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Simulation of bacterial content kinetics in fish after irradiation

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The use of radiation technology has become a common practice to extend the shelf life of agricultural commodities without compromising the quality of the end product. To compare with other treatment methods ionizing radiation is found to be the most environmentally friendly way of preserving food from spoilage which dramatically reduces bacterial content while preserving the nutritional value of foodstuffs. Being applicable to a wide range of packaged foods, this method has great potential in the food industry. Food irradiation uses gamma sources, bremsstrahlung radiation or accelerated electrons depending on the shape, geometry and density of products.

Considering that food product shelf life is determined by the amount of pathogens, accurate simulation is required to estimate the storage period. Mathematical models used in this study allow to assess the critical level of bacterial content in the processed food after irradiation in different doses to prevent it from spoilage.

This study shows the simulation of bacterial content in minced trout irradiated with 1 MeV electrons at different doses during 15 days of storage at the temperature of (2-4) °C. The model is based on the Lotka-Volterra predator-prey model, which describes the change in the number of two types of bacterial population species over time in the absence of abundant growth medium. The model agrees well with dependencies of viable cell kinetics in minced fish after exposure to accelerated electrons in various doses. This model was also used to estimate the expiration dates of the samples irradiated with doses ranging from 0.24 kGy to 5.6 kGy taking into account the maximum permissible value of pathogens.

Survival of tumor cells after proton FLASH therapy

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Recent preclinical studies have shown that irradiation with electrons and photons in FLASH mode (>40 Gy/s) significantly reduces side effects in normal tissues, but for tumor cells, it is just as effective as irradiation in standard modes (3-5 cGy/s). Today, proton therapy is an advanced method for a variety of tumor treatments. The physical properties of the proton beam make it possible to achieve high conformance of irradiation. Proton FLASH therapy is an innovative treatment method that involves high dose delivery in an ultra-short time. However, proton FLASH therapy is still only at the beginning of the study, and only a few proton accelerators can bring the necessary dose rate. In the Institute for nuclear research of the Russian Academy of Sciences (Troitsk), there is a proton complex that is best suited for flash therapy because it allows irradiation with a record dose rate. In December 2019, the Laboratory of medical physics, INR RAS together with RSCRR and Hospital of RAS (Troitsk) conducted a series of experiments on the irradiation of several types of tumor cells in FLASH mode and conventional mode. Human colon adenocarcinoma (HT-29) and human melanoma (Mel-x) were used as tumor cells. It was necessary to evaluate the effect of proton irradiation mode on cell survival. The main evaluation method applied was the MTT test, which is widely used to assess cell survival and cytotoxicity and is included in most protocols of molecular biology and medicine. Yellow tetrazole was used as a dye. The effects of radiation on tumor cells and unchanged human lymphocytes were compared. According to the results of the experiment, the percentage of survival of each type of tumor cells was determined depending on the dose and radiation regime. Flow cytometry methods were also used to evaluate parameters such as the level of radio-induced apoptosis and the distribution of cells by cell cycle phases. The Annexin V-PI paint was used for this purpose. The preliminary results obtained showed an increase in the level of apoptosis and a delay in proliferation processes in samples of tumor cells exposed to flash irradiation.

Digital mammography: Objective vs. subjective methods of image evaluation

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The constant challenge in mammography is to ensure high image quality while keeping the radiation dose to patients as low as possible. The introduction and subsequent development of flat-panel detectors has brought significant improvement in the field. However, most mammography evaluation methods remain subjective (e.g. visual), and do not take advantage the possibility of more precise digital image processing. In our work, we compared the results of simple visual analysis of phantom structures with two computable parameters: figure-of-merit (FOM) and detective quantum efficiency (DQE).

DQE was internationally accepted by its inclusion in Standard IEC 62220-1-2: 2007 of the International Electrotechnical Commission. DQE calculations are based on measurements of Modulation Transfer Function (MTF) and Noise Power Spectrum (NPS), followed by estimates of detector response in tube load function. Measurements were performed on a Siemens Mammomat Inspiration digital mammography system at MSCNRIO in Warsaw. Consistent with IEC recommendations, an additional 2mm Al filter was used. For MTF evaluation, we used an edge test device designed and manufactured at the NCNR. All calculation procedures were performed on user-friendly, Python-based software developed by NCNR. Additional calculations were performed to ensure that DQE measurements took place at the same detector-air-kerma point as in clinical exposure levels.

FOM is a wide range of parameters that describe contrast information in radiographic images. In this work, we used a version of FOM based on squared contrast-to-ratio (CNR) divided by exposure. CNR was determined as specified in the 4th edition of the European Guidelines. For a contrast object, we placed 0.2 mm Al foil placed on PMMA blocks.

Visual assessment was performed by examining phantom images with exposure levels based on automatic exposure control (AEC) system settings. A tissue-equivalent, anthropomorphic breast phantom was used to ensure clinical conditions of irradiation. The phantom we used mimicked an average firm breast with 50% glandular and 50% adipose tissue. Images were viewed on mammography dedicated displays. We paid particular attention to the visibility of microcalcifications (0.13 – 0.4 mm grains) and fibrous (0.3 – 1.25 mm diameter) elements.

We performed the first measurements and calculation of DQE, FOM and visual assessment of microcalcifications with W/Rh (a tungsten anode with rhodium filter) under clinical exposure conditions. In the next step we plan to use a different anode/filter combination with kilovoltage between 26 and 34 kV in order to assess the influence of target/filter combination on image quality and dose. The goal will be to describe DQE for optimal image quality.

Method of dose modification in foodstuffs during irradiation

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Medical devices and food products are directly linked to the most important aspects of people's life-sustaining activity and health. For this reason, it is necessary to develop and improve the existing methods of sterilization treatment. Radiation sterilization is the most effective and economically successful way of treatment. The international community has a growing interest in foodstuff irradiation to extend the shelf life. A series of researches suggest that food treated with up to 10 kGy retains its nutritional value and contain no toxic substances. However, to enable consistent quality of the product, it is important to carefully monitor the absorbed radiation dose. Failure to ensure the required dose can lead to undesirable changes in physical, chemical and organoleptic parameters.

The purpose of the studies performed in Moscow State University (MSU) in collaboration with Scientific Research Institute of Nuclear Physics is to measure irradiation parameters and doses and find the optimal combination of properties to insure fast and save treatment of food products.

Currently, there is the problem of uneven irradiation of objects of complex geometry. The ratio of the minimum dose to the maximum can reach 5 times. During the radiation treatment of a cylindrical object with a diameter of 7 cm with 9.5 MeV electrons, the minimum dose is 20% of the maximum. In particular, due to such an uneven distribution of the absorbed dose, sausage and meat products in a cylindrical package cannot be treatment. It is necessary to modify the dose distribution and make it more uniform.

This study provides the method for the modification of absorbed dose during 9.5 MeV electron irradiation. The use of correctly selected aluminum plates installed between the irradiated object and the beams of accelerated electrons can ensure uniform irradiation. The programming code GEANT 4 based on Monte-Carlo method was used to estimate the dose absorbed by cylindrical sample. The simulation considered the electron spectrum of industrial electron accelerator as well as the geometry of aluminums plates.

Computer modeling has shown that the developed method allows us to achieve a minimum dose of 60% of the maximum. This ratio of the minimum dose to the maximum is not critical, therefore, the developed method allows radiation sterilization of cylindrical objects at an industrial accelerator with an energy of 9.5 MeV.

