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Effects of a commercial detergent on the protease activity and biomass production of *Penicillium cyclopium*

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The proteases isolated from microbial sources have a large number of dilutions in various industrial sectors (laundry detergents, pharmaceutical, leather, food processing) and bioremediation. The largest application of protease is in laundry detergents where they remove protein based stains from clothes followed by in leather industry. The stability and compatibility of proteases with surfactants and detergents are necessary for their practical application in detergent formulation. Modern detergent industry requires efficient, eco-friendly and economical strategies for unwanted protein degradation. Fungal enzymes offer a distinct advantage over a bacterial protease in terms of easily mycelia removed by filtration.

This study investigated the production of alkaline protease by native isolate *Penicillium cyclopium* by submerged fermentation. The fungus was isolated from the riverbed of Western Morava (Čačak, Serbia), at a place where municipal wastewater discharged into the river. The fungus was grown in sterile Czapek-Dox liquid nutrient medium composed of (g/l): 3 $NaNO_3$, 1 K_2HPO_4, 0.25 $MgSO_4$, 0.01 $FeSO_4$, 30 sucrose, distilled water up to 1000 ml (control - C) and in same medium with addition of 0.3% commercial detergent "Merix" (Henkel, Kruševac) (D). Flask cultivation performed on an electric shaker (150 rpm) (Kinetor-m, Ljubljana) at ambient temperature (28°C±3°C) during 16 days. The proteolytic activity of fermentation broth was determined during fungal growth at 3rd, 6th, 9, 12th and 16th day by Anson's method. After 16 days of incubation, the total biomass dry weight was determined gravimetrically.

The results obtained in the present study showed that total biomass dry weight in C and D media was 1.41 and 0.94 g/L, respectively at 16th day. Therefore, the tested detergent caused an inhibitory effect on growth and biomass dry weight (33.4%). *P. cyclopium* produced maximum proteolytic activity in C medium (0.75 IU/mL) at 9th day. In D medium, maximum enzyme activity was recorded (0.64 IU/mL) at 6th day. In other words, the proteolytic activity retained a high percentage of activity (87.7%) in presence of tested detergent. Briefly, this study clearly indicates that alkaline protease of *P. cyclopium* has high percentage of compatibility with tested detergent, so it could be use as additive in formulation of detergent.

Keywords: Biomass, fungus, proteolytic activity

Capacity of *Penicillium cyclopium* for biodegradation of anionic surfactants

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Surfactants are among the most widely disseminated xenobiotics to enter waste streams and the aquatic environment. Considering its harmful environmental consequences, several technologies have been developed to address the problem and satisfy the strict environmental regulations. Bioremediation is the most promising option for the treatment of surfactants contaminated systems which has certain inherent merits (e.g., low costs, environmental friendly nature, in situ treatment capability) over other physical or chemical based processes.

The current study investigated the biodegradation rate of anionic surfactants as component of commercial detergent "Merix" (Henkel, Serbia) by *Penicillium chrysogenum* and its influence on fungal growth. The fungus was isolated from wastewater samples of Lepenica (Kragujevac, Serbia) at a place where sewage domestic wastewater discharged into the river. The Czapek-Dox liquid nutrient medium composed of (g/l): 3 $NaNO_3$, 1 K_2HPO_4, 0.25 $MgSO_4$, 0.01 $FeSO_4$, 30 sucrose, distilled water up to 1000 ml (control - C) was stored in Erlenmeyer flasks. The C medium and same medium with addition of 0.3% commercial detergent (D) were sterilized and inoculated with one ml spore suspension (1×10^4 CFU/ml). Erlenmeyer flasks were placed on an electric shaker (Kinetor-m, Ljubljana) at room temperature for 16 days. The total dry weight biomass (DWB) in media was determined at 3rd, 6th, 9th, 12th and 16th day from inoculation. Simultaneously, biodegradation rate of anionic components of detergent was determined by MBAS assay.

The fungus cultivated in D medium expressed monophasic exponential growth with stationary phase prolonged to day 16. The maximal total DWB in D medium was measured at 16th day and it was 61.84 % less compared to C medium. The initial concentration of detergent 3 mg/mL decreased continuously with the mycelial growth. The biodegradation study confirmed ability of fungus to degrade of anionic components of detergent. The fungus decomposed the highest percentage of detergent during the exponential growth phase whereas lesser amount of anionic surfactants degraded during stationary phase. Exactly, during the first 3 days, the fungus decomposed 15.63 % of the initial detergent concentration. From 3rd to 6th day the biodegradation rate was 26.73 %; from 6th to 9th day it was 31.03 %; from 9th to 12th day, 36.57 %; and at 16th day the detergent concentration was 1.51 mg/mL. In other words, the fungus degraded total 50.2 % of the initial detergent concentration for 16 days. According to obtained results the fungus acts as potential candidate for bioremediation of anionic surfactants contaminated environments.

Keywords: Anionic surfactants, biodegradation rate, biomass, fungus

Determination of the redox potential of bronchodilators (Ventolin)

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Chronic obstructive pulmonary disease (COPD) is characterized by persistent, progressive airway obstruction caused by an inflammatory response in these pathways and the pulmonary parenchyma to inhalant toxic particles or smoke. The main goals of the pharmacological treatment of COPD are to reduce the symptoms, frequency and severity of the exacerbation and to improve the endurance of physical exertion and health status. The mainstay of pharmacological treatment for stable symptomatic COPD is bronchodilators alone or in combination with inhaled corticosteroids. Ventolin (Salbutamol) is a selective β2-adrenergic receptor agonist. At therapeutic doses it acts on the β2-adrenoreceptors of the bronchial muscles, with little or no effect on the β1-adrenoreceptors of the heart muscle. Due to its rapid action it is especially suitable for the treatment and prevention of asthma attacks. In this paper, the electrochemical processes of Ventolin on a glassy carbon electrode (GC) were investigated using a cyclic voltammetry method to determine the redox potential of a bronchodilator. The effect of different substrate concentrations was monitored by cyclic voltammetry, and the effect of different scan rates on the appearance of voltammograms was examined. Cyclic voltammograms can provide information on the rate of charge transfer, the processes of charge transport, and the interactions that occur between enzyme segments at specific sites. We have come to the conclusion that with increasing Ventolin concentration, an increase in the current peak in the reduction region is observed. This concludes that the concentration of the test drug has a significant effect on the kinetic and redox characteristics, and therefore on the control of the disease.

In vitro magnetic targeted delivery of doxorubicin using iron oxide nanoparticles leads to enhanced cell death in glioblastoma

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Objectives. Being one of the most aggressive and invasive types of brain cancer, glioblastoma multiform leads to very low survival rates, caused by high recurrence and therapy resistance. The aim of this study was to obtain and evaluate iron oxide nanosystems for the magnetic targeted delivery of doxorubicin chemotherapeutic in human glioblastoma cell cultures.

Materials and methods. Iron oxide nanoparticles were synthesized using a modified chemical co-precipitation method and functionalized with polyethylene glycol by *in situ* conjugation (Fe_3O_4@PEG 6K), followed by doxorubicin (DOX) loading (during 24 and 48h). The morphology and structure of the resulted nanoparticles was assessed using scanning electron microscopy (SEM), high resolution transmission electron microscopy (HR-TEM) and selected area electron diffraction (SAED). Using high amplitude alternating magnetic fields, the DOX-loaded nanoparticles were subjected to controlled drug release testing and the Specific Absorption Rate (SAR) was calculated from the time-temperature dependence after magnetic stimulation. The *in vitro* evaluation of the nanosystems was done for U-87 MG human glioblastoma cells using the MTS tetrazolium- salt metabolic assay and microscopic characterization of the morphology. Internalization of the nanoparticles was quantitatively measured using particle induced X-Ray emission (PIXE).

Results. Highly crystalline Fe_3O_4@PEG 6K nanoparticles with spinel structure and an average diameter of 8.81±1.96 nm were obtained. The drug release was proportional with the corresponding thermal variation of the sample during magnetic stimulation, leading to a maximum release of 78.2% Fe_3O_4@PEG 6K/ DOX (24), respectively 72.12% for Fe_3O_4@PEG 6K/ DOX (48) (for 2 kW magnetic field). The maximum calculated SAR value (43.68±1.25 kW/kg) was obtained for Fe_3O_4@PEG 6K/ DOX (48) nanosystems. Unloaded Fe_3O_4@PEG 6K nanoparticles showed a biocompatible behaviour for all concentrations, while Fe_3O_4@PEG 6K/ DOX induced an improved cytotoxic effect of the nanoparticles after loading the chemotherapeutic substance. PIXE analysis showed a significant difference between the amount of internalized nanoparticles per cell, in case of Fe_3O_4@PEG 6K/ DOX (24) (1325.63±164.41 pg/ cell), compared to both Fe_3O_4@PEG 6K (601.48±152.65 pg/ cell) and Fe_3O_4@PEG 6K/ DOX (48) (828.2±22.3 pg/ cell) ($P<0.05$).

Conclusions. Magnetic targeting of Fe_3O_4@PEG 6K/ (DOX) determined their intracellular internalization in the peri- nuclear areas of U-87 MG human glioblastoma cells and local doxorubicin delivery leading to increased cytotoxicity.

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Drug delivery nanosystems for intracellular release of doxorubicin improve theclonogenic inactivation of X-Rays in human cervical adenocarcinoma cells

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Objectives. Radiosensitization using nanoparticles is a promising approach for the improvement of radiotherapy cytotoxic effects against chemo-/radio-resistant tumor cells and simultaneous reduction of adverse effects in surrounding healthy tissues. Here, we propose a method based on iron oxide nanoparticles (IONP) for the intracellular delivery of the anthracycline doxorubicin to enhance the cytotoxic effects of X-Rays.

Materials and methods. We synthesized and characterized iron oxide nanoparticles functionalized with polyethylene glycol ($IONP_{CO}$) in order to be used as drug delivery systems for doxorubicin ($IONP_{DOX}$). The biological effects were assessed in 2D and 3D cell cultures of human cervical adenocarcinoma cells (HeLa). Uptake and retention of IONP were evaluated using optical, fluorescence and transmission electron microscopy. Clonogenic survival was used to measure the radiosensitization effect of IONP at different doses of low (50 kV), medium (150 kV) and high (6 MV) X-Rays in both 2D and 3D cell models. Data are presented as mean ± SEM.

Results. Efficient internalization of $IONP_{CO}$ and $IONP_{DOX}$ in HeLa cells occurred through pino- and endocytosis, with both IONP accumulating in the perinuclear area. In 2D cell cultures, $IONP_{CO}$ enhanced the radiosensitivity (dose-modifying factor, DMF) of 50 kV X-Rays with a $DMF_{SFo.1}$= 1.13 ± 0.06, but did not determine any radiomodulatory effect after6MV irradiation. $IONP_{DOX}$ enhanced the clonogenic inactivation of 6 MV X-rays in 2D HeLa cell cultures with a $DMF_{SFo.1}$=1.3 ± 0.1 and $DMF_{SF=\ 0.1}$= 1.29 ± 0.02 in case of 150 kV. Efficient penetration of the $IONP_{DOX}$ was obtained after 48h of exposure in 3D spheroids and exposure to 150 kV led to a $DMF_{SFo.1}$=1.07 ± 0.07.

Conclusions. The radiosensitization effect was dependent on the radiation energy for drug-free nanoparticles, $IONP_{CO}$ showing a significant clonogenic inactivation compared to irradiation alone, in case of low energy X-Rays exposure, while $IONP_{DOX}$ determined radiomodulatory effects for both medium and high energy X-Rays. The IONP are good candidates for the controlled delivery of DOX to enhance the cytotoxic effects of ionizing radiation.

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Radiosensitization effects of doxorubicin-iron oxide nanosystem in charged particle radiation therapy for human chondrosarcoma

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Objective. Charged particle radiotherapy (hadron therapy) shows better specificity and lower toxicity for the surrounding normal tissue compared to conventional photon therapy being a standard care for some chemo-/radio-resistant tumors such as chondrosarcoma. Still, the efficiency of the hadron therapy can be enhanced. For this, we proposed an intracellularly targeted method based on doxorubicin/polyethylene glycol-conjugated iron oxide nanosystem ($IONP_{DOX}$) to improve the cytotoxic effects of proton therapy.

Methods. Core-shell IONP for the encapsulation of doxorubicin were previously synthesized and characterized. The biological cytotoxic effects were determined for 2D and 3D cell cultures of human chondrosarcoma (SW 1353). The 3D cell cultures were obtained using the liquid overlay technique. The long term cytotoxicity of $IONP_{DOX}$ and proton irradiation (0-4 Gy, 155 MeV) were assessed using the colony formation assay, while for the genotoxicity determination was employed the cytokinesis block micronucleus assay.

Results. Long term cytotoxicity measurements emphasized a statistically significant reduction in survival of 2D SW 1353 cell cultures after exposure to $IONP_{DOX}$ followed by proton irradiations at doses of 0.5 Gy and 4 Gy ($P<0.05$). In case of 3D cell cultures, a radiosensitization effect of $IONP_{DOX}$ was obtained at 1 Gy ($P<0.05$). Genotoxicity evaluation confirmed the clonogenic survival results.

Conclusion. The $IONP_{DOX}$ showed a potentiated cytotoxic effect of proton irradiated 2D and 3D chondrosarcoma cell models, proving the applicability of the nanosystem for radiosensitization purposes in charged particle radiation therapy of highly chemo-/radio-resistant chondrosarcoma.

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Biomechanical study of vertebral column after performing modified partial lateral corpectomy in dogs

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Disturbances in the structure of the intervertebral disc are inevitable during aging of medium and large chondrodystrophic dog breeds. However, veterinary data on the treatment of chronic discopathies are practically absent. Nevertheless, discopathy is a common pathology and causes paresis and paralysis in dogs.

Biomechanical studies to determine the region of elastic and plastic deformation were conducted. Also, maximum torque, resistance of the samples in various parts of the graph, and permanent deformation were found. Tests were performed on operating samples from 3 groups: native spinal specimens, samples with classical partial lateral corpectomy, and samples with modified partial lateral corpectomy. By the methods of correlation analysis of biomechanical parameters, the degree of destruction of various structures of the spines of the motor segment was determined and a directly proportional relationship between the angle of rotation and the resistance of the sample in the zone of elastic deformations was revealed.

When comparing the areas of elastic deformations in different groups, the following data were obtained. In all groups of samples, a directly proportional relationship between the load and resistance of the samples was obtained. Native vertebral specimens are the most resistant to stress, the next in strength are specimens with modified partial lateral corpectomy, the least durable ones with classical partial lateral corpectomy. The greatest resistance was exerted by native spinal specimens. The maximum torque values were (44.5 ± 1.5) N·m. To reduce stability, the groups were arranged in the following order: the group with a classical partial lateral corpectomy [maximum value (44.5 ± 1.5) N·m], with a modified partial lateral corpectomy [maximum value (49.5 ± 0.5) N·m]. The difference in indicators indicates the possibility of both changing the modulus of the radius vector and the angle between the vector indicated and the direction of the acting force. The values of rotation angles at which a transition from elastic to plastic deformation was observed were also different and amounted to 22.0° ± 1.0° and 28.0° ± 1.0° degrees.

Modeling of the chemical dosing process in raw water by an artificial neural network

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Artificial intelligence and machine learning based on artificial neural networks has found application in a variety of processes. One of them is treatment of raw water by chemicals. The aim of this research was to optimize treatment of raw water in water plant in Uzice from aspect of chemical dosing and amount of good quality sludge. Raw water comes from artificial lake Vrutci. Water quality is affected by eutrophication process and there are biological species that need to be treated. Treatment means dosing of aluminum sulphate (coagulation) and anionic polyacrylamide (flocculation), but also ozonization. As input layers in modeling of these process by artificial neural networks parameters used were: raw water flow, concentration of aluminum sulphate, concentration of anionic polyacrylamide, pH, temperature, total organic carbon, consumption of $KMnO_4$, turbidity, total suspended solids and chlorophyll A. Output layers were: doses of aluminum sulphate, anionic polyacrylamide, ozone and amount of sludge.

The structure of the network and time were optimized in accordance to neural architecture number of layers and neurons, learning rate, ξ, and momentum, μ. The aluminum sulphate and polyacrylamide doses received by artificial neural network calculation and Flock tests results in received are in well agreement.

When obtained these data should be applied to raw water. The chemical composition and biological species should be optimized in accordance to Serbian and European legislation for quality of drinking water and sludge. The sludge has to be free of micotoxine and with low Al^{3+} concentration. If it consits excessive amount of N, P compounds it should be composted.

For comparison, other regression models should be applied: multiple linear regression, based on step wise regression and multiple linear regression optimized by genetic algorithm. The stability of model should be checked by cross validation and then applied to process of raw water and sludge treatment.

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EPR identification of gamma-irradiated small berries of Bulgarian flora

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Increased interest and consumers demand for natural food products has led to an increased investigation of their antioxidant properties after gamma irradiation. Food irradiation is an internationally recognized method (Directive 1999/3/*EN 1787*) for effective long-term storage, improves hygienic quality and protects against oxidation processes. The present study for the first time reported radical-scavenging, antioxidant and radiation-protective properties in two varieties of small berries from Bulgarian flora, *Aronia melanocarpa L.* and *Rosa canina L.*, against 10 kGy and 25 kGy doses radiation. Both contain several components such as vitamins, polyphenolic acids, anthocyanins carotenoids, dietary fibre, organic acids, and minerals. Phytochemical composition of the small berries is responsible for its biological effects, e.g., antioxidative, hepato-, cardio-, gastro-protective, anti-diabetic, anti-inflammatory, hypoglycemic and anti-cancer activities. The freeze-dried berries were irradiated at ^{60}Co-dosimeter (*BioMax, at 8200 Ci*), powdered and extracted by 30% ethanol solvent (*v/v*) to the purity of 90% and 87%, respectively. X-band electron paramagnetic resonance (EPR) spectrometer e-scan (*EPR, Bruker ER 116 DS)* as promising techniques for food-stuffs identification, antioxidant capacity, and regulatory requirements was used. Spectral processing was identified by *Win EPR and Sim-Fonia* software. The ability of extracts to scavenge *in vitro* short-lived radicals the spin-traps BMPO• (5-tert-Butoxycarbonyl-5-methyl-1-pyrroline-N-oxide) and DPPH• (2,2-diphenyl-1-picrylhydrazyl) was expressed. Both extracts were analyzed five times. As a result, both extracts exhibit singlet, symmetrical line characterized by g-factor 2.00456 ± 0.0002 before radiation exposure. After 10 kGy irradiation, spectra with the same shapes were registered in both samples. 25 kGy radiation decreased signal intensity and change the g-value to 2.00412 ± 0.0002 in both. The kinetics of 10 kGy and 25 kGy radiation-induced EPR signals were studied for a period of 90 and 180 days post-storage. It should be pointed out that stable radical structures were registered in both samples for the mentioned periods for 10 kGy irradiated samples. In the case of the adducts formations, the signal intensity increases for *Aronia melanocarpa L.* and *Rosa canina L.* samples after 10 kGy radiation. The high dose radiation (25 kGy) statistically significantly decreased EPR signal intensity and ROS-adducts scavenging.

Keywords: Small berries, gamma radiation, antioxidants, protectors

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Comparison of two methods for measuring facial soft tissue thicknesses based on CT images

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Background. Facial soft tissue thickness (STT) represents the amount of soft tissue overlying the bone and measured at definite landmarks of the skull. The STT data have been used in the facial reconstruction for recreation of an individual's face based on the skull. In recent years, the computed tomography (CT) images have been widely utilized to derive STT measurements. The present study aims to compare the STT data obtained by two measuring methods based on CT images. The first method is based on 2D measurements on tomograms, and the second is grounded on measurements performed between the 3D surface models of both face and skull generated from the DICOM series.

Materials and methods. The CT images used in the study were generated with a CT system Toshiba Aquilion 64. Fifteen head CT scans of adult Bulgarians were used for the measurements. The STTs were measured at 25 anatomical landmarks. The 2D measurements were performed using the InVesalius software. The thicknesses were measured perpendicular to the bone surface in the axial and sagittal views. The measurements in the 3D space were performed after segmentation and generation of surface models of the face and skull in InVesalius. The distances between both surface models were computed in MeshLab and the STT in the particular landmarks were recorded. All measurements taken either on tomograms or on surface models were performed twice by one observer. The intraobserver reliability was evaluated using the Intraclass Correlation Coefficient (ICC) and the Technical Error of Measurement (TEM). For estimation of the intermethod differences, the mean values from the double measurements were used. The statistical significance of the metric differences between the two methods was assessed applying the paired t-test or the Wilcoxon signed rank test, depending on the results of the Kolmogorov-Smirnov normality test.

Results and conclusion. The ICC and TEM values shows excellent intraobserver reliability and a measurement error within 0.4 mm for the STTs measured by the first methods and within 0.6 mm for those computed by the second method. More than half of the intermethod differences are statistically significant, demonstrating an inconsistency between both measuring methods. Such differences are observed among the midsagattial and the bilateral landmarks. This result shows that the STT data provided by both 2D and 3D measuring methods are not interchangeable.

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Computed tomography: A non-destructive method for investigation of bone tissue structure

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Introduction. Bone is a connective tissue modified for the specific function to form a rigid framework and to provide the internal support of the body, protection of vital organs, and attachments for muscles. It is composed of living cells imbedded in an extracellular hard matrix which are sensitive to internal and external influences such as nutrition, mechanical stress, trauma, infection, and neoplastic growths. Depending on its gross architecture, the bone tissue is organized in two main types: cortical and cancellous bone. The compact bone is a dense lamellar bone, whereas the cancellous bone is a porous network of branching and anastomosing trabeculae. As a living tissue, bone undergoes continuous renewal by the opposing processes of bone resorption and formation. The pathological conditions lead to imbalance in the normal equilibrium of these processes. Bone reacts to abnormal conditions by an increase or decrease in the normal bone formation, resorption, or a combination of the two processes at different locations in the bone. Therefore, knowledge and understanding of normal bone structure, growth and remodeling are crucial for identification of various pathological conditions. This study aims to demonstrate the application of computed tomography (CT) for non-destructive examination of bone tissue.

Materials and methods. The volumetric images used in this study are obtained by medical CT system Toshiba Aquilion 64 and industrial μCT system Nikon XTH 225. The images are generated through scanning of patients for diagnostic purposes (medical CT) and scanning of dry skulls (industrial μCT).

Discussion. The CT is a powerful non-destructive modality, which allows investigation of mineralized bone tissue through virtual sectioning and visualization of the inspected specimen in the three orthogonal planes. The thinnest trabecular elements have a diameter of 70 μm, therefore the resolution of 0.3 mm achieved at CT scanning of patients is too low for calculation of morphometric parameters such as bone volume fraction (BV/TV), ratio of bone surface to bone volume (BS/BV), trabecular thickness (Tb.Th), trabecular number (Tb.N), trabecular separation (Tb.Sp) and degree of anisotropy. These images allow inspection of the whole specimen and searching for abnormality in the bone structure. The region-of-interest scanning by industrial μCT, however, generates images with high resolution which enables a reliable calculation of the morphometric parameters and the degree of anisotropy of bone tissue directly from the image datasets.

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Cytotoxic and antiproliferative effects of *Salvia officinalis* and *Melissa officinalis in vitro* plant extracts

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A large variety of studies illustrates the benefits of the active compounds present in plants from the *Lamiaceae* family on human health. Either if it is about the antioxidant or the antitumor effect, they are viable options as adjuvants to synthetic products in the therapy of various diseases. *Salvia officinalis* (sage) and *Melissa officinalis* (lemon balm) are important representatives of the *Lamiaceae* family.

The purpose of this study is to test the bioactive effects of these two *in vitro* plants extracts and to improve their biological activity by gamma irradiation of the plants' cultures.

Both types of *in vitro* plants were exposed to gamma irradiation with doses of 10, 15 and 20 Gy in order to evaluate if this treatment improves the biological effects of the extract compared to extract from non-irradiated plants. The sage and lemon balm extracts were investigated for their cytotoxic, antiproliferative properties using MTT assay on A431 human epidermoid carcinoma cell line and BJ human normal fibroblasts cell line. The cells were treated for 72h with extract concentrations in the range of 1-2000 μg/mL.

Both vegetal extracts exerted pronounced cytotoxic, antiproliferative effects against tumoral A431cells, their viability being decreased down to 30% in the case of *Melissa officinalis* and almost to 1% in the case of *Salvia officinalis* for the highest concentration used. Treatment of normal fibroblast cells (BJ cell line) with sage extract lead to a significant decrease of cellular viability (40%), while in the case of lemon balm exposure, their viability rate decreased down to 50%. No change with respect to irradiation was observed.

In conclusion, the results obtained hereby demonstrated the ability of both plant extracts to selectively inhibit tumor cells growth.

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Plant-derived vesicles as a drug delivery system to human cells *in vitro*

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Extracellular vesicles (EVs), including exosomes, are nanosized vesicles secreted by many cells that utilize them for cell-to-cell communications to facilitate transport of proteins and genetic material. EVs are found in human biofluids as well as in conditioned media of cultured cells [1].

To date, the development of drug delivery systems based on EVs is widely seen in the scientific literature. First, EVs are natural particles that make their toxicity and further immunogenic of medicine impossible. Secondly, vesicles carry large amounts of nucleic acids or proteins, saving their stability, which implies possibility of the delivery exogenous therapeutic molecules. Thirdly, EVs have effective natural penetration mechanism into recipient cells [2]. However, the further development of targeted delivery of drug-loaded EVs, as an availability of large amounts of pure exosomes for improved therapeutic outcome, is necessary for a wide applying of exosomes as carriers of bioactive molecules in humans. The extracellular vesicles, isolated from edible sources in significant numbers, are considered promising in solving of these tasks

Plant-derived extracellular vesicles (PEVs) are biocompatible, biodegradable and can be obtained in significant amount. Recent descriptions of vesicles derived from edible plants show that they might contain pharmacological active molecules [3]. It seems that the plant vesicles appeared to be promising carriers of different exogenous bioactive molecules to the human cells.

The purpose of this study is to test the delivery of functional proteins by plant vesicles to human cells *in vitro*.

In present work, PEVs from grapefruit juice were isolated by differential centrifugation and characterized in size, quantity, and morphology by nanoparticle tracking analysis, dynamic light scattering, atomic force microscopy, and cryo-electron microscopy. Cryo-EM experiments allowed us to obtain high-quality images of grapefruit membrane vesicles and accurately determine their size distribution.

Using *in vitro* cell culture models, we have shown that grapefruit-derived extracellular vesicles (GF-EVs) are highly efficient for delivering of the exogenous Alexa flour 647 labelled BSA and HSP70 proteins into human colon cancer HCT-116 and DLD1 cells. Additionally, the functional activity of being delivered by plant vesicles into the culture cells has been confirmed.

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Immune response and virus infection: Inspiring similarities

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The intrinsic features of life are (nucleotide) coding, transmission of information (DNA, RNA, etc) and protection of each organism from "pollution" with products of "foreign" genetic information, using a type of immunity. All features were originated at the beginning of life and were the prerequisites of evolution. This means that immunity evolved no later than the single-cell stage of life, when Burnet's Clonal Selection Theory was not applicable. Possibly, an ancient mechanism of molecular recognition of antigens existed. Nature is very conserved in its successful developments; therefore, it is unlikely that the molecular mechanisms of antigen recognition were omitted at the multicellular (metazoan) organisms.

We suggest that viruses and more simple RNA-protein complexes (miRNA-protein and siRNA-protein) possess features necessary for both: recognition of antigens, dissemination of the information inside definite specialized cell populations and for silencing of the auto-reactive immune reactions.

Our hypothesis is based on 2 prerequisites: 1) Existence of the molecular recognition mechanisms in the virus life cycle; 2) appreciated role of viruses as life-initiated entities and drivers of evolution. It is therefore likely that virus-adopted processes are used in eukaryotic organisms including humans. Indeed, more than 90% of the human genome represents sequences of retrovirus origin. We suggest contributions from the Human Endogenous Retroviruses (HERVs) together with miRNA-protein complexes, siRNA and retrotransposons to the mechanisms of acquired immunity.

To prove our hypothesis we've used UniProt Align, BLAST and FASTA similarity searching programs to identify homologous sites of proteins and DNA sequences. It was shown 10.5% identity (73 identical aminoacid positions) between Env protein of the HERV retrovirus and heavy chain of Human Immunoglobulin. 12.7% identity, 116 identical and 178 similar aa positions were found between Env protein of HERV and B-cell receptor (CD22). More critically, electrophoretic mobility of influenza virus polypeptide NP was equal to that of the Heavy chain of human sera Ig, and electrophoretic mobility of virus polypeptide M was the same as in the Light chain of human sera immunoglobulin.

Conclusion. We propose the Virus origin of the Immune response. We suggest to consideration of the Immune response as an aborted (atypical) Virus infection with Immune HERVs, characterizing by standard incubation period, infectious spread of the "Immunity virus" among immune competent cells and definite manifestations like exposure of virus proteins (the Ig) on cell membrane and their shedding/secretion by infected (immune) cells in the form of antibodies. According to this Theory, a faulty immune response is able to initiate cell transformation (the cancer) due to rise of retrotransposone's and telomerase reverse transcriptase activity in somatic cells primed by immune HERVs.

Silybum marianum (L.) ameliorate ochratoxin A-induced hepatic toxicity in acute models

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Ochratosin A (OTA), a secondary metabolite of *Aspergillus ochraceus* and *Penicillium verrucosum*, encountered mainly in forages. The consumption of OTA-contaminated feed showed easy distribution in the liver, kidneys, and spleen. The oxidative pathways, protein synthesis, and ROS mediation in metabolic systems were affected by OTA- toxicity. Over the last 10 years increasingly relies on herbal antioxidants that protect OTA-induced cytotoxicity and reduced DNA oxidative damages. *Silybum marianum L.* (*S. marianum*) as an isomers mixture of *silybin, silidianin, silychristin, and silipide,* contains mainly flavonolignans. *S. marianum* has a similarity with steroidal hormones and maintains the cell fluidity, the hepatocyte Ca^{2+} content, enhanced protein, and DNA synthesis. As antioxidant *S. marianum* has the ability to modulate the hepatic detoxification activity and to prevent oxidation processes by acting as oxygen-scavenger and hydrogen transferring agents. By the present study using *ex vivo* methods, we investigate the therapeutic potential and antioxidant efficacy against oxidative stress-induced conditions in hepatic tissues isolated from *S. marianum extract* IRC/w treated male mice in an acute model of OTA-induced oxidative toxicity. Mice were divided into four groups, i.e., a) untreated controls; b) *S. marianum* treated (*80 mg/kg b. wt. i.p., given 14 times/14 days*); c) OTA treated (*Isolate D2306, 1.25 mg/kg b.wt., i.p., given in every two days*); d) *S. marianum* (*80 mg/kg b.wt., i.p.*) pretreated 2hrs prior OTA-administration. Till the end of the 14 experimental days of OTA-administration, the mortality rate (±0) was not observed in mice. Liver tissues homogenates of the treated animals were subjected to ascorbate radical estimation, ROS production and the levels of oxidative stress markers, i.e., the GSH ratio, and non-enzymatic antioxidant capability of SOD and CAT. Treatment with *S. marianum* protected OTA-induced hepatic injury by suppressing oxidative stress damages with the statically significantly reduction on ascorbate levels ($p< 0.05$), ROS products ($p< 0.004$) in the liver cells, and the enhancement of the GSH ratio ($p<0.05$) and SOD ($p<0.005$) and CAT ($p< 0.03$). Reduction in oxidative disorders was observed in healthy mice which were treated with *S. marianum* only, compared to controls. Thus, it can be concluded that *S. marianum* treatment and in combination *S. marianum* +OTA neutralized OTA-induced hepatic toxicity associated with oxidative stress caused by OTA, not only by reducing lipid peroxidation but also by improving hepatic antioxidant status. By the present experiments *in vivo*, were demonstrated that *S. marianum* behaves as a potential free radical scavenger in the prevention and alleviation of acute OTA-toxicity.

Keywords: *S. marianum*, OTA, lipid-peroxidation, hepatic protection

FT-IR spectroscopy characterization of *Acacia catechu* extract-alkalized clinoptilolite microformulations

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FT-IR spectroscopy has been applied to quantify biologically active substances in semi-solid and solid formulations, to assess drug incorporation into artificial and biological matrices. Among the major advantages of the analytical technique is the possibility of spectral depth profiling.

Medical and pharmaceutical applications of natural zeolite type minerals have emerged as a promising field over the last decade, due to good performance of these materials in ion exchange, adsorptive and biocatalytic processes. Modified forms of clinoptilolites have been evaluated as a gastric antacid, antidiarrhetic agent, potential adjuvant in anticancer therapy. Therapeutic activities associated with pH balancing and radioprotective activity have also been established. One of the prospective pharmacological applications of clinoptilolite is the adsorption of various bioactive compounds and their subsequent controlled release.

The aim of the present study was to demonstrate the usefulness of the FTIR method for the evaluation of the encapsulation process of *Acacia catechu* extract into alkalized clinoptilolite framework. The absorption bands at 3516 cm^{-1} and 1282-1029 cm^{-1} in the extract spectrum are related to hydrogen bond formation. The slight shift of these wave numbers to lower frequencies observed in the spectra of catechin-clinoptilolite microparticles, depicts formation of H-bonds between the catechin-OH-groups and the two types of OH-groups present in the clinoptilolite. The spitted peak at 879 and 844 cm^{-1} is indicative for the presence of benzene ring in the polyphenol molecule. This band was found to shift to a lower frequency to broaden and become less sharp with decreasing catechin concentration in the three studied CAT-clinoptilolite samples. Similar trends were observed for the spectra at 565, 503 cm^{-1} responsible for C=C–C-aromatic ring asymmetric bending and C–H-out-of-plane aromatic ring bending. The gradual decrease of the peak intensities was directly proportional to the decrease of catechin initial concentration in the polyphenol-mineral composite systems.

The comparative analyses of the experimental data undoubtedly proved that catechin extract-clinoptilolite matrices exhibited predominantly the characteristic peaks of the polyphenol, and the quantity of the encapsulated bioactive organic molecules increased with increasing the initial concentration of catechin. In conclusion FTIR technique could be applied as an essential tool for the assessment of bioactive molecules incorporation into mineral frameworks and the mechanism of the encapsulation process offering wide spectrum of possibilities to investigate biomolecules diffusion.

Keywords: FT-IR, *Acacia catechu*, alkalized clinoptilolite, encapsulation

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Mathematical analysis of cow heart rate variability

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Method of studying of the heart rate variability (HRV) seems to be one of the promising areas of modern veterinary medicine because it is one of the most popular methods in physiology which needs methods of mathematical processing of results. The HRV-analysis proved to be modern, generally accepted indicator of the functional status of various parts of the regulatory mechanism. At present, the classical ideas that HRV is associated with the tonic influence of the nervous system only are subjected to correction. The method of HRV-analysis was used in order to study and to assess types of vegetative regulation. The *basis* of this approach is the need to plan the level of physical activity in accordance with the assessment of the type of vegetative regulation of the animal.

Since such a study is being conducted for the first time, it was decided to perform a study on the indices of heart rate variation in cows, totally, without dividing into groups according to age, weight, and functional state of animals. At the same time, in our study, before starting the recording of HRV, the studied animals were at rest for 5–10 minutes. The study of HRV was carried out no earlier than 1.5–2 hours after eating, exercise or stress, at a temperature of 20–22° C. At the time of the study, all interferences and noises resulting in emotional arousal were eliminated. When the HRV-recording, it was ensured that the experienced animals did not take deep breaths or exhale and did not cough.

For additional control of the objectivity of the developed methodology, the degree of adaptation of the cardiovascular system of cows, determined according to the results of the analysis of the cardiac rhythm, was compared with the change in the functional activity of the sympathoadrenal system. Analysis of cardio-intervals during long-term recording was carried out by analogy with the method of R. Baevsky. The main generally accepted parameters were considered. The cumulative effect of regulation was assessed by the heart rate (HR) and the duration of the R–R intervals. As a result of cattle cardiac activity study, the following gradations of heart rhythm were identified.

The method of mathematical analysis allows to control the work of the heart, the regulation of blood circulation and other parameters. HRV analysis has established itself as an indicator of adaptation-adaptive processes not only in relation to the cardiovascular system, but also to the whole organism. The facts of the connection of the formation of HRV with the inclusion of suprasegmental structures were obtained. This opens new opportunities for analyzing the nature of HRV.

Thermal processes in biological tissue during laser radiation

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Relevance. Lasers and LEDs are used in medicine as diagnostic devices for the treatment of the skin and internal organs, to carry out operations etc. It is necessary know the effect of radiation action on biological objects therefore.

Purpose of work is studying of action of the narrow beam of laser radiation on human skin and on tissue under skin. The spatial and temporal characteristics of the heat distribution in the biological tissue by heating of limited area: determine the time of heating and cooling at various modes of operation of the laser, find the dimensions of the heating region, temperature of tissue.

For this purpose heat conduction equation was solved and the temperature distribution on the skin surface and inside of the biological tissue by the action of laser radiation was finding. The wavelength of radiation is 0.8 mm (near infrared region), the radiation power is 1 W, the beam diameter is 1 mm. The depth of penetration of the radiation into the tissue is 50 mm by intensity level $1/e$. It is considered that heat sources are internal heat sources located in the cylindrical region 1 mm in diameter. The volume power density varies by exponentially taking into account the conductivity of heat and the blood beam.

Results. The mathematical model of the process by locally heating of region within the biological tissue of laser radiation was made. It is found the temperature distribution in the tissue and on its surface. It is calculated rate of heating and cooling. It is determines the power and wavelength of the radiation which are required for effective action on the object.

Conclusions. Temperature of biological tissue by laser radiation heating has strongly dependent on the wavelength, since it determines the depth of radiation penetration into the tissue. If it is necessary to heat the portion size of a few millimeters, it is necessary to use a green laser light (wavelength of 0.5 mm, the depth of penetration -1 mm), or CO_2 laser radiation (wavelength of 10.6 mm, the depth of penetration - 50 mm). If necessary, the heating of deep tissue it is necessary to use radiation of near-infrared range (wavelength of 0.8 - 1.5 mm). The characteristic value of the establishment of the temperature is a few minutes.

Spectral properties of hair (mathematical modeling, experimental determination of melanin concentration)

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Purpose of work is measuring the scattering and absorption of light in the hair of different colors. Mathematical modeling of the interaction of light with the hair was used. Optical parameters and their connection to the amount of melanin in the hair are determined.

Methods. The investigation contains several parts.

1. Image of hair in transmitted light in various ranges of the visible light was obtained using the microscope and the digital optics prefix. The intensity distribution and the transmittance were finding.
2. The task of scattering and absorption of optical radiation on hair was solved. Light falls on the hair for normal to its axis. Intensity distribution in the hair and in vicinity was found. The resulting pattern is compared with the light intensity distribution passing through the hair in the experiment. This allows find the values the refractive index and absorption index of the hair.
3. The method of calibrating (depending of absorption index versus the melanin concentration) was made.

Results. The comparison of the results of calculation and the experimental results which was obtained by photographing the hair by microscope was made. The method for measuring the optical constants of the hair was proposed. Their values are determined the concentration of melanin in hair and may be used to measure it.

Electrophysiological effect of long-lasting oxidants on Retzius neurons of the leech *Haemopis sanguisuga*

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Introduction. Electrophysiological studies have shown that reactive oxygen species (ROS) may affect cell membrane. Considering neuronal function, ROS can modify ion channels and transporters directly or indirectly via peroxidation of membrane lipids and by affecting associated signaling molecules. In the present study we examined the effects of long lasting oxidants on spontaneous spike activity and outward potassium current by exposing the Retzius neurons of the leech *Haemopis sanguisuga* to cumene hydroperoxide (CHP) and hydrogen peroxide (H_2O_2).

Methods. Experiments were carried out on Retzius nerve cells of isolated abdominal segmental ganglia of the ventral nerve cord of the horse leech *Haemopis sanguisuga*. Transmembrane action potentials were recorded with conventional microelectrode techniques and activity potassium channels were studied by using the voltage-clamp technique. Long-lasting depolarizing pulses in the point voltage experiments in leech Retzius neurons where the holding potential was more negative than -40 mV induced a progressive decay of the outward current which could be satisfactorily described by a triple exponential function.

Results. Exposure of Retzius nerve cells to CHP (0.25, 1 and 1.5 mM) prolonged the duration of the action potentials in a concentration-dependent manner. The prolonged action potentials showed an initial, spike-like depolarization followed by a plateau phase. In contrast, H_2O_2 at the same and much higher concentrations (0.25 to 5 mM) did not significantly change the duration of spontaneous spike potentials of Retzius neurons. Considering that the action potentials of Retzius neurons were elongated after exposure to CHP, the possibility of modification of membrane potassium currents was examined using the voltage clamp technique. In the voltage clamp experiments, outward potassium currents, needed for the repolarization of the action potential, were suppressed with 1 mM CHP. At the test potential of +17 mV, the fast and slow parts of the outward potassium current dropped by 42.86% and 36.12%. In contrast to the effect of CHP, application of the H_2O_2 (1 mM) failed to inhibit fast and slow outward potassium currents in the leech neurons.

