film Gafchromic® EBT3.

The biological *in vitro* tests have been carried out using two cell cultures: mice melanoma B-16 and Chinese hamster V-79. The cell samples were irradiated inside a water phantom at the center of Spread-Out Bragg Peak calculated for one or multiple irradiation fields by domestic treatment planning software. The tested dose range was 1.5 - 10 Gy. The doses reducing cells survival to 10 % levels have been assessed using colonies formation test. The similar cells in the same dose range were irradiated with ^{60}Co γ-rays. I*n vivo* studies were performed using rats with sarcoma M-1. Biological effects of 32 Gy proton and 28-36 Gy ^{60}Co γ-rays local dose to tumor were compared.

Results. The proton dose deposition analysis using various dosimetric and biological objects Monte Carlo simulations scenarios for proton scanning beam facility has shown a good agreement with experimental data and meeting all the quality assurance requirements for the medical needs. Different dosimetry techniques confirmed the overall dose deposition patterns within ± 5% uncertainty.

The RBE value for mice B-16 melanoma cells irradiated with 2 radiation fields has been found to be 1.2. For V-79 cells irradiated with proton beam either from 1 or 3 directions RBE values have been somewhat less, 1.0. The *in vivo* RBE values for rats with M-1 sarcoma ranged 1.1-1.2 with no skin reactions observed.

Conclusion. The dose field reconstructive Monte Carlo simulations, LET variation studies for multiple-fields irradiations, the dose uniformity assessment in accordance with treatment planning principles, dose visualization within the target volume, isodose field conformity, have shown that the therapeutic scanning proton beam facility meets all the technological and medical quality assurance requirements.

The absorbed doses measured or calculated within the biological samples irradiated both *in vitro* and *in vivo* using the proton beam with one/multiple fields, have allowed to assess RBE values that have been found to be 1.0-1.2 depending on the test-system chosen. This is a critical issue to be taken into account in the radiation treatment planning system.

The clinical trials for patients with brain and head-neck tumors, including the skull base sarcomas and cervical spine adjacent tumours have shown that additional methodical studies are required at the treatment plan preparation stage, particularly the lateral dose penumbra and local LET variation within lesion boundaries and zones at risk must be taken into consideration.

MEDICAL INFORMATICS IN CANCER RESEARCH: FROM IMAGES TO INFORMATION

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Medical images uniquely represent the anatomical and functional progress of diseases in 3D space and time. At the Division of Medical Image Computing, we strive to utilize the vast and unexploited potential in these images through computational image understanding and information processing.

Here, we will present our most recent methods that utilize "radiomics", traditional machine learning as well as deep learning techniques to comprehensively analyze and summarize imaging information from multiple time points and modalities. Our methods are developed for various clinical applications with emphasis on prostate cancer, breast cancer and brain tumors. Another focus of our research lies in processing, analysis and visualization of neurological datasets, especially from diffusion-weighted MRI. We develop techniques for white matter fiber tractography and segmentation, as well as for brain connectivity analysis (connectomics). Main fields of application comprise Alzheimer’s disease, autism spectrum disorder and borderline personality disorder.

CONSUMER *VS.* AN INNOVATIVE DEVICES' ABILITY TO GENERATE IMAGES FOR TELEDERMATOLOGY

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Type 2 diabetes’ incidence has dramatically increased over the last twenty years, especially in industrialized countries (USA, Europe, Australia, and Japan) [1]. About 20% of diabetic patients develop chronic wounds i.e. vascular ulcers. Such ulcers represent a huge economic burden: in 2004, 3 billion dollars were dedicated to such medical burden (71 000 lower-limb surgeries that cost 38 000 $ each) [2]. Since dermatologists density is very different from one area to another [3] and since dermatologists’ density is not increasing as fast as the general population is ageing and growing, tele-health appears to be a promising solution specifically in remote areas. Nowadays mostly devices from the “general consumer” market are used to perform tele-consultations dedicated to vascular ulcers diagnosis and care. Such general consumer devices typically are digital tablets, digital cameras as well as smartphones. Those user-friendly equipments allowed first experiments in tele-dermatology. However, imaging problems have quickly emerged because of *(i)* poor color rendering index resulting in poor color discrimination and poor color repeatability, *(ii)* resolution power smaller than the levels of resolution powers during in-person consultations and *(iii)* field of view’s areas misfit to wide areas required during teleconsultations (in order to evaluate the wound as well as surrounding skin). In a previous work [4], we proposed a set of optical criteria (along with corresponding threshold) that should be used to define an image quality that is of good enough level to be used in the framework of teledermatology. Based on such criteria and thresholds, we compared general consumer’s devices as well as medical devices’ optical performances. In the current work, we propose to complete previous data with data from the medical device we developed in order to outperform the medical devices currently found in most dermatologists' practices.

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ESTIMATION OF *IN VIVO* OPTICAL PROPERTIES OF HUMAN SKIN CARCINOMAS USING SPATIALLY RESOLVED MULTIMODAL SPECTROSCOPY: CLINICAL STUDY PRELIMINARY RESULTS

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Precise and robust estimation of biological tissues' optical properties is a key factor in the development of optical spectroscopic and imaging methods and in their applicability to non-invasive diagnostics in clinics.Pathological and early metabolic and morphological modifications induce changes in the optical properties of the biological tissues at sub-cellular, cellular and tissue scales. The data analysis challenge consists in extracting from the measured intensity spectra, discriminant information related to the characteristics and concentrations of the constitutive elements (absorbers, diffusers and fluorophores).Our research activities are oriented towards the development of multimodal « optical biopsy » modalities applied to early cancer *in vivo*detection. The benefit of coupling AutoFluorescence (AF) and Diffuse Reflectance (DR) spectroscopies has been demonstrated in several experimental studies for identifying the optical properties of *ex vivo* tissues [1] and for improving the diagnosis efficiency in several preclinical studies: skin hypertrophic lesions [5,9], bladder cancer [10,11,12], precancerous skin lesions [3,4,6,8,].In the framework of the collaborative project « SpectroLive » involving our laboratory and the Frenchcompany SD-Innovation, we developed a new prototype of bimodal spectroscopy, providing the simultaneous measurements of multiple excitation wavelengths (UV-Visible) AF intensity spectra and DR spectra, to be used in clinical settings [16]. A joint study within the Plastic Surgery Department of the Regional Hospital (CHR Metz-Thionville) is in progress for evaluating the performance of this prototype in improving the skin carcinoma detection and management (namely peroperativemarging delineation). The present contribution focuses on the question of tissue optical properties estimation which consists in solving a classically ill-posed (different sets of parameters may lead to close similar data set) and ill-conditioned (numerical instability of the solutions due to finite precision and errors in the data) inverse problem [2,15]. Preliminary results are given on healthy and carcinoma lesions by comparing the main features of AF and DR spectra and the estimated values of spectrally resolved optical properties in the case of mono- or bi-layered tissue models.

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MODERN INSTRUMENTAL AND METHODOLOGICAL APROACHES FOR BRAIN TUMORS THERANOSTICS

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One of the main conditions for delaying time to relapse after brain tumor surgical removal is the complete removal of all invaded brain tissues. Wherein the traditional technique of adjoining healthy tissue surgical removal has limitations related to the possibility of vital organs functionality disrupting. Thereby urgent tasks of the surgery success ensure is differential diagnosis of tumor micro-regions with subsequent removal or destruction of them. Recently, the new approaches to intraoperative navigation of brain tumors based on the using of fluorescent photosensitizers with selectively tumor accumulation. The most widely used photosensitizer is ALA-induced protoporphyrin IX. However, at nowadays there is no technical solution allowing simultaneous tissue sites differentiating by fluorescence signal at the micro level with their subsequent removal or destruction. At the same time there are technical solutions of both foreign and Russian groups at the macro level.

Diagnostic equipment available for clinicians does not allow to work under the bleeding, have a low depth of surface sounding, do not allow simultaneous monitoring of the original and fluorescent images. And the most important flaw is the spatial resolution of the removed tumor site which does not guarantee complete removal.

So we have developed the endoscopic system for the visualization of 5-ALA induced protoporphyrin IX distribution, which allows to combine a full-color and fluorescent images, and also to calculate the photosensitizer concentration in the surgeon's field of vision. The local maximum of protoporphyrin IX absorption in the so-called biological transparency window (in the red region of the spectrum) is used to excite fluorescence, which allows to increase the depth of tissues sounding and to avoid signal screening from the leaky blood, which increases the measurements accuracy and the system using convenience.

At the planning operations to remove high grade glioblastoma multiform, the main goal is the glial cells removing that have been diffused along the nerve fibers and blood vessels (that is not yet solved in the world). We are trying to solve this problem in four areas:

- Fiber-optic implants developing. The optic fibers are covered with a special composition which attracts glial cells at the same time under the light cause their death due to the photodynamic effect.

- The use of infrared photosensitizers, infrared lasers and radiation receivers to increase the depth of detection and photodynamic action.

-The use of activated nanophotosensitizers, which become to fluoresce and phototoxic in the interaction with tumor and tumor associated microglia. This approach will significantly increase the selectivity of theatronics.

- The use of Vavilov-Cherenkov radiation due to tumor phototheranostics by the using of radionuclides for photosensitizer activation which are selectively accumulating in malignant glioma cells and tumor-associated microglia.

There are experimental results demonstrating the validity of these approaches on laboratory animals and cell lines in the report.

The project was implemented with the financial support of the Ministry of Education and Science of the Russian Federation (agreement No. 14.607.21.0183).

PROBING BIOLOGICAL TISSUES WITH ELLIPTICALLY POLARIZED LIGHT

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Polarization gating is a popular technique in biomedical optics to classify and select photons based on their state of polarization. Surface of tissues is enhanced by selecting the polarization maintaining photons, usually using a collinear imaging channel, and, reversely, deeper volumes are probed by selecting the depolarized ones, usually by performing cross-linear measurements. Instead of using the conventional linearly polarized illumination, we propose to take advantage of using elliptically polarized light as it allows a more selective probing in terms of depth. Co-elliptical measurements allow accessing to deeper subsurface volumes than collinear measurements, the depth of probing being controlled by the ellipticity of polarization. Counter-elliptical measurements attenuates subsurface signal and, hence, enhances the signal coming from deeper volumes, provided mirror reflections are filtered too. We propose a new protocol of polarization gating data acquisition that combines co-elliptical and counter-elliptical measurements. Validations of the approach include measurements on phantoms, ex vivo and in vivo tissues. Furthermore, a new Monte Carlo algorithm, efficient in terms of computation time, allowed to perform modeling of polarized light propagation in various configurations. Its flexibility provides a versatile linear formulation for efficient resolution of inverse problems, allowing a step forward to the quantification of the optical properties of biological tissues at different depths.

INORGANIC-ORGANIC HYBRID NANOMATERIALS FOR TARGETED AND CONTROLLEDDRUG DELIVERY

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Nanomedicine offers unprecedented opportunities in the diagnosis and treatment of diseases. Key features of nanomedicine include ultra-sensitive diagnostics, multimodal bioimaging, targeted delivery, controlled drug release, and externally activated therapy. Inorganic-organic hybrid nanoparticles combine the benefits of active metal center/s and organic functionalities. We have synthesized drug-loaded hybrid nanoparticles, such as organically modified silica/titania and nanoscale metal-organic framework. The loaded drugs were found to release in a sustained manner. Furthermore, incorporation of optical or magnetic moieties within these nanoparticles allows for optically or magnetically guided delivery to target sites, as well as externally-activated localized therapies. This talk will present a brief overview on such topics, with representative examples from our research work.

APPLICATIONS OF MOLECULAR IMAGING AND MACHINE LEARNING METHODS FOR MEDICAL DIAGNOSTICS

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The focus of the report connected with applications of molecular imaging and machine learning methods for medical diagnostics. The problem is connected with separation of informative features from of molecular imaging data and construction of effective classifiers for medical diagnostics.

The experimental base for molecular imaging and molecular spectroscopy includes time-domain THz spectrometer "T-Spec" (EXPLA) with tuning range 0.3 – 3.5 THz and ability of regular position in the XY space, MPTflexMultiphoton Laser Tomograph (JenLab) with FLIM module, and laser OPO photoacoustic gas analyzer LaserBreeze (Special Technologies, Ltd, RF).

The used Data Mining methods include Canonical Correlation Analysis, Principal Component Analysis for selection of most informative features and reduction the dimension of initial feature space, a number of methods of results classification, such as Support Vector Machine, the combination of the latter and the Histogram of Oriented Gradients descriptor.

TRANSLATIONAL MEDICINE: MYTH OR REALITY?

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Personalized and Precision Medicine (PPM) as being the Grand Challenge to forecast, to predict and to prevent is rooted in a big and a new science generated by the achievements of systems biology and Translational Medicine (TM) whilst integrating and consolidating platforms of Genomics, Proteomics, Metabolomics, Interactomics, Cytomics, etc, and Bioinformatics as well.

The development and application of systems strategies to biology and disease are transforming medical research and clinical practice in an unprecedented rate. Translational research is the science that aims at making scientific discoveries available for practical application, especially in relation to life sciences, medicine and bioengineering. TM is thus an area of research that aims to improve human health and longevity by determining the relevance to human disease of novel discoveries in the biological sciences. Despite increasing use of the term, the translation of basic science discoveries into clinical practice is not straightforward.

TM seeks to coordinate the use of new knowledge in clinical practice and to incorporate clinical observations and questions into scientific hypotheses in the laboratory. Thus, it is a bidirectional concept, encompassing so-called *bench-to-bedside* factors, which aim to increase the efficiency by which new therapeutic strategies developed through basic research are tested clinically, and bedside-to-bench factors, which provide feedback about the applications of new treatments and how they can be improved. TM facilitates the characterization of disease processes and the generation of novel hypotheses based on direct human observation.

Digital medicine is a new strategy and engine of TM, encompassing electronic health record keeping, mobile medical device use, hospital information systems, laboratory information systems, and nationwide medical information architecture. These systems and networks connect patients, community health service centers, hospitals, remote clinics, and education centers to improve the quality and efficiency of health care.

The goals of TM in academia and industry are complementary. Thus, a balanced approach that encourages partnership between these entities, with small bioengineering enterprises bridging the gap, could establish a positive feedback loop in which benefits in the clinic fuel advances in academia, which in turn lead to the development of new products in industry.

To optimize translational research, policy could consider refining translational research models to better reflect scientists’ experiences, fostering greater collaboration and buy in from all types of scientists. Organizations could foster cultural change, ensuring that organizational practices and systems keep pace with the change in knowledge production brought about by the translational research agenda.

RECOGNITION OF LEUCOCYTES FROM BLOOD AND BONE MARROW IN THE DIAGNOSIS OF ACUTE LEUKEMIAS

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Diagnosis of acute leukemia is based on the study of morphological features of leukemic cells in the peripheral blood and aspirates of bone marrow.

Application of methods of clarifying the morphological characteristic of lymphoid elements is of considerable interest up to the present time.

Computer microscopy with using a multispectral camera is better able to study the structure of nuclear chromatin and allows to objectify the data obtained in the form of a numeric index compared to traditional visual analysis [1].

Digital image processing systems have not required level of performance and reliability of automatic analysis of blood smears and bone marrow aspirates at the present stage of development [2].

The work is dedicated to the creation of a program complex of the automated classification of leukocytes in blood smears and bone marrow aspirates.

As objects of the measurements were images of leukocytes, which were obtained from preparations of the blood and bone marrow fixed and stained by the method of May-Grunwald-Romanovsky. Morphological examination of blood smears and bone marrow aspirates was conducted by two experts in the laboratory of immunology and hematopoiesis of NN Blokhin Russian Cancer Research Center. The diagnosis was established on the basis of morphological, cytochemical and immunophenotypic studies.

The program complex was developed in the result of the work. It allows to segment blood cells from preparations of blood and bone marrow, count the characteristics of the leukocyte, count myelogram for the bone marrow aspirates and leukocyte formula for blood smear.

Fig.1 shows example of a comparison myelogram deemed by expert and software.

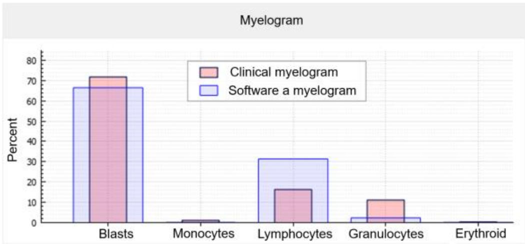

Fig.1. Myelograms built by expert (clinical myelogram) and software

The proposed software approach of myelogram building coincides with the expert calculation by 87%.

Planned step for further research is improving the recognition accuracy of leukocytes on images of bone marrow preparations.

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DIFFERENT WHOLE GENOME SEQUENCING STRATEGIES TO CHARACTERIZE OROPHARYNGEAL SQUAMOUS CELL CARCINOMAS AND HOW THIS COULD TRANSFORM THE CLINICAL TREATMENT OF PATIENTS WITH THIS CANCER

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Oropharyngeal squamous cell carcinomas are cancer of the base of the tongue and tonsils. While these cancers were traditionally caused by smoking and drinking, in the past several decades more and more of these cancers are found to contain human papilloma virus (HPV) sequences. In order to characterize how HPV has been involved in the development of these cancers we have used different genome sequencing strategies to characterize genomic alterations in these cancers and the physical structure of HPV in these genomes. The first strategy employed was mate-pair next generation sequencing which is a powerful technique to characterize genomic alterations but at a fraction of the cost of whole genome sequencing. Using this technique we’ve found that HPV is only integrated into the genome in 30% of HPV-positive oropharyngeal squamous cell carcinomas, which is very different from what is observed in cervical cancer. We have also started to explore whole genome sequencing as an alternative way to characterize these genomes. In collaboration with scientists at the Beijing Genomics Institute we have done 30X WGS of a number of these cancer genomes. We demonstrate that this is a very powerful way to characterize most of the genomic alterations that have occurred in these cancers. This not only detects the sites of HPV integration (when it occurs), but can also reveal the genomic structure at and around each integration. These strategies reveal a great deal about the alterations in each individual cancer and the knowledge gained from this could provide important information for the best way to clinically treat each individual cancer patient.

NEW TARGETS FROM THE HUMAN GENOME AND SECOND GENOME WITH METABOLOMICS

Carlos Malpica

PhD, MBA, Global Business Development Director, Metabolon Inc.

Metabolon has developed a platform technology capitalizing on advances in mass spectrometry, proprietary software and database analysis that provide unprecedented insight into biochemical pathways. Metabolomics has evolved to accompany tools like genomics in the quest to unlock human health and disease. The ability to collect so much data directly on human subjects and their microbiome offers the potential to deliver new targets that will have unequivocal relevance to human disease.

By producing a comprehensive read-out of their metabolic profile, metabolomics can give clinicians more insight to the patient's health status. We will discuss how metabolomics will play an integral role in the future of precision medicine.

INTERNATIONAL COOPERATION IN THE GLOBAL SEARCH FOR NEW ANTIMICROBIAL AND PHARMACEUTICAL THERAPIES - A JOINT NEW ZEALAND RUSSIAN MODEL TO ADVANCE THE SCIENTIFIC EFFORT

John Aitken

1000 Airplanes Ltd, New Zealand

New Zealand is relatively isolated from the rest of the world, and evolution of indigenous microorganisms has been driven by unique environmental pressures.

My work involves identification of microorganisms capable of protecting indigenous plants and animal, and identifying candidate organisms capable of being used for interventions in global plant and human microbial diseases.

My laboratory also investigates autoimmune diseases and has identified cell-wall defective microorganisms that may be acting as triggers for autoimmune diseases.

My talk will discuss biodiscovery of these organisms, and experimental procedures to help to understand the mechanisms of action.

Distance can also be a problem, and it is necessary for us to seek international partners in order to bring some of these organisms to commercialisation. I will discuss some possible models to achieve this synergistic outcome.

INTEGRATING GENOMIC AND CLINICAL DATA FOR PRECISION MEDICINE

Shawn Murphy

Partners HealthCare System Inc, USA

Although patients may have a wealth of imaging, genomic, monitoring, and personal device data, it has yet to be fully integrated into clinical care. We identify three reasons for the lack of integration. The first is that "Big Data" is poorly managed by most Electronic Medical Record Systems (EMRS). Big data is mostly available on "cloud-native" platforms that are outside the scope of most EMRS. The second reason is that extracting features from the Big Data that are relevant to healthcare often requires complex machine learning algorithms, such as determining if a genomic variant is protein-altering. The third reason is that applications that present the big data need to be modified constantly to reflect the current state of knowledge, such as instructing when to order a new set of genomic tests. In some cases, the applications need to be updated nightly. A new architecture for the EMRS is evolving which could unite Big Data, machine learning, and clinical care through a microservice-based architecture which can host applications focused on quite specific aspects of clinical care, such as managing cancer immunotherapy. Informatics innovation, medical research, and clinical care go hand in hand as we look to infuse science-based practice into healthcare. Innovative methods will lead to in a new ecosystem of Apps interacting with healthcare providers to fulfill a promise that is still to be determined.

MICROFLUIDIC APPROACHES FOR SMALLMOTILE ORGANISMS HANDLING AND TRACKING DURING MAGNETICRESONANCE MICROSCOPY

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The nematode Caenorhabditiselegans (C. elegans) possesses several attributes that make this organism attractive as a model system. The potential usefulness of C. elegans stems from a balance between biological simplicity and complexity, allowing one to address high-level biological questions and providing a unique opportunity to model human ailments, such as Alzheimer's and Parkinson's disease. Nuclear magnetic resonance (NMR) spectroscopy is one of the most information-rich methods, which provide a unique opportunity to link morphological, functional and chemically specific spectroscopic information from small volume (e.g., μL) samples. However, the motility of this small model organism poses a key challenge for the in vivo acquisition of magnetic resonance signals. Micro-fabrication techniques hold potential to yield intelligent probe and fluidic system in combination with other detection methods to achieve highly parallel signal acquisition. With the ultimate goal of NMR measurements of individual nematodes, a modular multifunctional platform for detection and immobilization ofC. eleganshave been developed. This approach has a potential to address the need for comprehensive NMR-driven analyses and provide a highly important tool to the molecular and systems biologists.

DEVELOPMENT OF A BIFUNCTIONAL TRANSLATIONAL PLATFORM TO DEVELOP THERAPEUTICS OF THE NEWEST GENERATION TARGETED FOR THE POST-INFARCTION CONDITION MANAGEMENT AND BEING APPLIED INTO BIOPHARMA

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Myocardial infarction (MI) remains a major clinical problem and the leading cause of mortality in the world: permanent loss of cardiomyocytes after MI results in an irreversible damage to the cardiac function, and the latter would strongly need cardiac repair which is, therefore, essential to restore function of the heart following MI. Existing therapies dictate a need for treatment to heal the infarcted area by replacing the damaged cells with functioning cardiac myocytes (CMs) after MI. In contrast to the experience trying to activate mature CMs or resident CSCs we are aiming to apply our data summarized in a series of papers published illustrating intracellular development of resident cardiac stem cells (CSCs) inside CMs to form "cell-in-cell structures" (CICSs). It was shown that CSCs undergo multiple rounds of division inside CICSs and eventually become partially differentiated in the cardiomyogenic lineage in the form of transitory amplifying cells (TACs). After ischemic heart injury, TACs are released into the myocardium and demonstrate marked proliferative potential and the ability to differentiate into matured CMs. The significant value of that phenomenon would allow to consider TACs as a powerful cell source for regeneration and thus the therapeutic tool to be applied in post-MI preventive therapy and rehabilitation. Exosomes may be a key mechanism by which may be stimulated the differentiation of TACs. We assume that the study the phenomenon of intracellular CSC development with formation of TACs, and the developing approaches for programming exosomes aimed at interacting with TACs will promote the regeneration of CMs pool in post-infarction period. Such multi-step studies illustrating so-called “translational pipeline”, i.e., starting up from the original idea through the development of the laboratory product, followed by preclinical and clinical trials with the following exit to biopharma updated sector.

HARNESSING DNA DAMAGE PROCESSING ENZYMES FOR BIOTECHNOLOGY AND HUMAN HEALTH

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DNA damage is ubiquitous and can perturb DNA replication, leading to sequencing errors, mutations, cancer, or cell death. DNA polymerases of the Y family possess the specialized ability to copy damaged DNA, although this ability comes at the potential cost of mutations. The Y-family DNA polymerase *E. coli* DinB and its human ortholog pol kappa specifically copy minor groove N^2-dG adducts and are inhibited by major groove adducts [1-2]. These polymerases also show a specific pattern of protection from hydrogen-deuterium exchange in the presence of preferred damaged DNA substrates and the correct incoming nucleotide, consistent with a conformation change that correlates with activity; these specific patterns of protection are not observed with non-preferred damaged DNA or the incorrect incoming nucleotides [3]. To probe the mechanisms of these DNA polymerases further, we applied the computational active-site prediction method Partial Order Optimum Likelihood (POOL) to *E. coli* DinB, which predicted that residues outside of the active site contribute substantially to activity [4]. We validated this experimentally and further determined that these so-called second shell residues contribute specifically to the ability of DinB to extend DNA primers beyond the site of DNA damage [5]. We are now applying POOL to other DNA polymerases to determine their active site architecture as well as to harness these insights to develop new polymerases and DNA repair proteins with useful properties. Our objective is to develop DNA polymerases specialized to copy DNA that has been damaged by cellular stress or certain types of environmental mutagens, such that the correct base sequence is maintained. These new proteins will have a number of applications in human health and biotechnology.

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CORRELATIVE MICROSCOPY: A POTENT TOOL FOR BIOMEDICINE

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The concept of correlation microscopy includes three points:

(1) obtaining structural information by high resolution microscopy (SEM, TEM, SPM);

(2) obtaining data on composition and functional properties (optical microspectroscopy);

(3) reconstruction of the three-dimensional structure by microtomography.

Traditionally, correlation microscopy included the combination of electron and optical microscopy, the so-called method of Correlative Light and Electron Microscopy, CLEM.

In the last decade, the circle of correlation microscopy methods significantly expanded. New tools combined electron microscopy and Raman spectroscopy, as well as electron microscopy and ultramicrotomography in one device are developed.

An alternative to the electron microscopy as ultra-high resolution technique is the scanning near-field optical microscopy, SNOM). We used this approach to design modern instrument in which scanning probe microscopy was combined with optical polarization microspectroscopy and mechanical ultramicrotomography. This combination allows solving all complex of correlation microscopy problems [1-3].

We demonstrated the opportunities of the approach on the example of investigation the nanomaterial: quantum dots in cholesteric liquid crystal matrix, QD/CLCM). It was found the correlations between the fluorescent polarization properties of a CLCM with QDs and the 3-D distribution of QDs in the CLCM. As the result the way to improve the characteristics of nanomaterial was proposed [4]. Another example was the determination of the structure of the elements of colloidal liquid microchips for medical diagnostics [3].

On the base of the approach the Unique Scientific Device "System for probe-optical 3D correlative microscopy" (http://ckp-rf.ru/usu/486825/) was build. In the device, all techniques of SPM are presented (contact, semicontact, dynamic contact, and tapping modes, force modulation, magnetic and electrostatic force, Kelvin-probe and scanning spreading resistance microscopy. Also, it has the possibility to use the confocal fluorescence, Raman, surface and tip enhanced Raman scattering spectroscopy (SERS and TERS), and SNOM. Instrument contains the hard and software for reconstruction 3-D reconstruction of the morphological/optical structure of samples. Potential and perspectives of the correlative microscopy approach and new instrument in the biomedical applications are discussed.

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BIOPHOTONICS, ELECTROSMOG, PREDICTIVE AND PREVENTATIVE MEDICINE

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Biophotonics research has been able to show ultraweak photon emission from the human body at the wavelengths of visible light, but longer wavelength photon emissions in the microwave spectrum have been much harder to isolate. Research in Kiev in the 54-78GHz range, in Prague at 42GHz and our own efforts with TE mode at 12GHz and TM mode at 4.8GHz have not been able to show convincing proof of microwave electromagnetic (EM) radiation from living organisms at levels above thermal noise - a substantially similar result to the ultraweak generation of visible photons. Living organisms clearly have evolved a finely balanced energy metabolism where minimal energy is wasted overcoming the molecular reaction potentials. This very absence of high-energy radiation is an important Biomarker for Medicine to assimilate, as it overturns a pervasive belief that only high-energy EM radiation is capable of altering human biology. Based on the ultraweak emissions, the Theorem of Reciprocity would predict that even miniscule levels of EM energy are likely to affect the molecular interactions in living organisms. Using Faraday Cages we have been able to show that humans with immune disease are indeed sensitive to levels which are orders of magnitude below current levels of Electrosmog. Further, we used Molecular Dynamic emulations to show that a key transcription factor, the VDR Nuclear Receptor, exhibited metastability when docking with its ligands. Potential resonances were found in the low GHz range - already widely subject to Electrosmog from cell-phones and WiFi. Our biophotonic radiation observations were corroborated when the VDR's hydrogen bonds typically settled into energy wells between 20 and 50 meV, energies just above the level of thermal noise at human body temperature. Yet Evidence Based Medicine (EBM) continues to study EM signal levels seven orders of magnitude (70dB) above this threshold, and puzzle over inconsistent experimental results. Conversely, we are seeing that low-level EM radiation consistently exacerbates existing human immune disease.

Mankind is at a precipice. Are modern communications technologies associated with the 50% reduction in human sperm count over the last 20 years? Is EM radiation associated with the projected doubling of diabetes prevalence within the next 10 years? Is it at least partly responsible for the spiraling rate of chronic immune disease? It is essential that we point the Evidence Base experiments towards asking the right questions about EM radiation and disease. It is clear that Predictive and Preventive Medicine research (PPPM) can only be successful if it is based around multi-disciplinary translational study teams capable of understanding not only human Physiology, but also the Molecular Physics.

LASER-TISSUE INTERACTION ON THE MOLECULAR LEVEL

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During the 1^{st} symposium I reported of advanced laser-tissue interaction of pulsed laser systems in medical application.

In this lecture I will present the opposite condition of the interaction of photons with biological tissue at lower laser intensities.

New knowledge has been accumulated about low intensity laser applications in vitro but also in vivo which opens insight into themolecular reaction mechanisms in cells and tissue. Not only cells reactions are influenced by photons, but also the extracellular matrixplays an important role. Such mechanisms will be explained and results presented.

POSTER REPORTS

TISSUE CULTURE OF BOVINE FOLLICLES IN COLLAGEN MATRIX GEL

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One of the new technologies attracting the attention of reproductive technologists in recent times is the isolation and the culture of preantral ovarian follicles from ovarian tissue for using them as an alternate source of fertilizable oocytes to produce embryos. Well known that the mammalian ovary contains a huge stock of resting follicles [1]. A very small number of these oocytes grow to the final size, mature, and are ovulated. In the ovary there are more early antral follicles than late antral or preovulatory follicles. The large store of these small follicles creates a potential source of oocytes for in vitro embryo production.

The aim of study was to establish a culture system to support the growth of small bovine oocytes as enclosed in granulosa cell complexes that extend in a three-dimensional collagen matrix supports a spherical structure of follicles and to determine the optimal conditions for in vitro growth [2] and fertilization of early antral animal follicles. Such systems have been established for mouse oocytes but are not applicable to larger animals because it is difficult to maintain an appropriate association between the oocytes and companion somatic cells. The present study examines integrity and morphological features, viability, and follicular forming capacity of early bovine oocytes cultured in vitro in collagen embedded matrix. This culture system may provide a valuable approach for study of the regulation of early follicular development.

The objectives of the study were to investigate the relationship between the morphological statuses of collagen embedded early antral follicles and conditions of culture of the oocytes. In the present study, we compared five culture conditions for growing bovine oocytes and examined the effect of hypoxanthine and hormone on oocytes growth. The oocyte-cumulus-granulosa cell complexes were embedded in collagen gels and cultured for 7 days in 4 different culture systems. When hypoxanthine and FSH were added to the culture medium, the number of granulosa cell-enclosed oocytes increased significantly. As result more oocytes enclosed by a complete cell layer and form follicle like structures were recovered from the medium. The percentage of follicles like strictures in this case was 82.86%. After a subsequent maturation culture of the oocytes, 84.2% underwent germinal vesicle breakdown and 14.3% of oocytes were fertilized. The viability of the oocytes to day 8 of culture was 73.1%. The results of in vitro growth of early bovine oocytes in a three-dimension structure demonstrate that using of combination of hypoxanthine with FSH in cultural media can maintained in the complex that developed follicle like structure similar to that observed in ovary.

The culture system has the potential to form the basis of oocytes in vitro growth system for the production of mature oocytes and the defined nature of the system makes it suitable as a tool for investigating early oocytes development. Finally, the culture of intact follicles within ovarian stromal tissue provides a unique opportunity to examine the regulation of cell differentiation and follicle growth, particularly at preantral stages. Our experiments suggest that it may be more difficult to maintain the proper association between the oocytes and granulosa cells on a collagen substrate in large animal species and the conditions of growth and fertilization in vitro should be improved and requires addition in-depth study.

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METHODOLOGICAL APPROACHES FOR THE NK CELLS IMMUNOTHERAPY OF CANCER

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Increasingly important in the treatment of various cancers become integrated approaches using methods adoptive immunotherapy based on in vitro cultured cells. Activated lymphocytes could open a new window of great interest in this setting. Immunotherapies based on natural killer (NK) cells are among the most promising therapies under development for the treatment of many types of cancer. Search of methodological approaches for the preparation of NK cells in vitro is relevant. New immunotherapies are focused in identifying factors that could increase the expression of activating receptors, to counteract inhibitory receptors expression, and therefore, to improve the NK cell cytotoxic capacities against tumor cells. In the last years, several cytokines have been extensively studied as potential therapeutic agents to manipulate the immune response against malignant cells due to their capacity of stimulate cell growth and survival as well as increase the cytotoxicity or cytokine production to boost immune reactivity. So far, only a small number of cytokines have reached clinical use probably due to the complexity of cytokine network. Among these cytokines tested in different in vitro and in vivo settings, interleukin (IL)-2 and IL-15 should be highlighted. The work describes a method of activation lymphocytes isolated from the peripheral blood of patients with melanoma and cultured in serum-free medium supplemented with IL-2 and IL-15. Assess the viability, proliferative, cytotoxic and functional activity of lymphocytes. The expression of activation markers (CD38, CD69, CD25, HLA-DR and CD314) and subpopulations of NK- and T-lymphocytes were evaluated by the method of flow cytometry [1-2].

It is shown that in this medium condition for lymphocytes cultures have better proliferate and activation potential in vitro. IL-2, initially described as a T cell growth factor, promotes CD8+ T cell and NK cell cytolytic activity and modulates T cell differentiation in response to antigen. Recently, IL-15 has emerged as a potential immunotherapeutic candidate for the treatment of cancer. IL-2 and IL-15 are structurally related and have overlapping functions including their role in T cell proliferation, promotion of cytotoxic T cell differentiation, production of immunoglobulin by B cells, and generation, proliferation, and activation of NK cells. It has been shown that the combination of cytokines IL-2 and IL-15 not only has a positive influence on the expression of activation markers CD38, CD25, HLA-DR and CD69 on lymphocytes, but also on their viability (>95%). Our results showed that IL-15 increased the surface expression of NKG2D on NK cells from healthy donors and cancer patients with the consequent improvement of NK cell cytotoxicity.

The methodological approaches based on medium with a combination of cytokines can be recommended for a longer cultivation of lymphocytes and for escalating of lymphokine- and cytokine-activated killer cells. The proposed method of obtaining a sufficient number of activated lymphocytes may be recommended for adoptive NK cell immunotherapy of cancer patients [3-4].

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SPECTRAL-FLUORESCENT STUDY AND OPTIMIZATION OF THE PHOTOSENSITIZER BASED ON CATIONIC DERIVATIVE OF BACTERIOCHLORIN FOR ANTIMICROBAL PHOTODYNAMIC THERAPY

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Photodynamic inactivation of planktonic bacteria and bacterial biofilms is considered as a treatment of infected wounds.

This work is devoted to the study of the properties of a new nanostructured cationic photosensitizer (PS) based on a cyclodextrin composition of 13^3-N-(N-methylnicotinyl)bacteriopurpurinimide methyl ester [1] in order to optimize the composition and to choose the time regime for the antibacterial photodynamic therapy (aPDT) for festering infected wounds. The main tasks accomplished in pursuit of this objective were:

- To study the absorption and fluorescent spectral properties of the cyclodextrin PS compositions in dependence on the ratio and concentration of components;
- To study the fluorescence of PS in organs and tissues of intact mice at different times after administration;
- To make the spectral-fluorescent study of the content and selectivity of PS accumulation in infected wounds to select the optimal time to start the irradiation;

Spectral studies of the absorption and fluorescence of PS nanodispersion showed that to reduce aggregation and increase the efficiency of

PS, the content of Tween-80 should be 0.1%, and the mass ratio of cyclodextrin to bacteriochlorin should be about 200:1.

It is shown that PS selectively accumulates in infected wounds, fluorescent contrast is 3-4. The optimal time interval for irradiation is 2-3 hours after administration, when high values of PS concentration and selectivity in infected wounds are achieved.

The new cationic PS in the optimized cyclodextrin composition showed high efficacy in the photodynamic treatment of septic wounds. As a result of aPDT, the time of epithelization of skin wounds on mice has decreased for wounds infected by *P. aeruginosa* from 15 to 8 days (Figure 1), and for wounds infected by *S. aureus* from 11 to 7 days.

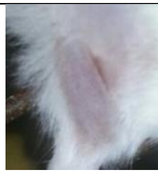
Days after aPDT	Before irradiation	2	8	15
A				
B				

Fig. 1. Wounds infected by *P.aeruginosa*:
A) after PDT, B) control without PDT

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POSITRON LIFETIME SPECTROSCOPY OF SILICON NANOCONTAINERS FOR CANCER THERANOSTIC APPLICATIONS

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In recent years, the possibilities of using porous silicon (por-Si) nanoparticles (NPs) for diagnostics and therapy of cancer tumors have been extensively studied. The great attention to por-Si NPs for applications in biomedicine is caused because of its important properties as (i) biocompatibility, i.e. an ability to be incorporated into the body without side effects, and (ii) biodegradability, i.e. an ability to be dissolved and to be excreted from the body. Advantages of por-Si NPs as carriers of drugs are also favorable due to the high surface area and large pore volume. Besides it is possible to control the parameters of the porous structure (porosity, pore diameter, surface area, hydrophobicity/hydrophilicity) in a wide range. Biocompatibility and biodegradability of por-Si NPs, as well as the fact that they can selectively accumulate in tumor tissues, allow us to use them as containers for delivery of diagnostic markers or drugs to the tumor [1]. To use por-Si NPs as nanocontainers it is necessary to have the comprehensive information about their porosity.

Positron annihilation lifetime spectroscopy (PALS) is a non-destructive technique of porosity investigation, which uses the positronium (Ps; an electron–positron bound state) as a probe [2]. Positronium localizes in pores and its lifetime is reduced compared to its natural lifetime (140 ns) due to the collision with the pore surfaces. Thus the Ps lifetime is correlated to the pore size and size distribution. Using the

RTE model [3] on the base of Ps lifetime it is possible to estimate the pore size in the sample under investigation. Total Ps intensity in measured lifetime spectrum is proportional to the pore concentration in the sample.

Samples of por-Si were prepared by electrochemical etching of heavily boron doped crystalline Si wafers in a hydrofluoric acid solution. The prepared por-Si films were dried and mechanically milled to obtain powder of NPs [1]. Then, the powder was pressed into tablets for PALS investigation. The measured lifetime spectra were analyzed by means of the decomposition on several exponential components. It allowed us to estimate two lifetimes of Ps in por-Si accounted about 3.4 ns and 33.5 ns with intensities 1% and 4%, respectively. These results indicate that the pore size distribution in por-Si NPs is bimodal with two peaks near 1 nm and 3 nm. The latter is probably favorable for loading of anticancer drug and therapeutic applications.

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COMPARATIVE STUDY OF SILICON AND SILICON CARBIDE NANOPARTICLES LASER ABLATED IN WATER

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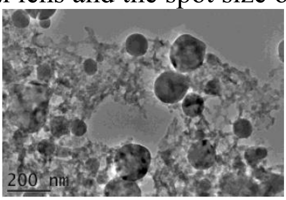
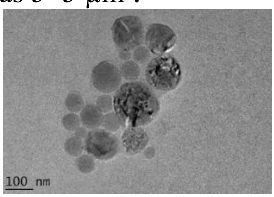
During the last decade different types of nanoparticles (NPs) have been extensively studied for applications in biomedicine, including simultaneous diagnostics and therapy (theranostics) of different diseases. Silicon (Si) nanoparticles (NPs) are promising for the theranostics of malignant tumors because of the biocompatibility and biodegradability of the former [1]. In our work NPs of Si and SiC prepared by laser ablation in water were comparatively studies to reveal their properties, which are important for applications in cancer theranostics.

NPs of were prepared by laser ablation of solid targets of crystalline Si and SiC in distilled water. The laser radiation with wavelength 1025 nm, pulse energy 100 μJ and repetition rate 10 kHz was focused with a 75 мм lens and the spot size of the target was $5{\times}5$ μm^2.



a



b

Fig.1. Transmission electron microscope images of Si and SiC NPs.

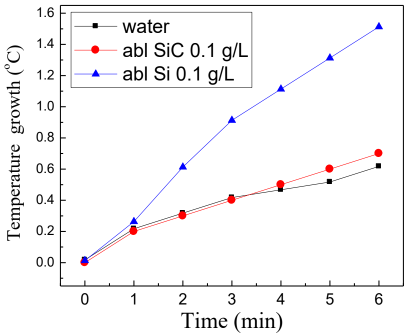


Fig.2. Temperature growth of aqueous suspensions of Si and Si NPs with concentration of about 0.1 g/L vs time under cw laser irradiation at 808 nm with power of 1.5 W.

According to the transmission electron microscopy (TEM) Si NPs had a broad size distribution from 5-10 to 100-200 nm (Fig.1a). The mean size of SiC NPs accounted 70-100 nm and the size distribution was narrow (Fig.1b).

It was found that aqueous suspensions of Si NPs under irradiation with cw laser at 808 nm exhibited continuous heating with mean rate 0.25 K/min (up-triangles in Fig.2). Suspensions of SiC NPs showed lower heating rate, which was slightly higher than that for pure water (see Fig.2). The observed heating of Si NPs can be obviously used for hyperthermia of cancer tumors, while their photoluminescent properties and Raman scattering are promising for the optical diagnostics of cancer cells.

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LASER THERAPY IN CORRECTION OPTIMIZATION SURGICAL ENDOINTOXICATION

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The endointoxication problem in modern surgery remains to one of urgent. Expressiveness of a syndrome of intoxication is defined not only intensity of intake of toxic substances in a blood stream from the defeat center, but also adequacy of functioning of the main mechanisms of elimination of toxins. Great interest is attracted by laser therapy which, as shown in many works, at various pathologies has a number of positive effects.

Research objective: to study efficiency of laser therapy in correction of endointoxication at acute peritonitis.

The clinical laboratory researches of 62 patients with acute peritonitis of various genesis divided into 2 groups are conducted. In the first (group of comparison) to patients after operation carried out (n=32) the standardized therapy, in the second (main) group (n=30) - and laser therapy sessions. For this purpose within 5 days after operation daily sessions of laser therapy by the device "Matrix" with use of a head of KLO3 were held (radiation with the wavelength of 635 nanometers, 2 mW). Laser radiation of blood through skin in a projection of an elbow vein within 30 minutes was carried out. Patients of groups were comparable on age, sex, associated diseases, weight and genesis peritonitis

Carried out the standard laboratory tests, a laser Doppler floumetria by means of the analyzer of microcirculation "LAKK-02", estimated intensity of peroxide oxidation of lipids, fosfolipaz activity, a hypoxia, endogenous intoxication.

Use of laser therapy for patients with acute peritonitis led to reduction of expressiveness of endogenous intoxication. Against the background of laser therapy use the level of molecules of average weight

(λ=280 nanometer) in comparison with control decreased by 13,3-26,2%, molecules of average weight (λ=254 nanometer) - for 15,5-32,6% ($p < 0,05$). Level of effective concentration of albumine increased for 8,3-15,2% ($p < 0,05$), an albumine binding reserve - for 9,1-18,3% ($p < 0,05$). The index of toxicity of plasma on albumine decreased by 12,5-23,4% ($p < 0,05$).

It is established that at use of laser therapy at peritonitis the level of diene conjugates in a blood plasma in comparison with control fell for 13,1-22,6%, triyen conjugates - for 16,1-19,7% ($p < 0,05$), low-new dial - for 13,2-18,3% ($p < 0,05$). Activity of a phospholipase of A2 decreased by 7,9-16,8% ($p < 0,05$).

Against the background of laser therapy the level of lactic acid in a blood plasma of patients with acute peritonitis in comparison with control decreased by 13,4-22,7% ($p < 0,05$), a hypoxia index - for 7,3-15,1% ($p < 0,05$).

Influence of laser therapy on microcirculation is noted. So, the microcirculation indicator in comparison with control increased by 10,2-17,9% ($p < 0,05$), an index of efficiency of microcirculation - for 16,8-26,3% ($p < 0,05$). At the same time the indicator of shunting fell - for 11,7-22,9% ($p < 0,05$).

Thus, use of laser therapy at acute peritonitis significantly reduces expressiveness of an endotoxemia. One of significant components of this treatment is its ability to improve microcirculation and, as a result, to adjust peroxide oxidation of lipids and a hypoxia that reduces the catabolic phenomena (one of sources of endogenous intoxication). Clinical laboratory researches established the fact that efficiency of such treatment falls at severe forms peritonitis.

MULTIPLEXED MEASUREMENT SYSTEMS WITH CODED APERTURES

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Single photon emission computed tomography (SPECT) is a nuclear medicine tomographic imaging technique using gamma rays. It is able to provide 3D information. This information is typically presented as cross-sectional slices of a 3D object, and can be freely reformatted or manipulated as required. Myocardial perfusion scan is a nuclear medicine procedure that illustrates the function of the heart muscle (myocardium). The function of the myocardium is also evaluated by calculating the left ventricular ejection fraction of the heart [1].

To reconstruct the space distribution of radiation sources the focal planes method (FPM) is used [2,3]. Volume source is divided into planes, which sequentially placed in focus of MMS. Obtained images on the detector are used in the decoding algorithm.

In the case of 2D object this focused image is the reconstructed object. Using this algorithm in case of the volume source we obtain focused images of focal planes with the contribution of all out-of-focus planes (Fig.1).

Back projection method (BPM) is developed on the basis of an idea of back projecting. The basis of BPM is an information about contributions of sources to every cell of PSD (Fig. 2).

Numerical experiments were carried out for different types of coded apertures. It was found that the use of BPM as well as SDM and DDM is more effective for coded apertures with a small average transparency

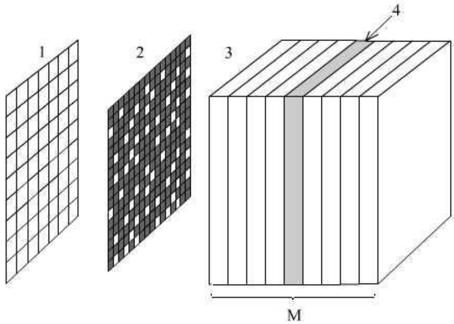

Fig.1. Focal plane method: 1 – PSD, 2 – CA, 3 – spatial distribution of radiation sources (object) with M planes, 4 – focal plane

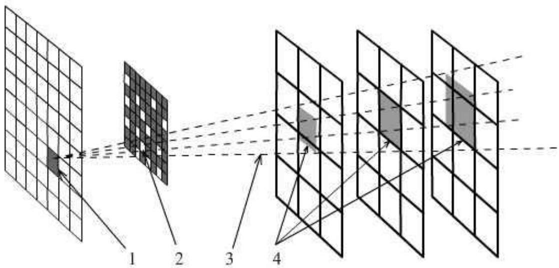

Fig.2. Back projection method: 1 – PSD cell, 2 – open pinhole, 3 – back projection cone, 4 – source cells, which contained in the cone

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PREPARATION NANOPARTICLES AND FILMS Si

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Performing research work on the search for optimum conditions on the preparation of the films and nanoparticles and study of their properties with the aid of scanning probe microscopy for issuing of recommendations regarding the formation of the nanoparticles, which can be used for the purpose of the detection of cancerous cells with the photodynamic therapy.

PVD Product's PLD/MBE-2000 is a completely integrated pulsed laser deposition tool capable of depositing thin films and nanoparticles. A Coherent/Lambda Physik COMPex PRO 110 excimer laser will be mounted on top of the electronic rack system at the correct height for the optical train. The laser comes with ceramic tube technology and operates at repetition rates 15 Hz at 150 – 250 mJ per pulse (248-nm, KrF) for a average power output of 3 Watts. Nominal angle of incidence of the laser beam on target: 60^{o}. Electro polished 304 SS cylindrical chamber was used with internal removable SS shields. Targets Si were silicon wafers 50KDB1-20 (100)0±1 thickness 280 mm, ø = 2". The system can handle substrates up to 2-inch in diameter. Operating pressure range: $5 \cdot 10^{-3}$ Torr base to 1 Torr standard (He, Ar). NT-MDT Product's "Nanoeducator" – scanning probe microscope was used in AFM techniques for studying samples Si with nanoparticles. Fig.1 presented scanning probe microscopy scan size 5×5 mkm with objects 10 – 200 nm.

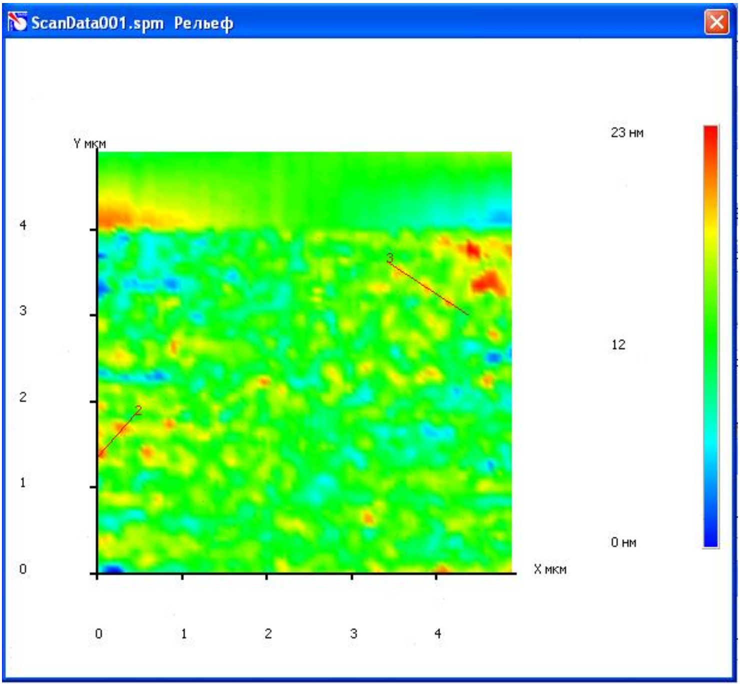

Fig.1. Scanning probe microscopy scan size 5×5 mkm

DETECTION OF GRAM-NEGATIVE BACTERIA BY SURFACE-ENHANCED RAMAN SPECTROSCOPY

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Detection of bacteria in biological tissues is one of the major world-wide challenges that need a quantitative, fast and reliable technique in order to avoid personal errors in diagnosis. Raman spectroscopy (RS) is a prompt and noninvasive technique capable of providing reliable information about molecular-level alterations of biological objects at their minimal quantity and size [1,2]. Owing to the poor efficiency of Raman scattering, the application of RS is limited, especially in the detection of liquid samples. In order to overcome the limitation, surface-enhanced Raman spectroscopy (SERS) has been employed for detection.

In the frames of this work carbon nanowalls (CNW) deposited with thin gold films are used as SERS substrates. CNW consist of graphene layers are arranged perpendicular to the surface, which provides a large surface area. Such structures are formed by plasma chemical deposition in a dc discharge in a mixture of H_2/CH_4 gases [3,4].

The synthesized substrates were used for the SERS study of Staphylococcus aureus, Escherichia coli and Klebsiella pneumoniae. Bacterial cultures were grown in a nutrient medium. Then they deposited on a substrate, inactivated and dried. The spectral measurements were fulfilled with the help of Raman spectrometer supplied by a 532-nm laser.

Raman signal amplification using SNW-Au substrate is demonstrated in Fig. 1.

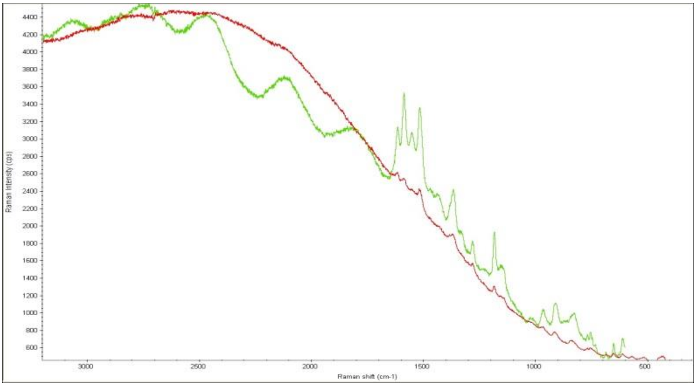

Fig.1. RS of *E. Coli* for CNW-Au (green) and Al-mirror (red) substrates

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INDICATIONS FOR L-CARNITINE USING IN SPORTS PRACTICE

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Objective. Pathophysiological justification of L-carnitine usage in a sports cardiology

Methods. An experimental part of study is executed using of white mice and white rats of both sexes. The dynamic exercise of daily swimming "up to the full stress" with weighting in 10% of body weight (14-20 days) was modeled. All the animals were randomized into three groups: I – intact animals, II – control (exercise stress), III – experienced (an exercise stress and a L-carnitine). For III group of animals the daily dose of L-carnitine was 50-100 mg/kg intraperitoneally in 30 minutes prior before swimming. Swimming duration was determined. In the end of an experiment (at rats) m. soleus and m. plantaris allocated of a muscle and carried out a histochemical identification of muscle fibers depending on expression of activity of a succinatedehydrogenase (SDG) and alkali permanent adenosinetriphosphatase (ATP-ase) of a myosin. A share of muscle fibers of various type was estimated and by method of a direct morphometry their diameter was determined. By method of a submicroscopy changes of intracellular structures of muscle fibers of both muscles were estimated. Clinical part of study was accomplished at purpose of a L-carnitine to young athletes (10-16 years old) with signs of a stress induced cardiomyopathy. Obtained data statistically by means of criterion of U (Vilkoksona-Mann-Whitney) and t-criteria's processed.

Results of a research. L-carnitine prolongs the duration of swimming of animal both types, to the end of the period of observation its effect becomes more stable. At the examination of histochemical characteristics of muscle fibers of m. soleus and m. plantaris it has been shown that dynamic physical activity doesn't change a ratio of muscle fibers of oxidative and glycolytic type. The L-carnitine also doesn't influence this indicator. On the background of a L-carnitine's administration physical activity hasn't provoked development of muscle fibers hypertrophy.

The electron microscopical study has revealed the damage of structure of muscle fibers induced by physical activity in the kontrational and power kompartment of muscle fibers. According to the obtained data the L-carnitine reduces negative consequences of physical activity to intracellular structures.

Clinical observation over effects of L-carnitine using in young athletes with signs of a stress induced cardiomyopathy the following effects have been shown:

1. The L-carnitine promoted correction of such signs of a stress induced cardiomyopathy: electric myocardium instability in the form of ventricular premature contraction and augmentation of QTc, a pathological hypertrophy of a myocardium of LV in combination diastolic dysfunction of LV.

2. Using of L-carnitine had stress protective effect, reducing levels the biochemical markers of a stress (troponin I, Brain Natriuretic Peptide, metanephrine, normetanephrine)

3. Complex effect of supplement, promoted augmentation level of physical working capacity to 3,2% according to the PWC170 test.

Influence of drug on a metastructure of the muscular system in an experiment found accurate confirmation in clinical observations that allows to use L-carnitine as one of effective remedies of pharmacological maintenance of sports activity.

OPTICAL DIAGNOSTICS OF SILICON NANOPARTICLES FOR CANCER THERANOSTIC APPLICATIONS

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Optical methods are widely used for both medical diagnostics and therapy and their combination, i.e. theranostics. In our work different liner and non-linear optical methods were used to investigate silicon (Si) nanoparticles (NPs) formed by laser ablation of c-Si targets at low pressure inert gas atmosphere and by electrochemical etching of c-Si wafers followed by mechanical grinding of the prepared porous Si layers. The prepared NPs and their aqueous suspensions were studied by means of the optical transmission measurements, attenuated total reflectance technique, photoluminescence (PL) spectroscopy, PL microscopy, Raman scattering, coherent anti-Stokes scattering, two-photon excited PL etc. The optical diagnostics was used to monitor uptake and dissolution of Si NPs in *in vitro*. The PL properties of microporous and laser-ablated Si NPs were explored for the bioimaging of cancer and normal cells. Porous Si NPs were found to be efficient sensitizers for the phototherapy of cancer *in vitro*. The obtained results demonstrate prospects of the optical diagnostics of Si NPs for the optical theranostics of cancer.

This work was supported by the state project 16.2969.2017/4.6.