Liposomes as the selective transport of the boron-10 into tumor cells for boron neutron capture therapy use

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Boron neutron capture therapy (BNCT) is based on selective accumulation of boron-10 inside tumor cells and subsequent irradiation with epithermal neutrons that results in destruction of only tumor cells. At the same time, surrounding healthy cells are not exposed to the damaging effects of radiation mainly due to lesser boron accumulation [Am J Roentgenol Radium Ther. vol. 36, pp. 1 – 13, 1936]. It is necessary to insert enough boron nuclei into the tumor cells for successful boron neutron capture reaction realization. Nowadays, boronophenylalanine (BPA) and borocaptate (BSH) are widely used for the BNCT method, but they have not selectivity enough to tumor cells. Alternative boron-10 delivery method to tumours is using liposomes [Proc. Natl. Acad. Sci. U.S.A., vol. 110, no. 16, pp. 6512 – 6517, Apr. 2013]. This approach increases boron-10 accumulation effectiveness in the tumor. It was previously shown [DOI: 10.37392/RapProc.2019.07] that the liposomes are absorbed by cells without violating cells structural integrity.

We carried out a series of pre-clinical experiments BNCT on and laboratory animals. The immunodeficient 8-10 week old male SCID mice of the SPF status were obtained from the "SPF-vivarium" Federal Research Center Institute of Cytology and Genetics SB RAS. The Mice were injected orthotopic xenograft human glioblastoma cells (U87). The PEG-liposomes with BSH were used as a drug for targeted delivery of boron-10. The organ of laboratory animals (blood, kidneys, liver, brain and tumor) were analyzed. The evaluation the effectiveness of the accumulation of liposomes-BSH in the tumor and construction the kinetic curves of excretion of drugs were made. The boron concentration was determined by the ICP OES spectrometer (iCAP-6500, Thermo) after acid digestion (HNO_3 or mixture HNO_3 & H_2O_2).

It was previously found the tumor/brain ratio does not exceed 1.1 for BSH [DOI: 10.37392/RapProc.2019.06]. The liposomes as boron transport increase the tumor/brain ratio up to 25-30 times. It should be noted, the boron concentrations in tumors are comparable when using BSH and liposomes-BSH. Thus, delivery boron-10 by liposomes-BSH increases the selectivity and the effectiveness of the BNCT.

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The comparison of the effectiveness of different administration methods of the drug for BNCT

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It is known that selective accumulation of boron-10 in cancer cells followed by epithermal neutron irradiation leads to death of tumor cells without affecting surrounding healthy cells. One of the problems of boron neutron capture therapy (BNCT) is the targeted delivery of boron to tumor cells. The effectiveness of the BNCT depends on many factors including the administration ways of the drug.

In the present report, we describe biodistribution studies that have been carried out with the immunodeficient 8-10 week old male SCID mice of the SPF status. The mice were model orthotopic xenograft human glioblastoma cells (U87). The L-p-borphenylalanine (BPA), borcaptat (BSH) and PEG-liposomes with BSH [DOI: 10.37392/RapProc.2019.07] were used as a drug for targeted delivery of boron-10. For construction the kinetic curves of drug excretions the boron concentration in organ tissues of laboratory animals (blood, kidneys, liver, brain and tumor) was determined by the ICP-OES [DOI: 10.37392/RapProc.2019.06].

The toxicity of standard drugs for BNCT (BSH and BPA) and PEG-liposomes with BSH was studied. The possibility of increasing the therapeutic dose of BPA and BSH was shown. The relationship between a safe therapeutic dose and the method of administration of BPA was founded. The intraperitoneal injection allows one to increase the dose of meds relative to the recommended value: for BPA at least twice (recommended value – 350 mg/kg body weight), BSH – at least 4 times (recommended value – 100 mg/kg body weight) with intraperitoneal injection. The toxicity of developed PEG-liposomal form of BSH was evaluated. No toxic effect in SKID mice was detected (at a dose of 100 mg/kg) and this form of the drug can be used for further research.

The intraperitoneal administration of BPA demonstrates better results in comparison with intratumoral administration. The concentration of boron-10 in the subcutaneous tumor with intraperitoneal administration is 4.4 times higher than with intratumoral administration.

The intratumoral administration of BSH shows grater effectiveness in comparison with the intraperitoneal ways. The concentration of boron-10 in the subcutaneous tumor with intratumoral administration is 2.3 times higher than with intraperitoneal administration.

The results show a high gradient of values at the border of the tumor/healthy tissue.

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In vitro assessment of gamma irradiation effects on regulatory T cells of lymphocyte culture in lymphoproliferative diseases

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Purpose. To assess the sensitivity of regulatory T (Treg) cells of lymphocyte culture to gamma radiation in lymphoproliferative diseases by in vitro tests.

Materials and methods. Primary lymphocyte cultures from peripheral blood of 5 patients between 53 and 70 *years* of *age* were examined. Four samples were taken from patients with chronic lymphocytic leukaemia and one sample was taken from a patient with CD5-negative B-cell lymphoma. The cells were irradiated with *2 Gy*, 4 Gy and 8 Gy at a *dose* rate of 0.98 Gy/min using a Rokus-AM *gamma*-ray *machine* for external beam irradiation. Lymphocytes were cultured in *RPMI-1640 medium* supplemented with *10%* fetal bovine serum, *gentamicin* (400 mkg/ml) and 100 IU/ml of IL-2. Mononuclear cells were incubated at a mean *concentration* of 1.2×10^6 *cells/ml* for 1, 3 and 5 days at 37°C. Treg cells were evaluated according to *expression of membrane molecules* $CD45^+CD4^+CD25^+CD127^{low/-}$ (FACS Canto II, BD Biosciences). Non-irradiated lymphocytes served as a control group. For the comparison of arithmetic means, the single-*factor dispersion analysis* was performed using *STATISTICA 8.0* software.

Results. In the *non-irradiated* control group, 68% of Treg cells survived in cell culture *over* the *5-day observation period*. Over the same time period, 48% of lymphocytes survived. When Treg cells and lymphocytes were exposed to a dose of 2 Gy, their survival rates decreased to 58% and 42%, respectively. Similar survival rates resulted from exposure to radiation doses of 4 Gy and 8 Gy. Thus, the viability of Treg cells was reduced to a lesser degree than that of lymphocytes and was, on average, 18% higher than within the general lymphocyte population. These data suggested that Treg cells were more *resistant to* radiation. The analysis of dose-dependent changes in the percent and absolute numbers of Treg cells demonstrated that the percentage of Treg cells slightly increased with elevation of radiation dose meeting the *threshold* for *statistical significance* of 8 Gy (from 10.2±3.9% of non-irradiated cells to 13.3±4.4% of cells irradiated with 8 Gy; $p < 0.05$). There was no *significant reduction* of *Treg cells* due to a wide range of data in the subgroups ($F_{3/55df} = 0.17$; $p = 0.91$), which pointed to heterogeneity in cell cultures regarding comparison parameters. The mean absolute number of Treg cells in all groups added up to 0.028×10^9 cells/L (*25th percentile*, *75th percentile* – 0.008 and 0.044×10^9 cells/L, respectively).

Conclusion. During the specified cultivation period after irradiation with 2, 4 and 8 Gy, the viability of Treg cells appeared to be higher than that of the general lymphocyte population. *Dose–response* analysis of the absolute number of suppressor regulatory T lymphocytes did not reveal any significant changes in the range of delivered radiation doses. A small increase in their percentage occurred following irradiation with 8 Gy. The obtained data indicate that Treg cells are more *radioresistant* than other types of lymphocytes.

Regulatory suppressor Treg cells in immunopathogenesis of radiation-induced pulmonary fibrosis

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Purpose. The aim of the study was to evaluate regulatory functions of Treg cells in radiation-induced lung injuries.