Conclusion. The present findings indicate that CHP is a more potent oxidant in our model of oxidative stress than H_2O_2. The effect of CHP on the electrophysiological properties of Retzius neurons may be due to the inhibition of the outward potassium channels which play a fundamental role in determining neuronal excitability and action potential duration.

Keywords: Leech, cumene hydroperoxide, hydrogen peroxide, action potentials, potassium currents

Hydrogen peroxide and copper induce electrophysiological disturbances in Retzius nerve cells of the leech *Haemopis sanguisuga*

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Introduction. Oxidative stress and the generation of reactive oxygen species (ROS) play an important role in cellular damage. Hydrogen peroxide (H_2O_2) is a neutral molecule, which is the least reactive among ROS and is stable under physiological pH and temperature in the absence of metal ions. In the presence of redox metal ions (such as iron or copper) and superoxide anion H_2O_2 can produce the hydroxyl radical ($HO^{\bullet}$). The aim of this study was to examine whether copper can enhance H_2O_2 toxicity and whether $HO^{\bullet}$, scavengers could protect leech Retzius nerve cells from toxicity induced by the H_2O_2/Cu(II) oxidizing system.

Methods. The experiments were done on Retzius nerve cells located in the first ten abdominal ganglia of *Haemopis sanguisuga*. The membrane and action potentials were recorded using standard single-barrel glass microelectrodes. Outward directed membrane currents have been studied in voltage clamp experiments on isolated Retzius nerve cells.

Results. In the present study, oxidative stress was induced by bath application of 1 mM of hydrogen peroxide (H_2O_2) and 0.02 mM of copper (Cu) for 20 min. Our previous results showed that H_2O_2 did not significantly change the electrical properties of Retzius neurons. However, the H_2O_2/Cu(II) produced considerable changes in the electrical properties of the Retzius nerve cells. Intracellular recording of the resting membrane potential revealed that the neuronal membrane was depolarized in the presence of H_2O_2/Cu(II). We observed that the amplitude of action potentials decreased, while duration increased in a progressive way along the drug exposure time. In order to examine the possibility that the broadening of action potentials of Retzius neurons were a consequence of the inhibition of the outward potassium current, we studied the effect of H_2O_2/Cu(II) on this current. Voltage-clamp recordings revealed a powerful inhibition of the outward potassium channels responsible for the repolarization of action potentials. To confirm whether the mechanism action of the H_2O_2/Cu(II) system on the electrical properties is in any way attributable to $HO^{\bullet}$, the action of the specific scavengers were investigated. The neurotoxic effect of H_2O_2/Cu(II) on Retzius nerve cells was reduced in the presence of hydroxyl radical scavengers, dimethylthiourea and dimethyl sulfoxide, but not mannitol.

Conclusion. This study provides evidence for the oxidative modification of outward potassium channels in Retzius nerve cells. The oxidative mechanism proposed in this study might have broader significance, pertaining not only to leeches but mammalian neurons as well.

Keywords: Hydrogen peroxide, copper, Retzius neurons, action potentials, potassium currents

Study of the dielectric properties of erythrocyte hemoglobin in patients with lung cancer before and after radiation therapy

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The study of the temperature behavior of the dielectric permittivity and conductivity the cells of the blood in the temperature range from 0 to 50° C is of great interest. Oxygen carriers - blood hemoglobin Hb and muscle hemoglobin Mb are well-studied proteins with a known spatial structure. Currently, the functioning of hemoglobin as reducing agents in biological systems of cells may be an important link in connection with the identification of the role of cellular proteins in maintaining the redox potential of the cell and overcoming oxidative stress during radiation exposure to the body during the treatment of the tumor.

In this paper the use of UHF-dielectrometry method makes it possible to differentiate bound water in the hydration shell of red blood cell hemoglobin according to structural and energy characteristics. Patients with lung cancer received radiation therapy as an independent course in the mode of classical fractionation (total dose of 45-50 Gy), with a single focal dose of 1.8-2.2 Gy. Radiation therapy was performed using gamma radiation ^{60}Co. Blood sampling was performed before and after irradiation. The complex dielectric constant of aqueous hemoglobin solution was measured at frequency 9.2 GHz. The temperature was varied from 5 to 42 °C.

The authors found that the temperature dependences of the dielectric permittivity of hemoglobin suspensions for donors and patients in the studied temperature range are characterized by nonmonotonic changes in dielectric permittivity and dielectric losses and a significant increase of the frequency of dielectric relaxation of water molecules of hemoglobin suspensions of patients in comparison with the frequency of dielectric relaxation of water molecules in the hemoglobin suspensions of donors.

In the suspensions of hemoglobin of donors and cancer patients there is a change in the activation energy of the dielectric relaxation time of water molecules on seven temperature intervals. The observed breakpoints of the Arrhenius dependences lie in the range of temperatures known as critical, where the rates of many physiological processes associated with erythrocyte hemoglobin change.

Monitoring of changes in enthalpy values in hemoglobin suspensions in cancer patients provides additional information about the course of the tumor process, which is of interest in connection with the development of methods for early diagnosis of malignancies.

The results of the dielectric permittivity of hemoglobin for cancer patients after radiation therapy show that the main fraction of water near the protein surface, the so-called bound water, is not at all immobilized what is connected involve a breaking and formation of hydrogen bonds.

Paramagnetic property of proteins in aqueous solution can be highlighted even at low intensity electromagnetic fields

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The main characteristic structure in the secondary structure of proteins is the α-helix, whose dipole moment allows possible orientation of proteins along the direction of an applied electromagnetic field. The aim of this study is to show that typical proteins have a paramagnetic property that can be evidenced applying an electromagnetic field even at low intensity levels. Spectroscopic analysis has been used by FTIR spectroscopy on typical proteins in aqueous solution exposed to high frequencies electromagnetic fields at the power density level of 0.1 W/m2. Statistical analysis highlighted a significant increase in intensity of proteins Amide I band after exposure. This result can be explained assuming that proteins α-helix aligned with the direction of the applied electromagnetic field, due to the circumstance that the ligands of C=O and N-H are oriented along the α-helix axis, giving rise to the Amide I mode intensity. The result which was found is that proteins in bidistilled aqueous solution have relevant paramagnetic property which can be evidenced even at low intensities level of an applied high electromagnetic field, below the limits recommended by the ICNIRP. Given that proteins in bidistilled aqueous solution can well schematize biological cellular environment in which proteins are embedded to carry out their functions, the paramagnetic property of proteins under low intensity electromagnetic field can induce change in cellular functions.

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Correlation between the thermodynamic features of blood plasma and polymorphisms in thrombophilia genes of women with pre-eclampsia and early pregnancy loss

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Differential scanning calorimetry (DSC), highly sensitive technique for resolving heat-induced conformational transitions of biological molecules, is increasingly applied for characterization of complex biofluids with the aim to establish specific characteristics for pathological conditions. In this work we combine the thermodynamic approach with capillary electrophoresis and ELISA test to identify calorimetric features of blood plasma proteome specific for women with pre-eclampsia (PE) and early pregnancy loss (EPL), and find out correlation with the level of the plasma proteins and cytokines.

The advancement of the pregnancy of healthy pregnant women (CP) is associated with increase in the excess heat capacity of the thermal transitions of fibrinogen and immunoglobulins in DSC profiles compared to those of non-pregnant women (Controls), which correlates with the values of the respective protein fractions determined by the capillary electrophoresis. The calorimetric profiles of blood plasma from nearly half of EPL and all of PE women were found to be distinct from those of the matched CP groups. The thermograms for women with EPL and PE exhibited altered shape, reduced heat capacity and up-shift temperature of the albumin-assigned transitions, higher enthalpy and weighted average center value compared to the matched CP groups.

Additionally, increased cytokine levels of TNF-α and IL-6 were establish in blood plasma of both groups, more pronounced for EPL women.

The polymorphism in the genes of thrombophilic factors (FVL, MTHFR C677T, 4G/5G PAI-1, and PLA1/A2 ITGB3) in EPL and PE women were significantly more prevalent than in both control groups.

Our data suggest strong correlation between the modified calorimetric features of the plasma proteome of women with pre-eclampsia and early pregnancy loss and the carriage of polymorphisms in thrombophilia genes.

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Morphological and nanomechanical properties of platelets derived from women with early pregnancy loss

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Platelets play a fundamental role in hemostasis. During normal pregnancy, the fine balance between the pro- and anticoagulation systems and the fibrinolytic system is strongly altered toward hypercoagulation state thus increasing the risk of thrombosis, especially in women with thrombophilic mutation. Herein, we used atomic force microscopy (AFM) and nanoindentation to examine the morphological and nanomechanical properties (Young's modulus) of platelets derived from women with early pregnancy loss (EPL) and control pregnant (CP) and non-pregnant (CNP) women. The morphometric parameters (height and surface roughness) and the membrane stiffness of CP platelets exhibited slightly lower mean values than of CNP. EPL patients' platelets are more activated than the healthy control groups, with prominent cytoskeletal rearrangement involved. Reduced membrane roughness and height and stronger increase in Young's modulus of EPL platelets, compared to the control ones, were found for 79% of women (EPL1 group), 70% of which carried of polymorphism in thrombophilia (FVL, FII20210A, PLA1/A2, MTHFR or PAI-1) genes. The height and membrane roughness of platelets isolated from the rest of patients – EPL2 group (all carriers of polymorphism in PLA1/A2 or FVL) did not differ from the corresponding values of control ones, while the elasticity modulus was almost twice lower. The pregnancy loss of EPL1 group occurred between 6-8 gestational week (embryonic stage), while in EPL2 group - between 9-11 (foetal stage). Thus, it appears that the structural and mechanical variations in the platelets from the women with EPL correlate with platelet hyperactivity, that is associated with the carriage of polymorphisms in thrombophilia genes and the stage of gestational development at which the abortion occurred. AFM of platelets shows potential as a novel biomarker technology for platelet-related disorders.

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Biophysical characterization of the structural stability of *Helix lucorum* hemocyanin

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Hemocyanins (Hcs) are oligomeric copper-containing respiratory proteins, freely dissolved in the hemolymph of many arthropod and mollusc species. Various aspects of biomedical applications of molluscan Hcs, associated with their immunogenic properties and antitumor activity, promoted us to perform structural studies on a representative of these proteins.

The structural stability of the Hc, purified from the hemolymph of garden snails *Helix lucorum* (HlH), was investigated by means of far-UV circular dichroism, differential scanning calorimetry and transmission electron microscopy.

Higher concentrations of Ca^{2+} and Mg^{2+} ions and pH values 6.5 – 8.0 promote the stability of the protein molecule. One transition, with an apparent transition temperature (T_m) at 82.3 °C, was detected in the heat capacity curve of HlH in 50 mM Tris-HCl buffer, pH 7.2, at a heating rate of 1.0 °C min^{-1}. The calorimetrically observed thermal transition correlates well with the unfolding transition monitored by CD measurements. The two-state kinetic model was used to analyse the process of irreversible thermal denaturation of HlH, E_a 451 ± 4 kJ mol^{-1} was calculated.

The data obtained will serve as a basis for the development of stable Hc preparations and will facilitate further study of the properties and potential biomedical applications of this oxygen-carrying protein.

Keywords: Hemocyanin, Mollusc, *Helix lucorum*, thermal stability

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Device for redox-potential measurement

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The invention relates to merchandising and forensic biological examination, and to identification of the species affiliation of a sample of mammalian hairline.

The essence of the technique is that a sample of the test material is subjected to alkaline hydrolysis until complete dissolution. The resulting hydrolysate is adjusted to pH = 12.5, after which the value of the redox potential (redox potential) of the resulting solution is measured. After determining the redox potential, the solution is exposed to light with a given exposure. Under the action of light, a change in the redox-potential occurs (photo-redox effect). The amplitude of the photo-redox-effect for hair hydrolysates of various types is strictly specific.

To measure the parameters of the photo-redox effect, a device (stand) was used that includes the following standard units: a laboratory Ph-meter/ionometer with the ability to connect to a computer, a sensor unit with appropriate electrodes, a computer with software, and a specially designed ring illuminator for light exposure to the object measurements.

The totality of the possible measurement results is as follows: the value of the redox potential before exposure to light, the magnitude of the change in the redox potential during exposure to light and the value of the redox potential after the termination of exposure to light. All measurement data depend on the etiology of the studied material and are its digital biological characteristics.

Implementation of methods for hair research in practice

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The study of the physiological skin derivatives such as hair is practically important. The study of hair for resistance to aggressive environmental factors is necessary not only in animal husbandry and fur production, but also in the cosmetic industry relating to human hair. The effect on the quality of the hair is studied after the use of dyes, brightening reagents and even chlorinated water. The study of the properties of hair electrification is necessary in the manufacture of products from fur of valuable breeds: such as mink or Arctic fox. Animal hair, which is used in the spinning industry, must have a certain elasticity and tensile strength, and not form spools.

Of great importance for the examination is the determination of the species of hair. This allows to identify falsifications of products of fur raw materials. The main method for examination is microscopy of hair in transmitted light. This method is subjective, as it depends on the qualifications of the specialist conducting it. In the course of our research, we successfully applied biophysical methods: redox-metry and spectrophotometry to determine objective indicators of the quality of raw materials, as well as for species identification of hair. Since these are hardware methods, they are more objective. But the main disadvantage is the loss of the test sample in connection with the production of alkaline hydrolysates. As was discovered during the study using spectrophotometry, it is possible to identify not only species, but also gender and age differences.

Plants of *N. tabacum* expressing the desC gene were tested for resistance to ultraviolet radiation

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At present, there is a decrease in the level of ozone in the atmosphere, which leads to the formation of ozone anomalies. Under the action of ultraviolet, unsaturated fatty acids are degraded to the state of saturated, and only then degraded as saturated. Therefore, the oxidation process in them takes longer. Desaturases are enzymes that promote the formation of double bonds in fatty acids and thereby transform them from saturated to unsaturated. Tobacco plants containing and expressing the *des*C gene encoding the Δ9-acyl-lipid desaturase of cyanobacteria *Synechococcus vulcanus*, which investigated the increase in the proportion of linolenic acid used in the work. As a control, wild-type *N.tabacum* tobacco and *N. tabacum* tobacco containing and expressing the *gfp*:*lic*BM3 reporter gene were used as controls. The activity levels of the superoxide dismutase (SOD) enzyme, the level of accumulation of malondialdehyde (MDA), the level of accumulation of flavonoids after the action of ultraviolet C at doses of 1308 J/m² and 2616 J/m² were analyzed. A study of flavonoid levels showed an increase in flavonoid content after a dose of 2616 J/m² in all transgenic plants including controls. There were no differences in SOD activity indices between the tested plants and controls; investigated a lower level of MDA accumulation in plants with desaturase genes.

Potential of bioengineered polyester beads for the bioremediation of a uranium mine effluent

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The exploration of uranium in Portugal from 1908 to 2001 resulted in huge hotspots of metal and radionuclide exposure. Despite the overall success of conventional remediation works to counteract the associated risks, there are still mine effluents and/or nonpoint discharges (leaching/runoff events) jeopardizing adjacent aquatic systems. Bioremediation has been an excellent alternative, being primarily focused on microbial potential. But the direct use of living organisms may fail to succeed due to their reduced tolerance ranges. As such, biogenic, biodegradable and non-toxic polyhydroxybutyrate (PHB) beads were engineered as to obtain bioremediation agents with improved capacity to adsorb metals and radioisotopes from mine effluents. Three PHB bead types were generated and tested: one nonfunctionalized bead type (NFB), and two differently functionalized bead types (B1 and B2). In order to evaluate the efficiency of those beads to adsorb radionuclides, we have performed adsorption experiments by exposing the three bead types to a uranium mine effluent collected in the Quinta do Bispo mine pit (Mangualde, Portugal). The experiments were run at pH 4 (the effluent pH) and pH 7 (adjusted pH), in triplicate. After ending the exposures, each replicate was filtered, being the filtrate and filter-retained material analysed for quantifying the levels of different radioisotopes (^{238}U, ^{235}U, ^{234}U, ^{230}Th, ^{232}Th, ^{226}Ra, ^{210}Po) by radiochemical separation followed by alpha spectrometry. The achieved outcomes indicate that the functionalized PHB beads B1 provided enhanced ability to remove ^{238}U, ^{235}U, ^{234}U and ^{226}Ra (up to 95%) radioisotopes from the effluent at pH 7, comparatively to B2 (up to 88%) or NFB (up to 84%) beads. Accordingly, the amount of radioisotopes retained in the filter was higher in B1-exposed effluent, than for the other bead types. In general, lower removal percentages were obtained under acidic pH values. Promising results were hence accomplished thereby proving the efficiency of engineered B1 beads as bioremediation agents for the cleansing of uranium mine effluents.

Cervical cancer in Ukraine and the possibility of its prevention by vaccination against papillomavirus infection

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Introduction. Infection with human papillomavirus (HPV) presents a serious problem for modern health care. According to the World Health Organization, around 2.5-3 million cases of infection are diagnosed annually in the world. HPV causes cervical cancer, which has the most common cancer in women. A large majority (around 85%) of the global burden occurs in developed regions, where it accounts for almost 12% of all female cancers. HPV-associated diseases and, in particular, cervical cancer are a significant health problem in Ukraine. According to the National Cancer Registry of Ukraine, in the structure of the incidence of women with malignant neoplasia, cervical cancer is 5.9% (ranked fifth). About 1,700 women (5.8% of patients with malignant tumors) die every year from the cervical cancer in Ukraine.

The only way to effectively prevent HPV-associated diseases is through vaccination. Three HPV vaccines are now being marketed in many countries throughout the world - a bivalent, a quadrivalent, and nonvalent vaccine. All three vaccines are highly effective in preventing infection with virus types 16 and 18, which area together responsible for approximately 70% of cervical cancer cases globally. The vaccines have a high prevalence of cervical diseases caused by these viruses. Therefore, one of the topical issues is the study of the possibility of including vaccination against a papillomavirus infection in a mandatory vaccination calendar in Ukraine.

The purpose of the work is to determine the economic feasibility of preventing cervical cancer in Ukraine by introducing a continuous vaccination against with a papilloma virus infection.

Materials and methods. Markov simulation was used to determine the incremental cost-effectiveness ratio (ICER) on the basis of epidemiological data on morbidity and mortality from cervical cancer in Ukraine. It was assumed that the effect of vaccination persisted through out life, taking into account it only in the vaccinated population.

Results. Taking into account the accepted assumptions and limitations of the introduction of HPV vaccination in Ukraine, it will prevent the preventionof 1592 cervical cancer cases, the preservation of 2059 quality-adjusted life-year and the reduction of the cost of medical care for cervical cancer in the amount of $1,534,778. The amount of additional costs for the vaccine and its introduction was $19,037,021 (all results per 100,000 vaccinated persons). The ICER index is $8,501, which is 3,3 times the gross domestic product in Ukraine per 1 person in 2017 ($2,640).

Conclusions. Given the assumptions and the actual cost of the vaccine, vaccination against HPV infection with a view of preventing cervical cancer in Ukraine is currently not economically feasible.

Localization and shape of stenoses in peripheral lung carcinoma diagnosed by VB and FB methods

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Introduction. The study aims to present the diagnostic capabilities of virtual bronchoscopy (VB) and fiberoptic bronchoscopy (FB) for determining the localization and shape of stenoses in patients with peripheral lung carcinoma.

Material and methods. A systemic study was performed on 90 patients. 61 patients of them (67.78%) are men and 29 (32.23%) are women, 44-85 years of age with the endobronchial disease, using the FB and VB methods, over the period 2013-2020.

Results. As a result of the study of 220 patients aged 11-83 years (54.36 ± 17.24), in 90 patients after VB (40.91%; 61 men - 67.78% and 29 women - 32.23%) and in 86 patients after FB (39.09%; 61 men - 70.93% and 25 women - 29.07%) peripheral lung carcinoma was found. Cases of men diagnosed with VB and FB with peripheral left carcinoma predominate (65.38% and 71.43%, respectively) compared to those in women (34.62% and 28.57%, respectively) and vice versa with regard to cases with peripheral right carcinoma. Significant differences in the size of the stenoses were found in both sexes with peripheral carcinoma (U = 4.112, P = 0.0000).

Conclusion. VB allows high-quality visualization of stenoses and poststenotic areas that cannot be achieved with FB in peripherally located processes. Through VB peripheral branches of 5-6 order can be reached. VB makes it possible to examine the areas located after the tumour formation.

Keywords: Peripheral lung carcinoma, localization, stenoses, VB, FB

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Monitoring of radioactive contamination of southern Baltic Sea in 2016-2018

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Central Laboratory for Radiological Protection performs regular observations on radioactive contamination of southern Baltic Sea environment since 1986. Current research includes determination of ^{137}Cs, ^{238}Pu, ^{239,240}Pu and ^{3}H in biota (fish), water and bottom sediments. Studies are coordinated by Helsinki Commission and carried out by all Baltic States.

Samples of fish (cod, herring, sprat and plaice) came from the Gdansk Bay, the Gdansk Basin and the Bornholm Basin. Water samples and sediment core samples were taken during the sampling cruises with r/v "Baltica" in permanently selected six sampling stations located in the Gdańsk Basin (3), Gotland Basin (1) and Bornholm Basin (2). Determinations of ^{137}Cs ^{40}K and ^{3}H in water were performed in surface and near bottom layers. In the bottom sediment determinations of ^{137}Cs and plutonium isotopes were performed in stratified core samples.

Determinations of ^{137}Cs and ^{40}K were performed by gamma spectrometry, plutonium isotopes were determined by radiochemical method and alpha spectrometry measurement. Tritium was determined by the method based on electrolytic quantitative enrichment of ^{3}H in samples, distillation of concentrates and measurement of their radioactivity using a liquid scintillation spectrometer.

In four fish species the highest concentration of ^{137}Cs was found in cod and the lowest in herring. Average ^{137}Cs concentration calculated for above mentioned species in 2018 was 3.10 ± 0.46 Bq kg$^{-1}_{ww}$, being almost five times lower comparing to the maximum recorded in 1989.

In the water samples concentrations of ^{137}Cs were in the range of 18.0 ÷ 31.6 Bq m^{-3}. The smallest value was determined in the Bornholm Deep and accompanied by the highest salinity. This characteristic is directly related to the impact of highly saline water from the North Sea that has lower concentrations of ^{137}Cs. In most locations' concentration of ^{137}Cs in surface waters was higher than in near bottom waters, which is in accordance with the long-term trend. Activity concentrations of ^{3}H in surface and near bottom water were 3.1 kBq m^{-3} and 2.4 kBq m^{-3}, respectively.

Contamination of sediments in the southern Baltic Sea was uneven. The concentration of ^{137}Cs and plutonium isotopes were higher in the Gdansk Basin than in the Bornholm Basin. The vertical distributions of mentioned isotopes show that the highest ^{137}Cs activity concentrations were found in the upper sediment layers, and in the Gulf of Gdansk reached up to 227 Bq kg$^{-1}_{dw}$ while in Bornholm Deep it was 52.5 Bq kg$^{-1}_{dw}$ (in 2018). In the case of plutonium isotopes, its higher concentrations were observed in deeper layers. The highest concentrations of ^{239,240}Pu were found in deeper layers of Gulf of Gdansk (5.4 Bq kg$^{-1}_{dw}$) while in Bornholm Deep (1.1 Bq kg$^{-1}_{dw}$).

Monitoring of radiological parameters of drinking water in large Polish cities and evaluation of doses received by its consumption

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In Poland, the quality of water is regulated by the Ordinance of the Minister of Health of 7 December 2017. Monitoring of radioactive contamination of tap water in 2019 included samples of water coming from the main water intakes in Warsaw and Kielce. Tap water was collected into polyethylene containers with a volume of 10 dm^3. Twenty liters of water were collected from each point. The water delivered to the laboratory was distributed for testing as follows:

- 15 dm^3 of water was allocated to the ^{137}Cs and ^{90}Sr content tests.

The samples were pre-evaporated to approx. 0.5 dm^3. First, ^{137}Cs content was determined, followed by ^{90}Sr.

- 4 dm^3 of water was dedicated to the study of total alpha and beta radioactivity.

- the remaining 1 dm^3 of water was allocated to the tritium content tests.

In the water samples concentrations of ^{137}Cs were in the range of 1.74±0.23 to 3.53±0.41 $mBq \cdot l^{-1}$. The average concentration of ^{137}Cs calculated for the examined water samples was 2.77±0.75 $mBq \cdot l^{-1}$.

In case of ^{90}Sr that range was from values 1.54±0.17 $mBq \cdot l^{-1}$ to 4.73±0.54 $mBq \cdot l^{-1}$. The average concentration of radioactive ^{90}Sr in drinking water tested was 2.80±1.44 $mBq \cdot l^{-1}$.

The tritium concentration in drinking water ranged from <0.5 to 1.9 $Bq \cdot l^{-1}$.

The total beta radioactivity in investigated water samples was very low and ranged from 0.05±0.01 $Bq \cdot l^{-1}$to 0.22±0.03 $Bq \cdot l^{-1}$. The total radioactivity exceeded the detection limit of a (0.015 $Bq \cdot l^{-1}$) only for water sample.

Based on the concentrations of ^{137}Cs and ^{90}Sr, the annual absorption of these isotopes with water in age groups was calculated.

On the basis of these data, the average annual absorption was calculated. These absorptions were 0.23±0.67 $Bq \cdot year^{-1}$; 0.32±0.49 $Bq \cdot year^{-1}$; 0.49±0.75 $Bq \cdot year^{-1}$ and 0.67±1.02 $Bq \cdot year^{-1}$ for ^{137}Cs. The ^{90}Sr absorption in appropriate age groups was: 0.23±0.39 $Bq \cdot year^{-1}$; 0.33±0.55 $Bq \cdot year^{-1}$; 0.50±0.85 $Bq \cdot year^{-1}$ and 0.68± 1.14 $Bq \cdot year^{-1}$.

Based on the annual absorption and appropriate conversion factors expressed in $Sv \cdot Bq^{-1}$, calculated weighing effective doses.

Doses from absorption of ^{137}Cs range from 0.003 to 0.009 $\mu Sv \cdot year^{-1}$, which is a small percentage (0.0003-0.0009%) of the annual border dose for people from the general population specified in the Regulation of the Council of Ministers dated January 18, 2005 on the radiation dose limits of ionizing radiation Dz. U. No. 20, item 168 (1mSv $year^{-1}$).

From ^{90}Sr absorption, the doses range from 0.019 to 0.054 $\mu Sv \cdot year^{-1}$, which is 0.0019% - 0.0054% of the limit dose.

The results obtained indicate that these doses are negligibly small and the tap water in all examined cities meet the requirements set out in the Regulation of the Minister of Health of 7 December 2017.

$^{234}U/^{238}U$ activity ratio and $^{87}Sr/^{86}Sr$ isotope ratio in ultra-fresh lakes of the Altai Mountains

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Previous studies have shown great potential for using the $^{234}U/^{238}U$ and $^{87}Sr/^{86}Sr$ isotope ratios to determine the duration of water-rock contact, and the difference or similarity of the rock composition (Chabaux et al., 2011). However, in this work the study was directed on the systems of salt and fresh lakes, which are mainly fed by groundwater. Our work focuses on ultra-fresh lakes with mainly meteoric and glaciers feed. Deep groundwater supply is absent.

The purpose of this work is to identify patterns of change in the values of the $^{87}Sr/^{86}Sr$ isotopic ratios and the activity ratios of $^{234}U/^{238}U$ in the ultra-fresh lakes water located in a relatively small territory of the Ulagansky region of the Altai Republic. All the studied lakes have the salinity of near 50-300 mg/l; the type of water in all cases is Ca-HCO_3.

As a reference for the region and averaging a large catchment area Teletskoye Lake were taken. Two samples were taken in Lake and one at Korbu Falls. The 234U/238U value in the Korbu waterfall is 1.8 ± 0.4, at the estuary of the Korbu river in Teletskoye $^{234}U/^{238}U$ = 1.9 ± 0.1 and in Teletskoye Lake near the source of the Biya River $^{234}U/^{238}U$ = 2.0 ± 0.3. The ^{87}Sr / ^{86}Sr ratio in the waterfall significantly exceeds the values for the lake itself and is 0.712630 ± 21 (hereinafter, the error in measuring the Sr isotopic composition is given for 2σ in the format 10-6). At the estuary of the Korbu River and at the source of the Biya River, the Sr / Sr ratio is 0.709925 ± 4 and 0.709877 ± 6, respectively. That is, we can assume that the composition of the waters of Lake Teletskoy is the same.

Small lakes, Ulagansky district, are located in a small area. They contain a fairly wide range of variations of isotope ratios. The isotopic activity ratio of U varies in the range from 1.8 ± 0.3 to 4.0 ± 0.1, the ratio $^{87}Sr/^{86}Sr$ varies in the range from 0.708054 ± 4 to 0.712036 ± 8. An inverse correlation was found between these parameters and a direct correlation between the content of Sr and U.

The value of the 234U/238 U activity ratio in the literature is interpreted as an indicator of the water – rock interaction time (Chabaux et al., 2011). Perhaps, in the case of the lakes of the Ulagansky district, this trend is also manifested. The highest isotopic ratios (4.0 ± 0.1 and 2.8 ± 0.1) have lakes located in a swampy intermountain basin. In turn, the water of the flowing lake “Mertvoe” formed several decades ago after a collapse blocking the river has $^{234}U/^{238}U$ = 1.8 ± 0.3 in the same way as in Lake Teletskoye. Other studied lakes located above lakes from the intermountain basin have intermediate $^{234}U/^{238}U$ values (2.6 ± 0.2; 2.3 ± 0.4 and 2.0 ± 0.6).

With respect to the 87Sr / 86Sr ratio, we noticed a clear territorial zonality. One can see the similarity of the isotopic compositions of the water of three lakes in the lowland (87Sr / 86Sr ~ 0.7082), as well as two closely located lakes located hypsometrically higher (87Sr / 86Sr ~ 0.71082). In addition, another lake located not far from them has higher values of $^{87}Sr/^{86}Sr$ = 0.712036 ± 8. The Mertvoe Lake also differs from the others (87Sr / 86Sr = 0.709127 ± 7). Obviously, the motley geological composition of the folded structure of Altai in this district is reflected in the isotopic composition of the Sr water of the studied lakes. There are igneous rocks of various compositions, metamorphic (green shales), and also sedimentary rocks. In addition, everything is complicated by fairly widespread madder deposits. Since the lakes are predominantly meteoric and the glacial ratio $^{87}Sr/^{86}Sr$ of each of them is a reflection of the isotopic composition of the bottom rocks.

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Hybrid advanced oxidation processes (AOPs) based on cavitation phenomena for water and wastewater treatment

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Advanced oxidation processes (AOPs) based on cavitation phenomena are nowadays extensively studied, especially as processes dedicated for wastewater treatment technologies [1-2]. Cavitation phenomena can be induced in the liquid by means of ultrasonic radiation – a so-called sonocavitation (acoustic cavitation) or by different approaches such as hydrodynamic or optic cavitation.

The paper presents up-to-date review of knowledge on cavitation-based AOPs and the most important results of applicational studies of this group of processes. During the presentation recent developments of our research group will be presented in respect to effective degradation of several pollutants present in industrial effluents, including volatile organic compounds (VOCs), BTEXs, organic dyes as well as selected ions. Details on optimization of process parameters will be discussed along with explanation of mechanism taking place during transformation or organic compounds during cavitational treatment [3-8].

Developed technologies will be discussed in terms of (1) instrumentation needed to perform the treatment in laboratory as well as process scale, (2) methods of process control and degradation monitoring (3) economical evaluation of process feasibility (4) scale-up aspects (5) hybrid – cavitation-catalytic processes (6) overall advantages and disadvantages on cavitation based AOPs.

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Application of hybrid approaches based on cavitation and advanced oxidation processes in water treatment containing organic pollutants

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Among the variety of technologies designed for the elimination of refractory organic compounds in liquid phase, advanced oxidation processes (AOPs) represent a promising alternative, which can achieve complete mineralization. Based on the oxidation potential of highly reactive hydroxyl radicals (HO•), AOPs were proven to ensure high degradation efficiency of target compounds avoiding secondary pollution. Compared to other AOPs (i.e., Fenton process, UV/oxidant, UV-photocatalyst, corona discharge, etc.), cavitation-based AOPs have low operational cost, low energy utilization and can be applied in large-scale wastewater treatment. In recent years, only acoustic and hydrodynamic cavitation is extensively used in various chemical processes. The application of cavitation conditions results in the thermal dissociation of hydrocarbon molecules by the subsequent collapse of generated cavities in the media. Cavities are generated through hydrodynamic cavitation (HC) and acoustic cavitation (AC). HC-based devices include orifice, vortex diode, and Venturi and AC consists of ultrasonic bath and ultrasonic horn-type devices. The principle is the same in both methods, where the reactive radicals are generated through the dissociation of molecules entrapped in the bubble, and under extreme conditions such as high temperature (5 000-10 000 K) and pressure (500 atm) inside the bubble, generated reactive radical species such as HO• H•, O•, HO_2• can be formed. The combination of HC with external oxidants (Na_2SO_8, H_2O_2, Fenton's reagent, CH_3COOH, HCOOH, etc.) is a novel approach aimed to increase the efficiency of existing AOPs by accelerating the generation of reactive radicals. Thus, sole HC induced by Venturi tube with inlet pressure 8 bar and cavitation number of 0.27 gave 46%, 49%, 56% and 47% of benzene, toluene, ethylbenzene and *o*-xylene (BTEX) after 240 min at mild conditions. The combination of HC with persulfate (PS) in molar ratio of PS to BTEX at 5:1 enhanced the degradation efficiency of benzene, toluene, ethylbenzene and o-xylene by 29%, 34%, 24% and 35%, respectively. The synergistic effect between HC and PS was attributed to PS activation followed by the increase of number of reactive species (SO_4•- and HO• radicals) responsible for BTEX degradation.

The treatment of hydrocarbon liquid with conventional methods requires harsh conditions such as high temperature > 300°C and high pressures > 30 bar, and still, it may lack in the complete removal of low reactive substituted benzothiophenes (BT) and dibenzothiophenes (DBT). In contrast, cavitation conditions provide the extreme temperature and pressure inside the bubble, which subsequently will break the carbon chains, and the presence of oxidants will oxidize thiophenes (TH), benzothiophenes (BT), and dibenzothiophenes (DBT) in sulfoxides and sulfones. The cavitation bubble can be considered as a micro or nanoscale reactor that contributes to low sulfur or nitrogen-containing compounds for the studied media. Effect of cavitation phenomena in the organic phase media consists of in the implementation of sole cavitation processes, sole oxidants processes, and the combination of the cavitation and oxidants. The evaluation of processes is made based on the (%) desulfurization yield, synergistic coefficient, and cost-effectiveness for the implemented experiments.

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Comparison between beta attenuation, light-scattering and gravimetric methods for sampling $PM_{2.5}$ fraction collected at Urinj, Kostrena, Croatia

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The initial measurements of hourly and daily $PM_{2.5}$ fraction obtained by beta attenuation (BAM) and light-scattering (LSM) methods are reported. Daily concentrations obtained by BAM and LSM are compared with gravimetric method (GM). For gravimetric method, the samples were collected on stretched Teflon filters in 24 h period. Sampling was performed at Urinj during a continuously 16-day period in July, and 10-day period in October/November 2019. Urinj is industrial area of a Croatian municipality Kostrena (Kvarner Bay, Croatia) with an active oil refinery and an oil-fired power plant.

The average daily $PM_{2.5}$ concentrations was (9.35 ± 2.12) μgm^{-3} by the gravimetric method, then (10.85 ± 3.29) μgm^{-3} by the light scattering method and (7.34 ± 3.62) μgm^{-3} by the beta attenuation method. Generally, the light-scattering results are higher (14%), and the beta attenuation results are lower (22%) than results obtained by gravimetric method. The statistical methods showed that there is no statistically significant difference among the daily results.

The purpose of this analysis was to evaluate the suitability of our new portable real-time detector designed to measure particulate matter dynamics in outdoor and indoor environment by light-scattering method (LSM).

Correlation between airborne radionuclides and selected trace elements in suburban environment

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Adverse health effects of ionizing radiation raise a concern related to the inhalable radionuclides in the ambient air, but the additional risk comes from the coarse, fine and ultrafine atmospheric particulate matter with complex predominantly non-radioactive trace elements. Assessment of these two pollutant categories usually includes different approaches and research methodologies although both obey to similar processes and influences in the atmospheric environment. Physical-chemical characteristics and correlations of Pb-210, Be-7 and Cs-137 activity concentrations in total suspended particles and selected trace elements concentrations in the fine fraction (PM2.5) of atmospheric particulate matter, observed at the suburban monitoring station have been a subject of this study. Radionuclides data, reported in the national annual radioactivity monitoring reports, had been obtained by gamma spectrometry analysis (HPGe) of monthly composite samples, collected on daily basis, using cellulose filters and high-volume sampler (air flow about 50m^3/h). Fine particulate aerosol fraction within our research had been sampled by European reference low-volume sampler (2.3 m^3/h) with nozzles passing the particles with aerodynamic diameter less than 2.5 μm onto preconditioned PTFE filters. In this case daily aerosol samples were analyzed by non-destructive nuclear analytical technique to obtain simultaneously concentrations of trace elements. The statistics of radionuclides and trace elements concentrations was done and correlations and mid-term trends have been analyzed and discussed based on the knowledge on the radionuclides origin in the atmosphere, nuclear data, meteorological and precipitation data at the sampling site. Results have shown various correlations between the cosmogenic Be-7 and naturally occurring Pb-210 (Rn-222 descendant, from U-238 radioactive series) with Al, Si, Fe, Pb, Ca, elements pointed as tracers of soil-related factor in source apportionment receptor analysis (EPA PMF). Although the observed correlations and meteorological parameters have shown a dominantly natural origin of these elements, the industrial emissions might still contribute in some extent. Differences between elemental lead and radionuclide Pb-210 concentration allow us to distinguish shares coming from local soil and from the antropogenic activities in the investigated environments. This study has shown a capacity of naturally occurring radionuclides to be the tracers of processes in lower layers of atmosphere or the indicators of pollution origin, especially in boundary urban areas.

Concentrations of some heavy metals in urban soils and tree leaves from several city areas in the Republic of Srpska

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This study analyzed concentrations of heavy metals (HMs) in the urban soils (a.k.a. urbosoils) and tree leaves in the several cities in the territory of Republic of Srpska, with the aim to identify urban tree species as potential bioindicators of urban pollution. Nowadays, although cities occupy only 3% of the total Earth's surface, they are home to over 50% of the world's population. As a result of rapid urbanization and population growth in urban areas, the amount of various urban wastes and pollutants, including HMs is highly increased, having a significant impact on the urban environment and human health. Urbosoils are very heterogenic soils, significantly different of traditional soil types due to their properties changes linked with the urbanization processes in a way that those soils are highly loaded with waste materials used in the construction of buildings or traffic. Besides, urbosoils usually contain high concentrations of many HMs with toxic environmental effects. Woody plants, especially tree species may be used as biomonitors and bioindicators of urban pollution with heavy metals originated from traffic, atmospheric deposition, urbanization processes and inappropriate management of urban soils. Taking into account all the above facts, concentrations of three heavy metals, nickel (Ni), chromium (Cr) and manganese (Mn) were analysed in soils and tree leaves sampled in parks of cities of Banja Luka, Prijedor and Bijeljina. Leaf material is sampled from two common tree park species: horse chestnut (*Aesculus hippocastanum* L.) and planetree (*Platanus* × *acerifolia* (Aiton) Willd.), to evaluate their ability to adopt and translocate Ni, Cr and Mn from urbosoils to leaves and thus contribute to biomonitoring and refining of urbosoils pollution with HMs. Obtained data showed that concentrations of analyzed HMs in urbosoils, depending on locations and cities, varied in range 63.6-178.8 mg/g Ni, 87.0-233.7 mg/g Cr and 1040.9-1979.6 Mn, which are considered significantly above world´s mean levels, indicating urban soils contamination. Also, significantly higher concentrations of the same HMs are found in leaves of analyzed tree species with values above toxic levels for plants (1.5-7.6 mg/g Ni,0.3-3.2 mg/g Cr and 22.3-103.4 mg/g Mn), depending on locations and cities. The results of the measurements of HMs concentrations in tree leaves from city parks showed the accumulation of Ni, Cr and Mn reflecting urbosoils contamination and that horse chestnut and planetree could be a good plant choice for refining and biomonitoring HMs pollution in urban areas.

Keywords: Heavy metals, urban pollution, urbosoils, tree species, nickel, chromium, manganese

Conforming to the harmonized UAV regulatory framework in European countries – Experiences from the Preparedness project

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16ENV04 Preparedness, Metrology for mobile detection of ionizing radiation following a nuclear or radiological incident", is a project within the EMPIR framework, specifically aimed at metrology institutes. One of its main goals is the development of Unmanned Aerial Measurement Systems (UAMS), along with the novel methods and procedures for their use. It is almost self-evident that drone mounted with an array of compact sensors, which may include specialized equipment, such as gamma spectrometer, would be of great help to first responders. Previously, one of the limiting factors for application of UAMS for emergency response was the legislative regarding UAVs, which was, while similar, not entirely harmonized in Europe, thus hindering development, testing and finally deployment of drones in emergency situations.