MONITORING OF REFRACTIVE INDEX DISTRIBUTIONS IN DEHYDRATED CELLS BY MEANS OF DIGITAL HOLOGRAPHIC MICROSCOPY

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Cell refractive index is an important parameter directly related to cell morphology and intracellular mass distribution. It can be used for characterization of many biological parameters and phenomena: protein concentration, membrane elasticity and cell death pathway [1]. Moreover, it is known that deviation of cellular refractive index from a normal value may indicate some pathological processes, e.g. viral or bacterial infection [2]. A variety of methods is applied for determination of cellular refractive index. Many of them utilize digital holographic microscopy with usage of two culture media with different refractive indices. This technique allows reconstructing spatial distribution of the phase shift introduced by the sample. The phase shift value depends on both integral refractive index and thickness of the cell. Therefore, reconstruction of two digital holograms of the cell in the two extracellular media is required to obtain these two parameters [3]. However, restrictions imposed on the culture media for maintaining normal processes in living cells limits the method accuracy.

In this work we present results on refractive index determination in fixed dehydrated cells of human oral cavity epithelium. Biological specimens used in experiment were intact oral cavity mucosa scrapings of a 45 years old patient having no signs of inflammation, or other pathology. Phase shift distributions of seven cells in air and physiological saline solution were obtained and processed. Examples of spatial distributions of cell thickness and refractive index are shown in Fig. 1. An average refractive index of the fixed cell was found to be about 1.478, which is in a good agreement with typical values of refractive index of living cells.

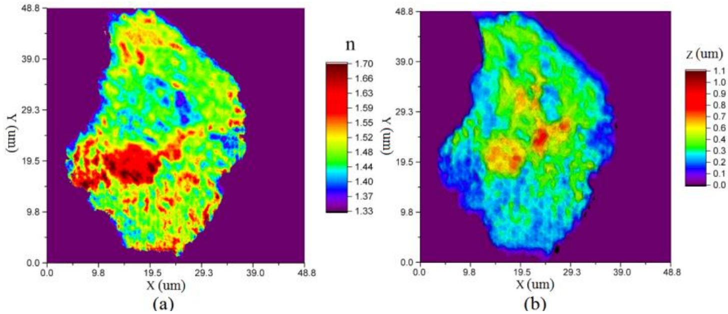

Fig.1. Spatial distributions of (a) refractive index and (b) thickness in the cell of human oral cavity epithelium.

It was shown that application of this methodology for fixed dehydrated cells provides a ten-fold increase of refractive index reconstruction accuracy. The suggested approach can be applied for investigation of specimens taken routinely from patients with no additional specific processing required. The results obtained demonstrate that measurements of refractive index distributions in non-stained label-free biopsic or histological samples are promising for the development of rapid diagnostics of pathological changes in cells and tissues.

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LOW-DOSE-RATE BRACHYTHERAPY FOR PROSTATE CANCER BY DOMESTIC MICRO SOURCES I-125

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Introduction. The prevalence of prostate cancer per 100,000 population in the Russian Federation was 116.4 in 2014, at the same time, it should be noted that the proportion of patients with stage I-II prostate cancer from 2004 to 2014 increased from 35, 5% to 52.5%, and the proportion of patients with stage III-IV decreased from 38.4% to 29% and from 22.7% to 16.5%, respectively. All this allows performing radical treatment: low-dose-rate (LDR) prostate brachytherapy to more and more patients with prostate cancer. Brachytherapy (contact or interstitial radiation therapy) of prostate cancer (PCa) is a method of radiation therapy in which a radioactive source (seeds) is implanted directly into the prostate tissue. In October 2015, for the first time in our country, the implementation of LDR brachytherapy by micro-sources I-125 completely domestic produced by the State Scientific Center of the Russian Federation – Institute for Physics and Power Engineering Named After A. I. Leypunsky - State Corporation "Rosatom" was started in The Federal State Budgetary Institution National Medical Research Radiological Center of the Ministry of Health of the Russian Federation.

Purpose. Improve the results of treatment of patients with localized prostate cancer.

Materials and methods. Low-dose-rate brachytherapy by domestic micro sources I-125 was performed by 36 patients with prostate cancer in stages T1-T2. Patients were divided into 2 groups according to the degree of cancer risk of progression: 30 - patients with low-risk cancer, 6 - patients with moderate cancer risk. The level of PSA was from 4.7 ng/ml to 17.1 ng/ml. For patients with low-risk cancer, LDR brachytherapy with domestic sources of I-125 was performed as monotherapy regimen. Patients with moderate oncological risk were undergoing LDR brachytherapy with domestic I-125 seeds in combination with laparoscopic pelvic lymphadenectomy. Extended pelvic lymphadenectomy was performed 4-5 weeks before brachytherapy.

Results. In group of patients (6 patients) who underwent previous pelvic lymphadenectomy, only in one case was metastasized prostate cancer in the lymph nodes. Side effects from the rectum (rectal toxicity) were also not observed in any case. At present, we continue to monitor this group of patients with the aim of evaluating the long-term results of low-power brachytherapy by domestic micro sources I-125. PSA level in patients of this group one year after the treatment is not more than 1.4 ng / ml, and in many cases less than 1 ng / ml.

Conclusions. Data from patient surveys after low-dose-rate brachytherapy show complete clinical efficacy, safety and compliance with international standards for domestic micro-sources I-125. At present, the National Medical Research Radiological Center of the Ministry of Health of the Russian Federation has completely switched to performing LDR brachytherapy with the domestic micro sources I-125.

INVESTIGATION OF FLUORESCENCE LIFETIMES OF A PHOTOSENSITIZER ON THE EXPERIMENTAL MODEL OF A TRANSPLANTED MOUSE TUMOR BY TIME-RESOLVED SPECTROSCOPY

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The most important indicator determining the effectiveness of photodynamic therapy (PDT) is the ability of cells to accumulate a photosensitizer (PS) at high concentrations.

The aim of this work was to estimate the fluorescence lifetimes of aluminum phthalocyanine nanoparticles on the experimental model of a transplanted mouse tumor.

To study the photoluminescence kinetics of the photosensitizer a measuring complex picosecond time-resolved stric-camera C10627-13 was used (Hamamatsu, Japan).

Tumor cells Colo-26 were administered subcutaneously to mice. After stabilizing tumor growth, PS was injected and fluorescence lifetimes were measured when excited by a laser with a wavelength of 637 nm (Hamamatsu, Japan).

It is known that PS exhibit photodynamic efficiency in an aggregated form to an insignificant degree. Also, the aggregated form is determined by the significantly reduced of fluorescence lifetime. Therefore, such a parameter as the fluorescence lifetime of PS is informative for determining the PDT conditions.

In this study, a mouse tumor was measured with and without skin. As a result, changes in lifetimes were revealed. The obtained data are given in the table.

Table 1. Lifetimes and pre-exponential factors of statistical treatment for a mouse tumor with PS

Mouse tumor	A1	τ1, ns	A2	τ2, ns
With skin	720	6,00	350	1,80
Without skin	3200	4,00	1100	0,50

From the data in Table 1, it can be seen that the lifetime of fluorescence decreased when measuring a tumor without skin, while the number of fluorophores with long and short components increased several fold, which is determined by the value of the pre-exponential factor. Therefore, the "parasitic" fluorescence of the skin must be eliminated, and to obtain accurate results, measurements of the tumor using time-resolved spectroscopy should be performed without skin.

IN VITRO CYTOTOXICITY OF CdSe/ZnS QUANTUM DOTS AND THEIR INTERACTION WITH BIOLOGICAL SYSTEMS

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Quantum dots (QDs) are luminescent inorganic semiconductor crystals [1] which are considered as promising tools for imaging of cellular processes, immunodetection [2,3], and proved to be useful for developing more sensitive multiplexed cancer diagnostic systems. Here, the interaction of CdSe/ZnS QDs with cell systems has been investigated in order to evaluate the QDs toxicity and the permeability of cell membranes for the QDs. In addition, the QDs physico-chemical properties while taken up by the primary cell culture were analyzed.

After the synthesis, the CdSe/ZnS QDs were transferred from organic solution to the water phase through the ligand exchange reaction replacing hydrophobic surfactants on the QD surface by the three-functional polyethylene glycol (PEG) molecules with the thiol (SH-) group having high affinity to the QD-surface and the hydroxyl (OH-) group at the outer end of the SH-PEG-OH molecules, to solubilize the QDs. The absorption and fluorescence spectra of the QDs were recorded, and their size distribution was measured (Fig. 1).

The *in vitro* toxicity of the QDs was measured in the SK-BR-3 human breast cancer cells and in developed *in vitro* model using monocytes, freshly isolated from the whole human blood by raising the primary culture. Fluorescent microscopy was used to study an uptake of the QDs by human monocytes. The solubilized CdSe/ZnS QDs were characterized by excellent homogeneity with the sizes varying from 10 to 12 nm (Fig. 1B) and the fluorescence maximum at 590 nm (Fig. 1C).

The data show that at the concentrations from 1.2 to 4 μg/ml the QDs exhibit low cytotoxicity, with the cell survival rate between 80 and 100%. At the concentrations superior of 3.7 μg/ml, the QDs became very cytotoxic, with the cell survival rate of 20% or less. These data permitted us to identify the limit of CdSe/ZnS QDs concentration at which they manifest themselves as a reasonably safe, nontoxic agents for cell culture biological applications. It has been also found that the monocytes take up the QDs within 48 h of incubation in primary culture and the cell vital activity in the presence of QDs was entirely preserved. It is worth mentioning that the QDs fluorescent properties within the human monocyte primary culture where unchanged.

A B C

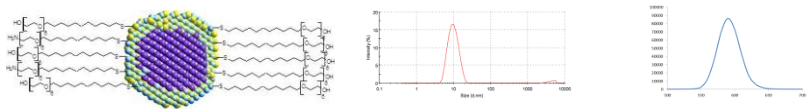

Fig. 1. “Anatomy”, size and optical properties of water-solubilized QD. A schematic representation of a water-solubilized CdSe/ZnS QD structure (A), their size distribution (B) and fluorescence spectrum (C) are shown.

In a glance, our data paves the way to development of safe QD-based tools for *in vivo* and *in vitro* diagnostic and therapeutic applications.

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REGIONAL ASPECTS OF NOSOCOMIAL INFECTION AS A MEDICAL AND SOCIAL PROBLEM

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Abstract. Prevention of nosocomial infection (NI) is an important medical and socioeconomic problem. And though certain organizational and practical measures are implemented in Russia every year to reduce NIs, the problem is still relevant from medical and social points of view. At risk of infection are both patients and medical workers. In Russia the minimum economic damage caused by Nis is 2,5 – 5 billion rubles annually. According to the Office of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare in the Republic of Mordovia, the total incidence of NI in the region is at a low level. The incidence rate was 0,01 per 1000 patients in hospitals. The dynamics of the last 5 years demonstrates a decrease in hospital-acquired infections. In the dynamics of the last five years, incidence rates of purulent-septic infections of newborns and postpartum women, postoperative purulent-septic complications and post-injection complications had an unstable downward trend. Thus, purulent-septic infections of newborns and postpartum women and post-operative infections are dominated in the structure of nosocomial infections. Analysis of dynamics of morbidity in recent years in the Republic of Mordovia suggests that the measures taken to prevent NI are quite effective and are manifested with consistently low rates.

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FEATURES OF POLYMERIC STRUCTURES BY SURFACE – SELECTIVE LASER SINTERING OF POLYMER PARTICLES USING WATER AS SENSITIZER

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Surface selective laser sintering (SSLS) is very effective in creating three-dimensional structures of a given topology within the rapidly developing direction of modern industry and science [1], called "additive technologies." The basis of the SSLS method is the sintering of the material particles as a result of their laser heating and melting. The controlled motion of the laser beam allows to obtain products of a given topology from finely dispersed powder materials layer by layer on a computer model.

Three-dimensional structures were obtained by the SSLS method, in which liquid water is used as the heating sensitizer in the sintering of polymer particles, and its effective heating is carried out by the emission of a thulium fiber laser at a wavelength of 1.94 μm, espcially promising for applications in the field of laser medicine[2]. When using such a laser, the possibility of using water as an effective sensitizer of polymer heating in the PSCM method is associated with the presence of a strong absorption band in the 1.94-μm region with an absorption index of ~ 130 cm-1[3].

As a source material for sintering and creation of matrix structures, we used powder PDL 02A (Purasorb), which was modified by treatment in a 1% solution of hyaluronic acid. This led to a change in its adhesion properties, namely, to a decrease in the contact angle of wetting from 126° to 41°. From the resulting material, layer by layer obtained a three-dimensional structure based on a computer model with a porosity of 51.2%.

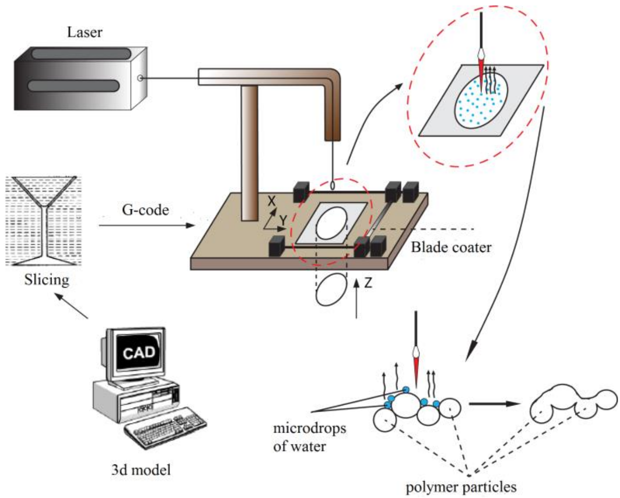

Fig.1. Experimental scheme for surface selective laser sintering

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SOLAR ENERGY MATERIALS AS THE PRECURSOR MATERIALS FOR BIOMEDICINE

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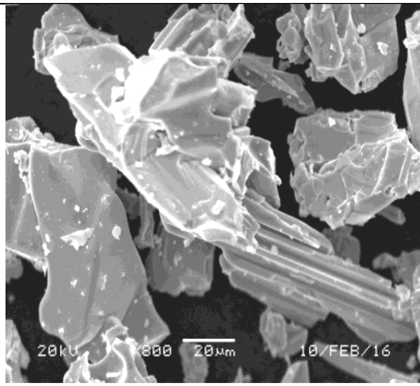
The particles specifically synthesized of high-purity materials and specific structures are used in biomedical industry. Known use for these purposes, chalcogenides of cadmium and zinc [1,2]. These materials are widely used for panels for solar energy. The company ADV-Engineering LLC is currently the only one producer in Russia of the compounds of group AIIBVI and supply these materials to the leading manufacturers of solar panels in the U.S. and Germany. Manufactured products a wide range can be used as precursor materials for Biomedicine (quantum dots etc.).

Found that after melting of the cadmium and reaching a certain vapor pressure of cadmium and sulfur starts the exothermic chemical reaction, which is characterized by high speed and heat generation. The result is a sharp rise in temperature in the reaction zone, the pressure in the reactor can reach values in excess of atmospheric. In this regard, you need periodically to harass the vacuum pumping of the reactor.

Found that the influence of the speed of movement of the reactor, and the temperature of the isothermal zone and the time of exposure to the process of producing the product, allowing to select and justify values of these parameters.

The study was carried out on the industrial equipment installed at the manufacture of ADV-Engineering company. (Fig.1).

Synthesis product is an easily crumbling speck of bright yellow. The conformity of its chemical composition to stoichiometric (22.2% wt. S ,77,8 % wt. Cd) installed on the x-ray fluorescence spectrometer with integrated diffraction.

	
Fig. 1 - Synthesis Installation	Fig. 2. The structure on the wall of the reactor.

The study of the structure of particles of Cadmium Sulfide using scanning electron microscope showed that in the synthesis process in the reaction zone formed particles of Cadmium Sulfide with different morphology and size (Fig.2). Developed synthesis modes are optimal, because the received product in its chemical composition corresponds to stoichiometric structure of Cadmium Sulfide.

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QUANTUM DOTS AS BIOMARKERS WITHIN BIOCONJUGATES WITH AUJESZKY'S DISEASE VIRUS ANTIBODIES

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Colloidal quantum dots (QDs) are promising candidates for fluorophores in molecular sensors, biochips and lateral-flow immunoassays [1]. QDs with the near infra-red (NIR) emission range are particularly important, because NIR light is poorly absorbed by the components of body tissues and markedly distant from the autofluorescence of biological materials [2] and nitrocellulose, which is the basic material of test strips for lateral flow assay (LFA).

CdSe/CdS/ZnS (600 nm), CdTeSe/CdS/ZnS (640 nm) and CdTeSe/CdS/CdZnS/ZnS (680 nm) QDs were synthesized and coated with hydrophobic ligands. Modification of QDs surface has been carried out according to our one-pot synthetic procedure for synthesis of heterobifunctional polythiol ligand (PTVP), suitable for conjugation with antibodies and further testing on LFA test strips.

For the evaluation and verification of synthetic approach, an LFA for the detection of glycoprotein B (gB) of Aujeszky's disease virus (ADV) based on gB-directed monoclonal antibodies have been developed. ADV glycoprotein B (gB)-directed QD conjugates were prepared by carbodiimide method.

BHK-21 cells were infected with the ADV. Cell lysates of uninfected and ADV-infected cells were prepared. The concentration of gB-antigen in the cell lysates were determined by the gB-specific two-site "sandwich" assay. gB-specific antibodies were immobilized on a nitrocellulose membrane at the test line. The control line was prepared using rabbit anti-mouse IgG antibodies. The ADV gB was diluted and mixed with gB-directed QD conjugates and pipetted onto the sample pad.

Intensities of the control lines and background were measured using fluorimeter equipped with solid-sample holder accessory. Repeated measurements of the samples were carried out after irradiation by UV light (312 nm) 225 mW/cm^2 in 1-160 min time range. Fluorescence intensity did not decrease for several hours of UV irradiation.

In the presence of ADV gB at a concentration of 200 ng/ml, fluorescence were readily detected in the test line area (fig.1, line 2). To quantify the results, a ratio of integral fluorescence intensity of test line to that of the background in the presence of 20 ng/ml ADB gB was used. The values of 1.27, 2.77, and 2.67 were obtained for the conjugates with emission peaks of 600 nm, 640 nm, and 680 nm, respectively. Thus, the conjugates QDs-PTVP-Ab with fluorescence maximum in a range of 640-680 nm were most suitable in LFA for the detection of ADV gB since the background intensity in this area of spectrum is low.

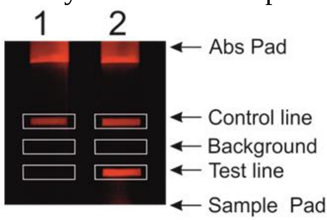

Fig.1. Photo of the LFA test strips with QDs (680 nm)-PTVP-Ab conjugates. (1) - control without ADV gB, (2) the sample containing 200 ng of gB antigen.

The developed and validated QDs-PTVP-Ab with fluorescence maximum in a range of 640-680 nm has a great potential for the development of LFA-based diagnostic tests.

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RADIATION MICRO SOURCE FOR CANCER BRACHYTHERAPY AND OTHER DISEASES

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The report examines the experience of transfer of previously developed technology based on glass microspheres shift at the molecular level glass precursor thermally decomposing into oxides, for the manufacture of radiation microsources (RMS) on the basis of short-lived radioisotopes β-active Y90, Au198, P32 and other radionuclides [1-3]. RMS technology is based on the manufacture of glass microspheres containing precursor radionuclide and activation of thermal neutrons nuclide.

The sol-gel microsphere technology allows to producing microspheres of different spectral compositions and formulations, the alkaline free, for example magnesium aluminum silicate, which is an analogue of yttrium aluminosilicate microspheres. High levels of mixing component RMS provides high chemical purity, chemical resistance, high radiation purity, stability, concentration of radionuclide, higher range radionuclide concentration, for example, the concentration of yttrium oxide (Y89) in the glass is 10 to 70% from weight. Microspheres, hollow and solid, small (about 10 μm) and large (up to 1000 μm) manufactured by foaming dispersion gelling solutions and dry of gels [4-6].

RMS is mainly used for cancer brachytherapy and other diseases as a minimally invasive therapy making more active radiation directly into the tumor (vascular embolization, interstitial brachytherapy) or a contact to the tumor (surface and intracavitary brachytherapy). In inoperable cases with metastatic, when disseminated and locally advanced tumors, in cases of restrictions permissible dose of radiation exposure, resistance or high toxicity of tumor and other organs to chemotherapeutic agents and contraindications of radical therapy, RMS is the only one therapeutic agent.

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NEW APPROACH TO UPGRADE SPM CONTROL SYSTEM

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Scanning probe microscope (SPM) is widely used device for medical and biological applications. The investigation with SPM allows measuring biological objects in liquid with molecular resolution/ So SPM techniques are very popular in topography and nanomechanical properties of biological samples, pharmacology, biotechnology, microbiology, structural biology, molecular biology, genetics and other biology related fields.

The tracking process in the control system of the SPM contains such blocks as flexure XYZ-stage with piezoelectric stack actuators, high-voltage amplifier (actuator's driver), capacitive displacement sensor, probe and probe excitation circuit [1]. Usually, the transfer function order is less than a third. That is enough to study the behavior of the SPM control system [2, 3].

In the SPM control system the flexure stage's some resonance on the vertical Z-direction occurs at frequencies of several hundred Hz and above [2, 3]. It is one of the most significant factors, which are limiting the speed of scanning. This leads to the appearance of the vibrational characteristics. The appearance of the measured signal oscillation is leading to image distortion. The influence of unwanted vibration on the behavior of the SPM feedback control loop can be reduced by increasing the controller integrator's time constant. This, in turn, leads to reduced scanning rate [3]. Therefore, the goal of this work is to find the way to upgrade and optimize the SPM control system with the scan time reducing and improving the SPM image quality at the same time.

There is obtained the simple approximate formulas for Q-factor and frequency of complex-conjugate poles of the third order transfer function with the dominant low-frequency real pole (the typical case of controlled process for SPM positioner control system). The ratio error of the obtained formulas did not exceed 10%.

There is explored the behavior of the control systems with a tracking process with both resonance properties and without oscillating. There is easy and conveniently showed that the overdamped transition measurement signal (case of the best SPM image quality) is only possible by using PID-controller when the tracking process is resonant. Using the ideal integrator and PI-controller in this case is not enough.

The scan time was significantly reduced with improving the SPM image quality by using feedback with the PID-controller with the selected parameters using the proposed new approach.

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MODELING AND OPTIMIZATION OF THE POROUS SILICON PHOTONIC STRUCTURES

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Porous silicon is a widely used material for fabrication porous structures which could be used in different devices including gas sensors and biosensors [1]. Ability to precisely control the porosity and hence the refractive index during the formation makes porous silicon suitable to obtain various multilayer porous structures including one-dimensional photonic crystals. Among them one of the most interesting for practical application are distributed Bragg reflectors and microcavities. In order to estimate the physical features of the structures with definite optical characteristics, appropriate mathematical models should be developed. In our study we have performed theoretical modeling of the optical properties of porous silicon one-dimensional photonic crystals using different approaches.

We have developed the model for calculating the refractive index of the layers with different porosities using three-component effective media approximation, taking into account the oxidation and refractive index dispersion of the silicon. Using these data we have performed the calculations for the optical properties of one-dimensional multilayer structures with different porosities applying transfer matrix [2] and numerical finite difference time-domain methods. In order to estimate the accuracy of the methods we compared the calculated results with the experiment. Photonic crystals have been fabricated using electrochemical etching of monocrystalline silicon wafers in hydrofluoric acid solutions. Semiconductor quantum dots have been used as luminophores for embedding in order to obtain luminescent structures. The influence of photonic crystals structure on the photoluminescence has been investigated as well.

We have shown that transfer matrix method is suitable for calculating reflectance of one-dimensional structures (Fig. 1). It does not require high computing powers and fits well with the experiment. However, numerical calculations are more accurate and could be used to investigate the luminescent properties of complicated structures.

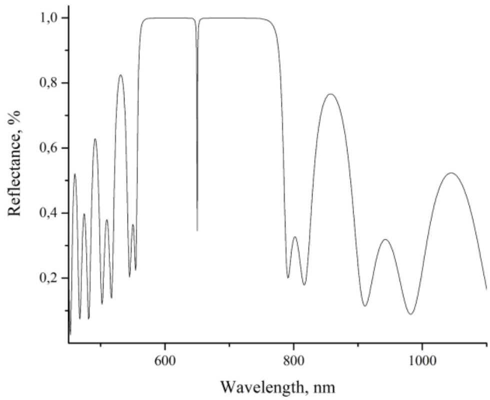

Fig. 1. Reflectance spectra of the porous silicon microcavity calculated using transfer matrix method.

Acknowledgement. This study was supported by the Federal Target Program for Research and Development of the Ministry of Education and Science of the Russian Federation, grant no. 14.616.21.0042 (ID RFMEFI61615X0042).

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POROUS SILICON PHOTONIC CRYSTAL AS A SUBSTRATE FOR HIGH EFFICIENCY BIOSENSING

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Improvement of detection efficiency in biosensing is of great interest due to the potential ability to reveal diseases at the early stages. One of the most widely used sensing methods is the measurement of luminescence signal obtained from the fluorescent markers which could selectively bind to the antigen in the analyte. Detection efficiency could be significantly improved with the use of highly luminescent markers such as semiconductor quantum dots (QDs), or by the use of more sensitive detection set-ups. Photonic crystals allow one to influence on the luminescent properties of luminophores embedded into their structure and provide the possibility to improve the efficiency of collection of luminescence signal. On the other hand the activated surface of the photonic crystal should be able to interact with the analyte in order to use it for sensing. Photonic crystals made of porous structures thus could be effectively applied in biosensor field [1].

One of the most interesting materials for fabrication of porous photonic crystals is porous silicon [1]. Ability to precisely control the fabrication process allows one to obtain highly ordered multi-layer structures and to construct one-dimensional photonic crystals such as distributed Bragg reflectors, Rugate-filters and microcavities. Due to the oriented cross-cutting pores liquid samples could easily infiltrate the whole porous structure and hence the entire surface could be activated and used for detection. Furthermore, after the embedding of the luminescent particles their luminescence could be enhanced with the Purcell effect at the certain wavelength.

In our study we have performed deep investigation of porous silicon as the material for sensor substrates. We have fabricated different types of porous silicon photonic crystals (Fig. 1) using electro-chemical etching, characterized them and measured their optical characteristics. In order to estimate the influence on the photoluminescence of the embedded luminophores, QD solutions have been embedded into the structures and spectra and spatial distribution measurements of the luminescence have been made. Finally, we have shown the possibility to improve the detection efficiency of biosensors with the use of porous silicon photonic crystals as the substrates.

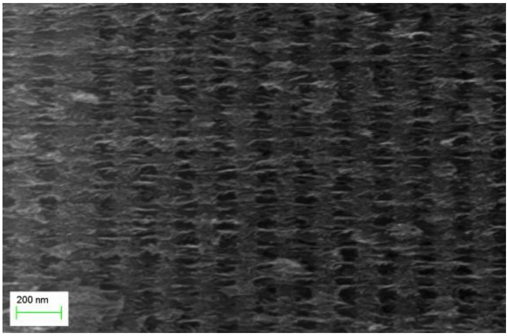

Fig. 2. Scanning electron microscopy cross-section image of the one-dimensional porous silicon photonic crystal

Acknowledgement. This study was supported by the Federal Target Program for Research and Development of the Ministry of Education and Science of the Russian Federation, grant no. 14.616.21.0042 (ID RFMEFI61615X0042).

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INTELLECTUAL EDUCATIONAL AND DIAGNOSTIC COMPLEX: HISTOLOGICAL ANALYSIS OF THYROID TUMORS

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The death rate from oncological diseases is steadily growing. The solution of this problem directly depends on the timely diagnosis. Early detection of problems and predispositions to them makes a significant contribution to solving the problem of treating thyroid diseases. The relevance of the work is to systematize and compare already existing knowledge with new data, which makes it possible to detect regularities in the signs, both benign neoplasms, and in developing malignant tumors[1-4].

The purpose of this project is the creation of an interactive intellectual training system based on the DBMS, which allows to organize and store information, transfer and copy data for employees. The already existing images and their characteristics are structured, a decision support system is developed for the recognition of tumors and suspicious cells, which saves time for an already experienced oncologist. This system allows to increase the accuracy of diagnosis. Educational and diagnostic complexes help to accumulate experience for young specialists in the field of image analysis, carry out comparative research, which speeds up the learning process, promotes professional development of the specialist.

Practical application of intelligent educational and diagnostic complex is in medicine. This complex allows building a knowledge base in which the images of the microscopic analysis of thyroid preparations and their description are systematized in accordance with the classification table of the preparation. The table developed in conjunction with the doctors of the Federal State Budgetary Institution "National Medical Research Center of Oncology. N.N. Blokhin "of the Ministry of Health of Russia[1-2].

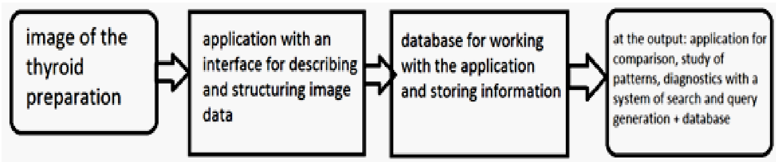

Fig.1. Structure of the project

Also, the complex allows you to work with this knowledge base afterwards: after specifying the image description, you can find out how many images of the preparation have the same diagnosis, search and compare objects on the basis. The whole process is visualized. The developed complex can be useful in describing the symptoms and in the formation of a diagnosis and treatment plan for thyroid tumors.

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THE COURSE OF ASYMPTOMATIC LONE ATRIAL FIBRILLATION DURING PREGNANCY

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Atrial fibrillation (AF) is one of the most common cardiac rhythm disorders with serious complications. According to available data, the body of a pregnant woman has electrical instability and increased arrhythmogenicity [1-3]. AF in a patient without an organic pathology of the heart is called lone AF. According to some authors, lone AF is up to 34% of all occurring AF in pregnant women [4]. Most often AF present with specific symptoms, like irregular heartbeat or palpitations. Nevertheless, a lone AF may not be accompanied by an obvious symptomatology, having an asymptomatic character. This asymptomatic arrhythmia is often not diagnosed on time, which creates a great danger in the development of complications in the patient [5].

The method of continuous 24-hour EKG monitoring (HM) allows to detect symptomatic and asymptomatic paroxysms of AF, as well as to evaluate the dynamics of arrhythmia flow [6]. This method is safe and routinely used in modern practice in non-pregnant women. However, the frequency of occurrence of extrasystoles and paroxysms of AF in pregnant women has not been estimated at different terms of pregnancy until now.

The purpose was to study the course of asymptomatic lone atrial fibrillation for trimester of pregnancy and after childbirth.

We examined 43 pregnant women with paroxysms of asymptomatic lone atrial fibrillation. It was revealed that the increasing of the gestational age leads to increase of number of single, paired and group supraventricular extrasystoles; single and paired ventricular extrasystoles;

number and duration of paroxysms of atrial fibrillation. However, the number of extrasystoles and paroxysms of arrhythmia decreased to baseline values after delivery.

Thus, it was proved that pregnancy contributes to the increase of paroxysms of lone atrial fibrillation due to the increased influence of modulating components on the triggering extrasystoles. The importance of the HM in the detection of arrhythmia in pregnant women is emphasized.

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MODELING HEMODYNAMIC PARAMETERS IN THE STAND CARDIOVASCULAR SYSTEM OF A CHILD

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Acute heart failure is one of the main causes of death worldwide. A medication of such disease doesn’t allow recover cardiac function. The only way to save life is heart’s transplantation or implantation of left ventricular assist device (LVAD). This kind of high-tech medical care is increasingly used for the treatment of acute heart failure in pediatric cardiac surgery. In developing systems of auxiliary blood circulation and the stages of testing and verification used stand simulation of the cardiovascular system.

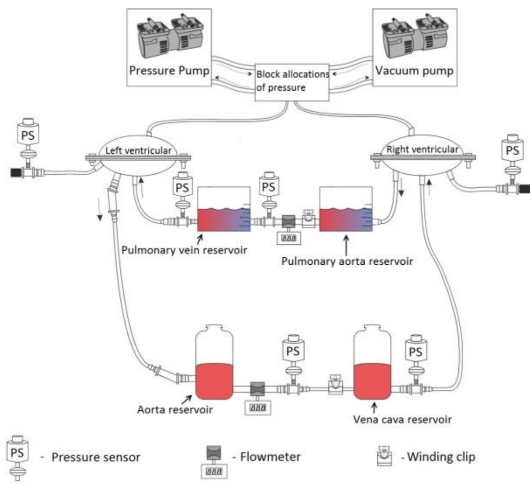

Fig.1. Structural diagram of the stand cardiovascular system of a child

Significant differences of hemodynamic parameters of the cardiovascular system of a adult and a child, which presented in table 1, does not allow use the stand simulate the cardiovascular system of an adult for testing systems of auxiliary blood circulation of the child. The aim of this work is design of stand cardiovascular system of a child and experimentation on modeling acute heart failure. This stand, which consists of the pneumatic system of control, hydraulic circuit and system of measurement, is able to modeling the wide range of conditions of the cardiovascular system of a child.

Table 1.Comparative characteristics of the main physiological parameters of cardiovascular system a child and a adult

	Child	**Adult**
The average heart rate, (beats/min)	85-110	60-70
Systolic volume, (ml)	20-45	50-70
Diastolic blood pressure, (mm.Hg.)	60-75	65-80
Systolic blood pressure, (mm.Hg.)	100-115	110-130
The mass of heart, (g)	95-260	250-300
Heart emission, (l/min)	1,3-1,6	4,8-5,6

In the work presented description of designed child's artificial ventricular, artificial valves, the module of piezoelectric valves and evaluation of result of the experiments.

The results of the experiments showed that the designed stand cardiovascular system of a child is able to simulate the wide range of conditions of the physiological parameters of the cardiovascular system.

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EVALUATION OF HEALING SKIN GRAFTS WITH USING ALUMINUM PHTHALOCYANINE NANOPARTICLES AND INDOCYANINE GREEN BY LASER SPECTROSCOPIC METHODS

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The evaluation of blood flow condition and lymph state with using luminophor gives wide understanding of the healing process stages. The use of aluminum phthalocyanine nanoparticles (nAlPc, molecular form authorized for clinical applications) allows to determine non-invasively the skin physiological condition and evaluate the degree and rate of engraftment or rejection of skin grafts by measuring and analyzing the spectral data in the monitoring mode via low-intensity lasers. nAlPc colloidal solution were added under the right graft «B» for cross skin transplantation of the mice’s back (Fig.1a), which does not fluoresce, but getting into biological inflamed tissue, AlPc molecules acquire fluorescence properties due to high concentration of macrophages [1].

The formation of new vascular and lymphatic networks within the skin graft tissue is a prerequisite for successful engraftment. The use of phosphors, such as indocyanine green (ICG), allows to record the fluorescence images of the vascular and capillary networks to follow the skin grafts healing process. ICG absorption maximum is observed in the near infrared spectral range (λ = 805 nm), which corresponds to a tissue transparency window, and allows to record the luminescence (λ = 835 nm) in the deeper tissue layers. The instrument complex for visualize the images, which consists of a highly sensitive video camera, an optical filter and the source of laser radiation (λ = 785 nm), was used for fluorescence visualization in real time.

In the fluorescent image (Fig.1b) the contrast is observed between the healthy skin areas and grafts, which is not observed after two months (Fig.1c), this can attest about new vasculature formation within grafts tissue.

The nAlPc fluorescence intensity in skin graft increases after cross skin transplantation, that fact indicates the occurrence of an inflammatory reaction in the tissue graft (Fig.1d).

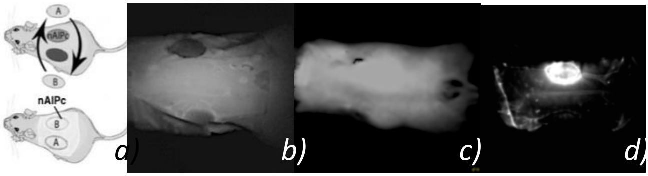

Fig.1. a) Cross skin transplantation scheme (A-control graft, B-graft with nAlPc), b) ICG fluorescence image in circulatory system of mice after 7 days of cross skin transplantation, c) ICG fluorescence image in circulatory system of mice after 2 month of cross skin transplantation, d) ICG fluorescence image in skin graft of mice after 7 days of cross skin transplantation.

The ICG phosphor intravenous injection allows to determine the rate of germination of new blood vessels and capillaries in engraftment tissue. Besides, nAlPc local application studies under the skin graft showed that the intensity of inflammatory reactions in tissues correlated with nAlPc fluorescence intensity that allows to evaluating the lymph flow state.

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RADIATION TREATMENT PLANNING BASED ON MRI ONLY: FIRST STEPS

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At present CT is used as imaging method in radiation treatment planning. It is impossible use only the MRI-based radiation treatment planning because of the lack of electron density information.

The lack of electron density information in magnetic resonance images (MRI) poses a major challenge for MRI-based radiotherapy treatment planning (RTP). In this study the authors convert MRI intensity values into Hounsfield units in the head region and thus can enable accurate MRI-based RTP for children cancer patients with tumors in head with varying tissue anatomy and body fat contents. The authors of this researches [1-3] showed – MRI-based RTP can be used for prostate cancer patients. The main task of this study – to adapt this method to treat children cancer patients in Moscow Children Hospital.

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SPECTRAL RESEARCHES OF MODEL OF AN OSTEOPOROSIS AT THE RATS WITH ASSESSMENT OF EFFICIECY OF ITS TREATMENT BY A HYDROXYAPATITE

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The osteoporosis is a general metabolic disease of which the depression of density of a bone leading to fractures is characteristic. It results in temporary and resistant invalidity, to restriction of ability to the movement, losses of a possibility of self-service and in general quality of life and also the raised mortality, especially elderly people [1].

The purpose of this work was carrying out spectral researches of model of an osteoporosis at rats with assessment of efficiency of its treatment by a hydroxyapatite.

Experiments were made on puberal females of rats by age of 6-9 months and mass of 180-230 g. As materials of a research femurs of rats were used. Animals were divided into three groups. The first group – group of healthy animals. In the second group the osteoporosis model by administration of drug Cortisonum was framed (hormonal drug of a steroid form with expressed high-speed antiinflammatory, the anti-exudative (antiedematous), desensitizing (antiallergenic) immunodepressive, antishock and antitoxic action). The third group – group of animals at whom carried out osteoporosis model by administration of drug of Cortisonum with the subsequent course of treatment powder of a hydroxyapatite (GAP). Amounts of the administered drugs per unit mass of a rat were 10 mg/kg and 40 mg/kg (the second and third groups were divided into two subgroups).

Spectral characteristics of bones were investigated by means of the stand realizing a method of the spectroscopy of combinational dispersion (SCD). The stand included the high-allowing digital spectrometer of Shamrock sr-303i with a spectral range of 200-1200 nanometers, with the built-in cooled DV420A-OE camera, the fiber-optic probe RPB-785 for KR spectroscopy combined with the laser LuxxMaster LML-785.0RB-04 module with a length a wave of the laser radiation of 785 nanometers and with a width of line of 0,2 nanometers [2].

Spectral differences between the studied groups of samples (control group, group with model of an osteoporosis and group with osteoporosis model after treatment by means of GAP) were taped on wave numbers 428 of cm-1 (PO43-Natrii phosphas ion (ν2)), 581 cm-1 (PO43-(□4) - (P-O deformation fluctuation)), 854 cm-1 (a hydroxyproline, the C-C fluctuation), 956 cm-1 (PO43-Natrii phosphas ion (ν1) (R-O symmetric valent)), 1033 cm-1 (phenylalanine), 1062 cm-1 (CO32-(ν1) replacement of B-type (S-O plane valent)), 1244 - 1271 cm-1 (Amidum PP of III) and 1659 cm-1 (Amidum PP of I).

The coefficients allowing to estimate efficiency of treatment of model of an osteoporosis with Cortisonum (10mg/kg) by means of GAP are also entered. For model with Cortisonum 40mg/kg at treatment of GAP changes weren't observed that in this case demonstrates noneffective treatment of this model of development of an osteoporosis.

Results of researches by method of a spectroscopy of KR are confirmed with mechanical tests for durability and on a break.

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POROUS SILICON NANOPARTICLES AS SENSITIZERS OF ULTRASOUND-INDUCED CAVITATION AND HEATING FOR SONODYNAMIC THERAPY APPLICATIONS

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An effect of ultrasound (US) irradiation for biomedical purposes can be significantly improved by using as called sonosensitizers. Porous silicon (PSi), which is biocompatible and biodegradable, can be used as a potential sonosensitizer for cancer therapy. The present work is devoted to experimental and theoretical study of the thermal effect and cavitation in aqueous suspensions of mesoporous PSi nanoparticles (NPs).

The temperature change T of the medium in which the US wave of intensity I propagates can be calculated using the following heat-transfer equation:

$$\frac{\partial T}{\partial t} = \chi \Delta T + \frac{2\alpha_a I}{\rho_0 c_p}, \tag{1}$$

where t is the time variable, Δ is the Laplace operator, $\chi = \kappa/\rho_0 c_p$ is the thermal conductivity, α is the US attenuation (absorption) coefficient in the medium, I is the US intensity, ρ_0 and c_p is the medium density and specific heat capacity, respectively.

A special setup was developed to measure the heating in the suspensions of PSi NPs. The core part of the setup consisted of a cylindrical sample chamber with two US transparent windows located between a flat transducer and a hydrophone immersed into the water tank. The external diameter of the chamber was 25 mm and the length was 30 mm. The transducer was connected to an amplifier, which transfers the sinusoidal signal from a generator. The central frequency of the transducer is 2.1 MHz. The temperature was measured with highly sensitive chromel-constantan E-type thermocouple. The thermocouple was inserted into the chamber center. The cavitation was also monitored by measuring scattered US radiation and its subharmonics.

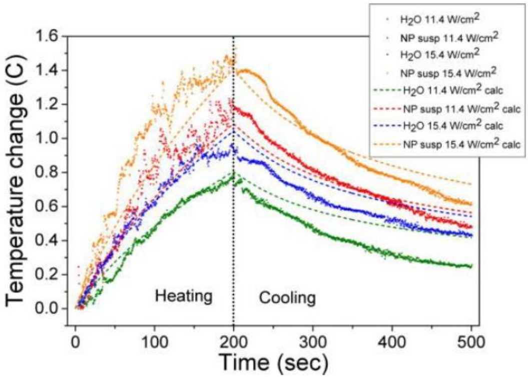

Fig.1. Transients of heating and cooling of PSi NP suspension obtained in the experiment. Dash curves are results of the calculations.

Fig. 1 shows experimental data on the heating of PSi NPs aqueous suspensions and pure water at USI intensity of 11.4 W/cm^2 and 15.4 W/cm^2. Also presents temperature curves calculated on the basis of the heat-transfer equation (1). The heating of suspensions was much stronger because of the additional absorption of ultrasonic waves PSi NPs.

The obtained results demonstrate outstanding sonosensitizing properties of selectively modified PSi NPs for the initiation of USI-induced hyperthermia in aqueous media under exposure to the therapeutic US. These remarkable properties PSi NPs look very promising for applications in the sonodynamic therapy of cancer.

This study was supported by the Russian Science Foundation (grant no.16-13-10145).

CHEMICAL SENSIBILIZATION OF CELLS AFTER EXPOSURE TO SPARSELY AND DENSELY IONIZING RADIATIONS

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Densely ionizing radiation is promising for radiation therapy due to their increased relative biological efficiency (RBE) and the reduced cell ability to recover from damage produced by radiation with high linear energy transfer (LET). One way to improve the effectiveness of radiation therapy is to inhibit the post-irradiation cell recovery. In literature there is no data related with comparative study of cell recovery suppressing by chemical agents after the action of ionizing radiations with different LET. It seems perspective to analyze the mechanism of radio-sensibilization by chemical drugs after application of ionizing radiation of various qualities.

Diploid (strain XS800) yeast cells of *Saccharomyces cerevisiae* was used in our experiments. Cells from the same suspension were exposed to ^{60}Co γ-rays (LET = 0.2 keV/μm, 20 Gy/min) and ^{239}Pu α-particles (25 Gy/min). The γ-ray dose rate was measured with a calibrated Siemens ionization chamber. The LET of α-particles reaching a cell monolayer was estimated to be of 120 keV/μm. Exactly at about this LET value the maximum of RBE-LET relationship was observed for most eukaryotic and some prokaryotic unicellular organisms [1]. Yeast cells are the simplest model of eukaryotes, radiobiological characteristics of which do not differ qualitatively from response of cultured mammalian cells.

After the treatment, the samples were diluted to the appropriate cell concentration and a known number of cells were plated in such a manner that survival cells would produce 50–300 colonies. Survival response was determined on the basis of the colony counts obtained at the end of 2–3 days of incubation at 30°C. Cell recovery in the post-radiation period occurred in non nutrient condition at 30°C.

In our experiments cell survival in the dependence of radiation dose and the duration of recovery have been obtained. To describe the kinetics of post irradiation recovery, the following equation was used $D_{eff}(t) = D_1\left[K + (1-K)e^{-\beta t}\right]$, where t is the duration of recovery, D_1 - the initial dose in which cells were irradiated, $D_{eff}(t)$ - the effective dose, e - base of natural logarithms, and β - recovery constant characterizing the probability of recovery from radiation damage per unit of time, K - is irreversible component of radiation damage.

The following chemical radiosensitizers have been tested: cisplatin, doxorubicin, bleocin, cyclophosphamide, camptothecin, difluoromitilornithine, 5'-iododeoxyuridine, sodium pyruvate, novobiocin, sodium lactate, nalidixic acid, 3-aminobenzamide, hydroxyurea.

It is shown that the mechanism of cell radiosensitivity increase after applying most of the compounds studied in the post-irradiation period, irrespective of the radiation quality, is associated with an increase in the proportion of irreversible radiation damage (K), and the probability of cell recovery constant (β) did not depend on the concentration of chemical compounds. It is concluded that the mechanism of cell recovery inhibition is mainly caused not by a violation of the process of recovery, but is connected with the formation of additional irreversible damage from which cells are unable to recover.

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DETERMINATION OF EFFECTIVE SPECTRUM OF MEDICAL LINEAR ELECTRON ACCELERATORS FROM DEPTH DOSE DISTRIBUTIONS

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Constantly increasing requirements for the accuracy of dosimetric planning and the values of delivered doses in external radiation therapy (RT) and in radiation technologies usually lead to the need to know the output energy spectra of bremsstrahlung generated by linear accelerators (Linac). These spectra depend essentially on the design of the Gantry and the beam collimation system. In addition, in many Linacs, to create a homogeneous dose distribution, as a rule, at a depth of 10 cm in a water phantom, smoothing filters are placed on the path of the beams. They have a complex cone-shaped shape, which leads to an increase in the absorption of low energy photons with a decrease in the angle between the direction of their trajectory and the geometric axis of the beam. As a result, the photon spectrum becomes dependent on the field size.

In modern treatment planning systems (TPS), using the Kernel method for calculating the dose, this effect is attempted to be taken into account by averaging the dose kernels according to different spectra, depending on the field size and the position of the dose calculation points.

The information available in the literature on this issue was mainly obtained either by calculation using the Monte Carlo method [1] or indirect method of spectrum reconstruction based on measurement of some integral characteristics of bremsstrahlung fields [2]. However, the spectra presented in these works differ quite strongly between each other and do not take into account the dependence of the spectrum on the field sizes. The spectrum of photons of clinical beams depends on the features of the design of the Linac, and these designs vary significantly from model to model, this is a reason to determine the spectra for each model and even a specific specimen individually.

Purpose of the work is a development of the spectrum reconstruction method for bremsstrahlung beams with different field sizes, generated medical electron linear accelerators, on the base of the depth dose distributions in a water phantom and determination of photon spectra for Varian Trilogy accelerator 6 MV.

The proposed methodology is based on the use of dose kernels algorithm of point monoenergetic monodirectional source (pencil beam (PB)) for the depth dose distribution calculation, created different cross-section beams of in a water phantom, and experimental measurements of these distributions.

Bremsstrahlung energy spectrum generated medical accelerator Varian Triology with different sizes of square fields from 3 x 3 up to 40 x 40 cm2 and average energy photons, depending on the size of the fields were received. Dose kernels for a set of defined energies PB were calculated. Depth dose distribution in a water phantom, calculated using the obtained spectra and dose kernels agree well with measurement dose distributions.

The proposed technique reconstruction of bremsstrahlung spectrum of medical accelerator is good adequate. Average energy of photon spectra for Varian Trilogy Accelerator in regime 6 MV varies from 1.71 to 1.43 MeV depending on the field size.

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EFFECT OF CHRONIC RADIATION EXPOSURE ON THE TEMPORAL DYNAMICS OF SEEDS GERMINATION IN SCOTS PINE POPULATIONS FROM THE BRYANSK REGION AFFECTED IN THE CHERNOBYL ACCIDENT

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Long-term monitoring of Scots pine populations inhabiting sites in the Bryansk region have shown [1] that the frequency of cytogenetic alterations in the root meristem of germinated seeds from the radioactively contaminated sites significantly exceeded the reference level during the entire observation period (2003-2015). However, an effect of an increased mutation rate on the reproductive potential of different species inhabiting areas with elevated levels of radioactive contamination is not clear yet. An objective of this work is to analyze temporal dynamics of germination level in Scots pine populations experiencing chronic radiation exposure, basing on unique monitoring data presented in [2].

Over a period of 8 years (2008-2015) seed quality was evaluated in six Scots pine populations. The calculated dose rates for the trees varied from background values at the reference sites to 40 mGy/year at the most contaminated site. The data combined over 8 years showed [2] no correlation of germination with the level of radiation exposure. Seeds from the studied populations have high interannual variability of viability. Thereby, the current dose rates at the study sites are insufficient to cause discernible changes in seed viability.

The analysis of temporal dynamics showed that germination of seeds from both reference and affected populations tends to decrease (Fig.1). In most cases, the best description of temporal dynamics of germination is reached with polynomial and nonlinear models.

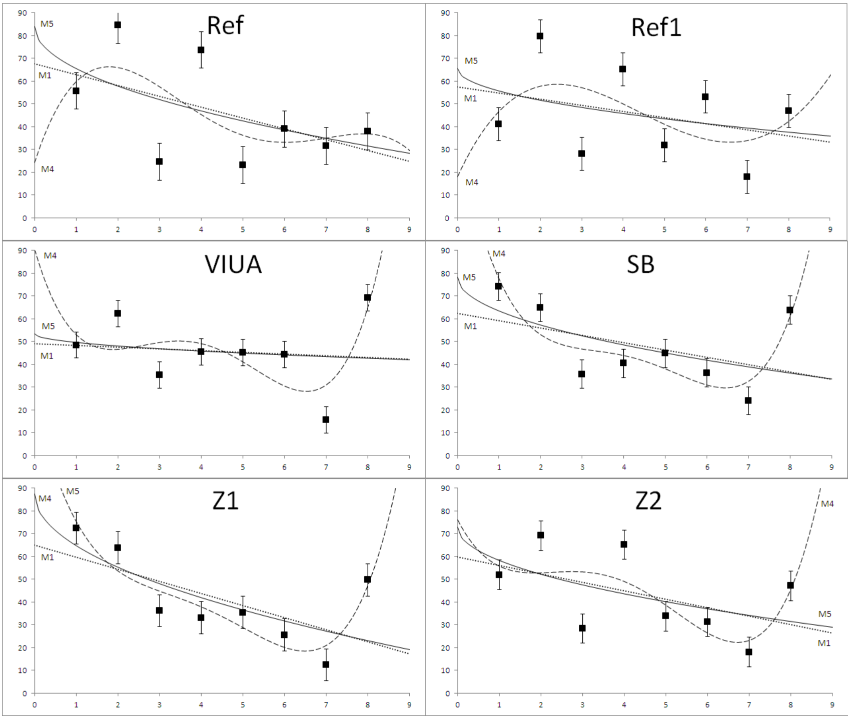

Fig.1. Proportion of germinated seeds from reference (Ref, Ref1) and impacted (VIUA, SB, Z1, Z2) Scots pine populations depending on observation year. Approximations with linear (M1), polynomial (M4) and nonlinear (M5) models are shown

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STUDY OF ANTIBACTERIAL ACTIVITY OF IRON OXIDE (Fe_3O_4) NANOPARTICLES

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Antibiotic resistance is one of the well-known phenomenon in public health. Antibiotic resistance has become a serious problem with economic and social implications throughout the world. Due to antibacterial activities, metallic nanoparticles represent an effective solution for overcoming bacterial resistance.

Iron oxide-based nanomagnets have attracted a great deal of attention in nanomedicine over the past decade because the Fe_3O_4 magnetic nanoparticles with size less than 100 nm have the ability to attach to microbials cells.

In our studies, we performed a chemical synthesis of iron oxide nanomagnets and investigated their antibacterial activity.

The iron oxide nanoparticles were synthesized by using co-precipitation method in alkaline media solutions with Fe^{2+} and Fe^{3+} in ratio 1:2 [1]. To stabilize the nanoparticles and prevent their coagulation, oleic acid was added to the reaction mixture. After synthesis and centrifugal separation, the nanoparticles were washed several times with deionized water and sonicated (150 W).The synthesis of iron oxide nanoparticles were validated by UV-Visible spectroscopy which showed higher peak at 370 nm as a valid standard reference. Antibacterial activities were studied by disc-diffusion method on agar against gram negative E.coli K-12, the square of inhibition zone was calculated by the special program "Image Repair".

Inhibition zone square under iron oxide nanoparticles (17μg/ml) influence was 2982±219 pixel^2, which is comparable to antibacterial activity of kanamycin at a concentration of 100 μg/ml.

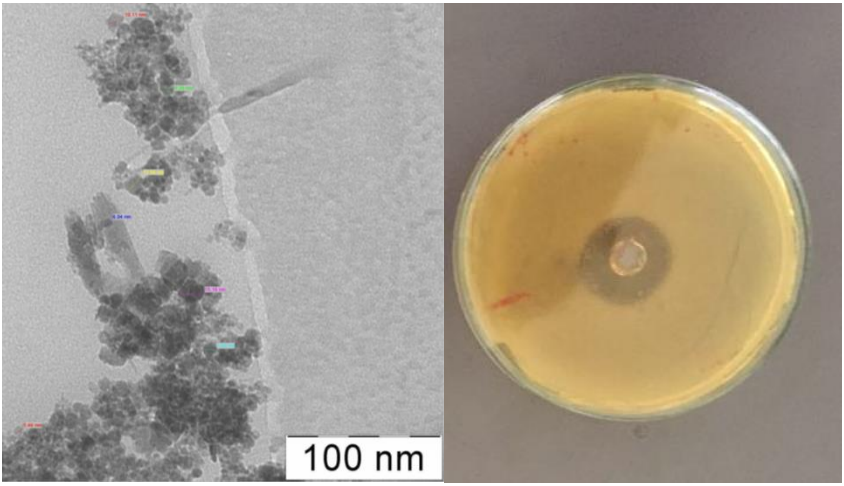

Fig.1. Scanning electronic microscope SEM image of: (left) Fe_3O_4 nanoparticles; Fe_3O_4 nanoparticles effect on the growth of E.coli K12.

As can be seen from Fig. 1 (left) Fe_3O_4 nanoparticles have rounded form and sizes in the range of from 6 nm to 15 nm and (right), the iron oxide nanoparticles show a high inhibitory activity (D>35 mm) relative to the growth of the Gram-negative bacterial culture. The obtained results testify to the high perspectivity of the use of iron oxide nanoparticles as antibacterial drugs.

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METHODS OF CORRELATION DIGITAL PHOTONICS IN THE DIAGNOSIS OF COMPLEX MEDICAL CONDITIONS

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Abstract: Quantum and wave information processing is highly suitable for classification of system's states because it offers unique possibilities of parallel processing two-dimensional data arrays, realizing the correlation algorithm in a simple way, handling information rapidly, and providing large memory density and capacity. Probability algorithms, exploiting statistical distributions, display the highest flexibility. Our proposed methods are suitable for diagnosing in the general case of no constraints imposed on the statistical function of system's states (correspondence method), and for the cases where the distribution is a histogram (deterministic method) or when the parameters of the system are statistically independent (Bayesian method), or when statistical sample has a limited size (metric method). This system retains all the well-known advantages of holographic methods – speed, multichannel, record-breaking high capacity of memory, flexible of data processing and representation of result. In distinction from the optical methods dealing with the signals and images in the natural form, this method allows to analyze information presented in multi-parametric form, thereby offering a qualitatively new way of photonics data processing.

REIRRADIATION WITH PROTON THERAPY FOR BRAIN TUMORS

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Keywords: brain tumors, proton therapy, reirradiation.

Historically, reirradiation for brain tumors is a very rare used therapeutic option because of concerns about risks of late central nervous toxicity. Anyway, according to the NCCN guidelines 2016 [1], radiotherapy can be an efficacious treatment, especially for recurrent gliomas. Ang et al. in 2001 showed that up to 50% of tolerance of the nervous tissue can recover after 12 months from previous irradiation [2].

So, there is an opinion that the cumulative dose for two courses equal to 100-110 BED (or 40 Gy for the second course) can be well tolerated by the patients [2]. By using active scanning proton beam we can extremely reduce the dose to the normal brain tissue, that can decrease the risks of toxicity. That’s why we also can provide a dose escalation to achieve the increasing of treatment efficacy.

The aim of our research was to define efficacy and safety of using active scanning proton beam for reirradiation in patients with recurrent, previously irradiated brain tumors.