Materials and methods. A total of 45 patients with radiation-induced pulmonary fibrosis were examined. Their medical history contained information about combination treatment for breast cancer, lung cancer and Hodgkin lymphoma including radiotherapy with total doses of 40-70 Gy. We evaluated T cells and their functional state [CD3, CD4, CD8; activated CD3+HLA-DR+; regulatory T cells (Tregs) including CD45+CD4+CD25+CD127–; naive and memory T cells (CD4+CD45RA+CD45RO–/ CD4+CD45RA-CD45RO+); apoptosis of CD3+CD95+, CD4+CD95+; proliferation according to l*ymphocyte blast transformation*]. Furthermore, B cells (CD19, concentration *of IgM, G, A classes*); natural killer (NK) cells (CD16); p*hagocytosis* of *Staphylococcus aureus were* evaluated too. A group of 50 *healthy persons served as a control*. The factorial and correlation analysis *was performed* using *STATISTICA 8.0* software.

Results. Suppression of T cell-mediated immunity prevailed. There was a *decrease* in both the percentage and absolute number of T cells (*mainly* naive CD4+ T cells) involved in providing anti-infectious and anti-tumor immunity. The *proliferative* potential of T lymphocytes in the l*ymphocyte blast transformation reaction* was reduced. Enrichment of T cell-specific immune memory was suggestive of the encounter with cells bearing viral and tumor-associated antigens. Increased levels of activated T cells and percentages of B lymphocytes, higher *serum immunoglobulin* (IgG) *concentrations* and more intensive phagocytosis pointed to the predominance of humoral responses reflecting an elevated level of the antigenic components in blood circulation.

Patients with pulmonary fibrosis showed a higher percentage of Tregs. *Spearman's* test revealed *multi-directional correlations* between the percentage or the number of Tregs and other parameters of immunity. Increased percentages correlated with decreased numbers of T helper cells, naive T lymphocytes and *T cells undergoing apoptosis* as well as with *T lymphocyte proliferation*. Direct correlations were noted between the percentage of Tregs and the percentage of cytotoxic T lymphocytes and activated T cells. The absolute number of Tregs correlated directly with the numbers of T helper cells and cytotoxic T lymphocytes, their death by apoptosis as well as with the numbers of lymphocytes and memory T helper cells. There wa**s** an inverse relationship between their increased numbers and decreased numbers of activated and *naive* cells of the lymphocyte pool and reduced percentage of NK cells.

Conclusion. Our results suggest that it is necessary to update treatment plans for lung damage after combination therapy. *Important* concepts for the *prevention* of *lung injuries* include new clinical approaches aimed at restoring immunity and protecting tissues from immunosuppressive factors such as elimination of excess Tregs or influence on the mechanisms of their function. It may promote immune recovery, *attenuate inflammatory manifestations* and prevent pulmonary fibrosis.

Gamma tomography of geological samples

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The study of intergranular permeability of granite for the purpose of assessing the safety of the deep deposition of radioactive waste into geological formations enables the characterization of migration processes taking place in the rock environment. Cylindrical samples with a diameter of 50 mm and a height of 10 mm are obtained from deep well boreholes in the monitored locality.

During the so-called diffusion experiment, the sample is placed between two reservoirs, where the inlet tank contains a radioactive tracer (e.g. 134CsCl, 137CsCl, etc.), the output reservoir is inactive (so-called diffusion cell). The sample is exposed to this solution for several weeks to months. The results were evaluated based on Fick's law.

After removal of the samples from the diffusion cell, they were cut to 1 mm slices by diamond saw, in the past. Each slice was then individually studied by autoradiography. The new gamma tomography device SPE-CT, constructed by experts from the Research Center Rez, now allows analysed the sample tomographically, i.e. by a non-destructive method, and display the activity inside the sample in 3D distribution.

The resulting 3D map of the radioactivity distribution can be used to determine the permeability of the sample for water labelled with a suitable radioactive salt. The 3D analysis of the spatial distribution of indicator activity in a geological sample shows the propagation of the indicator along with defects in granite, intergranular permeability of intact granite, etc.

Positron annihilation spectroscopy of irradiated polycarbonate

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The aim of the study was determined interval of the doses when the crosslinking in irradiated polycarbonate prevails and when on the contrary the degradation of polymer chain occurs. Polycarbonate is used as a reusable radiochromic integrating dosimeter for measurements of high doses of ionizing radiation.

In horizontal channels of the Research Reactor LVR-15, Research Centre Rez, pairs of pure samples of polycarbonate of different doses of mixed neutron/gamma field were irradiated. In parallel, other pairs of samples were irradiated with the same doses in Gamma irradiation facility equipped by a 60Co emitter with an activity of 200 TBq. Using alanine, eventual alanine and activation dosimetry, the dose of the photons and of the neutrons were determined.

The irradiated samples were analyzed by positron annihilation spectroscopy (PAS), which gives information about the distribution of free volume sizes in the polymer.

The crosslinking takes effect in a shorter lifetime of positronium, the formation of free radicals in the breakdown of polymer chains leads to a decrease in the probability of positronium formation. The study has shown that both processes can be detected by PAS, as well as the range of doses in which individual process predominates. The results were compared with previously published results.

Testing of the measuring instruments in non-governmental networks for the purpose of environmental monitoring of ionising radiation

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Non-governmental networks for environmental monitoring employ a wide range of radiation protection instruments from different manufacturers, which provide the public with often unreliable dosimetric data. These Measuring Instruments in Non-governmental Networks (MINN) are mostly based on Geiger-Muller tube gas detectors, which represent low-cost easily operated instruments. An extensive testing of these devices was performed in order to validate the data acquired with MINN within the 16ENV04 Preparedness EMPIR project. In total, 16 different dosemter types were selected, with a sample size of four dosemeters per dosemeter type. Performance testing included the energy dependence and the linearity tests of the dosemeter response. Additionally, during the Researcher Mobility Grant associated with the 16ENV04 project, two Geiger-Muller based dosemeter types, with a sample size of two dosemeters per type were included in the testing. These instruments were subjected to the angular dependence testing in both horizontal and vertical planes, besides the energy dependence and linearity tests in the reference Cs-137 field at Physikalisch-Technische Bundesanstalt (PTB). For all the dosemeter types, inherent background, response to secondary cosmic radiation and the response to small changes of dose rate were determined at the metrological facilities of PTB. The sensitivity of the measuring instruments used in non-governmental networks to small variations of the ambient dose equivalent rate was examined by exposing the dosemeters to low dose rate Cs-137, Co-60 and Ra-226 radiation sources, in order to estimate the effect of environmental radioactive contamination with artificially produced radionuclides. For the comparison purposes, besides the measuring instruments used in non-governmental networks, a previously characterized CdZnTe-based spectrodosemeter was irradiated with the aforementioned radiation fields. The measured values were compared with a reference Reuter-Stokes ionisation chamber used for low-dose rate level measurements.

Influence of air gap and chamber positioning on radiotherapy chamber calibrations

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Determination of dose in radiotherapy requires highly accurate dose measurements. Such measurements can only be performed by trained and competent staff, with calibrated equipment and QA/QC procedures in place. Chambers that are used for clinical measurements are usually calibrated in Secondary Standards Dosimetry laboratories in terms of dose to water. Calibrations are performed in water phantoms, usually in Co-60 beams at the depth of 5 cm. Chamber positioning is critical, because deviation from reference position of 1 mm along the beam axis introduces additional standard uncertainty of 0.5%. Deviation from reference position in other two directions is less important – standard beam size for radiotherapy calibrations is 10 cm x 10 cm, and beam non-uniformity within several millimeters of the beam center is usually insignificant.

Chamber positioning can be achieved by using special chamber sleeves, made of PMMA or other water equivalent materials. This allows precise and easy positioning, but only in case that the sleeve is specifically made for the phantom type and chamber type. Other option is using screws and clamps, but human errors are more probable in this case. There is also a high risk for chamber to be tilted along one of the axes, especially for waterproof chambers with rigid plastic-coated cables, which are often curved from storage inside the boxes.