This problem was recognized at EU level, and large efforts were put into development of harmonized drone legislation across all member states. The efforts were led by European Aviation Safety Agency (EASA). Besides increasing cooperation potential of manufacturers and research groups, goal of this effort was also to ensure the safety and security of all European citizens who could be affected by drone activities. This made Europe the "first region in the world to have a comprehensive set of rules ensuring safe, secure and sustainable operations of drones both, for commercial and leisure activities". [1]

While previous version of regulations [2,3] had maximum take-off mass as an important criterion in drone classification, the new unifying EU regulation introduces UAV operation categories based on the "risk level criteria". New regulation recognizes several categories of drone operations, namely: 'open', 'specific' and 'certified' category. Each category ups the level of needed authorization for drone use. Increased risk requires appropriate measures to be taken, for example, since the use of drones in emergency response may impose BVLOS operation, it is necessary to have integrated collision avoidance systems.

In this paper, experiences from Preparedness project, in the context of the new harmonized EU UAV regulatory framework are presented. Furthermore, planned and already held UAV exercises are briefly described, along with the specialized equipment developed and tested within Preparedness.

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Activity concentrations of ^{137}Cs in muscles of wild boars in Poland: 2012–2018 results

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The radiocaesium activity concentrations may still remain high in natural products such as game meat, wild mushrooms, and forest berries. The results of regular radioactivity monitoring of game meat in Poland showed wild boars as the most contaminated game animals. It has been well documented that some mushrooms, readily consumed by animals, show high ability to accumulate caesium radioisotopes. Furthermore, animals consuming various mushroom species may also digest highly contaminated soil components. Within seven years more than 430 samples were examined. Radiocaesium activity concentrations were determined by a gamma-ray spectrometry technique using standard 450 cc Marinelli beakers. Generally, the ^{137}Cs activity concentrations were very variable. Even in the same region they ranged from values below MDA to hundreds of Bq/kg. In eight samples, ^{137}Cs radioactivity concentrations exceeded 600 Bq/kg (maximum permitted level). The highest value reached 2850.6 Bq/kg. Moreover, the effective doses originating from ^{137}Cs were calculated. In conclusion, some precautions could be advised for consumers with elevated intake of wild boar meat – hunters with their families.

Application of new protein sources in food emulsions

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The composition and technology of oil-water food emulsions with two species of Bulgarian freshwater microalgae Spirulina and Chlorela were developed. The stability and rheological behavior of model emulsions was studied. A comparison was made with the results of similar systems with skim milk powder.

According to literature, unicellular freshwater algae Spirulina and Chlorella reduce inflammation and heart disease and have protective properties against certain types of cancer. A high protein content of Spirulina (43.7%) and Chlorella (43.7%) was established, which identifies them as suitable emulsifiers in food emulsions.

From the analysis of the rheological characteristics of the emulsions, with sufficient accuracy, we can conclude that emulsions with 20% and 40% of the oil phase have the behavior of an ideal plastic body. Emulsions with a higher oil content (60%) and an emulsifying component (8% and 12%), regardless of the type of emulsifier are pseudoplastic fluids. The highest values of plastic viscosity and consistent coefficient show emulsions with Spirulina. Those with skim milk powder have the lowest values.

Emulsions with 12% Spirulina and Chlorella, in all three oil phases, have high stability (90%). At the lower values of the emulsion agent, emulsions with skimmed milk powder are more stable.

Key words: Food emulsions, Spirulina, Chlorella, protein content, stability, rheology, viscosity

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Correlation study of different solvent extraction effects on phenolic contents and antioxidant activities of some dried spices

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Extraction of dried spices (fennel, anise, coriander, celery, parsley, dill, star anise pericarp, star anise seed, caraway and cumin) was examined using ethanol (75%), acetone (70%) and water. Content of total polyphenols (TP) and flavonoids (TF) in these extracts were determined spectrophotometrically. Screening of antioxidant activities of extracts was performed by DPPH, ABTS, FRAP, RP and CUPRAC spectrophotometric assays. Pearson correlations analysis was applied in order to evaluate inter-relationship of parameters. Results of this analysis showed that correlation coefficients between all parameters in ethanol ($r=0.85–0.98$) and acetone ($r=0.59–0.95$) extracts were highly positive, $p<0.05$. Water extracts demonstrated high values of Pearson's r between all applied antioxidant assays ($r=0.73–0.96$), while total flavonoids showed weaker correlations with other parameters. The highest correlation was calculated for TF and RP ($r=0.57$, $p<0.05$). In order to summarize effects of all the obtained antioxidant activity data in applied solvents, antioxidant composite indexes (ACI) were calculated for each spice in each extract. Analysis of these results showed that ethanol extracts of six (dill, fennel, parsley, star anis pericarp, cumin) out of ten selected samples had the highest ACI values. Dill showed the highest, while coriander showed the lowest ACI results in all three extracts. This is in accordance with TP and TF contents in examined extracts. Therefore, extraction of tested spices by appropriate solvent is important for obtaining fractions with high antioxidant activities.

Polyphenol-rich waste wood extract as natural preservative of cottage cheese

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The main idea behind this work was to use completely natural and eco-friendly wood waste extract for the treatment of cottage cheese. Heartwood is a rich source of different bioactive metabolites and wood extracts could be applicable in the food and pharmaceutical industries. Following initial phenolic screening [1] and proved antimicrobial activities on eight representative human pathogens, the main focus of this investigation was to test the potential of the extract of wild cherry wood (*Prunus avium* (L.) L.) to be used as a preservative to prolong shelf-life of cottage cheese. Different concentrations of cherry tree extract were directly mixed with chees samples and stored under refrigerator conditions (4 ^{o}C). Samples were tested on third, seventh and tenth day. Microbiological analysis included enumeration of total plate count, *Enterobacteriaceae*, yeast and molds and *Staphylococcus spp*., using ISO standard methods. Concerning the microbiological quality of cottage cheeses, cherry tree extracts showed strong antimicrobial effect leading to rapid reduction of the microbial groups in treated chees after 3 days, compared with initial count (0 day). Also, yeasts count was significantly reduced in samples after 7 days, while growth of molds was noticed between 7th and 10th day. Results of this investigation are promising in a view of the possibility of the wood extract utilization in preserving perishable foods with short shelf life.

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Health risk assessment of autochthonous and international grapevine varieties from Serbia

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In this research, health risk indices have been used to monitor the transfer of possible contaminants, such as toxic elements, from grapes to humans. The phenolic and elemental profiles of autochthonous and international grape varieties collected in a vineyard located in East Serbia were analyzed. The following results represent a continuation of our previous investigations [1, 2] on phenolic and elemental composition of different grapevine varieties. Here, phenolic acids were determined in skins, seeds, and pulp of grape samples, along with total phenolic content and radical-scavenging activity. Total phenolic content and radical scavenging activity were highest in the seeds of autochthonous variety 'Plovdina', and in the skins of 'Smederevka', where also the highest contents of ferulic, chlorogenic, and caffeic acids were found. Protocatechuic acid was detected only in the seeds of autochthonous varieties. Elemental composition was established for each variety, in the whole berry. 'Plovdina' grapes had lower quantities of Al, Ni, and Na in comparison to the other varieties intended for white wine production. Significant correlations obtained among the most abundant elements, pointed to some synergistic interrelations. The potential threat of non-carcinogenic and carcinogenic risk for adults and children who regularly consume the grapes was assessed by calculating daily intake rate, target hazard quotient, hazard index, chronic daily intake, and target cancer risk. Obtained results indicate that all studied grape samples were safe for human consumption.

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Investigating radon, pH values and fluorides in spring waters from rural areas and municipalities of Leposavić and Novo Brdo, Kosovo and Metohija

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This study presents the results of the research carried out on the territory of two municipalities in Kosovo and Metohija: Leposavić and Novo Brdo. Households typically take their drinking water from a well in rural areas of these municipalities. The purpose of this study is to investigate the water quality, primarily radiation properties of spring water used by the inhabitants for drinking and other purposes. It is known that radon is highly soluble in water, making it possible to seep into drinking water and therefore cause the radioactivity to enter into the human body. Radon concentration in water was determined by alpha spectrometric method using the system (RAD7 RAD H_2O) (DURRANGE Co.), and ranged from 5.05 Bq l^{-1} to 340.72 Bq l^{-1}, with mean value of 36.65 Bq l^{-1}. An important parameter of water is its pH value, which indicates acidic or alkaline properties. If the water is characterized by a low pH value, the presence of easily dissolved radium is enhanced, which leads to an increased presence of radon in it. Measured pH values ranged from 6.8 to 7.6, with mean value of 7.16. From the radiation point of view, spring waters from these areas can be used for drinking, but also for other purposes. In this study authors also investigated the fluoride concentration of the drinking water to get an idea of the overall water quality. Fluoride, if consumed at high doses, can weaken bones and reduce the quality of the tooth enamel. Fluoride concentration was determined by potentiometric titration with an ion-selective electrode. For this purpose, a WTW fluoride ion-selective electrode, a saturated Ag/AgCl reference electrode, and a HANNA pH/mV meter were used as the working electrode to measure the pH value. Values of fluoride concentration ranged from 2.08 mg l^{-1} to 25.04 mg l^{-1}, with mean value of 11.60 mg l^{-1}, which is ten times more than allowable concentration of fluoride in water.

Keywords: Spring water, radon, pH value, fluoride, water quality

Annual effective dose due to ingestion and inhalation of radon in water samples from public fountains in municipality of Kuršumlija, Serbia

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In the present study, the water samples were taken from public fountains in rural area municipality of Kuršumlija, in southern part of Serbia. Sampling of water from public fountains began subsequently according to establishment role and analyzed by alpha spectrometric method using the system (RAD7 RAD H_2O) (DURRANGE Co.). Values of radon concentration in water ranged from 4.4 Bq l^{-1} to 22.4 Bq l^{-1}, with mean value of 13.8 Bq l^{-1}. As can be seen, the radon concentrations in water samples from this region were well below the range prescribed by the WHO – 100 Bq l^{-1}. The annual effective dose due to ingestion of radon in water samples is varied from 0.03 mSv y^{-1} to 0.16 mSv y^{-1}, with mean value of 0.1 mSv y^{-1}, due to inhalation of radon in water samples is varied from 13.44 μSv y^{-1} to 62.72 μSv y^{-1}, with mean value of 39.09 μSv y^{-1}. Annual effective dose ingested by stomach due to consummation of water varied from 0.003 mSv y^{-1} to 0.019 mSv y^{-1}, with mean value 0.01 mSv y^{-1}. Annual effective dose received by lungs due inhalation of radon released from water ranged from 1.61 μSv y^{-1} to 7.53 μSv y^{-1}, with a mean value 4.72 μSv y^{-1}. Since the values of annual effective dose in investigating region are found below the recommended limit, hence it can be concluded that the areas are safe for health hazard point of view.

Keywords: Radon concentration, ingestion dose, inhalation dose, radiological risk

System analysis of the linkage of sporadic fluctuations in the incidence of childhood cancer with environmental factors

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According to traditional ideas, changes in the incidence rate (IR) of malignant neoplasm's (MN) are sporadic, random in nature. Therefore, to study the causes of tumors and identify hidden trends, these fluctuations are aligned. We put forward the opposite thesis: fluctuations in the incidence of cancer are causal in nature and are associated with environmental factors.

To study these linkages we used data on the incidence rate of MN in young children (YC) 0-4 years old, since tumor pathology at this age is predominantly prenatal. This allows to get results in a fairly short time.

We studied the dependence of cancer incidence in the YC population of the Khabarovsk Territory (572 cases) with the number of forest fires and Solar activity. A model of the ecosystem "Sun - Smoke of Forest Fire - childhood cancer" was created. The linkage between the Wolf number, the quantity of forest fires, and the incidence of cancer in the YC cohorts of 1972-1988 year of birth was investigated by multiple regression-correlation analysis.

It was established that the number of forest fires 2 years before the birth of children is associated with the incidence of Hodgkin's lymphoma ($r = 0.726$, $p = 0.001$), in the year of birth - with IR of neuroblastoma ($r = 0.736$, $p = 0.037$, cohorts 1976-1983 year of birth) and retinoblastoma ($r = 0.541$, $p = 0.046$, 1975-1988 year of birth). Fires that occurred 1 year after the birth of children had a linkage with the incidence of tumors of the central nervous system ($r = 0.533$, $p = 0.028$).

The activity of the Sun 1 year before the birth of children was associated with non-Hodgkin's lymphomas, in the year of birth - with sarcomas of soft tissues, 3 years after birth - with a Wilms tumor.

Leukemia incidence was found to be related both to the number of forest fires 2 years before the birth of children and to the activity of the Sun 3 years after their birth ($R = 0.614$, $F(2.14) = 4.236$, $p < 0.036$). For the combined group of embryonic tumors a significant link was found with the number of fires per year of birth, and the activity of the Sun 1 year after the birth of children ($R = 0.912$, $F(2.5) = 12.281$, $p < 0.012$).

Thus, fluctuations in the incidence of cancer in YC are associated with long-term changes over many years of the complex of environmental factors. We called this phenomenon "Alternative oncogenesis", implying a change in the incidence and spectrum of tumors over a certain period of time due to changes in the parameters of the complex of environmental factors.

It is known that smoke and electromagnetic waves cause the development of oxidative stress. Therefore, measures for the prevention of malignancies in children should include tools that help improve antioxidant protection in future parents, young mothers, and young children.

Since the absence of contacts with microbes at the early stage of life leads to a disruption in the functioning of the immune system, it is recommended for cancer prevention joint stay for children of different ages, long breastfeeding, and immunorehabilitation with Transfer Factor.

Key words: Solar radiation, ecology, environmental factors, smoke, forest fires, prenatal, postnatal, children, carcinogenesis, childhood cancer, system analysis

Indoor air quality of naturally ventilated Croatian classrooms

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Indoor air quality in schools has been a public concern for a number of years, as adverse effects of poor air quality have far-reaching effects on children's and students' health.

The present work aims to evaluate the effect of manual airing on indoor air quality in two naturally ventilated Croatian schools. Indoor air quality was studied in terms CO_2, sub-micron particle number and PM concentrations during the heating and non-heating seasons and compared with outdoor levels.

Closed windows over a prolonged period of time, result in alarmingly high CO2 concentrations (up to 4000 ppm), and consequently, poor ventilation rates. Longer windows opening periods reduce indoor CO_2 but simultaneously increase the outdoor –generated sub- micron particles.

Hyper-immune response from unfiltered drinking water

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The study was focused to assess the abnormal immune response from the intake of degraded water in local population Lahore. The home tap-water samples were collected from eleven regions of Lahore. The complete blood count (CBC) test was conducted from the individuals where water samples were collected, with written permission voluntarily. Following were considered: hemoglobin (HGB- g/dl), white blood cells (WBC-10^9/l), platelets (PLT-10^9/l), hematocrit (HCT-%), red blood cells (RBC-10^{12}/l), lymphocytes (LY %), monocytes (MO %), granulocytes (GR %), absolute lymphocytes count (Ab. LY absolute-10^9/l), absolute monocytes count (Ab. MO absolute-10^9/l) and absolute granulocytes count (Ab. GR absolute-10^9/l). The Mann-Whitney U test for non-normalized parameters values was applied to compare deranged values (high or low) of different parameters of water samples with the normal values found. The significance level was 0.05 (two tailed). Whereas, the two tailed t-test (independent samples) on normalized parameters (water or CBC) values was applied to compare deranged values (high or low) of different parameters of water samples with the normal values found. The significance of difference was considered at p values <0.050. Overall, the highest number of high MO (54%) values were found high among all CBC parameters. Second highest high values (38%) was found with RBC, third highest high values (32%) were found with Ab. MO, fourth highest high values (22%) were found with LY and fifth highest low values (18%) were found with GR. All deranged differences were found statistically significant at $p<0.0001$ as per Mann Whitney and t-tests. The immune system fights in case of infectious or cancerous diseases and a toxic exposure can alter this system. The agranulocytes regulate immune response. An individual may have some symptoms associated with altered monocytes levels. We looked hematological impacts of the residents of Lahore who are being exposed to an unsafe, polluted and bacterial contaminated water. Granulocyte cells are involved in immunity system, which comprises macrophages and neutrophils. Raised levels of monocytes (monocytosis) can be resulted in cases of blood disorders. Very few studies are available on altered levels of monocytes in humans from the intake of poor quality, contaminated water. Higher levels of lymphocytes indicate the lymphocytosis. Few individuals were found with low levels of granulocytes (granulocytopenia). The cell-lines variations in the form of monocytosis, lymphocytosis and granulocytopenia reported in this study, indicating an altered immune response in group of individuals who were exposed to polluted drinking water. Raised levels of monocytes and lymphocytes show a hyper immune response in individuals. An active immune cell lines indicates the presence of infectious causing microorganisms in population of Lahore. The citizens are experiencing unsafe with altered DO (dissolved oxygen) levels of drinking water (Shahid et al. 2018). There is a link between atmospheric oxygen pressure and higher RBCs in humans. A hypoxia (low oxygen) of water can pose significant health impacts. Adequate oxygen levels allow our body to successfully fight all microorganisms that are harmful to our body. With hypoxia, a human body can suffer with the infections caused by microorganisms.

Photocatalytic activity of titanium dioxide nanocomplexes in the visible spectral range

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Titanium dioxide is actively used in various fields of human activity due to its special photocatalytic and physicochemical properties, including high chemical resistance, biological inertness and low toxicity. However, one of the major disadvantages of TiO_2 as a photocatalyst is that its photochemical activity is in the UV-region. This significantly limits the potential areas and perspectives for its application.

One of the promising ways of increasing the photocatalytic activity of TiO_2 and shifting its absorption spectrum into the visible region is to modify the titanium dioxide structure by impurities of different materials. Particularly, modification by sulfur (S) and carbon (C) allows to extend the region of TiO_2 light absorption and, thus, to improve its photocatalytic properties in the visible range. Modified titanium dioxide can actively form highly efficient hydroxyl radicals $OH^{\cdot}$ and effectively oxidize harmful organic substances, destroying their molecular structure under the influence of visible radiation.

Another no less effective method of enhancing the photocatalytic action of the semiconductor photocatalyst is its combination with noble metals. For instance, deposition of thin silver shell on TiO_2 nanoparticles makes it possible to obtain plasmon absorption of such nanosystems in the visible spectral region and easily control the absorption peak position by changing the nanostructures geometrical parameters.

In this work, comparative studies of the photocatalytic properties of anatase nanopowders TiO_2 (P25) and TiO_2:S,C, which synthesized by the hydrothermal method, were carried out during the photodegradation process of selected organic compounds. The activation of bleaching process was performed using the semiconductor laser with a wavelength of 445 nm. During the experiment, a gel-like paste was prepared based on polyvinyl alcohol (PVA) aqueous solution, which contains hydrogen peroxide with limited concentration to 6%, rhodamine G dye, and TiO_2 or TiO_2:S,C nanopowder. It has been found that sulfur and carbon doped titanium dioxide shows significantly better photocatalytic properties in the visible spectral range and significantly reduces the reaction time. This is very important characteristic for the widespread practical application of nanophotocatalysts. In addition, it has been found that TiO_2: S, C nanostructures with silver shell, formed by laser-stimulated reduction, are characterized by intense absorption of the entire visible range due to the synergistic effect of plasmon resonance. Thus, it has been confirmed that such metal-semiconductor nanoobjects can be effectively used as photocatalysts in ecology to stimulate the chemical reactions of harmful organic substances oxidation under the solar radiation effect; in medicine, particularly in dentistry, for the hygiene and bleaching of tooth enamel under the influence of dental lamp radiation based on LED (420-480 nm) and other industry areas.

Polylactic acid film implantation into the anterior chamber of the eye *in vivo*

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Polylactic acid (PLA) is a biodegradable aliphatic non-toxic and eco-friendly polyester and is widely used as medical implants in the form of anchors, screws, plates, pins, rods, and as a mesh. Of particular interest is the use of PLA as a corneal implant for the bullous keratopathy treatment. The bullous keratopathy is the severe cornea disease and occupies one of the leading positions among the causes of corneal weak vision. One of the directions in the treatment of this disease is the use of stem cells. However, cultivation of stem cells and their landing on the inner surface of the cornea in order to replace the endothelial defect without using a substrate is a big surgical problem. There is a high probability of cell loss during surgical procedures. Using of scaffolds based on biodegradable thin films with controlled solubility as a temporary material for stem cells may be an alternative to existing insoluble polymers. The purpose of this research is the study of the influence of thin polylactic acid films implantation on the corneal morphology in vivo experiment.

The feedstock for the films was obtained by dissolving polylactic acid (PURASORB® PL 10, Netherlands) in the chloroform ($CHCl_3$). 8 pubescent female Sylvilagus bachmani rabbits weighing 2.0-2.5 kg were used. All animals were healthy and free of ocular diseases. All procedures were approved by the Siberian Medical State University Life Science Ethical Review Committee (protocol № 3898 from November 24th, 2014).

Polylactic acid films were implanted into the anterior chamber of one animal eye. All animals were instilled Tobramycin Drops (6 times per day), 0.1% Diclofenac Sodium Ophthalmic Solution (3 times per day) and 0.05% Vitabact (4 times per day) in the postoperative period.

The overall duration of the experiment comprised 21 days.

The following histological results were obtained. The anterior epithelium was represented by 4-5 layers of squamous epithelium with normochromic nuclei. Bowman's membrane was unchanged and visualized as a homogeneous eosinophilic strip. Collagen fibers were located compactly. In some places collagen fibers had increased twisted stroke. Descemet's membrane was visualized throughout. The endothelial layer was represented by a single layer of cells. In some places proliferation of endothelial cells in the form of process cells was observed.

Electron microscopy showed that fibroblast had the normal structure (big oval shaped nucleus with dimensionally pronounced chromatins, normal structure mitochondrion, not extended tanks of rough endoplasmic reticulum). In most cases collagen fibers were located compactly. In some places collagen fibers had increased twisted stroke.

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The effect of pigments on thermal properties of high-density polyethylene (HDPE) and polyethylene terephthalate (PET)

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High-density polyethylene (HDPE) and polyethylene terephthalate (PET) are widely used in packaging materials. Due to their chemical inertness, good mechanical and physical characteristics, these materials are suitable for packaging material of food, cosmetics, pharmaceuticals, etc. As everyday consumables are most often packed in HDPE foil or PET bottles, these materials give a high percentage of municipal plastic waste. The most significant examples of usage in the region of Vojvodina are thin HDPE bags for the package of consumables and PET bottles for water, soft-drink, milk and some dairy products. To reduce the amount of plastic waste, following environment protection tendencies in the last few years, stores have been charging for HDPE bags. Unfortunately, this regulative did not change their use significantly and a huge amount of bags ends up as environmental pollutants. The situation with PET bottles is similar. These items cannot be reused for packing, but can be recycled. There are several solutions for municipal plastic waste recycling. By melting and molding of selected plastic waste, new products can be prepared. The thermal degradation of plastic materials into simple hydrocarbons is an alternative way for gasoline production. Unfortunately, the conversion of plastics into gasoline is expensive. These materials may also be incinerated as trash, but due to CO_2 release, it increases the greenhouse effect. Besides the CO_2 release, the pigments and dyes used for coloring have an additional impact on environmental pollution. In this work, the effect of the coloring of HDPE and PET on the thermal stability, the decomposition mechanism, and the energy release was studied. It was found that pigments added into HDPE and PET do not affect their thermal properties significantly, except for the dark green and dark blue PET bottles. These samples had higher thermal stability and showed a lower energy release while burning than the samples with no color or with other colors.

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Swelling behavior of synthesized poly(1-vinyl-2-pyrrolidone-*co*-vinyl acetate) hydrogels

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Poly(1-vinyl-2-pyrrolidone-*co*-vinyl acetate) has great application in cosmetics, primarily in personal care products. It is used in drug delivery, and in a variety of biomedical applications. Also, significant is the application as an adsorbent of various pesticides. The aim of this paper is to examine structural characterization and the swelling behavior of synthesized poly(1-vinyl-2-pyrrolidone-*co*-vinyl acetate) copolymer hydrogels with 10 mol% of vinyl acetate and with 1.0; 1.5; 2.0; 2.5 and 3.0 mol% of cross-linker ethylene glycol dimethacrylate (EGDM). The characterization of the synthesized hydrogels was performed using FTIR spectroscopy. The swelling study was monitored gravimetrically until equilibrium was reached in solutions of different pH values (3.0, 6.0, 9.0) at a temperature of 25°C. The sensitivity of poly(1-vinyl-2-pyrrolidone-*co*-vinyl acetate) hydrogels to changes in external temperature was examined by monitoring the change in the equilibrium degree of swelling with increasing fluid temperature from 25°C to 80°C in a pH solution of 6.0. FTIR spectra of xerogels confirm the performed synthesis. Swelling of hydrogels poly(1-vinyl-2-pyrrolidone-*co*-vinyl acetate) was favored at a lower temperature (25°C), in a solution whose pH=6.0, when the sample with 1.0 mol% EGDM reaches the highest degree of swelling (α_e=87.23) compared to the achieved capacity at a temperature of 80°C (α_e=20.74). The most intense phase transition was observed in the temperature range of 40-45°C. Based on the obtained results, the synthesized copolymers can be classified into negative thermosensitive hydrogels that have a lower critical dissolution temperature (LCST). pH sensitivity analysis led to the conclusion that the highest value of the equilibrium degree of swelling (α_e=168.97) was observed in the hydrogel sample with 1.5 mol% EGDM in the solution whose pH=9 at 25°C. An increase in the molar content of cross-linkers in the hydrogels composition shows a decrease in swelling capacity at all pH values and temperatures.

Keywords: Hydrogels, 1-vinyl-2-pyrrolidone, vinyl-acetate, swelling capacity, LCST

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Morphology characterization of synthesized poly(1-vinyl-2-pyrrolidone-*co*-vinyl acetate) copolymers

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Hydrogels are defined as two- or multicomponent systems consisting of a three-dimensional network of polymer chains and water or fluid that fills the space between macromolecules. They are materials that are characterized by viscoelastic properties. The aim of this work is synthesis of hydrogels based on 1-vinyl-2-pyrrolidone and vinyl acetate as well as their morphology characterization. Synthesis of 1-vinyl-2-pyrrolidone monomer and vinyl acetate as comonomer (10 mol% relative to the amount of 1-vinyl-2-pyrrolidone) was performed using the free radical copolymerization method. Various amounts of ethylene glycol dimethacrylate (1.0, 1.5, 2.0, 2.5 and 3.0 mol% relative to the total amount of monomers) were used for crosslinking of polymer chains. The reactants were dissolved in methanol and the polymerization was initiated by the addition of the initiator 2,2'-azobis(2-methylpropionitrile). The synthesized hydrogels were purified from unreacted monomers, crosslinkers and initiators after extraction in methanol. The content of residual reactants from methanol extracts was examined using high pressure liquid chromatography (HPLC) method. Calculation of residual reactants in relation to their amount present in themixture at the beginning of the reaction shows that the values of unreacted monomers are in the range of 0.605-1.609% for 1-vinyl-2-pyrrolidone and 2.486-4.798% for vinyl acetate, and for the EGDM networker are the range of 0.889-3,240%. Morphology characterization of the obtained poly(1-vinyl-2-pyrrolidone-*co*-vinyl-acetate) hydrogels were performed using the scanning electron microscopy (SEM) method. SEM micrographs show highly porous honeycomb-like structures, with pores sizes dependent upon the cross-linker content.

Keywords: Hydrogels, synthesis, characterization, 1-vinyl-2-pyrrolidone, vinyl acetate

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Intrastromal implantation of track-etched membranes overlaid by prenatal stromal cells for the treatment of bullous keratopathy

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Bullous keratopathy (BK) is one of the leading causes of a chronic corneal edema and visual loss among corneal diseases. The track-etched membrane (TM) based on the polyethylene terephthalate polymer (PET) is the attractive material for bullous keratopathy treatment using. In addition, the layering of stem cells on the material surface can stabilize the pathological process and significantly increase the regeneration. The aim of research is to study the possibility of using track-etched membrane, including track etched membranes modified with cold plasma, followed by layering prenatal stem cells (PSC) on the material surface in the surgical treatment of the bullous keratopathy.

The study was conducted on 16 Sylvilagus bachmani rabbits, which after BK modelling were divided into 4 groups: the 1st group was a control group of 4 animals (4 eyes); the 2nd group was a group of 4 animals (4 eyes) which was implanted TM; the 3rd group was a group of 4 animals (4 eyes) which was implanted TM with cells; the 4th group was a group of 4 animals (4 eyes) which was implanted plasma modified TM with cells. Eyes were enucleated for histological examination after 8 weeks from the start of the experiment. The track membranes made of polyethylene terephthalate were obtained by irradiating the polymeric film with the 40Ar+8 ion beams and by the chemical etching. The modification of the track membranes surface was conducted using the atmospheric low-temperature plasma experimental device, based on the charge barrier. The time of the plasma exposure on each surface of the membranes comprised 30 seconds. TM was sterilized by the gamma radiation of the radionuclide ^{60}Co with the dosages of 1kGy (Si).

As a result of the research, it was found that the implantation of TM with a preliminary layering of human PSC promotes the growth of the fibroblast population in the cornea stroma and forming of the leukocyte (lymphocytic and eosinophilic-basophilic) infiltration compared with the implantation of PET TM without a cellular component. In addition the implantation of TM contributes to a twofold decrease in the induced by BK cornea edema. Modification of TM with cold plasma did not affect the studied histomorphometric parameters.

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Determination of temporomandibular joint condyle translation using magnetic resonance imaging

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Translation of the mandibular condyle represents the pathway that mandibular condyles make from the closed to the open jaw position.

When measuring and quantifying parameters of temporomandibular joint (TMJ), translation of the mandibular condyle is the distance that the most prominent point of condylar head crosses from the closed jaw (maximal intercuspation) to the open jaw position. It is measured on the sagittal tomograms obtained on magnetic resonance imaging. The values are expressed in mm, as the average of three sequential measurements.

Obtained values for the left and the right TMJ should not be significantly different. If so, it is associated with the asymmetry and dysfunction of TMJ and surrounding muscles.

Being familiar with dimensions of TMJ is very important in presurgical planning, before interventions on TMJ, since it reduces duration of operation and number of postoperative complications. In addition to the condylar translation measurement, it is essential to determine the width and length of the articular disc, inclination of the sagittal condylar path, intercondylar distance, width and depth of the mandibular fossa, and condylar mobility. Magnetic resonance imaging represents a reliable and reproducible method of determination of these parameters, and is very helpful for the presurgical planning.

X-ray examination of the temporomandibular joint in patients with dental alveolar and gnathic type of mesial occlusion

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Dental-facial abnormalities, combined with mesial occlusion, are one of the most complex clinical problems. In the Russian Federation, its prevalence is up to 14% among other occlusion abnormalities, and in the Samara region, the prevalence is 10.5% for children 6-15 years old.

Objective. To study the x-ray anatomy of the TMJ in patients with dental alveolar and gnathic type of mesial occlusion.

Research material and methods. All patients participating in the study had mesial occlusion. We divided them into age groups. Children 6-12 years old made up group I, children 12-15 years old-group II. We studied 40 computer tomograms of TMJ in the Central ratio of dentition: 5 children of group I with dental alveolar type, five children of group I with gnathic type, five children of group II with dental alveolar type, five children of group II with gnathic type. Both groups performed: the morphometry of the dentition and face; orthopantomography (OPG) and teleradiography (TRG) head inside view with cephalometric analysis in software Dolphin Imaging (USA); cone-beam computed tomography (CBCT); anthropometry of dentition on plaster models. We compared the dental alveolar and gnathic type in patients with mesial occlusion. The study presents the average and their errors (M±m). The significance level (P) corresponded to 0.05.

Results. Analysis of craniometry indicators of TMJ tomograms in patients of groups I and II with dental alveolar and gnathic type of mesial occlusion revealed the following. Signs of craniometry of tomograms of the right and left TMJ in group I of patients with dental alveolar and gnathic types of mesial occlusion do not have statistical differences. In the dental alveolar mesial kind of occlusion, the upper and posterior sections of the craniometry region of the TMJ correspond to the norm, and the anterior part is significantly smaller ($p=0.024$). The index of the posterior division in patients with the dental alveolar type of mesial occlusion is higher ($p=0.001$) in comparison with patients with the gnathic mesial kind of occlusion. Indicators of craniometry of right and left TMJ tomograms in group II in patients with dental alveolar and gnathic type of mesial occlusion do not have statistically significant differences. The index of the upper part in children with dental alveolar form is less ($p=0.021$) in comparison with patients with the gnathic type of mesial occlusion.

Conclusions. Treatment planning for patients with dental alveolar and gnathic forms of mesial occlusion at the age of 6-12 years and 12-15 years should include craniometry data for the ratio of TMJ elements detected by cone-beam computed tomography (CT).

Assessment of kidney viability in patients after extracorporeal resection under conditions of pharmacological cold ischemia without the intersection of the ureter with the orthoptic replantation of vessels with anuria in the early postoperative period

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Introduction. In the early postoperative period after extracorporeal kidney resection, there is a high risk of acute renal failure, which may be due to tubular and cortical necrosis. The kidneys are extremely sensitive to ischemia, so acute renal dysfunction is a common complication of hypotension. Also, early postoperative complications after extracorporeal kidney resection include formed hematomas and bleeding from the kidney resection zone. Thus, it may be necessary to assess the viability of the kidney. MSCT of the kidneys with the introduction of an iodine-containing contrast medium is not recommended to conduct in the early postoperative period, since contrast-induced nephropathy may occur.

The purpose: to develop and evaluate a research methodology that allows an accurate and reliable assessment of the state of the vascular bed of the kidney without radiation exposure and the administration of nephrotoxic contrast medium at the bedside of a patient with renal failure and other complications at intensive care.

Materials and methods. A study on the proposed method was performed in 9 patients with anuria in the postoperative period out of 47 operated patients with renal cell carcinoma with a central and intraparenchymal location of the tumor in the kidney; with tumors of large sizes, but potentially resectable; in patients with tumors of a single kidney; with billateral neoplastic tumor of the kidneys.

Results. In the early postoperative period, in the event of acute renal failure, an ultrasound research is performed in duplex scanning mode and with the introduction of an echo-contrast medium. Ultrasound duplex scanning is performed in Color Doppler and / or Energy mapping modes to confirm the presence or absence of intraorgan blood flow in the kidney. In case of clinical anuria, intraorgan blood flow in the resected kidney is not recorded. Next, perform an ultrasound with the introduction of an echo-contrast medium.

In all 9 cases, the kidney was recognized as viable and patients continued hemofiltration sessions until the appearance of urine. In 3 cases, it was necessary to conduct a study on this technique twice, in 2 - three times. Repeated injections were performed in patients with initially more compromised kidneys. The total duration of anuria ranged from 3 to 7-8 days.

Since patients have anuria, hemofiltration courses are possible. The study must be performed with the hemofiltration device turned off and the kidneys not forced to work.

Conclusion. The technique of contrast enhancement during ultrasound examination of patients with renal cell carcinoma in the early postoperative period after extracorporeal resection of the kidney under conditions of pharmacological cold ischemia without intersection of the ureter with orthotopic vascular replantation is very effective in assessing the viability of the kidney in controversial issues in case of complications in the early postoperative period.

Changes in liver metastases and parenchyma caused by transcatheter arterial chemoembolization using drug-eluting beads

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Background. This study investigated the changes in liver metastases and surrounding tissues due to transcatheter arterial chemoembolization using drug-eluting beads (DEB-TACE) based on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI).

Patients and Methods. 42 patients with unresectable hepatic metastases treated with DEB-TACE in an institutional review board approved protocol from 2011 to 2019 were studied retrospectively. The origins of the primary tumors were: colorectal region (40%), lung (15%), uterus and cervix (15%), prostate (10%), ovaries (5%), pancreas (5%), liver (5%), breast (5%).

This study included patients with a follow-up of 1 year to 7 years. CT and MRI with contrast enhancement were performed before DEB-TACE, after 8 weeks, 16 weeks, then every 3 months. 3–5 target lesions were selected according to the RECIST 1.1 for an objective assessment of treatment. The size of the lesion, contrast-enhancing area and necrosis were evaluated. Additionally, the density of the tumor in different contrast enhanced phases, apparent diffusion coefficient (ADC) on diffusion-weighted MR imaging were measured.

Results. After analyzing 205 target lesions and 615 nontarget lesions we identified the following types: 1) disappearance of the lesion with/without the reaction of the surrounding liver parenchyma (10%); 2) intratumoral hemorrhages (4%); 3) necrosis and/or cystic transformation (27%); 4) cavity formation without resizing (10%); 5) the size reduction on the first control, then the lack of dynamics (22%); 6) decrease in the total tumor size while maintaining the contrast-enhancing area (11%); 7) increase in the size of the lesion (11%); 8) increase in the size of the contrast-enhancing area (5%).

However, we encountered the problems: 1) the reaction of the liver parenchyma in 15% led to a transient increase in tumor size; 2) necrosis and cystic transformation of the lesion in 8% passed through an increase in size; 3) spontaneous recurrent intratumoral hemorrhages in some cases were accompanied by an increase in the size. When comparing these data with ADC and contrast enhanced series we noted: 1) the reaction of the liver parenchyma was not accompanied by restriction of diffusion; 2) necrosis and cystic transformation in 75% had a high ADC; 3) intratumoral hemorrhages reduced the intensity and speed of contrast enhanced.

A progressive increase in the size of the lesion and contrast-enhancing area were combined with the absence of an increase of ADC and prior pattern of contrast enhancing.

Conclusion. 1) the cytotoxic and cytostatic components of DEB-TACE may act independently of each other; 2) an increase in the size of the lesion does not always indicate process progression; 3) liver parenchyma reaction may influence lesion size; 4) ADC, patterns of contrast enhancing may be useful in evaluating treatment.

Intraductal papillary mucinous neoplasms: Radiology methods in the definition of treatment tactics

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Introduction. Intraductal papillary mucinous neoplasms (IPMN) of the pancreas is characterized by cystic expansion of the main and / or branch pancreatic ducts, which in most cases, but not always, forms papillary structures. The tumor grows from the epithelium of the pancreatic ducts and can be represented by various histological options from mild dysplasia to carcinoma, which, in essence, are biological stages of development and can be detected within a single tumor. The frequency of malignancy depending on the type of tumor (Crippa S. et al., 2010): type 1 - 48%; type 2 - 11%; type 3 - 42%.

Objective: to analyze the data of patients with IPMN and to evaluate the possibilities of radiology in determining the tactics of patient management and treatment.

Materials and methods. In A.V. Vishnevsky NMRC of Surgery 96 patients with IPMN were examined and treated in 2006-2019. At the preoperative stage, all patients underwent ultrasound, MSCT and MRI.

Results. Depending on the type of tumor (Lim J.H. et al., 2001), IPMN was divided as follows: type I - 19 (19.8%) patients; type 2 - 46 (47.9%) patients; type 3 - 31 (32.3%) patients.

Characteristic signs of IPMN according to radiology: the presence of expanded main pancreatic duct (MPD), expanded branch pancreatic ducts, compaction of the MPD walls, parietal papillary growths of varying severity, the presence of tumor masses around the MPD (with the accumulation of contrast substances).

Tumor malignancy criteria: obstructive jaundice; parietal papillary growths of more than 5 mm / presence of a solid component; the presence of tumor cells during cytological examination; the diameter of the pancreatic duct is more than 10 mm.

In accordance with these criteria, 56 (58.3%) patients were operated on, 40 (41.7%) were under observation:

Type 1: operated on - 17 (89.5%); are under observation - 2 (10.5%);

Type 2: operated on - 12 (26.1%); are under observation - 34 (73.9%);

Type 3: operated on - 27 (87.1%); are under observation - 4 (12.9%).

Thus, dynamic monitoring is carried out mainly for type II tumors.

The observation is carried out according to the following scheme: after 3 months, after 3 months, then 1 time in 6 months. The scope of the examination during the follow-up: MSCT and / or MRI and the tumor marker CA 19-9.

Criteria for malignancy: newly detected expansion of the pancreatic duct 5-10 mm; an increase in the cystic component over 5 mm in 1 year; newly identified parietal papillary growths up to 5 mm; the appearance of a solid component; transition to type III; an increase in CA 19-9.

Conclusion. Peculiarities of the growth of IPMN with a tendency to diffuse propagation along the MPD impose responsibility on doctors of instrumental diagnostics and surgeons in assessing the area of primary damage. Radiology research methods also play an important role in the dynamic monitoring of patients with IPMN (mainly type II) to determine possible malignancy.

Differential diagnosis of acute cholecystitis with an atypical ultrasound image

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Background. To improve the ultrasound diagnosis of the gallbladder (GB) pathology by developing a diagnostic algorithm for the atypical ultrasound image of acute cholecystitis.