The clinical material is based on the records of 15 patients treated by using active scanning beam with image guidance from 2015 to 2017. In 5 cases patients had anaplastic astrocytoma, in 5 cases – recurrent glioblastoma, 2 patients had low-grade glioma, in 2 cases – esthesioneuroblastoma, and one patient had hemangiopericytoma. For target definition we used MRI images (T1 with contrast, 1mm slice thickness), and for patient with recurrent gliomas we strongly also used PET scans with

C^{11}-methionyne or F^{18}-thyrosine. Total dose was from 40 GyE to 60 GyE (2-3 GyE per fraction, RBE 1.1), depending on recurrent tumor volume, previous total dose and regimen, patient status, and time from primary radiotherapy. Follow-up time was from 1 to 18 months.

We had positive clinical outcomes in 53.3% (8 patients): in 6 cases tumor presents partial response, and 2 times we saw stabilization disease. In three cases patients had tumor progression, and two patients died after 3 and 5 months after treatment, one is still alive. In all these cases patients had large tumor volume, high-grade, very aggressive gliomas, and low total dose of proton therapy (40GyE). For 5 patients we have no data because of short term after treatment. In all of our clinical cases we didn't see any late toxicity.

Radiotherapy with active scanning proton beam can be efficacious and safe treatment for reirradiation in patients with recurrent brain tumors because of reducing of irradiated volume of normal brain tissue and possibility for dose escalation.

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STUDY OF THE STRUCTURAL OF 3D COMPOSITES BASED ON CARBON NANOTUBES FORMED BY INSTALLATION OF LAYERED LASER PROTOTYPING

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Recently, 3D composites have been used to replace lost biotissues. 3D composites should have a certain porosity (pore sizes, specific pore volume, percentage porosity) to ensure cell proliferation and tissue regeneration [1]. It is necessary to select the optimal characteristics of porosity when restoring a certain type of tissue. The structure of 3D composites was studied by X-ray microtomography.

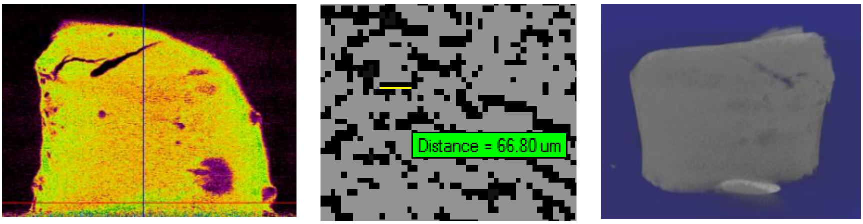
Porous composites were formed with the help of a developed installation of layered laser prototyping. The layers of 3D composites were formed by laser evaporation of an aqueous dispersion of carbon nanotubes in a protein matrix on a substrate. A protein solution of a mixture of proteins of bovine serum albumin (BSA) and bovine collagen (BC) was used as a template.

The installation of layered laser prototyping used a diode laser (power up to 2 W). The laser light was output by fiber, which was fixed on a 3-coordinate system of displacement (the displacement accuracy was ~ 10 nm). Further, laser light influenced the layer of the aqueous dispersion of carbon nanotubes in the protein matrix. The thickness of the layer was 100-500 μm. The laser light was focused into a spot with a diameter 1-200 μm. The laser beam is controlled by a control program.

The dispersion contained components with the following concentration: BSA – 25 %, BC – 1 %, single-walled carbon nanotubes produced by OCSiAl - 0.01 %, the rest - water. The time of making a 3D composite consisting of 5-15 layers is ~ 25 minute. The following parameters of X-ray microtomography were selected: the voltage at the cathode of the X-ray tube was 26 kV; the current at the cathode of the X-ray tube is

400 mA; the current at the cathode of the X-ray tube is 9 W; the rotation step is 0.15 (~ 4000 shadow projections); the spatial resolution is 12 μm.

A comprehensive analysis of 3D composite was carried out, including: 2D and 3D visualization of the 3D composite. In general, the 3D composite was homogeneous, but pore spaces were observed in its structure (Fig. 1a). To visualize the porous structure, the image was binarized (Fig. 1b). Three-dimensional visualization was carried out (Fig. 1c).



a b c

Fig.1. X-ray microtomography 3D composite image: a - two-dimensional visualization, b – binarized two-dimensional visualization, c - three-dimensional visualization

The shadow projections of the 3D composite were analyzed: the average pore diameter was 80 μm, the pore volume was 0.009 ml/g, and the percentage porosity was 23 %. The surface area is 1.089 m^2/g.

It is known that, with an average pore diameter of 1-300 μm, and a percentage porosity of 10-30 % of implantation materials, the proliferation and germination of blood vessels is accelerated [2]. These 3D composites can be used as an implant material to restore the integrity of bone-cartilage connections.

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NEW METHOD TO DETERMINE SINGLET OXYGEN CONSUMPTION DURING PHOTODYNAMIC THERAPY

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During photodynamic therapy, singlet oxygen molecules actively oxidize the substrate, and oxygen amount in the tissue decreases temporarily. It is very important problem for photodynamic therapy to keep the optimal oxygen amount during exposure for treatment efficacy. We propose to use special type of delayed fluorescence to monitor oxygen dynamic amount during therapy. This DF type origins when singlet oxygen molecule collides triplet excited sensitizer (we will call it as singlet-triplet annihilation delayed fluorescence, STADF). In this case, STADF intensity correlates directly to singlet oxygen amount in the sample. It is shown that STADF contributes significantly to the DF signal if the samples in vitro are in open air [1, 2].

In our experiments, we checked STADF changes during laser exposure for mice tissues in vitro. Special line BYRB mice have genetic feature that lead to mammary glands cancer at late stages of life [3]. Eosin and erythrosine as sensitizer were used. Under pulse periodic excitation, the STADF quenching was observed when excitation frequency exceeds 1 Hz. (see Fig. 1, curve 1) It was reversible if the exposure is suspended for several seconds. We assume that singlet oxygen is consumed via photochemical reactions, and new oxygen molecules cannot fill the tissue quickly. Less amount of singlet oxygen in tissue leads to STADF quenching. The quenching magnitude shows oxygen consumption level. It can be used as photodynamic action indicator.

It is possible to measure restoring time when tissue oxygen tension turn to its initial equilibrium value after it is changed under photodynamic action. After main exposure, a single pulse was provided due to different time. Then, STADF integral intensity was calculated for each pulse, and plot was created (Fig. 1, curve 2). We suppose that STADF technique will be useful to control tissue oxygen amount and to improve the therapy effectiveness.

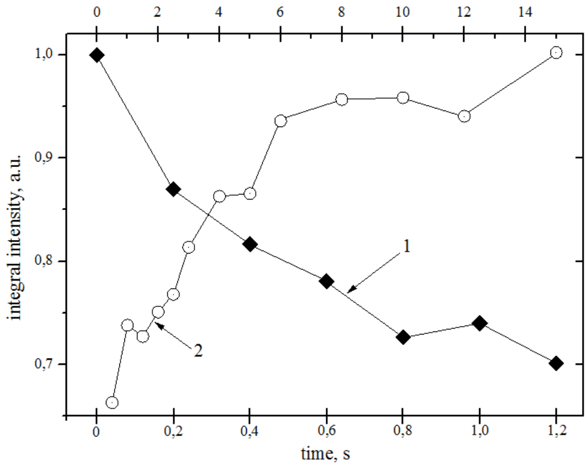

Fig.1. STADF quenching under pulse periodic excitation with frequency of 5 Hz (1 – bottom time axis) when STADF integral intensity calculated for each pulse; STADF signal restoring after laser exposure (2 – top time axis)

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COMPLEX FOR REMOTE MULTI-DIAGNOSTIC AND REHABILITATION OF PATIENTS WITH POSTURE DEFICITS

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The authors present remote multi-diagnostic system to perform long-term rehabilitation of patients with postural deficit. The rehabilitation process is carried out via the Internet. Recreation therapist can monitor rehabilitation process by analysis of changes if ECG, EEG, EMG and stabilographic signals, and conduct rehabilitation actions based on biological feedback (BF). The paper based on the results of the prototype testing on postural deficit patients.

The technique of determining the individual norm is to conduct a special survey, intended for the formation of personal norms on all parameters from all channels of data readout [1]. For the final formation of personal norms is required to conduct at least 5 surveys, preferably on different days. Individual rate is determined for each patient on the first five surveys, each of which has a duration of 1 minute, and averaged the values for all channels and retains all the state in which the patient was in the process of evaluating standards. After determining the individual norm of the program is determined not only the critical state (in deviations from group norms), but also deviations from their own individual norms of the patient under examination [2].

Stabilographic integral indicator is calculated according as

$$Ps=0.15*X+0.06*Y+0.38*SqDX+0.19*SqDY+0.22*V,$$

where X, Y (mm) is the average position of the center of pressure, SqDX, SqDY (mm) - standard deviation of the center of pressure, V (mm/sec) - the RMS velocity fluctuations of the center of pressure.

The overall rate specific rate is calculated as

$$Pn=Ps+0{,}03*MSA\_EEG+0{,}03*MSA\_EMG+0{,}02*HR.$$

Based on applying the principle of multichannel diagnostics and BF designed the system, increasing the efficiency of rehabilitation of patients with dysfunctions of musculoskeletal and neuromuscular disorders [3]. Improving the quality of results is achieved by an integrated synchronous recording, processing and analysis of diagnostic signals for multiple techniques for the study of body functions. Using the analyzer in the mode of BF allows you to explore and make timely adjustments in the training mode violation the degree of stability of patients with damage to the nervous system and musculoskeletal system [4].

Held to improve communication with the aim of determining the boundaries of individual standards allows to increase the efficiency of application of multi-channel training through visualization of the monitored parameters and representation of the boundaries of the norm\pathology in the form of accessible and understandable graphic images patients with the nervous system and musculoskeletal system. Thus, we can conclude that the created system provides new possibilities in the development of medical care of patients with different types of diseases. However, its application requires the expansion of professional skills of doctors with the aim of optimal utilization of the possibilities of multichannel diagnostics, BF and information technologies.

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OPTICAL METHOD OF ESTIMATION EFFICIENCY OF TREATMENT STAPHYLOCOCCAL INFECTIONS OF THE TONSILS

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According to the report on the state sanitary and epidemiological wellbeing of the population in the Russian Federation the leading place in the structure of infectious and parasitic diseases in 2016 as in previous years, is acute upper respiratory tract infection multiple and unspecified localization (ARI), which account for 84 %, acute tonsillitis – 3,7 % [1].

The most significant bacterial pathogen of acute tonsillitis (angina) is hemolytic Streptococcus group A. Less acute tonsillitis are caused by viruses and other streptococci, rarely, Mycoplasma and chlamydia. The pathogen is transmitted by airborne droplets. Sources of infection are sick and, in some cases, the disease carriers who have no overt symptoms. Chronic tonsillitis is the consequence of repeated disease, angina, a lack of treatment. [2].

Treatment of acute tonsillitis is through the use of various antibacterial drugs, most prevalent among them received antibiotics "Amoxiclav", consisting of amoxicillin and clavulanic acid [3].

The experiments investigated 12 samples with the content of the strain of Staphylococcus aureus ATCC № 29923 (culture I), and ATCC № 35591 (culture II) in the saliva of patients and in saline. Half the samples were treated with antibiotic, such as "Amoxiclav", the second half was a control.

Spectral characteristics were studied using an experimental stand including the high-resolution digital spectrometer Andor Shamrock sr-303i with the built-in cooled DV420A-OE camera, the fiber-optic probe for Raman spectroscopy RPB785, combined with the LuxxMaster LML-785.0RB-04 laser module (with Adjustable power up to 500 mW, wavelength 785 nm) [4]. The selection of the CD spectrum of background autofluorescence was conducted using polynomial approximation fluorescent component and subtracting it from the recorded spectra. Processing of the spectra of CU was carried out in the program Wolfram Mathematica 9. The studied range in the processing cleansed from noise smoothing by a median filter (5 points). On the selected interval 400-2200 cm-1 using the iterative algorithm has determined approximates a line (a polynomial of the fifth degree) autofluorescent component, and then subtracted this component, receiving the allocated spectrum CU.[5].

As a result of the study revealed spectral changes in the treatment of the tonsils with antibiotics "Amoxiclav", which is manifested in the change of lines at wave numbers of 667 cm-1, 735 cm-1, 992 cm-1, 1635 cm-1 corresponding to guanine, adenine, glycine, and proteins, and introduced the factors used to evaluate the effectiveness of treatment of staphylococcal infection with antibiotics "Amoxiclav". Found that antibiotics "Amoxiclav" more effective when exposed to a strain of Staphylococcus culture (I).

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INTRAOPERATIVE NEUROMONITORING AT THE THYROID GLAND OPERATIONS

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One of heavy complications at operative measures on a thyroid gland is injury of a recurrent guttural nerve. Frequency of this complication considerably fluctuates, making 2,8-22% of all observations and considerably increases at repeated operations.

The work purpose - assessment of efficiency of use of intraoperative neuromonitoring as prevention of injury of a recurrent guttural nerve at a thyroid gland operations.

The analysis of results of surgical treatment of 120 patients with various diseases to a thyroid gland is the basis for work, 60 of them were operated with use of a technique of intraoperative neuromonitoring.

For carrying out monitoring used the surgical neuromonitor "Neyrosayn 400" ("INOMED", Germany). The emergency detection and localization of a nerve, its exact differentiation among surrounding fabrics by means of a stimulator was the main objective when using intraoperative neuromonitoring. The device is capable to write down the 4-channel electromyogram much below than a threshold of visible muscular contractions that thereby significantly increases safety of the performed operations.

Performing surgery in a zone of a recurrent guttural nerve causes the associated reductions of motive groups of muscles. In response to them the device publishes a clear sound signal which level of force is proportional to the irritation felt by a nerve. The recurrent guttural nerve can be subjected to also direct stimulation via the stimulating sensor with use of current of weak size (0.5 мА, 30 Hz). Muscular stimulation is made only if neuromuscular blockade is absent, or is limited. Specially developed software package provides simplicity of operation of data collection and the analysis of forms of signals. The recurrent guttural nerve has an accurate minimum threshold of borders of stimulation. This minimum threshold makes about 0.5 мА. At the same time the age of the patient has no basic value.

Intraoperative use of neuromonitoring of a recurrent guttural nerve by means of the Neyrosan-400 device authentically reduced time of search of a nerve. So, in group of comparison time of search averaged 9,2±0,8 min. whereas in the main group - 3,1±0,7 min. ($p < 0,05$). As a result of it the general time of operation decreased. The general duration of operation at patients of group of comparison averaged 63,7±6,1 min., in the main group - 45,4±5,8 min. ($p < 0,05$). To all patients without fail for the 3rd days survey by the otorhinolaryngologist for assessment of a condition of phonatory bands was carried out. In group of comparison 2 patients (3,3%) with unilateral passing paresis of phonatory bands were revealed. In the main group of such problems it was revealed not.

Conclusions: 1. Its obligatory visualization is necessary for reliable prevention of injury of a recurrent guttural nerve during operation. 2. The recurrent guttural nerve has an accurate minimum threshold of borders of stimulation - 0.5ma, at the same time the age of the patient has no basic value. 3. Carrying out at operations on a thyroid gland of neuromonitoring by means of the Neyrosan-400 device allows to carry out the emergency and accurate identification of a recurrent guttural nerve in all cases and to avoid traumatic damage.

^{1}H MRS AS A NOVEL QUANTITATIVE METHOD FOR OSTEOPOROSIS DETECTION

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Osteoporosis is skeletal disease characterizing by a decrease in bone mineral density (BMD). It leads to an increased risk of fractures, for instance compression vertebral fracture (CVF) [1]. Dual-energy x-ray absorptiometry (DXA) and quantitative CT (QCT) are commonly accepted methods for assessing of the disease.

Spectra were obtained by localized proton magnetic resonance spectroscopy (1H MRS) from the cancellous bone (CB) of the vertebra (Fig. 1A). Figure 1(B) shows a typical spectrum from the CB. There are two main peaks in the spectrum: water peak (δ = 4,66 ppm) and peak from bulk methylene protons of fat (δ = 1,20 ppm). The fat fraction index (FF) was calculated using equation (1).

$$FF = \frac{I_{fat}}{I_{fat}+I_{water}} \tag{1}$$

Previously FF was shown to increase in adult patients with osteoporosis as compared to healthy volunteers [2]. The aim of the study was to explore the relationship between FF and BMD in children.

Seventeen patients (10.9 ± 2.4 years) with CVF were studied. QCT was used to determine the BMD [mg / cm^3] in vertebrae L3, L4 using Philips Brilliance 16. ^{1}H MR spectra (STEAM, TE = 12.8ms, TR = 3000 ms, voxel size = 20×15×10mm) were acquired from CB of lumbar vertebrae L3, L4 (Fig. 1A)) using MRI Philips AchievaTX 3.0 T.

Correlation analysis revealed significant inverse correlation link ($p<0.05$) between FF and BMD for all vertebrae of all patients (Fig.1C). Patients were classified into two groups: 7 mild CVF patients (1-2 damaged vertebrae) and 10 severe CVF patients (more than 2 damaged vertebrae). Intergroup analysis revealed significant increase FF and a reduction of BMD in patients with severe CVF as compared to mild CVF.

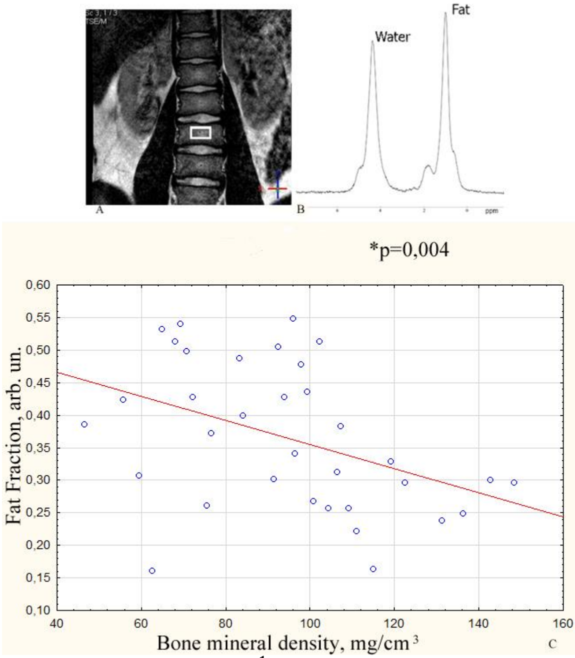

Figure 1. Location of the voxel for ^{1}H MRS (A). A typical spectrum (B). Correlation coefficient (R = -0.49) between FF and BMD values (C).

Revealed significant negative correlation between FF and BMD in children without osteoporosis suggests that the processes of increasing FF in the bone marrow and lowering the BMD are parallel. Therefore, ^{1}H MRS could be good alternative to QCT and DXA without radiation dose in osteoporosis detection.

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RADIOECOLOGICAL RESEARCHES IN TECHNOGENIC AREAS OF ISSYK-KUL REGION

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Technogenic uranium site "Kaji-Sai" is located on the southern shore of Lake Issyk-Kul. Mining Plant Mini USSR Ministry of Medium Machine Building for processing uranium ore-centered functioning from 1948 to 1969, it was subsequently converted into electrical engineering plant. Coal is mined in the local underground mine, previously burned a passing generation of electricity, after which the uranium oxide was removed by acid leaching of the ash. Wastes from the manufacture and industrial equipment had been buried, forming a radioactive dump, with a total volume of the uranium-400 thousand m^3 of moves. Exposure dose of radiation background in the field of uranium waste disposal is 200 - 300 mcR/h, and the individual destruction of the protective layer of radioactive dump to 1300 mcR/h [1].

Growth of herbaceous plants in the uranium dump deposit its print on their form - slow growth, poverty, specificity and uniformity of the flora [Fig.1]. The situation is aggravated by the action of the radiation factor, which can cause amplification mutational variability of plants. The level of chromosomal aberrations in wild plants growing in natural areas of Issyk-Kul region is on average 1 – 2 %. The level of chromosomal aberrations statistically significantly increased in plants grown in the radioactive dump, so for example, *Artemisia dracunculus* (4,2 ± 0,89%, t = 3,2, p <0,01) and *Peganum harmala* (3,4 ± 0,81%, t = 2,6 p <0,05) [Fig.2]. In addition, a decrease in mitotic activity of cell division and germination of seeds.

Increased frequency of chromosome aberrations Peganum harmala and Artemisia dracunculus growing in the radioactive dump and the techno-industrial area of genetically uranium site "Kaji-Sai", probably due to the influence of high background of the radioactive and the accumulation of radionuclides in plants.

Fig.1. In place of flowers *Peganum harmala*, 5 petals marked 6.7 petals, the sterility of flowers *Peganum harmala*.

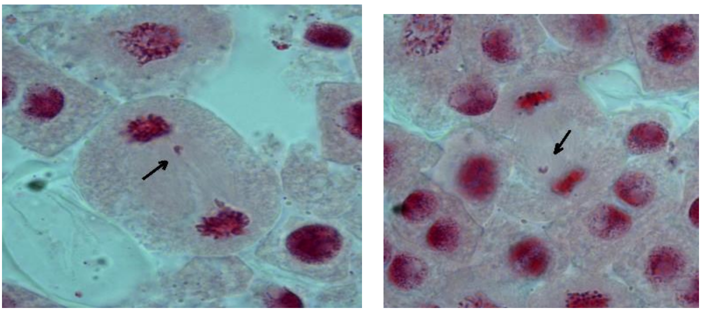

Fig.2. Ana-telophase plate *Peganum harmala* with chromosomal disorders.

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ENHANCEMENT OF THE PROTON SPIN RELAXATION IN AQUEOUS SUSPENSIONS OF SILICON NANOPARTICLES FOR MAGNETIC RESONANCE IMAGING APPLICATIONS

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Application of nanoparticles (NPs) in biomedicine is a very important direction in targeted therapy and diagnosis of cancer. The possibility of NPs to circulate in bloodstream, penetrate deep into tissues and cells can be used in biomedicine. However, it is necessary to take into account the safety of the used NPs. Silicon (Si) NPs seem to be a promising material for biomedicine. It is shown that NPs dissolve into orthosilicic acid $Si(OH)_4$ and then it is excreted from the body within four weeks through urinary system [1]. Si NPs can provide therapeutic modalities acting as sonosensitizers [2] and radiofrequency radiation induced hyperthermia sensitizers [3]. In addition Si NPs can provide diagnosis at the same time. Recently it was shown that Si NPs can be used as contrast agents for magnetic resonance imaging (MRI) [4]. We study porous and nonporous Si NPs as potential agents for enhancement of the proton spin relaxation in water.

Porous silicon (PSi) films were formed by the electrochemical etching of (100)-oriented lightly and heavily boron doped crystalline Si wafers in a solution based on hydrofluoric acid and ethanol. Mesoporous Si (MPSi) and microporous Si (μPSi) NPs were prepared by grinding the PSi films in water. Dispersed in water Si NPs were found to exhibit a week effect on the longitudinal proton relaxation. However, the transverse relaxation rate changed significantly and it was almost proportional to the NP concentration varied from 0.1 to 20 g/L (see Fig.1).

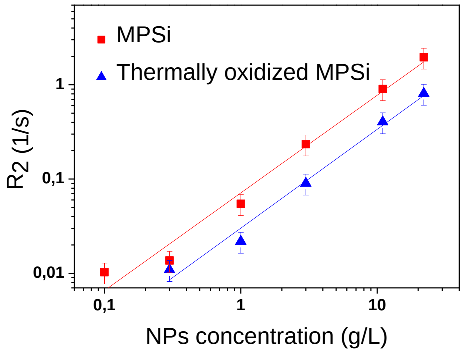

FIG.1. Transverse relaxation rate R_2 of aqueous suspensions of as-prepared (red dots) and thermally oxidized in air MSi NPs (blue dots) vs NP concentration in the suspensions. Solid lines are linear fits.

The investigated NPs were subjected to heat treatment in air or in vacuum in order to change the number of paramagnetic centers (Si dangling bonds). Maximal relaxation rate was observed for the thermally annealed in vacuum μPSi NPs with paramagnetic center density 10^{17} g^{-1} and it was about 0.5 L/(g·s). It should be noted that relaxivity calculated per Si dangling bond would be about 10^3 L/(mmol·s), which exceeds the corresponding value of commonly used Gd-based contrast agents.

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CONDUCTIVITY-BASED METHOD FOR THE INVESTIGATION OF BIODEGRADATION OF SILICON NANOPARTICLES KINETICS

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Since the discovery of porous silicon by Canham [1] , porous silicon and other types of silicon nanoparticles(NPs) attract a lot of interest. Their relatively small toxicity and luminescent properties allows their application in biomedicine [2]. The biodegradability of such particles makes them one of the most promising inorganic NPs proposed as agents for drug delivery [3], theranostics via activation with ultrasound [4], UHV-radiation and bioimaging. Silicon NPs, however, have a short (from hours to days depending on size) lifetime in the water solutions.

In the present work, we present the new method for in-situ degradation kinetics analysis for the silicon NPs. Conductometric method is based on fact that during dissolution in water, there is formation of extra ions into solution In case of low concentration, we can propose that the number of ions is proportional to the conductivity change.

By observation of the conductivity change rate, we can estimate the dissolution rate of NPs. Experimental studies on the silicon NPs produced by plasmochemical deposition (wide size distribution from 100 to 1000 nm) and modeling of conductivity-time dependence at fig. 1 shows, that the average NPs dissolution speed is 7±3 nm/h which is in accordance to data for bulk silicon. The dissolution rate for porous silicon in literature (crystallite size about 2-3nm) proofs that the dissolution occur only from the outer surface of the porous silicon NPs agglomerates.

So, it was shown that conductivity measurements could be used as precise in-situ method for the degradation kinetics measurements and it can provide extra information about the mechanisms of the agglomerates dissolution.

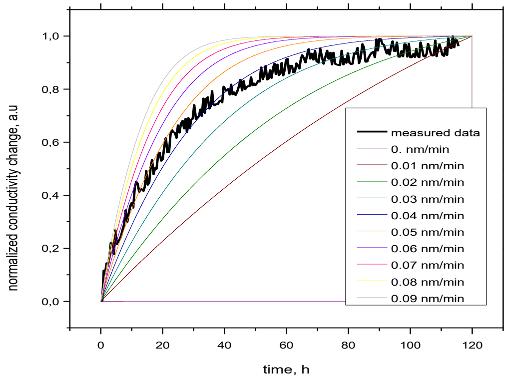

Fig.1. The experimental and modeled (at different dissolution rates) kinetics of conductivity for Si NPs solution

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THE PSYCHOLOGICAL CONSEQUENCES OF THE CHERNOBYL ACCIDENT IN REMOTE PERIOD

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Keywords: emergency situation, social and psychological problems of activity, Chernobyl accident, radiation factor.

Results of empirical research of social and psychological problems of activity of the population from contaminated ares of Russia after accident on the CNPP in the remote period (2004-2014) by results of monitoring are presented in article. Empirical material is based on the sample including results of inspection of 5988 people at the age of 16-89 years. 4003 surveyed live on is radioactive the polluted areas, 1985 surveyed – on is radioactive uncontaminated areas. Monitoring was conducted with Method research of social and psychological problems of population.

It is proved that in the remote period (2004-2014) after accident on the CNPP the level of expressiveness of social and psychological problems of activity of the population from contaminated ares of Russia considerably decreased. Level of expressiveness and structure of social and psychological problems at the population from contaminated ares have features in comparison with the population from uncontaminated ares.

Conclusions:

1. In the remote period after the Chernobyl accident the level of severity of the socio-psychological problems of life in the population of contaminated areas of Russia decreased significantly.

2. The severity of the factors of socio-psychological disadaptation were significantly higher in residents of contaminated areas.

3. The composition and nature of the complex of measures for socio-psychological adaptation and rehabilitation should encompass the population of all contaminated areas in remote period.

OPTICAL ANALYSIS OF IMPLANTS FROM THE DURA MATER

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In modern dentistry, the problem of restoring the tissues of atrophied gums, both in the region of the exposed neck of the teeth, and in the case of adentia, is extremely urgent [1]. According to different authors, the prevalence of gingival recession varies widely and amounts to 16 - 89% of all periodontal diseases [2]. For the first time in the world practice, in this pathology, it is proposed to use the allogeneic dura mater (DM) of a human, made as the plastic material by the original domestic technology "Lioplast" ® . The use of dura mater, in this case, is the most profitable solution, since it can be used for multiple recessions. The successful outcome of such operations depends on the quality and technology of production of materials, while preserving the necessary biological substances, such as collagen, glycosaminoglycans, proteoglycans and the removal of cellular components (DNA, RNA). Raman spectroscopy has certain advantages and allows real-time non-destructive, quantitative and qualitative analysis of the composition of biological objects and provides information on the molecular structure with high spatial resolution.

Since implants made on the basis of the dura mater are a multicomponent complex, their RS bands can overlap each other. Such overlap leads to a significant decrease in the information contained in the spectrum. Therefore, in order to carry out a full-scale spectral analysis, it is necessary to apply mathematical methods for the decomposition of the spectral contour [3] . To separate such a complex into components and improve the resolution of bands in the Raman spectrum, Fourier deconvolution and spectral profile (spectrum modeling) methods can be used.

Objective: to study the composition of implants from the dura mater by the method of Raman spectroscopy using the methods of decomposition of the spectral contour at various stages of its production.

The subjects of the study were dura mater (DM) samples measuring 10 * 10 mm. All samples were divided into 3 groups: 1 group- lyophilized, processed by the technology "Lioplast" ® (TU-9398-001-01963143-2004) after radiation irradiation (sterile); 2 group - before sterilization (non-sterile) and 3 group - native samples.

As a result of the research:

- A comparative spectral evaluation of the component composition of the surfaces of implant samples based on the dura mater, manufactured using the "Lioplast" technology, carried out sterilization and without it, as well as native samples was carried out.

- Deconvolution of spectra by the method of selection of the spectral contour and deconvolution of the Gauss function allows to carry out an expanded component qualitative and quantitative analysis of bioimplants on the basis of the dura mater of the main indices of biomatrix: collagens, proteins, glycosaminoglycans, proteoglycans, DNA / RNA. It was found that the main differences appear at wave numbers835 см$^{-1}$ (Tyrosine), 855 см$^{-1}$ (proline), 940 и 1167 см$^{-1}$ (GAGs, CSPGs), 1240 см$^{-1}$ (Amide III), 1560 см$^{-1}$ (Amide II).

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BACTERIA CARRIAGE OF PATHOGENIC AND ANTIBIOTIC RESISTANT STAPHYLOCOCCUS AMONG HEALTHY CHILDREN OF EARLY CHILDHOOD AND PRESCHOOL AGE

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Staphylococci belong to conditionally pathogenic microorganisms and they are part of normal human microflora. However, there are pathogenic strains that can cause purulent-inflammatory diseases. If treatment is not carried out, or it is performed incorrectly, then the person becomes a carrier and a source of proliferation of pathogenic forms of microorganisms. A significant role in the emergence of bacteria carrying is also formation of antibiotic resistance. This situation is particularly serious in children's organized collectives, where children are in close contact among themselves. Thus, the study of antibiotic resistance of pathogenic strains of staphylococci in the children's collective is relevant and worthy of attention. The purpose of this work is to identify carriers of pathogenic and antibiotic-resistant staphylococci isolated from the microflora of the oral cavity of children of preschool age that are considered healthy. The results of the study can be useful in public health practice, particularly in a paediatric practice.

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THE STUDY OF ANTIBIOTIC RESISTANCE OF HEMOLYTIC OROPHARYNGEAL MICROFLORA IN CHILDREN OF PRESCHOOL AGE

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The urgency of the problem of microbial drug resistance remains unchallenged today. Special attention should be paid to the questions of rational antibiotic therapy in children, as the future of humanity.

Taking this into account, the aim of this work was to study the resistance of hemolytic microorganisms, which are often the cause of upper respiratory infection in preschool children, to the main antibacterial drugs, that used in pediatric practice.

The results of this scientific research can be advisory in nature and useful to pediatricians and other specialists whose professional activities are related to the health of children.

In the work it is shown that about half of the children considered healthy at the time of visiting the kindergarten are pathogenic vectors of hemolytic microorganisms, among which are both opportunistic and pathogenic species, mainly represented by cocci forms. Morphological, cultural and biochemical features of the isolated hemolytic forms show their belonging to the species *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Neisseria perflava*, *Aerococcus viridans*, *Gemella haemolysans*. As a rule, these representatives of microflora cause inflammatory diseases of the upper respiratory tract in children with weakened immunity. In addition, practically all these representatives are able to cause infectious-allergic bronchial asthma in immunocompromised children. Unfortunately, the true infectious nature of colds and bronchial asthma is most often not investigated.

The most effective antibacterial drugs for opportunistic and pathogenic microbiota of throat with hemolytic activity in children of preschool age were clindamycin, amoxiclav and azithromycin. In addition, the expressed resistance of a number of hemolytic forms of pharyngeal microorganisms in preschool children to modern antibiotics used in pediatrics has been established: in *Staphylococcus aureus* — to amoxiclav and ceftazidime; in *Streptococcus pyogenes*, *Streptococcus pneumoniae* and *Aerococcus viridans* — to ceftazidime; in *Gemella haemolysans* — to ceftazidime and co-trimoxazole.

Confirmed resistance of opportunistic pathogens and pathogens to the antibiotics most often prescribed by pediatricians further exacerbates the situation with the incidence of upper respiratory tract infections and their treatment. Reception "useless" antibiotic, which is essentially a poison in small doses, disrupts unformed immunity of the child and can have serious consequences. Thus, the problem of uncontrolled using of antibiotics and non-compliance with the principles of rational antibiotic therapy still requires special attention.

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DETERMINATION OF SMALL PHOTONS BEAMS AXIAL DOSE DISTRIBUTION IN WATER BASED ON THE MATHEMATICAL MODEL OF PENCIL BEAM KERNELS

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The emergence of stereotactic radiosurgery, IMRT (Intensity-Modulated Radiotherapy) led to the development of a new formalism in the absorbed dose determination [1]. Despite this there are still many unclear issues that require careful study and detail [2,3]. In this paper, we propose a method for dosimetry of beams with a small cross section that combines absolute dose measurements at one reference point in machine-specific geometry and an analytical calculation of depth dose distributions using simple formulas for round beams.

The basis for the proposed method is the mathematical model of the dose kernels of PB (pencil beam). For all spectra of bremsstrahlung photons, it is divided into two components:

$$K_{\text{тл}} = K_{\text{тл},p} + K_{\text{тл},s}, \qquad (1)$$

where $K_{\text{тл},p}$ - primary component; $K_{\text{тл},s}$ – scattered component of the dose kernels.

For analytical approximation of the radial dependence of each component was used the following expression:

$$K_{\text{тл},j}(z,r) = \sum_{i=1}^{N} C_i(z) \cdot \mathrm{e}^{-k_i(z)\cdot r} \big/ r, \qquad (2)$$

where $j = p$ or s for the primary and scattered components, respectively; N - number of terms in the sum, depending on the beam quality and the type of component; C_i and k_i - empirical coefficients, which depend on the depth of [4]. The error in calculating the PB dose kernels for the proposed model is less than 5%. The comparisons the results of proposed method and the Monte Carlo method showed good agreement.

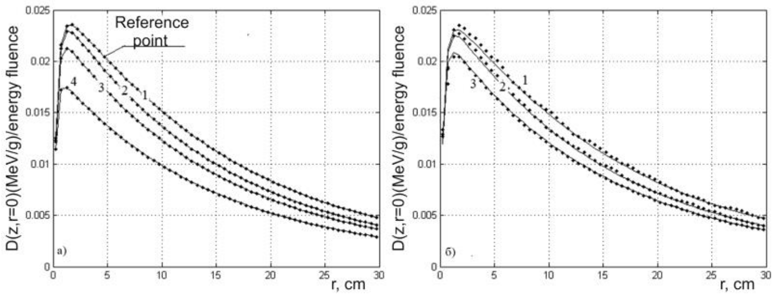

Fig. 1. Comparison of depth dose distributions obtained by the proposed method (formula 1, 2) and formed by divergent beams of circular cross section in the water phantom with (a) the results of the calculation by a combination of Monte Carlo method and the TL method, (b) with the results of direct Monte Carlo method (EGSnrs code) for different beams radii on the surface. The dose on the beam axis with a radius of 3 cm at a depth of 4.75 cm was taken as the reference dose. Designations: 1 - R_s = 3 cm; 2 - R_s = 1.0 cm; 3 - R_s = 0.5 cm; 4 - R_s = 0.25 cm

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SYNERGETIC EFFECTS OF OF IONIZING RADIATION WITH OTHER AGENTS

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Living organisms and ecosystems are never exposed to merely one harmful agent. Many physical, chemical, biological and social factors may simultaneously exert their deleterious influence to man and the environment. Risk assessment is generally performed with the simplest assumption that the factor under consideration acts largely independently of others. However, the combined exposure to two harmful agents could result in a higher effect than would be expected from the addition of the separate exposures to individual agents [1]. Hence, there is a possibility that, at least at high exposures, the combined effect of ionizing radiation with other environmental factors can be resulted in a greater overall risk. The problem is not so clear for low intensity and there is no possibility of testing all conceivable combinations of agents. Moreover, there are contradictions in literatures devoted to synergy problems relative to interaction effectiveness in the dependence of dose of applied agents and their intensity which resulted in various opinions about the importance of the synergistic interaction at low intensity of harmful agents found in biosphere [2-3].

It is well-known fact that the effectiveness of the synergistic interaction of ionizing radiation with other agents depends on the value or doses of these agents and the intensity of both factors. In particular, some authors notice that the synergistic effect of thermoradiation action increases with exposure temperature, while others believe that this effect is quite opposite. Similar contradiction exists for dose rate of ionizing radiation. For example, the synergistic effect could increases with dose rate and in some cases this effect could be decreased. These data indicate to the necessity to restore order among the chaos of the effects observed by the elaboration a novel conception of synergistic interaction.

Some general rules of synergistic interaction were reveled in our investigations. First, for every constant rate or intensity of exposure to physical factors or concentration of chemical agents, synergy can be observed only within a certain temperature range that is different for various cellular systems. Secondly, within this range, there is a specific temperature that maximizes the synergistic effect. Any deviation of temperature from the optimal one results in a reduction in synergy. Thirdly, the rate of exposure to physical agents or the concentration of chemical agents strongly influences the synergy; i.e. as the dose rate or concentration is reduced, the temperature providing the highest synergism decreases and vice versa. These general rules also show the existence of contradictions mentioned above.

To explain these new results a mathematical model of synergistic interaction has proposed. The model is based on the supposition that synergism takes place due to the additional lethal lesions arisen from the interaction of non-lethal sublesions induced by both agents. These sublesions are considered noneffective after each agent taken alone. In the model, one sublesion caused by irradiation or chemicals interacts with one sublesion produced by heat. This process is assumed to proceed until the sublesions of the less frequent type is used up. The model predicts the dependence of synergistic interaction on the ratio of lethal lesions produced by every agent applied, the greatest value of the synergistic effect as well as the conditions under which it can be achieved.

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OPTICAL PROPERTIES OF DROP OF BIOLOGICAL FLUID WITH HUMAN ALBUMIN AT SEPSIS ON THE SURFACE OF SILVER FILMS NANOPARTICLES CLUSTER

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Sepsis is a systemic pathology that can lead to complications and death [1]. World-wide, up to 13 million people develop sepsis each year, and as many as 4 million people have died [2].

Non-invasive diagnostic methods such as fluorescence and IR spectroscopy are [3], promising tools for the biomolecules investigation including conformational changes in human albumin molecules occurring at the molecular level during pathology. Modern nanomaterials (metal nanoparticles (NPs), quantum dots, fullerenes, etc.) used in nanotechnology can increase the sensitivity of optical methods of investigation, which makes it possible to detect pathology both at the early stage of diagnosis of the disease and when monitoring the dynamics of therapeutic treatment [4].

At present, the interaction of human serum albumin with silver nanoparticles of various sizes and shapes in aqueous solution has been well studied, it has been established that the fluorescence of protein molecules is quenched to form a protein complex with NPs [5]. In the present work, an optical study of the interaction of albumin molecules of a healthy person and in the pathology of sepsis with silver film nanoparticles clusters (NPCs) in an evaporating liquid drop and also in a protein film (facies) obtained by the method of a wedge-shaped drop dehydration [6] of the albumin solution at the concentration of $C=1\times10^{-5}$ M.

NPCs of were obtained by the electrochemical method of copper plates with subsequent by anodic dissolution at a current density of 5 mA /cm [7]. The hydrosol of Ag NPs with a radius of 32 nm was synthesized by citrate method. Optical study carried out drop of a protein solution with NPs and without (V=0,02 ml) on the surface of a glass slide and silver film with using a Raman scattering complex Centaur U.

In the Raman spectra of the samples, vibrational bands of 113 cm^{-1} and 423 cm^{-1}, responsible for the vibrations of the Ag_2O groups [8], were observed. In the presence of Ag NPs, these bands shift to the low-frequency region by 32- 34 cm^{-1}. We assume that this shift is due to the establishment of a link between the NPCs and the protein molecule at the level of these groups.

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A METHOD FOR ESTIMATION OF ADHESION FORCE IN THE MODEL SYSTEM "PROKARYOCITE – EUKARYOCYTE" WITH USE OF OPTICAL TRAP

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One of the causes of high mortality from infections is lack of knowledge about the subtle pathogenetic mechanisms disease. With regard to bacterial infections the first stages of microbial adhesion to target cells with subsequent penetration are still remain unexplored. The aim of the work was to develop a method for estimating the retraction forces between functionalized microspheres and eukaryocytes with use of optical trap.

Polystyrene microspheres (d = 1 μm) were coated with a lipopolysaccharide isolated from *Yersinia pseudotuberculosis* bacteria grown at +10 ºC [1]. A portion of the microspheres coated with LPS-10 (PS-LPS-10) treated with ascitic fluids containing MAb2 antibodies to LPS-10 O-side chains (PS-LPS-10-MAb2) [2] and MAb7 to the protein epitope of the outer membrane of *Y. pseudotuberculosis* (PS-LPS-10-MAb7) [3]. As negative control we used the microspheres treated with bovine serum albumin (PS-BSA). Murine macrophages J774 were reseeded aseptically onto a Fluorodish (d = 35 mm, WPI, USA) with 2 ml of full RPMI-1640 medium and incubated in 5 % CO_2 at +37 °C for 18 h. For measurements, the laser tweezer (λ=1064 nm) was used. All experiments were made in phosphate-saline buffer at +37 °C.

The analysis of these data shows, on average, a relatively high binding force between macrophages and microspheres "PS-LPS-10" and "PS-LPS-10-MAb7" (Figure 1).

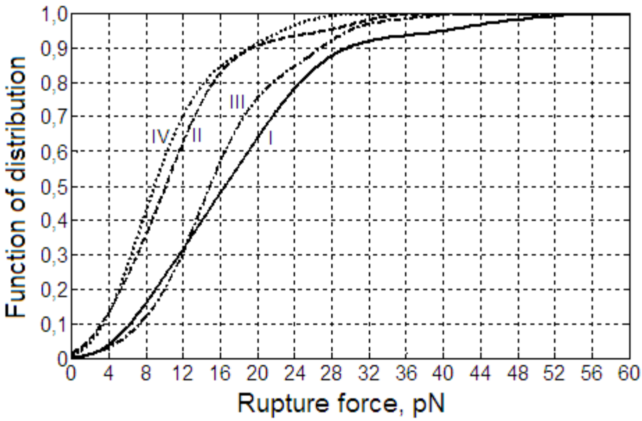

Fig.1. Integral distributions of measured rupture forces for microspheres functionalized with LPS-10: 1 – "LPS-10"; 2 – "LPS-10+mAb7"; 3 – "LPS-10+mAb2"; 4 – BSA (control)

The binding force for «PS-LPS-10-MAb2» microspheres was significantly smaller than for two above mentioned types and didn't differ from the control ("BSA" microspheres).

MAb2 binding to epitopes on the LPS O-side chains reduce the force of the estimated interaction. MAb7 recognize the proteinaceous antigenic determinant in outer membrane of *Yersinia* and unable to specifically binding with microspheres coated with LPS – so, they doesn't cause such effect.

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INTELLECTUAL SUPPORT SYSTEM OF DECISION MAKING AT DIAGNOSTICS OF INORGANIC RETROPERITONEAL TUMORS

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The oncology is the specialty demanding from the oncologist wide cross-disciplinary knowledge to carry out diagnostics and treatment of malignant tumors [1].

The Inorganic Retroperitoneal Tumours (IRT) are considered as the most difficult for diagnostics at early stages. It provocates the high level of mortality among patients with this diagnosis. Therefore nowadays, providing of highly qualified personnel lack, modern approaches in education acquiresis extremely high importance [2].

One of the most priority ways of informatization in oncology are the decision-making support systems by doctors performing as the multimedia training complexes with usage of knowledge bases, expert systems, network systems.

The purpose is the development of intellectual support system for medical decisions of inorganic retroperitoneal tumors diagnostics (IRT).

The intellectual support system of medical decisions (SSMD) at IRT diagnostics performs as the multimedia information training complex to diagnosing of IRT which is based on the training materials provided to N.N. Blokhin Russian Cancer Research Center.

The support system of medical decisions (SSMD) at IRT diagnostics accumulates knowledge and experience of medical experts and IT specialists [3]. It was developed for doctors, interns. We have made a pre-design research. It includes subject domain analysis, analysis of object medium and possible alternatives, unresolved problems and approaches to their decision. This research allowed to choose development tools and to formulate requirements for this complex and its systems [4]. The structure of SSMD was developed, its characteristics and structure of the entering systems it were defined. It consists of website for distance learning, testing system, clinical knowledge base of IRT clinical records and electronic manual [5].

The developed support system of decision making at diagnostics of inorganic retroperitoneal tumors for doctors was experimentally tested. Manuals of work with subsystems of SSMD and the electronic glossary were developed.

The main advantage of SSMD is the possibility of accumulation and transfer of knowledge to future experts in diagnostics of inorganic retroperitoneal tumors.

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ELECTROPHYSIOLOGICAL PARAMETERS OF SINUS NODE FUNCTION IN PATIENTS WITH PAROXYSMAL TACHYARRHYTHMIAS

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Aim: to analyze the indicators of the function of the sinus node in patients of young age with paroxysmal tachycardia.

Methods: the study included 11 patients with suspected paroxysmal tachycardia, with an average age of 17±28. The basis for holding transesophageal electrophysiological study (TE EPS) was the clinical and electrophysiological characteristics of paroxysmal tachycardia. According to the results of Holter monitoring ECG (HM ECG) analyzed the minimum and maximum heart rate, number of ventricular and supraventricular arrhythmias, the presence of pauses, rhythm and episodes of paroxysmal tachycardia. According to CHP, EFI estimated the initial heart rate (HR), the recovery time of sinus node function (RTSNF), corrected recovery time of sinus node function (CRTSNF), point of Wenkebach (p. W), the duration of the effective refractory period of the atrioventricular connections, the presence of aberrant complexes and episodes of paroxysmal tachycardias before and after administration of atropine at a dose of 0.02 mg/kg.

Results: Complaints characteristic of the tachyarrhythmia was diagnosed in 9 patients, episodes of heart rate more than 150 beats per minute in 7 patients. When conducting TE EPS obtained the following results: episodes of supraventricular tachycardia provoked in 8 patients (in two cases of paroxysmal tachycardia managed to provoke only after administration of atropine). Three of them have shimmer and atrial flutter episodes reciprocal tachycardia in five. Three patients provoke paroxysmal tachycardia failed, but they showed a shortening of the PQ interval and the appearance of aberrant QRS complexes when stimulated. In patients with paroxysmal SVT signs of sinus node dysfunction was detected in 6 patients, in the form of episodes of sinus arrhythmia (4 patients), migration pacemaker the atria (4 patients), sinoatrial blockade of II degree (3 patients), blockade of legs of bunch of gisa (2 patients), atrioventricular block degree II-III (1 patient), RTSNF more than 1500 MS in 1 patient, CRTSNF greater than 500 msec in 3 patients.

Conclusion: in 6 of 9 patients with supraventricular paroxysmal tachycardia revealed signs of sinus node dysfunction, probably has a vagotonic in nature.

ULTRASOUND-ACTIVATED SILICON NANOPARTICLES AS AGENTS FOR 3D BIOPRINTING PURPOSES

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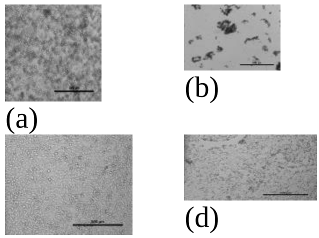
Since the discovery of porous silicon by Canham [1], porous silicon and other types of silicon nanoparticles (NPs) attract a lot of interest. Their relatively small toxicity and luminescent properties allows their application in biomedicine [2]. The biodegradability of such particles makes them one of the most promising inorganic NPs proposed as agents for drug delivery [3], theranostics via activation with ultrasound [4], UHV-radiation and bioimaging. 3D bioprinting with using tissue spheroids as building blocks is another potential new area for application of ultrasound-activated silicon NPs. We hypothesize that tissue spheroids biofabricated from cells labelled with ultrasound activated silicon NPs could enable the formation of lumenized tubes and cavities and 3D bioprinting of complex human organs with vascular and ductal systems.

The aim of this study was to demonstrate a principal feasibility the concept of sacrificial tissue spheroids and to show that ultrasound activation can induce cell death in cells labelled with non-toxic silicon NPs without injury of adjacent cells non-labelled with silicon NHs.

It was found that silicon nanoparticles with average diameter 80 nm produced via electrochemical etching of crystalline silicon [1], which are non-toxic at concentration 0.25 g/L, can penetrate inside the cell (rat myogenic cell line L6) and after activation with ultrasound 20 kHz (0.5

W/cm^2) the former can destroy the cells. In control experiments the treated cells without NPs have no effect under the same treatment (figure 1).

Thus, in the present work, we show that porous silicon NPs inside the cells after ultrasound activation can cause the cell death and detachment from other cells and the surface of the cell well, while the cells without NPs remain unaffected. These data opens an unique opportunity for biofabrication of sacrificial tissue spheroids from cells labelled with silicon NPs which will enable post-printed ultrasound mediated controlled formation of lumen and cavities in bioprinted 3D tissue engineered constructs with using tissue spheroids as building blocks [6]



(a) (b) (c) (d)

Fig.1. L6 cells
(a) –with NPs before sonication
(b) - with NPs after sonication
(c) - without NPs before sonication
(d) - without NPs after sonication

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THE POSSIBILITIES OF RAMAN SPECTROSCOPY IN THE DIAGNOSIS OF CERVICAL CANCER

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Relevance. According to Rosstat (M., 2015) for 10 years from 2005 to 2014, the incidence of cervical and uterine cancer increased by 31.8% from 30.2 to 39.8 thousand women [1]. Mortality of patients from cervical cancer (CC) in the first year after diagnosis in the Russian Federation for 2004-2014 was 16-20.8% [1]. Every fifth woman with a newly diagnosed CC dies within the first year after diagnosis. These data indicate the high urgency of the problem of early diagnosis of CC.

Purpose of the study. To study the possibilities of Raman spectroscopy in the diagnosis of cervical cancer.

Materials and methods. The research was carried out in Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences on a unique scientific installation "System of Probe-Optical 3D Correlation Microscopy". This installation was created in cooperation with scientists from the "Academician V.I. Shumakov Federal Research Center of Transplantology and Artificial Organs", LLC "SNOTRA" (resident Skolkovo) and NRNU MEPhI. The unit includes specially designed and optimized blocks: a surface modification system (ultramicrotome), a scanning probe microscopy system, an optical unit with a confocal module, a Shamrock 750 (Andor) monochromator with a CCD camera DU971P-BV (Andor Technology), an adjustable Ar- laser, He-Ne laser Melles Griot 25-LHP-928-230, photodiode laser

(532 nm). In this work, an argon laser with a wavelength of 488 nm was used for excitation (P=50 mW).

The spectral characteristics of the following cervical tissue samples were studied. 1 - As a control, we examined tissues of intact (without pathology) cervix (verification by histological examination). 2 - The main subject of the study is cervical tissue with histologically verified squamous cell carcinoma.

Results. Differences in the spectral characteristics between pathologically altered cervical tissue in comparison with normal tissues were revealed. Figure 1 shows 2 spectra: 1 - the spectral characteristics of the tissue of the unchanged (without pathological changes) cervix; 2 - spectral characteristics of cervical tissue with squamous cell carcinoma.

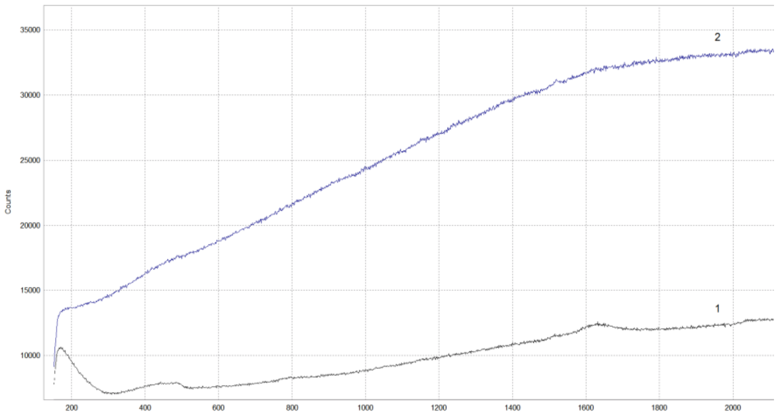

Fig. 1. Spectra of normal tissue of the intact cervix (1), cervical tissue with squamous cell carcinoma (2).

It was established that the intensity of Raman scattering in biopsies of cervical tissue with squamous cell carcinoma was higher than in biopsy specimens of intact cervical tissue. The difference in the intensity of Raman scattering was from 12.3 to 118.8%.

Conclusion. In the future, the Raman spectroscopy method can be used in the processing of biopsy and surgical material for diagnosis of cervical cancer.

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LUMINESCENT DIAGNOSTICS OF PATHOLOGICAL CHANGES OF THE CERVIX

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Relevance. In Russia, for 10 years from 2005 to 2014, the incidence of cervical and uterine cancer increased by 49.2% (from 39.4 to 58.8 cases per 100,000 women) [1]. These data indicate the high urgency of the problem of early diagnosis of cervical cancer. An accessible method that would allow examining large patient arrays for early diagnosis of precancerous cervical conditions has not yet been put into practice. The use of ytterbium complexes of porphyrins (YCP) luminescing in the near infrared (NIR) spectral region of 900 nm - 1100 nm opens up great prospects in this direction [2,3].

Purpose of the study. To study the possibility of using the ytterbium complexes of porphyrins and laser spectrofluorometry for the diagnosis of pathological processes in gynecology.

Materials and methods. Under supervision were 70 women, who were divided into two groups. Group 1 included women with squamous intraepithelial lesions of high grade (HSIL) in the Bethesda classification (The Bethesda System (TBS) 1988, 1991). In 2 (control) group included women without pathological changes of the cervix. Women measured the luminescence level of the cervix tissue after they were sensitized with YCP. The native gel Fliroscan was used as an YCP carrier. The gel is officially registered in Russia and the countries of the customs union. The registration number of the declaration on the conformity of the vehicle No.RU D-RU.AЮ18.B.06317 dated 09.02.2016.

To measure the luminescence intensity, a laser-fiber fluorimeter was developed in the Fryazino branch of the Institute of Radio Engineering and Electronics named after Yu. V.A. Kotelnikov [4]. Laser-fiber fluorimeter operates in the spectral range of 900-1100 nm. The IR region of the spectrum (760-1300 nm) is considered to be the "transparency window" of biological tissues and is characterized by minimal absorption and practically no background luminescence of endogenous chromophores in this spectral region. Laser-fiber fluorimeter allows simultaneous irradiation of the cervical tissues with laser radiation in the range of the Sore strips and measure the integrated intensity of the luminescence in the IR region of the spectrum.

Results. Reliable (P <0.001) differences between groups 1 and 2 in the level of luminescence were revealed. The intensity of luminescence from the cervical tissue without pathological changes ranged from 0.016 to 0.026 mV. The intensity of luminescence from the cervical tissues with squamous intra-epithelial lesions of high degree (HSIL) increased to 0.25-0.75 mV.

Conclusions. 1. IR luminescent diagnostics reveals objective differences between morphologically normal and pathologically altered tissues of the cervix.

2. The technique is highly sensitive - the intensity of luminescence from the tissues of the cervix with HSIL is increased by 10 - 47 times.

3 The difference in IL between normal and pathologically altered tissues is significant (P <0.001).

4. Study of the level of luminescence is a promising direction for developing a new method for diagnosing pathological conditions in gynecology.

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STUDYING THE PROCESSES OF OXIDATION OF MAGNETIC NANOPARTICLES

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Production of new metallic materials with unique properties is one of the actual problems of the modern technology. In turn, quality of metallic nanostructures depends on the production method, which determines its structural characteristics and physicochemical properties [1,2]. Recently, magnetic nanoparticles, in particular iron oxide (FeO) nanoparticles are of great interest because of their perspective application in making new materials for engineering, ecology and medicine. Nanoparticles are biocompatible and can be used in solving various medical problems. Materials based on metal nanoparticles are widely used due to their high specific surface values and the number of surface atoms ratio to the number of the volume atoms in particles. Furthermore, because of the possession of an unusual combination of electrical, magnetic and optical properties that are not characteristic to their bulky counterparts, specific electronic structure of nanoparticles are rather close to the semiconductors.