A waterproof IBA CC13 chamber was calibrated in terms of dose to water in Co-60 beam. Even though appropriate chamber sleeve was available, the chamber could not fit due to thicker chamber stem. Chamber was calibrated placed directly in water, by using clamps, and this value was considered as the reference value, because it is obtained according to standard protocols. Chamber was also calibrated in two sleeves designed for larger chambers – first with air gap between chamber and sleeve wall, and second in sleeves filled with water. There was measurable difference between reference position and chamber center in the plane normal to the beam axis – 3 mm and 7 mm for two sleeves.

For both sleeves, calibration coefficient increased when the sleeve was filled with water. The increase was 0.7% for larger sleeve and 0.4% for smaller. Maximum difference between reference value and calibration coefficient obtained when using sleeves was 0.5%. The differences are statistically significant when sleeves are dry, but when sleeves are filled with water, differences are smaller than statistical fluctuations.

The effect of inappropriate sleeve can be taken into account by increasing the measurement uncertainty. In this case, the uncertainty was estimated at 0.5% with rectangular probability distribution and k=1.73. The combined expanded uncertainty of calibration coefficient was increased from 1.2 % to 1.3 %, which is still within the uncertainty goals. This approach can be used for other calibrations, but uncertainty should be estimated in different laboratories and for different chamber types.

Activities of the Polish SSDL in radiation therapy

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The Polish Secondary Standard Dosimetry Laboratory (SSDL) was created in 1966, on the basis of the Physics Laboratory of the Oncology Centre in Warsaw founded originally by Maria Sklodowska-Curie as the Radium Institute in the year 1932. Since its beginning the Physics Laboratory was devoted to developing methods for measurement of radiation delivered to patients treated in the home institute as well as for the control of radiation delivery in other hospitals. The equipment of the SSDL in Warsaw had been acquired with significant support from the IAEA. Since 1988, the laboratory in Warsaw is a member of the IAEA/WHO network of SSDLs, and provides calibration of the therapy level dosimeters with cylindrical or plane-parallel ionization chambers in a Co60 beam, and with well chambers using a Ir192 source. Since 2014, the SSDL in Warsaw is an accredited calibration laboratory according to the PN/EN ISO/IEC 17025 standard and is annually audited by the Polish Centre for Accreditation – a member of ILAC association. The accreditation according to the PN/EN ISO/IEC 17025 standard was also obtained for postal TLD dosimetry audits, which are performed annually in all Polish radiotherapy centres. Due to the activity related to the dosimetry audits, the SSDL in Warsaw collects actual detailed data about the radiation machines, beams and radiation sources, used both for tele- or brachytherapy, in the whole country and keeps such database. Currently, the methods of auditing new and complex techniques, such as intensity modulated radiation therapy (IMRT) modality, are introduced and tested in collaboration with the IAEA. The tested audit methods were developed within the framework of the IAEA projects: CRP E2.40.16 “Development of Quality Audits for Radiotherapy Dosimetry for Complex Treatment Techniques” and CRP E2.40.18 “Development of Quality Audits for Advanced Technology (IMRT) in Radiotherapy Dose Delivery”. The activity of the SSDL and services provided for Polish radiotherapy centres results in a reduction of discrepancies between planned doses and doses delivered to patients. The newly tested IAEA methods of end-to-end on site dosimetry audits allow for monitoring and improving quality of IMRT in Poland. The traceability of standards used for the calibration of therapy level dosimeters from Polish radiotherapy centres is assured by the IAEA dosimetry laboratory. The service provided by the SSDL in Warsaw is highly evaluated by the participants of the organized audits, and by customers of the calibration laboratory in Warsaw. The personnel of the SSDL takes part in workshops and conferences organized by the IAEA in order to maintain a high quality of service, which is provided to radiotherapy centres in Poland.

Cumulative DLP (dose length product) exposure of oncology patients based on the data from the Dose Tracking System – Analysis of 8-year dose data

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Situation concerning cumulative exposure of patients are currently under investigation by international health care community. IAEA has already its technical meeting concerning this topic. Dose tracking systems provides relevant data and facilitate possible systematic analysis of group of patient for which total series of the exposures might be a part of the holistic approach to optimisation and radiation protection.

In our Institute, at the department of Radiology, first DTS has been integrated with one CT scanner in September 2012. This scanner has been replaced in November 2018, same time two other CT scanners (other manufacturer than first scanner) have been integrated with DTS. At the March 2018 new CT scanner, used only for Treatment Planning Purposes, has been installed in Radiotherapy department, and this scanner is integrated with DTS. There is still another CT scanner in Radiotherapy department not integrated with DTS, as well Nuclear Medicine department data are not collected in DTS (including PET/CT scanner). Dose Data from 4D breath gated CT examinations are not available in DTS due to some technical issues.

Cumulative data DLP (dose length product) from CT examinations collected by DTS has been analysed. Total 29146 records have been exported. One record means all cumulative DLP from any CT examinations registered by DTS for specific code "Patient ID number". Our DTS do not allow to automatically track cumulative effective doses. Effective dose can be checked separately for each CT procedure, only for CT scanner currently under operation. Exact estimation of effective dose would require checking of all 29146 records separately. Detailed data from old scanner are not available, but cumulative DLP is stored in data base and accumulated for each "patient ID". It has been found that 1100 records has cumulative DLP higher or equal to 10000 mGy*cm, which is 3.77% of all records exported. 1793 records has cumulative DLP equal or higher than 7700 mGy*cm, which is 6.15%), and this might reflect all the CED (cumulative effective dose) of 100 mSv level. More than 40 records has cumulative DLP that could reflect CED of 0.5 Sv. Effective dose has been roughly estimated using average correction factor determinate for the patient being 15th on the TOP20 list of highest cumulative DLP.

Many of the oncology patients, eg diagnosed with breast cancer, prostate cancer, Head&Neck (larynx) cancer, and Hodgkin Lymphoma, can be treated with great success and therefore their survival time after treatment can be longer than 10 years, therefore their cumulative doses might be of special interest for health care professions. Same time it is necessary to screen those patients in order to control possible secondary cancers or possible metastasis of the disease. This study is the first approach to evaluation of this issue.

Analysis of the TOP20 highest cumulative DLP (dose length product) exposures of oncology patients based on the data from the dose tracking system and other sources of information

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Situation concerning cumulative exposure of patients are currently under investigation by international health care community. IAEA has already had its technical meeting concerning this topic. Dose tracking systems provide relevant data and facilitate possible systematic analysis of group of patient for which total series of the exposures might be a part of the holistic approach to optimisation and radiation protection.

Currently not all modalities might be integrated with dose tracking system (DTS) and therefore analysis of total dose coming from any diagnostic system requires individualized approach. Analysis of patients doses, from TOP20 highest cumulative DLP based on the data from DTS, has been performed. Due to changes in the TOP20 during the time of analysis, a total of 21 patients, 8 female & 13 male, age 38 to 84 (avg. 59) has been taken into account. It has been checked if the patients from TOP20 underwent diagnostic Nuclear Medicine examinations, the data were taken from independent PACS system. Data concerning on-board imaging and CT for Treatment planning purposes, not integrated with DTS, has been derived from ARIA system.