Materials and methods. 5600 patients with acute pathology of GB were examined in CCH No. 68 in 2010-2018. Of these, 360 patients at primary ultrasound revealed changes in the GB that didn't allow them to be attributed to the image of acute cholecystitis. Patients were divided into 2 groups: the 1st group included 120 (33.3%) patients whose changes in the GB included thickening (change/poor differentiation) of the wall without increasing the size of the GB, the 2nd - 240 (66.7%) patients with an increase in the size of the GB, but without changes in the wall.

Results. In a retrospective analysis in the first group, the following changes were diagnosed: Mirizi syndrome - in 10 patients, GB tumor - 20, reactive changes in the wall against other diseases and conditions (liver disease, pregnancy, acute abdominal pathology located nearby) - 62, biliary digestive fistula - 12, perforation of the GB at acute cholecystitis - in 16 patients.

In the second group, only 30 patients were diagnosed with acute cholecystitis, including empyema of GB - in 8 patients, enlargement of GB wall' was regarded as a manifestation of congestive or "hungry" GB, which does not require specific treatment and observation, in 210 patients.

Against the background of conservative therapy, 240 patients (65 from the first group, 175 from the second group) showed a positive dynamics of GB state. Surgical treatment with laparotomy or laparoscopic access was performed only in the first group in 17 patients. Diagnostic punctures and drainage of GB were performed in 12 patients of the first group and 70 patients in the second group. Retrograde cholangiopancreatography, endoscopic and percutaneous drainage of the bile ducts were performed in 15 patients. 15 (4.2%) patients died (5 from the first and 10 from the second group).

Conclusions. After comparing the findings of ultrasound examinations of GB and final diagnoses (based on other imaging techniques, the clinical and laboratory picture of intraoperative and pathoanatomical studies), an analysis of inconsistencies and errors was performed. The main diagnostic criteria and algorithm to help make a differential diagnosis between various pathologies of GB were formulated.

Pseudolesions of the abdominal cavity by ultrasound: Causes of errors and recommendations that reduce their likelihood

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Background. Reduce the number of the most common errors in identifying pathological formations of the abdominal cavity.

Materials and methods. 1.45 million abdominal US-examinations were performed in CCH No.68 in 2010-2018. In 53 cases, pathological lesions of the abdominal cavity of inflammatory and tumor genesis, diagnosed at doctor's office call and weren't confirmed during further examination at clinic.

Results. The iliac-lumbar muscle was mistaken interpretated as neoplasm in the iliac region, in 7 cases. When the transducer turns over the muscle, it acquires a fusiform shape with a specific longitudinal striation.

The neoplasm of hypogastria turned out to be the spine in 6 cases. The transducer's turn over a transverse section of the spine allows you to see its characteristic structure, expressed uniform length, not characteristic of pathological lesions. The presence of a "clean" shadow from its upper contour, which is characteristic of dense structures, is another argument against lesion.

Hypertrophied additional spleen lobule after splenectomy simulated neoplasm in the left hypochondrium in 5 cases. A splenectomy in the anamnesis and the presence of solid lesion in the left hypochondrium with a homogeneous structure resembling a parenchymal organ make you think about the variant of the norm.

The lesion in the left hypochondrium turned out to be a stomach with heterogeneous contents, identified as pathological fluid accumulation in 15 cases. Oral fluid intake helps to clearly identify the stomach.

Hyperdiagnosis of liver neoplasms due to incorrect interpretation of hepatosis zones, as well as the imposition of acoustic shadows from the ribs, was in 7 cases. The specific form of hepatosis sites, the most frequent location in VI-V segments, and polypositional study help to conduct the differential diagnosis.

Epigastric preperitoneal fat is described as liver left lobe abscess in 5 cases. Differentiation of the abdominal cavity organs from the anterior abdominal wall during deep breathing, as well as knowledge of the structural features of the anterior abdominal wall, make it possible to exclude this diagnosis.

The liver left lobe was identified as a pancreatic head tumor in 3 cases. A polypositional study will help identify the liver caudate lobe.

In 3 cases, small intestine loops without contents, peristalsis and differentiation of the boundaries between them were diagnosed as neoplasm. The location in the left lateral region of the abdomen, the specific form and the presence of hyperechoic chaotic striation, as well as repeated review after a few hours will help to verify the absence of pathology.

In patients after surgery, including reconstructive ones, normal organs in atypical places were mistaken for pathological lesions in 2 cases. Knowing the surgery features will minimize the likelihood of error.

Conclusion. The analysis of errors, the causes of their occurrence was made, recommendations that reduce the likelihood of errors were formulated.

18-FDG PET/CT in evaluation of the effectiveness of the complex treatment of symptomatic pharmacoresistant epilepsy

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Objectives. To present the possibilities of clinical application of modern neuroimaging (NI) such as 18-FDG PET/CT at the example of a clinical case of treatment of symptomatic pharmacoresistant epilepsy and to evaluate the feasibility, tolerance of this type of imaging.

Methods. In March 2017 patient, 24 years old, about generalized seizures (since 2014 after fright from explosion of firecrackers) continued to be held anticonvulsant therapy, which led to a decrease in seizure frequency from 8 to 13 in month. Taking into account the progressive course of the disease, when any a combination of 2-3 essential anticonvulsants, including the latest, did not have a noticeable effect on the frequency and severity of attacks, the patient is treated by combination therapy, including antiepileptic drugs and autologous bone marrow stem cells (the AMSC CM transplantation).

Electroencephalogram (EEG) showed epileptiform activity. An irregular alpha rhythm with a peak frequency of 10.5 Hz is recorded on the patient's EEG. The frequency-spatial structure of the alpha rhythm is pathologically distorted. The structure of the maximum values of average coherence is represented as a triangle in fronto-central departments, which is characteristic of an active epileptic process. A moderate increase in low diffuse beta and theta activity is noted. Against this background, in the left frontotemporal region, epileptiform activity in the form of spikes is recorded in large numbers, the frequency of which reaches 30 per minute. Rare discharges of high, sharp, bilaterally synchronous alpha waves with a frequency of 1-2 per min. MRI of the brain showed diffuse cerebral subatrophy. The lateral ventricles are slightly enlarged, asymmetric S>D. Hippocampi are asymmetric (D> S), the volume on the left is reduced. Deformation of the soft tissue of the skull on the left.

PET/CT examination of the brain with F18 - fluorodeoxyglucose (18-FDG) after the first course of the introduction of AMSC CM revealed a pattern of increased metabolic active-STI of the left hemisphere of the brain. Significant a new increase in fixation of the radiopharmaceutical in the left frontal, parietal, temporal and occipital lobes.

On an EEG, after the first course of stem cell administration, significantly decreased the amount of epileptic formal activity. The frequency of spikes in the left temporal region STI decreased from 30 to 2 per min, the frequency of bilateral synchronization discharges of acute alpha waves remained at the level of 1-2 in minutes. At a frequency of alpha rhythm of 10.5 Hz, normalization occurred of its frequency-spatial structure, but the structure maximum mean coherence values are still was presented in the form of a triangle, which indicated the presence of an active epileptic process.

On the EEG, after the second course of stem cell administration, paroxysmal activity was not registered. On the EEG, a disorganized alpha rhythm was maintained with a peak frequency of 12.5 Hz with a diffuse increase in beta activity. Its frequency-spatial structure is largely normalized. A reduction in the pathological structure of the maximum values of mean coherence in the form of a triangle was also noted. In order to assess the functional state of the brain according to metabolic activity carried out repeated PET/CT with FDG after 5 months after the second course of the introduction of AMSK KM. The obtained data on the metabolism of the radiopharmaceutical in dynamics and when compared with relative reference regions testify in favor of stabilization (striving for reference values) of metabolic activity in the interested areas: in the left parietal, temporal and occipital lobes. Control PET / CT - study was performed under identical conditions, which is a prerequisite for assessing dynamics (the study was conducted on the same scanner, with the same entered activity, subject to variables of the research protocol).

Conclusions. Combining modern methods of NI including 18-FDG PET/CT are very useful tools in the evaluation of effectiveness of complex treatment for symptomatic pharmacoresistant epilepsy. The encouraging results of the evaluation of effectiveness of the proposed method of treatment of pharmacoresistant epilepsy on the clinical case of one patient have been obtained, which requires further study of the clinical application of the 18-FDG PET/CT on a more significant number of clinical cases in larger clinical trials.

Correction of the inflammatory reaction stages in patients with chronic trophic wounds of the lower extremities using photodynamic therapy

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Introduction. Trophic wounds are characterized by long-lasting inflammation, leading to extensive tissue damage. An obstacle to the healing of trophic wounds is a violation of the staging of the course of inflammatory processes.

The purpose of the work is to evaluate the effects of radiation from various parts of the visible spectrum and an exogenous photosensitizer on the course of the inflammatory process in patients with trophic wounds of the lower extremities at different stages of inflammation.

Materials and methods. Patients with trophic wounds of the lower extremities were examined, for the treatment of which photodynamic therapy was used. Dimegin was used as a photosensitizer. Irradiation was carried out with light from different parts of the visible spectrum: red (λ = 660 nm), green (λ = 530 nm), blue (λ = 440 nm). We studied indicators of phagocytosis, the level of vascular growth factor VEGF, the cytokine spectrum, the expression of regulatory T cells, the content of Ig classes A, M, G and the presence of an antinuclear component. Used methods of luminescence microscopy, enzyme immunoassay, flow cytofluorimetry.

Research results. After a single exposure to red light (λ = 660 nm), a decrease in the inflammatory response was observed after three days. A 2-fold increase in VEGF vascular growth factor, an increase in the level of pro-inflammatory cytokines, an increase in IgM content and stimulation of expression of Treg-lymphocytes were revealed. Activation of the inflammatory process contributed to the acceleration of wound cleansing. Seven days later, a decrease in the concentration of cytokines relative to reference values was observed. Irradiation of the wound with green light provided its purification from the microbial flora, enhanced microcirculation of the blood and accelerated tissue regeneration. Exposure to the wound with blue light (λ = 440 nm) reduced the content of VEGF factor by 9 times, which corresponded to the completion of inflammatory processes and revascularization with a further predominance of epithelization processes. Exposure to blue light inhibited all stages of the inflammatory reaction.

Conclusions. Phased light exposure with the sequential use of red (λ = 660 nm), green (λ = 530 nm) and blue (λ = 470 nm) light leads to the normalization of the studied immunological parameters. After conducting complex photodynamic therapy, it was possible to achieve complete cleansing of the wound from necrosis, the appearance of granulations and signs of regional epithelization in a short time (on the fifth or sixth day).

The response of the magic gel to external irradiation

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Polymer gels are relative chemical dosimeters. They allow to access to three-dimensional dose distribution. The aim of this study has been to investigate the preparation and the use of a polymer gel with a tissue equivalent density known as MAGIC gel from magnetic resonance imaging and x-ray computed tomography. This kind of gel is “normoxic” because it can be manufactured and used in normal room atmosphere. In the first part of this study, its accuracy and sensibility were studied using external beam irradiation by linear accelerator.

The response of the gels was revealed by relaxation rate measure (R_2) and Hounsfield units (HU). We got straight responses.

The simple assessment of the effects of uncorrected rotational movements

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Aim. Image guided radiotherapy (IGRT) provides an excellent solution to quantitative assessment and correct for patient set-up errors in the modern radiotherapy. However, the majority of linear accelerators are equipped with conventional couches that can be moved in three translational directions and perform only yaw rotation. Uncorrected roll and pitch result in rotational set-up errors, particularly when the distance from the isocenter to the clinical target volume (CTV) border is large. This study describes the simple method of assessment of the rotational set-up errors.

Materials and methods. Twenty-two patients with prostate cancer treated with VMAT technique had daily CBCT scans (570 CBCTs in total) prior to treatment delivery. The rotational errors remaining after on-line correction were retrospectively analysed. The shifts caused by uncorrected rotations were calculated with the use of the rotation matrix. The rotation matrix was formed by multiplying the pitch and roll rotation matrices. The point A was a hypothetical point. The (x y z) coordinates of the point A were equal to the maximum distance from the isocenter to the CTV border in the X, Y and Z axis directions respectively (X axis was defined as superior-inferior, Y as left-right and Z as anterior-posterior direction). The segment connecting the isocenter to the point A was the radius of the sphere that covered CTV. All CTV points were closer to the isocenter than the point A. This implies that the shift of each point of CTV was smaller than the shift of the point A.

Results. The method allowed a simple assessment of the effects of uncorrected rotational movements. 139 and 36 of the 570 rotational errors were larger than 1.5 degrees in pitch and roll direction respectively. 17 of the 22 patients had no treatment fractions with the shifts of the point A larger than 5 mm in X axis direction due to residual rotational error. The shifts larger than 5 mm were not noted in Y axis direction. 15 of 22 patients had no treatment fractions with the shifts larger than 5 mm in Z axis direction.

Conclusion. The presented method is useful and simple tool in quick verification of rotational errors. The obtained translations of point A approximate the shifts of CTV points resulting from uncorrected roll and pitch rotations. Mean values of pitch rotational errors demonstrate systematic errors (different for different patients) that were not corrected during treatment. Setup variations caused by uncorrected rotations cannot be ignored for prostate patients treated with “large field’ radiation therapy. Replacing the point A coordinates with the coordinates of selected CTV points in the mentioned method allows to calculate the shifts of these points with high precision.

Redox-active metal complexes with hydrazone and thiosemicarbazone derivatives of 4,6-di-*tert*-butyl-2,3-dihydroxybenzaldehyde

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The emergence of drug-resistant bacteria motivates the urgency of developing novel antimicrobials differing from antibiotics in their mechanism of action. Unlike many antibiotics, compounds of transition metals are able to realize several mechanisms of antimicrobial action (caused mainly by the metal ions) involving multiple targets which render the appropriate mutations required for microorganisms to become resistant unlikely [1]. In our view, it is transition metal complexes with redox-active phenolic ligands that are a particularly rich source of broad spectrum anti-infective agents. A design of the molecules carrying hydrazone or thiosemicarbazone as well as a sterically hindered *o*-diphenol moiety along with bioactive metal ions in a single scaffold was undertaken for the purpose of efficient inhibition of a broad spectrum of bacteria and fungi. Redox-active Mn(II), Fe(II), Co(II), Ni(II), Cu(II), and Zn(II) complexes have been synthesized using 4,6-di-*tert*-butyl-2,3-dihydroxybenzaldehyde isonicotinoyl hydrazone (L^{I}) and 4,6-di-*tert*-butyl-2,3-dihydroxybenzaldehyde thiosemicarbazone (L^{II}). These novel compounds were characterized by means of chemical, physicochemical and pharmacological screening methods. According to the data obtained from elemental analysis, TG/DTA, IR, ESR, UV-Vis spectroscopy and conductivity measurements, the complexes have the composition described by the general formulas $ML_2(H_2O)_2$ and ML_2. The ligands L^{I} and L^{II} coordinate in an *O,N*- or *S,N*-bidentate fashions. The complexes are characterized by distorted square planar or octahedral geometry of their coordination cores. The reducing properties of the ligands and their complexes were examined by cyclic voltammetry. Some metal complexes with L^{I} and L^{II} demonstrate the lowest MIC value (4 nmol×ml^{-1}) for bacteria and fungi, comparable with or even lower than those of some commonly used antimicrobials. The ligand L^{II} and its metal complexes are characterized by the highest rate of the reduction of bovine heart cytochrome *c* (determined spectrophotometrically) among the compounds under study. The results obtained are discussed in view of the presumed correlation between the capability of the compounds under study for reducing cytochrome *c*, their antimicrobial activity, redox properties determined electrochemically, and lipophilicity, and they give grounds to characterize newly synthesized complexes as potential antimicrobial agents with antioxidant activity.

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In vitro studies on the antioxidant efficacy of *Silybum marianum* (L.) against low-doses UV/γ irradiation

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Exposure to ionizing radiation leads to direct and indirect oxidative stress changes in biological systems, caused an increase in the free radicals, including reactive oxygen species (ROS) such as superoxide anions (O_2^-), hydroxyl (HO·), hydrogen peroxide (H_2O_2) and peroxyl (RCOO·) radicals. In the recent decades, plant antioxidants have been subjected to many investigations that have related their consumption to a reduction in the incidence of oxidative damage related to ionizing radiation.

Silymarin, derived from *Silybum marianum L.* (*S. marianum,* milk thistle) contains mainly flavonolignans, as a mixture of four isomers: *silybin, silidianin, silychristin and silipide. Silymarin* has similarity with steroidal hormones and its potential to: maintain the cell fluidity; the hepatocyte Ca^{2+} content; enhanced protein and DNA synthesis; anti-inflammatory; and ability to modulate the hepatic detoxification activity. As antioxidant *Silymarin* has the opportunity to prevent oxidation processes; reduce oxidation by reacting with free radicals and by acting as oxygen-scavengers and transferring hydrogen atoms to the radical structures.

Here, we report freshly-powdered milk thistle which reduces ionizing radiation activation and by an additional stage could be used to develop efficient radioprotectants. The effects were investigated under ultraviolet (UV) and gamma (γ-) irradiation on antioxidant and radical-scavenging properties of *Silymarin* by using *in vitro* spectrophotometrical and Electron Paramagnetic Resonance (EPR) methods.

The powdered *Silymarin* (percentage composition of silybin A and B (41% and 59.7%) purchased from Trakia University, Bulgaria was used. The samples were irradiated by using UVB-light (290-320 nm; UV–vis Transilluminator- 4000 Stratagene)/ rate of 2 hrs; ^{60}Co source at doses of 5, 10, 20, and 30 Gy (Gamma cell 5001, India; 1.42 Gy/h). Immediately irradiated samples were carried out in triplicate at 293K on an X-band spectrometer. The spectrophotometric radical-scavenging activities of *Silymarin* against superoxide (>73%), hydroxyl (>49.95%), DPPH (84.2%), ABTS (>51.4%), and NO radicals (>51.4%) were evaluated at dose of 20 Gy. The reducing power in the aqueous phase was (>52.4%, R^2 = 0.875). It was found, when the γ-radiation doses increased, modulatory and scavenging properties decreased. *Silymarin* inhibited lipid peroxidative stress in the case of membranes against ionizing radiation stress in the liposomal system. By the present EPR *in vitro* studies, we have demonstrated that *Silymarin* behaves like a good radical-scavenger. EPR signals registered at 20Gy were considerably stable and higher. Moreover, 60 days post-irradiation, antioxidant activity increases, presumably due to the generation of considerably stable radicals in the *Silymarin* chemical composition.

Keywords: Silymarin, low-level UV/ γ radiation, antioxidants, radioprotectors

Extraction-chromogenic system for nickel(II) based on 5-methyl-4-(2-thiazolylazo)resorcinol and Aliquat 336

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A water-isobutanol extraction-chromogenic system for Ni^{II}, based on the azo dye 5-methyl-4-(2-thiazolylazo)resorcinol (MTAR; H_2L) and the ionic liquid Aliquat 336 (A336), was studied. Under the optimal conditions (c_{MTAR}=2.0´10^{-4} mol dm^{-3}, c_{A336}=5.6´10^{-3} mol dm^{-3}, pH 8.5 and extraction time t=1 min), Ni^{II} is extracted as a ternary complex which can be represented by the formula $(A336^+)_2[Ni(L^{2-})_2]$. In the absence of A336, or in a slightly acidic medium, a binary complex, $[Ni(HL^-)_2]$, with an absorption maximum at l=548 nm and a shoulder at 590 nm is formed. The following extraction-spectrophotometric characteristics were determined at the above-mentioned optimal conditions: l_{max} (545 nm), molar absorptivity (5.0×10^4 dm^3 mol^{-1} cm^{-1}), Sandell's sensitivity (1.2×10^{-3} μg cm^{-2}), Beer's law limits (0.05–3.1 mg cm^{-3}), constant of extraction (Log K=6.1) and fraction extracted (99.2%). The effect of foreign ions was studied; the most serious interferences were caused by Co^{II}, Cu^{II} and Cr^{III}.

Keywords: Nickel(II); 4-(2-thiazolylazo)orcinol; ternary complex; solvent extraction; low-toxic solvent; spectrophotometry

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Photosensitized cholesterol oxidation with Zn(II)- phthalocyanines and exposure with UV or red visible light

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Photodynamic therapy (PDT) is a method based on combined action of a photosensitizer, proper light exposure and molecular oxygen. The general procedure of PDT involves application of a non-toxic photoactive drug which upon specific light excitation and in the presence of oxygen produces the highly reactive and cytotoxic oxygen species among them with highest amound is the molecular singlet oxygen. Phthalocyanines (Pcs) are well documented as prospective second generation photosensitizers for PDT applications. The ring molecule of Pc has highly conjugated chemical structure which facilitates the valuable far red absorbance (> 670 nm) and the high molar extinctions within the phototherapeutic window (630-850 nm). The Pc complexes with different metals or semimetals (MPcs) characterize with the relatively high singlet oxygen production without photodestruction (high photostability) during therapeutic red light exposure.

The presentation focuses on the photooxidation of cholesterol as a substance which appears in big amount in vessels and as a part of the cells membranes. The basic Zn(II) phthalocyanine (ZnPc) and novel ZnPc conjugate of phthalocyanine with biologically-active compounds are applied as photosensitizers together with exposure by two light sources with spectral maxima at 365 nm and 635 nm at a range of light doses. These studies are presented in comparison for the tested photosensitizers at various concentrations and light doses. The used ZnPcs are evaluated with high efficiency of photodynamic oxidation of cholesterol for very low ZnPcs concentrations (nmol/L) and mild doses of irradiation. The results suggested a good potential for application of new ZnPcs as PDT drugs.

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Bioconjugates of phthalocyanine complexes with steroid moieties towards pathogens

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Photodynamic inactivation (PDI) appears a promising approach for effective treatment of pathogens-associated infectious. The present knowledge on the PDI method focuses on the cationic photosensitizers and red light for effective inactivation of resistant pathogens. The structure - biological function investigations are still very actual in order to develop the optimal molecular structure for inactivation of the both Gram(+) and Gram(-) pathogenic species without harmful side effects of the chemotherapeutics.

The present study aims the further development of effective new generation Zn(II) phthalocyanines linked to biologically active substances (ZnPcs) for PDI application. The newly synthesized derivatives are on the basis of Zn(II) phthalocyanine by an linker group (ZnPcA), and with steroid units (ZnPcSt1 and ZnPcSt2). The main photosensitizers' properties of photophysics and photochemistry, and the photoinactivation potential towards pathogens are investigated. The results suggested that the new bioconjugated ZnPcs facilitate the improvement of photophysicochemical properties with low photoinactivation potential on fungus *Candida albicans*.

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Catechin hydrate desorption from newly-synthesized catechin-loaded biopolymer particles

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Catechins have been acknowledged as naturally derived biomolecules exhibiting profusive pharmacological and therapeutic activities like anti-inflammatory, antimicrobial, antitumor, antiaging, antioxidant, etc. This wide array of health effects, however, is significantly hampered due to the poor bioavailability, short halflife, stability issues, short shelf life, sensitivity to oxidation, limited gastrointestinal tract absorption and reduced biological activity of the bioflavanols. Modern scientific studies have recently developed various advanced methodologies to surmount these limitations and to reveal the full therapeutic potential of catechins by modulation of innovative encapsulation technologies and subsequent release studies. The increased search for the design and synthesis of bio-friendly carriers with enhanced bioactivities provoked the present investigations.

The aim of the recent study was to assess the extent of catechin hydrate release from newly synthesized bioflavanol-loaded chitosan-based particles. The biopolymer particles were prepared by a modified ion gelation method. The bioflavanol was incorporated into the acidic chitosan solution before the cross-linking and particle formation stages. The synthesized biopolymer particles were divided into two series: Series 1 - washed with ethanol and stored in 70% EtOH at 4^{o}C, and Series 2 - washed with EtOH, dried and stored at -18^{o}C. Both particle series were stable after 72 h storage. Desorption experiments were conducted by agitation of determined mass of catechin-loaded particles in PBS and at pH = 1.2 for 48 h. The maximum efficiency of catechin desorption from series 1 particles in PBS was 79.8 % after 24 h and increased to 91% after a subsequent step of desorption in strongly acidic medium after 48 h. Series 2 catechin-loaded particles exhibited slightly higher desorption extend in PBS. It has to be outlined that the size of series-1 particles significantly decreased, while the dried particles were completely degraded at the end of the experiment.

The latter results present valuable basis for future investigations on the applicability and efficiency of the synthesized bioparticles as bioflavonoid carriers in pharmaceutics, veterinary and human medicine.

Keywords: Chitosan particles, catechin hydrate, desorption

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The comparative analysis of anti-proliferative effect of natural products, catechin hydrate and epigallocatechin (extract), applied on leukemia lymphocytes

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Cancer is a problem with worldwide importance and is the second leading cause of death globally. It is widely accepted that the efficiency of conventional chemotherapeutics, as well as their harmful side-effect, are due to disruption of redox homeostasis and induction of oxidative stress in both cancer and normal cells. In this aspect, natural products from plants have recently attracted scientific interest, due to their possible application as supplements to conventional chemotherapeutics. The flavonoids are widely distributed in nature and it is well known that they possess multiple biological activities, such as antioxidant, antimicrobial, anti-inflammatory, antiviral, anti-allergic and anticancer properties. Scientific studies have shown that the natural products epicatechin and catechin (flavan-3-ol monomers), have the ability to scavenge free radicals, reduce the rate of LDL oxidation, inhibit lipid peroxidation, and participate in the modulation of the immune response in several biological systems. In the present study, the effect of catechin hydrate and epigallocatechin (extract) on cell viability of leukemia lymphocytes in low concentration and different incubation time (24, 48 and 72 h) were investigated. The aim is to provide an experimental basis for their future incorporated into chitosan carriers and to provide experimental results for their clinical application in cancer therapy. To evaluate of potential synergistic effect after combination with chitosan carriers, we need to select concentrations of the studied flavonoids, in which inhibition of cell proliferation activity is not more than 20 %. The MTT assay was used to report the activity of intracellular NAD(P)H dependent oxidoreductases and the NAD(P)H pools inside cells. Our data demonstrated that catechin hydrate and epigallocatechin (extract) showed anti-proliferative activity on Jurkat cancer cell line and IC_{20} is noticed when both natural extracts were applied at lower concentration (50 μM). The anticancer and anti-inflammatory *in vitro* mechanisms of these flavonoids, incorporated into chitosan microparticles need to be evaluated in future experiments on different cancer cell lines.

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Experimental study of anti-proliferative effect of quercetin applied on leukemia lymphocytes

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Flavonoids, a group of natural substances with various phenolic structures, are categorized according to their chemical structure to flavonols, flavones, flavanones, etc., and recently have attracted considerable scientific and therapeutic interest. Epidemiological studies have shown that the consumption of natural plant sources of flavonoids is associated with a low risk of cancer. Quercetin (3,5,7,3′,4′-pentahydroxyflavone) is the major representative of the flavonoid subclass of flavonols. Quercetin is abundantly present in diverse plant materials (leaves, grains, fruits, and vegetables) as well as in common foods and drinks, with onions, apples, berries, broccoli, tea, and red wine serving as typical examples. Due to its anti-oxidant, anti-tumor and anti- inflammatory activity, quercetin has been studied extensively as a chemoprevention agent in several cancer models. There is scientific information about the anticancer effects of quercetin, as well as its ability to promote apoptosis and autophagy due to modulation of PI3K/Akt/mTOR, Wnt/-catenin, and MAPK/ERK1/2 pathways. The experimental results indicated that applied at low dose (0 – 10 μM for 4 days incubation) quercetin lead to mild cytotoxic effect and cell cycle arrest in the G1 phase. At high concentration (50-130 μM) quercetin inhibited cell cycle progression from G0/G1 to G2/M phase in time- and dose-dependent manner due to increase levels of the pro-apoptotic biomarker surviving. The aim of conducted study was to evaluate anti-proliferative effect of quercetin in different concentration range (0,5 μM to 50 μM) on leukemia lymphocytes for 24, 48 and 72 hours incubation time. The MTT assay was used to report the activity of intracellular NAD(P)H dependent oxidoreductases and the NAD(P)H pools inside cells. The obtained results provide an experimental basis for future experiments linked with quercetin incorporation into chitosan carriers and their application in cancer therapy. But investigations on the *in vitro* mechanism(s) of action of these microparticles need to be deeply studied.

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Combined *in vitro* evaluation of antiparasitic and protective effect towards biologically important molecules of new 1*H*-benzimidazol-2-yl hydrazones

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Trichinellosis is a severe and sometimes deadly parasitic disease in carnivorous mammals and people, caused by infection with nematodes of the genus *Trichinella*. The main source in humans is infected wild or domestic pigs, whose meat and meat products are used for consumption without good heat treatment. Benzimidazole broad-spectrum anthelmintics as albendazole and mebendazole are widely used in the chemotherapy of human trichinellosis [1].

The benzimidazole nucleus is a heteroaromatic system of great interest for the medicinal chemistry. The various biological activities related to this pharmacophore (antineoplastic, antibacterial, antiviral, antioxidant etc.) support its importance for generating new therapeutic agents [2]. Furthermore, many benzmidazole derivatives were designed and synthesized as antiparasitic agents [3]. The mode of action of the compounds is by blocking the microtubule function [4].

Herein we present a study on the antiparasitic activity of a series of new 1*H*-benzimidazol-2-yl hydrazones, obtained from 1*H*-benzimidazol-2-yl hydrazine by condensation with various hydroxyl and methoxyl-benzaldehydes. The anthelmintic activity of the 1*H*-benzimidazolyl hydrazone derivatives was evaluated *in vitro* against *Trichinella spiralis*. The compounds containing two or three hydroxyl groups demonstrated the strongest larvocide effect ranging from 100% to 90% at concentration of 100 μg/mL after 24 h incubation period at 37°*C*. The compounds were subjected to a preliminary test for antiprotozoal activity on *Paramaecium caudatum* and several derivatives exhibited high efficacy by immediate extinction of the paramaecia cells.

The potency of the newly synthesized compounds to inhibit the oxidative molecular damage of biologically important molecules has been determined in model systems using as oxidisable substrates lecithin and desoxyribose. The observed trends in activity were rationalized based on DFT calculations of the antioxidant reaction enthalpies and related radical and ionic intermediates.

Keywords: Benzimidazoles, antiparasitic activity, *Trichinella spiralisl larvae, Paramaecium caudatum*, antioxidant activity

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DFT and IR spectroscopic study on the conversion of 2-[2-imino-5-nitro-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzimdazol-1-yl]-1-phenylethanone into radical and anionic products

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In various studies the presence of a nitro group has demonstrated a beneficial role for anti-cancer action [1,2]. A clinically evaluated 2-nitroimidazole containing lead compound (TH-302) was found to be selectively potent under hypoxia and stable to liver microsomes [3]. Some 5-nitroindazole derivatives have been examined and have shown antineoplastic activity against human colon adenocarcinoma (HT-29), human mammary adenocarcinoma (MCF-7) and human kidney carcinoma (TK-10) cell lines [4]. The structural similarity between the molecules of 5-nitromidazole, 5-nitroindazole and the 5-nitrobenzimidazole is evident. Studies revealed that nitro-anion radicals were generated by 5-nitroindazole derivatives through a one-electron process at physiological pH and that the mechanism of action was associated with the generation of reduced species of the nitro moiety [4]. The first step in the mechanism of action of nitroheterocyclic drugs as cytotoxic agents for cancer hypoxic cells is the reduction of the nitro group of the drug to the corresponding nitro radical anion [2]. On the other hand, the simultaneous presence of imino group is a prerequisite for deprotonation and generation of azanion products in biological conditions. Having all this in mind, we have decided to synthesize a series of nitro derivatives of 2-iminobeznimidazole and study the probable formation of nitro anion radicals.

The present contribution presents a computational and spectroscopic IR investigatrion on the conversion of 2-[2-imino-5-nitro-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzimdazol-1-yl]-1-phenylethanone into radical and anionic products. The propensity of the compound to generate radical anionic species was estimated based on calculated adiabatic electron affinity, while the stability and reactivity of the radical anions was characterized by spin density distribution and molecular frontier orbitals. The electrochemical reduction of the title compounds was studied in aprotic medium and followed by IR spectroscopy. Comparison of the calculated molecular parameters and spectroscopic data to those of other nitroaromatic compounds provided useful insights on the potential of the iminobenzimidazoles for development of bio-reductive anti-cancer drugs.

Keywords: Iminobenzimidazoles, anti-cancer action, radical anion, DFT, IR spectroscopy

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UV-Vis absorption spectra of $OsCl_6^{2-}$ in ethanol calculated by TD-DFT with SOC corrections

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The present work presents a investigation of Os(IV) hexahalide complex in ethanol with special reference to their UV-Vis absorption spectra employing methods rooted in density functional theory (DFT) and its time dependent extension. Geometric and electronic structures are obtained using Def2-TZVP basis set for BP86, B3LYP, M06-2X, and CAM-B3LYP functionals. TD-DFT is used to calculate the electronic transitions and absorption spectra of $OsCl_6^{2-}$ in the singlet and triplet states. The spin-orbit coupling (SOC) between singlets and triplets is calculated from TD-DFT using the quasi-degenerate perturbation theory. The influence of spin-orbit coupling on the spectra is considerable due to the triplet state T1 lies below the singlet state S0. Accounting for the SOC correction, M06-2X functional, overestimates excitation energies, whereas B3LYP and BP86 underestimate transition energies with respect to experimental results. The quantitative accordance between the calculated and experimental spectra shows CAM-B3LYP with the SOC correction. The calculations are performed using the ORCA 4.2.0 program.

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On the determination of uncertainty budget of electromagnetic field spectrum analyzers – A case study

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This paper presents detailed, step by step determination of uncertainty budget of a typical lab-grade electromagnetic field spectrum analyzer. Such analyzers exist for various parts of electromagnetic spectrum, and while this paper is mainly focused toward general principles, a case study that illustrates development of uncertainty budget for a high frequency electromagnetic field meter that has a frequency range of up to 6GHz (NARDA SRM-3006 with suitable probes) is presented alongside the general principles.

First, a general model of the electromagnetic field spectrum analyzer, consisting of field probe, cable and spectrum analyzer is presented. Most common ways of describing the performance of the individual components of electromagnetic field spectrum analyzer are stated. Each individual component can be described in a number of ways, and with different level of sophistication of the models used for description, e. g. models ranging from full wave representations to equivalent circuit models. This is an important step in the development of uncertainty budget, since data sheets and calibration sheets may use different models and simplifications, and it is important to have them in mind during uncertainty budget formulation.

Typical individual components of uncertainty budget such as probe isotropy, linearity, mismatch loss, temperature dependence etc. are considered in detail along with possible ways of modeling their share in combined uncertainty. Justification for use of specific probability distributions for individual components of uncertainty is thoroughly explained. Special attention is given to the mismatch loss. Furthermore, a commonly overlooked component of uncertainty budget, namely, a choice of measurement point is briefly discussed.

Once the final set of considered uncertainty budget components is determined, combined uncertainty is calculated. Two approaches are used and results of each approach are compared. In the first approach, combined uncertainty of the field level is estimated using analytical formulas, under typical assumptions (e.g. uncorrelated input variables). In the second approach, tools of numerical statistics are applied in order to check validity of the analytically obtained model. This yields more information about estimated uncertainty distribution, and offers a way of checking analytical estimates. Finally, obtained results are compared to the requirements of the relevant international standards for electromagnetic field meters.

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Development of low cost wireless network for solar UV irradiation monitoring in Bulgaria

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The global climate change in the recent years has increased the interest to atmospheric irradiation monitoring in wider format. Additionally, to Gamma-ray and X-ray sensors, UV-C, UV-B and UV-A sensing systems has been developed to respond to the human expectations about sustainable life and to prevent them from hostile factors. The deeper penetration of UV sensor equipment and dense disperse of monitoring points will improve further the accuracy of measurements, accuracy of forecasting and will convince the citizens in the responsibility of researchers and their work. This work presents UV sensing equipment developed for remote monitoring. Solutions include complex system of narrow band sensors, data logging units, Wi-Fi communication devices, solar PV charging and Li-Ion energy storing equipment. Most of the components and software technologies are based on open-source platforms and approaches as well as internet-shared results. The analysis of results from 3 UV sensor systems already installed in 3 high-mountain monitoring points reveals local UV spectral variations. The performance of UV sensors has been evaluated. The collected database during one-year field measurements is prepared for training and development of algorithms for short-term UV forecasting.

Keywords: Solar UV measurements, UV sensors, open-source platforms, UV databases

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Modulation of ATP-activated calcium intracellular signaling by methylglyoxal in brain microvascular endothelial cells

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The formation of advanced glycation end products is one of the major factors involved in diabetic neuropathy, aging, neurodegenerative diseases, as well as inflammation. *In vitro* models of neuroinflammation are commonly using the exposure of brain endothelial cells to methylglyoxal, ubiquitous product of cell metabolism, that activates $TRPA_1$, specific receptors present on the endothelial cells' plasma membrane [1].

The main objective of our study is to understand how MG affects the brain microvascular endothelial cells in inflammatory conditions. We studied the calcium ions dynamics based on the ratiometric calcium imaging technique in *in vitro* inflammatory conditions induced by treatment with MG for 24 hours of endothelial cells cultures from murine cerebral microvasculature (bEnd.3 cell line, ATCC). After treatment with different MG concentrations (1- 1000 mg/mL), the effects were tested on cell viability using MTT test and on cellular response to ATP quantified through calcium imaging experiments. For each calcium transient recorded, we used a MATLAB script previously developed [2] for characterizing a variety of specific parameters (duration, latency, asymmetry, rising velocity, decreasing velocity, area and amplitude), which are correlated with the molecular processes involved in a particular signaling pathway.

The MTT assay and the evolution of each parameter showed an inhibitory effect at high doses of MG. We also calculated the Pearson correlation coefficients for each pair of parameters with respect to the MG treatment concentration in order to establish a connection between different cellular processes.

Our study demonstrated that MG modulates the ATP-induced calcium signaling in brain microvascular endothelial cells and also the crosstalk between $TRPA_1$ and purinergic receptors. Considering the fact that bEnd.3 is a popular cell line used for BBB model, our data are valuable in understanding the behavior of the barrier in inflammatory conditions and may serve as a positive control for oxidative stress.

Keywords: Inflammation, blood-brain barrier, methylglyoxal, calcium imaging, bEnd.3 cells

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SiPM and ZnS:Li6 based neutron detectors

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Since 2012, active work is underway to developing scintillation neutron detectors based on ZnS:Li^6 and Silicon Photomultiplier(SiPM).

Basic requirements for the development of the first version of the detector:

1. The active area of the detector is 10x200 mm^2.

2. Neutron absorber - ZnS (Ag)/LiF scintillator with lithium concentration, ensuring maximum efficiency of neutron registration.

3. Transportation of scintillation light - optical fiber from plexiglass with optimal geometry.

4. Removal of the signal from the detector - two SiPM with an active area of 3x3 mm^2.

Parameters of the neutron counter:

- Variable active area of the counter.

- Scintillator ZnS(Ag)/LiF with efficiency of 46%.

- Own efficiency of the counter was 70%.

- The count rate of detector is better than 10^5/s.

- Gamma sensitivity on the order of 10^{-7}.

The efficiency of 70% was obtained for designed counters, comparable to the efficiency of the helium counters.

The time resolution of the counters is better than 1 μs, that allows the use of detectors for time-of-flight measurements.

The same values of power voltage and thresholds apply to all counters. No needs for individual tunings. Simple and noise-immune electronics.

It is possible to manufacture the detectors with the length up to several tens of cm.

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The use of radioanalytical methods for the detection and identification of selected drugs

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The increasing number of drugs in the black market and their rising consumption require efficient and sensitive methods for their control including the detection and identification of individual drugs seized by police or custom officers based on the analysis of a tiny amount of this substance from a contraband illegally smuggled over the borders and airports. This is why it is important to apply appropriate and selective monitoring techniques which can uncover the composition of imperceptible samples of unknown drugs and thus contributing to the revelation of their producers and distributors. Such results will surely contribute to the reduction of the drug availability to addict people where there are a high percentage of youngsters whose health may be affected by the consumption of these narcotics. The paper is summarizing the situation in the drug problems worldwide with special emphasis on these problems in the European Union and especially in the Czech Republic. Some details associated with the use of radioanalytical methods based on the neutron activation analysis are presented and discussed. The preliminary results of the analysis of some selected drugs like heroin and cocaine are interpreted in terms of the consequences of drug availability on the increased crime rate and the security of affected countries.

Compilation and application of Quality of Life (QoL) questionnaires: The NETs' patient treatment paradigm

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Introduction. Cancer constitutes the second largest cause of death worldwide. NeuroEndocrine Tumors (NETs) represent a rare class of neoplasms. Their therapeutic procedure requires interdisciplinary cooperation. A well-accepted therapeutic regimen of NETs is Peptide Receptor Radionuclide Therapy (PRRT). A common approach for monitoring therapeutic results includes patients filling in questionnaires regarding their Quality of Life (QoL).

Purpose. The purpose of this study is twofold; First, to present the parameters necessary for the structured compilation of QoL questionnaires; Second, to demonstrate the importance of QoL questionnaires' utilization in the assessment and monitoring of NETs during PRRT therapeutic approaches.