The resistance to oxidation and destruction in media with different acidity, which is determined by the concentration of H^+ and OH^- ions is one of the most important properties of nanoparticles.

In this paper, the degradation dynamic of Fe_3O_4 nanoparticles in media with various pH was examined, which determines the period for the nanostructures' applicability and their destruction rate. A detailed analysis of the changes in the structural properties was done. Morphological and structural properties have been studied using scanning electron microscopy, energy dispersive and X-ray diffraction analysis. The results of the phase composition assessment are presented in Table 1.

Table 1. Data on the phase state of nanoparticles, %

Time	1 pH		5 pH		7 pH	
	Fe_3O_4	FeO(OH)	Fe_3O_4	FeO(OH)	Fe_3O_4	FeO(OH)
Initial	100	-	100	-	100	-
1 day	100	-	100	-	100	-
3 days	96	4	100	-	100	-
5 days	91	9	100	-	100	-
7 days	85	15	92	8	100	-
10 days	79	21	86	14	100	-

The dynamic of the structural and phase composition of nanoparticles Fe3O4 in various pH media and the degradation degree dependence on acidity and residence time in the media has been studied. A sharp increase in the concentration of defects and vacancies in the crystal structure in acid media was observed by XRD and EDS analysis. This process is associated with the appearance of amorphous regions, which in its turn is due to the appearance of hydroxide compounds. The appearance of amorphous inclusions leads to an increase in the structure deformation, and a decrease in the crystallinity degree below 50% results in a high degree of amorphization of the structure and partial destruction of the structure. The causes are the high oxygen content and the formation of hydroxide compounds in the structure, as well as subsequent corrosion processes being capable of causing a destruction of the structure.

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THE DEVELOPMENT OF A KNOWLEDGE BASE FOR INTELLIGENT DECISION SUPPORT SYSTEMS FOR DIAGNOSTIC DECISIONS IN PROSTATE CANCER

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Prostate cancer is a malignant neoplasm arising from the epithelium of the alveolar cellular elements of the prostate. This is one of the most common types of cancer: in some countries prostate cancer takes 2-3 place in Russia – 7-8 place. The main problem is its late detection (already at stage 3-4), because in the first stages of prostate cancer flows without symptomes [1].

Analysis of the articles on this subject shows the main problems faced by most doctors. This is lack of accuracy of traditional diagnostic methods and difficulty in diagnosis definition. It is necessary to resort to advice from more experienced doctors, which are able to resolve your transaction dispute. It is often noted that even the slightest error in the interpretation of histological studies data immediately change the prognosis [2]. There are many ways of learning pathology, such as refresher courses, internships, etc., but they are not cost effective. Therefore, the creation of an automated, fast and objective method to aid pathologists in the evaluation of the prostate may improve the diagnosis of prostate cancer [3].

Considering the above, it is possible to determine the purpose of the work as follows: create a program that will simplify the work of the histologic analysis and the diagnosis. Thus, the program will serve as a virtual consultant to doctors when there is an ambiguous situation, as they will be able to access the statistics and to find similar cases.

The system allows you to operate in two modes. The first – filling of the knowledge base. To do this loads an image, analyzes it, selects the characteristic region and describes their respective characteristics. Then a set of "region – feature" is stored in the database. The second mode – search of images on signs. The user specifies the required characteristics, and the system pulls them from the database images which contain a region with the specified characteristics. Thus, in case of doubt in diagnosis, a physician can review the analyzed image with interesting characteristics, compare them with the sample and resolve the problem.

The practical importance of work consists in development of a knowledge base containing a set of images of histological preparations and their characteristics. This system can be used in clinical hospitals in the analysis of histological preparations and will allow to significantly simplify this process. The system also will significantly increase the diagnostic accuracy by eliminating subjective factors.

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LASER IRRADIATION AS A TOOL TO CONTROL THE RESONANCE ENERGY TRANSFER IN BACTERIORHODOPSIN-QUANTUM DOT BIO-NANO HYBRID MATERIAL

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Bacteriorhodopsin (BR) is a unique light-sensitive protein known for its ability to produce a pronounced electrochemical response to irradiation. The changes in the protein's absorption profile during photochemical transformations allow one to create optical logic gates based on BR. Owing to these properties, BR is a promising material for applications in optoelectronics [1]. However, the spectral region in which BR effectively absorbs light is limited to the band with a maximum at 568 nm, whereas its excitation in the UV, blue, and NIR spectral regions cannot be achieved. Semiconductor quantum dots (QDs), which have high one-photon and two-photon absorption cross-sections in a UV- and NIR spectral regions, respectively, can significantly improve the light sensitivity of BR by means of Förster resonance energy transfer (FRET) from QD to BR [2]. In turn, the high efficiency of the QD-BR nano-bio hybrid material implies a large number of FRET elementary actions from QD to BR per time unit, which is in strong correlation with the QDs' excited state population. The high intensity of laser irradiation makes it possible to turn a significant part of QDs ensemble into excited state and provoke, at the same time, various irreversible photo-induced processes leading to alteration of the QDs optical properties [3]. An important task is to study the effect of high-intensity laser irradiation on the FRET process inside the QD-BR nano-bio hybrid material.

In this work, we demonstrate the possibility to control an efficiency of the FRET from QD to BR within their electrostatically bound complexes. We have shown that UV laser irradiation of a QD at 266 nm leads to a drop of their luminescence quantum yield (QY), whereas QD irradiation at the 355 or 532 nm leads to an increase in their QY. Such photo-induced changes in the QY of QD lead to a corresponding change in the efficiency of FRET. We have compared efficiencies of FRET from QD to BR in the BR complexes with irradiated and non-irradiated QDs and found the pronounced difference between them. Indeed, for a fixed distance between the donor and the acceptor, FRET efficiency will increase with an increase of the Förster radius, which is proportional to the value of the QY of donor (QD) [4].

These experimental results not only allow one to optimize the operating conditions for nano-bio hybrid material based on QDs and BR, but can also be used to control an efficiency of FRET inside the QD-BR complexes without affecting their structure and geometry.

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DIAGNOSTIC FLUORIMETER WITH LEDS PULSED MODE OF OPERATION

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By researches it is proved that fluorescent assessment of maintenance of the final products of a glycation (AGE) in a skin of in Vivo allows prognosticating a mortality at diabetes and quality of operation at renal transplantation, the increased formation of AGE in a skin is observed at its aging and acute coronary heart disease. At illumination of a skin in the spectral range of 350 - 420 nanometers autofluorescence (AF) AGE therefore measurement of intensity of AF doesn't demand the procedures with injuring the patient.

Measurement of maintenance AGE in skin by intensity of its AF is complicated by two circumstances: 1) low intensity of AF at admissible power levels of exciting radiation; 2) variability of skin`s optical properties even at people of one race. The first circumstance forces to use highly sensitive photoreception channels of measurement AF intensity and to fight against different hindrances, and the second – to try in some way to neutralize influence.

Authors of this scientific work managed to realize the diagnostic fluorimeter on a direct current which allows revealing the age accumulation of AGE [1] and accumulation caused by coronary heart disease [2]. In the fluorimeter [1, 2] the variability of personal skin`s optical properties was compensated by a choice as diagnostic parameter the attitude of AF intensity offered in work [3] is elastic the exciting radiation dispersed by skin. The similar method of compensating variability is not unique. Similar results were shown by [4] normalization of AF intensity on intensity is elastic the radiation of white LEDs dispersed by skin. In case of trial operation of the fluorimeter on a direct current influence on its photoreceiving paths of external flares was shown. Therefore the version of the fluorimeter on an alternating current with a pulsed mode of operation of two LEDs was developed and realized. One of LEDs, with peak wavelength is 365 nanometers, serves for excitation of AGE AF, the second, with peak wavelength is 530 nanometers, is necessary for compensating variability on a method [4].

Transition to a pulsed mode of LEDs allowed to use in a photoreceiver`s path classical methods suppression of influence for the output signals of background flares - selective gain and the synchronous detection. Really direct flares were not shown by sunlight and lighting lamps in a digital signal on an output of 10-bit ADC.

Digital part of the fluorimeter is constructed on the platform Arduino. The software controls fluorimeter`s operation modes, provides carrying out the quantitative processing of results, visualizes and saves diagnostic data.

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DEVELOPMENT OF CASCADE PROCESSES IN METALS

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To study the effects associated with changes in the crystal structure of the material in the reactor core, it is often sufficient to conduct simulations of charged particle accelerators. It is very important task of studying the defect distribution profile along the depth of the damaged layer. At one time, for this purpose on the basis of theoretical research has been developed program for computer calculation of the profile distribution of displaced atoms in depth passage of heavy ions in the material. But any program, as it was neither an universal, yet can not take account all aspects of the complex process of the interaction of charged particles with the real crystal lattice, the more it can not be acceptable, when the research objects are multicomponent alloys.

Charged particles, moving in the matter, lose their energy. The energy loss of the incoming particles can occur in various ways, including on the ionization and excitation of the electron shells, the polarization of the atoms medium, the radiation loss and nuclear stopping, whose role in the formation of structural defects may be different. Consequently, the distribution profile of the defects in depth may also vary, the location, which depends on the species and the parameters of the bombarding particles, target material, the irradiation temperature, etc.. In this regard, the experimentally obtained parameters of defect structure can differ significantly from the theoretically calculated.

Since at least the passage of charged particles in matter, there is a consistent discharge of its energy, that to study of the profile distribution of defects in depth, in principle is the task of the study energy dependence of radiation damage metal. To solve this problem we can study defect structure of metal by consistently etching the surface or method, which based of alternating thickness absorber. Of course, the most appropriate is the second non-destructive method of investigation, the essence of which consists in irradiating a high energy charged particles and study stack of foils, the total thickness of which is the exceed length of free mileage of the particles in this material. In the result of using this method, each foil is irradiated particles of different energies and contains corresponding structural damage, which characteristics for the depth of the material. For the object of the study were used polycrystalline Mo and Ta, as well as stainless steel 10C18N10T-VD such as foil with the each thickness of 100 mkm and diameter is 17 mm. The initial state of metals was achieved by annealing at T=1200 ºC and steel at 1050 ºC during 1.5 hours in a vacuum of 10^{-5} Pa. The thickness of each foil Δd specifies the path element $\Delta x_i = \Delta d_i \rho$, where there is a loss of energy of protons $\Delta E_i = s_i(E)\Delta x_i$; the average energy of the protons on the other side of each foil will be $E_{xi} = E_i - \Delta E_i$. Hence, each foil is irradiated with protons of different energies by studying the degree of damage that can be installed its energy dependence.

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APPLICATION OF MDT METHOD FOR RADIOTHERAPY PLANNING IN PATIENTS WITH CARDIAC DEVICES

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The number of cancer patients with cardiac implantable electronic devices (CIEDs) receiving radiotherapy is increasing. Unfortunately, ionizing radiation can cause damage of CIEDs [1-2]. In this respect, it is necessary to make irradiation plans for these patients properly in order to minimize the dose received by the devices. Indeed, the metal implants can cause the streaks of different grayness (artifacts) on computed tomography (CT) scans. Such artifacts contribute uncertainty to calculation of the dose received by CIEDs.

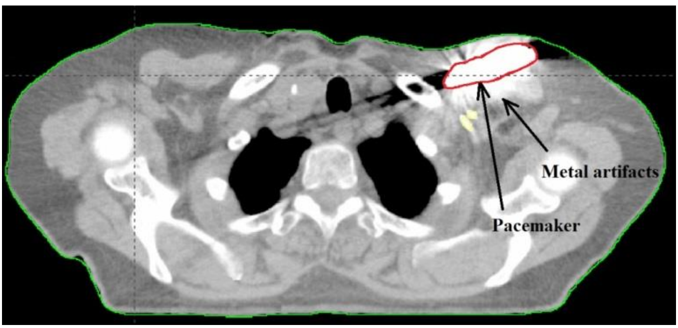

Fig.1. CT image with artifacts and cardiac device (pacemaker)

Metal Deletion Technique (MDT) has been tested on 9 cancer patients with different tumor localization. In the study, we have analyzed the influence of MDT application on the plan parameters. All radiotherapy plans were created in the VARIAN Planning System Eclipse 11.0

using 3D-CRT, IMRT, VMAT and SBRT irradiation techniques. The doses received by the CIEDs and electrodes before and after MDT method application were compared and analyzed.

The biggest inaccuracy in determining the maximum dose received by CIEDs was observed in 3D-CRT plan of breast and lymph node irradiation and constituted approximately 3.2 %. In most plans without application of MDT method, we have noticed a tendency to artificial reduction of maximum dose. In the analysis of the doses received by electrodes itself, the main uncertainty was observed in the calculation of medium dose and reached 3.5% in the case of esophagus irradiation.

The data obtained from this experimental study confirm the necessity of MDT application for artifact reducing for cancer patients with implantable electronic devices who are referred for radiotherapy. This approach contributes to the safe management of cancer patients with a cardiac device.

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INFLUENCE OF SR-90 ON THE MORPHOMETRIC INDICES AND THE LEVEL OF PROTEINS OF METALLOTHIONEINS IN THE SOFT TISSUES OF TERRESTRIAL MOLLUSKS *BRADYBAENA FRUTICUM* IN THE AREA OF LOCATION OF THE REGIONAL RADIOACTIVE WASTE STORAGE FACILITY

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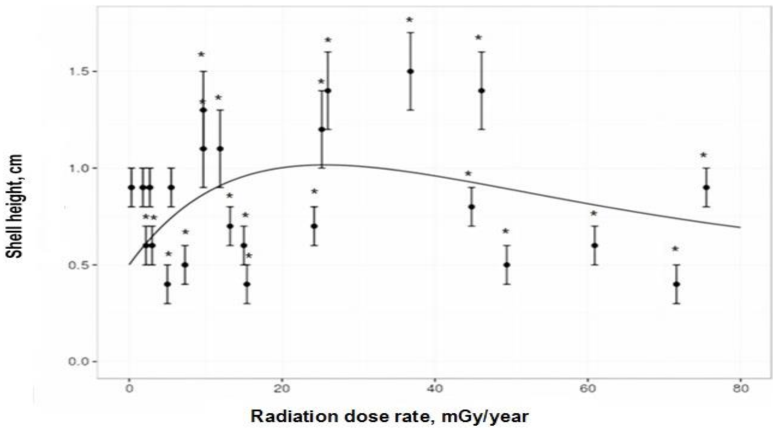
The concept of "conditional or reference animals and plants" proposed by the ICRP is the most developed in the development of an ecocentric radiation protection strategy [1]. At the same time, the set of 12 reference species proposed by the ICRP is not final, which requires justification of other representatives of the biota for inclusion in the reference set, including taking into account the formation of dose loads and radiation-induced effects. In this work it was estimated the effect of irradiation of terrestrial mollusks of the species Bradybaena fruticum with the radionuclide Sr-90 on the morphometric parameters of shellfish (height and diameter of the shell) and the level of proteins of metallothioneins in the field experiment. The site for research is the biotope of the regional storage of radioactive waste in the Kaluga region. In 1998 it was found that one of the storage tanks and leakage of radionuclides depressurized. As a result, an uncontrolled source of radionuclides entering the ecosystem components was formed in the soil. On the basis of many years of research it has been established that the radioecological situation in the study area is due to Sr-90 [2].

Based on the calculation of the dose load for terrestrial mollusks by means of the Monte Carlo method (taking into account the scenario of self-irradiation, irradiation from Sr-90 accumulated in the soil and accumulated in the nettle), it has been established that the absorbed dose rate of the mollusk varies in the range from 0.32 ± 0.07 to 76 ± 18

mGy/year. In the range of doses studied it was established a significant change in height of shell from 0.41 ± 0.06 to 1.5 ± 0.3 cm (Figure 1), which is described by an equation of the form y = 0.5 + 0.06xe (-0.04x) and change of the level of proteins metallothioneins from 12.4 ± 1.4 to 29 ± 1 μg / g, which is described by piecewise linear model with the threshold dose rate of 42.3 mGy/year.



Thereby, the terrestrial mollusk of the species Bradybaena fruticum can be considered as a candidate for inclusion in the list of reference species, and the height of the shell and the level of proteins of metallothioneins - as reference indicators.

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THE CONCEPT OF A LOW-POWER RESEARCH REACTOR FOR RADIOISOTOPE PRODUCTION

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Promotion of Russian nuclear technologies to world markets is one of the priority activities of SAEC Rosatom. At the present time agreements have been reached on the construction of scientific nuclear centers in Vietnam, Bolivia, Nigeria, etc. The list of tasks to be solved by the centers includes research on the use of nuclear technology for medical purposes. At the same time there are no nuclear reactors designed specifically for these purposes. The development of radiopharmaceuticals is carried out at the re-equipped facilities and optimal operating modes are not always achieved, that leads to a decrease in efficiency and a significant increase in the cost of the products.

The purpose of the present research is to develop the concept of a serial reactor designed to produce radioisotope products, potentially capable to overcome the threshold of commercialization. Due to the fact that the reactor is expected to be operated in countries with low experience in the use of nuclear technologies, one of the most important criteria is the requirement for operation without refueling during a long campaign.

The reactor is designed according to the scheme of a water-cooled reactor with a natural circulation of the coolant. A distinctive feature of it is the low level of the coolant temperature (below 90 °C), which avoids loading the hull with internal pressure and ensure a long safe operation. As the prototype serial reactors VVR and IRT [1] was chosen. The thermal capacity of the reactor is up to 10 MW. The size of the reactor tank is selected from the condition of a low level of activation of its material at the end of the campaign, permitting general industrial reprocessing without burial.

The reactor core consists of the shortened fuel assemblies of the VVER-440 reactor [2], which allows organizing their production on existing equipment. The active zone contains 37 shortened fuel assemblies and 48 cassettes with a beryllium reflector located around the fuel assembly (Fig. 1). The height of the core is 93 cm, diameter 100 cm. Each fuel cassette contains 120 fuel elements, fuel is UO_2, enrichment according to U^{235} is 4.4%. With such core configuration, the effective neutron multiplication factor at the beginning of the campaign is 1.2025 +/- 0.0017.

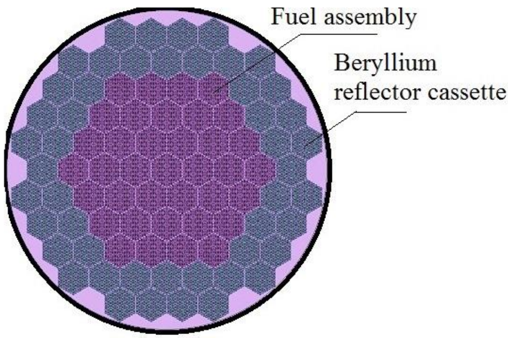

Fig.1. Cartogram of the core of the research reactor

The simple designs, small amount of activated structural materials, compactness of the plant as a whole make the present concept attractive not only from the technical point of view. The export potential is provided by using fuel with enrichment below 5%, which is in line with IAEA recommendations on the nonproliferation regime.

The research was carried out within the framework of the subsidy for financial support for the execution of the state task for the performance of public services. Theme No. 00-g-995-2203.

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THE EFFECT OF QUANTUM DOT SHELL STRUCTURE ON FLUORESCENCE QUENCHING BY ACRIDINE LIGAND

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The current strategy for the development of advanced methods of tumor treatment focuses on targeted drug delivery to tumor cells. Linking a fluorescent imaging agent to a biomarker-recognizing molecule conjugated with a pharmacological agent ensures real-time tracking of the delivery process of the active substance. Quantum dots (QDs) are semiconductor fluorescent nanocrystals with unique fluorescence characteristics: size-tunable light emission, high brightness, and long-term stability of optical properties. Thus, water-soluble QDs can be used as efficient biomedical fluorescent labels for real-time delivery control and tracking. Nitrogen heterocyclic compounds, such as acridine and its derivatives, being effective anticancer agents, can be used as pharmacological components of a multifunctional nanoprobe. However, the problem of QD fluorescence quenching caused by charge transfer can arise in the case when these compounds are bound to the QD. This hampers the use of acridines as targeting agents in designing QD nanoprobes.

Here, we addressed the problem of acridine derivative conjugation to QDs from the viewpoint of the effects of inorganic shell structure and shell thickness of CdSe-based core/shell QDs on the degree of fluorescence quenching. We have used an advanced procedure for the synthesis of highly luminescent core/shell QDs based on the hot-injection technique followed by coating of purified cores with three different types of shells using the SILAR approach.

It was found that typical CdSe/ZnS QDs (*d* ~ 5 nm) with a three-monolayer (3-ML) shell were completely quenched by addition of only 5 molar eq. of acridine, whereas QDs with a “giant” (5-ML) ZnS shell (*d* ~ 7 nm) and QDs with ZnS/CdS/ZnS “multishell” shell (MS) with a total shell thickness of 3 ML (*d* ~ 4.8 nm) exhibited a smaller degree of fluorescence quenching even, when the QD-to-acridine ratio reached 35. Thus, both MS and “giant” shell types provide more efficient protection of excited charge carriers in QDs from the quencher ligands than the “classic” thin ZnS shells. However, MS QDs are considerably smaller in physical size, which makes them more preferable as components of nanoprobes, since they could ensure better tissue and cell membrane penetration.

To conclude, the core/multishell QDs could be an ideal choice for engineering of small-sized fluorescence labels for tumor diagnosis and treatment systems employing fluorescence quenching ligands capable of penetrating into cells and cell compartments.

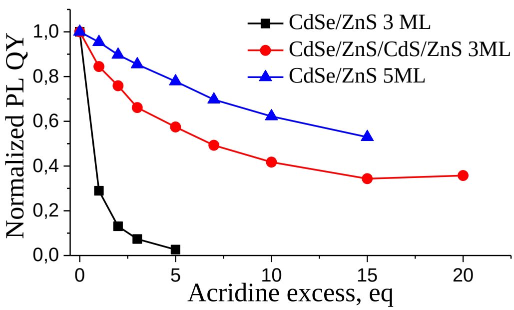

Fig.1. Kinetics of the photoluminescence quantum yield (PL QY) quenching of the types of QDs by acridine derivative.

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BACTERIAL CELLULOSE / ALGINATE NANOCOMPOSITE FOR ANTIMICROBIAL WOUND DRESSING

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Development of novel wound dressing has attracted more and more attentions in recent years. Bacterial cellulose (BC) is a biopolymer of great potentials, which features a distinctive three-dimensional structure consisting of an ultrafine network of cellulose nanofibers. This unique micromorphology enables it to have great water holding capacity, high porosity, high crystallinity, excellent mechanical strength and large surface area, which determines its potential application as an excellent wound dressing material [1-3]. Alginate, another natural polysaccharide product, is extensively used in many applications such as scaffolds and wound dressings due to its biocompatibility, biodegradability under normal physiological conditions and capacity for bioresorption of the constituent materials. Recently, hybrid nanocomposites of BC and alginate were developed for use as scaffolds for tissue engineering, films for wound dressing and supports for drug delivery [4]. However, both bacterial cellulose and alginate are lack of antibacterial property which limits the possibilities of application in wound dressing areas. There are several successful attempts to impart antimicrobial properties to BC. Bacterial cellulose-silver nanocomposites were successfully prepared and they exhibited excellent antibacterial activity [4].The synthesis of BNC/chitosan composites with high mechanical reliability and antibacterial activity was reported [3]. Antibiotics are used in combination with BC for the preparation of composite membranes with antibacterial activity [5].

Modification of bacterial cellulose can be made by two strategies: in situ, during the bacterial cellulose production, and ex situ after bacterial cellulose purification.

In the present study, nanocomposite bacterial cellulose films modified in situ by the addition of alginate during the static cultivation of *Gluconacetobacter sucrofermentans* B-11267 were produced and then enriching the polymer with an antimicrobial agent tetracycline hydrochloride.

The structure of bacterial cellulose and nanocomposites was analyzed by AFM and FTIR. The FTIR spectra displayed the specified interaction between the hydroxyl group of cellulose and the carboxyl group of alginate. The antibacterial activities of nanocomposites were investigated by disk diffusion method. The produced bacterial cellulose and nanocomposites were analyzed to determine tensile modulus. The resulting nanocomposite have high mechanical strength and antibiotic activity against *Staphylococcus aureus* and can be used in medicine as a wound dressing.

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SOLID ANGLE FRACTION IN POSITRON EMISSION TOMOGRAPHY

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Modern tomography is a powerful tool for visualization of internal structures of opaque objects [1]. Two classes of tomography are known: transmission computed tomography (TCT) and emission computed tomography (ECT). In TCT the object under investigation is irradiated by an external radiation. In ECT the spatial distribution of radiation sources (radionuclide atoms) is reconstructed. The ECT exists in two main forms. First one is single-photon emission computed tomography (SPECT) and second one is positron emission tomography (PET). In SPECT single gamma quantum originating from a decay of radionuclide atom is registered. In PET the detector register a pair of gamma quanta that arises from annihilation of a positron, which originates from a decay of radionuclide atom.

In ECT an additional distortion factor exists. This is so-called solid angle fraction that arises due to the different distance between an elementary source and an elementary detector.

Let $s(x,y)$ be the spatial distribution of radiation sources in a fixed coordinate system (x,y), $s_\theta(\xi,\zeta)$ be the spatial distribution of radiation sources in a rotating coordinate system (ξ,ζ), which is rotated by an angle θ with respect to a fixed coordinate system. In PET the projections $p(\xi,\theta)$ taking into account SAF can be written in the following form:

$$p(\xi,\theta)=\int_{l_1}^{l_2}\frac{s_\theta(\xi,\zeta)}{\left(R_1^2-\zeta^2-\xi^2\right)^2}d\zeta\ . \qquad (1)$$

In (1), the factor $\frac{1}{\left(R_1^2 - \zeta^2 - \xi^2\right)^2}$ is the factor SAF for PET. Neglecting SAF it can be obtained

$$\tilde{p}(\xi,\theta) = \frac{1}{R^4}\int_{-\infty}^{+\infty} s_\theta(\xi,\zeta)d\zeta = \frac{1}{R^4}\Re\{s(x,y)\}, \quad (2)$$

where $\Re\{s(x,y)\}$ is the Radon transform of the function $s(x,y)$. Therefore in PET in order to reconstruct the radiation sources spatial distribution the inverse Radon transform $\Re^{-1}\{\bullet\}$ is used:

$$\tilde{s}(x,y) = R^4\Re^{-1}\{p(\xi,\theta)\}, \quad (3)$$

where $\tilde{s}(x,y)$ is an estimation of the reconstructed function $s(x,y)$.

Usually the influence of SAF is neglected in comparison with attenuation due to radiation absorption in the substance of the object. [1] However, this neglection is not due to that the SAF is very small but it is not possible to take it into account exactly. Therefore it is interesting to study the influence of SAF on the quality of reconstructed tomograms and to develop methods for at least approximate correction of this influence.

To correct the distortion due to SAF a new method is developed that is based on the concept of the correction matrix [1,2].

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PET RADIOTRACERS AS THE CERENKOV RADIATION SOURCES INDUCED PHOTODYNAMIC THERAPY

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Photodynamic therapy (PDT) requires external light to activate photosensitizers for therapeutic purposes. However, light-based methods suffer from the rapid attenuation of the light in tissue. To overcome this limitation, we optimize the system by using Cerenkov radiation for PDT or radionuclides for photosensitizer activation that could serve as a depth independent light source for photoinduced inside cancer therapy [1].

Radionuclides are an ideal source for Cerenkov radiation because of their positron emission, which travel faster than the speed of light in the medium emitting from in the main ultraviolet light to visible spectrum (250-600 nm). Radionuclides such as Fludeoxyglucose (^{18}F-FDG) are widely used in positron emission tomography (PET) that allows observing metabolic processes in the body especially in clinical oncology. In its turn 5-Aminolevulinic acid (5-ALA) has become an integral part in the treatment of malignant glioma that is why in this research this photosensitizer (PS) used for CR-induced therapy.
The in vivo studies were performed on experimental animals with induced malignant glioma C6 in the groin. During the study intravenous injections of 5-ALA and tracer amounts of FDG were made successively at intervals of 2 hours respectively. Observation of metabolic processes and the FDG concentrations in tissues was imaging by the PET. 5-ALA acts as PS whereas the FDG induce the CR that in combination resulted in CR-induced therapy. The evaluation of photodynamic effect of CR-induced therapy was made using confocal laser scanning microscopy.

Histological analysis of tumor sections were visualized using confocal laser scanning microscopy posthumously. Analysis of tumor sections of 5-ALA-treated mice revealed efficiently proliferating of glioma C6 cells formed agglomerates (fig.1a). Analysis of tumor sections of FDG+5-ALA-treated mice revealed selective destruction of proliferating cells in the tumor region as well as pronounced necrotic zones that occupied approximately 20-30% of the tumor mass (fig.1b). Large areas of FDG+5-ALA-treated tumors exhibited a loss of cellular architecture and significantly high distribution of apoptotic foci (fig.1b). These findings suggest that the damage to cells probably was mediated by the CR-induced free radicals. Thus a comparison of the FDG-untreated (fig.1a) and FDG-treated (fig.1b) tumor sections using confocal microscopy shows predominantly apoptotic cells in the latter that confirms the selectivity of the method.

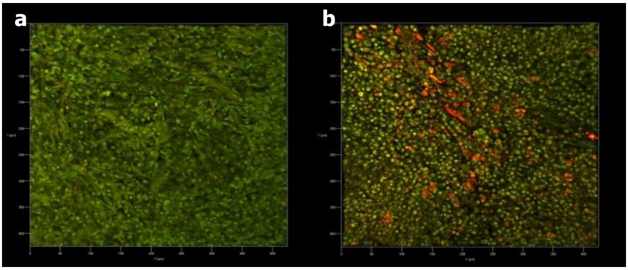

Fig.1. Histological analysis of tumor sections of a) 5-ALA-treated and FDG-untreated, b) FDG+5-ALA-treated by means of confocal microscopy

In this study, we have demonstrated a new approach using CR from PET radionuclides to activate 5-ALA for phototherapy. The effect of the complimentary radical-generation mechanisms enabled an effective CR- induced therapy using tumor-targeted PS. Thus the approach opens up the possibility of treating a variety of lesions by the depth-*inside therapy.*

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NEW METHODS OF STUDY OF RENAL DISEASES IN CHILDREN WITH HEMATURIA SYNDROME BY METHODS OF MEDICAL BIOPHYSICS

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At present, there is a need to develop new methods of study at a cellular level of difficultly diagnosable renal diseases in children with a hematuria syndrome for new types of diagnostics using high-technology physical equipment in connection with development of methods of medical physics. In this paper, research of blood samples of children ill with various types of chronic glomerulonephritis is carried out, including Berger's disease, using a scanning electron microscope with a Gentle Beam system with a Schottky heat-field cathode without sputtering, supplemented by studies on optical and atomic force microscopes and an IR spectrometer, as well as construction of physico-mathematical models of dynamics of erythrocytes under the influence of and depending on various physical factors, and realization of numerical experiments on their basis. Thanks to new approaches for performing experiments on the given equipment [1-3], unique images of blood erythrocytes of children ill with glomerulonephritis and other types of nephropathies, as well as a control group for comparison were obtained. Mathematical modeling allowed supplementing experimental data with important remarks and analysis of comparisons of theoretical and experimental data.

Results of these studies can bring a significant contribution to fundamental knowledge at the cellular level of human blood processes in normal and pathological conditions, form new less traumatic methods of diagnostics in a field of personalized medicine focused on rare difficultly diagnosable diseases, as well as allow making recommendations for improvement and adaptation of traditional physical equipment in an application in a field of medicine.

[1] Maksimov G.V., Mamaeva S.N., Antonov S.R. et al. Measuring erythrocyte morphology by electron microscopy to diagnose hematuria // Metrology. Quarterly supplement to the journal Measuring Techniques. 2016. No. 1. Pp.47-52.
[2] Maksimov, G.V., Mamaeva, S.N., Antonov et al. Measuring Erythrocyte Morphology by Electron Microscopy to Diagnose Hematuria //Measurement Techniques. June 2016. Volume 59 (3). P. 327-330.
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USE OF NANOCOMPOSITE MATERIAL BASED ON GRAPHENE OXIDE AND SILVER NANOPARTICLES IN RESEARCH OF BLOOD ERYTHROCYTES IN VARIOUS DISEASES

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Research of causes of emergence of various difficultly diagnosable diseases by methods of medical biophysics using modern traditional physical equipment with possibilities of nanotechnologies can become a basis for formation of effective methods of their diagnostics and monitoring of treatment. In this paper, it is considered a study by a method of scanning electron microscopy (SEM) of blood samples of sick children with a syndrome of hematuria and patients of a radiological department of an oncological dispensary with a diagnosis of cervical cancer. Studies of dry blood smears on substrates based on a nanocomposite material made from graphene oxide modified by nanoscale silver particles, using a scanning electron microscope Jeol JSM 7800F, are conducted. During the study, comparisons are made of obtained SEM images of erythrocytes of blood smears on a microscope slide [1-3] and on the substrate made from the nanocomposite material, as well as images of erythrocytes, when there is the cervical cancer, before and after radiation therapy. In the REM images on the graphene oxide substrate on a surface of erythrocytes, nanometer objects are more clearly observed (Fig. 1), dimensions of which are comparable with sizes of viruses, than nanometer structures on the microscope slide [1-2].

Results of these studies can indirectly confirm an assumption of authors about possible transportation of viruses by erythrocytes to various organs and viral etiology of renal diseases with the hematuria syndrome and cervical cancer, taking into account that the linear dimensions of the observed nanoparticles on the surface of erythrocytes basically coincide with the sizes of the viruses detected in the blood of patients using a method of PRC analyses.

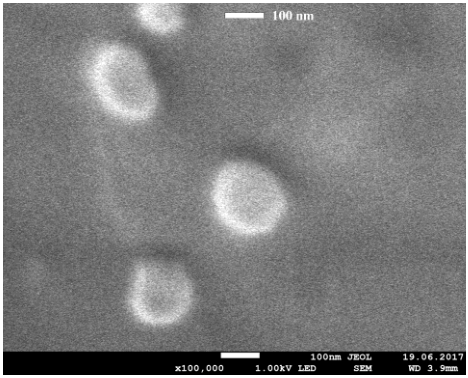

Fig.1 SEM image of nanometer particles on surface of erythrocyte of blood sample on substrate made from graphene oxide with silver nanoparticles in case of chronic glomerulonephritis at 100,000x magnification

[1] Maksimov G.V., Mamaeva S.N., Antonov S.R. et al. Measuring erythrocyte morphology by electron microscopy to diagnose hematuria // Metrology. Quarterly supplement to the journal Measuring Techniques. 2016. No. 1. Pp.47-52.

[2] Maksimov, G.V., Mamaeva, S.N., Antonov et al. Measuring Erythrocyte Morphology by Electron Microscopy to Diagnose Hematuria //Measurement Techniques. June 2016. Volume 59 (3). Pp. 327-330.

ABNORMAL ENERGY RESPONSE ON NEURONAL ACTIVATION IN EARLY-STAGE SCHIZOPHRENIA PATIENTS

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Introduction Brain metabolism in early stage of schizophrenia remains a subject of studies. The data on the local concentrations of proton-containing metabolites are contradictive. 31P MRS magnetization transfer study revealed decreased rate constant of forward creatine kinase reaction in frontal lobe of never medicated schizophrenia patients [1]. The purpose of this study is to reveal stimulation effects on 31P MRS detectible metabolites in activated cortex in the norm and in early stage schizophrenia patients.

Materials and methods Subjects of the study were 12 patients at early stage schizophrenia (F20, ICD-10) (mean age 21.2 ± 5.5) and 20 neurologically and psychiatrically healthy age-matched subjects. Philips Achieva 3.0T, Dual 31P/1H bird-cage coil for 31P 2D MRS and In vivo Philips station for visual stimuli transmitting were used. All participants passed fMRI (EPI, TE=35ms, TR=3000ms, FA=90°) revealing zones of visual cortex activation in response to watching a flashing checkerboard. Parameters of 2D 31P spectroscopy were pulse sequence ISIS, TE=0.3ms, TR=1200ms, FA=35°. fMRI activation map was used for better spectroscopic volume locating in visual cortex. (Fig. 1). Firstly, spectra acquisition were performed in resting state and then during continuous visual stimulation by a 6 Hz flashing checkerboard. Each spectrum acquisition took 6 minutes. Postprocessing and quantification were performed in jMRUI using AMARES algorithm. FIDs of two voxels containing visual cortex were averaged, amplitudes of individual resonances in spectrum recorded during excitation were normalized to corresponding values obtained from the spectra recorded in resting state. ATP concentration was measured using β-ATP peak.

Results.

No difference was found between [PCr]/[ATP] in visual cortex of healthy subjects and patients in resting state. Visual stimulation causes statistically significant (*$p<0.05$) decrease of [PCr] in visual cortex in the norm while no stimulation-induced effect on [PCr] in the group of schizophrenia patients was revealed. Visual stimulation had no effect on [ATP] in both groups; no statistically significant pH changes in any group were revealed either.

Discussion

The data obtained for normal subjects allow to conclude that in response to visual stimulation ATP is regenerated by creatine kinase reaction. No stimulation-induced [PCr] changes in schizophrenia may reflect disorders in creatine kinase system [1] and/or reduced energy consumption in the period of neuroactivation. The latter agrees with [NAA] resistance in motor cortex of early stage schizophrenia patients in response to the single stimuli [2]. NAA indirectly participates in energy metabolism [4]. The data obtained might reflect reduced energy expenses under neurostimulation in early stage of schizophrenia caused probably by decreased activity of energy dependent processes of glutamate transport [5].

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DYNAMICS OF T2* AND WATER CONCENTRATION IN ACTIVATED CEREBRAL CORTEX

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Introduction Physiological and biochemical mechanisms involved in hemodynamic response (HR) processes are not revealed fully. HR and metabolic processes are closely coupled; to reveal their relations dynamic spectroscopy was used [1]. HRF contains spin-spin relaxation (T2*) and water concentration (C) information. The purpose of this study is to separate T2* and C contributions to HR signal in premotor cortex zone activated by a single stimulus using dynamic spectroscopy.

Materials and methods 8 healthy subjects participated in the study. Philips Achieva 3.0 T and 8-channel Head coil were used. Spectroscopic voxel (PRESS, TE=30ms, TR=3s, size 20x10x15 mm^3) was positioned to activated zone of premotor cortex. Dynamic spectroscopy was performed, when FID signals were recorded at the moments t=0, 3, 6, 9, 12, 15, 18, 21 and 24 seconds after performing the same procedure as in fMRI. For each t, 97 FIDs were acquired, resulting in 776 FIDs for every subject. FIDs were processed individually: FT, phase correction, water peak amplitude and area quantitation were performed. Statistical significance of differences (*p*-value) was calculated using Mann-Whitney criteria.

Results.

Equations describing relationship between Amplitude and Area of water peak with T2* and C values were derived by FID signal interpreted in discrete form followed by Discrete FT application to it. For steady-state phase-corrected spectrum, signal intensity can be estimated as:

$$Ampl = A * C * \exp\left(-\frac{TE}{T_2}\right) * \frac{1}{[\exp\left(-\frac{\alpha}{BW}\right)-1]}, Area = A * C * \exp\left(-\frac{TE}{T_2}\right) * N$$, where

$\alpha = \frac{1}{T_2}$, BW – bandwidth, A – const, C – MR- detectible concentration, N – number of sample points of water signal

C(t) and T2*(t) values were calculated using these formulas. At maximum of HRF (t=6 s) we observe statistically significant ($p<0.01$) reduction of C that returns to its initial value after 3s, and T2* increase ($p<0.01$) with an undershoot ($p<0.05$) after 3s.

No statistically significant reduction ($p=0.07$) of C at (t=6s) as well as no increase of C at (t=9s) in schizophrenia, at this time point C differs ($p<0.05$) between norm and schizophrenia (Fig.3). T2* decrease (t=9s) in schizophrenia is smoothed: there is no undershoot and T2* is ~1% higher ($p<0.01$) than in the norm (Fig.4).

Discussion

In the norm at (t=6s) after single stimulus blood flow increases in activated cortex. According to Monro-Kellie hypothesis, the MR-undetectable (not irradiated by excitation pulse of PRESS) water from blood flow partly replaces MR-detectable water located in voxel before. The next spectrum of dynamic study reveals this water at (t=9s) after stimulus. This returns C to its initial value. Our estimation (based on neuronal glucose metabolism rate [2]) shows that the volume of metabolic water is 1.5–2 orders of magnitude less than the C change revealed in present study. T2* maximum at the HRF maximum is caused by increase of [oxiHb/deoxiHb]. The maximal increase of T2 obtained in this study using spin-echo (PRESS) is ~1%, while maximal increase of HRF obtained using gradient echo (GE-EPI) [2] is ~3.5%. This agrees with [3] ([GE-BOLD]/[SE-BOLD]~3.5). The T2* undershoot at (t=9s) in the norm is caused by blood deoxiHb accumulation [4].

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SIGNAL-TO-NOISE RATIO OF ^{31}P MR SPECTRA *IN VIVO* OPTIMIZATION

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Introduction ^{31}P Magnetic Resonance Spectroscopy is a unique way of *in vivo* energy and lipid metabolism investigation. The ^{31}P MRS studies demonstrated its effectiveness in MR negative pathology investigations, for example, schizophrenia [1]. Overcoming of the problems related with low 31P nucleus sensitivity, hence, low signal-to-noise ratio (SNR), is a practically significant task. The aim of this study is to optimize the method of 31P MRS acquisition in the context of time expenditure and SNR using proton-phosphorus decoupling and Nuclear Overhauser enhancement.

Materials and methods 11 healthy subjects participated in the study. Philips Achieva 3.0 T and ^{31}P/^{1}H RF coil were used. The spectroscopy volume of interest (voxel) sized 80x60x60 mm was located in such a way as to contain the most part of brain tissue. Pulse sequence (PS) ISIS was used for voxel localization, the parameters TE=0.1ms, FA=35°, BW=4000 Hz, NSA=64, broadband decoupling (waltz 4). In the first part of the study 3 spectra with TR=2, 3, and 4s were acquired. In the second part 11 spectra with TR = 3s and waltz16 NOE variating *mix time* = 0, 250, …, 2500 ms. Spectra were processed in SpectroView. In the first part the SNR increase (in %) with the increase of TR was calculated. In the second part the SNR of each peak for each *mix time* was normalized on the SNR of the according peak with *mix time* = 0.

Results. First part of the study: the greatest SNR increase keeping the time for spectrum obtaining constant was discovered when TR was increased from TR=2s to 3s. The increase of TR from 4s to 2s lead to increase of SNR mostly for lipids and Pi – no effective increase of SNR was demonstrated for main energy metabolism participants – ATP peaks.

Second part: the typical behavior of SNR as a function of *mix time* is demonstrated for PE peak on figure 1. The SNR gain for ATP, PC, GPC, GPX, DN resonance lines slows down at mix time values ~1250-1750 ms. For PCr, Pi, GPE, PE graphs the SNR increase is observed up to 2250-2500 ms values of mix time. The maximal SNR gain by means of NOE is from 20 to 35 % depending on metabolite.

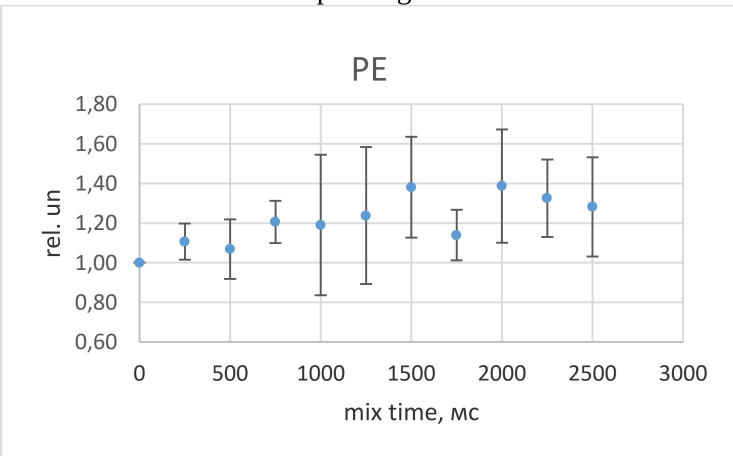

Figure 1. Relative SNR change for PE peak as a function of *mix time*.

<u>Discussion</u>

The *mix time* parameter that determines the time of proton irradiation for NOE is limited by TR and the time of spectra registration (~500 ms). The second part of the study revealed that the *mix time* values more than ~1500 ms will be effective only for PCr, Pi, PE and GPE peaks. This means that TR=2s is effective for energy metabolism investigations, available maximal *mix time* ~1500 ms is enough for maximizing NOE on ATP resonance lines. At the universally applicable TR=3s, shown in the first part of the study, *mix time* is constrained by ~2500 ms. This value is enough for a maximal SNR gain by means of NOE practically for all metabolites.

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LUMINESCENT BIOCOMPATIBLE NANOFIBER MARKERS

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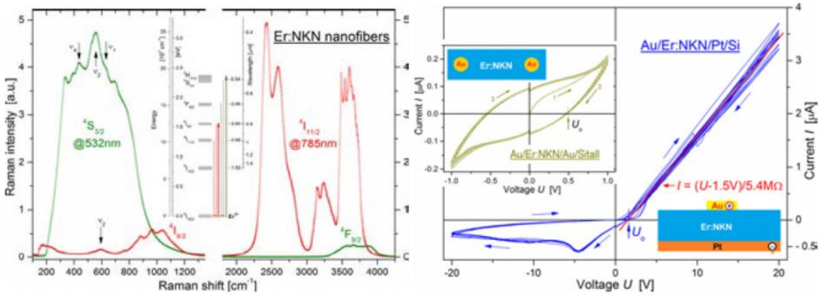
Ferroelectric sodium potassium perovskite $(Na,K)NbO_3$ (hereinafter NKN) ceramics was patented and FDA-approved (U.S. Food and Drug Administration) as a biocompatible material for implants. [1] Thorough toxicology tests showed that no bacterial products (endotoxin) appeared as well as viability of human monocytes was not negatively affected by the presence of NKN ceramics. We report properties of highly crystalline Erbium- and Ytterbium-doped NKN nanofibers.

Dense homogeneous NKN fabrics composed from 100 μm long and 100-200 nm in diameter nanofibers were sintered by sol-gel calcination assisted electrospinning technique. The process requiring neither catalysts nor templates yields continuous bead-free NKN nanofibers. [2,3] Rare earths Er and Yb doping with the concentration of 2 at.% provides readily detectable room-temperature broad-band photoluminescence (PL) centered at λPL = 0.55 and 0.98 μm being pumped, respectively, with 532 and 785 nm lasers (see the *left frame* in the figure attached). [4] Ferroelectric phenomenon in individual nanofibers was revealed by hysteretic electrical polarization as high as P = 21.2 μC/cm2 and strong electrostriction effect 75.8 pm/V.

Nanofiber fabric possesses diode-type current-voltage *I-V* characteris-tics (shown below in the *right frame* of the figure) that exhibit strong rectification effect. The *n*-type NKN fiber/high work function Pt cathode junction works as memristive memory cell. It demonstrates 102 times electric field induced non-volatile switching from a low- to a high-resistance state.

Photoexcited luminescence, enhanced piezoelectric and strong electro-striction effects promise great potential of NKN fibers as tensile and torsion sensors, electrically polarizable scaffolds for engineering, repair, and regeneration of damaged tissue as well as for energy harvesting biocompatible nanogenerators and implantable electronic chips.



Left frame - Unpolarized backscattered Raman spectra of Er:NKN nanofibers. In-tensive luminescence at λPL = 0.55 nm (Raman shift 556 cm-1) and within the λPL band 0.96 to 1.11 nm (Raman shifts 2300 to 3750 cm-1) is shown under excitation at 532 and 785 nm laser light pumping (green and red colors, respectively).
Right frame - Current-voltage *I-V* characteristics demonstrate nonvolatile resistance memory switching in vertical Au/NKN(260 nm)/Pt/Si and in planar Au/NKN(350 nm)/Au/Sitall cells.

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FEATURES OF DEFINITION OF SYMPTOM SHCHETKINA-BLUMBERG IN ACUTE APPENDICITIS IN PATIENTS WITH EXCESSIVE BODY MASS

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Overdiagnosis of acute appendicitis is relevant to this day [1]. It is known that the indications for appendectomy are symptoms such as local pain and tension in the right iliac region, combined with the increase in the level of leucocytes in the blood [2]. Along with the positive symptom Shchetkina-bljumberga these symptoms are absolute indications for surgery [3]. In people with excessive body mass can be observed false positive symptom Shchetkina-Blumberg, when subjective feelings of pain occur when sudden odergivaniya hands. Often soreness is caused by a sudden displacement of the internal organs with deep palpation. In this regard, we consider it appropriate to identify the symptom Shchetkina-Blumberg of fat people on a demarcated area of the abdominal wall. Palpation of the delimited area of the abdominal wall does not cause displacement of internal organs, and the manifestations of the symptoms of irritation of the peritoneum are more reliable. To confirm the reliability of our method, we conducted surveillance of 79th patients with excessive body weight, having a referral diagnosis of "Acute appendicitis", in which the traditional method was detected the symptom Shchetkina-Blumberg. When defining symptom on a delimited area of the abdominal wall symptom was confirmed in 52 patients. 48 of them in clinical blood analysis was observed inflammatory changes. As a result, these patients were operated. Intraoperatively, and subsequently histologically, was exhibited diagnoses of phlegmonous and gangrenous appendicitis. Another 8 patients were operated on because of their inability to exclude acute appendicitis – he was diagnosed with acute catarrhal appendicitis. The remaining 23 patients, the diagnosis of acute appendicitis was not confirmed.

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MICROVASCULATURE OF THE MYOCARDIUM IN ACUTE EXPERIMENTAL PERITONITIS

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The morphofunctional state of the myocardium in acute peritonitis is of great interest. This is because the heart, like all the internal organs exposed to pathological effects of toxic products generated during endotoxemia [1,2,3]. We conducted an experimental study on 22 mongrel dogs with experimental acute fecal peritonitis. The material sampling was carried out after 1 day, 3 days and 5 days after the onset of the disease. The study revealed that in the myocardium are observed destructive changes of the microvasculature, reflected in the swelling of the walls of arterioles and capillaries. Venular link of the myocardium is dramatically expanded, there is clearly microvariation. In Megalochori tissue swelling was observed. When electrocardiographic study experienced a decrease in voltage of the ventricular complex. The most significant damage was achieved on the 3rd day. Studies show that when you create acute experimental peritonitis in 72,7 % of the animals occur morphological and functional changes in the myocardium, indicating the involvement of cardiac muscle in the pathological process.

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STUDY OF THE EFFECT OF RADIATION DOSE RATE ON THE STABILITY OF VARIOUS ORGANOCHLORINE PESTICIDES

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Currently there are certain knowledge in the field of radiation technology, and results are obtained on effect of high-energy ionizing radiation on biologically active substances, such as organochlorineted pesticides (OCPs). These substances present in environmental and foods in microconcentrations. In radiation-chemical studies, there is no data about a dependence of OCPs stability on radiation characteristics. In this regard, it is difficult to predict the transformation degree of OCPs, the composition of the degradation products, and the toxicity of the newly formed substances.

Earlier we studied dose rate effect on the OCP degradation degree at exposure to a dose of 10 kGy of solutions of DDE, alpha-, gamma-HCH in hexane and 2-propanol with concentrations of 0.100 and 1.00 μg/ml.

The model solutions of an individual OCP were irradiated on "Issledovatel" (^{60}Co), "Luch-1" (^{60}Co) and Gammacell (^{60}Co) installations at doses of 10 kGy at dose rate varied from 0.0083 up to 1.35 Gy/sec.

The OCPs stability was estimated basing on their degradation under irradiation (P, %):

$$P = 100\% - \frac{C_{after}}{C_{before}} 100\%, \qquad (1)$$

where P – degradation degree, %, determined by liquid gas chromatography as ratio of their concentration before and after irradiation; C_{after} – concentration of pesticide after irradiation, μg/ml; C_{before} – concentration of pesticide before irradiation, μg/ml.

Data on the effect of irradiation dose rate on the stability of various organochlorine pesticides are presented in table 1.

Table 1. The degradation degree of OCP in hexane depending on dose rate of gamma-radiation

Pesticide	Dose rate, Gy/sec					
	0.0083	0.15	0.23	0.43	0.70	1.35
	C_{before} = *1* μg/ml					
alpha-HCH	6.91	-	-	14.72	13.97	12.94
gamma-HCH	21.80	-	-	32.52	27.32	23.10
DDE	15.83	29.67	38.66	42.39	23.76	23.00
	C_{before} = *0.1* μg/ml					
alpha-HCH	10.12	36.57	-	57.53	37.56	35.01
gamma-HCH	10.72	-	-	47.64	38.96	36.50
DDE	31.32	72.23	79.51	52.18	35.82	33.21

The data presented in table 1 indicate that the dependence of the OSPs degradation degree has complex nature within the studied range of dose rates. Table 1 shows that the OSPs degradation degree increases with dose rate, reaches its maximum (at about 0.23–0.43 Gy/sec), and then decreases. This dependence is best revealed on the example of DDE solutions, where the values of its degradation degree are obtained in full range of dose rates.

It is found that the shape of the degradation degree relatioship on dose rate is similar for different OCP in polar and non-polar solvents (hexane, 2-propanol) and does not depends on the concentration of initial substance.

SEGMENTATION TOOL FOR *IN VIVO* 2D PROTON MAGNETIC RESONANCE SPECTROSCOPY OF HUMAN BRAIN

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Localized proton magnetic resonance spectroscopy (^{1}H MRS) is a unique non-invasive method for quantification of metabolic concentrations in all human tissues and organs. In contrast to the traditional NMR experiment, MRS uses medical magnetic fields (lower than 7Tesla) and large field of views (MR spectra are acquired using MRI scanners). Using such little fields decreases SNR, thereby increasing time of study or volume of interest (VOI) size. MRS is classified into 2 types: single voxel (spectra are acquired from one VOI) and 2D MRS (spectra are acquired from several voxels in one VOI). Average voxel volumes are 3000 and 1000 ml in the case of single voxel and 2D spectroscopy respectively. Such big volume include different tissue contaminants of brain – grey (GM) and white (WM) matter as well as cerebrospinal fluid (CSF). Due to the differences in H_2O and metabolic concentrations as well as different T_2 and T_1 relaxations times. Therefore, main objective of this study was creation robust method for quantification GM, WM and CSF contamination in voxels in case of 2D spectroscopy.

First solved task was writing MATLAB tool for creation of binary masks of chosen voxels in VOI (binary mask – image where pixels which belongs to voxel =1, other pixels =0). 3D T1 images and geometry information of spectra were used as input data. Correctness of the program was tested using experimental phantom spectra (FOV-200×200mm; voxels size 40×40×30mm) and images (3DT1 sagittal, TR/TE: 8.1ms/3.7ms, flipangle 8°, 179 slices) Binary mask completely coincides with voxel geometry (fig.1).

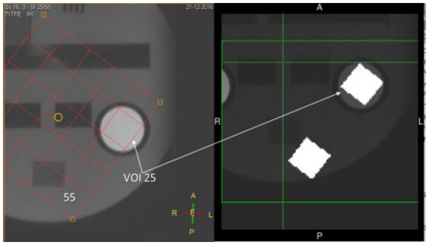

Figure 1. Comparison of binary mask and initial voxel geometry

FSL routine can segment T1 images into three contaminants – GM, WM, CSF using FAST algorithm. Resulted segmented images are presented on the fig.2.

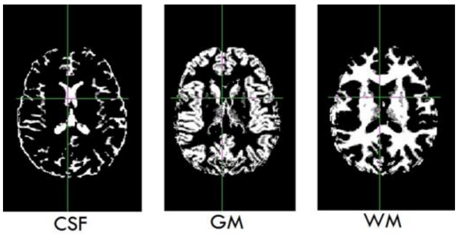

Figure 2. Segmented images.

The last step is to quantify contaminant using *$fslstats* function in the FSL routine with created mask.

This study for the first time revealed robust method for tissue segmentation spectroscopic in the voxel. Quantified GM, WM, CSF percentages can now be used for correction factors in the calculation of metabolic concentrations (1).

$$[M] = \frac{S_{met} \times (f_{GM} \cdot R_{H2O\_GM} + f_{WM} \cdot R_{H2O\_WM} + f_{CSF} \cdot R_{H2O\_CSF})}{S_{H_2O}(1 - f_{CSF}) \cdot R_M} \times \frac{\#H_{H_2O}}{\#H_{met}}[H_2O]$$

Calculated in this way concentrations do not introduce errors, associated with different tissue contamination of voxel, in the statistical analysis.

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NEUROTRANSMISSION DISTURBANCES IN THE BRAIN AFTER ACUTE PEDIATRIC MTBI

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Mild Traumatic Brain Injury (mTBI) or concussion heads the list of different types of TBI in amount of cases. The highest-risked group are children. Typically, there are not any MRI and CT-visible anatomical structure abnormalities of brain with concussion, but mTBI can result in a number of physical, cognitive and emotional disruptions1. These symptoms may be associated with disturbances of excitatory and inhibitory neurotransmission processes in central nervous system (CNS). Localized proton magnetic resonance spectroscopy (^{1}H MRS) is a unique non-invasive method for quantification of metabolic concentrations in all human tissues and organs. Extension of MRS with edited MEGA-PRESS pulse sequence [1] can estimate in vivo concentrations of major neurotransmitters: inhibitory-gamma-Aminobutyric acid (GABA) and excitatory-glutamic acid (Glu). Thus, the main aim of this work was to estimate changes in *in vivo* cerebral GABA and Glu concentrations after acute mTBI using ^{1}H MRS.