TOP20 Cumulative DLP (from DTS) was in the range of 45023.96 to 73939.74 mGy*cm, estimated effective doses 0.58 Sv up to 0.96 Sv. TOP20 patients underwent 11 up to 19 CT examinations (average 14), during 2 up to 8 years (average 3.5 years). 7 patients additionally underwent NM examinations: 3 patients underwent PET/CT among which one patient had 3 PET/CT examinations in the years 2014, 2016 and 2018; 4 patients had scintigraphy among which one had multiple 6 examinations (2016, 4x2017, 2018). 10 patients from TOP20 underwent radiotherapy treatment and therefore they had additional imaging during the treatment. This includes kvCBCT (2 up to 10 exposition) and EPID-MV imaging. Two of patients who underwent RT treatment had 4D breath gating CT, 5 patients had CT for treatment planning purpose done on the CT scanner which is not integrated with DTS. 16 (of 21) patients has been diagnosed with melanoma, 1 with Dermatofibrosarcoma protuberans, 1 sacroma, 1 (basal cell carcinoma of the skin), 1 breast cancer, 1 HCC (Hepatocellular carcinoma).

It is necessary to screen oncology patients in order to control possible secondary cancers or possible metastases of the disease, therefore CT examinations are performed quite often during the whole process of treatment e.g. in order to assess patient response to performed treatment. Holistic optimisation of the entire series of exposures means finding relevant balance between frequency of the exposure and the dose associated with a single CT, at the same time assuring image quality acceptable for this clinical situation, might be of interest and support process of justification of multiple medical examinations using ionizing radiation.

Tips and tricks to bear in mind while analyzing data from Dose Tracking System – Effective dose estimation issues

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Dose Tracking Systems (DTS) are very practical tools for systematic analysis of the patient doses. Some of this systems are Medical Device according to European legislation (MDD directive), and they are CE-marked. That means Medical Physics Expert should be involved in the commissioning and acceptance tests, preferable, before the clinical use of TPS. One of the DTS has been checked for its internality with Medical Devices (e.g. CT scanners), as well the quality of presented data in the DTS has been checked. 4 CT scanners from two different manufacturers are integrated with DTS. Effective doses are available only for the specific examinations, and no cumulative effective dose is collected by DTS. Conversion factors are fixed in DTS and for CT examinations are derived from Deak et all (Radiology 2010) and Saltybaeva et all (Radiologoy 2014): 0.0019 [mSv/(mGy*cm)] for Head, 0.0052 [mSv/(mGy*cm)] for Neck, 0.0146 [mSv/(mGy*cm)] for Chest, 0.0153 [mSv/(mGy*cm)] for Abdomen, 0.0129 [mSv/(mGy*cm)] for Pelvis, and 0.0004 [mSv/(mGy*cm)] for Extremities. Patient body region, for which effective dose conversion factor is applied, might not be the body region that has been scanned e.g. for some of the abdomen protocol and examinations – the head region has been reported and therefore associated estimated Effective dose has been significantly under estimated even by factor of 5. E.g. For the TOP highest DLP study (8458.31 mGy*cm) effective dose shown by DTS is 16.07 mSv, while 91.56 mSv is the correct number, another study (8340,71 mGy*cm) effective dose shown by DTS is 15.85 mSv, while 77.22 mSv is the correct number. For some of the protocols reported CTDIvol can be determined for incorrect IEC phantoms. E.g. It has been found that for one of the Head examinations the 32 cm body phantom has been used instead of 16 cm head phantom. This results in the underestimation of CTDIvol by factor of 2, leading to the underestimation of DLP and consequently to the underestimation of the calculated effective dose. Is has been found that some of the examination, e.g. 4D breath gating CT studies are not available in the DTS data base even CT scanner report status of the data as 'sent to DTS'. Described above tip-and tricks might be the issue also for other DTS, and therefore involvement of MPE seems to be crucial. Medical Doctors are one of the DTS's users, and therefore specific E&T concerning possible issues with analysis of the data is important. EU legislation – directive 2013/59/EURATOM emphasis MPE as a key professional to provide training to other staff in the topic of radiation protection of patients. Correct use of the DTS can be an important part of this king of E&T. It has to be underlined that systematic analysis and management of patient dose data without DTS tools is almost impossible. Therefore even some practical issues with full integration of DTS in clinical environment, it is recommended to use DTS in daily practice.

The character of radionuclide contamination of the water bodies formed in emergency situations at the Semipalatinsk Test Site

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Water bodies of man-made origin at the Semipalatinsk Test Site (STS) are craters which resulted from nuclear tests and filled with water. Bottom sediments and soil of water bodies formed by aboveground nuclear tests and excavation explosions are, certainly, highly contaminated of radionuclides. But for water bodies resulted from soil subsidence due to emergency situations during underground tests, it remains unclear what are the levels of water and sediment contaminations. This type of water bodies includes boreholes 101, 125 and 104 at 'Sary-Uzen' site and 'Glubokaya' borehole at 'Balapan' site.

According to literature data, during the nuclear underground test with a capacity of 20-150 kt conducted on December 18, 1966, the emergency with the outburst of approximately 10% of the radioactive explosion products into the atmosphere happened in borehole 101 of 'Sary-Uzen' site. Radiation levels on the soil in the vicinity of the borehole exceeded 1,000 R/h [Logachyov V., 1997].

The 70 kt underground nuclear test in borehole 'Glubokaya' at 'Balapan' site was conducted on November 30, 1977. 15 years later, on April 16, 1992, explosive inflammation of gasses occurred due to degasification of carbonaceous rocks in 'Glubokaya' borehole followed by formation of a crater, which was then filled with water. [Velikanov A., 2007]. There was no data on radioactive contamination of the area of borehole 'Glubokaya'. As well as there was no data on radioactive contamination of the area in the boreholes 125 and 104 of the 'Sary-Uzen' site.

Currently, the sizes of craters are as follows: borehole 101 – about 400 m in diameter, borehole 125 – about 150 m, borehole 104 – 15 m long, 5 m wide, 'Glubokaya' borehole – about 30 m in diameter. For this research at each water bodies were 1 to 5 sampling points which sediments and water were taken. The content of ^{137}Cs, ^{90}Sr, ^{241}Am and $^{239+240}$Pu was determined in each sample.

Maximum values of radionuclides are registered in sediments of borehole 101, the ^{137}Cs, ^{90}Sr and $^{239+240}$Pu are about $n\times10^3$ Bq/kg, ^{241}Am – $n\times10^2$ Bq/kg. Minimum values – in 'Glubokaya' borehole (^{90}Sr and $^{239+240}$Pu are about $n\times10^0$ Bq/kg). As a whole, the ^{241}Am varies from less 1 Bq/kg to 600 ± 60 Bq/kg, ^{137}Cs – from less 1 Bq/kg to $(8.4 \pm 1.7)\cdot10^3$ Bq/kg, ^{90}Sr – from less 1.2 Bq/kg to $(3.5 \pm 0.5)\cdot10^3$ Bq/kg, $^{239+240}$Pu – from 2.8 ± 0.9 Bq/kg, to $(5.3 \pm 0.5)\cdot10^3$ Bq/kg.

The content of ^{241}Am in water is less 1 Bq/l. Numerical values of ^{137}Cs are registered in water of boreholes 101 and 125 (0.05 ± 0.01 Bq/l), in other research areas is less 0.01 Bq/l. Numerical values of ^{90}Sr are registered of each area studied from 0.1 ± 0.01 Bq/l to 230±25 Bq/l. The $^{239+240}$Pu varies from less $3.8\cdot10^{-4}$ Bq/l to 1.0 ± 0.3 Bq/l.

Thus, the most contaminated water body is borehole 101 at 'Sary-Uzen' site, next, in the descending order, are boreholes 125 and 104, the least contaminated – 'Glubokaya' borehole at 'Balapan' site.