Materials and methods. Two studies, which have been carried out worldwide and assess utilization of QoL questionnaires on NETs treatment procedures (based on either PRRT or combined PRRT-octreotide regimens) are reviewed.

Results. The structure of the QoL questionnaires is based on the theory that human QoL has the form of a pyramid. This pyramid comprises of various domains of human life (physical, social, psychological etc).QoL questionnaires can be generic or disease-specific. The first paper reviewed assessed the results of a PRRT therapeutic procedure on patients with GastroEnteroPancreatic (GEP) NETs. This study validated the efficacy of PRRT therapy, in accordance with the existing bibliography. The second paper used the QoL questionnaires in order to compare the PRRT-octreotide vs. octreotide therapeutic regimens in the case of midgut NETs. The former therapy was proved to have better efficacy, mainly on the global health domain of patients.

Discussion. QoL questionnaires have been proven to be an important tool for the assessment and monitoring of the therapeutic regimens in NETs' patients, as well as in other types of cancer and other diseases. By incorporating the patient's voice in the decision making process, QoL questionnaires have become essential not only for monitoring, analysis and assessment of patients' health, but also for individualizing a patient's treatment regimen. Additionally, QoL questionnaires can be used beyond clinical practice (such as in pharmaceutical companies in the framework of product development or in statistical studies), while their flexible nature allows corresponding data to be collected online, so as to be subsequently studied.

Genus *Cistus* – A general overview and biological potential

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Genus *Cistus*, one of the 8 genera in family Cistaceae, includes perennial evergreen shrubby plants, commonly called rockroses. These species are widely distributed throughout Mediterranean and represent one of the first inhabitants in stony and infertile areas, but also on terrains affected by fires, as germination of theirs hard-coated seeds can be induced by higher temperatures. Genus is divided into three subgenera: pink or purple flowered *Cistus* (e.g *C. parvifolius*, *C. incanus*, *C. albidus*), and white flowered Leucocistus (e.g. *C. ladanifer*, *C. salviifolius*, *C. laurifolius*, *C. monspeliensis*) and Halimioides (e.g. *C. libanotis*). Concerning the phytochemistry, species are characterized by presence of essential oil, with terpenes being the dominant components. Depending on the abiotic factors and type of trichomas present in species, essential oil is rich either in monoterpens and sesquiterpens, or in diterpens especially of labdane and clerodane type. Commonly mistaken for essential oil and used in perfume industry, oleoresin labdanum is present in some species of the genus, *C. ladanifer* being the most prominent source. Various flavonoids, phenolic acids and tannins were detected in several representatives of this genus. In general, subgenus *Cistus* is abundant source of flavonoids and devoid of elagitannins, while two other subgenera are rich in elagitannins, and contain fewer amounts of flavonoids. Both essential oils, labdanum and various types of obtained extracts showed *in vitro* activity against both gram-positive (*Staphylococcus* sp., *Enterococcus* sp., *Bacillus subtilis* and others), gram-negative (including *Pseudomonas aeruginosa*) and other (*Borrelia burgdorferi sensu stricto*) bacteria. Extracts obtained from several species of this genus demonstrated potent antifungal activity against *Candida* sp. but also against pathogens affecting citrus fruits, thus giving potential for use as ecological fungicides. Antiviral activities recorded *in vitro* support the traditional application of tea-drinks in common cold and influenza cases. Numerous and various testing of antioxidant activity suggested high potential of these herbs. This type of activity is complementary with antihyperglycemic effects, mediated by potent inhibition of α-amylase and α-glucosidase. Several species have been tested *in vitro* for anticholinesterase activity, giving positive effects against acetylcholinesterase. In cell cultures, prominent activity of *Cistus spp.* against cancer cell growth was recorded. All of the mentioned activities suggest biological potential of *Cistus* species. Further investigations in pharmacological and clinical studies would give justification of traditional uses as wound-healing, anti-inflamatory and antiulcerogenic remedy, but also as antidiarrheic, antacid and antispasmodic agent.

Stability of rosmarinic acid in human gastrointestinal tract

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Numerous *in vitro* and *in vivo* conducted studies have demonstrated high biological and pharmacological potential of rosmarinic acid (RA). This compound can be found in representatives of subfamily Nepetoideae of family Lamiaceae (e.g. rosemary, sage, lemon balm, thyme) and in family Boraginaceae (e.g. borage, comfrey), as well as in several other plants. Chemically, RA is an ester of caffeic and 3,4-dihydroxyphenyllactic acid. It is considered that specific structure contributes to its high and diverse activities, antioxidant potential being the most prominent. As it can be seen, RA is present in aromatic spices, used both culinary and in pharmaceuticals. Thus, peroral application can be considered as the most important. However, the environment of human gastrointestinal tract (GIT) exhibits a high impact on this compound. Throughout GIT, pH values vary widely. Highly acidic gastric environment can affect RA content, and it is considered that low pH values can lead up to ≥50% reduction of RA's concentration. However, the reduction rate is affected by presence of other herbal compounds. Pure RA is relatively stable in acidic medium, while RA in extracts obtained from thyme, winter savory and marjoram is less stable and the content can be reduced up to 99%, in the example of thyme. The presence of other compounds can increase the stability of RA; in the example of oregano, it is considered that high content of luteolin and apigenin can protect the RA from GIT-related degradation. Intestinal environment has slightly alkaline reaction, and it is demonstrated that stability of RA is better in given pH values. Again, stability of pure RA is higher than stability of RA in herbal extracts, due to the same reasons. A loss of 61% of RA content in rosemary extract is recorded after use of artificial digestive juices. However, it should be taken into consideration that different approaches to GIT digestion simulation can lead to differences between results, where digestive juices collected from patients should have advantage in reporting compared to synthetic, commercial mixtures, as human digestive juices are much more complex systems consisted of digestive enzymes, enzyme inhibitors, minerals and bile acids and their salts. It is estimated that only minor portion of RA can be absorbed by paracellular transport in enterocytes. Majority of RA reaches intestine and its microbiota. Microorganisms have enzymes which cleave the ester bonds, leaving the simple phenolic units which are further easily absorbed. Studies suggest that microbes take an important part in RA metabolism. Approximately 14% of RA is lost through process of *in vitro* colonic fermentation (using rat feces as microbiota source). Even higher percent of RA (>90%) can be hydrolyzed *in vitro* by using *Lactobacillus* strains. Further studies evaluating RA stability in human GIT are needed, in order to provide the complete data on compound's pharmacokinetics and potential for clinical studies.

Evaluation of the influence of different irradiation types on the physicochemical properties of chloramphenicol eye ointment

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Commonly used methods for sterilisation of pharmaceutical preparations are sterilisation with moist heat under pressure, dry heat, gas, filtration, ionizing irradiation or high intensity visible light. In this study we used eye ointment in a form of a suspension containing chloramphenicol as active substance (API) and white paraffin, lanolin and castor oil as ointment base. The most effective method, thermal sterilisation, was not applicable considering the low melting point of ointment base and heat sensitivity of the API. Sterilisation with ethylene oxide and preparation with aseptic manufacturing process were avoided – the former because of toxic residues problems and the later due to the high cost of the process. The chosen method for sterilisation of the chloramphenicol eye ointment was sterilisation by irradiation.

The aim of this study is to evaluate the influence of different types of irradiation, such as gamma-rays (dose of 25 and 40 kGy), E-beam (15, 25 and 50 kGy) and X-rays (15, 25 and 40kGy), on chloramphenicol eye ointment and identification of the minimum dose required to achieve the desired sterility level. Evaluation of the product stability was performed for a period of 3 months when stored at 25°C/60%RH and 30°C/75%RH with monitoring of the quality parameters: appearance and colour, assay of chloramphenicol, related and degradation products, and sterility of the product.

Generated stability data showed that after sterilisation by the aforementioned types of irradiation, all of the evaluated samples met the established acceptance criteria for the parameter appearance. Slight changes of colour were observed in samples treated by X-rays (40 kGy) and by E-beam (50 kGy) irradiation when stored at 30°C/75%RH. After sterilisation by three types of irradiation, slight decrease in the assay of chloramphenicol was observed, however, during the stability study the assay of chloramphenicol remained constant. The impurity profiles were similar after sterilisation, however, with increment of the dose, an increase in the number of radiolysisproduct was noticed. From the data obtained for the unspecified impurities and the total impurities, it can be concluded that all the results are below the established specification limits and remain constant throughout the stability study. Sterility testing showed that product sterility is achieved with all evaluated types and doses of irradiation. Although X-rays have penetration comparable with gamma-rays, based on the literature data, this type of irradiation may cause nuclear transformation, limiting its use for pharmaceutical products. E-beam irradiation was avoided since low dose uniformity ratio cannot be achieved. According to the obtained results from the screening stability study of the tested eye ointment, gamma irradiation (25 kGy) was evaluated as a most suitable method for sterilisation by irradiation, considering the product characteristics.

Lipid peroxidation induced by UV-A irradiation of protoporphyrin in lipid mixture: TBA-MDA test

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Lipid peroxidation (LP) is the phenomenon involved in the oxidative damage to cell structures and in the toxicity processes that lead to cell death. On the other hand, LP is considered as process applied in various fields in medicine (photodynamic therapy) and pharmacy. Lipid peroxidation can be a free radical chain reaction, or, occurred through a non-radical pathway, by direct reaction with singlet oxygen, created in the presence of a photosensitizer. As a consequence of lipid peroxidation processes, alcohols, ketones, alkanes, aldehydes and ethers can be found as breakdown products. The most prominent and currently used assay for detection and recording of LP is the spectrophotometric thiobarbituric acid - malondialdehyde test (TBA-MDA), based on the reactivity of a product of lipid peroxidation, malondialdehyde with thiobarbituric acid (used as reagent in this test), to produce a red adduct absorbing at 530 nm.

In this study, a special type of LP initiator, photosensitiser protoporphyrin IX dimethyl ester (PPIX), was used. Lipid peroxidation was initiated by photosensitization reaction of PPIX with continual UV-A irradiation in lipid mixture, in methanol. The formation of the LP product MDA, was measured by using TBA-MDA test. UV-A irradiation treatment of lipids mixtures in methanol (with or without the photosensitizer PPIX) was performed in cylindrical photochemical reactor with emission maximum at 350 nm and total measured energy flux 12.9 W m^{-2}, 10 cm from the lamps. Time of irradiation was 5-30 min. Simultaneously, one sample lipid mixture with PPIX was kept in the dark.

The continual UV-A irradiation of lipid mixture sample in presence of PPIX resulted in lipid peroxidation process - continuous increase in absorbance band at 530 nm. Lipid peroxidation process obeys first-order kinetics - results obtained from the kinetic analysis. The calculated rate constant of TBA-MDA growth is 0.0189 min^{-1}. Lipid peroxidation process was not observed in the samples without photosensitizer, or samples with photosensitizer kept in dark. Detected lipid peroxidation processes under conditions of UV-A light implicated great possibility for PPIX use as photosensitizer agent.

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Study of structural changes in irradiated polycarbonate by positron annihilation spectroscopy, NMR spectroscopy and nanoindentation

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The aim of our study was to determine interval of doses for radiation crosslinking occurs in irradiated polycarbonate and interval of doses in which the degradation of polymer chains already prevails.

On horizontal channels of the LVR-15 research nuclear reactor of the Research Center Rez, Ltd., pairs of pure polycarbonate samples were irradiated with different doses of radiation. In parallel, other pairs of samples were irradiated with the same doses in a high-activity irradiation facility equipped with a ^{60}Co gamma emitter with an activity of 200 TBq. The dose from photons and neutrons was accurately determined.

The irradiated samples were then subjected to positron annihilation spectroscopy (PAS) analysis (which gives information about the distribution of free volume sizes in the polymer), NMR spectroscopy (which measures the mobility of molecular chains) and finally was used the nanoindentation method (which indicates changes in the mechanical properties of the irradiated polymer).

Lift-off lithography process for fabrication of TlBr gamma-ray detectors

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TlBr gamma-ray detectors have been fabricated by lift-off lithography process using a positive resist. The resist was coated on TlBr crystals with thickness of around 0.4 mm and the crystals were baked at 100 ºC for around 5 minutes. After developing process and Au electrodes formation by the vacuum evacuation on the crystals, deposited Au on the resist were removed with the resist film by immersing them in N-methyl-2-pyrrolidinone. Influence of the lithography process on the TlBr detector performance has been evaluated by measuring leakage-current of the TlBr detectors and estimating charge transport properties of electrons and holes in TlBr detectors. Current-voltage characteristics and energy spectra show that resistivity and mobility-life time products for TlBr detectors prepared in this study were comparable to the results on detector performance obtain from TlBr detectors fabricated by typical electrode formation process using a metal mask.

Correction of fogging effect on Gafchromic® HD-V2 film response for its use in gamma-ray dosimetry

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Gafchromic® HD-V2 film dosimeter is a reliable dose measurement device, thin, flexible, inexpensive, ease to handle and simple to analyse data. The interest in this dosimetric system is related to the use of gamma radiation in industrial processing, such as sterilization of medical-sanitary material, food-processing and others. The response in terms of net absorbance with respect to absorbed dose was found to be linear in the selected dose range, which supports the feasibility of using the film dosimetry in many applications. For its use for high-energy photon dosimetry, a preliminary calibration of the film response versus dose was performed with reference to international standards. However, the temporal analysis of the dosimeter responses shows a "fogging" growth over the time both in irradiated and non-irradiated films mainly due to the instability of the active component of the film. This effect must be taken into account since film response changes with time.

In this work, the fogging effect was investigated for more than 400 days with reference to a dose range up to 300 Gy. A correct calibration curve was obtained determining, prior to each use, a time dependent background value through reading of non irradiated dosimeters and evaluating for each dose value a mean net absorbance. The behaviour of mean net absorbance versus dose was well fitted with a straight line passing through the origin of axes. This corrected calibration curve can be considered valid for any irradiation time.

Testing of low-cost dosimeters used in non-governmental networks within 16ENV04 Preparedness project

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Recent advances in microelectronics and information technologies, along with the expansion of citizen science, have changed the way measurements are done in many scientific fields, including ionising radiation dosimetry. Many low cost user-friendly instruments are now available for purchase over the internet. Most of the instruments can be connected with applications for real time measurements, and some of them provide possibilities for real time upload to the specialized public websites. Low cost and low requirements for technical knowledge allow many laymen to perform measurements, and results can be easily disseminated via social networks and media outlets. These results are often not verified and low-cost instruments are usually not type tested, so there is a significant possibility for such results to cause misinformation of public or even unwarranted panic.

Research on non-governmental dosimetry networks has been conducted within the Work Package 3 of 16ENV04 Preparedness, scientific project within the European Metrology Programme for Innovation and Research (EMPIR). The research has identified non-governmental networks with the densest networks and most active websites, because such networks have the largest potential impact on the public. Measuring instruments used in non-governmental networks (MINN) have been identified, and a total of 16 types of MINNs have been sourced, commissioned and tested in dosimetry laboratories of Vinca Institute of Nuclear Sciences (VINS), Serbia, Physikalisch-Technische Bundesanstalt (PTB), Germany, National Physics Laboratory (NPL), United Kingdom and Italian National Agency for New Technologies, Energy and Sustainable Economic Development (ENEA). The tests included linearity and energy dependence of the response in photon fields generated at each institute, determination of inherent background, response to cosmic radiation, response to small changes of background radiation and tests of dependence of the response on climatic conditions – humidity and temperature, at PTB facilities.

The research has shown that most of the MINNs are based on non-compensated Geiger Mueller tubes, with the consequence that the energy dependence does not conform to the requirements of relevant standards. Dead time correction is not performed in most low-cost instruments, but the linearity is within ±15 % in the dose rate range of interest for environmental monitoring. Response to small changes in background dose rate is dependent not only on the radiation detector, but also on the software and the mode of operation selected by user. In field tests, most dosimeters were sensitive to small changes in background radiation.

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Dose-rate measurements based on commercial phototransistors using a modified reader unit

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Introduction. The main application of photodiodes and phototransistors is to measure visible, ultraviolet or infrared light. However some authors have reported their use as dose rate sensor for X-ray photon beams (M.S. Andjelkovic et al., Radiation Measurements 75, 2015).

Our research group previously developed a reader unit for MOSFET dosimeters (M.A. Carvajal et al., Sensors and Actuators A 247, 2016). Our aim in this work was to extend the sensor interface capability of our reader. Therefore, a connectable module to measure dose rate with phototransistors is presented as well as its application for phototransistors as dose rate sensors.

Current voltage converter. This is the main analog processing system. It is based on the operational amplifier TL072 (Texas Instruments, USA) with a feedback resistor of 4.7 MΩ. The output is low pass filtered and level adapted to our reader unit input. Finally, data are digitalized with the converter ADS8320 (Texas Instruments, USA), achieving a resolution of 0.2 nA. The biasing voltage, -10 V, was obtained filtering the output of a DC-DC inverter based on the PWM controller MC3463 (Texas Instruments, USA).

Experimental setup. Two experiments were carried out with an irradiation field of 10x10 cm^2 in electronic equilibrium condition, and placing the devices at the isocentre of the radiation sources (at 100 cm) of the linear accelerators:

- Siemens Artiste, 6 MV: Devices to test BPW85B (Vishay Siliconix) and VTB8440BH (Excelitas Technologies).
- Siemens KDS, 18 MV: Device to test OP505 (Optek).

Dose rates of 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0 Gy/min were applied to characterize the response of the reader module and the phototransistors. The reader unit was placed in the bunker and connected via USB extension cable with a computer place outside the irradiation room. To study the effect of the accumulate dose, the response of the devices were monitored from high to low dose rate (High -> Low), and after, from low to high dose rates (Low -> High). In order to minimize the effect of ambient light, the devices were painted with nails polish and placed into a black plastic box.

Results. Linear dependence of the current with dose-rate was found in all the experiments (bias voltage during irradiation: -10 V) for the following devices:

OP505: High -> Low: (11.01 ± 0.23) µC/Gy (R^2= 0.998);
Low -> High: (10.73 ± 0.08) µC/Gy (R^2 = 0.9998).
BPW85B: High -> Low: (9.85 ± 0.18) µC/Gy (R^2 = 0.998);
Low -> High: (7.32 ± 0.05) µC/Gy (R^2= 0.9998).
VTB8440BH: High -> Low: (10.8 ± 0.4) µC/Gy (R^2 = 0.9947);
Low -> High: (7.7 ± 0.2) µC/Gy (R^2= 0.9970).

Conclusions. The designed reader unit has been successfully tested to measure dose rates in the usual range of radiotherapy treatments. Regarding the response of phototransistors, high linearity and sensitivity was found, however the response of the BPW85B and VTB8440BH showed a response degradation higher than 26% after the first 12 Gy. The OP505 presented a better response to be used as dose rate sensor with our reader module, and it will be further characterized with photon beams of 6 and 12 MV. The current tasks are focused to development a specific reader unit for dose measurements using the topology of the I/V converter described in the present work and characterizing another model of photodiode.

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Study of optical and luminescence properties of undoped $Gd_3(Ga,Al)_5O_{12}$ scintillating single crystals

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The Ce-doped garnet scintillator crystals with general formula $Gd_3(Al,Ga)_5O_{12}$ (GAGG) are perspective for medical applications, e.g., in a single photon emission computed tomography. These crystals attract attention due to the combination of high density, chemical stability, high light yield and good energy resolution. The tailoring of luminescence and scintillation properties of GAGG crystals can be achieved using the method of the bandgap engineering, which consists in gradual variation of substitutional cations concentration. The influence of such variation on optical properties and, in particular, on the bandgap values has been studied previously for the Ce doped GAGG crystals only. However, Ce absorption bands distort the fundamental absorption edge. Therefore, the studies on undoped crystals are required. Here we present the results of the study of the influence of partial substitution of Al for Ga cations on the structural, optical and luminescence characteristics of the undoped $Gd_3Al_xGa_{5-x}O_{12}$ (x = 2,3) crystals.

Single crystals were grown by the Czochralski method at the Fomos-Materials (Moscow, Russia). Characterization of crystal structure has been performed using XRD, SEM and TEM techniques. Absorption spectra were measured using an Agilent Technologies Cary-5000 spectrophotometer at 300 K and PerkinElmer Lambda 950 spectrophotometer in temperature region 80-500 K. Luminescence excitation and emission spectra under excitation in the UV-VUV region were measured using the photoluminescence endstation of the FinEstBeAMS undulator beamline at the MAX IV synchrotron facility (Lund, Sweden).

Unit cell parameters and space group were obtained using XRD analysis. Chemical compositions of the crystals were determined using SEM-EDX and TEM-EDX techniques. It was shown that the increase of Ga content results in the decrease of bandgap. Bandgap values were estimated from the temperature dependence of the fundamental absorption edge and its approximation using Urbach formula. In the luminescence spectra, narrow emission lines were detected at low temperatures in UV, visible and IR spectral regions and ascribed to the $^6P_J - {}^8S_{7/2}$, $^6G_J - {}^6P_J$ and $^6G_J - {}^6I_J$ 4f-4f radiative electron transitions within Gd^{3+} ions. In the excitation spectra, electronic transitions from $^8S_{7/2}$ to ^6P_J, ^6I_J and ^6D_J were observed in crystals transparency region. The transitions from $^8S_{7/2}$ to ^6G_J were observed for the GAGG crystals with x = 3, while for the crystal with x = 2 these transitions were enveloped by interband electronic transitions. The threshold of photon multiplication process was determined.

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Dose measurements with clinical electrometers and Light-Dependent Resistances

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Introduction. Light Dependent Resistances (LDR) are widely used as visible light detectors, due to its low cost, and very well-known response with light intensity. In our previous works, it was tested experimentally that some models of LDRs present a promising performance as dose-rate sensors (P. Escobedo et al. RAD2018, J. Román-Raya et al. SEFM-SEPR2019, Burgos, Spain). As reader units, a digital multimeter (P. Escobedo et al. RAD2018) or a clinical electrometer (J. Román-Raya et al. SEFM-SEPR2019) were successfully employed, respectively. In the present work, a clinical electrometer as a reader unit for monitoring LDR radiation response with dose rate was tested.

Experimental setup. LDR model NSL-19M51 (Luna Optoelectronics, USA) was characterized for 6 MV photon beams produced by an Artiste linear accelerator (Siemens, Germany). LDRs were painted with black nail polish and located inside a carton box, to reduce the effect of environmental illumination. For an irradiation field of 10x10 cm^2, the carton box was placed between slabs of solid water in order to achieve the electronic equilibrium condition, with the LDRs situated at the isocenter (at 100 cm from the source).

LDRs were connected to a PC Electrometer (Sun Nuclear, USA) situated inside the treatment room and connected to a computer with an USB extension cable. This electrometer provides a bias voltage from -400 to 400 V, with a maximum current range of 50 nA.

Results and conclusions. Currents produced with a bias voltages (80 V and 100 V) were monitored with dose rates values of 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0 Gy/min. The current was zeroed before each irradiation and the charge was calculated integrating the current with time. The accumulated charge was fit as total dose function, obtaining an average sensitibity. Three LDRs were characterized at 80 and 100 V, obtaining an average sensitivity of (56 ± 5) nC/Gy and (68 ± 7) nC/Gy respectively, with a minimum $R^2 = 0.987$. Linearity and the low price suggest that the LDRs could be a promising candidate for low cost dose measurements. A thermal characterization will be carried out to study the temperature interference with dose measurements.

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Characterization of the response of microMOSFET detectors with the distance for *in vivo* dosimetry in high dose rate brachytherapy

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Purpose. *In vivo* dosimetry allows to monitor the dose administered to patients enabling an independent verification in radiotherapy treatments. In the last decades, different devices have been used for high dose rate brachytherapy (HDRBT), such as termoluminiscent dosimeters (TLDs) or semiconductor diodes. However, TLDs do not provide real-time measurements whereas the semiconductor diode response strongly depends on measurement conditions. Metal Oxide Semiconductor Field Effect transistors (MOSFETs) provide real-time measurements and their size is small enough to be introduced into the needles used for HDRBT. Nevertheless, their response may depend on measurement conditions. In this work, we have studied experimentally how the Best Medical Canada microMOSFET response depends on the source-to-detector distance, in order to establish the influence of the radiation spectrum and dose rate.

Materials and methods. The Flexitron Afterloader and the Flexisource ^{192}Ir source (Elekta, Stockholm, Sweden) were used. Dose distributions were calculated with the Elekta Oncentra Prostate Planning System and depth-dose curves were measured with GafChromic EBT3 film (Ashland Advanced Materials, USA). Calculations and measurements were made in both, water and air. The microMOSFETs were inserted in metallic and plastic needles, and introduced into a PMMA phantom designed for this experiment, which had several holes made for the needle positioning.

Results. The voltage variation in the microMOSFETs was measured as a function of the source-to-detector distance in water. An increase of the detector response of (1.4±0.2)% per cm and (2.3±0.3)% per cm was observed when using metallic and plastic needles, respectively. No changes in the detector response were observed in the case of the in-air measurements. As a consequence, the microMOSFET response shows up to be independent of the dose rate, though it is affected by the modifications of the radiation spectrum due to the material surrounding the device.

Conclusions. A strong dependence of the microMOSFET response with the distance was found and therefore it must be corrected in clinical applications. This distance dependence can be attributed to the sensitivity of the device to the details of the radiation spectrum. Currently, Monte Carlo simulations are being carried out to obtain the change in the radiation spectrum with distance in water and to estimate its effect on the microMOSFET response.

Generational impacts of paternal irradiation in a cricket: Damage, life-history features and hormesis in F1 offspring

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Animals exposed to significant stress express multi-modal responses to buffer negative impacts. Ionizing radiation can inflict considerable damage to molecular, cellular and epigenetic aspects, both directly and via generation of reactive oxygen species. Impacts on germ cells may also transmit transgenerational alterations to F1 offspring. Transgenerational impacts have been mainly studied in maternal lines, and paternal lines have received less attention. Here we assess damage and life history alterations arising from irradiation of juvenile (4th instar) male crickets (*Acheta domesticus*) and their F1 offspring. Paternal transmission of radiation impacts emerged in multiple life history traits. Irradiated males and F1 offspring expressed hormetic responses in survivorship and life span at mid-range doses (i.e., 7Gy & 10Gy doses extended F0 longevity by 37% and 31%, respectively). F1 offspring of paternal 7Gy and 10Gy sires lived 30% and 79% longer, respectively. Although irradiated F0 males had reduced growth rates, F1 offspring did not. Results indicate that irradiation directly impacted males but also mediated significant alterations in life history features (particularly longevity and survivorship) of F1 offspring.

Electromagnetic radiation at resonance frequencies: Possible harmful and beneficial effects

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Resonance is a phenomenon represented by the oscillation at high amplitude of a material, which occurs if a material is forced mechanically, or electrically, or acoustically, at a specific frequency named natural resonance frequency. If the frequency of the external forcing is close to a natural frequency of a system, a large vibration occurs giving rise to a resonance phenomenon.

Modern technology has led to the achievement of wireless technology, based on the transmission by electromagnetic radiation in RF and MW regions. Otherwise, it was already shown in several studies that biological systems exhibit natural resonant frequencies in the MWs region, precisely at frequencies most used by wireless devices. In particular, the 5G technology is planning working at above 20 GHz or more, also requiring an increasing in intensity of electric and magnetic fields, so that we cannot know if such frequencies can be close to some resonant frequency of human organism inducing a drastic increase of harmful effects for livings. In contrast, it was recently demonstrated the existence of non-resonant frequencies at which wireless communication systems could be designed (1,2).

On the other hand, beneficial effects of resonance frequency electromagnetic radiation can be represented by using it at some natural resonant frequency of cancer cells or of some particularly lethal virus such as SARS-CoV-2.

Indeed, the result that the displacement of cell channels α-helices depends on the frequency of applied high frequency electromagnetic fields (3-6) leads us to deepen the search for frequencies in which this effect is amplified, since an alteration of cellular membrane channels should induce a change in ions flux across channels and the consequent damaging of cancer cells.

Furthermore, proteins denaturation is a necessary condition to inactivate virus capsid and it was shown that exposure to electromagnetic fields induces proteins denaturation (7-9). Hence, we can plan to use an electromagnetic radiation at a resonant frequency in order to emphasize this effect (work in progress).

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Bystander effects induced by proton-irradiated human chondrosarcoma cells

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The radiation-induced bystander effect was highlighted in non-irradiated cells that received stress signals sent by the irradiated neighbour cells. The bystander effect depends on a number of conditions such as radiation dose, dose rate, LET, cell type, culture system and its contribution is appraised for conventional therapy as well as charged particle therapy (hadron therapy). Hadron therapy presents better specificity and lower toxicity for the surrounding normal tissue compared to conventional treatment and is standard care for some chondrosarcomas.

This study focuses on analysing cellular effects induced in bystander cells by 2D and 3D chondrosarcoma cells irradiated with protons of high and low energy versus X-rays.

Bystander effects were induced through media transferred from 2D and 3D irradiated chondrosarcoma cells (SW1353) to normal chondrocytes (T/C-28a2) and endothelial cells (EA.hy926). Cell survival and DNA damage were assessed in bystander cells.

Irradiated 2D chondrosarcoma cells triggered bystander effects in both chondrocytes and endothelial cells. Interestingly, X-Ray irradiated 2D chondrosarcoma cells caused a more efficient bystander effects in chondrocytes than proton irradiated cells at the lowest dose used (0.1 Gy). On the contrary, in endothelial cells the most effective bystander response was caused by the low energy proton irradiation at 2 Gy. Proton irradiated 3D spheroids induced a similar response in 2D bystander cells.

Our results showed the ability of chondrosarcoma cells to secrete bystander signals that were received by normal chondrocyte and endothelial cells.

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Effect of prolonged UV irradiation on model and wild Poaceae species in laboratory and in mountain conditions

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This study aims to assess the potential of prolonged UV irradiation both in laboratory and mountain conditions to induce genotoxic alteration in model and wild Poaceae plants. It is well known that changes in natural environment increase at a great extend with the altitudes. As sessile, photosynthetic organisms plants are exposed to more than one environmental factor: increased levels of UV irradiation, altitude, temperature, humidity and etc. Plant response differ when environmental factor is single or in combination with other abiotic stress factors. Two types of plants from family Poaceae were studied depending on the experimental conditions. A model plant *Hordeum vulgaris* L. was used in laboratory conditions. 5 days old plants were exposed to UV irradiation during periods of 10, 20, 30 and 43 days. On the other hand four wild species: *Poa alpina* L., *Sesleria coerulans* Friv., *Festuca valida* (R. Uechtr.) Penzes, *Dactylis glomerata* L., characteristic of the ecosystems in Rila Mountain at three altitudes (1500m, 1782m, and 2925m) were collected in three successive growing seasons (2017, 2018, 2019). Micronucleus assay was applied as endpoint. Frequency of micronuclei (MN) increased in a time-dependent manner and plant organs susceptibility was observed in laboratory conditions. Wild genotype *D. glomerata* L., growing at 1500 and 1782 m.a.s.l was with higher sensitivity for three seasons. The highest susceptibility of this genotype was measured for 2019 at 1500 m.a.s.l. Similar values were established for this genotype at 1782 m.a.s.l. for three seasons. The larger UV intensity on Moussala Peak supposed a higher frequency of MN, but the yield of induced MN was relatively low. The other three Poaceae genotypes sampled on Moussala Peak were not very sensitive comparing with *D. glomerata* L.. Their sensitivity were similar and lower in comparison with *D. glomerata* L. Variability in the response between model and wild plant species was found to UV irradiation alone or in combination with other abiotic stress factors. The frequency of MN was higher in laboratory conditions than that in mountain conditions. It could be due to the fact that in laboratory conditions was studied the effect of a single factor, while in natural environment, effect of prolonged UV irradiation is combined with other abiotic stress factors. On the other hand plant species at the highest altitude were with well pronounced low level of damage. It is well known that plants response is modified while effect of UV irradiation is combined with other factors. Further studies are needed for better understanding the mechanisms of interaction between factors and plant responses to the changing environmental conditions. Based on this and future monitoring studies could be posible to select sensitive monitor/model Poaceae species for the following comparative environmental impact assessments in laboratory and in mountain conditions.

Key words: Genotoxic effect, micronuclei (MN), UV irradiation (UV-A; UV-B), *Hordeum vulgaris L.*, *Dactylis glomerata* L., *Poa alpina* L., *Sesleria coerulans* Friv., *Festuca valida* (R.Uechtr.) Pénzes, Poaceae

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Effects of ionizing radiation on the synthesis of carotenoids of microscopic fungi Aspergillus versicolor with radiotropism found in the Chernobyl exclusion zone

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There is a constant search for producers of biologically active substances that can be used as immunostimulants, adaptogens, anticancers, compounds as substances that maintain homeostasis, regulators of biorhythms, cardiac activity, have hypolipidemic, antisclerotic, thrombolytic, antihypertensive and antihypertensive effects. All these properties are inherent in carotenoids. In humans and animals, carotenoids are not synthesized de novo, but come with plant foods. Previously, studies of the biological role of carotenoids in humans and animals were dominated by the "provitamin concept", according to which these pigments were considered precursors of vitamin A, and now the study of carotenoids has formulated a concept of a wide range of biological non-vitamin functions in humans and animals. As a result, these pigments are widely used in various sectors of the economy, and recently there is an active search for new producers of carotenoids.

A number of studies performed on fungal cells have shown the connection between the synthesis of carotenoids and the protection of the body from the photodynamic action of ROS, which are formed by light in the presence of oxygen. Carotenoids have a powerful antioxidant activity, which is manifested in the deactivation of highly reactive oxygen free radicals, peroxides, quenching of lipid and superoxide radicals and stopping free radical processes. Previous studies have shown that one of the species of micromycetes that was constantly found indoors in the Shelter was Aspergillus versicolor, and certain strains of this species showed positive radiotropism, i.e. the ability to activate metabolic processes under high doses of radiation. It has been suggested that such unique properties of these fungi are realized to some extent due to the peculiarities of the functioning of their antioxidant system, in particular carotenoid pigments, and additional irradiation may induce the synthesis of these pigments.

The aim of the study was to conduct a comparative study of the effect of radiation on the synthesis of carotenoid pigments in strain *A. versicolor* 99 with radiotropism and *A. versicolor* 432, which did not have such properties.

Thus, we noticed differences in the content of carotenoid pigments in strains of *A. versicolor* with a sign of positive radiotropism and control. It was found that ionizing radiation is an inducer of synthesis of β-carotene and lycopene in the strain with positive radiotropism and synthesis of lycopene in the control strain *A. versicolor 432*.

CT examination for treatment planning purposes in the mediastinum of a pregnant patient with Hodgkin Lymphoma

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In pregnancy, Hodgkin Lymphoma is one next most common type of tumour after breast cancer. Our institute has more than 30 years of experience with successful treatment of pregnant patients including 147 with Hodgkin Lymphoma. Patient treatment schemes included chemotherapy, radiotherapy, surgery performed either alone or combined, according to the type of cancer and clinical indication. For patients who undergo radiotherapy, it is essential to perform a CT scan for treatment planning.

It has been found, based on the retrospective study, that due to ALARA principle, the extension of the CT scan has been set as short as possible. In some cases, for patients treated in the mediastinum region, the CT scan was too short, and did not cover the whole lungs and whole heart of the patient, which made it impossible to use these organs correctly for optimizations of treatment plan, as well as for the calculation of whole organ doses.

The CODE (Conceptus Dose Estimation Tool) has been used to determine the dose to foetus during CT scan on SIEMENS Somatom Open machine. For the protocol which covers the whole organs at risk, 2.5mGy has been estimated, while for the very short procedure, this was 0.5mGy foetus dose. Although for a technically better CT scan, the dose is 5 time larger, it is still very low and below 5mGy set by ICRP as a very safe level, below which no relevant radiation effects can be estimated based on the LNT model, the probability of not having cancer at the age 0-19 years is 99.7%, and is the same as for the background radiation for children who had not been exposed in the foetus period.

The CT scan which covers the full organ at risk and allows to calculate the dose is a ‘must’ procedure during Hodgkin Lymphoma treatment, and for the future probable re-irradiation purposes. Benefits for the mother, coming from proper optimisation and assessment of the treatment plan significantly overcomes potential risk for the foetus associated with wider CT examination. This means that the CT, extended enough to cover all OAR, for a pregnant patient with Hodgkin Lymphoma is justified and should be performed.

The estimation of the effective dose as a factor for the comparison of the total toxicity and long time effects of various treatment plans for radiotherapy patients with Hodgkin Lymphoma

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Over time, treatment approach has evolved due to technological and clinical changes. Over the last years the ISRT (Involved Site Radiation Therapy) has replaced the MANTEL fields approach for patients diagnosed with Hodgkin Lymphoma, which has contributed to lower long term toxicity of the radiation treatment. Optimization in radiotherapy signifies the delivery of prescribed dose to the target volume while keeping the dose to the organs at risk (OAR) as low as possible. This is especially important for young patients and those with predicted long life expectancy after treatment, which concerns most patients.

The issue faced by Radiation Oncologists is to choose the best treatment plan, which involves the setting out of special protocols and criteria. Even for Pareto optimal plans, there is a whole group of plans from which one might be chosen as “the best for a given patient” based on the criteria of the optimisation eg. the lowest dose for the lung or the lowest dose to the heart, or any other. It is well known that the conformal therapy VMAT/IMRT, a large part of the body can be exposed to low doses, especially in comparison to 3D treatment plans. Comparing effective doses for a number of different treatment plans might be useful, as it takes into account exposure of the whole body, acute toxicity of the radiation, as well as probability of the induction of secondary cancers. Despite the limitation of using an effective dose for cancer patients, there is a number of advantages that might make this quantity appropriate to help the radiation oncologist to take the final decision concerning the ‘best treatment plan’ for patients with long life expectancy after treatment, and CTV delineated in large part of body eg. lymph lodes in head&neck and mediastinum.

For a 33-years old woman diagnosed with Hodgkin's disease, lymphocytic predominance (ICD C81.0), two plans have been created (MANTEL fields and VMAT. 2Gy per fraction, 15 fraction, 30 Gy per treatment), effective dose (ICRP103) has been estimated based on the calculation by treatment planning systems. Due to the fact that Lymphatic nodes and the Thymus are the CTV (clinical target volume), two numbers have been estimated (excluding and including those organs). Only photon radiation has been taken into account, while neutron radiation (for 15 MV) has been omitted. For a single fraction of the treatment 0.53 Sv and 0.50 Sv (for MANTEL) and 0.33 Sv / 0.30 Sv for VMAT has been estimated, which means a reduction by 40%, mostly due to a lower dose to bone marrow, breast, salivary glands, skin, oesophagus and heart (reminder tissue). This calculation allows to show that 8 fraction of this treatment with MANTEL fields might be considered as quite toxic with a result of 4.2 Sv, while for VMAT it is 2.62 Sv.

We find effective dose an interesting and useful quantity which allows to compare treatment plans, when the choice of the best one from Pareto optimal family is not a simple task.

Evaluation of individual *in vitro* radiation response in PBMC samples of H&N cancer patients correlated with severity of side effects following radiotherapy

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Radiotherapy induces mild to very severe side effects on normal tissue of cancer patients which can profoundly affect life quality or lead to long term damage. The possibility to develop personalized treatment plans based on individual response to radiation would represent a major improvement in cancer patients' life expectancy and life quality.

We aimed to investigate the correlation of *in vitro* radiation response of PBMC isolated from head and neck (H&N) cancer patients with severity of adverse events following radiotherapy.

Blood samples of 23 head and neck cancer patients were collected before undergoing radiotherapy. All donors were male, age 40-71 years. DNA damages (gamma-H2AX foci and micronucleus yield) were assessed following *ex vivo* irradiation of isolated PBMC, using the same system that was used in the treatment of the patients (Linear accelerator Primus Mevatron, Siemens). Plasmatic cytokine levels were measured in samples collected before treatment and following 20 fraction of irradiation. *In vivo* radiotherapy side effects were determined using the criteria given by European Organization for Research and Treatment of Cancer (EORTC). Cellular and plasmatic parameters were analyzed in relationship to severity of *in vivo* radiation effects.

Radiotherapy induced side effects with variable severity levels. Both gamma-H2AX foci and micronucleus yield increased drastically in all samples, following *in vitro* irradiation. Some of the samples presented complete repair in 24has measured by gamma-H2AX foci, while in others residual foci were still present. Basal DNA damage markers and cytokine levels showed a large variation among donors.

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Development and creation of the method of information retrieval and recording electronics for a 2D position-sensitive neutron detector

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In the thermal neutron detector for detecting particles, a cathodic method for acquiring information on an electromagnetic delay line is implemented. This method is widely used to register particles using multi-wire proportional chambers (MWPC).

The information retrieval from the delay line, consisting of 200 channels, was developed, and the recording electronics of the prototype 2D detector were also developed.

The recording electronics connected to the cathode strips of the delay line contains signal preamps, time-to-code converters (TDC), amplitude-to-code converters (ADC), and a computer with a PCI interface card.