Two groups of participants were included in the study: patients group consisted of 11 children hospitalized in the Clinical and Research Institute of emergency Pediatric Surgery and Trauma, Moscow (5 males, 6 females, mean age - 16±2 years, mean time between trauma and MRI examination 40±20 hours, Glasgow Coma Score (GCS) - 15) with acute phase of mTBI; group of healthy volunteers consisted of 8 children (2 males, 3females, mean age - 16±1 years) without history of any TBIs and other cerebral pathologies. All investigations were performed on scanner Phillips 3.0T Achieva TX. GABA (TE/TR=80ms/1900ms, NSA – 8, 12ms editing pulses applied at 1.9 ppm and 1.5 ppm , 42 averages.)

edited spectra were obtained using MEGA-PRESS sequence. REST slabs was used for suppressing unwanted water signal from ventricles. Corresponding PRESS spectra with the same parameters (TE/TR=80ms/1900ms, NSA – 64) were also performed for obtaining NAA, Cr, Cho and unsuppressed water signal intensities. All Voxels in size of 25×25×30mm were located in the frontal lobe. (fig.1.). Participants and their parents signed an informed consent.

The main effect on the [GABA] was found (Z=2.03, $p<0.05$), with the patients having higher [GABA] as compared to the control group (36%) (Fig. 2). Absolute concentrations of NAA+NAAG, tCho, tCr and glutamate were unchanged.

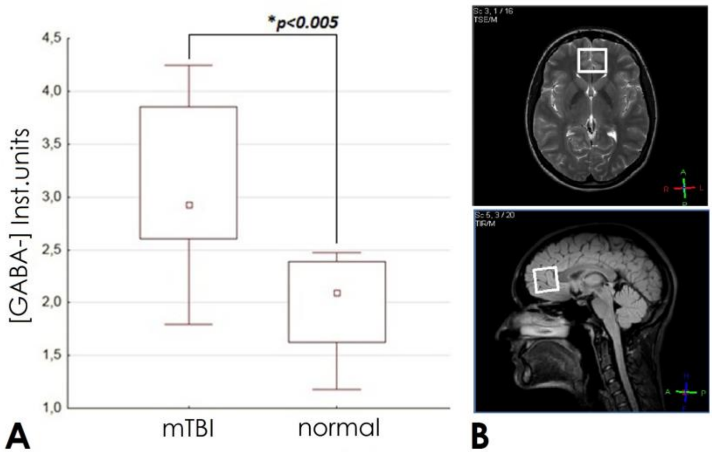

Figure 1. (A) Significant GABA increase after acute mTBI (B) VOI placement

This study for the first time revealed increased cerebral [GABA] as well as disorders in the [GABA]/[GLX] balance in the pediatric acute mTBI. The most likely cause of [GABA] increase is growth of free pool of GABA (non-related to GABA receptors). Postconcussion changes of neurotransmitter revealed in the present study could be promising for understanding of functional consequences of MRI negative TBI

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EQUIPMENT FOR RADIOPHARMACEUTICALSQUALITY CONTROL

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In accordance with the State Pharmacopoeia quality control of the radiopharmaceutical should be madefor the specific activity and radio-chemical purity. Activitymeasurements should be made in accordance with the requirements of the 102-FZ Federal Law «About the assurance of uniformity of measurements» and the Ministry of Healthcare Order N81n “About approval of the list of measurements in the field of the State assurance of uniformity of measurements for healthcare and their mandatory metrological requirements including accuracy parameters”. Therefore, in particular, activity measurementsof radiopharmaceuticals must be traceable to the State Primary Standard of Radionuclides Activity. It means that the relation between of the measurement device and the Primary Activity National Standard should be established. Routine activity measurements are made with the well-type ionization chamber radiometers (Dose Calibrators) and volume measurements – with dispensers and syringes. In the report it is demonstrated that traceability by direct or indirect methods for each radionuclide of the radiopharmaceutical used in hospitals should be provided. It was made for RIS-A Dose Calibrator. Indirect calibration based on radiopharmaceutical aliquot comparison with reference 1st category standard point OSGI-type radionuclide source. Direct calibration based on comparisons of the reference Dose Calibrators with the State Primary Standard of Radionuclides Activity. In the report it is also shown that uncertainty of direct and indirect calibrations are comparable. The problem of high activity measurements up to 10 Ci and even 200Ci should be solved for radiopharmaceutical manufacturing (for example, manufacturing of Tc-99m generators or F-18 PET network). Obvious traceability methods (calibration) cannot be used because the operation with high activity radiopharmaceutical samples is impossible out of the hot cell. In this case traceability can be assured by a decay curve analysis for radiopharmaceutical radionuclides or by sequential measurements of radiopharmaceutical aliquots with reference to standard Dose Calibrator. However the limitation of measurements accuracy for activitiesabove 100 Ci is caused by the destruction of ionized gas equilibrium in sensitive volume of the Dose Calibrator. Methods of the measurements under suchnon-equilibrium conditions are also discussed in the report.

Radiochemical purity is the ratio between the radionuclide activity inthe specific chemical formand its totalactivity in the radiopharmaceutical. The strong criteria for Radiochemical purity of the modern radiopharmaceuticals (95 - 99 %) define requirements for the measuring techniques. In particular, accuracy of the measurements should be higher than "traceability accuracy". In the report the theoretical model of the radiochemical purity determination by thin-layerchromatography and its implementation to the special radiometer GammaScan-01A are established.

POTENTIAL OF ANTIFUNGAL DRUGS AS PHOTOSENSITIZERS

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In the present work, using commercially available formulation of polyene antifungal antibiotic amphotericin B, it is shown that its antifungal activity could be enhanced in combination with light corresponding to the absorption band of amphotericin B due to photodynamic effect.

We have studied the effectiveness of usage of aforementioned drug as photosensitizer in molecular (glycolytic enzyme - lactate dehydrogenase - LDH), cellular (BGM cells from African green monkey kidney) and animal models (in a model of the contact dermatitis on depilated areas of the skin of rats).

It is shown that the exposure of amphotericin B-LDH solutions to optical radiation with λ = 405 nm causes irreversible damage of LDH which is accompanied alteration (decrease) of its enzymatic activity (Table 1).

Table 1. Enzymatic activity of LDH upon exposure to laser radiation with λ = 405 nm (70 mW/cm^2) in the presence of amphotericin B

Irradiation time, min	Without additives	10^{-2} M NaN_3	4´10^{-5} M NAD^+	10^{-4} M L-cystine	D_2O
0	100%	100%	100%	100 %	100%
5	55%	97%	70%	89%	98%

Apparently, the radical processes rather than reactions involving singlet oxygen are dominant in the mechanism of photodynamic damage of enzyme. The confirmation of that is a sharp decrease in photoinactivation effect when adding the donors/acceptors of electrons to mixture being irradiated. Besides, upon changing the aqueous solutions to D_2O (where lifetime of singlet oxygen is one magnitude higher than in H_2O) we have not revealed a sharp increase in photobiological action. In this respect the observed decrease in the effect of LDH photoinactivation sensitized by amphotericin upon irradiation of solutions in the presence of sodium azide (NaN_3) can be also explained by quenching of excited states of antibitotic by sodium azide.

Photodynamic activity of amphotericin B has been also demonstrated in BGM cells from African green monkey kidney using MTT assay. The results obtained show that exposure of the cells preincubated with photosensitizer to optical radiation corresponding to the absorption band of amphotericin B leads to decrease in cellular survival.

The ability of optical radiation (λ = 405 nm, fluence rate – 100 mW/cm^2) corresponding to the absorption band of amphotericin B to enhance its fungicidal action is demonstrated in a model of the contact dermatitis on depilated areas of the skin of rats (Figure 1).

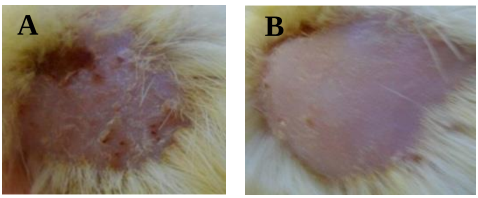

Fig.1. Area of skin inflammation of experimental model of dermatitis before (A) and after (B) photodynamic therapy with amphotericin B as photosensitizer.

Thus, we demonstrate that amphotericin B can be used as potent photosensitizer and its fungicidal action can be enhanced in combination with optical radiation corresponding to the absorption band of drug.

BIOCOMPATIBILITY OF NANOPARTICLES BASED ON SILICON AND GOLD FOR NERVOUS CELLS

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Solid state nanoparticles (NPs), which are able to penetrate deeply into tissues, cells and nuclei, are prospective for applications in biomedicine, particular in theranostics (simultaneous therapy and diagnostics) [1]. However, recent studies reveled that some type of NPs are able to provide cytotoxic effects to the human organism, especially to the nervous system [2]. Therefore, it is important to evaluate biosafety of the emerging NPs for brain cells and tissues. Development of new non-toxic NPs will open new possibilities in molecular neuro diagnostics and therapy. In this regard, the aim of our investigation was to study the biocompatibility of NPs based on silicon (Si) and gold (Au) and with primary cells of the nervous system.

Dissociated hippocampal cells were taken from C57BL/6 mice embryos (E18) and cultured on coverslips during 14 days *in vitro* (DIV) according to the previously developed protocol [3]. NPs of Si and Au were provided by femtosecond laser ablation the corresponding solid targets of high purity in deionized water [4]. The initial concentration of NPs was about 0.1 mg/mL. 1%, 5% and 7% of cultural medium were replaced by NPs solution on 14 DIV. For viability determination of primary hippocampal cultures on the 7th day after treatment, we estimated the ratio of the number of dead cells stained by propidium iodide (Sigma, P4170, Germany) and the total number of cells stained by bisbenzimide (Invitrogen, H3570, USA). The metabolic activity of primary hippocampal cells was studied by using MTT-test.

Substitution of the cultural medium by 7% suspensions of Si and Au NPs gave numbers of the dead cells about 30±5%. This fact indicates cytotoxicity of such NPs concentration. On the one hand, 5% replacement of the cultural medium to the corresponding volume of NP suspensions did not induce significant metabolic changes in the primary hippocampal cultures. On the other hand, this concentration of NPs was not optimal, since its application led to marked morphological changes of the primary culture, manifested as an increase in the number of dead cells (20±7% for Au NPs and 23±7% for Si ones). Replacing of the cultural medium with 1% solutions of both types of NPs did not result in morphological and metabolic changes in the cells, and it holds promise for application as a working NP concentration in further studies.

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NEPHELOMETRIC METHOD FOR DETERMINATION OF GROWTH PARAMETERS OF CHLORELLA CULTURE

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Cultivation of microalgae is of great interest all over the world. In this connection use of nephelometric method, which is fairly accurate and simple in performing measurements of optical density, is especially relevant. Aim of research – to evaluate the possibility of using a nephelometric method for determining the growth parameters of chlorella strains in suspension culture. Nephelometric method for determination of growth parameters of chlorella culture using a photoelectric colorimeter was described. Use of photoelectric colorimeter for cell counting in suspension requires periodic calibration of meter readings using chlorella standard culture (with a certain cell concentration). *Chlorella vulgaris* IPPAS C-66, IPPAS C-111 and IPPAS C-2019 strains served as object of research. Cultivation was carried out during 12 days on a Hoagland medium. Sample selection for analysis and measurement was carried out daily, three times per day. Based on the obtained data, readings of photoelectric colorimeter KFK-3.01 were calibrated via direct count of chlorella cells quantity in Goryaev's chamber. Use of calibration curve made it possible to reduce significantly time and error in determination of cell number in suspension cultures. The proposed technique can be used for comparative determination of the growth parameters of strains in vitro, standardization of suspension cultures, semiquantitative determination of chlorella biomass in order to predict the yield of desired product.

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CARBON FRICTION PAIR IN TOTAL HIP REPLACEMENT

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With the increase in the number of revision hip joint replacements is increasing and the number of postoperative complications [1]. The most common reason for revision replacement is a developing bone loss around the implant, which is a cause of aseptic instability [2].

In a healthy joint, the friction coefficient is 0,01 — 0,06. When using modern materials, which include metal, ceramics, polyethylene, to achieve such performance is not possible.

To solve the problem of aseptic instability we have proposed material isotropic pyrolytic carbon (pyrocarbon), the tribological properties of which are closest to the healthy hip joint of the person superior to modern materials used in friction pairs of hip joint replacement.

The purpose of the work

Experimental substantiation of the possibility of using isotropic pyrolytic carbon (pyrocarbon) in endoprostheses of the hip joint and its advantages in comparison with other pairs of friction.

Materials and methods

To determine the margin of safety node mobility of pyrolytic carbon. used mathematical modeling, which was conducted by the finite element method in the medium "ANSYS 5.7". The calculation was performed under the condition that the application angle of 45^{o}, under a load of 2500 N.

A study of the torque was carried out on the installation ElectroPuls E10000, designed for testing mechanical and tribological properties of components of the hip implant and was conducted in accordance with GOST R 52640-2006. The rotation speed of the bowl was 0.5 Rev/s, the axial load of 2250 N. Recording the torque produced for 600 s, during which the bowl was made of 300 full turns. The load and displacement components of a friction pair is consistent with GOST R ISO 14242-1-2012.

A comparative study was carried out of the volumetric wear of a friction pair from pyrolytic carbon and a ceramic friction couple on the device ECRB.942623.110-07.00 intended for testing the friction pair of a hip joint endoprosthesis for volume wear.

Results

According to the findings of mathematical modeling, the maximum voltage that occurs under load, does not exceed the ultimate strength of the material and was 450 MPa.

The study of torque, this ratio was 1.1 Nm, on the surface of samples out free products wear, the coefficient of restitution of joint mobility was 134%, which meets the requirements of GOST R 52640-2006.

The data obtained volumetric wear of the friction couple made up of ceramic 0,00085 mm/year, a pair of friction of the pyrolytic carbon. 0,00058 mm/year, which is 31.8% less than in a friction pair made of ceramics.

Conclusions:

1. The ultimate strength of the material equal to 450 MPa, which is greater than the possible load on the friction in the joint.
2. Torque was 1.1 Nm, which is 26.6% below the maximum permissible figure.
3. A pair of friction of the deposited pyrocarbon has less volumetric wear than a pair of friction of ceramics by 31.8%.

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TECHOLOGY OF CREATION AND DETAILED ANALYSIS OF POLYMER COMPOSITE WITH UNIFORM DISTRIBUTION OF QUANTUM DOTS AND LIQUID CRYSTALS

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The most actual biotechnology task for today is construction of new generation of nanobiosensors with improved brightness, photostability and high level of localization. Composites of polymers and colloidal quantum dots (QDs) are the most promising base for such sensors. [1]

QDs provide the high level of photostability, narrow and intense fluorescence band that varies from infrared to ultraviolet region and a wide range of absorption that allows to excite different types of QDs by same laser. [2] The large market of commercially available polymers, in it`s turn, allows to construct composites sensitive to a wide range of physicochemical factors. The composite from CdTe QDs and molecularly imrinted polymer sensitive to cytochrome c [3] is the good example of use of such type of composites for biosensoric technologies. The main problem of such structures is the extremly low concentration of uniformly distributed QDs into that [4].

This work contains the technology of creation and detailed analysis by methods of optical microscopy, AFM, SPM and confocal fluorescence microspectroscopy of nanostructured composite films based on polypropylene matrices with uniformly distributed CdSe/ZnS QDs and liquid crystals. The presence of liquid crystals in the composite makes it possible to carry out additional control of QDs` fluorescence, which was shown earlier in the work of this research group [5-7].

The suggested methodology is applicable not only to polypropylene, but also to other porous polymers. The results of this work are an indicator of the fundamental possibility of creating high-quality polymer/QDs composite materials and demonstrate the possibility of qualitative integration of an additional fluorescence regulating factor-liquid crystals.

This study was supported by the Ministry of Education RF, project no. 14.616.21.0042 (project unique identifier, RFMEFI61615X0042). The study was carried out with use of unique scientific setup "System for probe-optical 3D correlative microscopy" IBCh RAS (http://ckp-rf.ru/usu/486825/).

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DESIGN OF RATIOMETRIC POLYMER NANOBIOTHERMOMETER BASED ON QUANTUM DOTS

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Advances of nanotechnology allow creating more and more powerful tools for processes in cells and tissues monitoring. Development of nanosensors based on nanoparticles is able to provide quantitative data on the physico-chemical parameters distribution such as pH, temperature, ion concentration etc.[1].

The relevant task for today is the development of the nanothermometer operating in the range of physiological temperatures for providing the high local control over the various exo- and endothermic reactions, such as trypsin digestion of bovine serum albumin or to provide control over the local temperatures of the heated cells during the procedure of hyperthermia in cancer patients.

In this study we suggest an original nanosensor`s architecture containing a polymer core and a lamellar structure around. At least two layers contain fluorophores of different colors separated from each other with silane layer, and the outer layer is formed from a so-called "smart" polymer, capable of changing its properties when environmental conditions change. It is known the "smart" polymers, capable of selectively responding to certain parameters of the environment [2]. As fluorophores, we used here the quantum dots (QDs), which are demonstrated the most stability and brightness [3].

The operation of nanosensor is based on the compression by "smart" polymer of all composite structure when the controlled parameter changes. Due to the compression, the separated layers containing QD approach each other, which induce a resonance transfer of energy between QDs of different colors. The degree of resonance transfer, in turn, determines the ratio of the emission peaks of the two types of QDs relative to each other, which is a parameter for measure the temperature.

The proposed principle was realized on the example of a thermosensitive polymer poly-N-vinylcaprolactam with temperature sensitivity range (20-50)°C. We have shown that for maximum nanosensor sensitivity, longer-wave (Red) QDs should be located on the inner layer of the nanosensor. To prevent QDs migration between layers and penetration them into the core, QDs containing layers must be isolated by layers of tetraethoxysilane.

The results obtained in this work indicate the fundamental possibility of constructing multicoded ratiometric nanobiosystems based on colloidal quantum dots. The proposed architecture of ratiometric nanosensor is universal and can be extended to measure other parameters in local nano-areas. In particular, microstructures based on "smart" polymers with included QDs are described in [4]. Fluorescence of such nanocomposite materials is responsed on the variation of environmental factors: pH, concentration of copper ions. Nanocomposites can be used for ratiometric nanosensors.

This study was supported by the Ministry of Education RF, project no. 14.616.21.0042 (project unique identifier, RFMEFI61615X0042). The study was carried out with use of unique scientific setup "System for probe-optical 3D correlative microscopy" IBCh RAS (http://ckp-rf.ru/usu/486825/).

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MODERNIZATION OF IRT-T RESEARCH REACTOR FOR BNCT APPLICATIONS

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At the present time a significant step towards implementation of Boron Neutron Capture Therapy (BNCT) as a clinical modality is extending BNCT application to various types of cancer. Therefore, the development of new boron compounds synthesis, delivery, and evaluation is one of the most important issues that should be resolved. Conducting experimental "in vivo" and "in vitro" trials on biological samples is an important step for developing new boron compounds. For this purpose, a new irradiation facility for BNCT applications was developed at the horizontal experimental channel HEC-1 of IRT-T research reactor.

IRT-T Research Reactor is a 6 MW pool-type reactor using IRT-3M fuel assemblies. IRT-T reactor has 10 horizontal experimental channels, a beryllium thermal column, and 14 vertical irradiation channels in the reflector. In order to create an experimental irradiation facility for preclinical NCT studies the reconstruction of the horizontal experimental channel HEC-1 is in progress. At the initial phase of facility modernization, the preliminary design of sample irradiation facility is the prime objective to ensure that the designed beam line meets IAEA requirements for neutron beam "in air" parameters. Sample irradiation facility includes a sample positioning system, temperature regulation system and beam forming system, which are placed into an aluminum tube delivered by the conveyor into/out of the reactor. The beam forming assembly consists of a set of moderator/filter disks, used for providing the proper neutron spectra and a reflector installed in the channel before the sample irradiation point. The MCU-PTR code was chosen for the purpose of IRT-T reactor simulation and design calculations. The detailed geometrical model of the IRT-T reactor [1] was developed using MCU-PTR code, including fuel assemblies, reflector blocks, control rods, main structural components, horizontal beam tubes and vertical irradiation channels. Each fuel assembly was modeled independently. All calculations were performed for the "fresh" load of the reactor.

At the first step of the modernization project, the neutron spectra in two possible beam lines (HEC-1, tangential to the core, and HEC-10, radial to the core) applicable for sample irradiation have been calculated. Due to the low contamination of fast neutrons, the HEC-1 was selected for irradiation facility installation. To improve performance of the HEC-1 beam line and to obtain the characteristics, suitable for BNCT, the position, material composition and thickness of the beam forming assembly components (neutron scatter, neutron moderator/filter and gamma filter) were optimized. In all tested cases three-group neutron fluxes, gamma dose and fast neutron dose per one thermal neutron were calculated. Several core configurations were investigated [2], the effect of replacing part of the beryllium reflector blocks adjacent to the HEC-1 with lead, aluminum and fuel assembly (FA) on the neutron flux was studied.

The design stage of the project on preclinical BNCT studies at IRT-T research reactor was finished. The developed irradiation facility obtains the thermal flux of $\sim 10^{10}$ n cm^{2} s^{-1}, which allows to complete irradiation in a short time. Both fast neutron and gamma contamination are maintained below IAEA recommended limits.

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DEVELOPMENT OF AQUATIC BIOASSAY WITH LEMNA MINOR AND SPIRODELA POLYRRHIZA FOR SCREENING AND INTERPRETATIVE RISK ASSESSMENT OF WATERS CONTAMINATED WITH TRITIUM

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Introduction. Tritium (H-3) is the unique radionuclide widely evidenced in the biosphere constituents, atmosphere, water reservoirs and soil, in particular. Being actively introduced into living organisms, it can violate the structure of biologically important molecules in cells not only via internal beta-radiation but also as a result of H-3 transmutation into He-3. It induces disruptions in DNA chemical bindings and the following cell death and violations in the organism activity [1]. Such discovered disturbances allowed the ISO specialists in 2005 and Russian hygienists in 2010 to develop a bioassay with Lemina minor for recording harmful compounds in the chemical production wastewater [2]. Since H-3 is a chemical agent as well as a radiator, it was decided to use Lemna minor as the bioassay for detecting natural and technical water contaminated with tritium as a part of tritium oxide (HTO) and organically bounded tritium (OBT) [1].

Aim. The research is aimed at studying the morphometric features of Lemna minor and (for comparison) the allied species Spirodela polyrrhiza to develop the radiation (or combined chemical and radiation) bioassay for screening surface and groundwater contaminated with tritium compounds. In future the data will allow to interpret the results of ecological and health risk assessment when drinking water with small amounts of tritium.

Materials and methods. The suggested method of bioassay is based on the route chart of risk assessment for chemical substances (all at once radiators) developed by Momot O.A [3]. The specific activity of tritium in water after special sample preparation was determined by a scintillation spectrometer Quantulus-1220 with internal standards and reference water samples. Morphological indices of algae and polyrrhiza were estimated by a special camera microscope; the statistical data processing has been realized with the information space R software. 100 algae and polyrrhiza plants were used for any sampling site. Distribution functions were plotted from the corresponding parameter values, for which estimated were the indices corresponding to median values, the first and the third quartiles of the distribution function.

Results and conclusions. It is found that the specific activity of tritium in different Protva river oxbow areas separated by lintels changes from 550 up to 3600 Bq/l; on 6 July 2017 in the nearest Protva river oxbow area the specific activity was 21 Bq/l; the average activity in the rivers of Russia was 4 Bq/l and according to the Russian standard HRS/2009 the intervention level was 7600 Bq/l.

Spirodela polyrrhiza plants do not respond to tritium radioactivity in the revealed concentrations and this gives evidence of its relatively high radio resistance. On the contrary, according to the indices, algae plants reveal stimulation in their growth and development at high values of tritium radioactivity.

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PERSONAL FLUORESCENT TEST STRIP READER FOR IMMUNOCHROMATOGRAPHIC DIAGNOSTICS WITH USING QUANTUM DOTS AS LABELS

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Rapid development of the instrument-making technical base for receiving and processing data stimulates the process of modernization of scientific and technical methods, as well as the creation of new software and hardware systems for solving applied problems in almost all fields of science. The emergence of medical diagnostic systems using express methods of immunochemical analysis (ICA), in the form of programs and plug-in hardware modules based on modern personal devices, was not an exception.

Modernization and personalization of devices provides immersion in the modern universal wide-spread (mass) technical solution of the part of the upgraded single queuing device, which are possibly unavailable earlier due to technical and economic limitations of standalone devices. Also, the modernization process contains design, the main target of which is to simplify and miniaturize unique nodes that are not available in the base hardware platform, in the form of plug-ins parts. Personalization leads to a significant simplification and often to the elimination in the design of personal devices of elements of mass service of laboratory instruments, and a natural replacement of these elements on distributed processing and protection of personal data. Note that some elements of the technology can also be provided with special requirements for operating conditions with special user guides.

Thus, taking as a basis, an innovative laboratory robotic complex [1], which is a specialized queuing system, and choosing the technical platform for personalization, a modern smartphone with an operating system which is open for software development, and has an ergonomic user interface, advanced optical means, illumination means, etc., we can present the option of creating a software-hardware, personal, affordable for mass consumer solution for the application of the quantitative express method of ICA for the early diagnosis of dangerous infections [2].

Describing the physical processes implemented by the laboratory installation, we define the main parameters that ensure the quality of the analysis that must be preserved or improved in the device being designed:

1. The thermostating of test strips ensures the presence of immunochromatographic biosensors in the operating temperature range;
2. The initial light (including excitation light and background light) is characterized by the light spectrum, power consumption, illumination of the surface area of the test strip with marks;
3. Fluorescence of quantum dots - the spectrum and intensity of fluorescence;
4. Optics of image focusing - light transmittance;
5. Band-pass filter - transmission spectrum;
6. Photodiode array - the physical size of the matrix, the number of photodiodes, the spectral sensitivity of the matrix;
7. Analog-to-digital converter - transfer function of ADC, conversion speed, bit depth.

Proceeding from the comparative analysis of the elements of the laboratory instrument and the base platform, the part of the device that must be designed and implemented as a plug-in module is determined.

The approach described above allowed to create a personal device for diagnosing dangerous infections that meets the basic requirements of the technology of analysis and measurement accuracy.

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PEGYLATION MODULATES THE SPECTRUM OF SECONDARY ELECTRONS UPON IRRADIATION OF GOLD NANOPARTICLES: A MONTE-CARLO CALCULATION

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Gold nanoparticles (GNP) are the candidates for sensitization in antitumor radiation therapy due to their interactions with X- and γ-rays. GNP absorb the energy of ionizing radiation and generate secondary particles such as photo-, Compton and ionizing electrons. These particles distribute their energy in different areas depending on LET. The low energy, short-range ionizing electrons (Auger, Coster-Kronig and fluorescent ones) deposit very high energies in the close proximity to the GNP surface. The GNP surface can be modified by different ligands, e.g., polyethylene glycol (PEG), for targeted delivery and prevention of aggregation in the blood. The impact of the PEG shell on the spectrum of secondary radiation initiated within GNP must be taken into account since this parameter may influence the therapeutic efficacy of the radiosensitizer.

We performed a Monte-Carlo simulation (a Geant4 algorithm) to reveal the influence of ionizing radiation on low energy secondary electrons. A 17 nm GNP was modified with the PEG shell (thickness 8.5 nm; M_{PEG}=5000 g/mol). GNPs were virtually irradiated by a circle photon beam (D=60 nm) using a ^{60}Co source (1.17 MeV and 1.33 MeV) (Figure 1). The amounts of secondary electrons that left the gold core and the PEG shell were recorded and analyzed.

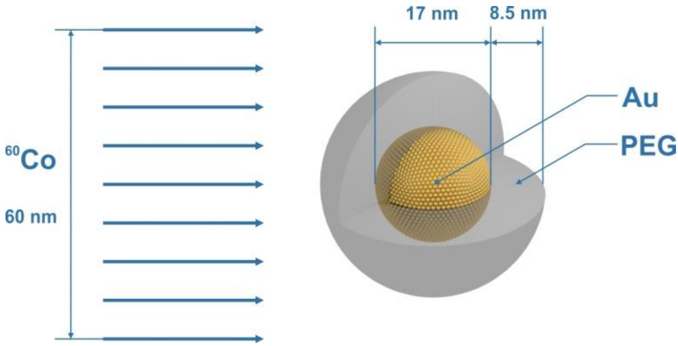

Figure 1. Scheme of Monte-Carlo simulations.

We found that the PEG shell is critical for spectral characteristics of low-energy ionization electrons and Compton electrons (Table 1).

Table 1. Energy spectra of secondary particles.

Secondary electrons	Quitting electrons	Quantity	Total energy, MeV
Ionization	Gold core	1812 ±42	0.263±0.013
	PEG shell	883±30	0.170±0.015
Compton	Gold core	10275±101	4205±56
	PEG shell	13092±114	6020±68

Conclusions:

1. Even though PEG consists of light chemical elements, the shell forms an additional barrier for low energy electrons. To initiate water radiolysis, a key event in tumor cell death by radiation, electrons have to leave not only the gold core but also the PEG shell. About one half of generated in the gold core low-energy ionizing electrons was absorbed by the PEG shell. These electrons lost ~35% of their total energy.

2. However, more Compton electrons (1.27-fold) were generated within the shell due to predominant Compton scattering in the interaction of primary photons with the PEG shell.

3. No changes were revealed for photoelectrons and secondary photons.

A COMPREHENSIVE ASSESSMENT OF TUMOR RESPONSE IN PATIENTS WITH GASTRIC CANCER

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The gastric cancer (GC) is one of the most common malignant neoplasms today. In 2012, approximately 952,000 new cases of GC were detected, which is 6.8% of all diagnosed malignant tumors [1]. It is not just the high prevalence of this pathology, but also the associated mortality.

In order to improve both immediate and long-term results of the treatment, the neoadjuvant radiotherapy and/or chemotherapy are being increasingly used lately. To study its effectiveness, as well as to select the extent of the subsequent intervention and control of the course of the disease, it is necessary to study the patterns of tumor response to the therapy and the development of universal and nonspecific criteria for evaluation of the therapeutic pathomorphosis.

In the diagnosis of the tumor response of the GC the widespread methods are the contrast radiography, EUS, EGD and CT. However, the informativeness of these methods in assessing the therapeutic pathomorphism of tumors raises doubts. By some accounts, these methods are not enough for the correct assessment of the tumor response. Despite the improvement of imaging methods, many authors note that histological examination is the most demonstrative and accurate method, while other methods tend to overestimate or underestimate the results of neoadjuvant therapy. It allows to evaluate the scope and nature of changes in tumor tissue even in the absence of a noticeable clinical effect. According to the observed changes in the histological pattern, one can judge the degree of the tumor response. Most classifications are based on evaluation of necrosis and fibrosis spread and and the measurement of the proportion of the residual viable part of the tumor. The prognosis heavily depends on the size of the residual viable tumor tissue.

Evaluation of therapeutic pathomorphosis is a highly important stage in the management of patients with GS. It allows to estimate the effectiveness of neoadjuvant therapy, to predict the further course of the disease, to confirm the need for surgical intervention. Currently, the most indicant method in the analysis of the tumor response of the GC is the CT examination, which allows to estimate the change in the volumetric dimensions of the tumor and lymph node, as well as its structure. However, the data obtained with CT and other instrumental methods, especially the detection of a complete tumor response, require histological confirmation. Therefore the development of a system of complex clinical and histological evaluation of pathomorphism of the GC is required.

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IMMUNOHISTOCHEMICAL MARKERS IN THE ASSESSMENT OF TUMOR RESPONSE

Mozerov S.A. [1], **Komin Yu.A.** [2], **Yuzhakov V.V.** [1], **Pashkin S.B.**[3], **Larkin A.A.**[4], **Mozerova E.S.**[1]

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According to a WHO report in 2014, the oncological diseases are one of the leading causes of death worldwide. In 2012, about 14 million new cases of cancer and about 8.2 million deaths from malignant neoplasms were detected [1].

Today, treatment of a malignant tumor often involves neoadjuvant radiotherapy and/or chemotherapy. The tactics of managing the patient and the prognosis of the course of the disease after neoadjuvant therapy largely depends on the degree of therapeutic pathomorphism of the tumor-the tumor response. With an incomplete (partial) response of the tumor to treatment, the choice of further tactics becomes ambiguous. This circumstance dictates the need to search for new methods for studying therapeutic pathomorphosis, in particular, to the study of the possibility of using IHC for it. It is expected that a change in the content of different markers in resected tissues after treatment may allow more accurate assessment of the degree of pathomorphosis and determine the prognosis, as well as adjust the patient management tactics.

The use of an immunohistochemical method of staining the slices to evaluate the pathomorphism of neoplasia after neoadjuvant therapy primarily concerns the proteins of cell proliferation (Кi-67, PCNA, EGFR, CyclinD1, COX-2, $p57^{kip2}$, AURKA, HER2), apoptosis (BAX, bcl-2, p53), cell adhesion (E-cadherin), and also angiogenesis (VEGF).

The high efficacy of antitumor therapy was indicated by a decrease in proliferative activity, which was accompanied by a decrease in expression of Ki-67 and PCNA markers in neoplastic cells [2].

CyclinD1 and E-cadherin are among the least studied markers in the evaluation of pathomorphosis.

One of the main problems of managing patients receiving neoadjuvant therapy for cancer is evaluation of the results of therapy and predicting the course of the disease. There are many classifications and systems for assessing therapeutic pathomorphosis, but none of them takes into account the results of immune staining of tumor tissue. At the same time, contradictory data, which were obtained by different researchers, indicate the possible importance of IHX staining for the evaluation of pathomorphosis. In addition, for this purpose it is necessary to develop a system of complex analysis, including the inclusion of clinical, pathomorphological and molecular-genetic parameters [3].

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SPECIFIC ABSORPTION RATE OF ASSEMBLIES OF MAGNETIC NANOPARTICLES WITH CUBIC AND COMBINED ANISOTROPY

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Superparamagnetic magnetite nanoparticles of various average diameters are used in magnetic hyperthermia [1] for local heating of biological media in an alternating magnetic field. These nanoparticles have cubic or combined type of magnetic anisotropy. In this paper the specific absorption rate (SAR) for assemblies of spherical magnetite nanoparticles with cubic anisotropy is calculated in the range of diameters D = 30-60 nm taking into account both thermal fluctuations of the particle magnetic moments and strong magneto-dipole Interaction [2] in assemblies of fractal-like clusters of nanoparticles.

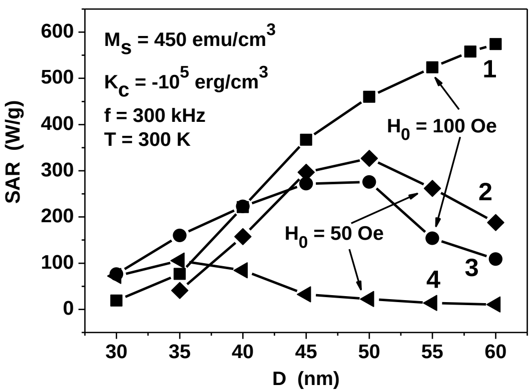

Fig. 1. SAR of assembly of magnetic nanoparticles with cubic anisotropy as a function of particle diameter: 1), 2) – assemblies of non interacting particles, 3), 4) assemblies of fractal clusters with strong magneto-dipole interaction.

As Fig. 1 shows, at a typical frequency of the alternating magnetic field f = 300 kHz and the field amplitudes $H_0 = 50 \pm 100$ Oe SAR of dilute nanoparticle assemblies (curves 1) and 2) in Fig. 1) can reach large values, on the order of 300-500 W/g. However, the presence of strong magnetic dipole interaction in assemblies of fractal clusters of such nanoparticles, which arise in a biological medium loaded with magnetic nanoparticles, leads to a significant decrease in SAR (curves 3), 4) in Fig. 1). For example, at the field amplitude $H_0 = 100$ Oe, in the range of optimal particle diameters, D = 45-55 nm, the SAR of assembly of fractal clusters decreases by 30-40% compared to that of a dilute nanoparticle assembly.

Similar calculations are also carried out for assemblies of spheroidal magnetite nanoparticles with a small semiaxes ratio, a/b = 1.1-1.2, having combined magnetic anisotropy. It is shown that, due to large saturation magnetization of magnetite, $M_s = 450$ emu/cm^3, even a small perturbation of the nanoparticle shape leads to the appearance of the shape anisotropy. This substantially changes the parameters of the low-frequency hysteresis loops, as well as the SAR, of assemblies of magnetite nanoparticles with combined anisotropy .

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FABRICATION OF A MICRO-HOLE ARRAY IN THIN Ag-FILMS AS A CHEMOSENSOR AND BIOSENSOR

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The micro-hole array with diameter ≈ 4 μm and period ≈ 6 μm in a 30 nm thick silver film on a CaF_2 substrate as a chemo- and bio-sensor was produced by femtosecond pulsed laser (Fig. 1a, b). IR unpolarized transmittance of the clean sensor and sensor with a monolayer of R6G and Staphylococcus aureus (SA) bacteria was measured by using a FT-IR spectrometer V-70 (Bruker) [1, 2].

Selective IR absorption at 1261 cm^{-1} enhanced by 455 times, was demonstrated for rhodamine 6G molecules, covering a 2D-photonic crystal (Fig. 1c) [1]. A novel optical platform for surface-enhanced IR absoprtion/reflection spectroscopy, based on a micro-hole array in a supported silver film, was tested, demonstrating 10-fold analytical enhancement of the characteristic absorption bands of SA, while the buried carotenoid fragments, as the fingerprints of such bacteria, were also detected in the IR-spectra (Fig. 1d) [2].

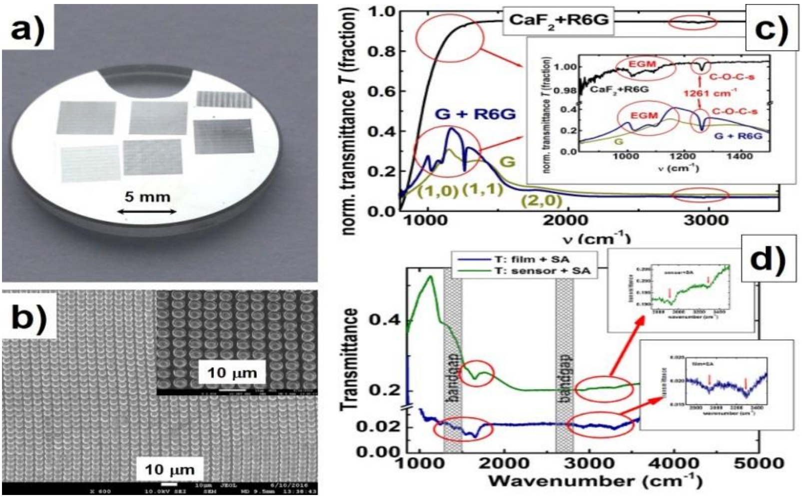

Fig.1. (a) Optical image of the 11-mm wide CaF_2-slab with the top 30-nm thick Ag-film and a number of micro-hole arrays (typical square – 4×4 mm^2). b) Top-view SEM image of the array with diameter D = 4 μm and period P = 6 μm (inset: its magnified view). c) Normalized FT-IR transmission spectra of the array and of the array with the R6G monolayer atop (G+R6G); FT-IR transmission spectrum of the CaF_2 substrate with the R6G monolayer is given for comparison. Inset: the magnified view of their normalized low-ν transmittance with the assignment of the R6G absorption bands on the CaF_2 substrate and the array. d) IR transmission (T) spectra of the film (bottom curve) and the sensor (upper curve) with the SA-layer.

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EFFICIENT ENCODING OF MATRIX MICROPARTICLES WITH NANOCRYSTALS FOR FLUORESCENT POLYELECTROLYTE MICROCAPSULES DEVELOPMENT

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Development of theranostic agents serving simultaneously as therapeutically active agents and imaging tools for early diagnosis of various diseases is an important task in designing the systems for controlled drug delivery [1]. Engineering of polyelectrolyte microcapsules is an efficient approach to combine both functions. Existing technologies of microcapsule fabrication allow biologically active compounds, metal, magnetic or fluorescent semiconductor nanoparticles to be incorporated within or tagged with the capsules [2].

Quantum dots (QDs) are fluorescent semiconductor nanocrystals characterized by a high photostability, wide absorption spectrum, and narrow and symmetrical fluorescence spectrum with position determined by the size of nanoparticle. Owing to the optical characteristics of QDs, a single source of radiation can be used to excite QDs of different fluorescent colors, what makes them promising fluorophores for multiplexed imaging [3].

Here, we are developing technology of encoding of template matrix microparticles with semiconductor nanocrystals with a modified method of alternate layer-by-layer application of oppositely charged polymers and water-soluble QDs onto calcium carbonate microspherolite cores, and apply them further to fabrication of fluorescent polyelectrolyte microcapsules. The CdSe/ZnS core/shell QDs were solubilized with polyethylene glycol derivatives as described earlier [4]. The solubilized QDs were characterized by a narrow size distribution (from 10 to 12 nm) and a negative surface charge (–21.9 ± 0.4 mV), which ensures their efficient adsorption between polyelectrolyte layers during the process of encoding. The efficiency of the encoding was estimated spectrophotometrically. The morphology and size distribution of the microbeads were analyzed by fluorescence microscopy.

The size of developed QD-encoded microbeads has varied within a narrow range, from 3 to 6 μm. Fluorescence microscopy data have demonstrated that the used encoding procedure provides the QD-content in the microbeads sufficient for contrast imaging.

The data show that obtained QD-encoded microbeads are characterized by an optimal dispersity and bright fluorescence thus demonstrating efficiency of developed procedure of microbeads encoding and paves the way to development of fluorescent polyelectrolyte microcapsules on their basis.

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CYTOTOXICITY OF POLYELECTROLYTE MICROCAPSULES ENCODED WITH SEMICONDUCTOR NANOCRYSTALS

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The use of polyelectrolyte microcapsules as a tool for targeted delivery and controlled release of pharmaceuticals, contrast agents and fluorescent probes for *in vitro* and *in vivo* imaging is a promising approach to personalized diagnosis and treatment of various human diseases [1]. Quantum dots (QDs) are fluorescent semiconductor nanocrystals from 2 to 10 nm in diameter characterized by a wide absorption spectrum and a narrow emission spectrum. A high photostability and a bright fluorescence signal make QDs advanced nanophotonic detection and imaging labels [2]. However, the presence of heavy metals in the cores of the best QDs and related potential toxicity make the possibility of QD *in vivo* application a questionable issue.

Here, we evaluate an *in vitro* cytotoxicity of diagnostic agents based on polyelectrolyte microcapsules optically encoded with the semiconductor CdSe/ZnS core/shell QDs. Doing this, home-made calcium carbonate microbeads were used as the matrix cores. The formation of multilayer polyelectrolyte shell on the surface of the carboxylated microparticles and their encoding with CdSe/ZnS QDs were carried out by alternately applying oppositely charged layers of polymers and water-soluble QDs, as it was described earlier [3]. The polyelectrolyte microcapsules were further obtained by removing the calcium carbonate core from the prepared encoded microparticles. The morphology, size distribution and fluorescent properties of microcapsules were analyzed using microscopy analysis. The toxicity of the polyelectrolyte microcapsules was evaluated *in vitro* in the SK-BR-3 human breast carcinoma cells.

Microscopy study has shown that the size of the resultant polyelectrolyte microcapsules ranges between 3 and 6 μm. The microcapsules are spherical hollow structures whose walls are intensely fluorescent due to incorporation of QDs.

Developed polyelectrolyte microcapsules exhibit low *in vitro* toxicity in the cell model used, with more than 75% of the cell viability within 24 h, in a wide range of microcapsule concentrations, from 2 to 2×10^4 capsules per cell.

The data show that the developed polyelectrolyte microcapsules encoded with CdSe/ZnS QDs are characterized by bright fluorescence and low cytotoxicity, what offers an opportunity for development of new diagnostic and theranostic agents and drug delivery systems on their basis.

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GENERATION OF TERAHERTZ PULSED RADIATION WITH PHOTOCONDUCTIVE ANTENNAS BASED OF LOW-TEMPERATURE-GROWN GALLIUM ARSENIDE AND ITS APPLICATIONS

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Terahertz (THz) radiation generally refers to the frequency band spanning 0.1–10 THz, which lies between the microwave and infrared regions of the electromagnetic spectrum. The area of the electromagnetic spectrum of THz radiation with wavelengths of about 0.1 to several millimeters used: new devices are being intensively created to ensure life safety; medical diagnostics; nondestructive technological and operational control. Because of the innocuous action on natural objects and sufficiently high penetrating power.

There is great interest in applying THz spectroscopy to probe and characterize various biomaterials because most low-frequency biomolecular motions, including vibration and rotation of the molecular skeleton, lie in the same frequency range as THz radiation. Therefore, various biomolecules can be effectively recognized and characterized according to their distinctive spectral fingerprints. Additionally, by sensitively probing the fast hydration dynamics around biomolecules whose key large-amplitude motions coincidently occur on the picosecond timescale of THz frequencies, THz spectroscopy has demonstrated unique advantages for detecting the coupling between biomolecules and their hydration shells.

One of the most important applications of THz PCA in medicine is the early detection and diagnosis of diseases. Successful examples are the identification of caries [1], the assessment of the degree of skin burns [2], the control of wound healing and scarring, the detection of subdermal carcinoma [3].

We investigated the dependence of terahertz response power on ex-situ annealing temperature of low-temperature-grown gallium arsenide (LT-GaAs) and voltage-current characteristic. Molecular-beam-epitaxy obtained LT-GaAs samples at temperatures of 230℃ and 260℃ and different arsenic pressures on GaAs (100) substrates. THz waves excited by femtosecond laser pulses emitted from photoconductive antennas (flag type) formed on LT-GaAs, and the radiation power measured with a pyroelectric detector. The THz output power of the photoconductive antennas (PCA) showed the quadratic increase with the bias voltage.

Based on the analysis of the literature data on the annealing of LT-GaAs and our experiments, it was decided to increase the annealing temperature to 700℃ and conduct a new series of experiments. The choice of parameters and the control of the annealing process are of fundamental importance since the latter affects not only the relaxation of structure imperfections but also the formation of precipitates As in the crystal layer, which determines to a large extent the electrophysical properties of LT-GaAs. As a result of the measurements of the I-V characteristics made for the samples at annealing temperatures of 673.8℃ and 716.2℃, a THz response was recorded with a power of 5 and 4.2 μW and a current-to-power conversion factor of 0.36 and 0.21 mW/A respectively.

The spectral characteristics of THz radiation measured by time domain spectroscopy method. These graph shows the THz waveforms and their Fourier-transformed spectra. The graph (Fig.1) shows a comparison between the radiation waveforms for the antennas and crystal ZnTe (Zinc Telluride). The intensity of THz radiation from the PCA on LT-GaAs is 2 orders of magnitude greater than the intensity of the THz radiation from a nonlinear crystal of ZnTe.

The characteristics of an optimized photoconductive antenna made it possible to establish that the design of a photoconductive THz antenna based on LT-GaAs low-temperature gallium arsenide with the flag type geometry of the contacts developed by the method of molecular beam epitaxy has a high THz response power. Figure 1 shows that the main part of THz radiation is concentrated in a rather narrow spectral range from 0 to 2 THz.

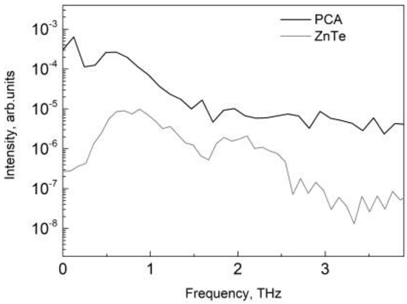

Fig. 1. The intensity of the THz response of the PCA as a function of frequency in the interval 0-4 THz, the bias voltage of 100 V, the pump power is 300 mW and the probe power is 150 mW.

The useful terahertz bandwidth extends from 0.1 to 2.7 THz and the source of terahertz wave usually used nonlinear crystal ZnTe in the biomedicine applications. However, in comparison PCA on LT-GaAs with ZnTe have better results in the intensity and the power of the THz response. Therefore, it will be possible to detect a lower concentration of biological objects.

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THE METHOD OF LIGHT DOSES MEASUREMENT OF PHOTODINAMIC THERAPY IN VISIBLE AND NEAR INFRARED RANGES

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In planning the PDT of the peritoneum, it is required to consider not only the target laser therapeutic radiation within the calculated light spot, but also additional radiation sources that can deform the resulting light dose received by the tissue at a work point. Monitoring of the light dose during photodynamic therapy of various points of the irradiated area and its surroundings allows to achieve maximum selectivity of treatment.

A new fiber-optic four-element sensor was created to rich the goal, which represents in four optical fibers connected by SMA connector from one end, and four white plastic ellipsoids (sensors), which recording radiation with a frontal projection area of 1 cm^2. Signal recording with sensors using fiber-optic spectrum analyzer LESA-01-BIOSPEC. The density of energy value in each measurement, which taking into account the coefficients, obtained as a result of preliminary calibration. The amount of light dose was calculated automatically during the monitoring process. For this purpose, a special software module was created.

The sensors were placed under a laser spot 4 cm in diameter with a homogeneous intensity. A laser unit for photodynamic therapy of LFT-630 / 675-01-BIOSPEC (668.9 nm) with a power of 1.04 W was used as a source of laser radiation.

As a result, it was shown that in the neighboring field of laser spot the light dose does not significantly affect the absorbed dose of laser irradiation during PDT.

At the same time, during the resection stage of surgical intervention, the size of the light dose during irradiation of the operating field from the operating lamp is large enough to be taken into account when planning PDT.

RESEARCH OF NEURAL NETWORK CLASSIFIER FOR THE DIFFERENTIAL DIAGNOSIS OF ACUTE LYMPHOBLASTIC LEUKEMIA

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Diagnosis of acute lymphoblastic leukemia (ALL) and their variants based on morphological, cytochemical and immunophenotypical features of leukemia cells poole. Using light microscopy plays an important role in accurate estimate of the number of parameters of blasts: the shape and size of cells, shape of nuclei, features of the structure of chromatin.

A comparative study of blasts in different variants ALL with the help of modern high technologies will allow to expand our knowledge of the biology of leukemic cells and to identify possible patterns in differences in the nuclear structure of blasts in different types of ALL[1-2].

The aim of this work is the study of possibilities of neural network classifier for the differential diagnosis of acute lymphoblastic leukemias.

Studies were carried out on stained smears of peripheral blood and bone marrow. Morphocytochemical and immunophenotypic studies were conducted in the laboratory of immunology of hematopoiesis of N. N. Blokhin Russian Cancer Research Center.

As a result of work the system was designed with the use of the library "FANN" for the research of neural network classifier.

Implemented a neural network classifier takes as input a format file "*.csv". In experiment precision neural network classifier at 250 periods was 89%.

Table 1. The test results for 250 periods

Sample #	Classification group	Test sample data	Test results
1	Norma	206	101
	Lymphoma	0	47
	T-ALL	0	33
	B-All	0	25
2	Norma	0	21
	Lymphoma	299	214
	T-ALL	0	11
	B-All	0	53
3	Norma	0	0
	Lymphoma	0	1
	T-ALL	483	129
	B-All	0	353
4	Norma	0	12
	Lymphoma	0	21
	T-ALL	0	226
	B-All	601	342
5	Norma	206	134
	Lymphoma	299	283
	T-ALL	483	399
	B-All	601	773

Further development of the system consists in the possibility of implementing a neural classifier, the input of which receives images, and improving the accuracy of the existing neural network classifier.

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COMPUTER 3D MODELING OF HEAVY IONS IMPACT ON DNA

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In order to understand the cage response to radiative effects it is necessary to study mechanisms of induction of DNA primary damages such as single-strand breaks (SSBs) and double-strand breaks (DSBs), including the hardly repaired cluster damages. Non-repaired damages are capable to lead to various negative consequences, such as genomic instability, chromosomal aberrations, carcinogenesis and death of a cage.

In radiobiology the special attention is drawn by heavy ions as the effective tool for investigation of the fundamental mechanisms induced mutational process of biological fabrics. The accelerated heavy ions successfully are applied at treatment of oncological diseases in view of optimum distribution of the absorbed radiation dose in a tumor at radiation by them. That is why a studying of mechanisms of genetic action of heavy ions is very actual.

Information about DSBs induction by accelerated heavy ions with various energies is very limited and often inconsistent. Information about regularities of a reparation of these damages by cages with various genotypes at action of radiations of wide range of linear transmission of energy is very poor. Induction and reparation of cluster SSBs and DSBs induced by heavy charged particles with high energies are studied is not enough.

The particles used in experiment were received on the cyclotron complex U-400 in Joint Institute for Nuclear Research intended for receiving the accelerated bunches of ions of elements practically of all table of D.I. Mendeleyev with energy 15–120 MEV/nucleon. Heating of electrons in plasma of an ionic source with an electronic and cyclotron resonance allows to receive unique bunches of multicharging ions.

Mathematical modeling methods application allows to study more deeply regularities of a cage reaction to the ionizing radiation, to make a numerical experiments, too labor-consuming, expensive or impossible in working with original system, and also capable to put considerable damages to the system sensitive to external influence.

In work approach to the mathematical description of induction of different types of DNA damages after action of heavy ions with different physical characteristics is offered (^{11}B, ^{16}O, ^{12}C, ^{56}Fe), and also p+.

Mathematical modeling was carried out with use of the program Geant4-DNA environment (GEometry ANd Tracking) – a software package on the basis of the Monte-Carlo method created for modeling of interaction of a particle with substance. The program Geant4-DNA environment allows to consider a contribution of different physical and chemical and biological processes, including interaction with the used substance, to allocate and consider the dominating processes, and also to set target geometry (the size, a form of sensitive area), to consider character of the environment of a target (in this work – homogeneous water solution). After that modeling of spatial structure of charged particles tracks, that is determination of the total saved-up energy, location for each interaction is carried out.

In research spatial distributions of energy release and the absorbed dose at action of various heavy ions in the wide range of LET at a cage kernel scale are calculated. The number of primary DNA damages and their spatial distributions according to structure of a particle track are estimated.

Our results and results of other researches are in agreement in general. But the number of primary DNA damages differs a little because of mathematical modeling results have the bigger accuracy than practical experiments.

ANALYSIS OF CLINICAL, DIAGNOSTIC, THERAPEUTIC, AND REHABILITATIVE ASPECT IN ISCHEMIC STROKE

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Abstract.

The analysis of clinical, diagnostic, therapeutic, and rehabilitation aspects in ischemic strokes at the multidisciplinary city clinic was made. Study group included 100 patients with ischemic stroke aged 45 to 92 years (mean age 69.4 years), including 56 men (mean age 63.7 years) and 42 women (mean age 76.6 years).

The study permitted to grade the average age of disease onset with gender-specific, significancy of analyzed risk factors. The main risk factors are hypertension (85%), atherosclerosis of cerebral arteries (62%) and ischemic heart disease (58%).

The most common forms of the disease were: the middle cerebral artery occlusion (71%), and atherothrombotic stroke (74%).

According to clinical, diagnostic, treatment and rehabilitation characteristic of patients the study confirmed the necessity of implementing high-tech methods as well as multidisciplinary approach in the rehabilitation of patients with ischemic stroke.

Keywords: ischemic stroke, atherosclerosis, multidisciplinary rehabilitation

CLINICAL AND GENETIC STUDY OF NEUROFIBROMATOSIS TYPE I

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Abstract.

A study of clinical and genetic characteristics of neurofibromatosis type I by results consultation of a doctor geneticist, neurologist regional hospital.

The study included 37 patients with a clinical diagnosis of "neurofibromatosis type I" aged 3 months to 19 years (mean age 9±0.65 years).

The result of the genealogical and population-statistical studies revealed an uneven distribution of the disease within the region and among major ethnic groups.

Analysis of the clinical polymorphism of the disease in the burdened families confirmed compliance to the international diagnostic criteria. In 54.1% of cases was severe, rapidly progressively disease, at 45.9 % – moderate and mild, slowly progressive. Installed low availability of molecular-genetic typing.

Keywords: neurofibromatosis type I, epidemiology, molecular-genetic typing.

EPIDEMIOLOGY, CLINICAL AND GENETIC CHARACTERISTICS OF THE CHARCOT-MARIE-TOOTH DISEASE

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Abstract.

The results of genetic counseling of families with the Charcot-Marie-Tooth disease at regional clinical hospital was studied, the analysis of the epidemiological, clinical and genetic features of disease to was made.

Clinical, genealogical, population-based statistical, electroneuromy-ographic and molecular genetic methods were applied. The studing signs, taking into account the population characteristics, were analyzed in 35 unrelated families (40 patients).

As a result of inquiry, the prevalence of the disease, according to the territorial units of the region, ethnic characteristics, clinical polymor-phism and genetic heterogeneity have been obtained.