Estimation of the content of natural and artificial radionuclides in water bodies of the East Kazakhstan region

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The East Kazakhstan region with an area of about 283 thousand km² is among the richest of water resources region of the Republic of Kazakhstan, which is determined by its natural and climatic conditions. The water fund of the region includes rivers, lakes, swamps, ponds and reservoirs. The central place in the hydrographic network of the region is occupied by the transboundary Irtysh River, which flows through the territory of three states: China, Kazakhstan and Russia. The length of the Irtysh River within Kazakhstan is 1698 km. There are more than 700 tributaries in the Irtysh basin, of which 4 are large rivers, the rest are classified as small rivers. The river flow is regulated by a cascade of reservoirs – Bukhtarma, Ust-Kamenogorsk and Shulbinsk.

East Kazakhstan is also a large industrial center, where the basic sector of the economy is non-ferrous metallurgy. The activities of mining, mining and processing, metallurgical and machine-building enterprises, as well as nuclear weapons tests conducted at the Semipalatinsk test site, can have a significant impact on technogenic contamination of the aquatic environment in the territory of not only this region, but also outside it.

According to Kazhydromet, the water fund of the East Kazakhstan region has a “moderate and high level of pollution” in chemical indicators: exceeding the maximum permissible concentrations of sulfates SO_4^{2-}, nitrites NO_2^-, ammonium NH_4^+, and some heavy metals (Cu, Zn, Mn). However, the radiation indicators of water bodies of the East Kazakhstan region are poorly studied, there is practically no reliable information on the levels of radionuclide concentration in the waters of this region.

The aim of this work was to assess the content of natural (^{40}K, ^{232}Th, ^{226}Ra, ^{210}Po, ^{238}U) and artificial (^{3}H, ^{137}Cs, ^{90}Sr, $^{239+240}$Pu) radionuclides in the waters of East Kazakhstan region. For this, water objects of various types were investigated: dynamic – the Irtysh, Bukhtarma, Ulba, Ayagoz and Shar rivers; and static – Lake Zaysan, Shulbinskoe and Bukhtarma reservoirs. According to the obtained data, the contents of ^{232}Th, ^{226}Ra, ^{3}H и ^{137}Cs in water are below the detection limit ($<7.0\times10^{-3}$, $<4.0\times10^{-3}$, <4 $<1.0\times10^{-3}$ Bq/l, respectively). The content of other radionuclides does not exceed the following values: for ^{40}K – 0.9±0.09 Bq/l, for ^{210}Po – $(2.8\pm0.5)\times10^{-3}$ Bq/l, for ^{238}U – $(9.9\pm0.68)\times10^{-2}$ Bq/l, for ^{90}Sr – $(1.8\pm0.3)\times10^{-2}$ Bq/l, for $^{239+240}$Pu – $(1.2\pm0.5)\times10^{-4}$ Bq/l.

The obtained data on the content of radionuclides in water is 2-3 orders of magnitude lower than the permissible level, according to the Hygienic standards established in the Republic of Kazakhstan.

Fukushima nuclear disaster

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On March 11, 2011, the 9.0 Mw Tohoku Earthquake occurred at 14:46 on Friday with epicenter near Honshu Island. The disaster was the most severe accident since the April1986 Chernobyl disaster and the only disaster to be given the Classification of the International Nuclear Event Scale (INES 7). Its direct causes were all foreseeable. The report discovered that the plant was incapable of withstanding the earthquake and tsunami. The plant was located in Japan, like the rest of the Pacific Rim, is in an active seismic zone. The International Atomic Energy Agency (IAEA) had expressed concern about the ability of Japan's nuclear plants to withstand seismic activity. We experienced the greatest disaster of Fukushima Nuclear Disaster (INES 7). Many lessons to learn: the fragility of human life, its vulnerability, man's omnipotence and helplessness. We live in the age of atoms. It is absolutely necessary to prevent man-made disaster to come because the most important reason and purpose of human being are peace and happiness. Future science should be science of safety. Humanity's greatest strengths are our ability to dream a better world to imagine a future and inspire generations to bring it life. Let there be life!

Optical and electrical characteristics of fabricated three-layered Al/Er_2O_3/Eu_2O_3/SiO_2/n-Si/Al MOS capacitors for radiation sensors

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In the development of radiation sensors, the process of enhancing the gate dielectric radiation responses, which is the sensitive area of the sensors, should be considered. In this study, optical and electrical Characteristics of fabricated three-layered Al/Er_2O_3/Eu_2O_3/SiO_2/n-Si/Al MOS capacitors for radiation sensors were comprehensively studied and investigated. MOS capacitors with 15 nm thin SiO_2, 25 nm thin Eu_2O_3, and 110 nm thick Er_2O_3 stacked gate oxide layers were grown on an n-Silicon substrate by thermal oxidation and electron beam evaporation system, respectively. The aluminum gate and back contacts of the capacitors were formed by RF magnetron sputtering. The optical and electrical properties of the thin films and capacitors were analyzed by studying reflection, transmittance, refractive index and absorption coefficient, Capacitance–Voltage, Conductance–Voltage and Current density–Voltage measurements. It is observed from these studies that interfacial layers, which appeared to cause interfacial dipoles, are used to reduce the interface trap charge density and oxide trap charge density, in order to improve the charge storage capacity of the device.

Keywords: n-Si/SiO_2, Eu_2O_3, Er_2O_3, MOS capacitors, reflection, capacitance–voltage, conductance–voltage

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Effects of annealing temperature on the crystallographic, morphological and electrical characteristics of E-Beam-deposited Al/Eu_2O_3/n-Si (MOS) capacitors

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Rare earth oxides (REO's) play an important role in semiconductor technology. Europium oxide (Eu_2O_3) is one of the REO and it has been used in many applications such as optoelectronics, telecommunications, microelectronics and optical devices. However, in this study, Eu_2O_3 MOS capacitors have been fabricated by using the Electron Beam Evaporation (E-Beam) technique and the effects of different annealing temperatures on them have been investigated. Before and after annealing, the crystallographic and morphological of the Eu_2O_3 films have been analyzed by X-ray Diffraction and Atomic Force Microscopy. The electrical properties of the devices have been investigated using measuring C-V, G/ω-V characteristics. The results show that Eu_2O_3 rare earth materials can be a good candidate for microelectronic applications.

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Investigation of electrical characteristics and surface morphology of vanadium oxide-VO_2 MOS devices

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In this study, the Electrical Characteristics and Surface Morphology of Vanadium Oxide-VO_2 MOS Devices have been studied. VO_2 thin films were deposited onto n-type (100) silicon wafer by using RF magnetron sputtering system. Thin films were annealed at different temperatures in Ar ambient. The FTIR and XRD measurements were performed to check surface morphology, crystal structure and bond structures, of VO_2 thin films, respectively. The back and front Ohmic contacts were established by Al evaporation. The electrical characterization of Al/VO_2/p-Si MOS devices were investigated at various frequencies by analyzing Capacitance-Voltage (C-V) and Conductance-Voltage (G/ω–V) measurements. The obtained results demonstrate that VO_2 may have potentials to be used in MOS-based applications.

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Frequency-dependent electrical characteristics of Er_2O_3/SiO_2/n-Si/Al MOS capacitor deposited by E-beam

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In this study, the frequency-dependent electrical characteristics of the Al/Er_2O_3/SiO_2/n-Si/Al MOS capacitor deposited by E-beam were studied and investigated. The Er_2O_3/SiO_2 films were annealed in nitrogen ambient for 30 min at 550°C. The crystal structure and surface morphology were examined by XRD and AFM. The capacitance-voltage (C-V) and conductance-voltage (G/ω-V) measurements have been performed in the frequency range of 50 kHz – 1MHz at room temperature. Furthermore, the frequency effects on the series resistance (R_s) and interface state density (D_{it}) through the C-V and G/ω-V curves were studied and analysed. It is observed that R_s and D_{it} decreased with an increase in frequency. The measured and calculated results reveal that frequency has a significant impact on both R_s and D_{it} of the fabricated MOS characteristics. These effects are supposed because of the interfacial SiO_2 layer that is contained in between n-Si and Er_2O_3.