From the ends of the delay line, the current signals are fed to the detector electronics, which provides the formation of logical pulses with a time reference to the input signal, independent of its amplitude. Thus, the coordinate of the center of gravity of the electron avalanche is calculated by the difference in the arrival times of the logical pulses to the corresponding TDC (Stop) inputs.

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Variations in dosimetric EPR signals induced in touch-screen glasses by ionizing radiation after their exposure to light

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Electron paramagnetic resonance (EPR) signals induced by ionizing radiation in touch-screen glasses have been reported as useful for personal dosimetry in people accidently exposed to ionizing radiation [1]. Stability of the radiation–induced signal (RIS) was shown to be sufficient for dosimetry even weeks after exposure of screen samples to radiation [2, 3]. However, the RIS signals (i.e. the dosimetric signals) induced in gorilla glass, in mineral glass and in tempered glass (used for protective screens) by radiation, as well as the native, background EPR signals can be strongly affected by exposure of the samples to light. This effect can lead to significant deviations of the radiation doses reconstructed by EPR from the real ones. In the presented study the EPR spectra from glass samples unexposed and exposed to X-rays and/or to natural sunlight and UV lamps were numerically decomposed into three model spectra: background (BG), RIS and light-induced signal (LIS). The results showed, that sunlight and light from common UV lamps (nail lamps, lamps from tanning salons) reduce the magnitude of the dosimetric RIS components by 50-70% of their initial values. Only five minutes of exposure of the irradiated glass to sunlight caused reduction in magnitude of the RIS by factor of three. These effects put a strong limit on achievable accuracy of retrospective dosimetry using EPR in glasses from mobile-phones, unless their exposure to light containing a UV component can be excluded or the light-induced reduction in magnitude of the RIS is quantitatively estimated.

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Full-Energy-Peak Efficiency evaluation for a $LaBr_3$(Ce) scintillator using a Virtual Point Detector approach

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The use of a Lanthanum Bromide scintillator, $LaBr_3$(Ce), as a tool for measuring activity (or concentration) in a given sample, requires the evaluation of Full-Peak-Energy Efficiency (FEPE) or the knowledge of a corresponding calibration curve. In addition to the usual methods based on the use of calibrated sources with the same shape and composition of the sample under examination, or Monte Carlo methods, a rapid tool for evaluating efficiencies can be represented by the application of the Virtual Point Detector (VPD) approach. With this approximation, the detector is assumed equivalent to a virtual point inside the crystal where all interactions can be considered to take place, all the physical quantities vary with the square of the distance from the VPD and each efficiency, even elementary, can be calculated starting from an experimental reference value.

The VPD approach to evaluating efficiencies has already been positively used for Si(Li) detectors and, mostly, for HPGe detectors, while in recent years NaI(Tl) and BGO scintillators have been also involved.

The aim of this work is to investigate, in a wide range of gamma emission energies, the validity of the VPD simplification for a $LaBr_3$(Ce) scintillation detector through experimental measurements of point sources and the use of transfer algorithms of elementary efficiencies.

The results are compared with the experimental ones related to already characterized reference measurement geometries, for which secondary standards are available and the efficiency curves have been evaluated.

OSL study of ion-substituted hydroxyapatites

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Hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH)_2$) is a calcium orthophosphate which due to its similarity to mineral part of hard tissue is best known as biomaterial hard tissue regeneration [1]. However, HA has also been among the most studied dosimetric materials in the high dose and retrospective dosimetry, by the EPR (electron paramagnetic resonance) spectroscopy. As HA substituted with different ions is the one occurring in biological systems, ion-substituted HA are increasingly attracting attention as hard tissue biomaterials [2, 3]. But they could as well be used as OSL (optically stimulated luminescence) dosimeters [4].

To test this hypothesis, in this study influence of Mg and Si substitutions on the OSL response of irradiated HA was determined. Mg and Si substituted HA were synthetized by hydrothermal method. Obtained ion-substituted HAs were characterised by powder X-ray diffraction and scanning electron microscopy. EPR spectroscopy were used to follow and control the changes in relation with substituted ions and correlated with pure HA.

Obtained results indicate that Mg and Si ion substituted HA can be potential dose indicator material using OSL technique. However, more detailed study of the influence of the ion substitute concentration and type is needed to confirm their applicability as OSL dosimeters.

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Application of the new matrix method to coincidence summing effects in gamma spectroscopy

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A new method has been developed for deriving counting rate equations describing coincidence summing of gamma and X-rays for germanium spectrometers. The coincidence summing effects occur whenever two or more cascading photons are emitted from the same nucleus and detected within the resolving time of spectrometer. The application of analytical approaches to coincidence summing effects makes it possible to predict all summation peaks that occur in the spectrum. Our work includes solving the problems of coincidence summarizing by introducing the new method with simpler algebra. The new analytical approach that we have developed also allows us to determine the activity of radioactive sources directly without calibration of the detector, which is very important in metrology of radionuclides. Accordingly, based on the value of the peak area in the spectrum and knowledge of probability transitions between excited states of a nucleus, it is possible to determine the efficiency of detection. This method is successfully applied to the decay of radionuclides ^{139}Ce, ^{57}Co, ^{133}Ba and ^{152}Eu. Results, obtained using the proposed method, are achieved in a much clearer and simpler way.

Dosimetric evaluation of two intracavitary brachytherapy modalities in treatment of inoperable cervical cancer

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Introduction. Brachytherapy comprises an integral part of inoperable cervical cancer definitive treatment. Mostly used is intracavitary brachytherapy (ICB) with its primary role of boosting the total dose needed for obtaining disease local control. ICB uses intra-uterine probe and ovoids/ring placed inside the natural cavities combined with after-loading source placement in several applications following external beam radiotherapy treatment (EBRT). Although three-dimensional (3D) ICB planning is used, sometimes plans are calculated with two-dimensional planning (2D), especially when shorter treatment time is needed due to various reasons.

Methods and materials. 20 patients were treated with ICB, with prior EBRT dose of 50.4Gy. 10 patients received high dose rate (HDR) ICB in three applications (once a week) with dose of 7Gy/weekly and total dose reaching 21Gy. 10 patients received their HDR ICB in two applications with dose of 9Gy and total dose of 18Gy. All patients had 2D planning. Organ at risk (OAR) constrains were adequate for 2D planning (70% of the prescribed dose for rectal points and 80% of the prescribed dose for bladder point). Radiobiological equivalent for 2Gy daily dose (EQD2, alpha/beta=10) for 3x7Gy ICB treatment is 29.8Gy and 28.5Gy for 2x9Gy ICB respectively.

Results. Organs at risk absorbed doses were evaluated in bladder and rectum. 2x9Gy ICB whole treatment doses for rectum averaged at 4.04Gy, while doses for bladder averaged at 3.93Gy. 3x7Gy ICB doses for rectum averaged at 3.47Gy and averaged at 2.57Gy for bladder.

Conclusion. OAR absorbed doses were comparable and both maintained the prescribed dose constraints. Keeping in mind that three-dimensional (3D) ICB is the mainstay, yet in some situations where patient conditions differ or when 3D planning resources are limited, both modalities (2x9Gy and 3x7Gy) of 2D HDR ICB can be equally used successfully.

Keywords: Cervical cancer, intracavitary brachytherapy, high dose rate brachytherapy

Volume correlation of bladder, rectum and intestines in gynecological pelvis radiotherapy

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Introduction. One the greatest challenges in gynecological pelvis radiotherapy are internal movements of organs at risk (OAR) in target volume close proximity. Since there is a direct correlation in between OAR volume, thus obtaining relatively constant bladder volume during the whole radiotherapy treatment is one of the key factors for reducing irradiated intestine volume. This is provided with sustainable bladder filling protocol. Cone beam computed tomography (CBCT) provides needed quality assurance of absorbed doses in OAR.

Materials and methods. 30 patients with diagnosed gynecological malignancies were included and their data analyzed. Median age was 57 years (30-75) at University clinic of radiotherapy and oncology – Skopje. All patients received three-dimensional conformal radiotherapy (3D-CRT) in post-operative setting (25 fractions, daily dose of 2Gy with total dose of 50Gy) with adequate bladder filling protocol (500ml of liquids, 1hour prior irradiation) expected to fill the bladder with 200-300cc. CBCT was used twice a week in comparison with simulation computed tomography (CT). OAR volumes compared were bladder, rectal and intestine volumes. Dosimetric volumes constrains for bladder were less than cumulative 60Gy, for rectum less or equal to 46.3Gy (50% organ volume) and intestines constrains used were less of equal to 42Gy for 25%, 37Gy for 50% and 33Gy for 67% organ volume. Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) constraines of 45Gy for 195cc were used for intestines as well.

Results. Pre-treatment average CT volume for OAR was 283cc, 75cc and 1084cc for bladder, rectum and intestines respectively. CBCT control average OAR volumes were bladder 198cc, rectum 68cc and intestines 940cc (inside CBCT range). QUANTEC intestines volume averaged at 245cc.

Conclusion. For rectum bladder filling protocol did not have significant impact. Bladder and intestinal absorbed doses directly correlated with bladder filling protocol. However, considering the absence of uterus and parametria, even with sufficient bladder filling protocol, intestines can not be sufficiently protected due to retrovesical loop placement. Thus increasing bladder filling protocol volume may be needed.

Keywords: Organ at risk, CBCT, gynecological pelvis radiotherapy

Evaluation of the effectiveness of the treatment of infected radiation skin lesions using photodynamic therapy in the experiment

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Radiation therapy is often accompanied by the development of damage, both general and local. The most severe type of radiation damage to the skin and soft tissues are radiation ulcers. Bacterial infection exacerbates the course of radiation ulcers, significantly complicating treatment. In addition, there is a significant risk of infection of radiation-induced ulcers with antibiotic-resistant nosocomial strains of bacteria. The prevalence of antibiotic-resistant microflora conditions the search for alternative methods of infection control such as photodynamic therapy (PDT).

The purpose of the study was to increase the effectiveness of treatment of infected radiation skin lesions by experimentally developing a new method using photodynamic therapy.

In the course of *in vivo* experiments in rats with *S. aureus* infected skin lesions, a scheme of photodynamic therapy was developed and tested. Optimal physical parameters of light exposure in red spectrum (630 nm) and exposure time were previously determined *in vitro*. Methylene blue was used as photosensitizer.

Reference strain *Staphylococcus aureus ATCC 6538* and antibiotic resistant clinical strain *Staphylococcus aureus No. 450* were used as test strains for infection.

The study showed that in infection of radiation ulcer with reference strain, 100% bacterial elimination occurred after the first PDT session. This was not enough in infection with a clinical strain of *Staphylococcus aureus No. 450*. 24 hours after the first PDT session, these animals showed only a decrease (almost 1000 times) of bacterial counts compared to pre-treatment levels in the control group. This prompted a second PDT session.

After the second PDT session, only one animal (6.6%) was found to have a small degree of colonization of ulcer surface test strain. Control examination in 7 days after treatment showed no *S. aureus* test strain in the specified animal, as well as in all other animals of the experimental group. The obtained results were stored until the end of the observation period, namely for 45 days. In the control group, self-elimination of infectious agent occurred only on the 27th day from the date of infection in 22.3% of the animals, and at the end of the experiment a third of the rats remained infected.

Thus, it has been shown experimentally that PDT is an effective alternative to antimicrobial therapy in treatment of infected radiation skin lesions. However, several sessions of PDT should be performed if the condition is caused by antibiotic resistant strains of bacteria, to improve the effectiveness of treatment.

Forecasting and optimization of the kilovoltage X-ray therapy office within the framework of the new clinical guidelines

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One of the elements of the quality of medical care is its accessibility, which depends on the material and technical base of the institution, as well as on the availability of stuff and work management. Implementation of the new clinical guidelines revealed the problem of increasing the load on stuff and equipment.

Aim. To identify clinical and organizational changes in the technology of kilovoltage X-ray therapy for non-melanoma skin cancer (NSC) after the implementation of the new clinical guidelines; to identify patterns and derive a mathematical model of the kilovoltage X-ray therapy room in order to ensure the optimal mode of work for employees, providing quality treatment and maintaining the availability of medical care.

Materials and methods. Data from the radiotherapy room of the Sverdlovsky Regional Oncologyc Dispensary (SROD) were used. The economic method of mathematical modeling was used for planning and rational use of material and human resources. Also, to assess and calculate the average duration of x-ray therapy session per patient, timing was carried out.

Results. The analysis of the radiotherapy room of radio unit No. 2 of the radiological building of the SROD for 3 years showed an increase from 10.4 to 17.3 of the average number of therapeutic fractions in one patient using the clinical recommendations of the AOR. An increase in the average number of radiotherapy sessions leads to a doubling of the length of the average bed-day stay of the patient in a Day hospital (24 vs. 12).

To address the issue of ensuring optimal working conditions of staff and availability of medical care, a formula was proposed for calculating the number of treated patients with NSC by one day hospital radiotherapist, as well as a formula for the number of patients admitted to the day hospital Department per week. There is a clear correlation between the duration of treatment, the dynamics of hospitalization and the number of treated patients. The calculated results, obtained using a mathematical model, fully correspond to the real performance of the office of radiotherapy for the period from 2017 to 2019.

Conclusion. To ensure optimal availability of medical care, it is necessary to match treatment technologies with available resources of the organization. The introduction of new treatment programs may require both the expansion of staff (medical, nursing), and an increase in the number of units of medical equipment. The obtained mathematical model of the kilovoltage X-ray therapy room allows to predict the optimal mode of work of employees.

Keywords: Kilovoltage X-ray therapy, radiotherapy, quality of medical care, availability of medical care, organizational optimization of the treatment process, clinical guidelines, non-melanoma skin cancer, mathematical model of the kilovoltage X-ray therapy office

Photo-single and photo-double ionization and fragmentation of isoxazole molecules

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The five-membered heterocyclic rings containing oxygen or nitrogen atoms are incorporated into a wide variety of structures that play a vital role in many biochemical processes. In particular, isoxazole molecule due to its unique ring structure that consists of one oxygen atom and one nitrogen atom at adjacent positions appears in many bioactive compounds and is utilized as the fundamental structure in the synthesis of new pharmaceutical medicines. The unique atomic composition and bond arrangement of isoxazole imply its specific electronic properties that cause exceptional dissociation mechanisms. The understanding of the role and possible control of electron dynamics in these reactions and chemical reactivity is itself a problem of fundamental importance. Therefore in the present communication, we present results on the photo-single and photo-double ionization and fragmentation of isoxazole molecule. The dissociative processes where only one electron is emitted are quite well known. However, double ionization is a unique mechanism producing the doubly charged parent ion after the emission of two correlated electrons. Both the single and doubly charged parent ions are very reactive entities that can dissociate into several ionic fragments. The current study aims to unravel the dissociation processes of the parent ions of isoxazole, leading to the formation of different ionic products in the photon energy range of 9–34 eV, using ion time-of-flight (TOF) spectrometry combined with the photoelectron-photoion coincidence (PEPICO) technique.

Colliding the pyridyne molecules with low-energy cations

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Carbon-rich meteorites contain many biologically relevant organic molecules. The most recent studies have provided evidence of extraterrestrial amino acids, nucleobases, and ribose in those primitive rocks. Thus it is believed that meteorites could have been carriers of biological material needed to create life on the early Earth. But the question arises: how these molecules were formed and how they could have survived the bombardment of the solar wind consisting of photons, electrons, protons, and a few percents of heavier nuclei. The laboratory investigations of collisions of the DNA building blocks or their analogs with a different kind of radiation may shed some light on these issues. Therefore, in the present communication, we present results of collisions of low energy cations with the pyridine molecules, the hydrocarbon building blocks of agrochemicals, pharmaceuticals, and vitamins.

Assessment of ^{137}Cs and ^{90}Sr intake with food by the inhabitants of Warsaw in 2004-2019

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One of the pathways of radiation exposure in humans is consumption of contaminated food. The composition of an average diet is diversified for various groups within the population and depends on age, sex, habit and performed work.

The aim of the study was to assess the intake and to estimate the dose received by the inhabitants of Warsaw from trace quantities of ^{137}Cs and ^{90}Sr isotopes in the consumed food. The assessment of intake has been based on the analysis of main food products available in stores in Warsaw and all-day meals prepared in several canteens during two periods: 2004-2013 and then five years later in 2018-2019. The impact of individual products in dishes, e.g. mushrooms, on the annual intake of ^{137}Cs was also analyzed. In addition, in years 2006–2009 an assessment of the intake of ^{137}Cs and ^{90}Sr isotopes with food by children (8 month -12 y) and teenagers (13-17 y) was conducted. The effect of milk and milk products on the content of ^{137}Cs and ^{90}Sr in 2-3 year old children's daily meals was also examined. Gamma spectrometric and radiochemical methods were used to determine the radioactive concentration of the mentioned isotopes. Based on those results, the annual intake was assessed and the dose received by urban residents could be estimated.

Annual doses received in period 2004-2013 by the adult inhabitants of Warsaw from ^{137}Cs ranged from 1.0 μSv to 2.0 μSv excluding dishes with mushrooms while the dose related to dishes with forest mushrooms reached 7.0 μSv. Doses from ^{90}Sr ranged from 0.6 μSv to 1.2 μSv. In 2018-2019, the dose received from ^{137}Cs was below 1μSv. The dose from ^{137}Cs was connected with the consumption of products like: milk, meat (mainly beef and veal) and some fish species. The dose from ^{90}Sr is related to eating milk, cereal and vegetables.

Doses received by children ranged from 0.5 to 2.5 μSv depending on age and those received by teenagers were on the level of 2.0 μSv from ^{137}Cs. For these two groups, the values from ^{90}Sr were 1.5-2.1 μSv and 2.5 μSv, respectively.

Doses received by the inhabitants of Warsaw from the food consumption constitute only a fraction of a percentage of the annual permissible dose limit of 1 mSv. They do not differ significantly from the doses received by residents of other Polish cities (1.4 -7.5 μSv) as well as most European countries.

Radioprotective effect of human lactoferrin against gamma-irradiation with sublethal dose

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The pathogenic processes induced by ionizing radiation are currently being extensively researched. Radiation damage is basically due to DNA injury caused by the ionization effect of radiation. This process involves hyperoxidation by the free radicals produced. Lactoferrin (Lf) is a multifunctional protein of the transferrin family that is widely represented in various secretory fluids of mammals. Previously, it was shown the therapeutic effect of Lf purified from cow's milk after single whole-body X-ray irradiation [Nishimura et al, 2014; Feng et al, 2018].

The aim of research was to investigate the effects of Lf in mice after acute gamma irradiation at a sublethal dose. Human Lf (hLf) was isolated from colostrum by preparative ion-exchange chromatography followed by purification with affinity heparin-sepharose sorbent. C57Bl/6 2-2.5 months old male mice were used for the experiments. Animals were randomly divided to experimental and control groups (three and four, respectively). Mice from experimental groups were treated with whole-body γ-radiation from a cobalt-60 (^{60}Co) source at 7.5 Gy (at a dose rate of 0.6 Gy/min) followed by the intraperitoneal administration of hLf (4 mg/animal; «exp Lf» and «exp Lfx2» groups) or saline («exp» group). The control mice were sham irradiated. Mice from «exp Lfx2» and «cont Lfx2» groups were injected with hLf second time after 24 h. The assessment of the effect of Lf on the behavioral functions of irradiated animals (locomotor and research activity) was carried out using the "Open field" test on the 10th, 20th and 30th days. The survival rate at 30 d after irradiation was investigated. The body weights of the mice were measured every three days following irradiation.

Analyses of the data obtained from the "Open field" test revealed that 20 days after irradiation, the animals of the «exp Lf» and «exp Lfx2» groups did not differ from the control ones in the number of rearings. By day 30th, they were no different in terms of time spent in the central zone. While for the «exp» group, these parameters were significantly changed. The survival rate in Lf-treated mice 30 d after irradiation was 76% («exp Lfx2» group) and 71% («exp Lf» group), significantly higher than in mice treated with saline 29% («exp» group). Lf administration had a compensatory effect, which was manifested in an increase in the 30-day survival rate of irradiated animals and life expectancy, in a faster normalization of the dynamics of body weight changes. These findings suggest that Lf may inhibit radiation damage. Further studies are required to determine to clarify the value of Lf within the field of radiation protection.

Investigation of oxidative stress in tobacco plants with cyanobacteria desaturase genes after ionizing radiation

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We are currently watching the effects of the rapid development of nuclear energy. Unsaturated fatty acids are degraded more slowly by ionizing radiation compared to saturated fatty acids. Desaturases are enzymes that contribute to the formation of double bonds in fatty acids and thereby convert them from saturated to unsaturated. Plants of *Nicotiana tabacum* containing in their genome and expressing the *des*C gene encoding the Δ9-acyl-lipid desaturase of cyanobacteria *Synechococcus vulcanus*, or the *des*A gene encoding the Δ12-acyl-lipid desaturase of cyanobacteria sp. PCC 6803 were used in the work. An increase in the proportion of linolenic acid was investigated in plants with the *des*C gene, and an increase in the proportion of linoleic acid was investigated in plants with the *des*A gene. As a control, wild-type *N.tabacum* tobacco and *N.tabacum* tobacco containing the genome and expressing the *gfp*:*lic*BM3 reporter gene were used as controls. The activity of the enzyme superoxide dismutase (SOD), the level of accumulation of malondialdehyde (MDA) after the action of 1 Gy, 5 Gy, 10 Gy were investigated. They found an increase in SOD activity and a decrease in MDA accumulation, which may indicate a lower degree of lipid peroxidation after the action of 5 Gy and 10 Gy in plants with desaturases genes compared to controls.

Assessment of feasibility and consequences of a potential radiological terrorist attack

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While for the time being the access of terrorists to nuclear weapons is almost unrealistic, this is not the case if it comes to availability of other CBRN components, namely chemical, biological and radiological agents. The use of high activity specific radioactive sources in a radiological dispersal device, also known as a dirty bomb, can cause severe health effects in affected persons, environmental radioactive contamination of the site as well as panic and fear among the general population. Because of the atomic bombing of Hiroshima and Nagasaki in Japan at the end of WW2, people have feared nuclear explosives more than any other weapons of mass destruction, mainly due to the ability of these weapons to cause immediate devastation and trauma, and because radiation, undetected by human senses, could cause ongoing morbidity and mortality, including cancer, years after exposure. Recently there have been some visible signs that terrorists are interested in the construction of a dirty bomb where they may use intensive radioactive sources used in irradiators, radiotherapy machines or industrial radiography equipment where the security of these sources in some countries is not adequate and in line with international standards and requirements especially those set by IAEA. This is why the relevant national authorities and other law enforced agencies should be prepared to deal with such emergency situations in order to minimize the impact on the afflicted persons and the surrounding of the attack. The paper presents an overview of the latest assessment of this threat and the preparedness to protect people against exposure to the spread radioactive material following the terrorist attack.

Exposure to medical low-dose ionizing radiations and influence on haematological indices

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An exposure to ionizing radiations (IR) can reduce bone marrow production where blood forming cells both immature and rapidly dividing cells locate. We examined the effects on hematological indices through Complete Blood Count (CBC) test in workers who were chronically exposed to low-dose medical ionizing radiations in Radiotherapy (RT), Radiology (RD) and Nuclear Medicine (NM) units. The IR workers were exposed to Annual Average Effective Dose (AAED) 0.29-1.91 mSv. Most of the parameters i.e., HB (hemoglobin), WBC (white blood cells), PLT (platelets), HCT (hematocrit), MCH (mean cell hemoglobin), MCHC (MCH concentration) & NEUT (neutrophils) were found low in majority of IR exposed workers. Workers of both RD and RT departments had more CBC parameters affected as compared to NM department workers. From t-test, significant differences were observed in the mean values MCHC and LYM. The correlation was significant for following: PLT ($p = 0.021$), HCT ($p=0.024$), LYM ($p=0.026$) and NEUT ($p=0.014$) with the AAED. Three significant CBC parameters, i.e., PLT ($r =-0.240$), HCT ($r=-0.235$) and LYM ($r = -0.232$) were having weak negative associations, whereas, NEUT ($r=+0.254$) was having a weak positive association with AAED. Regression analysis indicated that 5.8% of variance ($R^2 =0.058$) in PLT, 5.5% ($R^2 =0.055$) in HCT, 5.4% (R^2 -square=0.054) in LYM and 6.5% ($R^2=0.065$) in NEUT can be predicted from the variable AAED. For every unit increase in AAED, there is -37.774 unit decrease in PLT, -2.401 unit decrease in HCT, and -5.129 unit decrease in LYM is predicted. NEUT is found to be higher by 7.181 points for every increase of one point on the variable AAED. The odds of developing low MCHC were 6.84 times higher, the odds of developing low NEUT were 9.69 times higher and the odds of developing a low ANC (absolute neutrophil count) were 6.89 times higher for those who were IR exposed compared to IR unexposed workers. Long term exposure of low dose IR can alter hematological indices due to decline in hematopoietic stem and progenitor cells. Decreased number of circulating lymphocytes and granulocytes by radiations can lead to infections and long term work on IR can induce anemia or leukopenia. Long term use of IR can affect their immune system even at low doses of radiations as leukocytes and lymphocytes are highly radiosensitive. The long-term impacts of low IR doses on the immune functions in relation to occupational health should be continuously monitored.

Evaluation of the permissible depth of tumor invasion as a part of the HDR brachytherapy re-irradiation of recurrent esophageal cancer

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The rate of locoregional recurrence after chemoradiotherapy for esophageal cancer is more than 50%. The “salvage” therapy is a good treatment way for such a patient. But it is enough dangerous after following definitive chemoradiotherapy, considering the radiation exposure to the organs-at-risk (OARs), including the lung, trachea, esophagus and spinal cord. One solution to the problem might be a high dose rate (HDR) brachytherapy. In this situation, the mucosal has focused attention as the main OAR. That is why it is so important to evaluate the maximum of the permissible depth of tumor invasion and possible modes of fractionation.

For this purpose, tissue-equivalent phantom modeling of the oesophagus was developed. Inside the phantom, a 10 mm diameter oesophagus bougie with an internal radio-opaque catheter was placed. Control of the source position was carried out by computed tomography (CT). In the dosimetric planning system, the radiation exposure process was simulated using different PTV (planning target volume) depth of 0.5-2 cm (in 0.5 cm increments). Context of evaluation: V_{100} = 90 %, the control point an at the PTV middle, at a distance of 1 cm from the center of the source. The mucosa is created at the distance of 1 mm outer from the bougie wall, 2 cm longer on each side of the PTV. Calculations have shown that with the 5-7 cm tumor spreads along the esophageal wall and its 0.5 cm invasion, the average single dose to the mucosa will be equal to 8.5 Gy. Depth increasing leads to the higher dose exposure to the main OAR. So, the average dose to the mucosa is 13.3 Gy at the depth of 1 cm and 19.3 Gy with the 1.5 cm lesion. Therefore, the invasion depth is a very important criterion for patient selection. From the obtained results, it can be seen that the single dose value at the control point does not exceed 14.8 Gy anyway. It is allowable value according to the European Society for Radiotherapy and Oncology (ESTRO) and the American Brachytherapy Society (ABS) recommendation. In this regard, the main limiting factor is the total dose to the mucosa. Also, there were some dose and radiation mode recalculations including linear-quadratic (LQ) and Time-Dose-Fractionation (TDF) models. They have shown that the most suitable fractionation mode is 5 fractions of 5 Gy every other day. Then TDF dose is 37.7 Gy (TDF factor = 63) and EQD_2 (α/β=5 Gy) = 35.7 Gy. At the same time, the total dose to the mucosa equal to 42.5 Gy with a 0.5 cm tumour invasion and 66.5 Gy when a lesion is 1.0 cm. For tumors of 1.5 cm thick, palliative brachytherapy will be performed to prevent dysphagia. Calculations will be performed as a case with a 1.0 cm invasion.

Re-evaluation of CBMN test reference values for occupationally exposed persons in Serbia

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Cytohalasine-block micronucleus (CBMN) test reference values were established and periodically re-evaluated in routine Cytogenetic biodosimetry laboratory (CBL) practice, according to recommendations of reference documents. In a three year period (2013-2016) CBL performed large – scale cytogenetic study on genetic damage of general and occupationally exposed population in Serbia and established reference values of CBMN test. Since then, 209 new occupationally exposed persons were examined for genetic damage by the means of CBMN test and served as a test group for re-evaluation of established reference values. For this purpose 410 occupationaly exposed persons were screened for genetic damage: 201 from previous laboratory base and 209 new examinees. Comparison of the groups for gender, age, smoking habit and duration of exposure showed no significant difference, however statistically significant difference was found in the mean number of micronuclei, with higher values in new examinees. Nevertheless, mean micronuclei values for both examined groups were in previously established range, which encouraged us to continue using current reference values for interpretation of test results.

Micronuclei and occupational exposure to physical and chemical genotoxic agents

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MN scoring is widely employed in human biomonitoring studies as a surrogate marker of chromosomal damage inflicted by clastogenic agents or by aneugens. It is used: (a) to compare genetic damage rates between populations exposed to different environmental, occupational and lifestyle factors; (b) to assess differences in radiosensitivity between individuals; (c) to evaluate the genotoxic potential of new chemicals produced by the agrochemical and pharmaceutical industries and (d) for quantitative analysis and biodosimetry in cases of radiological accidents.

In this study we evaluated cytogenetic status of persons occupationally exposed to ionizing radiation (nuclear medicine and diagnostic radiology) and chemical genotoxic agents (antineoplastic drugs).

Studied population comprised of 953 persons from two healthcare institutions: 516 from institution 1 (I1) and 437 from institution 2 (I2). Within both institutions three groups were formed: nuclear medicine workers (147-I1 and 137 - I2); workers from diagnostic radiology department (178 – I1 and 145 – I2) and workers exposed to antineoplastic drugs (190-I1 and 156 – I2).

Statistical analysis showed no significant difference between groups in all analyzed parameters, except for micronuclei values between nuclear medicine and antineoplastic drug workers, with higher values in the first group. Furthermore, mean values of micronuclei were in accordance with previous findings as well as within predefined reference range for exposed persons.

Micronucleus test provide reliable and valuable data in the evaluation of changes in genetic material due to occupational exposure, which is why is always recommended to use it in biomonitoring of exposed persons.

Biological efficiency of a scanning proton beam under different irradiation modes *in vitro*

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The use of pencil beam scanning technology in proton therapy reduces the dose to patient healthy tissues and increases the uniformity of dose distribution in the tumor volume. It results also in more complex dose and LET distributions in irradiated volumes which may be field multiplicity, proton energy, tumor volume and localization specific. Emerging spots of elevated proton LET values throughout the target volume might cause the RBE variations in the tumor.

Biological efficiency of a scanning proton beam in different irradiation modes was investigated by the cells clonogenic activity test. Chinese hamster V-79 fibroblasts and B14-150 fibrosarcoma cells in the stationary growth phase were used. Eppendorf tubes (5 ml) with cell suspensions (3×10^4 cells per ml) in a cylindrical water phantom were irradiated with 95–135 MeV protons ("Prometeus", PROTOM, A. Tsyb Medical Radiological Research Centre, Obninsk). The dose range was 2–10 Gy. Different ways of dose delivery to the irradiated volume were studied: irradiation mode No 1 – single field, without dose fractionation, irradiation mode No 2 – three fields (0°, 90°, 180°), without dose fractionation, irradiation mode No 3 – single field, 2 Gy fractions in 30 s, irradiation mode No 4 – five fields (0°, 90°, 180°, 240°, 300°), 2 Gy fractions in 30 s. The doses in modes No 3 and 4 were delivered by repeating the irradiation plan for 2 Gy.

The survival of V-79 and B14-150 cells following proton irradiation showed that the ways of dose delivery to the irradiated volume do not affect the results obtained. Survival curves in all cases were linear-quadratic, both α's and β's being independent on irradiation mode. Comparison of the regression curves did not reveal statistically significant differences in the biological effectiveness of protons regardless of the dose delivery ways ($p>0.05$). The RBE at 10% cell survival level did not have statistical differences too. The $RBE_{10\%}$ values were 0.96 (irradiation mode No 1), 0.94 and 0.96 (irradiation mode No 2) for V-79 and B14-150, respectively, 0.99 and 1.02 (irradiation mode No 3), 1.02 and 1.03 (irradiation mode No 4) and are actually equal to 1.0. These values differ slightly (about 10%) from the 1.1 adopted in radiation therapy. But they are consistent with it, if one takes into account the differences in the values of the absorbed doses planned and those measured by the ionization chamber (5–6%).

So, studies of the biological effectiveness of the scanning proton beam on Chinese hamster cells in vitro under different irradiation modes showed that the way of dose delivery to the irradiated volume does not significantly affect the irradiation result.

The effect of combined proton and carbon ion irradiation on Chinese hamster B14-150 cells

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Carbon ions are effective in the treatment of radioresistant tumors. However, concomitant irradiation of healthy tissues with high LET radiation can lead to significant radiation damage in cells adjacent to the tumor. In some research centers, carbon ions are used as boost to photon or proton therapy to reduce the risk of possible complications. In terms of radiobiology, it is of interest to study interactions of cell damage induced by sequential exposure to protons and carbon ions. In the case of carbon ions, contribution of high LET particles to the total effect is not completely clear. The LET spectrum of these particles is close to that of heavy recoils C, N, O (HR) induced by 14.5 MeV neutrons.

The aim of the study was to assess the importance of irradiation order when Chinese hamster cells are exposed to protons and carbon ions or protons and heavy recoils.

The survival of Chinese hamster cells B14-150 (fibrosarcoma) in the stationary growth phase was studied using clonogenic assay. Cell monolayers were irradiated sequentially with protons and carbon ions or with protons and HR. Protons with energies 65–85MeV were produced using the Prometeus accelerator (MRRC, Obninsk). The irradiations with a ^{12}C ion beam (initial energy 454 MeV/u) were carried out at the U-70 synchrotron (IHEP, Protvino) in a water phantom at the center of spread out Bragg peak. The portable neutron generator NG-14 (MRRC, Obninsk) was the14.5 MeV neutrons source. For studying the effects of HR cell monolayers were irradiated with 14.5 MeV neutrons through a glass Carrel flask bottom (1 mm) under the conditions of the proton equilibrium absence.

Time interval between two fractions was 2 hours. The irradiation schemes for protons (p) and carbon ions (^{12}C) were as follows: 1) 6 Gy (p) + 1 Gy (^{12}C); 2) 1 Gy (^{12}C) + 6 Gy (p); 3) 4.5 Gy (p) + 1.7 Gy (^{12}C); 4) 1.7 Gy (^{12}C) + 4.5 Gy (p). Those for protons and HR were: 1) 6 Gy (p) + 0.5 Gy (HR); 2) 0.5 Gy (HR) + 6 Gy (p); 3) 4.5 Gy (p) + 1.0 Gy (HR); 4) 1.0 Gy (HR) + 4.5 Gy (p).

The results obtained showed that the cell survival was higher when protons were given as the first dose fraction. On the contrary, the first dose fraction of carbon ions or HR followed by proton dose fraction resulted in lower cell survival. It suggests that cell lesions induced by low-LET protons were repaired between the fractions while those induced by high-LET carbon ions and HR were mainly unreparable. Thus, the order of sequential combined cells exposure to low- and high-LET radiations is of importance. The proton irradiation followed by carbon ions or HR is less effective than the opposite order of sequential irradiation.

The effect of Resveratrol on the change in vitality of breast cancer cells in combination with ionizing radiation

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Introduction. Breast cancer (BC) is the most common cancer among women worldwide, making this disease a leading cause of morbidity and mortality. One of the most common treatments of this cancer is radiotherapy. The therapy is based on activity of ionising radiation (IR) which directly affects malignant cells by changing DNA structure stability and repair processes. However, even though it is widely used and provides good outcome this treatment, it has some limitations. It has been observed that cancer cells might become radioresistant and therefore repopulate. Hence, it is important to find molecular mechanisms by which radioresistance occur and find new therapeutic alternatives that can inhibit the viability of the cancer cells and sensitize them to radiotherapy. For a while, investigation using phytochemicals has drawn attention of the scientists. It is known that a number of phytochemicals possess anti-cancer properties. In addition, these substances might enhance cancer cells sensitivity to IR. Therefore the aim of this study was to evaluate human BC MCF-7 and MDA-MB-231 cell line response to a single dose of IR combining it with phytochemicals.

Methodology. MCF-7 and MDA-MB-231 BC cell lines were used to test Resveratrol (RSV) effect. RSV was dissolved in dimethyl sufoxide. Initially, we examined cell viability after the exposure solely to RSV. In order to assess survival we incubated cells with different RSV (0, 10, 25, 50, 80, 100, 150, 200 μM) concentrations for various incubation times (24, 48, 72 h). For cells survival analysis MTT test was performed. Afterwards, the combination of RSV and IR (0, 2, 10 Gy) on cells survival (MTT method) was analysed.

Results. The study showed that chosen substances had different effect on BC cell viability. Firstly, MTT assay results indicated significant decrease in cells survival after the exposure to RSV. In addition, viability of both cell lines declined depending on concentration. According to these results we chose most suitable conditions for further treatment. Subsequently, results after the combined effect revealed that 50 μM RSV combination with IR showed significantly lower cell viability than using IR only.

Conclusions. Our study results revealed that RSV had negative effect on cells by significantly decreasing their viability. Moreover, a significant sensitization combining RSV and IR for both cell lines was observed.

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Breast cancer cell response to ionizing radiation

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Background. Nowadays breast cancer is one of the most common cancers around the world and the radiotherapy is one of the highly targeted and effective ways to destroy cancer cells. There is still an urgent need of clinical and basic research in order to improve the effectiveness of radiotherapy in cancer treatment. Lithuanian University of Health Sciences participates in Horizon 2020 project "INfraStructure in Proton International Research" (*INSPIRE*) in the Framework Programme for Research and Innovation. The aim of *INSPIRE* project is to integrate infrastructures in proton beam therapy research. Consequently, in this project we aimed to study the molecular basis of breast cancer cell resistance to ionizing radiation. For this purpose, the survival, the extent of apoptosis and cell cycle delay in irradiated MDA-MB-231 breast cancer cells were analyzed.

Materials and methods. Commercially available MDA-MB-231 breast cancer cells were exposed to different doses of ionizing radiation (IR) from Clinac 2100C/D linear accelerator. Colony forming assay was performed for cell survival analysis following irradiation. The intensity of the radiation-induced apoptosis and cell-cycle delay were measured via flow cytometer analysis.

Results. In colony forming assay the fraction of surviving cells was 51.6%±2.15 following the exposure to 2 Gy. The survival decreased with IR doses, however, the results suggested that MDA-MB-231 cells were rather resistant to IR. Furthermore, the early radiation-induced apoptosis analysis showed no apoptotic response after 24 hours following the exposure to IR. A significant amount of apoptotic cells was found at 48 hour time-point following the exposure to 8 and 10 Gy of IR. In addition, the cell cycle analysis revealed IR induced arrest of MDA-MB-231 cells in the G2/M phase, which indicated that entry into mitosis had been delayed.

Conclusions. We concluded that MDA-MB-231 cell line is radio-resistant and it may be associated with a delayed apoptotic response and G2/M phase arrest following the exposure to IR. The molecular mechanism of MDA-MB-231 breast cancer cell line radio-resistance is under investigation.

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The impact of target volumes of Ehrlich ascites carcinoma irradiated with a pencil scanning beam of protons at a total dose of 60 Gy on the tumor growth and remote effects in mice

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The purpose of the work is to study the growth of solid Ehrlich ascites carcinoma (EAC) and the remote effects (duration of remission, relapses rate, and average lifespan (AL)) in tumor-bearing mice that were exposed to oligofractionated irradiation with a pencil scanning beam of protons (PBS) at a total dose of 60 Gy depending on the volume of the tissue being irradiated.

The experiments were carried out with SHK male mice weighing 24–28 g, which were maintained under the standard vivarium conditions. Each group consisted of 10–30 animals. The solid form of EAC grafted intramuscularly into the femur of the left hind paw served as the tumor model. Mice were irradiated two fractions of 30 Gy each. Irradiation was carried out in a proton synchrotron accelerator “Prometeus” (Russia, Protvino) with a PBS from two opposite directions. In order to determine the volume of irradiated tissue, a tomogram of a mouse in the water phantom was obtained and a gross tumor volume (GTV) that is equal to the average size of 0.47 cm^3 was specified using a specially developed 3D planning system. In another group of animals the irradiated tissue region was increased to the planning target volume (PTV) which was equal to 1.5 cm^3. The dynamics of tumor growth was monitored during the first month, then antitumor efficiency parameters that characterize the remote effects of radiation were recorded: the date of the occurrence of secondary tumors (remission time), the number of mice with EAC relapse, and the AL of mice with tumors and without them.

Analysis of the dynamics of EAC growth during the month showed that higher irradiation efficiency in mice that received a dose of a smaller volume (GTV group) compared with the PTV group. In this work we observed remote radiation effects in mice with a complete regression of tumor nodes in one month after PT. At the beginning of the observations tumors were absent in 81% of the animals following irradiation by GTV and 45% following irradiation by PTV. The occurrence of EAC relapses in the same place was observed within a month after the complete disappearance of the primary tumor in all groups. The relapses rates following irradiation using GTV and PTV also did not differ. In the group with GTV irradiation, survival was higher: the maximum life expectancy in mice without relapse was 5 months longer, and in mice with relapse it was 3 months longer. The AL of mice with EAC relapses in the group with GTV irradiation was higher compared to the group with PTV irradiation (96 and 77 days after irradiation or 58 and 31 days after the occurrence of a relapse, respectively; $p \leq 0.01$). The AL of mice without tumors was also notably longer in the GTV group: 283 days compared to 228 days after PTV irradiation ($p \leq 0.01$).