The diagnostic algorithm of the Charcot-Marie-Tooth disease, based on the data of research was developed and it would be contribute to the effectiveness of genetic counseling in the region/

Keywords: disease Charcot-Marie-Tooth, epidemiology, molecular-genetic typing

THE ANALYSIS OF PSYCHOLOGICAL ISSUES AFFECTING THE QUALITY OF PSYCHOSOMATIC HEALTH OF STUDENTS

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Abstract.

The some peculiarities of psychological status of 1st year University students were investigated. The study used the following methods: a brief WHO questionnaire of quality of life; the test of differentiated self-assessment of functional status; the scale of reactive and personal anxiety Spielberg – Hanina. In a voluntary anonymous questionnaire was attended by full-time students of 1 course, aged 17 - 21 years old (male - 35, female – 64).

The results revealed a high level of anxiety in 98% of cases and 16.3% of respondents exposed to neuroticism, indicating overload of the mental sphere. At 56.6% of respondents with low adaptive capacity, and 16.2% were depressed, and in 6.1% of these figures reach a critical level.

28.1% have dysfunction of the autonomic nervous system, and 23.3% of the respondents was a chronic disease.

The obtained results indicate the necessity of psychological support, conducting by professional psychologist for 1st year students, with the aim of increasing their adaptive capacity and improve the quality of physical health.

Keywords: psychology, depression, autonomic dysfunction

THE GENEALOGICAL ASPECTS OF SCHIZOPHRENIA AND THE ANALYSIS OF ADHERENCE TO THERAPY

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The analysis of the clinical features of schizophrenia (97 cases) on the basis of the specialized Department of the city multi-field hospital was made.

It is established that the proportion of individual cases (89 patients 86,3%) predominated over the family (4 families: 8 patients and 7.8%), which is not contrary to the polygenic etiology of the disease.

To study the clinical features revealed a wide polymorphism – 27 syndromes, which are dominated by affective-delusional (19,6%) and hallucinatory-delusional (23.9 percent).

In the analysis of the spectrum of schizophrenia identified 11 variants with a predominance of the paranoid form (69,1%), rarely met sluggish (3,9%) and neurosis-like forms (4,9%), simple (3,9%), circular (3,9%) and paranoiac form (4,9%); psychopathic – 3 cases (2.9 percent). A wide range of forms confirms the genetic heterogeneity of schizophrenia.

The most important factors in the progression and exacerbation of the disease were: low adherence to therapy after discharge from the hospital (43 cases – 44,3%), adverse social environment (35 cases – for 36.05%), alcohol abuse (10 cases and 10.3%) and continuous flow (9 cases of 9, 27%).

Keywords: schizophrenia, paranoid syndrome, adherence to therapy

UNIVERSAL BIOMEDICAL ANALYSIS SYSTEM

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The universal analytical system for recording, storing, combinig samples of different users, performing statistical analysis of normal and pathological characteristics of biological objects, including humans (diseases, sex, age, ethnic, etc.) was developed. The program can be applied both in research and in biological and medical education, and in the future – in the practical medicine. It will be possible to adapt the system for aims of different specialists, to create of additional applications (statistic, information and educational, diagnostics, etc), to update the eprogramme depending of changing standarts.

Keywords: biomedical analytical systems, education, medicine, statistics.

BIODISTRIBUTION STUDIES OF A NEW ANTITUMOR COMPOUND BASED ON NANOPOROUS NANODIAMOND COMPOSITE LABELED WITH RHENIUM-188

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This study evaluated a new drug delivery system for local radiotherapy on the base of nanoporous nanodiamond composites (NDC) labeled with rhenium-188 (^{188}Re). NDC consists of nanodiamond particles with a mean size of 4–6 nm and a nanosize graphite-like matrix coating the surfaces of the nanodiamond particles and bonding them into a composite [1]. They possess a high biocompatibilty with human cells and a high porosity, which may be used for takeover, storage and long-term emission of drugs and/or radionuclides by creating durable containers. Local application of radionuclide-carrying containers based on nanoporous NDC allows to circumvent the problems inherent in systemic radionuclide delivery – low tumor accumulation and exposure to healthy tissues.

NDC are cylinders with the length of 40 μm and the diameter of 20 μm. The biodistribution of labeled nanoporous NDC was assessed after intratumoral (i.t.) and intramuscular (i.m.) injection. 24 mice-bearing solid Ehrlich carcinoma xenografts received i.t. injections of 0.370 ± 0.074 MBq (10 ± 2 mCi) ^{188}Re-nanoporous diamond composites. Another 24 intact mice were injected with the same preparation intramuscularly. The samples of different organs and tissues were collected for gamma count.

After i.t. and i.m. administration of ^{188}Re-nanoporous NDC a considerable amount of radioactivity retained at the site of injection. In tumor tissue the total amount of activity decreased from 92.68 % to 9.63 % of injected dose (ID) throughout the study. The removal of injected activity from muscular tissue was faster as compared with tumor tissue, and declined from 81.06 % to 8.40 % ID for up to 72 h.

Therefore, after i.m. injection the accumulation of radioactivity in healthy organs and tissues was slightly higher than after i.t. injection. In conclusion, it was demonstrated that ^{188}Re-nanoporous NDC had the potential for clinical applications in radiotherapy and can be further evaluated for establishing as a radiopharmaceutical for human use.

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PRECLINICAL EVALUATION OF ANTITUMOR EFFICACY OF A NEW RADIOPHARMACEUTICAL BASED ON THERMORESPONSIVE CARRIER AND SAMARIUM-153

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Intratumoral radiation therapy can be a highly effective treatment for solid tumors. Thermoresponsive polymers with the cloud temperature between the room and body temperature are attracted considerable interest as a radionuclide carrier. When heated above 37 ^{0}C, the polymer chains collapses and forms unsoluble gel that restricts its motility at the site of injection and distribution the radioactivity throughout the body.

Among the therapeutic radionuclides, samarium-153 with the favorable radiation characteristics ($T_{1/2}$ = 1.93 d, β_{max} = 0.81 MeV [20%], 0.71 MeV [49%], 0.64 MeV [30%], and γ =103 keV [30%]), is the most promising radionuclide for cancer therapy.

We have designed a new thermoresponsive system for local radiotherapy. This system consists of thermoresponsive copolymer based on N-isopropylacrylamide and allylamine labeled with beta-emitting radionuclide ^{153}Sm (^{153}Sm-KARP-CheM). This work is devoted to evaluation of antitumor efficacy of this injectable system *in vivo*.

The study of *in vivo* antitumor efficacy was performed using mice F1 and C57Bl/6 with transplanted subcutaneously sarcoma S37 and melanoma B16, respectively. The animals received single intratumoral bolus injections of 37 MBq (1 mCi), or 18.5 MBq (0.5 mCi) of ^{153}Sm-KARP-CheM, or saline in a volume 0.1 ml. The tumor sizes were measured every 3-4 days during 25 days. The efficacy of antitumor treatment was evaluated using tumor growth inhibition index (TGI, %) and increase of average life span (ILS, %).

The most meaningful therapeutic efficacy after intratumoral injection of ^{153}Sm-KARP-CheM was observed in melanoma-bearing mice C57Bl/6. The highest values of TGI for melanoma B16 were 79.5% and 79.6% after treatment with 18.5 MBq or 37 MBq, respectively. An increase of average life span by 17.1% was found in group of melanoma-bearing mice treated with 37 MBq of ^{153}Sm-KARP-CheM only.

Tumor growth inhibition of sarcoma S37 was slightly lower as compared with melanoma B16: 62.5% and 59.0% in 37 MBq and 18.5 MBq groups, respectively. ^{153}Sm-KARP-CheM didn't increase average life span of treated animals.

In conclusion, ^{153}Sm-KARP-CheM seems to be an effective agent for local radiotherapy of cancer.

PRELIMINARY BIOLOGICAL EVALUATION OF LEUCINE LABELED WITH GALLIUM-68 – A POTENTIAL AGENT FOR TUMOR IMAGING

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Many cancers exhibit increased consumption of amino acids as compared with normal cells. Amino acids play an important role in the synthesis of a variety of nitrogen-containing compounds, such as proteins and nucleotides during cell growth, and their increased transport and utilization are be associated with early events in carcinogenesis [1]. So radiolabeled amino acids can serve as alternative PET tracers to ^{18}F-FDG for tumor imaging.

Among the positron emission radionuclides, ^{68}Ga has several advantages. One of them is its cyclotron-independent availability via the ^{68}Ge/^{68}Ga generator system, which would facilitate widespread use of PET. In addition, ^{68}Ga has excellent physical properties for PET, such as high positron emission (89%) and low γ emission (1077 keV; 3.22%) [2].

In this study, we evaluated the biodistribution of natural amino acid leucine labeled with ^{68}Ga in Wistar rats bearing cholangioma RS-1 tumor xenografts. Tumors were grown for 10 days, and then ^{68}Ga-leucine (0.37 MBq in 0.1 ml) was injected through the tail vein. Animals were sacrificed at different time intervals (5 min, 1, 3 and 5 h) after injection; tumor, blood, and other organs and tissues were isolated, weighed and counted in automatic gamma counter. Results were calculated as the percent injected dose per gram of tissue (% ID/g).

It was shown that tumor uptake of ^{68}Ga-leucine was about 2-4 times higher when compared to $^{68}GaCl_3$ (Tab. 1). Among the soft tissue only kidney had a high uptake (up to 4.60% ID/g), indicating that the excretion of radioactivity is occurred through the urinary routes. In other organs and tissues the amounts of activity were relatively low. The results suggest that ^{68}Ga-leucine has the potential to be a new additional diagnostic tool for the imaging of tumors.

Table 1. Tumor accumulation of radiactivity after intravenous injection of ^{68}Ga-leucine and $^{68}GaCl_3$ (control) (in % ID/g). The data are presented as mean ± standart error (M ± m)

	Time after administration			
	5 min	1 h	3 h	5 h
^{68}Ga-leucine	0.79±0.02	0.36±0.03	0.32±0.06	0.29±0.05
$^{68}GaCl_3$	0.34±0.07	0.32±0.03	0.13±0.04	0.07±0.01
p	p<0.001	p>0.1	p<0.05	p<0.01

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THE INFLUENCE OF CARRIER ADDITION ON THE BIODISTRIBUTION OF BONE-SEEKING AGENT «^{188}RE-OXA-BIS(ETHYLENENITRILO)TETRAMETHYLENEPHOSPHONIC ACID»

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Metastatic lesions in the skeleton are revealed in more than 70% of patients with breast, prostate, lung, colon, thyroid, uterine, and skin cancers [1]. Bone-seeking radiopharmaceuticals are known to be the most promising agents for the palliative treatment of the pain of bone metastases. A generator-produced radionuclide rhenium-188 (^{188}Re) is an attractive candidate for therapeutic use due to its nuclear characteristics ($T_{1/2}$ = 16,9 h, $E_{\beta max}$ = 2,1 MeV, E_{γ} = 155 keV). It is known that carrier addition is essential for stability and biodistribution of many bone-seeking radiopharmaceuticals [2, 3]. The goal of the current work was to investigate the pharmacokinetic properties of ^{188}Re-oxa-bis(ethylenenitrilo)tetramethylenephosphonic acid (^{188}Re-OENTMP) with gallium carrier and without carrier and to compare them. A comparative accumulation study of both ^{188}Re-OENTMP formulations was carried out in healthy wild-type rats after intravenous administration up to 48 hours.

It was revealed that for carrier-added ^{188}Re-OENTMP the bone samples from femur, skull, ribs, spine and knee joint all had higher uptake in comparison to that of ^{188}Re-OENTMP without carrier. The values of carrier-added ^{188}Re-OENTMP in skeleton were ranged from 7,82 % to 57,37 % of injected dose (ID), when the amount of ^{188}Re-OENTMP without carrier varied from 5,76 % to 22,75 % of ID. Both formulations showed rapid clearance from blood. Among the soft tissue organs, only thyroid gland and kidneys had a relatively high uptake. Most of the activity excreted via the urinary tract. The femur/soft tissue ratios for both formulations of ^{188}Re-OENTMP had no significant differences. In conclusion, it should be pointed out that carrier addition strongly affects bone uptake of ^{188}Re-OENTMP. High and selective uptake in bone of carrier-added ^{188}Re-OENTMP after intravenous injection indicated that this complex could be useful to deliver radiation to skeletal metastases from soft tissue cancer.

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GENETIC FACTORS OF HEARING IMPAIRMENT IN POPULATIONS OF THE KARACHAY-CHERKESS REPUBLIC

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The population analysis and medical genetic counseling of patients with a hereditary non-syndromic neurosensory hearing loss in Cherkessk and ten districts of the Karachay-Cherkess Republic (Ust-Dzhegutinsky, Karachaevsky, Malokarachaevsky, Abazinsky, Nogaysky, Prikubansky, Khabezsky, Adyge-Khablsky, Urupsky, Zelenchuksky) were performed. The population-genetic survey covers a total population of 387,231 people.

A total of 207 patients with a hereditary neurosensory hearing loss (NHL) from 161 families were identified. 137 patients with NHL from 87 families (Russians, Karachays, Cherkess, Abazins, etc.) underwent DNA diagnosis for the gene *GJB2* mutations. A spectrum of mutations in the *GJB2* gene was determined, and a contiguous 101 kb deletion (delGJB2-D13S175) was screened. The incidence of all pathological changes in the *GJB2* gene in patients with NHL was 34.67% (in Russian patients – 52.68%, in Karachays – 7.69%, in Circassians – 50.00%, in Abazins – 25.00%).

The population frequency of the mutation c.35delG in *GJB2* gene was determined among 507 healthy individuals of the three ethnic groups (Russians, Karachais, Circassians). The population frequency of the c.35delG mutation in the Russian population of the republic was 0.0143 (heterozygous carriage rate 1:35), in Karachays 0.0014 (heterozygous carriage rate 1:370), in the Circassians – 0.0098 (carriage rate 1:51).

In general, the spectrum of mutations in the gene *GJB2* in the Republic corresponds to the spectrum of most European populations. According to the revealed frequencies of pathological mutations in the *GJB2* gene, Circassians and Abazines are most similar to the Russians of the Karachay-Cherkess Republic, the spectrum and frequencies of mutations in these ethnic groups are closest to those in the samples of Eastern Europe and Central Russia. A peculiarity of the mutations spectrum of Karachays is similar to the populations of Turkic origin.

Keywords: population and medical genetic examination, hereditary isolated neurosensory hearing loss, c.35delG mutation, *GJB2* gene, the Karachay-Cherkess Republic

LIPOSOMES WITH PHTHALOCYANINEOXYALUMINIUM AND GOLD NANOPARTICLES FOR COMBINED PHOTODYNAMIC AND PLASMON RESONANCE THERAPY

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Currently, there are several methods of binary antitumor therapy, some of them based on the use of laser radiation. Such methods are photodynamic therapy (PDT) and plasmon resonance hyperthermia (PRH). PDT is a method of tumors treating based on the administration of a photosensitizing agent followed by external laser irradiation. When the laser radiation interacts with the photosensitizer, the active forms of oxygen are generated, which causes damage and necrosis of the tumor tissue at the site of irradiation. PRHis a methodbased onsurface plasmon resonance in gold nanoparticles under external laser irradiation. Interacting with this radiation gold nanoparticles emit secondary infrared radiation which leads to a significant increase in the temperature of the particle and its environment. Gold nanoparticles (GNP) were obtained by reduction of gold chloride acid (HAuCl4) with sodium citrate in the presence of dextran sulfate (DS). Liposomes were obtained by hydration of thin lipid films. The main components of the liposomes were phosphatidylcholine and cholesterol. The active substances (PO and GNP) were incorporated into the liposomes by the passive loading method. Dispergation of the liposomes was performed by extrusion through a polycarbonate filter with a pore diameter of 200 nm. The average size of liposomes was185±30 nm.

A comparative study of the antitumor efficacy of liposomes containing GNP and PO in C57B6 mice with transplanted lung Lewis carcinoma (LLC)was performed. Animals were divided for 4 experimental and 1 control groups.Depending on group animals were treated according to the following schemes: liposomes with GNPand PO +laser irradiation (group 1), liposomes with PO + laser irradiation(group 2), liposomes withGNP+laser irradiation (group 3), laser irradiation only (group 4). Investigated substances were administrated in the tail vein. The tumor zone was irradiated by a 670-nm laser in 24 hour after drug administration. Animals in control group were not treated.

To evaluate the efficiency of antitumor therapy, the tumor growth inhibition index (TGII) was determined.It was calculatedby the formula: TGII= $(V_k-V_{exp})/V_k * 100$, where V_k and V_{exp} are the average tumor volume in the control and experimental groups respectively. The results are shown in Table 1.

Table 1. Efficiency of different schemes of the antitumor therapy

Group	Scheme	TGII, %		
		7days	14 days	21 days
1	Liposomes withPOand GNP+ laser irradiation	21	62	84
2	Liposomes with PO + laser irradiation	25	49	61*
3	Liposomes withGNP+laser irradiation	18	39 *	54 *
4	Laser irradiation	4,2 *	-2,1 *	-5,8 *

* a significant difference from the TGII of the 1-st group.

The inhibition of LLC growth was observed in all experimental groups. Treatment with liposomes with GNP and PO was more effective than other schemes. TGII in the 1-st experimental group on the 14-th and 21-st day of therapy was significantly different from the one in the 2-nd and 3-rd groups. Laser irradiation of the tumor did not inhibit its growth. Thus, the proposed drug provides an increase in the efficiency of PDT and improves the results of LLC treatment.

MECHANISMS OF ANTIOXIDANT PROTECTION AND THE PHOTOINDUCED DEATH OF CISPLATIN-SENSITIVE AND -RESISTANT OVARIAN ADENOCARCINOMA CELLS

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Introduction: Oxidative stress is the most important mechanism of tumor cells photodamaging in photodynamic therapy (PDT). The effectiveness of PDT is due to the accumulation of a photosensitizer in cancer cells and the functioning of mechanisms that ensure the realization of oxidative stress. However, in cells resistant to antitumor drugs (in particular, cisplatin), antioxidant systems can prevent photodamaging. It is required to evaluate the redox balance in cisplatin-sensitive and resistant cells as a factor determining the possibility of their death under PDT.

Aim: Study the expression of genes that encode enzymes able to produce active forms of oxygen (NADH oxidase) and the antioxidant system enzymes (superoxide dismutase, catalase, glutathione peroxidase). Moreover, we are aimed to study the death of cisplatin-sensitive and -resistant cells of ovarian adenocarcinoma in the presence of a new chlorin derrivative fluorboronchlorin (FBC).

Materials and methods. In this work we used the ovarian adenocarcinoma line SKOV-3 and subline SKOV-3/CDDP, resistant to cisplatin. Estimation of gene expression by quantitative polymerase chain reaction in real time (RT-qPCR), FBC dark toxicity (MTT-test), intracellular accumulation (flowing cytometry), and cell death under FBC photoactivation (fluorescence microscopy) were used.

Results. The change of the controlling the cellular redox status genes expression was revealed: a 4-fold decrease in the expression of the NADH oxidase (NOX5) gene, a 3-fold increase in the expression of the glutathione peroxidase (GPx1) gene and growth of the mRNA of superoxide dismutase (SOD1 and SOD2 by 1.7 times; SOD3 by 2 times). Low dark cytotoxicity in FBC (IC_{50}> 50 μM) was revealed earlier. The maximum intracellular accumulation of FBC in both lines was achieved in 36-48 hours. Illumination of SKOV-3 and SKOV-3/CDDP cells (20 min., 30 J/cm^2) after incubation with 5 μM FBC resulted in rapid (in the first minutes) cancer cells death accompanied by manifested changes of morphology and the introduction of propidium iodide – marker of necrosis. Consequently, the revealed changes in the mechanisms of antioxidant defense in cells resistant to cisplatin do not prevent their lethal damage under photoactivation of FBC.

Conclusions. Development of resistance of adenocarcinoma cells of the ovary SKOV-3 to cisplatin changes the expression of genes controlling the cellular redox status. These changes are not accompanied by an increase in cell resistance to the action of a new photosensitizer (FBC) under the conditions studied. Water solubility, low dark toxicity and the possibility of induction of unreparable photodamage of tumor cells (sensitive and resistant to cisplatin) allow us to consider FBC as a promising candidate for medicinal drugs.

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A CONTROL ALGORITHM OF FLOW BALANCE FOR A BIVENTRICULAR ASSIST DEVICE

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The use of rotary blood pumps (RBPs) as biventricular assist devices is a complex task associated with the high mortality rates of patients [1]. One of the main challenges is to control of RBPs in order to ensure a flow balance in systemic and pulmonary circulation, which arises due to the use of the same RBP for the circulatory support of the left and right ventricles, ventricular interaction and different systemic and pulmonary vascular resistances [2].

The aim of this study is to propose a control algorithm for a biventricular assist device, which should ensure the flow balance in systemic and pulmonary circulation using pump speed as a control variable.

The study was done with a mathematical model of the cardiovascular system [3], where RBPs described by the mathematical model of rotary blood pump HeartMate II (Thoratec Inc., USA). The pump speeds were varied from 3000 rpm to 10,000 rpm in 200 rpm increments.

The balance of flows in systemic and pulmonary circulation was considered as the equality of the following variables: pump flows, aortic valve and pulmonary valve flows, cardiac outputs of the left ventricle and right ventricle of the heart.

As a result the ratios of the speeds are selected at which pump flows, valve flows and cardiac outputs are differed not more than 0.1 L/min. These ratios are considered as pump operating points listed in Table 1. Therefore, the control algorithm involves searching and maintaining of the operating point. There are varieties of operating points characterized by the different end-systolic pressures. Thus, ESP can act as a constraint during the searching, where minimization of ESP_{LV} and maximization of ESP_{RV} may be used as a control objective.

Table 1. Operating points of the rotary blood pump HeartMate II; ω(RBP) – pump speed, Q (RBP) – pump flow, Q_V – valve flow, CO_V – cardiac output of the ventricle, ESP_V – end-systolic pressure in the ventricle

	Operating point 1	Operating point 2	Operating point 3	Operating point 4
$\omega(RBP_{LV})$	7400 rpm	8000 rpm	8400 rpm	8600 rpm
$\omega(RBP_{RV})$	6600 rpm	7200 rpm	8200 rpm	7800 rpm
$Q(RBP_{LV})$	3.47 L/min	4.06 L/min	4.61 L/min	4.63 L/min
$Q(RBP_{RV})$	3.46 L/min	4.02 L/min	4.69 L/min	4.58 L/min
Q_{AV}	0.54 L/min	0.25 L/min	0.08 L/min	0.00 L/min
Q_{PV}	0.55 L/min	0.28 L/min	0.00 L/min	0.05 L/min
CO_{LV}	3.32 L/min	3.27 L/min	3.24 L/min	3.23 L/min
CO_{RV}	3.23 L/min	3.26 L/min	3.31 L/min	3.32 L/min
ESP_{LV}	21.69 mmHg	24.29 mmHg	32.69 mmHg	27.22 mmHg
ESP_{RV}	-2.32 mmHg	-2.37 mmHg	-2.45 mmHg	-2.43 mmHg

The obtained results show that the balance of flows in systemic and pulmonary circulation can be achieved with the same RBPs as the biventricular assist device. It also represents a basis for a development of control method for the biventricular assist device towards a patient-specific treatment of biventricular heart failure.

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BIOLOGICAL EFFECT OF CONTINUOUS, QUASI-CONTINOUS AND PULSED LASER RADIATION

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Despite progress in the practical use of low-intensity laser radiation in medicine and agriculture, question about mechanism of biological activity of mentioned physical factor is still open. As a rule, the basic studies are carried out using a continuous radiation; biological effect of pulsed radiation of nano- and picosecond ranges is studied poorly.

In the present work we compare the biological activity of laser radiation of different regimes (continuous, quasi-continuous, pulsed –nano- and picosecond time ranges).

Zooplankton (branchiopod crustaceans) *Artemia salina L.* and sturgeon sperm were used as objects. The percentage of nauplii hatched from cysts (protective shells) after activation of eggs in salt water in a stable thermal regime, the data on duration of sperm motility as well as its curvilinear velocity after activation with water were chosen as indicators of biological activity of laser radiation. The exposure was realized using the second-harmonic radiation (wavelength λ = 532 nm, average output power ~ 30 mW) of Nd:YAG-lasers working in continuous and quasi-continuous (pulse repetition rate – F = 1 kHz, pulse duration – τ = 100 ns) regimes, as well as in pulsed regime with generation of nanosecond (τ = 15 ns, F = 10 Hz) and picosecond (τ = 60 ps, F = 20 Hz) pulses. Comparative studies upon exposure to radiation of red (632.8 nm, He-Ne laser) and near IR (808 and 976 nm – diode lasers; 1064 and 1342 nm – diode pumped Nd:YVO_4 laser; 1176 nm – diode pumped Nd:YVO4 laser (1064 nm) with intracavity Raman self-frequency conversion) spectral region were also carried out. Power density (P) – 3 mW/cm^2.

The results on sperm motility (λ = 532 nm, P = 3 mW/cm^2) show that the optimal dose of optical radiation which initiates the stimulation of functional characteristics of biosystems is strongly dependent on the regime of acting radiation. For example, using the aforementioned parameters of acting factors, the optimal stimulating dose when controlling the sperm motility is 135 mJ/cm^2 for continuous radiation; 90 mJ/cm^2 - for quasi-continuous and nanosecond and 60 mJ/cm^2 – for picosecond radiation. At the same time, maximal stimulating effect is (140±6)% for continuous; (163±9)% – for quasi-continuous; (122±6)% – for nanosecond and (115±7)% – for picosecond regimes. Even more pronounced stimulating effect (180±9)% has a continuous radiation of red spectral region. It is typical that stimulating effect in the case of nano- and picosecond regimes is observed in a very narrow dose interval: 30–60 mJ/cm^2. The rapid suppression of functional characteristics of biological systems is observed upon increasing the dose: at a dose of 1.8 J/cm^2 duration of sperm motility reduced more than two times compared to the control. Similar bell-shaped dose curves are registered when controlling the curvilinear sperm velocity and percentage of nauplii hatched from cysts after activation of eggs in salt water.

Studies have also shown that photobiological effects initiated by laser radiation (the hatching of the nauplii *Artemia salina L.*) is strongly dependent on the wavelength of incident radiation: if radiation exposure with λ = 632,8 nm, λ = 976 and λ = 1064 nm has an inhibitory effect on the hatching of the nauplii, then the radiation with λ = 808 nm, λ = 1176 nm and λ =1342 nm has stimulating effect.

Thus, we demonstrate that biological effect of laser radiation controlled on functional activity of zooplankton and sturgeon sperm is strongly dependent on the regime and wavelength of acting radiation under conditions with equal average power density. Laser radiation of different regimes, in a certain range of dose rates, is able to have both stimulating and inhibiting effect on all studied parameters of functional activity of biological systems.

REFLECTION SPECTROSCOPY IN THE STUDY OF BIOLOGICAL TISSUES OF ANIMAL ORIGIN

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Native and subjected to various types of chemical treatment (water and saline, alkaline, lyophilisation) pork muscle tissue and blood serum from healthy people and patients with multiple myeloma (MM) and chronic lymphoid leukemia (CLL) were investigated by attenuated total reflectance Fourier transform infrared (ATR FTIR) spectroscopy.

The comparative analysis of the biological tissues of different origin and nature revealed many similarities in their spectra, allowing to point out to similarities between them in interpreting the position and intensity of the bands of the lipid, protein and carbohydrate components.

The study of spectral characteristics of pork muscle tissue, muscle fibers, stroma and stroma proteins obtained by sequential chemical treatments and freeze drying was conducted. According to the results, pork muscle fibers are the closest in their spectral characteristics to dried human blood serum .

ATR FTIR spectroscopy analysis of human blood serum from patients with multiple myeloma and chronic lymphoid leukemia uncovered the discrepancy in their spectral characteristics not only between the group of healthy people and patients with both diseases but also between patients with MM and CLL.

Thus, it is possible to consider the ATR FTIR spectroscopy as an applicable method for the analysis of biological tissues.

THE RELATIVE BIOLOGICAL EFFECTIVENESS OF ALPHA PARTICLES IN THE MANIFESTATION OF HERITABLE LATE DAMAGE

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In this work, survival curves and delayed appearance of clones by haploid homozygous (S288C) and diploid (XS800) strains of *Saccharomyces cerevisiae* yeast cells in stationary stage of growth were studied. The aim was to analyze the relative biological effectiveness (RBE) of ionizing radiation with high linear energy transfer (LET). Most of radiobiological responses of yeast cells (a form of survival curve, the dependence of RBE on LET, oxygen effect, radiosensitizers and radioprotective effect) are qualitatively similar to the response of cultured mammalian cells. We used sparsely (gamma-rays of Co-60, 0.2 keV/μm, 20 Gy/min) and densely (alpha particles of Pu-239, 120 keV/μm, 23 Gy/min) ionizing radiations. Just at this value of LET a maximum in RBE-LET relationship is observed for most eukaryotic cells [1].

The effect of the late formation of colonies of yeast cells surviving after irradiation is an example of the manifestation of genetic instability [2]. For all yeast strains studied, the efficiency of densely ionizing radiation was nearly identical for cell survival and delayed appearance of clones produced by single cells surviving the radiation. RBE value for cell survival of wild-type diploid yeast cells (4.9 ± 0.4) was practically the same as for the delayed appearance of colonies (RBE = 4.7 ± 0.3). RBE value for both survival and genetic instability of haploid wild-type yeast cells varied in 1.8–2.7 range for both test-effects. These findings are not new for cell survival, while they are fundamentally new for genetic instability. Isoefficiency exposure to radiation of various qualities indicates that the number of effective (lethal) radiation damage is strongly related with the number of sub-lesions responsible for the later formation of colonies by cells surviving radiation exposure.

The obtained experimental dependence of the late formation of colonies by diploid yeast cells surviving ionizing irradiation shows more significant manifestation of this effect after exposure to α-particles, than after irradiation with gamma-rays. This may be due to the greater efficiency of densely ionizing radiation to produce a lethal radiation damage and the corresponding sub-lesions responsible for the late appearance of clones. In other words, the effect of the late appearance of the colonies is associated with the accumulation of inefficient for cell inactivation of sub-lesions [1]. These sub-lesions stored in the remote descendants of the surviving cells after irradiation, thereby causing destabilization of the genome, what results in the formation of colonies and their phenotypic differences. New results obtained in this work may be useful in providing novel basis for understanding the underlying mechanisms of radiation-induced genetic instability.

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ACTIVATION OF NANOCOMPOSITE VESICLES BY EXTERNAL ELECTRIC OR MAGNETIC FIELDS

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Problem of effective ways and methods of encapsulating, address delivery and controlled release of biologically active molecules, especially drugs in vivo is important and actual today. Such methods can greatly improve efficiency of drug therapy. Biomimetic membraneous vesicles called liposomes are of great interest in development of drug delivery and controlled released carriers due to their biocompatibility and submicron size, which promote their distribution through blood flow in vivo.

This article presents results of study of electric and magnetic impacts on nanocomposite liposomes, functionalized by polymer molecules and non-organic nanoparticles, which provide sensitivity to external physical effects. Phosphatidylcholine liposomes, synthesized by our scientific group contains in their composition molecules of amphiphilic polycation stearoylspermine, which provide bounding of magnetite and gold nanoparticles or polyanions on liposome surface. Magnetite nanoparticles provide the sensitivity of such vesicles to nonthermal physical effects-the impulses of the electric field and magnetic fields.

To quantify the effects of decapsulation under the influence of external physical effects, we have used a standard experimental technique, based on measuring the changes in the conductivity of a suspension of liposomes after external influences, which cause the release of the electrolyte (NaCl) contained in the liposomes. To this end, liposomes containing a concentrated NaCl solution in the internal volume were preliminarily formed. To investigate the effect of a pulsed electric field on vesicles, a tube with solution containing nanocomposite liposomes was placed between the plates of the apparatus capable of generating pulses of an electric field of nanosecond duration with a voltage of up to 45 kV. It is established that with a field strength of more than 15 kV such pulses lead to the destruction of nanocomposite liposomes and the escape of cap-sulphurized substances to the outside [1]. The effect of the magnetic field on nanocomposite liposomes was also studied. In this experiment, a tube with an aqueous suspension of liposomes was incubated in the field of a permanent magnet (2000-7000 Oe) for an hour, after which changes in the conductivity of the solution were investigated. Under the influence of an external magnetic field, the shape of the liposomes changed from spherical to ellipsoidal.

The results obtained in this paper show that nanosystems based on liposome-functionalized nanoparticles can serve as a basis for the creation of new efficient means of encapsulation, targeted delivery and controlled release of various biologically active substances in aqueous media that are promising for biomedical and other applications.

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CRYSTALLINE ZN SUBSTITUTED HYDROXYAPATITE COATING FOR BIOMEDICAL APPLICATION

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Amount of artificial joints and fixation devices comprise half of all devices used in medical practice. More and more implants are coated by bioactive calcium phosphates in order to increase their service life and enhance osseointegration.

Recently, the problem of peri-implantitis caused by unwanted bacteria at the implantation site was recognized by the global healthcare. Therefore, bactericidal activity of implants recently became important research trend due to the growing amount of implantation surgeries. Publications devoted to substituted hydroxyapatites by Ag, Cu, Zn and other ions drastically increasing [1,2]. It is reported that HA-Zn coatings enhance proliferation and differentiation of osteoblasts [2].

In our work thin Zn substituted hydroxyapatite coatings with columnar crystal structure were formed on heated to 400 °C Ti substrates by radio frequency magnetron sputtering. Coatings crystallinity state and elemental composition were evaluated by TEM and in-column EDX.

In our previous work, HA-Zn was deposited on the substrates that were uncontrollably heated by the glow discharge plasma. In contrast, present work Ti substrates were heated by the custom made sample holder with a built-in heater to the temperature of 400 °C. Figure 1 shows bright-field image of cross-section TEM (XTEM) of the HA-Zn coating deposited from RF magnetron source at the discharge power level of 250 W. Note, that the HA-Zn coating had a gradient structure with a nanocrystalline layer at the interface. The HA-Zn film is well defined, dense and homogeneous. Preferential growth orientation in (002) plane was seen. In-column EDX confirmed that HA-Zn elemental composition is close to stoichiometric for HA Ca/P ratio.

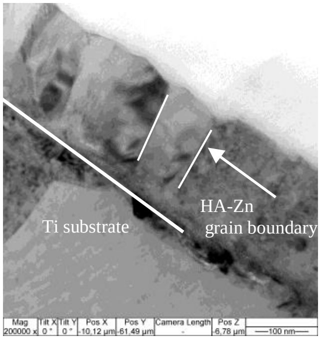

Fig.1. Cross-sectional bright field TEM image of a 200 nm thick HA-Zn layer.

Resulted columnar polycrystalline structure is in good agreement with results published in reference [3]. The reason for (002) preferential growth is in the fact that this plane has the lowest surface energy for HA. The other reason is a shadowing effect which is well-known for magnetron sputtering.

In conclusion, we show that it is possible to enhance crystallinity state of the HA-Zn coating and form columnar type of film structure on Ti by applying additional heat during the process of RF magnetron sputtering.

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CLINICAL APPLICATION OF NEW IMMOBILIZATION SYSTEM IN SEATED POSITION FOR PROTON THERAPY

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A special mobile patient positioning and immobilization unit has been developed within the proton therapy complex "Prometheus". This unit is much cheaper than a gantry and is suitable for a low-cost system designed to be used with a fixed treatment beam and a rotating seated patient. This paper reports the results of the verification (process which is carried out immediately before the proton therapy session) for the first 50 patients gone through clinical treatment at this facility. It contains a list of advantages of the presented system of patient positioning and immobilization in contrast to the standard methods and a gantry used in cases of head and neck cancer treatment. This system has been adapted for proton and ion therapy facilities working with the pencil beam scanning (PBS) technique.

Purpose: To report the first clinical experience of using new patient setup unit in a seated treatment position.

Materials and Methods: a patient positioning and immobilization unit as a part of proton therapy complex "Prometheus", civco thermoplastic masks, an X-Ray cone-beam computer tomograph, daily verification procedures.

Results: The obtained results of patient setup displacement were slight. We got measurements for each of the dimensions: at the X-axis: -0.1±0.8 mm, at the Y-axis: -0.4±2.0 mm, at the Z-axis: 0.1±1.5 mm. 530 daily verification procedures were held for 50 patients. The average time of treatment session was 5 min 39 sec.

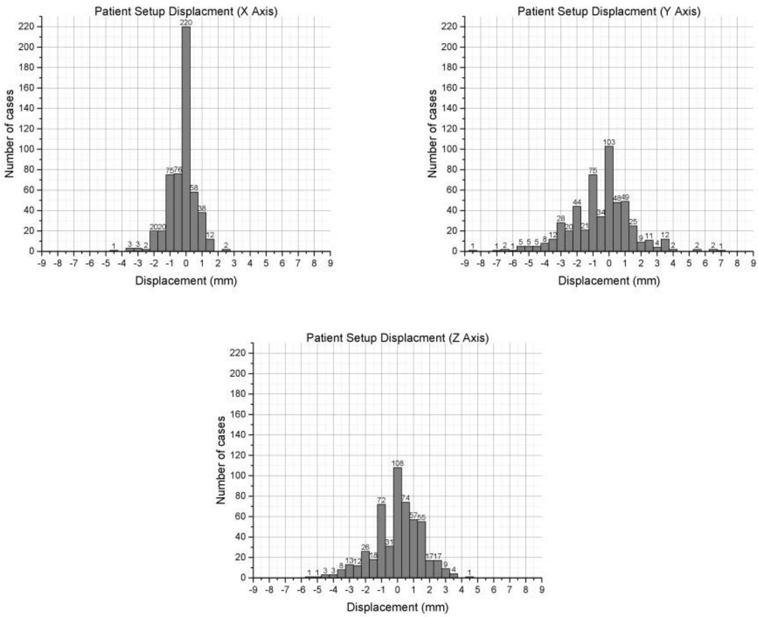

Fig.1. Patient setup errors.

Conclusion: this study demonstrates that the “Protom” patient setup unit is a real alternative for gantry systems in cases of head and neck cancer. It meets all clinical requirements. This device can be used as an independent system of patient positioning and immobilization, or can be a part of complex facilities with gantries and other systems.

Key words: proton therapy, ion therapy, pencil beam scanning.

DEVELOPMENT OF MAGNETIC LEVITATION OF THE ROTOR OF A CENTRIFUGAL BLOOD PUMP

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Due to the high rate of heart disease and a shortage of donor hearts, every year the need for more reliable and durable mechanical replacement of the heart grows [1]. Modern implantable devices of supporting circulatory using the mechanical suspension method, unfortunately, have almost exhausted their resource. Often, their lifetime is not enough to extend the life of the patient prior to transplantation of the donor organ. But before modern implantable blood circulation apparatuses, the task is not only to become a "bridge" for transplantation, but also, in more cases, simply maximally prolong the life of the patient, for example, with contraindications to donor organ transplantation [1].

To solve this problem can the technology of magnetic levitation. This development is a very important step on the way to extending the life of devices for more than 10 years, reducing the number of parts, simplifying the design and, as a result, reducing the size and weight of the device[1,2]. Moreover, magnetic levitation has useful properties and owing to them hydrodynamic bearings and magnetic levitation have recently become the focus of research for using them in centrifugal VAD/TAH blood pumps in many foreign firms [3].

The purpose of the presented work is the development of the magnetic levitation drive, and then the implantable third-generation centrifugal pump. This topic has a high practical value, because the contactless suspension method has been little studied in Russia, whereas in foreign countries the third generation of pumps have already been widely introduced into clinical practice. The results of the research will be useful to developers who are conducting research in the field of mechanical support of the heart's blood circulation and facing the problem of the stability of magnetic levitation.

As a result of the research of scientific and technical literature were advantages of technology as: higher reliability and durability, less weight and dimensions, less heating of parts, lowering of hemolysis and potential thrombosis. To conduct a theoretical study, were chosen analytical methods for calculating the magnetic field, their analysis was carried out, after that the choice of the most convenient and effective method of calculations was made. The paper presents important practical conclusions about the structure of the drive and its components. Also you can see a comparison of axial force and rigidity of bearings with axial, radial and perpendicular polarizations. There were investigated bearings from multi-stage annular magnets with alternating polarizations of three kinds: axial, radial and perpendicular (Halbach array). These calculations are useful for identifying the structures, which are required for providing greater axial force and rigidity.

Conclusions are done about the most advantageous structure of the passive component. Theoretical calculations and mathematical modeling of the selected Halbach structure in the Ansys Maxwell medium have been carried out. On the example of the considered structure, the effect of a magnetic potential well is investigated. Also you can see an analysis of the active component of the drive, namely, a DC brushless motor. There were considered its various types, their working principle. A choice of one of the presented engine types is made and substantiated.

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11C-CHOLINE PET/CT IN 217 PROSTATE CANCER PATIENTS AFTER RADICAL TREATMENT WITH PSA LEVEL < 10 NG/ML

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Prostate cancer (PCa) is the most frequent cancer among older men in Western countries and the second leading cause of cancer-related death among men [1, 2]. Detection of relapse site (local or distant) in patients with biochemical recurrence after radical treatment is crucial for further treatment approach [3, 4].

Purpose: To evaluate the usefulness of 11C-Choline PET/CT in the detection of recurrent PCa in patients with biochemical relapse after radical treatment.

Materials and methods: This retrospective study included 217 PCa patients who underwent 11C-Choline PET/CT in the Department of Nuclear Medicine of Bakoulev Scientific Centre over the period from January 2013 to May 2017. All patients had biochemical relapse 3±2 years after radical treatment for locally advanced PCa (T1–3 N0–1 M0): radical prostatectomy (n=159) and radiation therapy (n=41). The mean PSA value in the group was 2.1±2.5 (0.2–9.7) ng/ml, median – 1.9 ng/ml. Imaging was performed on PET/CT scanner (Biograph-64, Siemens) 10 min after injection of ^{11}C-Choline (400–550Mbq). All PET/CT results were validated by following criteria: histological analysis in 13% of cases, and in 87 % – findings from other imaging techniques, repeated PET/CT, clinical follow-up, further PSA dynamics, treatment response, as well as the combination of all mentioned above within 9±3 (1–12) months after performing PET/CT.

Results: Overall, 11C-Choline PET/CT detected PCa relapse in 56% (121/217) of cases: in 50% (80/159) after radical prostatectomy and in 71% (41/58) after radiation therapy.

The mean PSA value in PET-positive cases was 3.1±2.2 (0.2–9.7) ng/ml, while in PET-negative cases – 1.8±1.7 (0.2–4.6) ng/ml. The majority – 68% (65/96) patients with PET-negative scan had low PSA levels (< 2 ng/ml). Although the median PSA value was significantly higher in PET-positive than in PET-negative patients (2.4 ng/ml vs 1.4 ng/ml, $p < 0.001$), PET/CT confirmed its ability to detect relapse in patients with low PSA levels (from 0.2 ng/ml).

PET/CT was positive in 43% (50/115) patients with PSA of < 2 ng/ml, in 63% (45/72) with PSA of 2 to 5 ng/ml, and in 87% (26/30) with PSA of > 5 ng/ml.

Local relapse was detected in 51% (62/121) patients: prostate bed (n=11), prostate bed and pelvic lymph nodes (n=7), pelvic lymph nodes (n=44). Distant metastases were identified in 28% (34/121) cases: bone (n=23), extrapelvic lymph nodes (n=9), lymph nodes and lungs (n=1), bone and lungs (n=1). Both local and distant metastases were diagnosed in 21% (25/121) cases: regional lymph nodes and bone lesions (n=11), regional and extrapelvic lymph nodes (n=9), regional and extrapelvic lymph nodes and bone (n=5).

Lymph node metastases were detected in 38% (86/217) of all patients included in the analysis, of which 28% (24/86) had lesions in lymph node of normal size (median 7 mm).

Of all PET-positive patients bone metastases were detected in 33% (40/121), of which 60% (24/40) had isolated skeletal involvement. Importantly, that 27% (11/40) of PET-positive patients with bone metastases had no structural abnormalities on CT images (CT-negative cases), corresponding to isolated involvement of bone marrow. And half of these CT-negative patients (5/11) had single lesions. The mean PSA value in patients with revealed bone metastases was 5.0±3.7 (0.4–13.6) ng/ml, median – 3.8 ng/ml.

11C-Choline PET/CT revealed oligometastatic PCa recurrence in 38% (82/217) of all patients, of which 62% (51/82) had local relapse only. Distant oligometastatic lesions were detected in 38% (31/82), of which 13% (4/31) were presented by normal-size lymph nodes and 19% (6/31) – by early bone marrow metastases.

Conclusion: 11C-Choline PET/CT has been shown to be a single noninvasive accurate technique for detection of recurrent PCa in patients with rising PSA after radical treatment, which allows to differentiate patients with local and distant metastases in one study, as well as identify oligometastatic process, and therefore is useful in determining the further personalized therapeutic approach.

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ELECTROCARDIOGRAPHIC AND ELECTROPHYSIOLOGICAL TRIGGERS OF ATRIAL FIBRILLATION IN COMBINATION WITH CORONARY ARTERY DISEASE AND SUBCLINICAL THYROTOXICOSIS

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In recent years, there has been a trend towards growth and rejuvenation of patients with atrial fibrillation (AF) [1]. In this regard, the diagnosis and treatment of this disease have acquired medical and social significance.

AF is often associated with thyroid pathology, which affects its course and prognosis [2]. Given the importance of thyroid hormones in the regulation of the cardiovascular system, it can be assumed that functional disorders of the thyroid system can trigger the occurrence of cardiac arrhythmias [3].

The presence of concomitant thyroid pathology in the patient with coronary artery disease (CAD) increases the risk of the onset and progression of AF, reduces the quality of life and the prognosis [4]. According to available data, the symptomatic and asymptomatic course of AF also differs [5-6]. Despite this, the triggering factors of atrial fibrillation in this group of patients have not been described in detail so far.

The purpose was to evaluate the electrocardiographic and electrophysiological triggering factors of asymptomatic and symptomatic atrial fibrillation in the combination of CAD with subclinical thyrotoxicosis (ST).

We examined 202 patients with paroxysms of symptomatic and asymptomatic atrial fibrillation (AF), some of whom suffered from coronary artery disease (CAD) and subclinical thyrotoxicosis (ST). Healthy individuals acted as a comparison group.

It was revealed that in all studied groups, extrasystoles and paroxysms of reciprocal atrioventricular orthodortic and nodal tachycardia was the role of the triggering factors of AF. In patients with ST without CAD and in healthy persons, the paroxysms of tachycardia are short and unstable. When CAD combined with ST, the number of extrasystoles and AF paroxysms is significantly higher than only in ST and in healthy individuals. It was found that in patients with asymptomatic AF the total number of extrasystoles and paroxysms of tachycardia is greater than in the case of symptomatic. Thus, the identification of concomitant subclinical thyrotoxicosis in a patient with CAD should alert the clinician to the development and progression of atrial fibrillation. It should be given great attention to screening thyroid pathology in patients with CAD.

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DATA ANALYSIS AND FEATURE ENGINEERING ON OCT IMAGES OF SKIN CANCER

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Skin cancer is a result of uncontrolled growth of abnormal skin cells. Basal Cell Carcinoma (BCC) is the most common cancer in humans. Over one million new cases of BCC are diagnosed in the U.S. each year. Malignant Melanoma (MM) is a cancer that develops in melanocytes, the pigment cells presented in the skin. It can be more dangerous than other forms of skin cancer because it may spread to other parts of the body (metastasis) and causes serious illness and death.

The need for more objective and quantitative methods to support the diagnosis is a priority for physicians, biologists, physicists, and engineers. Many new optical imaging and spectroscopic techniques have been developed in order to answer to this demand. Optical techniques can provide noninvasive, low-cost methods for a variety of applications. Optical Coherence Tomography (OCT) is a good solution to study optically heterogeneous medium with a micron resolution. OCT provides the advantage of real-time, *in vivo* imaging of suspicious lesions without having to proceed directly to a tissue biopsy.

The post-processing software techniques can be used for improving the precision of diagnostics and providing solutions to overcome limitations for OCT. Image processing can include noise filtration and evaluation of textural, geometric, morphological, spectral, statistic and other features [1]. The main idea of this investigation is using information received from feature engineering on 2D- and 3D-OCT images for building effective classifiers to differentiate skin tumors. The many different methods as decision trees, regression, Fisher discriminant analysis and others have been utilized.

Table 1. The quantity of 2D/3D OCT images/species in data collection

Tissue	BCC	Healthy	MM	Nevus
Quantity(images/species)	229/10	229/10	229/11	229/4

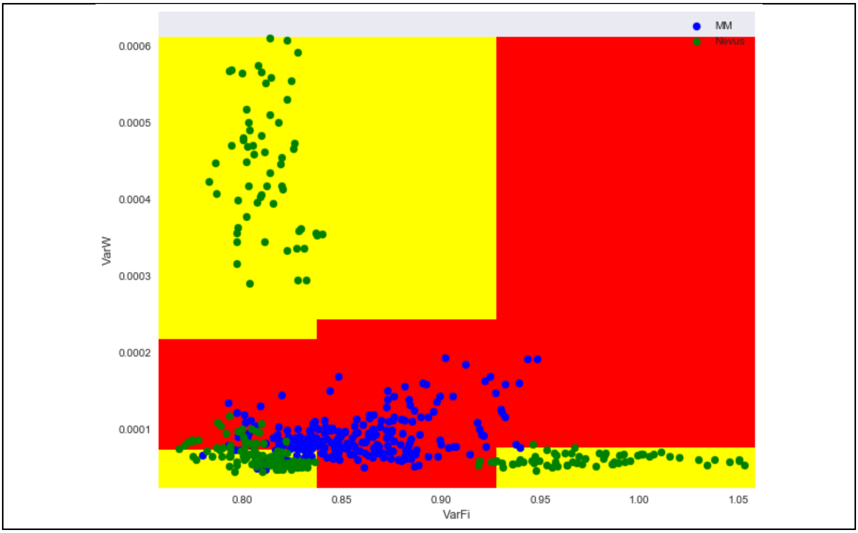

Fig.1. Decision tree classifier (depth=3) for MM – Nevus case (MM – blue, nevus – green points) using complex directional fields [2] features (X – variance of directional field, Y – variance of weight function). Red – area of predicted MM, yellow – area of predicted nevus. Accuracy for decision tree classifiers (the best depth is 5) from 83% to 90% on holdout and cross-validation with 5 folds

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POSSIBILITIES OF LASER SPECTROSCOPY METHODS FOR PREDICTION OF THE RADIOTHERAPY RESULTS

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Statistical analysis of malignant neoplasms in Russia has shown that more than 11,000 people fall ill with squamous cell carcinoma of the oral mucosa per year, and the mortality rate due to this pathology in the first year from the moment of diagnosis is about 45% [1]. The main reasons for this low survival are the resistance of tumor cells to different types of therapy and the use of standard treatment methods which do not take into account individual tumor reactions to the treatment. It has been established that the multiple drug resistance (MDR) of malignant neoplasms is one of the main reasons for their progression. Tumor cells are able to acquire MDR in response to many effects including therapy [2].

The effectiveness of photodynamic therapy (PDT) is determined, mainly, by the activity of cells' consumption of photosensitizer (PS) and the oxygen status of the tumor. The mechanisms linking MDR and the photosensitizer's uptake by tumor cells have already been described [3]. The question remains whether the fluorescence of exogenous fluorophores in the tumor and its oxygen status could also predict the radiotherapy (RT) efficiency.

In a pilot experiment (N=7), tumors of the oropharyngeal zone at stage II-III exposed to RT were investigated. Dynamic Multifractioning Schedule (DMS) of the radiation doze was applied. The total radiation dose was 60 Gy (120 units of TDF). The studies were performed before treatment, after reaching the total radiation dose of 10.8 Gy, of 34.8 Gy and after interruption in the middle of the RT course. A photosensitizer "Radahlorin" was intravenously injected 2 hours before the measurements. Fluorescence was excited at the wavelength of λ_e = 635 nm. The tumor area and the intact area were studied using laser diagnostic system LAKK-M. The mean value of blood perfusion index (I_m) for the measurement period (about 10-15sec), the mean value of functional tissue saturation of the oxyhemoglobin fraction in the mixed peripheral blood (S_tO_2), the mean value of relative volume (V_b) of hemoglobin fractions, and fluorescence intensity at wavelength λ_f = 690nm were evaluated. Based on the registered parameters, the previously developed diagnostic criteria DC [4] reflecting the oxygen status of tissue were calculated for each measurement. The obtained data were compared with the clinical observations of the treatment results.

The obtained data showed that the value of DC after interruption in the RT course, normalized to the initial once correlated with the observed volume of the residual tumor. Analysis of fluorescence spectra has shown that the fluorescence intensity of the tumor at the wavelength λ_f not always exceeds intact once. However, this parameter does not fully reflect the ability of the tumor to accumulate the FS. The tissue's optical properties, the power of the laser irradiance et al affect the result spectra. This in turn confirms the need for the development of algorithms for estimating the content of the FS in tissues. Perhaps, the introduction of some complex criteria, reflecting both the ability of the tumor to accumulate the FS, and its oxygen status, will allow the development of personalized treatment regimens for oncological diseases.

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SPECIFIC ABSORPTION RATE OF FRACTAL-LIKE AGGREGATES OF MAGNETIC NANOPATICLES

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A specific absorption rate (SAR) of fractal-like assemblies of iron oxide nanoparticles in alternating magnetic field has been calculated using Landau-Lifshitz stochastic equation [1] which simultaneously takes into account both the presence of thermal fluctuations of the nanoparticle magnetic moments, and magneto-dipole interaction between the nanoparticles of the clusters. Fig. 1 shows the structures of CC and PC types of fractal clusters created using Filippov's et. al. algorithm [2]. The number of the nanoparticles in the clusters $N_p = k_f\left(R_g/a\right)^{D_f}$, where R_g is the radius of cluster gyration, a is the nanoparticle radius.

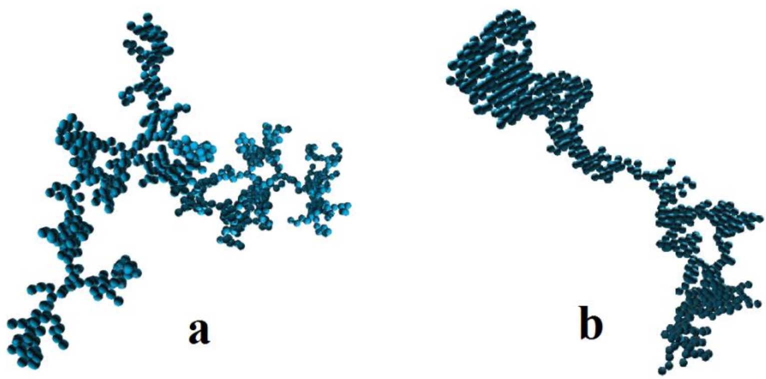

Fig.1. The structures of fractal aggregates of CC (a) and PC (b) types with fractal parameters D_f = 1.9, k_f = 1.7, and nanoparticles number N_p = 640.

The fractal dimension and pre-exponent of the clusters created were fixed at D_f = 1.9, k_f = 1.7, the number of the nanoparticles varied within the range N_p = 192 – 1280. The low frequency hysteresis loops at a frequency f = 300 kHz and magnetic field amplitude H_0 = 100 Oe were averaged over several, 20 – 30, independent cluster realizations.

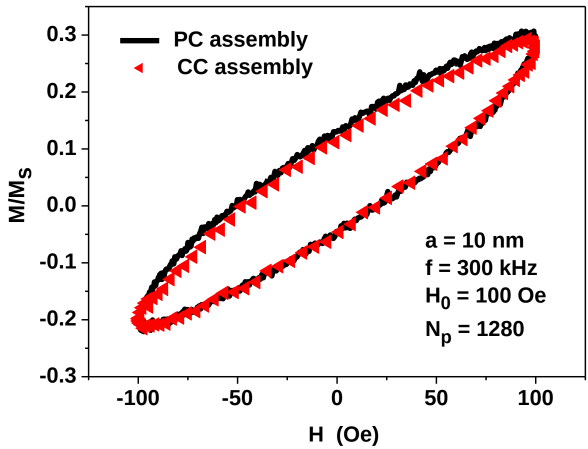

Fig. 2. Low frequency hysteresis loops of dilute assemblies of fractal clusters of PC and CC types.

As Fig. 2 shows, there is no appreciable difference in the hysteresis properties of fractal clusters of both types considered. It is also found that the SAR of dilute assemblies of fractal clusters of nanoparticles shows only weak dependence on the number of the nanoparticles within the clusters.

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SODIUM-23 MAGNETIC RESONANCE IMAGING

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Sodium is a vital component in the human organism. It is an important electrolyte that helps maintain the homeostasis of the organism through the osmo- and pH-regulation [1]. Sodium is a crucial element in cell physiology, which regulates the transmembrane electrochemical gradient and so participates in heart activity, the transmission of nerve impulses and muscle contractions. Sodium concentration (intracellular 10–15 mM and extracellular 140–150 mM) is very sensitive to changes in tissue metabolic state and to disruption of cell membrane integrity. In many pathological states, the sodium concentration increase is detected.

The sodium flux in and out of cells may occur by different mechanisms: voltage- and ligand-gated Na^+ channels, Na^+/Ca^{2+} exchangers, Na^+/H^+ exchangers, Na^+/HCO_3^- cotransporters, $Na^+/K^+/2Cl^-$ cotransporters, Na^+/Mg^+ exchangers and Na^+/K^+-ATPase [2].