Keywords: Er_2O_3 thin films, series resistance, interface state density, E-beam

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Structural and electrical characteristics of the $Al/Al_2O_3/SiO_2/n\text{-}Si$ metal-oxide-semiconductor capacitor

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In this study, the structural and electrical characteristics of the $Al/Al_2O_3/SiO_2/n\text{-}Si$ Metal-Oxide-Semiconductor (MOS) structure were investigated. Al_2O_3 films were deposited on the n-type Si wafer by RF magnetron sputtering after the growth of SiO_2 by dry oxidation. The Aluminum (Al) front and back contacts were deposited by RF magnetron sputtering. The fabricated MOS structures were annealed at 250°C, 450°C and 750°C in a N_2 ambient. XRD and AFM measurements were taken in order to examine the crystal structure and the surface topography of the MOS structure. C-V and G/w-V measurements were performed at low and high frequencies with the aim of analyzing the electrical characteristics. The discrepancy in the C-V curves for different frequencies stemmed from the defects and dangling bonds at the interfaces and in the oxide layers.

Keywords: Co-gamma irradiation, thin films, defects, dangling bonds

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Comparison of electrical properties of NÜR-PIN photodiode and BPW34 PIN photodiode

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The Silicon PIN photodiode (NÜR-PIN) with active area (3.5. x 3.5. mm2) was designed and fabricated by using conventional photolithography process at Nuclear Radiation Detectors Applications and Research Center (NÜRDAM). To get NÜR-PIN and BPW34 specifications, capacitance-voltage (C-V) and current – voltage (I-V) measurements were accomplished at room temperature by using Keithley 4200-SCS and results were compared. The dark current and capacitance at -10V are 20 nA and 17.7 pF for NÜR-PIN, 32 nA and 27 pF for BPW34. Even if NÜR-PIN has good results at low reverse voltage, it is unstable at high reverse voltage compared to BPW34 photodiodes.

Keywords: Silicon PIN photodiode, BPW34, current–voltage, capacitance–voltage

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Structural properties and radiation response of neodymium oxide

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Neodymium oxide (Nd_2O_3) was deposited by sol–gel method and deposited on P-type 〈100〉 silicon wafer. The chemical characterization of neodmiyum oxide was determined by Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), energy-dispersive spectra (EDS) and atomic force microscopy (AFM) and surface morphology was examined scanning electron microscopy (SEM).

In order to examine the neodymium oxide radiation responses, samples were irradiated using a Co-60 gamma-ray source from 1 gray to 100 grays at a dose rate of 0.015 Gy/s. A dramatic variation was observed in capacitance and conductance with increasing in irradiation dose. Irradiation creates a large number of e-h pairs and defects in the structure. For this reason, significant changes can occur in the electrical characteristics of the device. Consequently, Neodmiyum oxide dielectrics may have significant usage for microelectronic technology as a radiation sensor.

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Lowering synthesis temperature of Hbn by improvement of precursor

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In this study, hexagonal boron nitride (hBN) was synthesized with the modified O'Connor method in presence of different additives. Structural properties of the synthesized materials were determined by X-Ray Diffraction, (XRD), Fourier Transform Infrared Spectroscopy, (FTIR), and Scanning Electron Microscopy, (SEM). It was found that improving the precursor using different additives played a positive role by lowering the formation temperature. The average grain sizes (21–24 nm) and graphitization index (2.44–3.45) of hBN samples were calculated from XRD pattern.

Keywords: Hexagonal boron nitride, nanocrystalline materials, O'Connor method, characterization

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Radiobiological facility of the INR RAS for experiments on proton FLASH therapy

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One of the most relevant areas of research in the field of radiotherapy is the study of the so-called FLASH effect when targets are irradiated with short pulses of radiation with a high dose rate. This effect allows avoiding radiation damage to healthy tissues when bringing cancericidal doses to the tumor, while maintaining the effectiveness of the irradiation on pathological cells. It is believed that to achieve this effect, the dose rate applied to the target must be more than 40 Gy/s. This is a complex technical task for many accelerator systems of proton therapy centres that use active scanning techniques to generate dose distributions. The linear proton accelerator of the INR in Troitsk is ideally suited for conducting flash therapy experiments using passive proton scattering. According to our estimates, for typical beam parameters of this accelerator, corresponding to an energy of 209 MeV, a pulse current of 8 mA, a pulse duration of 100 microseconds and a pulse frequency of 1 Hz, the average dose rate applied to a 1l target can reach the level of 1 MGy/c. This dose rate corresponds to the ultra-FLASH irradiation mode, is many orders of magnitude higher than the values achievable on known clinical cyclotrons and synchrotrons, and opens the possibility for research in the unexplored field of radiobiology. As part of the preparation of our experiments, we calculated, created and tested a device for bringing a homogeneous dose field of at least 4x4x4 cm3 to biological objects in the region of the modified Bragg peak. The stand for radiobiological experiments, including a double proton scattering system, collimators, compensator and ridge filter, was modelled by the Monte Carlo method using the GEANT4 code. The position of the beam and the amount of dose delivered to the target are monitored by scintillating and Gafchromic films and TLD detectors. As part of the experiment conducted in December 2019, an average dose rate of about 0.3 MGy/s was achieved and applied to biological objects weighing more than 100 g. As a result, standard laboratory tablets with cell cultures were irradiated with a record dose rate. This stand allows study and comparison of radiobiological effects in the widest range of irradiation modes from ultra-FLASH to conventional irradiation modes using both cell cultures and laboratory animals.

Monte Carlo verification of ArcCHECK(R) detector output to radiation of Ir-192 sources in brachytherapy

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Verification of treatment planning is key to the safety and effectiveness of radiation therapy. External beam radiotherapy (EBRT) uses a number of proven methods to verify planned treatment, but there is not yet a standard way to check the efficacy of a treatment plan for radiotherapeutic implants (brachytherapy). We investigated the potential use of the ArcCHECK(r) radiation detector to verify brachytherapy. The ArcCHECK(r) detector is a three-dimensional matrix of 1386 semiconductor diodes, arranged spirally around the cylindrical space inside the device. The internal dimensions of the detector (32 cm length, 15 cm in diameter) make it possible to reproduce, in an appropriate phantom, the distribution of sources planned in the therapeutic procedure. The response from the detectors is presented as a two-dimensional dose distribution map on the diode surface. ArcCHECK(r), however, is a device with energies in the range of 6 – 22 MeV. To examine its potential application in brachytherapy, we determined the values characterizing the output of the detectors to Ir-192 radiation (energy of 380 keV) in a Monte Carlo simulation, and compared it with the signal actually recorded by the ArcCHECK(r) detector diodes. Experimental treatment plan measurement was performed in the detector using standard Elekta micro-Selectron-v3 sources containing the iridium-192 core. To avoid unit inconsistencies, both the signal from each of the diodes and the simulation results for individual diodes were normalized to the maximum value. We hypothesized that the results would show similar statistical parameters – expected value, variance, STD, etc. – indicating the same statistical distribution. Differences in diode indications from the simulation and the measurement were also subjected to statistical analysis, which showed the degree of general inconsistency of the measurement with the simulation. The results obtained provide an initial quantitative indication of the potential usefulness of the ArcCHECK(r) detector in brachytherapy verification.