The results show higher antitumor efficacy and a considerable increase in the AL of mice after hypofractionated irradiation with a pencil scanning beam of protons at a total dose of 60 Gy of the GTV compared with the PTV.

Mitochondrial proteins are involved in bystander response induced following chemical and physical genotoxic stress

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Damaged cells send intercellular molecular signals to their neighbor cells that respond through a signaling process that lead to so-called bystander effect. They were first considered detrimental secondary effects of genotoxic exposure, given their manifestation as increased DNA damage, chromosomal aberration, and increased apoptosis. However, newer studies suggests potential beneficial, adaptive role for bystander signaling. Few very recent studies are focused on connection of mitochondrial pathways with DNA damage response (DDR) HtrA2 is a mitochondrial serine-protease that induces expression of transcription factor CHOP, leading to upregulation of components of the integrated stress response.

Our aim was to evaluate mitochondria-nucleus implication in bystander response following various types of genotoxic stress.

We used Mouse Embrionary Fibroblasts (MEF) obtained from Wild-type (WT) mice and mitochondrial dysfunctional genetically modified mice – HtrA2 Knock Out (KO), CHOP KO, or double KO. Genotoxicity was induced by physical (X-rays, proton beam) and chemical factors (bleomycin - BLM). Bystander effects were induced by medium transfer method, from WT MEFs to WT, HtrA2 KO, CHOP KO or double KO at 24h following genotoxic treatment.

We proved exacerbated sensibility to all DNA-damaging factors in CHOP KO and HtrA2/CHOP KO cells. Protons exposure exhibited a slightly higher genotoxic effect in all cell lines compared to X-ray. CHOP KO MEFs cells proved to be more sensitive to DNA damage, independently of HtrA2. Bystander effects visible as increased micronuclei (MN) proportion were induced in WT but not in any of the cell lines with mitochondrial deficiency.

Our study showed therefore that mitochondrial signaling pathways of HtrA2/CHOP are involved in DDR and response to bystander signaling following exposure to physical and chemical genotoxic stress.

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Monte Carlo simulations of charged particle beams for radiobiology experiments at IFIN-HH

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Accelerated ion beams cancer therapy is an accurate radiotherapy technique capable of improved local control of the beam that allows a more efficient sparing of the healthy tissue. Very effective in delivering the desired (or expected) dose to target volume, hadrontherapy has a tremendous advantage over photon-based radiotherapy. Beneficial therapy outcomes come from a thorough understanding of the radiobiological effects on various types of cells, either healthy or tumoral. At IFIN-HH there are two facilities dedicated to ion beam irradiation for *in vitro* radiobiology studies [1], namely the 3MV Tandetron™ and the TR19 cyclotron facility [2]. We employed a simulation strategy based on Monte Carlo particle tracking, implemented using the Geant4 toolkit [3].

The geometry and primary generator classes were constructed and integrated to the simulation environments, based on experimental setups. This way, we obtained realistic spatial sampling and energy distributions of both facilities as well as track recordings and single particle scoring. We described the physical processes inside the target volumes using the Geant4 EM physics lists.

We ran the simulations for different physics lists, geometries, and source configurations. The results were compared against each other towards picking the most accurate description according to the experimental measurements.

Following the geometrical description and source parametrization of the two simulated systems, we established a complex scoring protocol capable of both single particle and spatial sampling energy determinations. We inferred the kinetic energy distributions of the beam at the interface between water and the adjacent medium, before entering the region in which the biological sample is placed. We also tested the lateral uniformity of the beam by scoring the energy of each particle at the air-target interface, along a lateral profile. The LET was determined, in both cases, in a 1 μm thick cylindrical water scoring volume, replicated along the beam propagation axis. The mean LET has been inferred inside the first 10 μm of water, where the cells are found in irradiation experiments. For proton beams of ~10^6 particles and the Geant4 EM option 4 physics list, our results indicated the closest resemblance with experimental measurements.

This study shows that Geant4 simulations are useful in validating the feasibility of ion-beam irradiation experiments at the 3MV Tandetron™ and TR19 cyclotron facilities. The models provided high-fidelity representations of geometry, source parameters and physical processes, as well as flexible dose and energy measurements.

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Radiobiology with the Alpha Magnetic Spectrometer (AMS02) experiment on the International Space Station

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The Alpha Magnetic Spectrometer (AMS) experiment has been operating on the International Space Station (ISS) since 2011. In this data-taking period, more than 145 billion cosmic ray events were acquired, measuring their characteristics with an accuracy never reached before.

These measures constitute a reference point for the solution of the problems of fundamental physics and cosmology currently open. This information is also crucial for a correct understanding of the radiobiological phenomena that are observed in space in order to improve the construction of dose-effect models.

This knowledge is an essential prerequisite for identifying and reducing the risk factors for ionizing radiation associated with human exploration and colonization of the solar system.

Radiosensitizing effect of boron to enhance the effectiveness of proton therapy *in vitro*

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Radiotherapy nowadays has a key role in cancer treatment. Proton therapy is used today to treat many cancers and is particularly appropriate in situations where surgery options are limited, and conventional radiotherapy presents unacceptable risks to patients. A few years ago, it was suggested that an increase of up to a factor of two of the doses at the proton Bragg peak could be achieved if boron is accumulated in the tumor tissues [1]. The mechanism responsible for a higher dose was suggested to be related to proton-boron fusion reactions, leading to the production of low-energy, and hence high Linear Energy Transfer (LET), α-particles. Nowadays there are single works showing effectiveness of proton beam irradiation boron-11-containing cancer cells [2]. Limited number of the studies devoted to application of 11B(p,3a) nuclear reaction in proton therapy and contradictoriness of the obtained result do not allow to judge so far about the future prospects of the boron containing drugs utilization in proton therapy to increase its antitumor efficacy [2,3]. However, this approach looks very attractive because of the already existing boron drugs successfully being applied in boron neutron capture therapy. In this work, we experimentally test possibility to enhance proton biological effectiveness in boron-11-containing cancer cells *in vitro*.

Human prostate and glioblastoma cancer cells were pre-incubated with boron compound ($Na_2B_4O_7$, sodium tetraborate) and irradiated with increasing doses 0.5-20 Gray at the proton Bragg peak at the synchrocyclotron SC-1000 of the PNPI. To test whether the physical nuclear reaction 11B(p,3a) results in an enhancement of the cancer cell death by high-energy proton beam irradiation, cell lines were also irradiated with graded doses 2-20 Gray using lift-up type ^{60}Co γ-ray source "Researcher". Then radiation sensitivity was determined by MTS-test and cologenic assays using crystal violet for staining.

In our study the ability of boron compound to activate the cancer cell death with protons at the Bragg peak irradiation was shown *in vitro*. At the same time, a weaker similar effect was determined for gamma-irradiation, which may indicate not only physical nature of influence boron at irradiated cancer cell viability but a specific biological effect. The data suggest that the combined effect of proton therapy with sodium tetraborate on cancer cells increases their sensitivity to proton irradiation with low toxicity of the boron drug for cells of normal morphology.

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The cranial irradiation with high-energy protons affects the visuomotor instrumental behavior of non-human primates

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During long-duration space flights unavoidable early damage to perceptive, integrative and executive brain systems of humans is caused by exposure to galactic cosmic rays, consisting mostly of protons (92%) (NPJ Microgravity. 2018. 4:8). Subsequent behavioural and cognitive deficits may affect operator activity of astronauts.

Although there is a substantial amount of model studies of the effects radiation has on central nervous system of rodents (Life Sci. Space Res. 2019. 21:1), usage of these results to predict outcomes of radiation exposure for humans is questionable. Oculomotor behaviour is central to operator activity and requires interaction among visual, integrative and executive systems. Therefore, non-human primates can serve as the most adequate model to study possible effects of radiation on humans as their oculomotor behaviour is similar to human.

We studied conditioned instrumental task performance of two male monkeys (*Macaca mulatta*) to visual stimuli of different eccentricities presenting in 34 locations within visual field of 39x26 deg. One monkey (O+) was exposed to a single cranial proton irradiation (170meV, 3Gy). For the control animal (O-) irradiation was simulated.

Monkeys were trained to fix gaze on a small square (0.38 deg. in size) in the centre of the visual field and then execute a saccade to peripheral stimulus of the same size, fix gaze on it and respond to its dimming by pressing manually the ipsilateral lever, at which point they received reward. Sometimes the animals executed predictive manual reactions that were not rewarded or missed the task ('misses'). We ended experimental sessions when 'misses' started to occur in more than 10% of trials. Therefore, the number of trials in sessions can be used as measure of motivation of the animals. All sessions were separated by 2 to 5 days.

During three month after irradiation the percent of correct reactions of O+ varied in the range 80-90%. A weak increase of this parameter ($r=0.413$, $p=0.036$) after irradiation can be attributed to effects of prolonged learning. In the same time we found a significant decrease of the number of trials ($r=-0.624$, $p<0.001$) in consecutive sessions. Therefore, the number of trials was negatively correlated with the percent of correct reactions ($r=-0.562$, $p<0.005$) for irradiated animal.

Control animal (O-) also showed a weak increase in the percent of correct reactions ($r=0.361$, $p=0.02$) (between 80 and 92%), but we found non-significant decrease in the number of trials ($r=-0.156$, $p=0.329$) in consecutive sessions. We also found these parameters to have a weak positive correlation ($r=0.379$, $p=0.015$) for control animal.

We suppose that proton irradiation caused decrease of motivation resulting from damage to dopamine system in experimental animal, but integrative processes necessary for conditioned instrumental task performance remained unaffected.

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Cytogenetic damages in lymphocytes of radiotherapy cancer patients followed by previous radiation exposure

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The cytogenetic effects studies in cancer patients due to radiation therapy have been of great importance for better understanding the radiobiological mechanisms of partial body radiation exposure in non-tumor cells. The estimation of the cytogenetic damages in peripheral blood lymphocytes of cancer patients is an important task in the development of radiobiological basis of radiotherapy.

The aim of study was to estimate the cytogenetic effects in cultured lymphocytes of cancer patients following radiation treatment, depending on previous irradiation.

Chromosome aberrations were analyzed in lymphocytes of 20 radiotherapy patients: with lung cancer and with head and neck cancer. Blood sampling was performed during γ-^{60}Co radiotherapy or megavolt radiotherapy course on linear accelerator: before radiotherapy, at the middle of treatment, at the end of first and second part of radiation therapy course, reaching an average the dose of 40 Gy and 65 – 70 Gy for the first and second part accordingly. Dose per fraction was 1.8 – 2 Gy.

The quantitative yield and quality range of cytogenetic damage in lymphocytes of patients before and during radiation therapy in the presence of a break following exposure were identified. The different pace of chromosome aberrations accumulation in groups of patients with various tumor localizations was found. The increase of radiation-induced aberrations from the beginning to the end of the first part of treatment before scheduled radiotherapy break in patients with lung cancer and less pronounced changes in these parameters in patients with head and neck tumors were demonstrated. Undergone the second part of the radiotherapy course the range of chromosome aberrations in patients with head and neck tumors did not expand. These data are of importance for correct assessing the impact of therapeutic irradiation on the chromosomal level.

The peculiarities of cytogenetic data treatment considering the absence or presence of previous radiation exposure will be discussed.

Impact of O-GlcNAcylation on the repair of DNA double-strand breaks induced by different qualities of radiation

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Introduction. DNA double-strand breaks (DSBs) are considered the most dangerous type of radiation-induced damage. The repair of DSBs is critical as its failure leads to loss of genetic integrity and/or cell death. Recent findings revealed that O-GlcNAcylation plays an important role in the repair of DSBs. O-GlcNAc is a posttranslational modification where a single N-acetyl-glucosamine molecule (GlcNAc) is attached to the oxygen atom of specific serine/threonine residues within proteins. O-GlcNAcylation is nutrient sensitive and controls activity, localization, or stability of numerous proteins. In addition, O-GlcNAcylation impacts on chromatin remodelling. We aimed to understand how O-GlcNAcylation affects the repair of X-ray or heavy-ion induced DSBs and cell survival as well as chromatin compaction upon irradiation.

Methods. HeLa CCL2 cells were irradiated with X-rays or C-ions in the absence or presence of the O-GlcNAcase inhibitor PUGNAc or O-GlcNAc transferase inhibitor ST060266. DSB repair was analysed with the γH2AX-foci assay in dependence of the cell-cycle phase. The influence of inhibition of O-GlcNAcylation on recruitment kinetics of GFP-tagged NBS1 was determined with live-cell microscopy up to 30 min after X-irradiation. Furthermore, to detect if O-GlcNAcylation has an effect on the chromatin status we performed fluorescence lifetime imaging of the DNA-binding dye Hoechst 34580 in living cells.

Results. Promoting O-GlcNAcylation enhanced the repair capacity of X-ray-induced DSBs in S/G2 cells, whilst inhibiting O-GlcNAcylation impaired or slowed down the repair of both X-rays and C-ion-induced DSBs. Upon iron-ion irradiation, DSBs were O-GlcNAc decorated indicating that this posttranslational modification is required for the break processing. Clonogenic assays revealed that elevated levels of O-GlcNAcylation improved cell survival whilst inhibition of O-GlcNAcylation displayed increased radiation sensitivity after X-rays. Life cell experiments revealed that inhibition of O-GlcNAcylation results in a more transient binding of the DSB-repair factor NBS1 to DSBs.

Conclusion: Our studies showed that DNA damage affects local O-GlcNAcylation at sites of DSBs where it is required for the retention of the repair factor NBS1. We confirmed that O-GlcNAcylation is important for DSB repair and yet more, showed that it is important for the survival of radiation-inflicted damage. These findings support critical links between O-GlcNAcylation and DNA-damage response.

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The eye and hand movement impairments during visuomotor task performance in non-human primates at cranial irradiation by high energy protons

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During long-duration space flights exposure to galactic cosmic rays leads to unavoidable early damage to human central nervous system, causing operator activity impairments in astronauts. A substantial amount of model studies of irradiation effects on central nervous system of rodents cannot be used to predict its effect on humans because human visual and motor systems are more complex and developed. Therefore primates are the most adequate model animals to study the ways radiation affects key constituent elements of operator activity (eye and hand movements), as systems providing visuomotor adaptive behaviour are quite conservative among primates.

We studied the latencies of saccades (SL) and manual reactions (ML) of two male monkeys (*Macaca mulatta*) in conditioned instrumental task. These temporal parameters are believed to reflect coherence of integrative processes such as attention focusing on targets, programming of movements and their execution. One monkey (O+) was exposed to a single cranial proton irradiation (170meV, 3Gy). For the control animal (O-) irradiation was simulated.

Monkeys were trained to fix gaze on a square (0.38 deg.) in the centre of the visual field and then execute a saccade to peripheral stimulus of the same size, fix on it until its dimming, then press the ipsilateral lever and receive reward. Predictive manual reactions and omissions were not rewarded. The stimuli of different eccentricities were presented in 34 locations within visual field of 39x26 deg. All sessions were separated by 2 to 5 days. Proton irradiation had no negative effects on instrumental performance efficacy in course of three month after irradiation, but SL and ML were affected.

Irradiated animal demonstrated a weak (by 4 to 5%) increase in SL at the 32nd day after irradiation; quite substantial SL increase (by 11 to 17%) occurred from 63rd to 87th day, and then reducing to the previous level by days 92-94. These results suggest that radiation caused a short period (for two months) of significant SL increase (r=0.543, p=0.013). On the contrary, SL of the control animal in this period decreased marginally significantly (r=–0.337, p=0.093).

The dynamics of ML was similar: from the 46th to the 87th day they increased substantially (by 13 to 20%), but by the 92nd day reduced to the previous level in exposed monkey, remaining unchanged in control animal (r=0.105, p=0.515) this whole time. Therefore, proton irradiation had a negative effect on ML only in exposed monkey (r=0.555, p=0.007), in which SL and ML highly correlated (r=0.837, p<0.001).

We can conclude that integrative processes, crucial for conditioned instrumental behaviour, turned out to be widely resistant to proton irradiation, although temporary increase in SL and ML suggests its early and transient negative effects on mechanisms of attention focusing on targets, movements programming and their execution.

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Adaptation of the ^{226}Ra determination method in water using liquid scintillation spectrometry

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^{226}Ra is a natural radioactive isotope with a half-life of 1600 years. ^{226}Ra is found in the Earth's crust and water, atmospheric air, soil and all living organisms. A particular risk to humans is ^{226}Ra after intake.

In Poland, what came into force was the Regulation of Minister of Health on the quality of water intended for human consumption in order to control the consumption of ^{226}Ra contained in water in which the acceptable content of ^{226}Ra is specified.

One of the known methods for determining ^{226}Ra is the emanation method. It is based on measuring the α-radiation of radon daughter nuclides in equilibrium with radium parent. Radium is separated from the solution by co-precipitation with barium carrier. The $Ba(Ra)SO_4$ precipitate is dissolved in alkaline solution of EDTA. After transfer to special vessel called bubbler, sample is purged with argon and stored for at least 8 days to allow ^{222}Rn to grow and come to equilibrium with its daughters. Then the solution is again de-emanated with aid of argon and radon is collected in scintillation chamber (Lucas cell). The measurement, which last for 3 hours, can start after storing cell for 2 hours. This method is selective and sensitive and can be used for the determination of ^{226}Ra activity in water and food samples. Limit of detection for this procedure is 5 mBq/L. However it is quite time consuming and quantity of samples that can be measured is limited to number of scintillation probes.

For this reason the development of a method for the determination of ^{226}Ra in water by using of liquid scintillation spectrometry was needed, which would significantly shorten the measurement time. This method is based on the co-precipitation, isolation and purification of the $Ba(Ra)SO_4$ precipitate. At the final stage of the procedure the $Ba(Ra)SO_4$ precipitate is dissolved in EDTA. The solution is then transferred to scintillation vial and mixed with scintillation cocktail. For this purpose a naphthalene-based scintillation was used (Optiphase Hisafe 3). It is important that sample was homogenous and measured almost immediately after preparation to avoid extensive ingrowth of progeny. During the tests, it was noticed that the storage temperature of the samples is a very important factor. Storage of sample at room temperature causes the precipitate to fall, resulting in a clear solution of water with a scintillator and a several millimeter layer of precipitate on the bottom of the scintillation vial. Such sample is not homogenous and its measurement is disturbed. It is necessary to store samples at low temperatures.

^{230}Pa isolation by extracting and chromatographic agents containing oxo- and hydroxo-groups

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Protactinium is poorly explored element having only one long-living and difficult of access isotope ^{233}Pa. Nevertheless, it has a wide application spectrum: geology, nuclear forensics, nuclear medicine. Institute for Nuclear Research (Russia) can produce Ci-amounts of ^{230}Pa ($T_{1/2}$=17.4 d) together with other useful alpha-emitters ^{225}Ac ($T_{1/2}$=9.9 d) and ^{223}Ra ($T_{1/2}$=11.4 d) [1] by irradiation of natural thorium with protons having energies 140-60 MeV. ^{230}Pa partially decays to ^{230}U ($T_{1/2}$=20.8 d), which has potential application in targeted alpha therapy (TAT) of cancer due to 5 emitting a - particles with total energy 33.5 MeV. ^{230}U can be utilized directly or as a parent of ^{226}Th ($T_{1/2}$=31 min) in a generator system.

Separation methods such as liquid-liquid extraction and ion exchange chromatography are usually used for isolation of pure Pa radioisotopes. But in aqueous solutions Pa(V) forms mono-oxo cation PaO^{3+} having strong tendency to hydrolysis, polynuclear species formation as well as complexation with various anions. Pa displays strong affinity to hydroxyl groups and easily forms oxo-complexes. These facts motivated us to investigate Pa extraction with ketones and alcohols as well as chromatographic behaviour of Pa on organic and inorganic sorbents.

Extraction separation. Extraction of Pa from HCl and HNO_3 solutions with methyl-isobutyl ketone, octanol and fluorinated alcohols was investigated. The distribution coefficients were compared. ^{230}Pa was quantitatively extracted from the HCl in the concentration range from 5 to 9M HCl. Octanol extracted up to 95% ^{230}Pa from 6-9M nitric acid. For back-extraction, various media were tasted and it was shown that oxalic acid solutions showed optimal distribution coefficients. Main impurities in Pa after extraction were radioisotopes of Sb, Nb, I and Ru.

Chromatographic separation. According to the literature, Pa forms strong complexes in concentrated HCl solutions, which are destroyed in diluted solutions. Catalytic amounts of HF also resulted in instability of these complexes. This fact was used for Pa separation by anion exchange chromatography on AG 1x8 and Dowex 1x8 in 8M HCl. The most part of radionuclides (mono- and bivalent cations, Th, Ac, Ra, lanthanides and others) were passed through the column. Pa, Nb, partially Sb, Zr, Ru were sorbed onto the column. Then ^{230}Pa was stripped off the column with 8M HCl with the addition of 0.3M HF or 3M HCl. Pa contains Sb as an impurity. One of the most effective method for Pa(V) separation is based on silica gel sorption from acid solutions. It may be used for final purification of Pa.

Thus, pure ^{230}Pa fraction was produced with combination of extraction and chromatographic methods. The total chemical yield of ^{230}Pa was about 80% and radionuclidic purity >99%.

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Radiochemical bioassay on Am-241 traces for internal contamination evidence

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Americium-241 is an artificial transuranic radionuclide with high specific activity of 0.13 TBq/g and long half-life $T_{1/2}$=432.2 years. Besides the nuclear and space industries it has a wide application in non-destructive testing, as a thickness gauge and in smoke detectors. Due to a high radiotoxicity surpassing its chemical toxicity a long-term internal contamination by low americium quantities may be a serious health issue. We have developed a bioassay procedure for americium-241 tests for persons occupationally exposed to risk of americium intake by inhalation and ingestion. The procedure is suitable for low-level activities determination and it includes decomposition and pre-concentration of complex organic samples, precipitation of lantanide group elements, followed by selective multiple solvent extractions and acid/alcohol-based separations using the anion-exchange (DOWEX resin) chromatography. Optimization of the acidity of alcohol solutions especially for final fraction eluation was the crucial step in this procedure. The concentration measurements may be performed by ICPMS immediately, while in the case of alpha spectrometry using properly calibrated PIPS detectors, thin layer americium alpha sources had to be prepared by modified Talvitie's electroplating procedure prior to activity measurements. The efficiency of the proposed radiochemical separation procedure had been evaluated by the Am-243 tracer addition and it exceeded 30% that is quite good in compare with other reported values. On the contrary, the electroplating efficiency was about 50% that is significantly low if compared with over 90%, reported for uranium and thorium, probably due to a low distribution coefficient for trivalent Am against lanthanides. It has consequences on the thickness of the alpha source and measurement efficiency. The advantage of the procedure is high sensitivity but issues with selectivity may be avoided by using ICPMS measurement technique instead of alpha-spectrometry in order to avoid electrodeposition step and time consuming activities counting. This procedure may be recommended in cases when there is a doubt on systematic low-level internal contamination so that operational procedures may be modified accordingly, and the workers awareness and risk perception affected. The internal dose assessments based on the bioassay results on Am-241 contents in analyzed samples may be assessed using available biokinetic models.

Optimization of Zr-89 production with a variable energy cyclotron

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Introduction. Over the last several years, immuno-positron emission tomography (immuno-PET), based on ^{89}Zr-labeled antibodies radiopharmaceuticals, proved to be an attractive tool for non-invasive tumor detection and antigen profile characterization, due to the high sensitivity of PET combined with the high antigen specificity of mAbs. There are several advantages of using ^{89}Zr for antibody labeling, one of them is that the decay half-life of ^{89}Zr (3.27 d) matches the biological half-life of antibodies. ^{89}Zr has one of the lowest maximum energies of emitted positrons, which allows for high resolution PET images.

Methods. At the Radiopharmaceutical Research Centre (CCR), ^{89}Zr radioisotope was produced by cyclotron bombardment of natural ^{89}Y, by ^{89}Y(p,n)^{89}Zr nuclear reaction, on TR-19 cyclotron (which allows native 14-19 MeV variable energy of the proton beam). The irradiated ^{89}Y foil-target was dissolved in HCl 6M, then ^{89}Zr in form of zirconium chloride ($ZrCl_4$) was separated from the target and purified by ion-exchange chromatography. The chemistry has been optimized to provide high yields of ^{89}Zr separation, with high purity and high molar (specific) activity. Sterile filtration was used in order to ensure the sterility of the product. Quality control of the final product was carried out for each batch. Irradiation yield, separation yield, pH, radiochemical purity (by TLC/HPLC) and radionuclidic purity (by gamma spectrometry) were assessed.

Results. The target used was a foil of ^{nat}Y (99.9%, Alpha Aesar), 10 mm diameter and 250 μm thickness. Nuclear reaction starts at 3.7 MeV, maximum proton beam energy at 13 MeV (according to Talys code simulations). The irradiation process parameters were studied and the optimal values were set at: proton energy 14 MeV degraded to 10.5 MeV with a pure Al foil (40 μm thickness), beam intensity I = 8 μA, irradiation duration t = 4 h, with 32 μAh integrated current on target. After irradiation, the target was dissolved in 5 mL HCl 6M and purified on a C18 column resulting 2 GBq [^{89}Zr]$ZrCl_4$ at the end of process. The radiochemical purity, assessed by radio-HPLC, was higher than 99% after purification.

Conclusions. Due to the increasing demand of high purity and high-specific activity [^{89}Zr]$ZrCl_4$ solution to be used for radiopharmaceuticals formulation, we developed and optimized an efficient and reliable method of ^{89}Zr production using a low energy cyclotron, based on irradiation of ^{nat}Y targets by ^{89}Y(p,n)^{89}Zr nuclear reaction. The [^{89}Zr]$ZrCl_4$ solution meets the specifications and quality requirements for biomolecules (antibodies) radiolabeling. This method can facilitate the use of ^{89}Zr in subsequent research studies and clinical investigations of immune-PET.

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Accumulation of ^{90}Sr by *Betula pendula* in the zone of radioactive contamination (East Ural Radioactive Trace, Russia)

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Soil is the main depot preserving the stock of radionuclides in forest ecosystems. Woody plants are the second most important component that retains radionuclides for a long time. It is known that up to 80% of radionuclides falling out of the atmosphere can be accumulated by woody plants. However, the level of plant pollution decreases with time and can amount to 2–4% of the ^{90}Sr content in the soil. Many studies are devoted to the radionuclides entry into plants in the initial period (1–10 years) after the accident. Data on radionuclides inventory over long periods of time are very poor. The East Ural Radioactive Trace (EURT) was formed in 1957 as a result of the accident at the "Mayak" enterprise. Now the main pollutant is ^{90}Sr. A study of woody plants growing in a contaminated area for more than 60 years enables to reveal patterns of radionuclides distribution within a trees and evaluate the total stock of ^{90}Sr.

The aim of the investigation was to study the accumulation of ^{90}Sr by the aboveground organs of *Betula pendula* Rott., growing in the EURT zone.

We ranked the EURT territory according to the ^{90}Sr soil contamination density: impact part (5–30 km from the accident epicenter along the central axis, soil contamination density 100–70000 kBq·m^{-2}), buffer part (30–100 km, contamination density 10–100 kBq·m^{-2}). Control plots were selected outside the EURT (soil contamination density 0.5–2.9 kBq·m^{-2}). Samples of soils, leaves, branches 1–5 years old, branches 5+ years old, trunk (wood, bark) of birch were taken. The distribution of ^{90}Sr in the aboveground organs of birch growing in the EURT and in the control plots was similar. The concentration of ^{90}Sr increases in the line: trunk < large branches < (leaves + small branches). It is shown that the ^{90}Sr content in the bark is higher than in wood. The concentration of ^{90}Sr in wood (trees age were over 60 years) does not depend on the age of the wood layer. Its level rises only in heartwood, which was characterized by a high content of ash elements. In all cases, there is a positive correlation of ^{90}Sr concentration with the ash elements content in the organs of *Betula pendula* (R = 0.64–0.99, p = 0.95).

The concentrations of ^{90}Sr in air-dry matter and plant ash were increased with increasing soil contamination density in accordance with the exponential dependence. Aggregated transfer factors (t_{ag}) have been maintained at the same level over the past 25 years.

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Informatization of radioecological research during drilling waste treatment

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Drilling cuttings is large-tonnage waste generated during well site construction on oil and gas fields. According to current environmental legislation drilling cuttings are to be neutralized and utilized. While applying modern developed technological solutions for the utilization of drilling waste and its further use, there is a need for timely and continuous monitoring.

In particular, one of the most resource efficient methods for utilizing of drilling waste is producing of soil-like reclamation mixtures used for the construction of embankments, deboning of technological sites and other earthworks.

To justify this method of utilization timely chemical and analytical studies of drilling cuttings determining the content of natural radionuclides and heavy metals are required.

The aim of this work is to increase the information content of the applied radioecological studies of drilling cuttings and to assess its timeliness during the utilization of this type of waste.

Data obtained from long-term studies of drilling waste show that drilling cuttings, sludge and produced water generated during oil production contain mainly natural ^{232}Th, ^{226}Ra and ^{40}K. This group of natural radionuclides accounts for up to 95% of the total radioactivity, therefore these elements are defined as a focus group that limit the technological possibilities of drilling cuttings utilization and the fields of further application of produced reclamation mixtures.

The main radioactive element that accumulates in solid fractions is ^{40}K. Moreover, the specific activity of this element can be up to seven times higher than the corresponding value of the remaining natural radionuclides contained in the drilling waste.

In order to prevent possible radioactive contamination of the area, as well as for timely monitoring of the radioactivity of drilling cuttings treated on technological sites, the following types of work are recommended:

1. Collection and separate storage of sludge from a horizon with abnormal radioactivity;

2. Continuous express radiometric assessment of drilling sludge with measuring of the ambient dose equivalent rate or exposure dose rate of photon radiation during the operational monitoring of the radiation situation;

3. In case an increased above the natural background of the area is found to be 2 times higher or more, sludge must be tested and analyzed with increased intensity (gamma spectrometry, chemical analysis of U, Th, Ra, K);

4. After penetration of the alleged radioactive zone, current gamma-ray logging is obligated.

Therefore, the use of rapid methods for the effective radiation activity of natural radionuclides (primarily ^{40}K) determining will allow to timely identify the waste with excessive radioactivity parameters, the use of which as soil-like reclamation mixtures is prohibited.

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Comparison of Pavlotskaya and Tessier methods for assessment of radionuclide speciation in soils

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The purpose of this study was to compare two methods used for sequential extraction of forms of radionuclide occurrence: the Pavlotskaya (Goryachenkova et al., 2005) and the Tessier methods (Tessier et al., 1979).

A comparison of the Pavlotskaya and Tessier methods in relation to the fractionation of various forms of technogenic radionuclides (^{137}Cs and ^{90}Sr) gives substantially consistent results. The sum of the water-soluble and exchangeable fractions extracted using the Pavlotskaya method and the sum of the exchangeable and carbonate fractions extracted according to the Tessier method should be used for the assessment of the availability of radionuclides to plants. The sums of the mobile fractions extracted using the Pavlotskaya method (the water-soluble, exchangeable, and mobile fractions) and the sum of the exchangeable fraction, carbonate fraction, and the fraction bonded with Fe and Mn oxides extracted according to the Tessier method should be used for the assessment of the geochemical mobility of radionuclides.

The application of the above methods for the speciation assessment of natural radionuclides (^{226}Ra, ^{232}Th, and ^{238}U) gives poorly consistent results. The Tessier method indicates higher contents of compounds available to plants and mobile compounds in comparison with the Pavlotskaya method. The main reason behind this may be the complexity of the soil chemistry of ^{232}Th and ^{238}U that feature polyvalence and a strong tendency for hydrolysis and complex formation; in addition, their behavior may be affected by various carriers. Therefore, these elements form a broad range of compounds that change one into another with changes in the chemical conditions; this complicates accurate comparison of the composition of their forms extracted by the reagents.

An advantage of the Tessier method is the selective extraction of radionuclides bonded with organic matter, while in the Pavlotskaya method, radionuclides bonded with organic matter constitute parts of the mobile and acid-soluble fractions. On the other hand, the Tessier method does not include the extraction of water-soluble compounds constituting the most available and mobile portion of the soil radionuclide pool. In addition, the Tessier method does not include the extraction of compounds bonded with crystalline iron and aluminum oxides, which makes comprehensive assessment of the behavior of natural radionuclides (^{226}Ra, ^{232}Th, and ^{238}U) impossible.

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Evaluation of variants of the calculation of meteorological dilution parameters

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One of the important tasks of assessing the radiation impact on the environment of regular emissions of nuclear fuel cycle enterprises is to determine the average and integral volume activity of radionuclides in the surface layer of the atmosphere, the density of radioactive substances that have fallen on the Earth's surface.

More accurate results allow us to obtain models using the lagrangian approach (RECASS NT, NOSTRADAMUS, ROM and others) [1]. Models realizing a solution of the semi-empirical equation of turbulent diffusion give acceptable accuracy in estimating the volumetric activity and density of the radionuclide fallout resulting from regular emissions [1]. Their practical application is justified in the form of a Gaussian model for continuous emissions.

The possibility of using the Gaussian model to take into account the repeatability categories of meteorological conditions during regular radioactive emissions of nuclear fuel cycle enterprises was assessed by comparing three calculation options that differed in complexity and requirements of the source data.

In the first variant, data on the repeatability of weather conditions for lines rumba with the highest probability of implementation in the circular wind rose are accepted [2]. In the second version, the parameters of meteorological dilution were calculated for each category of atmospheric stability at a weighted average wind speed, in the third - for the most probable category of atmospheric stability and the corresponding average weighted wind speed [2]. According to the results of the calculating options 1 and 2 the differences in the value of the average multi-year meteorological dilution and its integral do not exceed 10% in the range of distances of 1-100 km relative from the source of emission. For all calculation options at distances greater than 10 km, comparable results are observed for the parameters of meteorological dilution, which do not differ by more than a few percent.

Thus, it is possible to use relatively simple methods for calculating the average multi-year meteorological dilution factor and his integral to assess the parameters of the radiation environment as a result of regular radioactive emissions from nuclear fuel cycle enterprises.

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Estimation of absorbed dose of coniferous woody plants in emergency radioactive emissions

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Purpose of scientific research. Development of a migration-dosimetric model of irradiation to coniferous woody plants during in emergency radioactive emissions.

Methods. Analytical and numerical methods.

Results. The migration-dosimetric model consists of two migration and one dosimetric calculation blocks.

The first migration block is designed to calculate the volume activity of atmospheric air and the intensity of radionuclide deposition on the Earth's surface. The calculation block is based on the application of the gaussian model of the dispersion of impurities for brief emissions.

The basis of the second migration block is represented by system linear differential equations of 1st order with constant transfer coefficients between the studied components of the system. The calculation block allows us to estimate the dynamics of the activity of radionuclide deposition in the system "surface of aboveground phytomass of woody plants-ground cover-surface layer of soil".

The dosimetric calculation unit is intended for estimating the absorbed dose rate from external b- and g-radiation at different heights of coniferous woody plants from sources containing radionuclides from the emergency release composition. The sources are: a cloud of radioactive emergency release during its life cycle, the surface of the above-ground phytomass, the soil cover (green moss or forest floor), and the top layer of soil during the remaining growing season after radioactive releases. The geometry of the radiation sources: the cloud of an emergency radioactive release is a semi-infinite space, and the rest of the radiation sources are an infinitely extended layer of finite thickness in the longitudinal direction. Each of the radiation sources adopted uniform distribution of activity radionuclide.

Conclusion. The migration-dosimetric model developed is designed to assess the radiation-ecological situation in forest biogeocenoses and the radiation impact on coniferous woody plants.

^{7}Be, ^{210}Pb and ^{137}Cs in the atmospheric precipitation of the Southern and Arctic part of Western Siberia

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In modern studies, ^{7}Be and ^{210}Pb are often used as indicators in the study of various surface geological processes. In particular, information on their activities is used in assessing the conditions and rates of formation of lake sediments, studying the patterns of transport of aerosol particles in the atmosphere and their fallout on the earth's surface [Baskaran M., 1993, 2001; Branford D., 2004; Gourdin E., 2014; Renfro A. A., 2013]. An important component of such studies is the identification of the patterns of ^{7}Be and ^{210}Pb entering the earth's surface in the composition of dry (dust, aerosols) and wet (snow, rain) precipitation.

Currently, the literature does not contain widely known data on the combined atmospheric intake of ^{7}Be, ^{210}Pb, and ^{137}Cs in the Arctic and southern regions of Western Siberia. The purpose of the work is to eliminate this gap and conduct a comparative analysis of the nature of the intake of ^{7}Be, ^{210}Pb, and ^{137}Cs in atmospheric precipitation in the studied territories of Western Siberia in the winter.

Snow cover is a natural storage, accumulating information on atmospheric income for a sufficiently large period of time from the first precipitation in late autumn to its melting in spring. Its study can provide information on the integral supply of ^{7}Be, ^{210}Pb, and ^{137}Cs and other chemical elements to the earth's surface over the entire period of snow accumulation without separation of the contributions of the dry and wet component.

The objects of research are integral snow samples taken to the entire depth of snow cover without separation by layers at the end of April 2019 in the Arctic zone (Nadym, Purovsky, Tazovsky regions of the Yamalo-Nenets Autonomous Okrug) and in mid-March 2019 in the southern region of Western Siberia (Novosibirsk, n. Kolyvan, Altai Territory, Seminsky Pass, Altai Republic).

The activity of the studied radionuclides was determined by the method of high-resolution semiconductor gamma spectrometry using a gamma spectrometer based on HPGe low-background well detector GWL-220-15 using analytical gamma lines 477 (^{7}Be); 46.5 (^{210}Pb) and 661.7 (^{137}Cs) keV. The lower detection limit of these radionuclides was 0.02 Bq. The duration of measurement of a single sample varied from 12 to 48 hours and was chosen so that the statistical error in determining the areas of analytical photopikes of 46.5 keV and 477 keV does not exceed 5%.

As a result of the studies, it was found that in samples representing the Arctic zone the average contents of ^{7}Be, ^{210}Pb and ^{137}Cs in snow-melted waters are 262, 103 and <1 mBq/L, for the southern region of Western Siberia - 273, 171 and <1 mBq/L, respectively.

A comparative analysis of the data shows that, despite the difference in geographic location, the concentration of ^{7}Be in the meltwater of the northern and southern regions is almost equal. At the same time, the specific activity of ^{210}Pb in the suspended matter of meltwater taken in the south is 1.7 times higher, which may indicate a much higher level of dust material intake in winter. A significant part of ^{7}Be (the Arctic zone —78.6%; the southern region — 54.6%) is associated with a fraction of dimension less than 0.45 μm (nanosized dust, aerosol particles, colloids, and dissolved component). The amount of ^{7}Be associated with the coarse fraction in the north is 2 times less than in the south. The fractions of ^{210}Pb located in this fraction practically coincide for both regions (52 and 55.7%). For the southern region of Western Siberia, in the fraction <0.45 μm, the specific activity of ^{7}Be is 3.4 times higher than the activity of ^{210}Pb. The Arctic zone is characterized by a higher value of this ratio - 5.9.

As a result of the studies, data on the combined atmospheric intake of ^{7}Be, ^{210}Pb, and ^{137}Cs in integral snow samples, including atmospheric precipitation, dust, and aerosols, in the Arctic (for 7 months) and southern (for 5 months) regions of Western Siberia were firstly obtained.

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Distribution of ^{7}Be, ^{210}Pb and ^{137}Cs in moss biomass as a result of the SET experiment

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Biomass fractionation was carried out using large-volume moss samples taken in the Altai region. The apical green part (1-3 cm) of moss (part of the plant that has grown during the last vegetative period) was separated from the moss pad and subjected to fractionation by sequential elution technique (SET) (Perez-Llamazares et al., 2011). During sequential elution, 4 fractions are being extracted: 0) adsorbed on the plant surface; I) intercellular elements; II) extracellular; III+IV) intracellular elements + solid residue.

The isotopes distribution in biomass for samples taken in different places coincides well and, apparently, reflects the general patterns of isotope distribution in moss biomass.

The experiment showed that all isotopes that came to the surface of the moss in any form (sorbed on dust, dissolved in rainwater, etc.) are associated with biomass one way or another and no further washing out.

The isotope content in 0 fraction is 0.2–0.3%, and only the ^{137}Cs exceeds 1% (1.1–2.6%). The further distribution of isotopes in the biomass fractions is different.

The ^{210}Pb isotope is predominantly concentrated in I fraction (79-80%), to a much lesser extent in II fractions (17-19%); in III+IV fractions is only 2%. The Pb coming from the atmosphere and deposited on the surface of plants leaves easily penetrates into plants, including into cells (Kabat-Pendias and Pendias, 1984), but further transfer from leaves to other parts of plants does not occur, because one of Pb toxic effects is a change in cell membranes permeability.