The natural abundance of NMR-active isotope ^{23}Na is 100%. The gyromagnetic ratio of sodium nucleus is 11.26 MHz/T. Its Larmor frequency is ~5% larger than the one of ^{13}C, and ~26% of the ^{1}H frequency. ^{23}Na has spin 3/2 and thus has nuclear quadrupolar moment. The NMR sensitivity of sodium is 9.2% of the proton sensitivity, and the sodium concentration *in vivo* is ~2000 times lower than the hydrogen concentration. Therefore ^{23}Na MRI has SNR which is $(3–20)\times10^3$ times lower than ^{1}H MRI SNR. The interaction of the nuclear quadrupolar moment with the electric field gradients generated by the electronic environment of the nucleus results in a biexponential T_2 relaxation in biological tissues. A short T_2 component $T_{2,fast}$ = 0.5–5 ms gives 60% of the MR signal, while a long T_2 component $T_{2,slow}$ = 15–30 ms corresponds to 40% of the signal. It is necessary to apply pulse sequences with ultrashort echo time in order to detect both T_2 components [3].

To our knowledge, we are the beginners in ^{23}Na MR spectroscopy (MRS) and MRI in Russia. The problem which is being considered by our group now is to make an optimal protocol of ^{23}Na MR study for small animals (rat, mouse) on 7T MR scanner Bruker Biospec 70/30 USR. We made 14 phantoms with different concentrations of NaCl (0.05, 0.1, 0.14 and 5.3 M) and gelatine (0, 1, 2 and 4%). Distillated water was used as a solvent in all cases. Each phantom was enclosed in a plastic vial with the volume 14 ml. The protocol of study comprises two parts: proton and sodium. The first one consists of shimming and localizing. The ^{23}Na part includes obtaining of ^{23}Na MR spectrum and image. The FID signal for ^{23}Na MRS was acquired with a 90° single pulse of duration 90 μs. The linewidth of ^{23}Na peaks is in the range from 35 to 45 Hz. 3D FLASH method is applied for ^{23}Na MRI with the following parameters: TR/TE = 10/3.8 ms, FA = 30°, FOV = 6×4×4 cm, MTX = 64×64×8. We used RARE-VTR and MSME pulse sequences to measure T_1 and T_2 values. Sodium nuclei excitation and signal reception were implemented by means of a radiofrequency surface coil with 2 cm internal diameter. The ^{23}Na coil is a modified proprietary transceiver coil T6614 originally tuned to the ^{13}C frequency.

Sodium MRI is a quantitative *in vivo* method allowing to estimate cell integrity and tissue viability. Examples of clinical application include cerebral stroke, brain and breast tumors, cardiac infarction, Alzheimer's disease, multiple sclerosis, hypertension, osteoarthritis, renal failure. The use of ^{23}Na MRI in conjunction with ^{1}H MR techniques will help the diagnosis, prognosis of diseases and treatment outcomes.

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MOBILE HEART MONITORING AND DIAGNOSTICS DEVICE PROTOTYPE

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This paper describes a design of a prototype of mobile heart monitoring system based on the Texas Instruments hardware, such as ADS1298R ECG frontend and CC2541 wireless transceiver System-on-Chip (SoC).

Nowadays, there are various similar systems, such as eMotion ECG Mobile [1], allowing to perform continuous ECG monitoring in real time both at home and at work, CardioQVARK [2] that allows the user to record ECG from his two fingers, and a few other systems.

However, most similar systems have a problem of battery life, which can be partly solved with the help of a competent distribution of available energy resources.

The authors propose to control three parameters: amplitude of the excitation signal, gain coefficient and transmitting power [3].

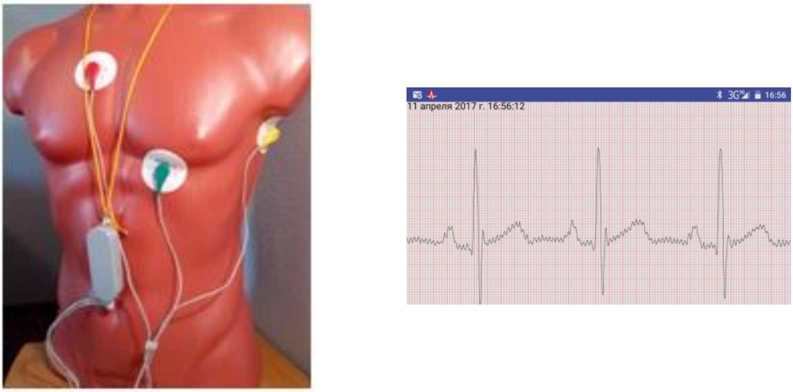
In terms of energy consumption, the gain coefficient should be as small as possible, but to exclude complex filters and amplifiers from the construction of the device it is necessary to provide the maximal gain using the existing software. The current consumption is increased significantly with the increasing gain. The choice of operation mode will depend on the value of threshold criterion of overall efficiency.

Another important parameter is the power of the transceiver. The authors propose to reduce it depending on the distance to the receiver in which the smartphone acts. This functionality is provided by the built-in capabilities of the SoC CC2541 and the control application on the smartphone which can measure the data loss to adjust the transmitting power.

Table 1. The power of the transceiver depending on the distance to the receiver

Distance	Less than 1 meter	From 1 to 5 meters	More than 5 meters
TX Power	-23 dBm	-6 dBm	0 dBm

The proposed prototype could be a base for implementation of ECG analysis, physical activity monitoring and electrical activities of the heart analysis algorithms, and could play a role of ECG data collecting element in other projects concerned with mobile ECG data analysis.



a) b)

Fig.1. The ECG data collecting prototype (a) and control software (b)

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OPTICAL PROPERTIES OF COMPLEX CORE-MULTISHELL QUANTUM DOTS

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Colloidal quantum dots (QDs) have gained enormous success in biomedical applications [1]. Several approaches to preparation of these fluorescent nanomaterials with a quantum yield close to 100% have been advanced in the past decade, with the core-multishell (MS) concept of QD structure developed by our group attracting significant attention [2]. The "core-MS" concept relies on strong confinement of charge carriers due to the strictly monolayer (ML) thickness of each shell layer ensuring the highest confinement potential created by each layer.

In this study, we present detailed analysis of the optical properties of core-MS QDs where the total number of shell layers varied from 3 to 7 MLs. The QD samples were synthesized by the previously reported method using a modified SILAR procedure and exact calculation of precursor quantities required for deposition of every single ML. The schematic representation and fundamental optical properties of the core-MS QDs are illustrated by Fig. 1. During the synthesis of each type of core-MS QDs, the deposition of the first CdS interlayer provoked a strong redshift of the absorbance and photoluminescence (PL) maxima, which is evidence of exciton wavefunction leakage into the shell. On the other hand, in QDs with 5- to 7-ML MSs, the deposition of the second and third CdS interlayers did not lead to a noticeable redshift of either absorbance or PL bands. This could be interpreted by assuming that the exciton wavefuctions are localized only in the inner shell space of the multishell structure, i.e., inside the first three ZnS-CdS-ZnS layers.

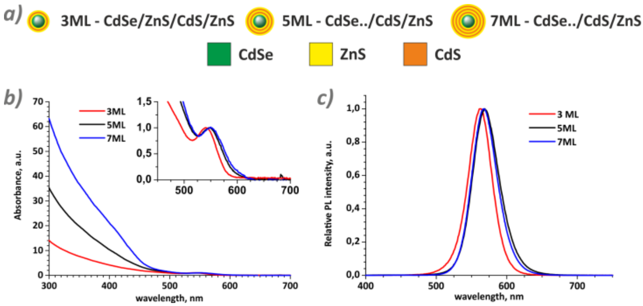

Fig. 1. "Anatomy" and optical properties of core-MS QDs. Schematic representation of core-MS QDs (a) and their absorbance (b) and fluorescence (c) spectra for with 3 (red), 5 (black) and 7 (blue) MS MLs.

The study of PL kinetics revealed another important feature of core-MS QDs. The sample with a 3-ML MS exhibited a single-exponential fluorescence decay with a lifetime of 24 ns upon excitation at 532 nm, while the fluorescence of the samples with 5- and 7-ML MSs had a single-exponential decay with a lifetime of 29 ns upon 532 nm excitation. Although the latter QDs had longer fluorescence lifetimes, their PL quantum yields were lower than that of the 3-ML core-MS QDs. This difference in PL kinetics could be explained by the existence of an alternative excitation mechanism in thick-shell samples. We suppose that infra-dot FRET excitation of the CdSe core by the outer CdS interlayer, or direct excited charge carrier transfer might underlie this discrepancy.

Acknowledgements. This study was supported by the Ministry of Education and Science of the Russian Federation, grant no. 14.587.21.0039 (ID RFMEFI58717X0039).

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LOW-COHERENT INTERFEROMETRY APPLIED TO *DAPHNIA MAGNA* HEARTBEAT COUNTING AND CONTRAST ENHANCEMENT IN RADIOBIOLOGY AND BIOMEDICINE

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Daphnia magna is a semi-transparent crustacean. *D. magna* is widely used as a key model in the field of radiobiology and ecotoxicology where low-doses and concentration long-term effects are analyzed. The heart rate of *Daphnia* is mainly studied in screening of pharmaceutical substances at the stage of pre-clinical drug trial. A number of highly advanced HR counting techniques have been proposed in time and frequency domains. Video sequence of the daphnia heart beating obtained by a high speed camera was processed manually [1] in slow motion. Video segmentation has been proposed to automate HR counting [2]. Doppler OCT has been applied to obtain HRV and spatio-temporal heart shape variation of *Drosophila* [3]. Here we show that low-coherent interferometry can be applied to enchase daphnia HR imaging.

Daphnia heart rate was determined by means of image correlation. A video sequence of a magnified 20x microscope image of daphnia was recorded at 100 fps rate. The segment with the heart occupied the region of about 250x250 pixels, 12 bit each. Maxima of the correlation indicate heart's return to its original position. The spectrum of the signal gives the average heart rate frequency. The accuracy of the method is about 0.1 Hz. *Daphnia* heart rhythm was also measured in terms of the toxicity of the environment. Ten-second measurements were carried out each 1.5 minute. The heartbeat rate might vary in time. We applied windowed Fourier transform (S-transform) to track these changes. The change of the fundamental frequency of the cardiac rhythm and moments of heart-failure are shown in figure 1. *Daphnia* heartbeat was also observed using low-coherence interferometry. A sample object O − *Daphnia magna* − is placed into one arm of Mach-Zehnder interferometer and is illuminated by supercontinuum source.

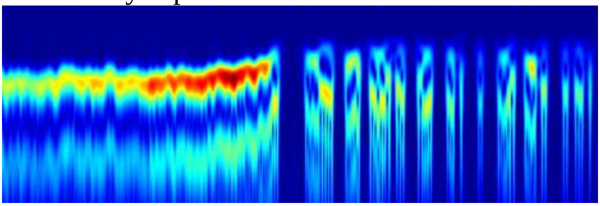

Fig.1. *Daphnia* heart rate. Frequency (Hz) vs time (min) representation. Temporal heartbeat failure

We used NIR radiation range (0.7 − 1μ) because illumination in the VIS range leads to noticeable speckling. A mircoobjective MO projects an enlarged image of the object onto the camera's cmos sensor. The other arm includes another MO to form a reference wave of the same curvature and a corner reflector CR based on a PZT, which is used to set zero path length difference. The obtained results will be illustrate. The latter reveals the contours of the heart with higher contrast. The absence of speckling in NIR range seems promising for extending this study from low-coherent interferometry to hyperspectral digital holography [4, 5] in order to obtain temporal-volumetric information of the daphnia heartbeat.

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THE DEVELOPMENT OF METHODOLOGY FOR ANALYSIS OF FORMIC ACID ANALYSIS IN PHARMACEUTICAL SUBSTANCES BY METHOD OF GAS CHROMATOGRAPHY

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In the production of medicines, it is necessary to control the content of extraneous impurities and residual solvents in pharmaceutical substances. Volatile thermostable impurities and solvents are usually analyzed by method of gas chromatography (GLC). The most common and universal detector in gas chromatography is the flame ionization detector, which has the greatest versatility in combination with speed response sensibility [1]. Most of the techniques in the Russian and foreign pharmacopoeias have been registered and certified just for a flame ionization detector.

However, some impurities are poorly recorded by FID. Seeing the principle of FID operation is the ionization of intermediate species during the combustion of matter, a hypo sensitivity is observed with respect to those substances that have already "burnt out", i.e. highly oxidized molecules such as trifluoroacetic acid, trichloroacetic acid, carbon tetrachloride, trifluoroacetic anhydride, formic acid. An additional disadvantage in the determination of acids is their high polarity (wide peaks). Formic acid is thermally unstable.

There are many methods for determining formic acid after derivatization (conversion into less polar and thermostable derivatives) in gas chromatography [2]. However, they use either mass-spectrometric detection or an Headspace Sampler (HSS). Headspace Sampler often does not allow obtaining the convergence of results required by pharmacopoeias, and mass spectrometry has not yet become a widespread method. The main task is to develop a simple and reliable method for determining formic acid, without going beyond the equipment available in conventional factory laboratories.

In the course of the work, various parameters of convergence and reproducibility, satisfactory sensitivity and selectivity were obtained, and a catalytic system for derivatizing , ensuring the required reproducibility, unattainable when using a headspace sampler, was selected. Thus, we solved the problem of quantitative analysis of formic acid in pharmaceutical substations with limit of quantitative definitions 0.005% and mean square deviation 5% on conventional equipment of analytical laboratories.

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NONTHERMAL PLASMA-JET FOR BIOMEDICAL APPLICATIONS

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The problem of the acquired resistance of bacteria and parasites to antibiotics is already taking dangerous scale. It was discussed at the 71st session of United Nations General Assembly in September 2016. For this reason, the development of medical drug-free treatment methods (excluding the using of antibiotics) is a very important research problem in modern medicine and veterinary.

One of perspective medical drug-free methods of septic wound cure is a treatment of disease site by flow of gas-discharge plasma with low gas temperature. Gas-discharge plasma is used in medicine last 15 years; there are plasma coagulators and plasma scalpels, but it can't use for therapy. Low-temperature plasma jet generates ozone, charged particles (electrons and ions), nitrogen- and oxygen-containing radicals, UV radiation (200-300 nm of range), so it can destroy the membranes of pathogenic microorganisms without damage to human cells. Therefore low-temperature plasma treatment is not specific, meaning the absence of acquired tolerance of the pathogens [1].

Only flow of plasma with a low-temperature of gas in the torch (less than 40°C) can use for painless therapy. Plasma of such type named as nonthermal. Main problem of development of nonthermal plasma jet sources is achievement of low of gas temperature at low working gas flow rate. Moreover these conditions must provide in closed current circuit without any sensitive current leakage to body.

Authors of works [2-3] achieved high efficiency of excimer DBD lamps due to feeding of discharge by short pulsed voltage. A sine-voltage power supply or other long pulse one has long current pulses that lead to the discharge contraction and increasing of gas temperature in discharge channel. The gas discharge contraction can be limited by the use of short duration current pulses followed by long pauses allowing plasma relaxation.

A result of investigation of atmospheric pressure helium plasma-jet excited by capacitive, one- or two-barrier discharges at various method of excitation is presented. Homogenous discharge of plasma jet and 34°C of gas temperature at helium flow 0.5L/min was achieved at short pulsed voltage excitation.

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USE OF PHYSICOCHEMICAL METHOD FOR EVALUATION OF MUCILAGE PRODUCING ABILITY OF THE *LINUM USITATISSIMUM L.* SEEDS

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In the modern medicine of many European [1-3] countries flax is used as a medicament with a wide range of use. Wholesome effect of flax seeds is determined by the large amount of enveloping substances (mucilage – up to 10% and glycoside linamarin). Flaxseed polysaccharides also possess anti-inflammatory effect. In literature data on intervarietal variability of mucilage producing ability is limited [4-5]. Therefore, its complex study based on physicochemical characteristics of seeds is especially relevant. Comparative evaluation of mucilage producing ability of flax varieties with different morphotypes was aim of work. The research of micromorphological characteristics of seed coat and mucilage production dynamics was carried out and it was established that mucilage producing cells are localized predominantly in the external layer of seed coat.

It was established that Bahmalskiy, Nebesnyy, Kustanayskiy yantar varieties possess the highest level of mucilage production. Morphotype and varietal specificity of mucilage production are determined, consequently it can be used as a marker feature of *L. usitatissimum* new forms. The proposed technique is based on the determination of seed physicochemical characteristics and can be used for express analysis of the vegetal samples and their differentiation by the directions of use: as a fatty oil or mucilage-containing raw material.

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EFFECTS OF LOW AND SUBLETHAL DOSES OF γ-RADIATION ON ADIPOSE MESENCHYMAL STROMAL CELLS

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In radiation oncology adipose mesenchymal stromal cells (AdMSCs) systemic cell therapy has shown significant restoration and improvement of radiation therapy induced normal tissue injury. MSC cultures contain subpopulations of mesenchymal stem cells and committed progenitors that can differentiate into mesodermal derivatives: adipocytes, chondrocytes, and osteocytes. Investigation of stem cells compartment is based on the unique dye efflux properties of stem cells. This subpopulation is called side population (SP), when analyzed by flow cytometry. SP proliferation rates can be increased to replenish cell population after insults such as cytotoxic agents exposure or irradiation.

The aim of this work was to investigate the sensitivity of mouse AdMSCs to low and sublethal doses of γ-radiation and to study the effects of low doses on these cells. Cells were exposed to γ-radiation at the doses of 0,1 to 8 Gy at a dose rate of 0,1 Gy/min (^{60}Co). Cell survival was assessed by counting living cells after staining with trypan blue in the Goryaev's chamber. SP fraction was measured by flow cytometry after incubation with rhodamine123. For CFU assay samples were stained with crystal violet and colonies of more than 50 cells were counted. Staining with Oil Red O was performed to confirm adipose differentiation. The ability of AdMSCs to differentiate to adipocytes was not inhibited after exposure to doses of 0,1 to 6 Gy. At the same time clonogenic activity of AdMSCs was dramatically reduced 2 week after irradiation at all doses, including 0,1 Gy. The maximum decrease in the cell number was observed on the seventh day after irradiation, but two weeks later cell number increased in case AdMSCs were irradiated at doses of 0,1 - 1 Gy; however, the cell number remained lower than in non-irradiated controls. The size of SP fraction increased one week after exposure at doses ranging from 1 to 10 Gy, but at the dose of 0,1 Gy it remained identical to the non-irradiated control. At the same time, the size of SP fraction significantly decreased two weeks after radiation exposure at the doses ranging from 0,1 to 1 Gy, but increased reliably at the dose 8 Gy as expected. The relationship between the cell number and the size of SP fraction suggests that SP fraction may be enriched for radioresistant AdMSCs, which are involved in replenishment of general population of cells after radiation exposure.

Thus, the stimulation of cell proliferation after γ-irradiation at low doses is accompanied by the redistribution of distinct cell subpopulations: the decrease in the SP fraction and the increase in the general population of cells were observed. AdMSCs possess a time-dependent repopulation, stable multi-lineage differentiation capacity and clonogenic activity. So the AdMSCs can be reliable candidates for cell therapy in radiation oncology regenerative medicine.

THE RELATIONSHIP AND LOCATION OF THE MAJOR COMPONENTS OF FIBER-OPTIC RATE SENSOR AND PARAMETERS OF THE LIQUID FLOWS IN LIFE SUPPORT SYSTEMS

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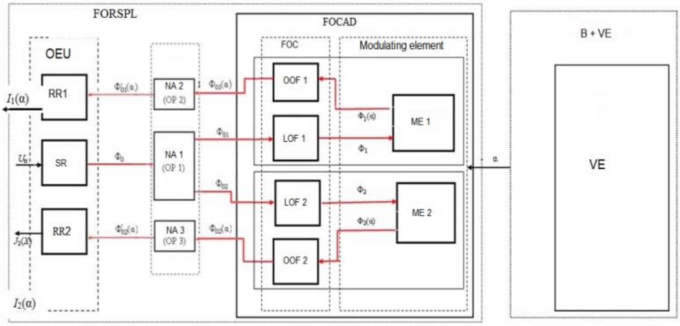
In the article [1] is discussed fiber-optic rate sensor and the parameters of the liquid (FORSPL). The problem of control of fluid parameters such as fluid pressure, flow and volume existed for a long time, but with the advent of new, modern high-tech sensors and monitoring systems, it was partially solved. At the same time, the need for obtaining the most reliable information on these parameters, the search for new structural and technological solutions by which the installation and operation of the sensor will be the most simple and convenient, still exists.

At this point in life-support systems there is a need of improvement of existing means of measurement of parameters of liquid media.

During the carried-out analysis of existing principles, we can conclude that in hydropower systems, it is advisable to use fiber-optic flowmeters because first of all it concerns electrical and fire safety, environmental impact, ease of installation and ease of maintenance, lack of effects of saturation and hysteresis in case of short circuits on power lines and electrical equipment. In addition, fiber-optic Converter allows you to make measurements without any additional energy consumption from the line while current measurement using conventional transducers leads to electrical energy losses (by some estimates, a total of up to 5%). A key feature of the fiber optic Converter is the submission of initial information about the measured current into digital form. This fact allows additional transformations to collect, process, store and transmit information at any distance in real time. Not less important feature of the fiber optic Converter is the extremely high degree of noise immunity its sensitive element [2].

Consider a block diagram of a fiber optic sensor liquid flow.

A generalized block diagram of fiber optic flow sensor and fluid parameters is presented in figure 1.



FORSPL - fiber-optic flow sensor and the parameters of the liquid; OIU – optoelectronic unit; RR 1,2 – the radiation receiver 1,2; NA 1,2 – node alignment 1,2; OOF 1,2 – outlet optical fiber 1,2; FOC – fiber-optic cable; LOF 1,2 – lead optical fibre 1,2; ME – modulating element; RE – receptive element, FOCAD – fiber-optic converter of angular displacements, SR - source of radiation, B – bellows.

Fig.1. Structural scheme of the model differential fiber-optic transducer with an optical input and output

The principle of differential FORSPL reflective type, in the General case is the following.

The sensor is simple, robust design, resistant to aggressive environments. The manufacture of the sensor does not require complex technological and adjusting operations for the production of optical parts.

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THE METHODS OF SUBSTRATE FUNCTIONALISATION WITH AGNPS

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Bacterial infections related to dental implants are currently a significant complication. A good way to overcome this challenge is functionalization of implant surface with silver nanoparticles (AgNPs) as antibacterial agent [1].

The aim of this study was to introduce the methods of samples functionalization with AgNPs by dropping method, dip-coating and electrophoretic deposition (EPD). The process of dropping method based on forming of a drop 120 μL of the working solution with the concentration 60 μg mL^{-1} and following drying at 55.5°C. The AgNPs were dispersed in distilled water by ultrasonication. The second method was a dip-coating where the sample was dipped in 5 mL of working solution with the same concentration and keep it at 24 hours with following drying at 55.5°C. The last approach was an EPD in water and ethanol solutions of the PVP coated AgNPs on titanium substrate and hydroxyapatite (HA) coating.

The AgNPs stabilized with polyvinylpyrrolidone (PVP) were synthesized in aqueous solutions with a diameter of the metallic core of 70 ± 20 nm, negative charge of -15 mV and polydispersity index of –0.192, indicating the absence of large agglomerates and presence of a monodisperse system. Dynamic Light Scattering (DLS), Nanoparticle Tracking Analysis (NTA), X-ray diffraction (XRD) and scanning electron microscopy (SEM) have been used to characterize the prepared AgNPs. The concentration of silver was determined by atomic absorption spectroscopy (AAS).

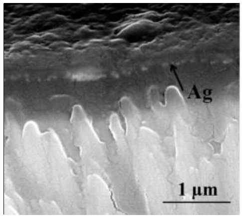

Fig.1. Backscattered electron images of cross sections of the three-layer hydroxyapatite-silver nanoparticles-calcium phosphate coating on titanium.

According the SEM and AAS data the most effective method of surface functionalization was EPD. SEM showed that the AgNPs were evenly distributed over the surface moreover, the particles had a spherical shape. In addition, in case of practical application, the EPD method has the advantage associated with the easy way of deposition process on special structural implants. Three-layer coatings based on HA-AgNPs and calcium phosphates were obtained by combining EPD AgNPs and radiofrequency (RF) magnetron sputtering of nanoparticles of ultra-thin HA coatings. Scanning electron micrographs of the cross section of three-layer coatings with backscattering reflections (BSE) confirmed the multilayer structure (Fig. 1). The XRD data obtained for the PVP-stabilized AgNPs on Ti substrate by EPD method showed the typical peaks of Ag at 2 Theta angles of 44.3° and 77.3° with the coherent scattering region of 14 nm. The similar results of X-ray diffraction analysis were obtained elsewhere [2,3].

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SPECTRAL-OPTICAL PROPERTIES OF NUTRITION COATED OPTICAL FIBERS FOR GLIOMA CELLS GROWTH ORIENTATION

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Brain neoplasms considered to be the most dangerous and difficult to treat tumors due to their anatomical location. It was explored in previous studies [1] if deep-lying brain tumor random proliferation can be controlled by guiding tumor to external surface where malignant cells could be registered and therapeutically affected.

Optical fibers structurally imitating white matter channels and blood vessels seem to be promising for brain tumor cells growth orientation [2]. Moreover, such optical fiber scaffolds are suitable for carrying out subsequent fluorescent diagnosis (FD) and photodynamic therapy (PDT) [3] as they conduct optical signal.

As gelatin is a nutritional medium favorable for cells seeding and growing, the oriented tumor cells proliferation improvement along the scaffolds can be achieved by coating optical fibers with gelatin compound [4]. In this way, current paper introduces the results of spectral-optical properties research of gelatin coated optical fibers.

Experiments were carried out by FD method using the model sample: a brain tissue phantom with photosensitizer (PS) agent addition. Aluminum phthalocyanine nanoparticles (nAlPc) were used as a PS (synthesized by Organic Intermediates & Dyes Institute (NIOPIK), Russia).

Spectral signal was obtained by fiber-optic spectrometer LESA-01 "BIOSPEC" (Russia). The fluorescence was excited by a laser source at a power density of ~ 100 mW / cm^2 and λ = 632.8 nm wavelength, chosen in accordance with nAlPc absorption maximum.

Gelatin coated optical fibers allow obtaining a fluorescent signal with high accuracy, not interfering with phototherapy or photodiagnostics.

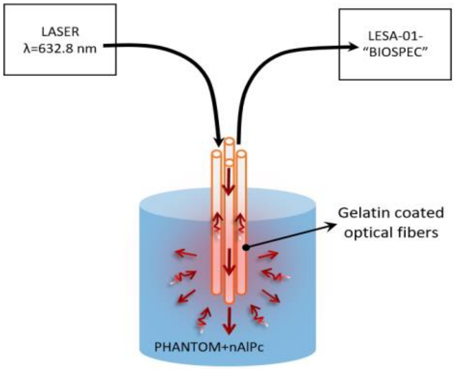

Fig.1. The scheme of experiment in FD mode. (Gelatin coated optical fibers in a brain tissue phantom with nAlPc PS addition)

To sum up, in order to carry out deep-lying tumor phototheranostics by guiding tumor cells to the external surface, further studies of the developed gelatin coated optical fibers in vivo seem to be promising.

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DYNAMIC ^{13}N-AMMONIA STRESS-PET/CT POSSIBILITIES IN THE DETECTION OF FUNCTIONAL SIGNIFICANCE CORONARY ARTERY STENOSES USING ABSOLUTE VALUES OF A MYOCARDIAL BLOOD FLOW AND CORONARY FLOW RESERVE

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Introduction. The unique characteristics of positron emission tomography combined with computed tomography (PET/CT) are the quantification of myocardial blood flow (MBF) and coronary flow reserve (CFR) in absolute terms. Recent results of foreign studies suggests diagnostic accuracy of semiquantitative myocardial perfusion imaging for the detection of hemodynamic significance of coronary stenosis can be improved by integrated application with a quantitative assessment of MBF and CFR. Thus, stress-PET/CT with quantification of myocardial blood flow and coronary flow reserve in absolute terms is a perspective direction in the non-invasive assessment of the hemodynamic significance of coronary stenosis [1-3].

The purpose. The goal of the study was to estimate the possible contribution of the application of MBF in absolute units and CFR for evaluation the functionally significant coronary stenoses in patients with coronary artery disease (CAD).

Material and methods. 63 patients with known CAD underwent ^{13}N-ammonia stress-PET/CT, measurements were performed using a dynamic PET protocol. Dynamic protocol allows to determine the myocardial blood flow both at stress and at rest in absolute units and coronary flow reserve. CFR was defined as the ratio of MBF at stress after adenosinetriphosphate infusion to MBF at rest. Exclusion criteria were coronary artery bypass graft surgery and presence of scar tissue defined by echocardiography or perfusion ^{13}N-ammonia stress-PET/CT. We also analyzed control group with low likelihood of CAD. None of the control subjects had a clinical history or evidence of CAD or other cardiac disease, they had normal invasive coronary arteriograms (stenoses didn't exceed 30%).

Results. We compared two groups of patients with ≥75% (n=36) and <75% (n=27) coronary artery stenoses by invasive coronary angiography (ICA) and group of healthy patients (n=11). When the groups of healthy patients and patients with CAD were compared, significant difference of the MBF at rest was not revealed (p=NS). Whereas the MBF at stress was significantly lower (p<0,001) in group with ≥75% diameter stenoses (1,44 [1,21; 1,85] mL/min per g) compared with group <75% diameter stenoses (2,42 [1,75; 2,89] mL/min/g) and the normal group (2,54 [2,31; 2,86] mL/min/g). Significant difference between stress MBF in patients with <75% diameter stenoses was similar to that in healthy patients (p=NS). CFR was significantly lower (p<0,001) in the group of patients with ≥75% stenoses (1,85 [1,54; 2,31]) in comparison with <75% stenoses group (2,73 [2,19; 3,21]), and also in comparison with the norm group (3,12 [2,75; 3,23]), (p<0,001). Beanlands R.S.B. with et al. [2] presented comparable results in the study: CFR was significantly lower in group with 95-100% coronary stenoses, whereas significant difference between CFR in groups with mild and moderate stenoses (50-69% and 70-94%) was not revealed (2,09±0,47 and 2,02±0,51, respectively, p=NS). Lee J.M. et al. [3] compared the quantitative ^{13}NH3-PET measures between lesions with low and high FFR by ICA. So lesions with FFR≤0,80 showed significantly lower stress MBF than those with high FFR>0,80 (1,71±0,05 versus 2,24±0,05 mL/min/g, p<0,001).

Conclusion. The value of myocardial blood flow at stress and coronary flow reserve is significantly lower in patients with severe coronary artery stenoses in comparison with the patients group with mild and moderate stenoses. The value of myocardial blood flow at rest independently has no diagnostic utility for detection of functional significance of coronary stenoses.

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LECTIN-MODIFIED NANOPARTICLES FOR CANCER CELL TARGETING

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Lectins are proteins that can specifically and reversibly bind to carbohydrates in biopolymers, e.g., glycans in glycoproteins, and this binding can be blocked by specific sugar. The use of lectins as targeting moieties for cancer cells treatment seems very promising since the glycosylation profile of cancer cells can differ from that of normal cells.

Here, we describe the construction of lectin-modified nanoparticles that were used for cancer cell labeling and quantification.

Despite unique intrinsic properties of nanoparticles, their biomedical potential for therapeutic and diagnostic applications can be varied on demand by incorporation into their structures various biomolecules. We have used nanoparticles of different nature – namely, magnetic, magneto-fluorescent and gold nanoparticles for modification with lectins of natural origin (namely, *Wheat Germ Agglutinin* – WGA, *Lens Culinaris Agglutinin* – LCA, lectin from *Canavalia ensiformis* – ConA, and *Soybean Agglutinin* – SBA).

We have synthesized gold (40±5 nm) and magnetic/magneto-fluorescent nanoparticles of magnetite Fe_3O_4 and modified them with the said lectins. The obtained nanoconjugates retained their aggregation and sedimentation stability after the modification. The binding specificity and selectivity of these structures to various glycoproteins have been previously studied in a cell-free system in the immunochromatography format [1]. All types of the obtained conjugates have been demonstrated to be highly specific during the interactions with the selected glycoproteins. For the quantitative investigation of interactions of the obtained structures with cancer cells we have used developed by us highly sensitive method which we called the MPQ-cytometry [2]. We have shown that lectin-modified magnetic nanoparticles specifically and, what is worth noting especially, reversibly bind to eukaryotic cells (structures have been eluted from the surface of living cells with a monosaccharide specific to a certain lectin). Moreover, it was found that conjugates of nanoparticles with WGA can be used for cell lines separation (i.e., Jurkat and 7.16.4 cells). The obtained data were used for the development of new generation theranostic structures, namely, nanoparticle-based biorobots [3]. It has been shown that these structures can perform a full set of Boolean functions and specifically bind to the surface of target cells based on a logical analysis of the molecular microenvironment of cells, thus acting as promising agents of theranostics, simultaneously analyzing several parameters of biochemical information and making a predetermined decision. Moreover, we have shown that lectin-modified fluorescent magnetic nanoparticles can be used for specific cancer cells visualization.

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

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TWO-PHOTON POLYMERIZATION AS A TOOL FOR TISSUE ENGINEERING

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One of the main critical points in tissue engineering is the fabrication of 3D scaffolds. They should ensure necessary mechanical and biological microenvironment and nutrient, oxygen and grow factor delivery to proliferating cells. Modern laser fabrication methods, which provide high accuracy of positioning and energy focusing and allow the precise porous scaffold formation, are interesting. Two-photon polymerization is a promising laser-based technique and permits the use of a large material variety, inc. polymeric, ceramic, and hybrid photoresists. This technique also allows the scaffold fabrication with the possibility of controlling accurately their microarchitecture using CAD models. Moreover, the use of two-photon polymerization in combination with other microfabrication methods can significantly increase the reproduction rate of tailor-made scaffolds and make the application of even more different materials possible. Thus, two-photon polymerization enables the fabrication of tailor-made cell-laden matrices, which can reproduce native tissue structure, and the translation of its use into clinical practice.

SYNTHETIC POLYMER HYDROGELS AS INNOVATION DECISION FOR BIOMEDICAL APPLICATIONS

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Synthetic polymer hydrogels constitute a group of materials, used in numerous biomedical disciplines, and are still developing for new promising applications. The self-healing behavior is a general phenomenon in nature, now is a field of a modern researches of synthetic polymers in which most organisms have the ability to self-heal upon encountering damages. It is highly important for the healed organisms to retain not only the structure, but also primary functionalities. For example, the human skin maintains the ability for sensing the external environment after constant self-repair processes.

For over fifty years hydrogels have been used in numerous biomedical disciplines, in ophthalmology as contact lenses and in surgery as absorbable sutures, as well as in many other areas of clinical practice to cure such illnesses as diabetes mellitus, osteoporosis, asthma, heart diseases and neoplasms. That was synthetic poly-2-hydroxyethyl methacrylate, used - soon after its discovery - in contact lens production. The main advantage of that revolutionary biomaterial was its stability under varying pH, temperature and tonicity conditions. Nowadays, hydrogels are obtained from new materials using the latest techniques to make them safe and non-toxic. The final hydrogel product is present in very advanced applications, e.g. tissue engineering and regeneration, where they can be applied in a non-invasive manner. They can serve in the prevention of thrombosis, post-operative adhesion formation, drug delivery systems, coatings for biosensors. Most often, a hydrogel is considered to be a material made when a water-insoluble polymer absorbs a large amount of water, or else it is simply a water-swollen polymer network. Polymer hydrogels can be of either synthetic or natural origin, homopolymers or copolymer.. Chemical hydrogels may be prepared either by cross-linking water-soluble polymers or by converting hydrophobic polymers into hydrophilic polymers that are then cross-linked to form a network. With such a structure, hydrogels are able to swell, absorbing a large amount of water without the polymer dissolving, which gives them characteristics similar to those of soft tissue. Although the water content in hydrogels may be as little as a few percents or as much as over 99 %, hydrogels retain the properties of solids.

Hydrogels do not disintegrate during swelling thanks to their cross-linked bonds.

Water in hydrogels not only provides a moist environment (important, for example, in wound healing) but also controls the permeation of nutrients into the cells and of cellular products out of the hydrogels. Dried hydrogels can swell in water or saline up to 1000 times their own weight.

It is also common to divide hydrogels into groups by structure: amorphous, semicrystalline, bound by oxygen molecules, with a supermolecular structure, or hydrocolloidal aggregations. Nowadays, hydrogel nanocomposites with mechanical properties superior to those of traditional hydrogels are becoming popular Poly(hydroxyethyl methacrylate) (polyHEMA, PHEMA) is one of the most important and most widely applied hydrogel biomaterials, and has been applied in the production of contact lenses and dressings, and for drug delivery and tissue engineering purposes.   Synthetic polymer hydrogels differ in their characteristics due to various chemical structure, synthesis technique, water content or cross-linking. Moreover, the hydrogel still possesses shape memory abilities after self-healing, and is capable of self-healing during the shape memory performance, which is comparable with natural biomaterials that can retain primary functionalities after constant self-repair processes. Taking advantage of the double network structure and dual non-interfering supramolecular interactions, the science offered a simple and universal approach to construct a mechanical stretchable supramolecular hydrogel with triple shape memory properties, which could broaden the list of shape memory polymers and promote the design and fabrication of novel shape memory systems for a variety of potential biomedical and optical applications. New material returns to its original shape even when cut into pieces.

It is still possible to design new hydrogel fulfilling specific functions for specific needs. A change in chemical composition, or even a change in one of the synthesis factors (cross-linking method, cross-linking agent, synthesis method, conditions of the synthesis) may lead to new intelligent biomaterials.

FLUORESCENCE LIFETIME SPECTROSCOPY FOR IDENTIFICATION OF PITUITARY ADENOMA

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A large number of studies in recent years have been devoted to the search for sensitive, accurate, and fast methods of diagnosing benign and malignant tumors and the limits of tumor growth. Optical methods are currently considered to be the most promising way to solve this problem. It is well known that human tissues contain biomolecules that fluoresce well in the UV, visible, and near-IR regions because they incorporate endogenous chromophores. The latter include tryptophan, tyrosine, dinucleotides, collagen, flavins, lipofuscins, porphyrins, etc. The characteristics of the intrinsic fluorescence of the chromophores depend on their distribution in the tissues, the concentration of ions, the properties of the microenvironment, and other factors. The appearance of a pathological process affects the physicochemical microcharacteristics of the tissues and therefore changes the autofluorescence parameters of the tumors.

The measurements were made on samples of healthy and tumorous tissues of the pituitary taken after an operation carried out at the Republican Research and Clinical Center of Neurology and Neurosurgery, Ministry of Health of the Republic of Belarus. The tissue samples were fixed in 0.9% physiological solution and were investigated a few hours after being taken. The presence of a tumor was estimated macroscopically immediately after taking the sample and microscopically from the results of a histological study. Nineteen tissue samples were investigated, from which there were eight samples of pituitary adenoma and eleven samples of healthy pituitary tissue.

The system for exciting and registration the fluorescence decays includes HORIBA PicoBrite pulsed semiconductor LED (emission wavelengths 342 nm, pulse width at half–height 700 ps, pulse-repetition rate 10 MHz), a SOLAR ML-44 monochromator (inverse linear dispersion 18,7 nm/mm), a Hamamatsu H5773 photomultiplier (wavelengths range 185–820 nm, time resolution 180 ps) and a Becker& Hickl SPC-130 time-correlated single photon-counting module. The fluorescence is excited and recorded via optical fiber probe, which consists of one central optical-fiber for transporting the excitation light from the LED to the tissue and six optical fibers located around the central optical fiber for recording the emission signal.

Our studies showed that the autofluorescence kinetics of the tissues in the spectral range 380–600 nm have two subnanosecond components with lifetimes, respectively, of 0.39–0.53 and 1.9–2.5 ns and a slower nanosecond component with a fluorescence lifetime of 6.9–8.2 ns. The mean lifetimes of the short-lived components are less in tumorous tissue than in healthy tissue, and the mean lifetimes of the slower nanosecond component is about the same in the various objects of investigation. It is found that a significant difference in the mean fluorescence lifetime of tumorous and healthy pituitary tissues is observed and has the highest value of 1.6 ns at emission wavelength 600 nm

Discriminant analysis is used to analyze the data obtained here. Mean fluorescence lifetime at emission wavelengths 380, 400, 420, 440, 460, 480, 500, 520, 540, 560, 580 and 600 nm were selected as discriminant variables. The sensitivity and specificity of the identification of pituitary adenoma, determined by means of discriminant analysis, are 100%.

Rapid and high-sensitivity identification of pituitary adenoma can be carried out by measuring the autofluorescence decays at emission wavelengths 380-600 nm. The method can be improved further by using excitation wavelengths of about 260 nm, which makes it possible to additionally record the UV autofluorescence of tyrosine and tryptophan.

DIRECT INTERACTIONS OF *DROSOPHILA* MUSCLE PROTEINS WITH SPECIFIC REGIONS OF GENOMIC DNA AS A PROSPECTIVE TOOL FOR FINE MANIPULATIONS WITH BIOLOGICAL NANOSCALE OBJECTS

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Human and Drosophila genomic DNA contains natural hot spots of double strand breaks (DSB) named FT (forum termini) [1]. It is known that genomic regions between two neighboring FT contain coordinately expressing genes and molecular mechanism of this coordinated expression still unknown. Apart from ability for specific interaction with nuclear proteins, such as HNRP and PARP [2], we find out that FT regions also possess extremely high affinity to several muscle proteins, including γ-actin and paramyosin B. Previously it was declared that γ-actin is required to organize desmin to crosslink myofibrils for nuclear movement [3] and spindle orientation during mitosis in vertebrates depends on the distribution of actin retraction fibers . Myosin 10 also colocolised with retraction fibers and dynamic actin clouds but it does not modify their dynamics or assembly (Pietro et al., EMBO Rep, 2016). Paramyosin B has ATPase domain homologous to chromosome segregation ATPases. We propose that identified FT-specific muscle proteins probably involved in distant inter- and intrachromosomal interactions characteristic of FT regions [5].

According to our experiments with FT immobilized on paramagnetic particles, muscle proteins are able for direct interactions with specific DNA regions situated in the immediate environment of FT. We speculate that technology based on actin-mediated relocations of DNA can be adopted for precise manipulations with nanoscale biological objects, in particular for controlled gene activation through formation of chromosomal loops connecting enhancer elements with the promoter.

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RETROSPECTIVE LUMINESCENCE DOSIMETRY METHOD USING SINGLE GRAIN TECHNIQUE IN APPLICATION TO INSTRUMENTAL ESTIMATION OF CUMULATED DOSE USING QUARTZ CONTAINING SAMPLES FROM FUKUSHIMA PREFECTURE: FIRST REPORT

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Introduction. As it was published in [1,2] the calculational estimates shows essential values of cumulated doses caused by irradiation of beta-particles from the soil in some high contaminated locations around Fukushima Daiichi nuclear power plant (FDNPP). Despite the lack of information regarding the dose estimations from beta irradiation following the FDNPP accident [1,2,3], this problem is important as far dose from beta particles can contributes to dose in flora and fauna and to human skin. In the presented international study, we conducted the first instrumental estimations of dose profiles in the bricks sampled from contaminated locations around FDNPP using Retrospective Luminescence Dosimetry (RLD) method [4,5]. For this purpose, the single grain OSL method for dose reconstruction using quartz containing samples from Odaka, Minamisoma city, and Maeda, Iitate town, ("witness "of the fallout from Fukushima-1 NPP accident) was applied in order to measure depth-dose profiles in sampled bricks. It was suggested that dose-depth profiles in thin layers of bricks can be useful in order to investigate the input from beta-irradiation or low-energy gamma-irradiation to total beta-gamma dose.

Results.

1.Single grain OSL method for dose reconstruction using quartz containing samples from Odaka, Minami-soma city, and Iitate town ("witness "of the fallout from Fukushima Daiichi nuclear power plant accident) was successfully applied in order to measure depth-dose profiles in sampled bricks. The usage of this method was useful in order to avoid the interfering effect of inclusions in samples of micro-particles of biotite.

2.It was estimated that at the depth in the brick of 5-20 mm from the outer surface the cumulated doses are equal to 25±6 mGy for sample from Minami-soma city and 73±18 mGy for sample from Iitate town (after subtraction of background doses).

3.Comparison of cumulated gamma-dose in the air estimated on the base of the results of single grain OSL measurements in the Minami-soma and Iitate village brick samples with available calculated estimates of cumulated gamma-dose in the air for Iitate village [6] showed that that the results of the comparison of instrumental and calculated estimates are in a good agreement.

4.It was found that at the depth of 3-5 mm the cumulated doses were quite high and equal to 50 mGy and 140 mGy, consequently. Meanwhile gamma-dose at the depth 3-5 mm should be lower as far as there is no electrons equilibrium near the brick surface. It was suggested that the elevated values of cumulated doses at the depth 3-5 mm were presumably caused by irradiation of beta-particles, or low-energy gamma-irradiation.

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RETROSPECTIVE LUMINESCENCE DOSIMETRY TECHNIQUE - PRELIMINARY RESULTS OF THE BETA-DOSE ESTIMATIONS: HIROSHIMA

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Introduction. Retrospective Luminescence Dosimetry (RLD) is currently being used for instrumental retrospective dose estimations in situations of uncontrolled irradiation of population. RLD employs the measurement of thermos - or optical stimulated luminescence (TL or OSL) from quartz crystals extracted from bricks, tile or other ceramic materials sampled in contaminated territories [1,2]. The intensity of this luminescence is proportional to dose of irradiation. This enables the cumulated dose to be measured. One of the possible ways to confirm or not to confirm the essential beta component of irradiation due to residual radioactivity is the analysis of dose-depth profile in surface layers (up to 1-2 mm) of tile samples sampled from the site of irradiation.

The following steps of the study were performed (methods and materials: Measurements of the dose-depth profile in the thin (0.3mm) surface layers of the tile from the Hiroshima University (HU) building, which was a "witness" of Hiroshima A-bombing using OSL single grain (quartz) retrospective dosimetry technique; gamma-irradiation: calculations by Monte Carlo method of the dose-depth profile in the surface layers of HU tile (using the real geometry of the HU building and corresponding gamma spectrum of irradiation); beta irradiation: measurements by TL technique of the dose-depth profile in the "quartz equivalent" Al_2O_3:C crystals ($^{90}Sr/^{90}Y$ source); comparison of dose-depth profiles from beta and gamma irradiations with measured dose-depth profile in HU tile sample.

Conclusions.

1.The observed dose-depth profile in HU tile sample is the result of superposition of two different dose-depth profiles in surface thin layers caused by two kinds of irradiation: contact beta-irradiation and highpenetrating gamma irradiation.

2.It's mean that residual radioactivity was essential following Hirosima A-bombing – as a result of radioactive dust, elevated after the blast. But there were a very small intention to these aspects in DS86 and DS02 as far as main purpose of these Systems was to estimate only the input to irradiation from primary neutrons and gammasafter A-bombing [3].

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CARCINOGENICITY SCREENING OF CHEMICALS USING POSITRON ANNIHILATION SPECTROSCOPY

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Chemical carcinogens are the main cause of cancer. Hundreds of thousands of new chemical compounds are synthesized annually in the world, unknown part of which is carcinogens. New dangerous compounds may enter a human body with water, food, etc., then they dissolve in the aqueous or lipid media, integrate into the biochemical processes inside the cells, violate the mechanisms of self-regulation of cells and lead to their degeneration into malignant tissue. There are several methods, which are currently used for testing the carcinogenicity of chemicals (screening of carcinogens): epidemiological studies; experiments on animals; short-term tests (Ames test); correlation of molecular structure and its biological activity (QSAR - quantitative structure activity relationship); physicochemical methods.

The most reliable data is provided by experiments on animals. However, they are very long and allow testing only a small part of the synthesized substances. The fastest are the physicochemical methods. Available data on luminescence of organic molecules, their electrophilicity etc. indicate that studying particular physical properties of molecules is not enough to conclude about their possible toxicity, mutagenicity and carcinogenicity [1]. However, the complex application of physicochemical methods makes it possible to accelerate and reduce the cost of carcinogen screening significantly.

One of the most effective physicochemical methods is Bakale's method based on the pulsed radiolysis [1]. The criterion of carcinogenicity in this method is the rate constant of the chemical reaction with electrons produced by the nanosecond pulse of ionizing radiation generated by an electron accelerator. It was shown that results of Bakale test with the probability of 80% correlates with the indices of carcinogenic activity, independently established by biological methods. The drawbacks of this method can be attributed to the fact that it is quite complex and requires the use of expensive and large-sized scientific equipment.

We suggest the alternative method of fast carcinogens screening using positron annihilation spectroscopy. This method is based on the two facts: 1) formation of positronium (Ps) atom in a condensed medium proceeds as a result of combination of a thermalized positron with one of the quasi-free electrons of the positron track; 2) carcinogenic substances, being very strong electrophiles, are effective scavengers of quasi-free track electrons. Therefore, the presence of carcinogen significantly reduces Ps formation probability. To measure this probability and predict carcinogenic hazard of the tested substances, one may use standard techniques of positron annihilation spectroscopy [2].

The proposed method also makes it possible to estimate anticarcinogenic properties of chemical compounds by the presence of an anti-inhibition effect of Ps formation [3].

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THE UTILIZATION OF MODERN TECHNOLOGIES OF WIRELESS SENSOR NETWORKS IN MEDICINE

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Nowadays wireless sensor networks are widely used. They are self-organizing networks of a plurality of spatially distributed autonomous sensors and actuators that communicate with each other via a radio channel and serve to collect data on various environmental parameters such as temperature, sound, vibration, pressure, noise level, movement of objects, chemical indicators, etc [1].

Promising is the possibility of their wide application in various fields of medicine, such as outpatient monitoring of health, detection of cancer cells, monitoring of allergens in the air.

The standards of wireless data transmission for wireless networks of sensors, their common features and differences are considered, and also modern technological decisions connected with the collection, storage and analysis of the received data are described in this work [2], [3].

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INTELLECTUAL INFORMATION AND TRAINING SYSTEM FOR DECISION SUPPORT IN THE HISTOLOGICAL DIAGNOSIS OF TUMORS OF THE ESOPHAGUS

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To date, one of the most urgent problems of oncology is the improvement of the quality of early morphological diagnosis of cancer, in particular, cancer of the esophagus. There is no doubt that timely diagnosis is a reserve that will change the situation with the treatment and survival of patients for the better along with other factors. However, this problem (early diagnosis) is complicated by the presence of a large variety of forms of malignant processes, rather complex systems of signs used to verify the morphological diagnosis and their weak formalization. Therefore, the qualification and experience of pathomorphologists participating in the diagnosis is extremely important here, since the final diagnosis is based on the results of the morphological histological research and the tactics of the patient's treatment are determined.

The aim of the work is to create a system of formalizing knowledge in the histological diagnosis of esophageal tumors and systematic transfer of knowledge to less experienced specialists. It is also a system that will provide support in making a decision in a histological diagnosis.

As a result of the analysis of the subject area and the object environment, two main categories of users are identified: pathologist-expert and trained physician, for which Automated Work Places (AWP) should be developed. The AWP of an expert pathomorphologist differs from the trained physician's AWP with the presence of a microscope and a video camera for image input, the shell of the system to form sets of histological signs and their meanings and a list of nosological forms for describing the input images. An expert doctor can work with the archive, with reference books and cases. The inexperienced specialist, in turn, can work with the archive of images, can get consultations and undergo training in various modes.

The conceptual model of an intellectual information-training system for the support of medical decision making in the histological diagnosis of tumors of the esophagus includes: a training system, a knowledge base, an expert system. The modes of operation have been developed: the "Atlas" regimes, the control sample and the training sample. The modes have been successfully tested in the N.N. Blokhin Russian Cancer Research Center with the participation of young specialists. Filling the database of the information and training system with histological images of tumor and precancerous processes in the esophagus was carried out using archival and advisory materials of the N.N. Blokhin Russian Cancer Research Center. According to the conclusions of the expert doctors, the developed information system implements all the necessary functions and capabilities to improve the quality of morphological histological diagnostics and professional development of young specialists.

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CURCUMA LONGA EXTRACT AS A SENSITIZER FOR SINGLET OXYGEN GENERATION

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Photodynamic therapy (PDT) is a promising procedure for destroying cancer cells at this time [1]. PDT employs two components: a photosensitizer whith triplet states and specific wavelength to activate the photosensitizer.

Water solution of the curcuma extract was prepared by dissolving of the extract powder m= 0,0066 g in volume V=10 ml.

The fluorescence spectra and excited state lifetimes of this extract were measured on Fluorolog-3 optical system (Horiba, Japan-France). The fluorescence spectra (fig.1) of curcuma longa are containing two maximum. The location of the first maximum depends on excitation wavelength. The location of second maximum is λ=677 nm. The most intensity peak according to excitation wavelength λ=400 nm. There were calculated a kinetics attenuation curves to get a some knowledge about possibility of singlet oxygen generation in Curcuma solution. The biexponential model was used for experimental curves:

$$\tau = A + B_1 e^{-i/T_1} + B_2 e^{-i/T_2} \qquad (1)$$

The results of kinetic experiments are present in table 1. The excited state lifetime of curcuma extract (λ=677 nm) is τ ≈ 5 ns. We also observed delay fluorescence spectrum at λ=680 nm. It is prove that there are a triplet states.

The luminescence spectrum of singlet oxygen at the excitation wavelength λ = 430 nm is observed in the extract solution.

Table 1. The lifetimes fluorescence of the curcuma longa excitated states

Times, ns	λ_{em}= 500 nm	λ_{em}= 677 nm
T_1	0,86	1,76
T_2	4,96	5,03

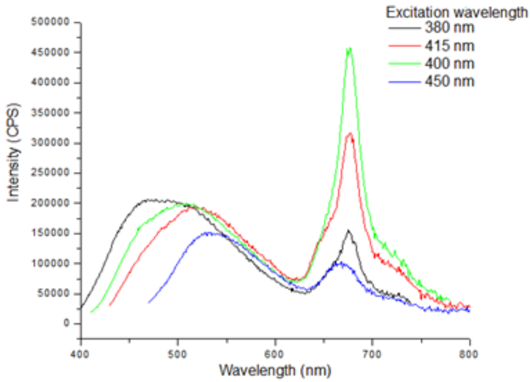

Fig.1. Fluorescence spectrum of curcuma longa water solution

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COMPARATIVE SPECTRAL ANALYSIS OF THE SURFACE OF AORTAL VALVES OF THE HEART OF BARANES BEFORE AND IN THE PROCESS OF THEIR DECELLULARIZATION

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Annotation

Keywords: Raman spectroscopy, Aortic valve, Decellularization.

The problem of treating heart valve diseases in humans is one of the priorities of modern medicine. One of the most radical methods of treatment is the replacement of valves [1] Even though the quality, design and properties of prosthetic heart valves are constantly being improved, they can not be compared in their properties with native valves. Therefore, clinical cardiosurgery needs to create new types of implants and improve the technology of their production. [2]

Objective: to analyze the qualitative composition of the surface of the heart valves using the Raman spectroscopy method before and after performing their decellularization.

Aortic valves of sexually mature rams are used as a research material. Decellularization of the valves was carried out according to the protocols [3,4] in the modification based on the Institute of Experimental Medicine and Biotechnology of SSMU. Stage 1 of decellularization was isolated before enzymatic treatment and stage 2 after it. Samples of biomaterials were stored before the study in phosphate-saline solution with the addition of antibiotics at a temperature of 4 ° C.

When studying the surfaces of aortic valves before and during their decellularization with the help of Raman spectroscopy, it was established that even after the first stage of decellularization, the intensity at the wave numbers 812 cm-1, 1062 cm-1 and 1440 cm-1 corresponding to the phosphodiester RNA ; OSO-3 symmetrical stretching of glycosaminoglycans and chondroitin-6-sulfate; Proteins, lipids. After the completion of the second stage of decellularization, an insignificant decrease in the intensity at a wave number of 1340 cm-1, corresponding to deformation of proteins and nucleic acids (DNA).

Optical coefficients were introduced, in the two-dimensional analysis, the efficiency of the process of decellularization of aortic valves was established. With the introduced optical coefficients, it is possible to monitor the efficiency of the valvular heart valve decellularization process.

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ESTIMATED INPATIENT HOSPITAL STAY IN INDIVIDUAL WARDS. GUIDELINES ON RADIATION SAFETY AFTER RADIOIODINE THERAPY

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Radionuclide therapy safety requirements are regulated by the Russian Radiation Safety Standards (RRSS), which state the maximum allowed radionuclide activity in the body and the equivalent dose rate (EDR) of gamma radiation. Therefore, it is necessary to estimate the time of an inpatient hospital stay in specially designed radionuclide therapy wards. The article presents the findings of individual ^{131}I biokinetics studies in 64 patients admitted to radioiodine therapy of thyrotoxicosis and differentiated thyroid cancer. We developed a method to calculate the time interval to reach the EDR of 20μSv/h and the recommended EDR of 3 and 0.3μSv/h for adults and children, respectively. It is based on the measurement of the ^{131}I excretion constant.