The ^{137}Cs isotope, as K chemical analog, easily enters the intracellular space through specific K^{+} ion transporters and distributed approximately equally between fractions I and II: 57% and 38-40 %. The contents of ^{137}Cs in fractions III+IV do not exceed 2.2%.

The ^{7}Be isotope is mainly concentrated in the extracellular (II) fraction, where its content can reach 80-90%. The reason for this, most likely, is the small ionic radius of the Be, which allows the Be^{+} ion enter the cell through Mg^{2+} and Ca^{2+} ion transporters. The isotope's entry into cell occurs at a sufficiently high rate, taking into account the ^{7}Be half-life. It can be explained by the high affinity of Be for phosphate groups and active centers in ATP (adenosine triphosphate) and ADP (adenosine diphosphate) as universal sources of energy for all biochemical processes (Kabat-Pendias and Pendias, 1984). In the intercellular (I) fraction, the content of ^{7}Be varies from 7.8 to 17%, with cell walls and an insoluble residue (III+IV fractions) no more than 5% of ^{7}Be is associated.

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Content of ^{137}Cs in components of floodplain biogeocenosis in the Krasnoyarsk MCC middle impact zone

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We investigated the ^{137}Cs distribution in floodplain biogeocenosis components (soil, rhizosphere, aerial parts of coastal plants) in the Krasnoyarsk MCC middle impact zone (20-250 km downstream from KMCC). From beginning of the middle impact zone (Kan River mouth) to Novokargino village, the substrate ^{137}Cs specific activities are almost identical: 17-70 Bq kg^{-1} in soil, 15-40 Bq kg^{-1} in rhizosphere. There is an obvious increase in the ^{137}Cs content in the substrate towards the far boundary of the middle impact zone. On the shore of Lopatin Island near Strelka village (the confluence of the Angara River and the Yenisei River), the ^{137}Cs specific activities in soil and rhizosphere are 2000 and 1000 Bq kg^{-1}, respectively. Below the confluence of the Angara River on coast of Gorodskoy Island in Yeniseisk city the ^{137}Cs specific activities in soil and rhizosphere are 190 and 230 Bq kg^{-1}, respectively. The background content of ^{137}Cs in the substrate is 15 Bq kg^{-1} (Shivera village, 5 km upstream from the MCC).

The wide variation of the isotope content at several neighboring sample points can be explained by differences in the hydrological regime: conditions favorable for the fallout of silt leads to increase in the isotope content in the substrate.

The ^{137}Cs content in the upper parts of the coastal sedge (*Carex* L.) varies from 1.1 to 26 Bq kg^{-1} and does not have such clear trend to increase with the distance from source of isotope input to the floodplain biogeocenosis. However, in points near the border of the middle and near impact zones, increased the isotope contents in the upper parts of plants correspond to a decrease its content in the substrate and vice versa. Apparently, there is a change in speciation of the isotope. ^{40}K as chemical analogue of Cs should behave similarly in the system; ^{40}K and ^{137}Cs distributions in the substrate more or less correlate with each other, but in the upper parts of plants, the ^{40}K distribution is opposite to the ^{137}Cs distribution in almost all sample points.

To verify our assumption, we examined the change of ^{40}K and ^{137}Cs transfer factor (TF). For both isotopes, TF does not exceed 1.000 and correlated with isotopes contents changing in upper part of plants. However, in two sampling point, the ^{137}Cs TF sharply increase by contrast ^{137}Cs content decrease in the substrate; so ^{137}Cs is present in easy mobile form and form easily accessible to plants. Most likely, due to floods there is a constant ^{137}Cs influx into the soil layer, from top to bottom, in sample places with low TF. At the same time there is constantly flushes out some part of the isotope that managed to pass in mobile or easily digestible by vegetation forms under the influence of the plant rhizosphere, but did not manage to be absorbed by the plant.

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From vulnerability to resilience in CBRN risk management

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Understanding the determinants of CBRN risk is the first component in promoting and strengthening the concept of CBRN resilience at the level of individuals, organizations, regions and states. As defined by UNISDR, vulnerability represents the conditions of an entity determined by physical, social, economic and environmental factors or processes which increase the susceptibility of an individual, a community, assets or systems to the impacts of hazards. At the other hand the same strategy defines the resilience as ability of a system, community or society exposed to hazards to resist, absorb, accommodate, adapt to, transform and recover from the effects of a hazard in a timely and efficient manner, including through the preservation and restoration of its essential basic structures and functions through risk management. The aim of this paper is to present the CBRN risk mitigation activities with a dual purpose: vulnerability reduction and resilience betterment. The key finding of this paperwork shows that there is a constant need of strengthening intrinsic resilience capacities of one society in order to effectively mitigate CBRN risks. In this sense, the proper application of CBRN risk management methods facilitates their effect.

Merging the requirements of radiological safety standards into an integrated safety management system

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Integration of existing safety standards/systems is considered as an indispensable process in all complex organizations, in order to enable efficient use of available, usually limited, resources of protection, and to adequately respond to the occurrence of adverse events and reduce their effects on employees, working conditions and the surrounding environment. An integrated safety management system, with complex management mechanisms, requires effective integration process to be implemented. In this sense, radiological safety should not be treated as an independent organizational activity, but should be included in all activities within the organization as an integral part thereof. An integrated safety management system is significant in all complex organizational structures, because it enables much more efficient use of organizational, human and technical resources. Working together in an integrated system, which involves the exchange of acquired knowledge and experience on protection, the occurrence of adverse events, occupational safety issues, is very important in the process of merging the radiological safety into the existing integrated safety management system. The aim of this paper is to analyze and present the most prominent radiological safety standard requirements, as well as to identify the common system procedures that are to be implemented at the organization scale.

Anomalies of the axial skeleton structure of the common roach (*Rutilus rutilus*) in water bodies contaminated with radionuclides

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Radioactive contamination is one of the main anthropogenic stressors of aquatic ecosystems within the Chornobyl Exclusion Zone (CEZ), which necessitates to study of deviations in the development of aquatic organisms. The common roach (*Rutilus rutilus*) is the one of the most widespread and numerous fish species in the European water bodies. Due to intensive accumulation of ^{90}Sr (chemical analogues of calcium) and transuranic elements by the bone structures of animals in the CEZ, the skeletal disorders can be one of the main problems in the development of fish and affect their morphology, growth and survival. The purpose of this study was to identify the main forms of skeletal development anomalies in the juvenile roach under long-term radiation exposure in water bodies within the CEZ. All sampled specimens were cleared and stained with alizarin red S by T. Potthoff method (1984). The studied young fish were on D_2, E and F stages of development and sampled from the north-western part of the Chornobyl NPP cooling pond (CP) and Yanivsky backwater within the CEZ and from Pidbirna Lake (environs of Kyiv City) with background levels of radioactive contamination as reference water body. The current absorbed dose rate due to main dose-forming radionuclides for parental fish from the CP on average was 17.4 μGy h^{-1}, from Yanivsky backwater - 8.7 μGy h^{-1} and from reference lake - 0.06 μGy h^{-1}. Anomalies such as ribs deformations of various degrees, additional processes of neural and haemal arches and their bifurcation, partial or total vertebral fusions, deformation of the spine etc. were found. Among the observed anomalies in fish from all studied water bodies, the rib deformities consequence prevailed: Pidbirna Lake - 93%; CP - 95% and Yanivsky backwater - 98% of the total individuals. At that the degree of complexity of this anomaly was different. In reference lake the deformation of the ribs was least expressed. Also, among the anomalies, the appearance of additional processes of neural arches was determined: Pidbirna Lake - 15%, CP - 13% and Yanivsky backwater - 22% of the total individuals. Among the revealed deformation of the spine for juvenile fish was noted: lordosis in Pidbirna Lake (11%); kyphosis in the CP (23%) and scoliosis in Yanivsky backwater (16% of the total individuals). In addition for the juvenile common roach from contaminated water bodies the multiple and severe vertebral anomalies, as well as deformation of neural and haemal arches were discovered. As a result of our studies the 13 types of anomalies localized in two parts of the skeleton were diagnosed. It was found that the number of observed anomalies depends from the level of water bodies' contamination and radiation absorbed dose rate for fish. The individual spectrum of anomalies for the reference water body did not exceed 4 anomalies per individual, and for contaminated water bodies there were cases of 5-7 anomalies per individual, and also multiple vertebral anomalies.

Diagnosis and treatment of patients with renal cell carcinoma with renal vein and/or inferior vena cava involvement

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Introduction. A distinctive feature of renal cell carcinoma (RCC) is the frequent, compared with other tumors, spread of the tumor through the venous collectors (along the renal and inferior vena cava (IVC) up to the right atrium), as the path of least resistance to invasive growth.

Objective: to analyze the data of patients with RCC with tumor invasion of the renal and/or IVC and to evaluate the possibilities of radiology.

Materials and methods. In A.V. Vishnevsky NMRC of Surgery 35 patients with RCC with tumor invasion of the renal and/or IVC were treated. At the preoperative stage, all patients underwent US, MSCT and MRI. All patients were operated on.

Results. Tumor thrombus were distributed according to the Mayo Clinic classification: 0 - 10 patients; I - 4; II - 8; III - 10; IV - 3. The damage of the only kidney with venous thrombosis was at 5 patients (nephrectomy of the contralateral for cancer - 3). Tumor thrombosis was combined with metastases at 14 (40.0%) patients (synchronous/metachronous). Target organs: lungs-6; liver-5; adrenal gland-4; lymph nodes-5; pancreas-1; diaphragm leg-1. Process prevalence: metastases in one organ - 9 cases; in two - 2; in three - 3.

Based on the analysis, an algorithm for evaluating a tumor thrombus was developed:

Stage I (preoperatively, US, MSCT / MRI).

- When a kidney tumor with central location is detected, especially with the involvement of the sinus, the lumen of the renal vein is evaluated for the possible presence of tumor thrombosis.

- When they are detected, the level of spread of the tumor thrombus is evaluated. If a thrombus is detected in the IVC, its lumen is evaluated along its entire length to determine the extent of the lesion and the level of thrombus head localization is clearly fixed (note if it is not one).

- When the tumor thrombus spreads to the diaphragm level, it is assessed whether there is its spread in the heart cavity.

It is necessary to note the presence / absence of thrombus biases in the IVC (forced breathing), identify fixation areas if possible.

- Obligatory assessment of the structure of the thrombus and the degree of vascularization.

Stage II (intraoperative US-study).

- After isolation of the IVC, the localization of the thrombus head is assessed with reference in mm to the anatomical structures.

- After clamping the renal arteries and veins, the localization of the thrombus head relative to the previously selected anatomical structure is also assessed, fixing whether there has been a shift as a result of a reduction in blood flow.

Conclusion. Despite the technical complexity of nephrectomy with thrombectomy from IVC, especially in the presence of a supraphrenic spread, they have no alternatives when achieving radical treatment. An important aspect of the preparation of such patients is the step-by-step follow-up of the patient using radiology methods, which makes it possible to determine the exact volume of the lesion and non-invasive assessment of the surgical treatment results.

Evaluation of the reasons for urinary stenosis: Possibilities of radiology

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Background: to evaluate the possibilities of radiology in assessing the causes of ureteral stenosis.

Materials and methods. Ureter diseases are rarely detected. In four large Russian clinics 47 patients with such lesion were treated in 2014-2018. Of these, in 14 (29.8%) cases, ureteral stenosis was diagnosed, in which there were "creeping" changes in the walls without extraorgan spread. All patients underwent US, MSCT and MRI.

Results. US allows to determine the level of ureter damage due to expansion above stenosis. It is practically impossible to differentiate the tumor and fibrous nature of the lesion at US, since the volume of the lesion is insignificant and, even if visualization of the violation of the wall layers differentiation is visualized, it is difficult to detect bloodflow in the tumor tissue, due to the extremely small caliber of the tumor vessels. It was possible to register the bloodflow at US in 2 cases only, in 1, a long-standing kidney stone disease (KSD) formed an inflammatory cushion around the ureter with increased bloodflow. The level of damage and the ureter dilated higher was also diagnosed in MSCT and MRI in all cases, tumor lesion was diagnosed in 4 cases, KSD in 6 A urothelial tumor diagnosed in 4 (28.6%) cases, KSD confirmed by calculi in the kidney in 6 (42.8%), it wasn't possible to determine the cause of ureteral stenosis (the tumor was excluded) in 4 (28.6%).

With damage to the ureter muscle layer, the nature of the ureteric discharge can significantly change. Ureteric discharge is observed in CDI at transabdominal US (transrectal if necessary). The absence of ureteral discharge in all cases indicated both obstruction of the ureter and damage to the muscle layer. With incomplete obstruction, the nature of the ejection changed, asymmetry was revealed in the frequency, intensity and direction of the ejections. Damage to the muscle layer of the ureter was suspected in 6 cases.

All patients were treated: urothelial cancer - radical surgery (n=4) with plastic in 2; stenosis of the ureter due to KSD in 4 cases and stenosis of undiagnosed etiology in 4 - stenting of the ureter; in 2 cases with KSD - resection of the ureter with plastic surgery. Comparison the morphology of ureteral stenosis and ureteral discharge data: the muscle layer is damage - the flow is at an angle <45°, has a rounded apex and non-intense staining; in the absence of the muscle layer damage - the flow is at an angle >45°, has a sharp peak and intense staining. The ejection frequency didn't depend on the wall lesion volume.

Conclusions. Currently, it is difficult to differentiate the damage to the muscle layer of the ureter with its stenosis (tumor or fibrous) according to radiology at "creeping" damage. The nature and quality of the ureteric discharge from the damage side may be differential diagnostic sign. However, this symptom allows you to differentiate the lesion of the muscle layer, but doesn't allow to determine the nature of the lesion.

Spleen cysts and cystic lesions: Differential radiology diagnosis

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Background: on the basis of the analysis of a significant number of spleen cysts and cystic lesions (C&CL), to assess the possibility of differential radiology diagnosis of individual morphological forms.

Materials and methods. In A.V. Vishnevsky NMRC of Surgery 289 patients with C&CL from 15 to 77 years old (women prevailed (68.2%) were examined and treated (1998-2019). All patients underwent ultrasound, MSCT and/or MRI were performed depending on the difficulties of differential diagnosis. Most of the patients underwent surgery - (82.0%), uncomplicated spleen cyst of insignificant size performed dynamic observation (verification by puncture biopsy).

Results. Morphological verification of C&CL (generally accepted differential diagnosis of "true" and "false" cysts based on histological detection of the epithelial lining is not always possible, because if they exist for a long time, the cell lining of the cyst may atrophy under the pressure of the contents or, when the inflammatory process is attached, it can be shed during the operation or during puncture and evacuation of contents)-151; true cyst-23; mesothelial cyst-4; dermoid cyst-3; pseudocyst-16; pancreatogenic-33; echinococcus-21; lymphangioma-24; lymphoma-9; ovarian cancer metastasis-2. When analyzing data from radiology research methods, differential diagnostics comes to the forefront according to MSCT data. The evaluation was carried out according to two parameters: lesions' capsule and the nature of the liquid contents (Table 1).

Table 1. Comparison of data obtained

Nosology	Liquid component (native phase)	Lesions' capsule
Cyst	0 - +15	thin-walled, doesn't accumulate contrast medium (CM)
True cyst	+15	thin-walled, doesn't accumulate CM
Mesothelial cyst	+35 - +60	thin-walled, doesn't accumulate CM
Dermoid cyst	-10 - +40	capsule is expressed unevenly, can be very dense, with calcium, doesn't accumulate CM
The malignant dermoid cyst	-10 - +40	capsule is expressed unevenly, can be very dense, with calcium, accumulates CM in the arterial and venous phase
Pseudocyst	+10 - 40	thick dense capsule, calcium inclusions are possible, doesn't accumulate CM
Pancreatogenic	+10 - +50	capsule is uneven, calcium inclusions are possible, doesn't accumulate CM
Echinococcus	+25	bypass capsule, doesn't accumulate CM
Cystic lymphangioma	+25 - +45	thin-walled, doesn't accumulate CM
Lymphoma	+15 - +40	true capsule missing
Ovarian cancer metastasis	0 - +15	unevenly expressed capsule, accumulates CM in the arterial and venous phase

Malignant tumors were revealed in 3 cases: malignant epidermoid cyst - 1; ovarian cancer metastasis - 2.

Conclusions: primary and parasitic spleen cysts are well differentiated according to radiology; false spleen cysts, depending on the cause of their occurrence, can create difficulties in their identification and differentiation; cystic tumors of the spleen should be differentiated with malignant lesions and metastases with cystic structure, when they are detected, there should always be a similar alertness.

Clinical evaluation of a Monte Carlo software for patient specific QA in VMAT

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The verification of radiotherapy plans is an essential step in the treatment planning process, and Patient Specific QA (PSQA) is very important in the RT workflow, especially for highly conformal plans which produce non-intuitive fluence maps and complex 3D dose distributions. However, conventional PSQA process to measure data prior to patient treatment and verify the accuracy of dose calculations is intensive and fairly time consuming for clinical staff and is improper for busy radiation therapy centers. Moreover, time-machine necessary for the phantom-based measurements is stolen from treatment patients time. The innovation proposed within this work is to introduce a new MC software (SciMoCa) in the RT workflow, which can be used as a fast-secondary dose check and an independent plan QA evaluating tool. The aim of the study was to evaluate the accuracy of SciMoCa dose calculation and the feasibility of the MC-based PSQA for VMAT treatment plan in clinical workflow.

SciMoCa was benchmarked against TPSs (Monaco and Pinnacle, based on MC and CCCS dose calculation algorithm, respectively) in use in our clinic and measurements. SciMoCa uses DICOM RT suite, namely the CT dataset, plan and structures, exported from TPS to perform an independent dose calculation on patient or phantom CT geometry. All software were commissioned for the same 6MV Elekta LINAC using same measurement set.

50 patients of six clinical classes (CNS, H&N, breast, lung, prostate and bone metastasis) were randomly selected from clinical database and computed with dose engines using same calculation parameters. Dose accuracy and dose distributions were evaluated by assessing isocenter point dose differences and statistics of 2D gamma index (GI) analysis, respectively.

Measurements rely on ArcCHECK phantom, to evaluate dose differences in a homogeneous phantom and SciMoCa performances respect to the current treatment plan verification paradigm. Comparisons were performed with the same setting as before.

On average, percent dose difference between TPS and SciMoCa is -1.8±1.8% (Monaco) and -0.5±1.1% (Pinnacle) while software to ionization chamber measurements is -0.6±1.7%, 0.4±1.4% and 0.8±1.7% for Monaco, Pinnacle and SciMoCa, respectively.

Comparing the SciMoCa dose distributions to those of Monaco and Pinnacle, average GI are 94.5±5.4% and 96.5±3.5%, respectively. Comparing TPSs and SciMoCa to ArcCHECK measurements, on average GI is 94.0±3.3% (Monaco), 95.3±2.5% (Pinnacle) and 93.1±3.2% (SciMoCa).

A very good agreement was found between SciMoCa, TPSs and measurements. This innovation provides an accurate secondary dose verification system and it could become a fast and positive chance for the PSQA, saving a lot of time both for physics and machine. This method allows to measure only those treatments that do not pass the minimum acceptance criteria. It could also be useful in adaptive RT for checking the impact of the approved RT-plan on the daily patient anatomy modifications.

Health risk related to environmental and clinical radon sources: Necessity to increase public awareness

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Introduction. Lung cancer is associated with high levels of incidence and mortality both in men and women. Despite the fact that a mortality percentage of approximately 80% due to lung cancer corresponds to smokers, mortality level is also significant in the group of non-smokers. The radioactive radon gas constitutes the most important environmental risk for lung cancer development for the whole population, also being no. 1 risk for non-smokers.

Purpose. The aim of this study is to review the current literature, in order to systematically present data regarding radiation burden and the corresponding risk due to exposure to radon and radon progeny. Radon sources might be either environmental or medical practices adopted in a hospital environment.

Materials and Methods. 22 large-scale studies that have been carried out worldwide, aiming to examine the consequences of radon exposure to human health were reviewed.

Results. Increasing residential radon exposure by 100 Bq/m^3 has been correlated with an excess relative risk of lung cancer development equal to 11% in USA-Canada studies, 16% in European Union studies and 33% in studies carried out in China. Additionally, the synergy of smoking and radon exposure as far as lung cancer development is concerned has been proved, which has led official bodies to establish acceptable threshold levels of radon concentration. For instance, WHO has set the reference radon concentration at 100 Bq/m^3 (or 2.7 pCi/l), whereas the action level of EPA has been set at 148 Bq/m^3 (or 4 pCi/l). Finally, radionuclide therapies being conducted in Nuclear Medicine Departments are present, during which high levels of radon concentration are generated in the course of patients' exhalation (~2 MBq/m^3).

Discussion. The significant mortality due to lung cancer is possible to decrease by increasing public awareness about the role of living-working in places with increased values of radon concentration, in addition to the well-known and widely accepted role of smoking. It is absolutely essential to conduct expert measurements of radon concentration in buildings that already exist (residences, educational institutions, workplaces) and adopt radon mitigation techniques as required. In addition, incorporation of radon-related measures during the process of upgrading the national building code can be extremely important, because it will facilitate the compliance of new establishments with internationally acceptable norms.

Radon anomalies as precursors of a recent earthquake: A case study of Kosovska Mitrovica environment

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Spike-like peaks in the concentration of radon gas prior to a major earthquake are attributed to release different gases (CO_2, CH_4, H_2S, SO_2, H_2 suitable for the transport of radon to the earth's surface) due to pre-seismic stress or fracturing of the rock. Passive radon technique based on charcoal canister test kit conducted in the environment of Kosovska Mitrovica in summer and autumn period showed inexplicable results. Since radon levels are sensitive to short-term fluctuations, an active technique for indoor radon monitoring was performed with RAD7 device (Durridge Company Inc.) in two selected sites (at 2 km distance) from 11-13 November 2019. Radon results for one measuring site in two proceeding days varied: from 103±44 Bq/m^3 during the afternoon; then strongly increased to 2843±217 Bq/m^3 in the midnight, afterward dropped to 1449±104 Bq/m^3 in the morning over the time scale of one day. These radon anomalies occurred within 1 hour for another site: from 200±94 Bq/m^3 to 2146±262 Bq/m^3 and radon values abruptly decreased in another day to about 40 Bq/m^3. We consider that these changes in radon levels have been precursors of an earthquake of M_L=6.4 which occurred in Albania (41.315°N, 19.479°E, H = 7 km), approximately 13 days later. It was preceded by a few weaker earthquakes (M_L>4.0), and a series of small earthquakes still appearing. The existence of deep fault zone and seismotectonic zone in Kosovska Mitrovica environment allow radon transport through fissures due to pressure gradient. These results showed that indoor radon measurement can be a useful predictor in an earthquake occurrence, even at a distance of 200 km.

Relationship between outdoor radon concentrations and meteorological parameters

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In order to establish radon levels in outdoor atmosphere radon measurements were performed during the fifteen days by alpha spectrometric measuring method with detector Airthings Corentium Home. Measuring point was at 0.5 m height. Since meteorological conditions can have a significant impact on radon measurements, parameters such as temperature, humidity, precipitation, wind speed were also noted by SENCOR SWS 9700. The results of short term outdoor radon concentration were read out daily and varied from 4 Bq/m^3 to 23 Bq/m^3 (values were averaged from hour to hour), until values of long term measurements (averaged daily) varied from 13 Bq/m^3 to 21 Bq/m^3. Average outdoor radon value strived to 15 Bq/m^3. During the measurements temperature ranged from 7.1-16.5°C, humidity varied from 62-95%, barometric pressure had a span from 710.6-753.2 mmHg. A weak correlation was found between outdoor radon levels and temperature (r=0.312). No correlation was found between outdoor radon levels and other meteorological parameters like humidity and pressure. The highest value of short term radon activity concentration was noted in a day with the lowest temperature, and highest humidity (and during the precipitation). Since precipitation presents a barrier to radon penetration through soil pores, at relatively high humidity the concentration of radioactive aerosols in the ground air layers are higher than radon concentration.

Calibration of recycled open-faced charcoal canisters for two- and one-day radon concentration measurements

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Charcoal canisters have been used for indoor radon concentration measurements for more than 40 years. Although there are several methods that use charcoal canisters, the basic principle is the same. As air passes through the canister, radon is being adsorbed and the quantity of adsorbed radon is proportional to the radon concentration in air. Radon canisters can be modified in different ways, e.g. by adding diffusion barriers, and different techniques can be used for counting. The method used in Vinča Institute of Nuclear Sciences (VINS) uses open-faced canisters, which are measured on gamma spectrometers, according to US EPA method. In this method, it is necessary to wait 3 hours after closing the canisters in order to reach equilibrium, because radon is determined via gamma emissions of radon progeny - ^{214}Pb and ^{214}Bi. Canisters are commonly exposed for periods between 48 hours and 144 hours.

Open faced radon canisters are typically used with calibration factors provided by manufacturers, or with EPA calibration factors. Calibration in EPA method is performed with canisters as received from manufacturers, but most laboratories recycle canisters by drying in order to reuse them. Since calibration factor is calculated based on the canister mass change (due to water adsorption) and duration of exposure, different moisture content due to recycling may introduce a bias in the measurement. A correction for this influence might be necessary. In order to investigate this effect, recycled canisters used in VINS have been exposed to different radon concentrations in a radon calibration chamber in Montenegro Bureau of Metrology. Exposures lasted for 48 h and the results have been used to assess the validity of used calibration factors. Additional measurements lasting (24±2) h have been performed at several selected measurement locations, covering two orders of magnitude of concentrations. Simultaneously, concentrations were measured with an AlphaGUARD detector, which was used as a reference instrument. This experiment allowed determination of calibration factor for short term measurements lasting 1 day. It is, however, necessary to perform additional study of uncertainty before using charcoal canisters for one-day measurements.

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Continuous measurements of indoor radon concentration with CR-39 detectors in two thermal spas – A case study

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Radon (^{222}Rn) is a radioactive gas, which may be found in indoor environments such as caves, homes, schools, and workplaces. It is produced from the natural radioactive decay series of uranium (^{238}U), which is found in several types of soils and rocks such as granite and volcanic ones.

In Portugal, the geological settings are mostly comprised of granite rocks with uranium mineralizations, which represents a potential risk for the exposure to high indoor radon levels, particularly in some specific regions.

Radon is the most important cause of lung cancer after smoking. It is estimated that radon is responsible by 3 to 14% of the lung cancers occurrences in a country, depending on the average radon level and the smoking prevalence.

In Portugal, the increasing concern about indoor air as a vehicle for pollutants and contaminants has become very important in recent years. Therefore specific law was published accordingly (Ordinance Nº 353-A/2013) and replaced the existent non-specific one (Decree-Law Nº 79/2006). It standardizes all procedures related to the operation and maintenance of the IAQ (Interior Air Quality) in several situations. The Portuguese Decree-Law Nº 108/2018 transposes the EURATOM Directive 2013/59 establishing the legal regime for radiological protection, setting the rules safety precautions for protection against the dangers arising from exposure to ionizing radiation.

This study addresses the radon concentration in the indoor air of thermal spas. The assessment was performed with a passive method for all therapy rooms and technical areas within two establishments (Spa “A” and Spa “B”). Radon measurements were carried out with solid-state nuclear track detectors (SSNTDs), such as CR-39, for approximately 12 months covering continuous periods. The CR-39 detectors were enclosed in small cylindrical (5-cm height, 3-cm diameter) diffusion chambers and placed at approximately 1.5 meters from the ground.

In the case of the thermal spa “A”, the measurements took place in two periods: 1) winter - 21/12/2018 to 15/04/2019 (113 days); 2) Spring / Summer - 15/04/2019 to 26/08/2019 (102 days).

In the thermal spa “B” the measurements took place simultaneously in the two buildings between 15-04-2019 to 26/08/2019 (102 days). The overall study is to be finished by January 2020.

The results showed that 94 % (17/18) of the indoor air radon concentration values of spa A do not comply with Portuguese legislation (300 Bq/m^3) and that 100 % of the sites do not comply with WHO recommendations for radon concentration in indoor air (100 Bq/m^3).

However, concentrations within the thermal spa vary widely, with a minimum of 280 Bq/m^3 and a maximum of 1941 Bq/m^3. In the Berthelot therapy rooms (application of the heat and thermal steam in the vertebral region), nozzle shower, Vichy shower and ORL’s spaces the radon concentrations in the indoor air are higher than in the other spaces. The explanation for these results is due to the fact that, in these places, there is the use of natural mineral water, which can also be an additional source for radon presence.

Is z-score adequate for evaluation of laboratory achievements in proficiency tests covering radioactivity measurements?

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Proficiency testing (PT) is perceived as the most important tool for the assessment of laboratory measurement achievements. So, adequate performance indicators are needed for the reliable evaluating the laboratories. One of the most popular and most commonly used assessment criteria is the z-score. The biggest disadvantage of this approach is that the measurement uncertainty is not taken into account. An alternative evaluation scheme has been elaborated by IAEA. This method uses accuracy and precision criteria and takes into account the measurement uncertainty estimated by participants. In the present PT study an IAEA reference material (RM) with certified activity concentration values was chosen as a test object. It is homogenous and stable for a long time, thus a sequential PT model with a circulating item could be adopted. Of the 12 results submitted by participants one laboratory obtained an unsatisfactory result in the precision criterion, while obtaining an “excellent” value of accuracy and z-score. The reason for this assessment was too high measurement uncertainty reported by the laboratory. In conclusion, it could be stated that the IAEA methodology in proficiency testing is a precise tool for assessing the results of laboratories conducting radioactivity measurements.

Single-stage radiation technologies for polymer nanofunctionalization

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γ-radiation and electron beam (EB) technologies offer a variety of methods for polymer formulation enhancement. Radiation-chemical method was used for metal nanoparticles (NPs) synthesis in reverse micelle solution (RMS). Metal NPs were chosen as functional nanoscale agents for polymer modification with the goal of influencing polymer granules and textiles desired diverse properties. Extrusion being prime fabrication process in studied of chemically and thermally stable PET textiles production case, suggest demanding requirements (Table 1.) for functional compound additives administered at pre-extrusion stage. Fine talcum powder and silica were successfully tested in a role of carriers for Ag NPs, along with granulated PET itself. The latter proved to be most "compatible" Ag NP-carrier for antimicrobial PET fibers production and justifying nano-smart-concentrate (NSC) approach development for polymer industry formulations.

The system of the object's modification with metal nanoparticles was employed for a) simultaneous processing of γ-irradiated metal NP synthesis in RMS, b) PET granules adsorption properties increase through controlled surface destruction with RMS components combined with irradiation impact, and c) modification of PET granules with Ag NPs in situ during the synthesis of NPs.

Applicable UV-VIS, DLS, HPLC, LIBS, and AFM had been used for the NPs synthesis process control, particle characterization and analysis of NSC granules and extruded strands. Expected antimicrobial and non-toxicity properties of the fibers and non-woven textile samples produced with addition of 10 - 35% of Ag NP PET-based NSC (in NSC CAg=0.00354 m. %) were appropriately tested and validated.

The process control approaches based on radiation dose dependence or reverse micellar system (RMS) parameters tuning, such as micelle's water content, i.e. solubilization coefficient, ω_0, adjustments are discussed. Dozes 25 kGy, or less prove to be efficient for reported application. Both, gamma and EB (with adjustments) radiation single-stage technologies reveal unique potential for effective multifunctional polymer Me NP-modifications in liquid RMS media.

Comparison of thermodynamic pK_{BH^+} values of aromatic benzoylhydrazones determined spectrophotometricaly

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Many chemical, physical and biological properties of organic compounds depend on the interactions of acidic and basic groups present in their molecule. The degree of ionization of molecules in solution at different pH values can be predicted knowing the value of the acid dissociation constant (pK_{BH^+}). The biological activity of hydrazones depends on the ionic form in which they exist in solution influence. The subject of this study was fifteen benzoylhydrazones with different substituents. All investigated hydrazones have following substituents on the benzene ring on the hydrazide part of the molecule: –H, $–CH_3$, $–OCH_3$, –Cl, –OH. Five of them (H_1-H_5) have no substituent on the benzene ring of benzaldehyde, five (H_6-H_{10}) have metohy group ($–OCH_3$), and five (H_{11}-H_{15}) have nitro group ($–NO_2$) on the benzaldehyde group of the molecule.

The investigated hydrazones were structurally characterized by UV spectroscopy, infrared spectroscopy (IR), nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR), as well as, by elemental analysis.

One of the main methods for determining the pK_{BH^+} values of a compound is UV-Vis spectroscopy. The pK_{BH^+} values can be determined from the spectrophotometric data using experimental and reconstructed spectra. The influence of the solvent can be eliminated by employing method of Characteristic Vector Analysis (CVA), which has been tested and proven to be applicable in the analysis of spectroscopic data. The pK_{BH^+} values were determined at three different ionic strengths (0.1, 0.25 and 0.5 mol/dm^3) in acidic media (1K_{BH^+} values were evaluated graphically as an intercept with extrapolation of the curve pK_{BH^+} = f(), to zero ionic strength.

The obtained results showed that there are no significant differences in the values of thermodynamic dissociation constants of investigated hydrazones with no substituent and metoxy group ($–OCH_3$) on hydrazide part of the molecule. Namely, in the molecules of these hydrazones the same substituents (–H, $–CH_3$, $–OCH_3$, –Cl, –OH) are present in *para* position on the benzene ring. The only difference between them is the –H (H_1-H_5) and $–OCH_3$ (H_6-H_{10}) group. The differences in the pK_{BH^+} values (but still not significant) were noticed for hydrazones with -NO_2 group (H_{11}-H_{15}) on the benzene ring of benzaldehyde. Theese hydrazones have lower pK_{BH^+} values, probably due to the influence of the $–NO_2$ group in their molecule. The obtained pK_{BH^+} values were in accordance with those for similar class of compounds.

Keywords: UV-Vis spectroscopy, Characteristic Vector Analysis, protonation, thermodynamic dissociation constant

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QSPR analysis of substituted hydrazones using experimentally determined constants of protonation and set of physicochemical descriptors

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The hydrazone functional group (C=N–NH-), has been involved a great deal of interest because of its ease of synthesis, modularity and functional diversity [1]. Configurational isomerization of the C=N bond, nucleophilicity of the hydrazone nitrogen, electrophilicity of the imine carbon, and acidity of the N–H proton, are functional characteristic that make hydrazone useful for diverse applications, ranging from biology (such as pharmacology), materials science to supramolecular chemistry.

The chemistry of hydrazones always attracts the investigators, as incorporation of these moieties in medicinal compounds due to their biological potential [2]. The hydrazones are known to exhibit wide variety of biological activities: used as antibacterial agent, anti-tubercular agent, analgesic, anti-inflammatory agent, antiviral agent, antifungal agent, muscle relaxants and antihistamines etc [3,4]. Some new synthesized hydrazone derivatives of coumarin-derived pyrazoles are good inhibitors of MRSA and B subtilis [5]. According the literature hydrazone derivatives of eugenol possess significant anti-tubercular potential [1].

According the literature, a hydrazone photos was integrated into a liquid crystal to yield a polymer network that responds to light with large shape transformations [6]. QSPR (Quantitative Structure - Property Relationships) analysis of a series of 15 *p*-substituted aromatic hydrazones was performed using experimentally determined constants of protonation (pK_{BH}+) and set of physicochemical descriptors.

The pK_{BH}+ values were determined numerically from the absorbance values of the experimental spectra by characteristic vector analysis. In order to obtain thermodynamic pK_{BH}+ values, measurements were performed at ionic strengths of 0.1, 0.25 and 0.5 M ($NaClO_4$). Surface tension, Molar Refraction, Molar Volume, Parachor, Index of Refractivity, Density and Polarizability were selected as set of physicochemical descriptors.

Multiple linear regression method was used to linearly correlate the selected descriptors and pK_{BH}+ values. Several well-known variable selection methods: stepwise, forward, backward and best model selection methods were performed by XLSTAT program package. Preliminary statistically assessment of the QSRR models were made according the values of preliminary statistical parameters as correlation coefficients and the standard error of the coefficient of each descriptor and of the global model. Further statistical evaluation of models with the best regression performance was made by: p-values; Fisher test for significance of the equation and Cross-validation squared correlation coefficient.

Six statistically best QSPR model were selected and disused: in all models correlation coefficients is above 0.85; Molar Refraction, Molar Volume and Index of Refractivity are important descriptors for QSPR modeling.

Keywords: QSPR, hydrazone, pK_{BH}+ values, statistical parameters

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Approaches to the treatment of patients with end-stage renal disease in Ukraine

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The number of patients with chronic kidney disease (CKD) is increasing worldwide, with CKD now seen as a global epidemic enhanced by increasing rates of diabetes and hypertension. The World Health Organization (WHO) estimated that there were 230 million people globally with CKD in 2015. This is a concern as it is believed currently only a few countries are able to fully meet the medical needs of these patients. This situation will get worse unless this is addressed as a result of increasing rates of hypertension and diabetes mellitus, especially in lower and middle-income countries (LMICs), which includes Ukraine. It is estimated that by 2030 > 70% of patients worldwide with end-stage renal disease (ESRD) will be in developing countries unless key issues and concerns are addressed.

ESRD contributes significantly to morbidity and mortality, decreasing life expectancy, whilst its management consumes an appreciable proportion of healthcare resources across countries including developing countries. It is estimated that up to 6% of the annual healthcare budget is spent on patients with ESRD in developed countries. The optimal management of ESRD requires renal replacement therapy in the form of either dialysis or renal transplantation. In the context of constrained budgets and rising patient demand for renal transplantation, many countries resort to dialysis as the initial preferred option for the management of ESRD. As a result, dialysis programs have shown an annual growth approximately 10% over the past 20 years in developing countries.

Due to an increase in the prevalence and financial burden of ESRD, a number of countries have undertaken studies to determine the cost of renal transplantation as well as haemodialysis (HD) and peritoneal dialysis (PD). However, these studies have drawn different conclusions, primarily due to the economic differences between high-, middle- and low-income countries. The disparities in the cost of HD and PD between high-income countries and LMICs might be attributed to a number of factors including lower wage rates among healthcare workers in low-income countries, which may result in lower costs of HD when compared with PD. PD will generally also cost less in countries that have capacity for local manufacture of materials used in PD as well as in countries with a higher prevalence of patients undergoing PD owing to economies of scale. This mix of factors will have an impact on overall dialysis costs in each country. Although PD is typically less expensive compared with HD in many parts of the world, the choice of dialysis modality may be influenced by other factors such as patient-population considerations, financial reimbursement, and incentives.

In Ukraine, in 2018, according to the «National Register of CKD Patients», there were 8810 patients with ESRD. Among them, 6765 patients were treated by the hemodialysis (for the first time this year, 1414 patients), 786 patients were treated by the peritoneal dialysis (137 of them for the first time). Kidney transplantation was performed for 1259 patients, of which 112 for the first time.

The accessibility index for treating patients with hemodialysis and peritoneal dialysis in Ukraine is 39% (in the European Union - 92-100%). The prevalence of treatment with these methods in Ukraine is 210 per 1 million of the population, and in the European Union - 823 per 1 million. The rate of ESRD treatment with kidney transplantation in Ukraine is 3 per 1 million people, which is the lowest in Europe (average 32 per 1 million).

Therefore, it is necessary to conduct a comparative analysis of the cost of treating patients with ESRD by kidney transplantation and hemodialysis or peritoneal dialysis to inform future policies in Ukraine.

Comparison of sensory and motor blockade during peripheral nerve blockades with 1.33% liposomal bupivacaine, 1% ropivacaine and 2% lidocaine dexamethasone

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Introduction. Mail goal of nerve blockade is to provide analgesia that will outlast duration of pain as long as possible. Deficiency of currently available local anaesthetics is relatively short duration of action. The aim of this study was to compared sensory and motor blockade after perineural application of liposomal bupivacaine, ropivacaine or lidocaine with addition of dexamethasone during peripheral nerve blockade in Wistar rats.

Materials and methods. A rat sciatic nerve block model was used. The study was conducted in accordance with the principles of Laboratory Animal Care and was approved by the Laboratory Animal Care and use Committee. Thirty adults Wistar rats both sexes studied. After induction of general anaesthesia, sciatic nerves were exposed unilaterally. Sciatic nerves were randomly assigned by the method of sealed envelopes to receive: 2 mL perineurally 1.33% liposomal bupivacaine, 1% ropivacaine or a solution of 2% lidocaine with addition of 4mg/mL dexamethasone. Neurological examination protocol was followed to determine motor function by extensor postural thrust test and nociception by withdrawal reflex.

Results. The rare of recovery of motor and sensory function after perineural administration of liposomal bupivacaine is statistically slower compared with perineural administration of ropivacaine or lidocaine with addition of dexamethasone. Liposomal bupivacaine significantly prolonged analgesic effect when used as a single - injection perineural nerve block.

Conclusion. Liposomal bupivacaine has favourable profile when it comes to the duration of action compared with ropivacaine and lidocaine in combination with dexamethasone.

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