Results and discussions

The dose rate conversion factor K is 53 ± 18 (ε = 33%). The dosimetric method of calculating the $T_{1/2}^{eff}$ has a 15% error regardless of the activity administered. The scintigraphic method with the tracer activity has an 18% error.

The average effective half-life in patients with thyrotoxic disease with therapeutic activity from 0.5 to 1.1GBq is 81 hours, according to scintigraphy, and 79 hours by dosimetry. $T_{1/2}^{eff}$ increases to 99 hours when the tracer activity is introduced.

When the dosimetric method with the administered tracer activity is applied, the $T_{1/2}^{eff}$ error at the therapeutic stage is 23%.

The mean effective half-life of patients with thyroid cancer with therapeutic activity administered from 1.1 to 5.5GBq (2.6 ± 1.5GBq) is 20 hours, according to whole body scintigraphy, and 20 hours, according to dosimetry.

Fig. 1 shows 95% CI time reaching $\dot{D}_{threshold}$ at 20/3/0.3μSv/h interval in relation to the administered activity in thyrotoxicosis and thyroid cancer cases.

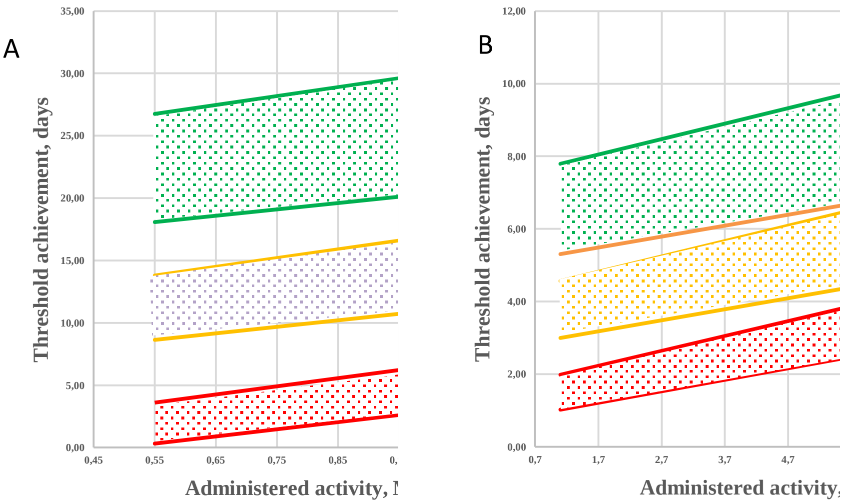

Fig. 95 % CI intervals for $\dot{D}_{threshold}$ (20μSv/h – red, 3μSv/h – yellow, 0.3μSv/h – green) in thyrotoxicosis (A) and thyroid cancer (B) cases.

SPECTRAL STUDIES OF THE MODEL OF OSTEOPOROSIS IN RATS ASSESSING THE EFFECTIVENESS OF TREATMENT WITH HYDROXYAPATITE

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Osteoporosis is a systemic metabolic disease, which is characterized by a decrease in bone density, leading to fractures. This leads to temporary and permanent disability, limited ability to move, loss of self-service and, in general, quality of life, as well as increased mortality, especially of the elderly [1].

The experiment was performed on mature female rats aged 6-9 months and weighing 180-230 g. As the study materials, the femoral bones of rats were used. The animals were divided into three groups. The first group is a group of healthy animals. In the second group, a model of osteoporosis was created by administering cortisone (a hormonal preparation of a steroid form with pronounced high-speed anti-inflammatory, anti-exsessive (anti-edematous), desensitizing (antiallergic) immunosuppressive, anti-shock and antitoxic action). The third group is a group of animals who have performed the model of osteoporosis by administering a cortisone drug followed by a course of treatment with hydroxyapatite powder. The amounts of drugs administered per unit weight of the rat were 10 mg/kg and 40 mg/kg (the second and third groups were divided into two subgroups).

The spectral characteristics of the bones were investigated using a stand that implements the Raman spectroscopy method. The stand included a high-resolution digital spectrometer Shamrock sr-303i with a spectral range of 200-1200 nm, with an integrated cooled camera DV420A-OE, a fiber-optic probe RPB-785 for Raman spectroscopy, combined with the LuxxMaster LML-785.0RB-04 laser module. The wavelength of the laser radiation is 785 nm and the line width is 0.2 nm [2].

Spectral differences between the study groups of the samples (control group, the group with the model of osteoporosis and the group with the model of osteoporosis after treatment with hydroxyapatite) were detected at wave numbers 428 cm^{-1} (phosphate ion PO_4^{3-} (ν2)), 581 cm^{-1} (PO_4^{3-} (ν4)-(P-O deformation vibration)), 854 cm^{-1} (hydroxyproline, C-C vibration), 956 cm^{-1} (phosphate ion PO_4^{3-}(ν1) (P-O symmetric valence)), 1033 cm^{-1} (phenylalanine), 1062 cm^{-1} (CO_3^{2-}(ν1) B-type substitution (C-O planar valence)), 1244 - 1271 $см^{-1}$ (amide III) и 1659 $см^{-1}$ (amide I).

In addition, coefficients were introduced to evaluate the effectiveness of treatment of the model of osteoporosis with cortisone (10 mg/kg) with the help of hydroxyapatite. For the model with cortisone 40 mg/kg, no changes were observed in the treatment of hydroxyapatite, which in this case indicates an ineffective treatment of this model of osteoporosis development. The results of investigations by the Raman spectroscopy method are confirmed by mechanical tests for strength and fracture.

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NANO-TECHNOLOGIES IN THE CREATION OF COMBINED DRUGS FOR THE TREATMENT OF OSTEOPOROSIS

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New compounds and substances obtained with the help of nanotechnology are especially attractive for pharmacology, the main task of which is the search for new effective drugs [1]. Directional transport of drugs to the focus of the pathological process makes it possible to achieve an increase in the effectiveness of the existing drug therapy.

Iron oxide (Fe_3O_4) based on a nano-magnet is a very promising tool for delivering of drugs to pathological cells to control cellular functions, such as adhesion, proliferation, differentiation, etc [2].

The main criterion of magnetic nanoparticles in nanomedicine is superparamagnetism. In the presence of an external magnetic field, magnetic nanoparticles spatially orientated with the direction of the external field. By means of an external magnetic field complexes of magnetic nanoparticles with the pharmaceutical preparats can be spatially orientated with the direction of the external field and sended to the focus of the pathological process. In modern pharmacology the phenomenon of synergistic action of two or more different active substances (preparations) is widely used.

For the application of encapsulating coating we used the method of vacuum thermal evaporation. Treatment of osteoporosis requires a drug therapy aimed at preservation of the existing and the formation of new bone tissue.

The experiments were performed on Wistar male rats (200-250 g), which were divided into 7 groups. In order to obtain a model of osteoporosis, prednisolone was administered intra peritoneally at a dose of 50 mg / kg for 14 days [3]. The effect of the new preparation (sodium fluoride in combination with iron oxide nanoparticles) on the course of osteoporosis in the experimental groups of rats was studied with the introduction:

- of sodium fluoride
- iron oxide nanoparticles
- a combination of sodium fluoride and iron oxide nanoparticles.

In the blood serum of rats total calcium and alkaline phosphatase were determined. The results of the study are presented in the Table 1.

Table 1.Dynamics of biochemical parameters of blood in rats under different conditions

Animal groups	Calcium (mmol/l)	Alkaline phosphatase nmol/(c·l)
Control	2.472±0.080	385±3,1
NaF	2.399±0.323	389±2,9
Fe_2O_3	2.412±0.120	287,1±1,9
NaF + Fe_2O_3	2.647±0.135	269,3± 3,9
Osteoporosis	3.044±0.179	351,1±1,15
Osteoporosis + NaF	2.822±0.037	448,9±4,89
Osteoporosis +Fe_2O_3	2.480±0.105	194±1,23
Osteoporosis + NaF+Fe_2O_3	2.684±0.011	255,7±2,75

As can be seen from the table 1 the treatment of osteoporosis by new preparation testify to their high biomedical activity.

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INFLUENCE OF HBO ON PHOSPHATE METABOLITIS OF THE HUMAN BRAIN

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Introduction Hyperbaric oxygenation (HBO) is a therapeutic method aimed at enriching all cells with oxygen. Many physiological effects of HBO are currently known [1]. However, the biochemical effect of HBO at the cellular level *in vivo* on human metabolism has not been fully studied. The purpose of this work is determination of the effect of HBO on brain metabolism using MRS on ^{31}P nuclei.

Materials and methods 17 healthy subjects participated in the study. Philips Achieva 3.0 T and ^{31}P/^{1}H RF coil were used. Spectroscopic study was carried out twice – before and immediately after a fifty-minute HBO session, and each of them lasted for 15 minutes. The field of view (FOV) of 200×200 mm was divided into individual voxels with a size of 40×40 mm (fig.1.). The slice was localized and spectra were obtained using the Image Selected Invivo Spectroscopy (ISIS) pulse sequence.

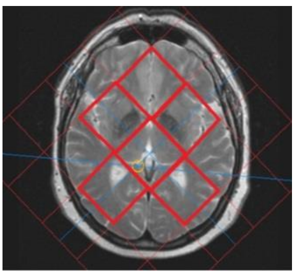

Fig.1. Location of spectroscopic volume with separation into individual voxels

Processing of the ^{31}P MR spectra was performed in the jMRUI 5.2. program. The obtained values of the intensity of the resonance lines in the voxel were normalized to the total phosphorus (Total ^{31}P) of this voxel. The values obtained in the spectra after HBO in each voxel in each subject were normalized to the corresponding values before HBO. Also for each voxel the value pH_{after}/pH_{before} was calculated. To estimate the intergroup differences of each parameter, the Student's t-test with a significance level of $p<0.05$ was used. Processing was performed in STATISTICA program.

Results. The results of significant ($p<0.05$) changes in the intensities of metabolite signals during HBO are presented in Table 1.

Table 1. The effect of HBO on the behavior of creatine phosphate (PCr), α-resonance of the ATP molecule (a-ATP) and intracellular pH in the human brain.

	mean	**abnormality**	**p-value**
$\mathbf{[PCr]_{after} / [PCr]_{before}}$	0.957	0.015	0.033
$\mathbf{[\alpha\text{-}ATP]_{after} / [\alpha\text{-}ATP]_{before}}$	1.033	0.015	0.0003
$\mathbf{pH_{after} / pH_{before}}$	0.995	0.002	0.006

There was no reliable influence of HBO on other metabolites.

Discussion ATP is used during HBO, although [ATP] doesn't change since it is supported by creatine-kinase reaction. The change in α-ATP peak area while [ATP] is constant indicates on the change of concentration of another metabolite that is overlaid by a massive peak of α-resonance of the ATP molecule. NAD^+ is such a metabolite.

To conclude, for the first time we have shown that HBO directly activates energy metabolism and increases the NAD^+ level, probably, in response to the oxidative stress hence to HBO [2].

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NEOGLYCOLIPIDS MICELLE-LIKE STRUCTURES AS A BASIS FOR DRUG DELIVERY SYSTEMS

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Advance in nanotechnology opens the new windows for creating new systems for medicine, in particular, in the targeted delivery systems of drugs. The new compounds are proposed and investigated.

The present work is aimed at studying the possibility of forming drugs carriers in the form of neoglycolipids micelle-like structures. A typical structure of neoglycolipid is shown in Fig.1. The neoglycolipid molecule contains three fragments: (1) a polar "head", a carbohydrate, (2) a polypeptide chain, and (3) a fatty acid residue.

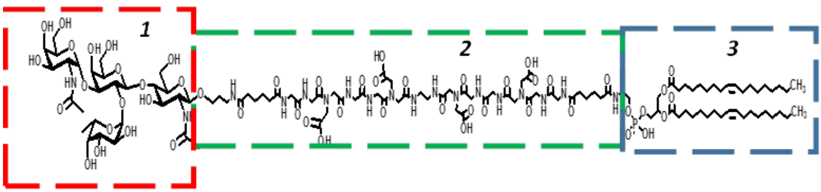

Fig. 1. Structure of neoglycolipid molecule.

Earlier, we found that such type of oligopeptide congugates are able to agregate in very stable structures [1]. The lipid fragments can play an orienting role. Due to their hydrophobicity, they have to localized inside the micelle. The carbohydrate fragment can fulfills the recognition function, due to the ability to recognize specific targets on the cell surface.

To study the association of neoglycolipids and stable micelle-like structures forming, methods of atomic force microscopy, dynamic light scattering, and small angle X-ray scattering were used. Experimental results allowed us to construct a structural model of complexes by molecular dynamics computation (the GROMACS package was used). Examples of the structures obtained are shown in Fig. 2. Dependences of the form of micelle-like structures on the parameters of the polypeptide chain and polar head of neoglycolipid have been found.

This study was supported by the Russian Science Foundation (project no. 14-50-00131). The study was carried out with use of unique scientific setup "System for probe-optical 3D correlative microscopy" IBCh RAS (http://ckp-rf.ru/usu/486825/).

1 2

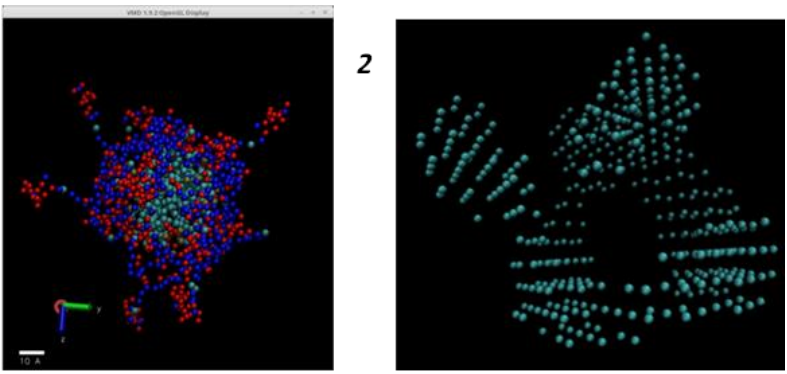

Fig.2. Micelle-like neoglycolipide structure (1) and electron density distribution on the result of small angle X-ray scattering investigations.

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OPTIMIZATION OF REPARATIVE PROCESS OF WOUNDS

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Now in surgery postoperative complications from wounds are quite frequent phenomenon. For the purpose of acceleration of reparative regeneration various medicines and physical ways are widely used. However still effect of aeroions of oxygen on process of a wound repair is not studied.

The purpose of the real research was studying of influence of aeroions of oxygen on regeneration of fabric structures postoperative wounds of an abdominal cavity.

Clinical laboratory researches are conducted by 48 patients with acute peritonitis of an appendicular origin who are divided into two groups. In the early postoperative period the patient of the main group carried out an aero ionotherapy. Aero ionization of hospital chamber was made daily within the first 7 days after operation by a dose in 20 biological units. Character and rate of regeneration of a wound estimated on a woundtenziometriya and a cytologic research of wound exudate. Control terms of observation - 1, 3, 5, 7 days.

When studying in dynamics in wound exudate of neutrophilic leukocytes it is revealed that at patients of group of comparison in a day after operation their quantity made 114±19,2 in 10 fields of vision, in 3 days increased by 71,3% ($p < 0,05$). In many neutrophilic leukocytes homogenization, swelling, fragmentation, pycnosis and final fracture of kernels with formation of granularity is observed. In 5 days the quantity of neutrophils increased by 2,3 times ($p < 0,05$). Kernels of many of them are increased in sizes, in some neutrophils they are loosened. The phenomena of a physiological degeneration of neutrophils were observed what fragmentation and pycnosis of kernels testified to.

Only by the end of the observed period the amount of neutrophilic leukocytes decreased to 38,3±4,8 ($p < 0,05$). To this term against the background of reduction of total number of neutrophils the progressing decrease in their degenerative forms was noted. It indicates end in these terms of a phase of an inflammation.

The regenerative-degenerative index also testifies to it. At patients of group of comparison in a day after operation it made 0,27±0,03, in 5 days - 0,46±0,06 ($p < 0,05$) and only by 7 days its value approached unit.

The maintenance of lymphoid polyblasts in the first 5 days after operation varied from 4,4 to 20,3 in 10 fields of vision.

When using an aero ionotherapy reparative process proceeded quicker and more perfectly. Effect of aeroions of oxygen is followed by acceleration of course of inflammatory reaction that is shown quick migration of cellular elements on a wound surface and their differentiation in connective tissue. This important fact explains antiinflammatory effect of such therapy, its ability to oppress alterativny process and to stimulate reparative. In the studied group force of biological consolidation considerably differed from that control group. In 3 days after operation it was above control value for 23,2%, through 5 - for 37,7%, in 7 days - for 35,6% ($p < 0,01$).

Thus, the obtained data give the grounds to note that negative aeroions of oxygen have rather expressed regenerator effect.

COMPUTER MICROSCOPY OF BIOLOGICAL LIQUID DRIED PATTERNS FOR MEDICAL DIAGNOSTICS

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A number of papers devoted to heat and mass transfer into colloidal solution evaporating drops on a flat substrate have been published over the last years, mainly due to the importance of this problem for fundamental and applied sciences and technologies. Report demonstrates some capabilities of the hardware-software complex Morfo in the field of solving the diagnostics problems of the human body in normal state, and when pathology states are being developed (Fig.1) [1,2]. The complex's application has allowed obtaining of interesting results not only in biomedical applications, but also acquisition of interesting data on the processes of dried pattern structure formation.

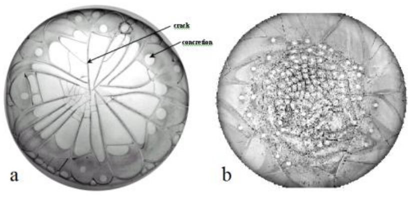
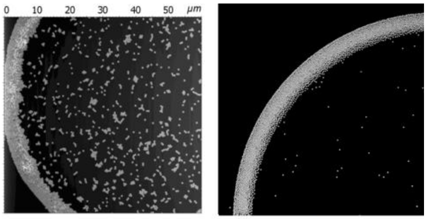


Fig.1. Blood serum dried pattern: a – norm; b – pathology

Also we are elaborating the useful software complex to predictive modeling of setup, spreading, evaporation of liquid droplet of inkjet size, as well as self-assembly of solvated monodisperse nanoparticles from the drop during evaporation (Fig.2) [3]. The most difficult case for modeling is a drop of biological liquid (blood serum, tear, saliva et al.) which consists of many different components of solution and forms the complex dry pattern onto substrate as a final stage of solvent evaporation process.



a b

Fig.2. a – ASM image of inkjet droplet pattern with monodisperse colloidal particles; b –DPD computer simulation pattern

Mathematical algorithm for computation the stage of endogenous intoxication by image of saliva patterns was created. Our algorithm is based on scientific researches in the field of analysis of structural changes in saliva patterns depending on the stage of endogenous intoxication. During the development of our algorithm we analyzed saliva probes belonged to 70 patients (training set) and received expert scores for these probes. After that the developed algorithm was tested on 30 saliva probes belonged to the others patients (test set). This testing has shown 75% agreement between computational and expert scores.

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TWO-STAGE SHELL COATING OF $CuInS_2$ QUANTUM DOTS FOR EFFICIENT PHASE TRANSFER

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The use of quantum dots (QDs) for bioimaging has significantly improved its capabilities. When compared to the previous generation of luminophores – organic dyes, QDs have superior properties such as size-tunable fluorescence, unique flexibility in excitation wavelength, high fluorescence quantum yield, large two-photon absorption cross-sections [1]. The most popular types of QDs are based on CdSe, and thus have a significant disadvantage for use in biomedical applications, because cadmium is a toxic material and its presence ceases *in vivo* applicability of CdSe QDs .

In this work we synthesized non-toxic $CuInS_2$/ZnS (CIS) QDs and developed a two-stage procedure for ZnS shell coating for adaptation of such QDs for biological applications. The synthesis was carried out by heat-up method. The mixture of dodecanthiol, indium acetate and copper iodide as precursors of sulfur, indium, and copper, respectively, were mixed and heated to 230 ^{o}C for 5 minutes. In order to increase the fluorescence quantum yield and stabilize QD's optical properties, their surface was coated by the first ZnS shell via the dropwise addition of zinc 2-ethylhexanoate and trioctylphosphine sulfide into the mixed dodcanethiol/octadecene QDs solution at 210 ^{o}C. We used this method of the ZnS shell coating instead of earlier developed procedure involving amine/octadecene solvent because of minor stability of CIS QDs in the latter media even under mild heating. Correspondingly, the temperature during the shell deposition was raised to enhance the rate of thiol molecules detachment from QD's surface and thereby to accelerate shell growth.

In order to make quantum dots synthesized in an organic medium compatible with biological fluids and tissues, it is necessary to convert their hydrophobic ligand shell into hydrophilic one. This can be done by solubilization procedure, a process of replacing hydrophobic ligands with hydrophilic cysteine or similar bifunctional thiol compounds. Hydrodynamic size of the solubilized CIS QDs prepared by the previously described procedure was found to be in the range of 40-60 nm, measured with using of the dynamic light scattering. This indicates the formation of aggregates during the solubilization, presumably because of the incomplete hydrophobic ligand displacement. $CuInS_2$ QDs synthesized in this work are capped with alkanethiol ligands which form strong covalent bonds with QDs surface, what causes the low efficiency of the ligand exchange during the solubilization. In order to overcome this undesirable effect, we developed a procedure for additional covering of the QDs surface with the ZnS shell in the amine/octadecence media. Solutions of the zinc 2-ethylhexanoate and tiourea were added dropwise to the solution of QDs in octadecene:oleylamine (1:1 by volume) under the argon atmosphere at 180 ^{o}C. The amine excess during the synthesis leads to the formation of the amine ligand layer on the QD surface, which is easily exchangeable to cysteine. The obtained QDs were solubilized by the standard procedure, and hydrodynamic size of these QDs was in range 10-15 nm, what indicates absence of QDs aggregation in the aqueous solution. This is due to the much more lower energy of complex bond formation between amine and QD's surface, and thus a higher efficiency of ligand exchange during the solubilization.

This study was supported by the Ministry of Education and Science of the Russian Federation, State Contract no. 16.1034.2017/ПЧ

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COMBINATION OF CRIOGENIC DIAGNOSTICS AND TREATMENT OF ONCOLOGICAL DISEASES TO VARIOUS DIFFERENT WAYS OF FIGHT AGAINST THEM

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The cryogenic surgery is known, but works on cryogenic oncological diagnostics it was revealed not. Therefore this direction of researches can be of particular interest. Main ideas. It is known that sick cells react to fall of temperature more weakly, than healthy. Besides we consider diagnostics on cytologic but not at the histologic level, leaving cells alive. It gives the chance to use dynamics of their body height and development as indexes and symptoms of a disease or their health. Let's consider gradual cooling of cells and change of their behavior under the influence of this cooling. In the beginning the speed of manifolding of these cells will change and healthy cells will have it more slowly, then sick cells. On the difference of these speeds it is possible to try to distinguish sick cells from healthy ones.

Then in process of cooling differentiated cells will perish gradually, and growth rate and the movements of living healthy cells will also be slowed down. Influence of cooling on undifferentiated cells is subject to a research, but it should not be too big

Besides there is a question whether there are among undifferentiated cells sick cells. Let's leave it without consideration so far.

We take the picture of cells or filming and we keep them for definition what cells are sick cells and what healthy. Slow-motion shots can be rather useful.

The further fall of temperature can lead to death of the other differentiated cells . Then there will be only sick and undifferentiated cells. It will be possible to distinguish sick cells and to photograph or remove them. It is at the same time possible to organize also their destruction, using the treatment methods which are not mentioning or poorly mentioning the remained undifferentiated cells. The same can be done earlier, in parallel with diagnostics and at the same time to check quality of destruction of sick cells. All these processes can go in parallel. Further at continuation of cooling also sick cells will begin to perish and to remain only undifferentiated cells. Here along with diagnostics there is also a treatment or a cryosurgery of sick cells. Again it is possible to return and check, how well it was succeeded to get rid of sick cells. At last, there is one more problem. This receiving from the differentiated cells their differentiated analogs or restitution of healthy fabric in situ the sick cells.

It is possible to clean an organism, to be exact a concrete type of cells from sick copies. There is a question further to what types of fabrics and bodies such diagnostics along with their treatment can be applied.

It is known that by cryosurgical methods kinds of a carcinoma cutaneum and also breast cancer and cancer of a kidney treat. It is possible to try to expand this combined method of cryodiagnostics and a cryosurgery on other tissues, bodies and the systems of a human body.

Its advantage is a noninvasive surgery

ONCOLOGICAL DISEASE AGAINST ONCOLOGICAL DISEASE

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It is well known. what adaptability have onco cells which are generated in an organism by thousand a day. The immune system copes with most of them and they are destroyed by macrophages. However some of them manage to survive. They pretend to be cells of the organism and besides are represented by sick cells and macrophages do not destroy them any more, and, on the contrary, protect. The organism also helps them, allocating padding vital resources. They strenuously breed and occupy the territory., occupied by earlier healthy cells. Their colonies expand, forming the tumor quite often deadly to the organism.

But if neither the immune system, nor an organism, nor his healthy cells cope with invasion of the enemy, then it can be possible to try other thing. Namely to use one oncocells against others oncocells, same the fissile and hardy, same impregnable for protective forces of an organism and to try to force them to fight for survival not with healthy forces of an organism, and with each other. To try, to use the destructive force of one type an oncocells against the destructive force of other type oncocells. And to force them to try forces in fight for survival not with healthy forces of an organism, and with each other. Here, probably, different options and the inferior of them are possible if oncocell of one type unite with oncocell of other type and will begin the joint fight against healthy forces of an organism. However such option seems improbable, considering aggression of a nature oncocells and their aspiration to boundless individual domination.

If it occurs after all, it is possible to try other couples or even combinations various oncocells. To select them so that they entered fight with each other. It makes sense to interfere with the course of this fight. To help the strongest against the weakest or on the contrary, equalizing chances of opponents. It is necessary to tell that different types of oncological diseases constitute different danger to an organism and it makes sense to seek to replace more dangerous oncological disease less dangerous, helping to win the against the last. Use of various chemical medicines striking more dangerous disease is possible, forcing out it less dangerous or even invasive intervention, including different ways of fight against an oncology. In principle it is quite good to reduce, for example, all other types of an oncology. let's tell, to a planocellular oncological disease. However all this should be checked in practice, opening new absolutely unknown area of fight against one types oncological diseases by means of other types of oncological diseases.

THE SIZE OF VESICLES PRODUCED BY DIFFERENT STEM CELLS

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We have previously demonstrated [1] that intravenous injection of human bone marrow multipotent mesenchymal stromal cells (BM-MMSC) to irradiated mice promoted partial recovery of their physiological parameters. Extracellular vesicles (EVs) secreted by practically all cells are now intensively studied as effectors of the paracrine mechanism of the therapeutic effect of MMSC on the irradiated organism. These particles are supposed to participate actively in cell-cell communication and cell interaction with the microenvironment. Our aim was to isolate and characterize extracellular vesicles produced by various types of stem cells.

To this end, suspensions of extracellular vesicles isolated from culture media (CM) of passage 2 human BM-MMSC (cells previously used in the therapy of irradiated animals; CM-1) and passage 4 rat adipose tissue-derived MMSC (AT-MMSC) (CM-2) were analyzed by transmission electron microscopy and nanoparticle tracking analysis (NTA). The cultures expressed typical surface markers of MMSC culture and did not express markers of hemopoietic and lymphocyte cells: BM MMSC CD105+/CD90+/CD73+/CD45-/CD14-/CD34-/CD49b-; AT-MMSC CD105+/CD90+/CD29+/CD45-/CD11b-/CD34-.

EVs were isolated by differential centrifugation at +4^{o}C. CM was centrifuged for 10 min at 300g for cells sedimentation. The supernatant was centrifuged at 16,500g for 20 min for more complete removal of cells and debris, filtered through a 0.2-μ filter to remove particles >200 nm, and then centrifuged at 100,000g for 2 h for EVs sedimentation. The pellet was resuspended in 1.5 ml PBS.

The preparations were absorbed on copper formvar-coated meshes, contrasted with 2% sodium uranyl acetate for electron microscopy, and examined in a JEM-1400 electron microscope (JEOL, Japan) at ×40,000. In CM-1, 36-45-nm near-spherical particles were detected. CM-2 contained two types of particles: 79-106-nm particles with morphological signs of extracellular vesicles and 37-53-nm particles corresponding to very-low-density lipoproteins present in the serum added to the culture medium.

The mean size and concentration of the particles in the samples were evaluated by the NTA method (Nanosight LM10-HSBF, Great Britain) based on tracing the Brownian motion of individual nanoparticles and measuring their standard mean square shift over a time interval related to particle size by the Stokes–Einstein formula. According to NTA results, the mean particle size and their concentration in CM-1 sample were 86 nm and 6.6×10^{10}/ml, respectively; for CM-2, the corresponding parameters were 101 nm and 7.9×10^{10}/ml, which can reflect secretion specificity determined by the cell type [2].

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IDENTIFICATION OF THE PATHOLOGY OF THE JOINT WITH THE HELP OF SPECTROSCOPY OF RAMAN SCATTERING

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Synovial fluid in the joint cavity is a unique biological medium, based on biophysical, physicochemical properties and composition [1] for the timely and correct diagnosis of joint disease and, as a consequence, more precise assignment of subsequent treatment of the patient is analysis synovial fluid.

Objective of the work is research the synovial fluid samples of the joint. The following results have been obtained: in norm and with pathology of the knee joint using the Raman spectroscopy method.

The SC fusion was performed with a disposable syringe by puncturing the joint, directly with arthrotomy or arthroscopy with careful hemostasis.

Materials of the study were samples of synovial fluid obtained from the articular knee bag. Samples were divided into two groups: 1 - conditionally healthy (control samples), 2 - developed osteoarthritis.

The spectral characteristics of the samples were studied using an experimental stand including a high-resolution digital Shamrock sr-303i spectrometer with an integrated DV420A-OE cooled camera, an RPB785 optical fiber probe for Raman spectroscopy compatible with the LuxxMaster LML-785.0RB laser module -04 (with adjustable power up to 500 mW, wavelength 785 nm).

As a result of the studies, the following spectral features of the SC were recorded. With the development of the destructive-dystrophic process in the synovial fluid of the affected joint, the total amount of protein components on the wavenumbers increases: 1001 cm^{-1} Respiratory ring of phenylalanine), 1155 (Hyaluronic acid (C-O, C-C)), 1206 cm^{-1}, 1125 cm^{-1} (C-C, C-O-C stretching of glycosidic bonds), 1250 cm^{-1} (Amide III), 1442 cm^{-1} (CH2 / CH3 deformation twisting), and 744 cm^{-1} (C-C-O)), 948 cm^{-1} (Secondary protein structure (N-Ca-C stretching, α-helix)). As well as, the component composition of the test substance can be identified at different stages of OA.

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DEVELOPMENT OF THE PROGRAM SYSTEM FOR DETECTING GLOMERULOID STRUCTURES ON THE PICTURES OF THE HISTOLOGICAL PREPARATIONS OF THE PROSTATE

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In the global structure of oncological morbidity, prostate cancer ranks sixth, and among men - the third. It is remarkable that at least 75% of men aged 85 years and older have histological changes in the prostate that correspond to the diagnosis of cancer. Nevertheless, in the overwhelming majority of cases (90 97%), the presence of malignant growth islands in the prostate does not lead to a pronounced clinical manifestation.

A critical problem of oncological urology seems to be the inability to allocate that small proportion of men in whom the presence of malignant islets in prostate tissue is a threat to health [1].

To date, the development and implementation of automated software systems for diagnosing pancreatic cancer are urgent tasks, the solution of which will automate the diagnosis of cancer, increase its accuracy and, therefore, accelerate the decision-making process about methods of medical intervention.

The aim of the work is the development of a software system whose function is the detection of glomeruloid structures, the presence of which on the images of histological preparations of the prostate indicates pathology.

Glomeruloid carcinoma of the prostate is represented by rounded or oval epithelial complexes resembling the glomeruli of the kidney [2].

The presence of glomeruloid structures on the photographs of histological preparations of the prostate gland indicates the presence of a cancer tumor corresponding to four points according to Glysson.

The software system has an intuitive interface (Fig. 1). The result of the algorithm for detecting glomeruloid structures can be observed in the appeared window "Original" (Figure 2). Green areas are allocated to 76 areas corresponding to glomeruloid structures, blue - areas that are not sufficiently appropriate for them.

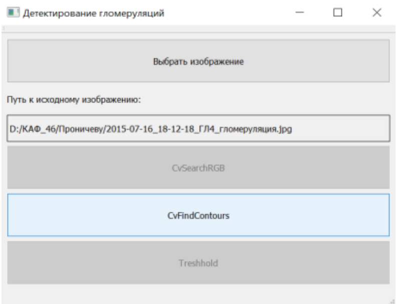

Fig.1. The launch of the algorithm for detecting glomeruloid structures

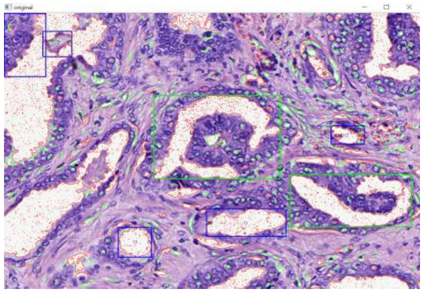

Fig.2. The result is the detection of glomeruloid structures

According to the test results, it can be concluded that the present system can be useful in the diagnosis of prostate cancer because the presence of glomeruloid structures detected by the system on histological specimens shows the presence of a cancer with a fourth degree of Glisson differentiation.

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INTELLIGENT TECHNOLOGIES OF CANCER MORPHOLOGY: A MULTIDISCIPLINARY ANALYSIS

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Widespread introduction of methods and means of pattern recognition in the diagnosis of malignant tumors is hindered by a number of existing problems: the complexity of the spatial brightness structure of the histological preparations images, the large variability of the objects, the lack of qualified doctors-pathologists and the long duration of their training(10-15years)[1-4].

The aim of this work is to develop methods and tools of pattern recognition for histological diagnostics of cancer diseases.

Key objectives to achieve the goals are associated with the formation of the feature space, the creation of reference base of the histological images, the choice of the method of making diagnostic decisions. Three main groups of conceptual alternatives have significant (relevant) importance in the area of pattern recognition of micro specimens (the most problematic in the clinical histological diagnosis). They are model characteristics (quality or quantity), classification model (the only result of the classification of the diagnosis or rating a list of options of diagnosis), degree of automation(fully automatic or interactive, with the participation of a physician).

Given the fact that the formulation of the histological diagnosis in Oncology is complex, ambiguous and informal procedure, when the same symptoms can correspond to different nosological forms, the choice of the classification model should be guided by the rating (probabilistic) system diagnoses.

The structure of the reference knowledge base of images of histological micro specimens in the system of pattern recognition for the diagnosis of cancer is based on the hierarchical principle.

This approach is implemented in the knowledge base created by experts of the Department of medical computer systems of the National research nuclear University "MEPhI" and the doctors of the Department of pathological anatomy of human tumors of the N.N. Blohin Russian Cancer Research Center[6]. The knowledge base contains 7988 images at 2615 cases of tumors of the pancreas, thyroid, breast, esophagus, stomach, colon, lymph nodes, kidneys.

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THE STUDYING OF THE METHOD OF LEUKOCYTES SEGMENTATION IN BONE MARROW IMAGES IN MULTICELLULAR CONDITIONS

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The use of methods and means of digital image processing for automation of diagnosis of acute leukemia is of considerable interest, because the composition of the cells and their morphological affiliation are paramount importance in the diagnosis of acute leukemia.

The procedure of blood cells recognition in image processing includes the following stages: registration of the images, preprocessing, segmentation, description, classification. One of the most important steps is segmentation, in which the nucleus and cytoplasm are detected, and then characteristics of the cells are measured. Closely located cells on images of bone marrow present challenges for automatic segmentation.

The analysis of publications showed that there is no approach for reliable segmentation of pathological cells in multicellular conditions.

The aim of this work was to study the effectiveness of methods of distance converting and watershed in resolving of the problem of segmentation of leukocytes in terms of their proximity ("clumping") on the images of bone marrow smears.

The following steps for image processing were proposed to solve the problem of segmentation – background and erythrocytes removal based on the analysis of the color components histogram, selection of objects (filling), screening artifacts, the identification of "sticky" white blood cells. The contour of an object is searched for touching leukocytes. Internal void areas are searched in the contour. The distance transform method and modified watershed method are used for the separation of "sticky" white blood cells.

The proposed solution is implemented as a software module in C++ using Qt library.

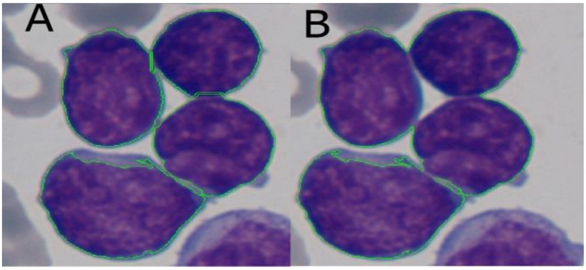

Fig.1. The result of proposed leukocytes segmentation method (A); white blood cells stuck together and are not separated (B)

This approach allowed us to effectively separate white blood cells, which stuck together (Fig.1), and highlight their core. The type of the analyzed object influences on the correctness of the algorithm results: if the white blood cells stuck together in a closed structure, the separation can be improper. The calculated shape factor makes it easy to distinguish a rounded nucleus from the nucleus of irregular shape that provides valuable information for recognition.

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STRUCTURE AND BIOCHEMICAL STUDY OF NANOCOMPOSITE BIOCONSTRUCTION FOR RESTORATION OF BONE-CARTILAGINOUS DEFECTS

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Today various bioconstructions are widely used in tissue engineering as scaffolds for growth and regeneration of damaged tissues of the body [1]. To replace lost or damaged tissues, bioconstructions must have a certain porosity, strength, adequate to the strength of native tissues, and high biocompatibility [2].

Porous and strong nanocomposite bioconstructions can be formed by laser evaporation of an aqueous dispersion of carbon nanotubes (CNTs) in a protein (bovine serum albumin (BSA) and collagen) matrix. The homogeneous dispersion were exposed to laser irradiation to create a solid constructions. Continuous laser radiation with a wavelength of 970 nm and a power of 5-7 W was used.

The porosity of nanocomposite bioconstructions was studied by the method of low-temperature nitrogen porosimetry, the tensile strength and relative elongation of bioconstructions were evaluated, and their biocompatibility was tested in vitro.

The results of a study of the strength and porosity of nanocomposite bioconstructions are presented in Table 1. Thus, it was found that with an increase of the carbon nanotubes concentration, a slight decrease in strength (3-15%), a decrease in the pore size (20-40%), and an increase in the degree of deformation (10-12%) was observed. At the same time, the mechanical parameters of the bioconstructions met the requirements for the materials for the restoration of bone-cartilaginous defects.

Using optical microscopy and the MTT-test, proliferative activity and structural features of bone tissue cells on the surface of nanocomposite bioconstructions were evaluated. Studies have shown no toxic or inhibitory effect on cells.

Table 1 - Structural parameters of nanocomposite bioconstructions

Sample	Specific surface area, m^2/g	Specific pore volume, ml/g	Average pore diameter, nm	Average tensile strength, MPa	Average relative extension, %
I. SWCNT 90A (0,01 %), BSA (25 %), collagen (1 %)	0.476	0.008	31.956	3.7	12.2
II. SWCNT 90A (0,1 %), BSA (25 %), collagen (1 %)	1.124	0.068	26.628	3.6	13.7
III. SWCNT 95TA (0,01 %), BSA (25 %), collagen (1 %)	1.089	0.008	46.877	3.9	11.9
IV. SWCNT 95TA (0,1 %), BSA (25 %), collagen (1 %)	0.583	0.001	27.935	3.4	13.1

The results of the studies can talk about the advantage of nanocomposite bioconstructions using as an implant material for improving the growth of biological cells and regenerating damaged biotissues.

The work was supported by the Ministry of Education and Science of the Russian Federation (agreement No. 14.578.21.0221, RFMEFI57816X0221).

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DEVELOPMENT OF TOTAL SKIN ELECTRON IRRADIATION TECHNIQUE

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Total irradiation of the patient's skin with the electrons is an effective method for treating of many skin oncological diseases in case of massive lesions. Practice has shown that the most optimal approach in this case is the use of medical electron accelerators in the energy ranges 4-9 MeV. In this paper, an experiment was performed with the prototype of the installation, comparative analysis of the dosimetric results of the actual experiment and the values obtained using the generated TSEI calculation code (Total skin electron irradiation) in the same geometry was made.

There are other methods of irradiating skin, for example, using short-focus X-ray machines, but with massive skin lesions, there are number of factors limiting the applicability of this equipment. These include: technical impossibility to form a sufficiently large field of irradiation, a feature of the formation of spatial distribution of the dose in the tissue.

For the development, a rotational irradiation technique has been chosen, in which the patient stands on a platform and irradiated by electron beam of large field size. In this case the most conformal dose distributions for the patient's skin can be achieved according to results of preliminary calculations. Before the measurements, it was required to select from among 175 TL-detectors 75-100 (the number of detectors required for the experiment) to be homogeneous in sensitivity. For this purpose, a series of irradiations of the entire set of detectors was carried out. The result of irradiation under identical conditions is a charge accumulated by each of the detectors. Based on the results of this series of measurements, a set of detectors was taken.We excluded those detectors whose rms deviation exceeds 2%. The measurements were made with

TLD detectors located inside the Alderson-Rando phantom at various depths. Phantom was placed on a rotating platform . Special computer code TSEI was created to calculate electron-photon transport in a medium. The code is based on well- known DPM code. The verification of the TSEI code was carried out by making a comparison with the analogous results of calculations using the EgsNrc code. The coincidence of the measured and calculated data is within 5%. The contribution from the bremsstrahlung from the head of the accelerator and the scattered contaminating radiation was not taken into account at this stage.

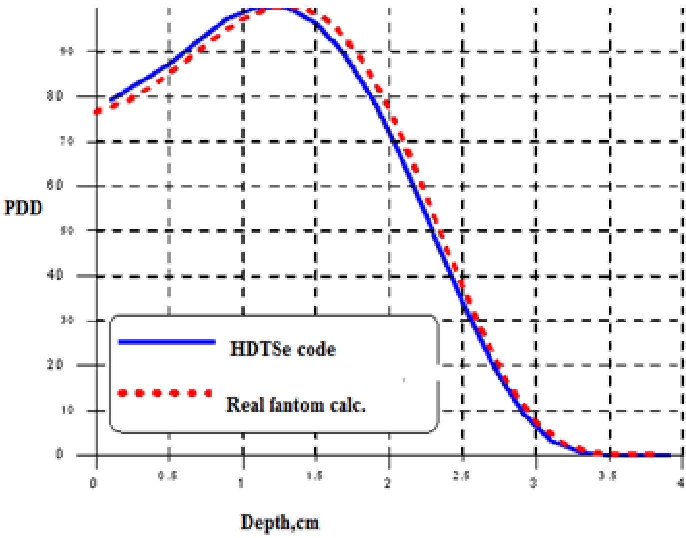

Fig.1 Comparison of the PDD measurement results for electrons with a nominal energy of 6 MeV and an applicator 10x10 cm2 with the results of calculations using the HDTSe code with a reconstructed spectrum.

COMPARATIVE QUANTITATIVE IMMUNOHISTOCHEMICAL CHARACTERIZATION OF TONGUE CARCINOMA

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There are 400 thousands cases of oral cavity carcinomas which have diagnosed every year all over the world and one forth part of these cases are tongue carcinomas [1]. The high mortality this group of diseases may be explained by lack of specific biological markers which can predict tumor progression [2]. The tumor stage is considered as one of the predictors for prognosis of the diseases [3].

The aim of investigation: quantitative comparison of expression different predictive antibodies by the tumor cells depend from tumor stage (T1, T2, T3, T4).

Materials and methods: We have investigated 80 observations of tongue carcinoma and classified them according to TNM system classification of tumors. There were 53 (66%) observations of the males and 27 observations (34%) of the females from 33 to 88 years old. We have used hematoxilin and eosin stain and immunohistochemical stains with antibodies such BCL-2, p53, Ki67, Cyclin D1, CD82, MMP9, CD138 to tumor cells. For antibody expression estimation we have used microscope Nikon optiphot-2 with magnification x100 (eye-piece lens x10, objective lens x10). We counted all tumor cells which expressed antibody in all fields of vision and estimated this data by Geisinger's scoring scheme (from score 1 to score 4 depend from percent of positive cells). Statistical significance was evaluated by Kruskal-Wallis and Mann-Whitney analysis. The significance level α= 0,05.

Results: There were 17, 31, 26, 4 cases of squamous tongue carcinomas with T1, T2, T3 and T4 stages respectively. By Kruskal-Wallis analysis we have compared expression each of investigated antibody in different tumor stage and we could detect statistically significant difference only between T1 and T2 tumor stage in p53 expression by the tumor cells. Supplement Mann-Whitney analysis revealed, that number of tumor cells with p53 expression in T2 stage more than number of tumor cells with p53 expression in T1 stage ($p=0,032$). On the other hand expression BCL-2, MMP-9, CD82, Ki 67, Cyclin D1, CD138 in all stages and p53 expression in T1/T3, T1/T4, T2/T3, T2/T4, T3/T4 tumor stages were not significant difference ($p>0,05$).

Conclusion: significant difference only in p53 expression between T1/T2 stage from one hand pay our attention to this protein, but from the other hand recommends us investigate new biological markers which can influence to tongue carcinoma behavior.

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NEW MEDICAL TECHNOLOGY OF FUNCTIONAL MICROWAVE THERMOGRAPHY: EXPERIMENTAL STUDY

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Practical applications of physical methods to control development of malignant tumors with "characteristic times" about times of the interaction between tumors and therapeutic factor (drug, radiation therapies, thermal effects, etc.), i.e. seconds, minutes and hours, become very important.

A malignant tumor is a complex, dynamic morpho-physiological system, which can be analyzed by considering the heat balance in a zone of tumor growth, e.g. a ratio of the of thermo-protective and termiticidal processes, which are detected by a local microwave broadband electromagnetic radiation on the basis of the principles of the contact radiometry. Design and engineering-technical decisions were developed on the basis of the Institute of experimental diagnostics and therapy of tumors of N. N. Blokhin NMRS. It allowed us to obtain a method of functional microwave thermography (FMT), which is currently at the stage of preclinical testing and patent registration.

The FMT method is based on comprehensive radio-physical measurements of biological objects and analysing the results of these measurements, the mathematics of nonlinear dynamics. Technical features of registration of the signal result in the possibility of discovering new information about metabolism, blood supply (microcirculation) and cell kinetics of malignant tumors. The theoretical methodology for the analysis of primary data, which are obtained in the form of non-stationary time series of a certain length, is performed by using the mathematical apparatus of nonlinear dynamics. The optimal regimes for the registration of the intensity of thermal radiation from internal tissues of laboratory animals in the microwave range of wavelengths. Examples of using this method in the application of various therapeutic agents in preclinical studies are chemotherapeutic agents, photodynamic therapy, continuous therapy in combination with temperature-sensitive nanoparticles and nano-complexes. Thus, an implementation of the FMT method can greatly facilitate the search for optimal parameters for the use of drugs and physical factors in experimental studies and clinical practice in the field of oncology.

This study was partially supported by the state project №16.7917.2017/8.9 at National Research Nuclear University MEPhI.

IN-VIVO STUDIES OF ULTRASOUND-ACTIVATED DRUG-LOADED POROUS SILICON NANOPARTICLES FOR CANCER THERAPY APPLICATION

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Porous silicon (PSi) nanoparticles (NPs) are biocompatible, biodegradable, and promising as an agent for both cancer therapy and diagnostics, i.e. theranostics [1]. The present work is devoted to experimental study of a combined effect of PSi nanoparticles (NPs), which were loaded with anti-tumor drug, and therapeutic ultrasound (TUS) irradiation to suppress cancer tumor growth in vivo.

We use one of the models of experimental oncology, i.e. malignant Lung Lewis adenocarcinoma (LLC) grafted at legs of mice of BDB line, to explore the therapeutic efficacy of combined action of TUS and of PSi NPs loaded with anticancer drug doxorubicin. Measurements of the thermal dynamics of the zone of tumor with introduced NPs and without them under the TUS treatment. Time dependences of the tumor growth for mice with introduced NPs and without them, as well as the life duration of the animals with grafted tumors with introduced NPs, and without them, after exposure to TUS with the specified parameters were studied.

PSi films were formed by electrochemical etching of (100)-oriented heavily boron doped crystalline Si wafers in a solution based on hydrofluoric acid and ethanol. PSi NPs were prepared by grinding the PSi films in ethanol by using a ball mill. The prepared NPs were loaded by doxorubicin (DOX) in 3:1 weight ratio and then they were dried in air.

Prior to in-vivo experiments DOX-loaded PSi NPs were suspended in saline (0.9% NaCl in water) by shaking for 1 min. Prepared suspension with NP concentration 0.1 g/L in a volume of 0.2 mL per animal was injected into LLC tumors grafted on legs of BDF mice. A part of the mice were treated with PSi NPs without DOX. Then tumor regions of the mice were irradiated by TUS at 1 MHz with intensity of 1 W/cm^2 for 2 min.

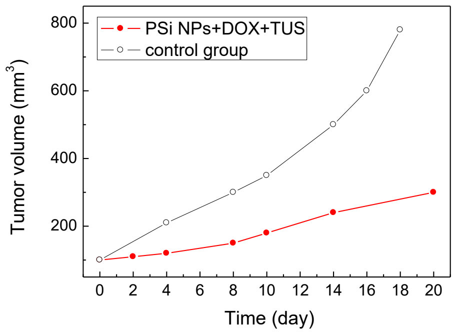

Fig.1. Time dependence of the tumor volume for mice after therapeutic ultrasound (TUS) treatment with doxorubicin (DOX)-loaded PSi NPs as well as for control group.

Figure 1 shows that the treatment by TUS with DOX-loaded PSi NPs resulted in a strong suppression of the tumor growth. Furthermore, the life duration of mice TUS-treated with DOX-loaded PSi NPs was found to be almost 2 times longer than that of the control group. Note, the same TUS-treatment without DOX or PSi NPs did not influence significantly tumor growth. These observations look very promising for applications of PSi NPs in the sonodynamic and combined therapy of cancer.

This study was supported by the Russian Science Foundation (project #16-13-10145).

MANGANESE-DOPED MESOPOROUS SILICA NANOPOWDER FOR PHARMASUTICAL APPLICATIONS

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Nanoparticles are widely used for biomedical applications, including targeted drug delivery, due to their dimensions and the ability to act at the tissular or cellular level. The advantages of such systems include targeting the specific locations in the organism and decreasing the drug concentration minimizing severe side effects [1].

In the study manganese-doped mesoporous silica nanopowder (NP SiO_2-MnO_2) with different dopant concentrations has been researched. It was produced by the physical method of electron beam evaporation in low-pressure gas (4 Pa) on NANOBIM-2 installation [2].

BET/BJH-analysis of NP properties demonstrates high porosity and increasing specific surface area with increasing dopant concentrations. The porosity mainly determines the loading capacity of the NP thus for the further experiments the sample with 3 % dopant concentration was chosen.

Table 1. BET/BJH-analysis of NP SiO_2-MnO_2

Dopant concentration, %	Pore size, nm	Sssa, m^2/g	Pore volume, cm^3/g
0,1	20,6	75,78	0,36
3	26,4	134,18	0,88
5	20,8	176,35	0,52

Basic toxicity experiments on cells showed that NP exerted low toxicity. Low toxicity is one of the main conditions for the use of NP for biomedical applications.

The qualitative loading experiments of antibiotic Amoxicillin in the NP showed the drug encapsulation in the pores and interaction with the surface of NP. The manganese-doped NP also is a perspective contrast agent for signal enhancement in magnetic resonance imaging by the reason of magnetic properties [3].

These all results of experiments allow considering the produced NP SiO_2-MnO_2 as a promising model for developing a targeted drug delivery system.

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ALUMINIUM PHTHALOCYANINE NANOPARTICLES FOR FD AND PDT APPLICATION IN DENTISTRY

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Early diagnosis of tooth-enamel microcracks is of great importance in modern dentistry for caries prevention [1]. Aluminum phthalocyanine nanoparticles (nAlPc) may be used for enamel microcracks diagnostics when pathogenic microflora is abundant. Also nAlPc is suitable for clinical application for fluorescence diagnostics (FD) because it does not fluoresce in the nanoparticle form in distilled water but in the monomeric form it does [2].

The purpose of this work is studying the application conditions of nAlPc for early diagnosis and prevention of caries.

Material and methods. The water colloid of nAlPc (in concentration 10mg/kg) was used for in vitro studying. For fluorescent measurements LESA-01-BIOSPEC and the diode laser (632.8 nm) for fluorescence excitation of nAlPc were used. The different surfactants (Tween 80, Propyleneglycol, Protelan MST-35, Plantacare 1200 UP and Sodium lauryl ethoxy sulfate) were used as additional activators of nAlPc. For investigation, the samples of human teeth of various age groups were removed for a various reasons.

Results. It was observed that the maximum fluorescence intensity (IF) of nAlPc appears in 60 minutes at interaction with enamel surface. It is too march for FD in dentistry. That is why it was decided to use surfactants as additional activators for nAlPc to reduce FD time. It was revealed that very strong IF of nAlPc appears approximately in 4 days after interaction with all surfactants. Also it was noted that the fluorescence wavelength of nAlPc at interaction with Sodium lauryl ethoxy sulfate is shifted to the right for 15 nm compared to others surfactants (Fig.1).

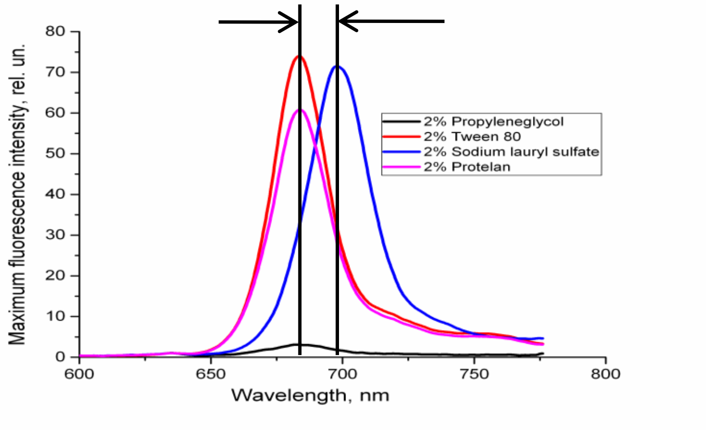

Fig.1 Fluorescence spectra of nAlPc at interaction with different surfactants in 40 min after application

In vitro study at interaction with enamel surface showed that the combined using of NP with the surfactant enables to spend FD after 3-5 min after application.

Discussion and Conclusion. Joint using of nAlPc and surfactants can allow to increase the sensitivity and effectiveness FD and PDT methods in dentistry for detection not only enamel microcracks but also inflammation processes in periodontal tissue.

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FINE-TUNING OF SILICA COATING PROCEDURE FOR PREPARATION OF BIOCOMPATIBLE AND BRIGHT PbS/SiO2 QDS

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In the past decade, a variety of vivid applications of quantum dots (QDs) as *in vitro* and *vivo* bioimaging probes has been demonstrated [1,2]. Since the human body has so-called "transparency windows" in the near infrared (NIR) region of optical spectrum, PbS QDs fluorescing in the NIR-region attracted a lot of attention as a promising *in vivo* labels. However, the intrinsic toxicity of lead and PbS QDs photoluminescence (PL) instability prevent their direct utility in biological experiments. One of the approaches used to render QDs biocompatible is coating of a QD with silica shell [3]. Yet, the PL quantum yield (QY) of QDs after the silanization procedure can be significantly reduced. Thus, the problem of reliable maintaining high PL QY and initial optical properties of the PbS-coresafter their coating with the SiO2-shell is in-demand.

Here, we investigated the effect of reaction parameters on the QY and PL spectra of silica-coated PbS QDs. The method for silica coating reported in [4] was taken as a basis and adapted in order to reduce the amount of sodium bis(2-ethylhexyl) sulfosuccinate (AOT), high content of which is undesirable by virtue of its destructive effect on the living cells. As AOT is a necessary component that reversibly caps the growing silica layer on the surface of QD, and prevents coalescence of the neighboring nanoparticles in solution, it may not be excluded but should be minimized to the quantity sufficient for stable passivation of the QD surface during the silanization procedure.

In our study, we have reduced the amount of AOT introduced into the reaction mixture down 40 times of the original value, and varied the quantities of TEOS and NH_4OH to achieve the best optical performance of PbS QDs. We have found that the eight-fold reduction in the quantity of these components results in the highest QY of silica-coated QDs, which was by a factor of 2.6 higher than that for the samples obtained in the synthesis done with four-fold components reduction. It is worth mentioning than proposed modification of synthesis procedure didn't provoke the widening or shift of the PbS/SiO2 PL spectra. In the same time, a twelve-fold components decrease led to sharp drop of PL QY and broadening of the PL spectrum. This result is most likely due to incomplete formation of silica shell due to the lack of silica-forming components in the reaction solution.

Our findings show that the PL QY of silica-coated QDs strongly depends on the parameters of the coating procedure. Thus, it is possible to make a proper choice of precursor amounts and reaction parameters to minimize the AOT surfactant content, making possible further QDs bioadaptation, always maintaining high PL QY and stable shape of their PL spectrum.

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