Prevention of chemotherapy-induced nausea and vomiting (CINV) in breast cancer patients receiving adjuvant chemotherapy: Single institution experience

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Introduction. The modern treatment of malignant diseases and the use of antineoplastic agents pose numerous challenges in terms of the side effects from applied specific oncological treatment. Despite to the significant progress in recent years, emesis and nausea are the two most common and most stressful side effects of cancer treatment and their successful management is still a great challenge. Chemotherapy-induced vomiting or nausea (CINV) significantly affects the quality of life of patients, can cause metabolic disorders, diarrhea, eating disorders and general physical and mental disorders and can question the further anti-tumor treatment of the patient. The prevention and the treatment of CINV and antiemetic therapy have central role in modern protocols for oncological treatment of malignant diseases, including breast cancer patients.

Aim. The aim of our study was to obtain data about the efficacy of antiemetic prophylaxis in patients with breast cancer who received chemotherapy following the EC75 protocol in adjuvant setting and the compliance of the patients for the both acute and delayed emesis and nausea.

Materials and methods. A prospective study was conducted in 32 breast cancer patients receiving chemotherapy following an EC75 protocol in an adjuvant setting for four consecutive chemotherapy cycles between February 2015 and June 2015. All patients received adequate premedication on day 1 prior to chemotherapy and appropriate oral postmedication was recommended in day 2-5 (with 5-HT3 antagonist and corticosteroid).

The occurrence of acute and delayed nausea and emesis as well as taking the recommended postmedicaton by patients was evaluated through a specially structured questionnaire that beside general information contained the following information: the appearance of emesis and nausea within 24 hours after receiving chemotherapy and within the next 10 days, taking the recommended postmedication and the number of taken tablets and taking additional therapy besides the recommended.

Results. Out of 32 patients, acute onset of nausea, nausea till day 5 and nausea from 5 to 10 day was recorded in 50%, 44% and 31% of patients, respectively. The results of the occurrence of acute emesis, emesis to to day 5 and nausea from 5 to 10 day were 16%, 9% and 0% respectively. Patients who received complete postmedication have reported acute nausea, nausea till day 5 and nausea from 5 to 10 day in 50%, 50% and 20%, while in patients with partial postmedication 50%, 59% and 39%, respectively.

Conclusion. The obtained results do not indicate that acute and delayed nausea are more difficult to control. In patients' good compliance, better control of both acute and postponed emesis is achieved, although the results obtained in patients with partial compliance may be due to failure to follow the recommended treatment. Despite the effectiveness of antiemetic prophylaxis and good compliance, there is a possibility for its improvement with introduction of new generations of antiemetics.

Keywords: Chemotherapy, emesis, nausea, breast cancer, compliance

Adjuvant chemotherapy plus concurrent chemoradiotherapy (CCRT) in advanced gastric adenocarcinoma treatment as standard of care

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Introduction. Despite a worldwide decline in incidence based on GLOBOCAN 2018 data, stomach cancer is the 5th most common neoplasm and the 3rd most deadly cancer. In 90% of cases, its histology is adenocarcinoma, either of the intestinal type or of diffuse. Helicobacter pylori infection, smoking, salt and nitrate-rich foods are the most important factors of risk. The interactions between dietary factors, environmental factors and the development of gastric cancer are well described with clearly identified dietary exposures strongly associated with gastric cancer induction and prevention. Postoperative fluoropyrimidine-based CCRT and chemotherapy is standard adjuvant treatment of resected gastric adenocarcinoma.

Materials and methods. Patients with subtotal gastrectomy and D1 lymph node dissection were treated with 2 cycles of Capecitabine (DD 2500 mg/m2 po bid/21day cycle) followed by chemoradiotherapy and another of 2 cycles chemotherapy with Capecitabine (DD 2500 mg/m2 po bid/21d cycle). CT simulation with oral contrast application was performed followed by delineation of target volumes and organs at risk according to CRITICS protocol. 3D conformal postoperative chemoirradiation was delivered with standard fractionation (TTD 50.4 Gy/1.8 Gy) with concurrent application of Capecitabine 1650mg/m2/bid/d1-5. Adjuvant treatment was delivered in postoperative period of 6 months.

Results. Adjuvant chemotherapy and chemoradiotherapy prolongs disease free survival (DFS) and improves quality of life. CT-based 3D conformal treatment planning and delivery of postoperative chemoirradiation is minimum standard of care of gastric cancer treatment.

Conclusion. Multidisciplinary decision making team approach is preferred. Primary treatment option for patients with potentially resectable locoregional gastric tumors is surgery. The guidelines have included postoperative chemo/chemoradiotherapy treatment depending of tumor stage, nodal status, extent of lymph node dissection and other risk factors (differentiation, lymphovascular invasion, neural invasion, surgical margins). Adjuvant chemotherapy and chemoradiotherapy prolongs disease free survival (DFS) and improves quality of life.

Keywords: Gastric cancer, chemoirradiation, CCRT, DFS, 3D conformal, postoperative

The role of P53 status in response to ionizing radiation

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Radiation therapy is a major therapeutic modality in cancer. However, in response to gamma-irradiation cells may survive and give rise to a secondary tumor and disease progression. Among the molecular determinants of tumor cell response, p53 pathways have long been established as key regulators of the balance between cell survival and death.

In this study, to assess the effect of irradiation, we used a pair of isogenic cell lines with the wild type and non-functional p53, that is, the HCT116 human colorectal carcinoma and its HCT116p53KO variant with both alleles of the *p53* gene deleted. In HCT116 cells a dose and time dependent arrest in G2/M phase of the cell cycle was detectable at days 1 through 7 after irradiation with 1-4 Gy. In contrast, a bigger percentage of apoptotic (subG1) cells was found after the same exposure of HCT116p53KO cells indicating that p53 inactivation was detrimental for survival of irradiated cells. Clonogenic assays demonstrated a 3-fold lower long-term (14 days) survival of p53 negative counterparts compared to the wild type p53 cells. Furthermore, p53 protein was accumulated in HCT116 cells at days 1-10 post irradiation with 2 Gy; this effect was paralleled by p21 increase at days 1-7, what was determined by immunoblotting. One may hypothesize that, in cells carrying the wild type p53, irradiation-induced DNA damage activates Chk1/2 protein kinases that, in turn, stimulate Cdc25 phosphatase. This pathway also stimulates expression of tumor suppressor p53. The accumulated p53 activates p21 cell cycle inhibitor thereby arresting the cells via Cdc25 suppression and prevention from traverse through G2/M phase. In p53 negative cells no block occurs in response to DNA damage, and Cdc25 drives the damaged cells through mitosis leading to apoptosis. Furthermore, disruption of p53-Mdm2 interaction with Nutlin-3a followed by irradiation, caused a more pronounced death of cells with wild type p53 compared to p53-null counterparts treated with Nutlin 3a, therefore proving that the effect of Nutlin 3a is dependent on the presence of p53.

Altogether, our results provide evidence for therapeutic combinations aimed at the increased cytotoxic, rather than cytostatic, response of irradiated cells.

Cell ageing in dermal fibroblasts of patients with breast cancer and patients at risk of tumors

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Genomic instability leads to many diseases, including cancer. Chromatin protein HP1gamma and histones H3K9me3 and H3K27me3, as well as histone deacetylases SIRT1, SIRT6 and SIRT7 play an important role in the regulation of chromatin and genomic stability maintenance.

The fluorescence intensities of cell markers of ageing: HP1gamma, H3K9me3 and H3K27me3 and histone deacetylases: SIRT1, SIRT6 and SIRT7 were studied in dermal fibroblast lines from patients with breast cancer, lines from people at risk of tumors and healthy donors.

Each study group is represented by several lines from donors of different ages: 30 and 40-55 years.

Features of fluorescence intensity's distribution depending on cell line category (cancer patients, tumors risk group or healthy donors) and on donor's age were obtained.

The average fluorescence intensity of the HP1gamma cell ageing marker in the dermal fibroblast cells of a 30 years old patient with breast cancer is distinctly higher than that in the cells of a 55 years old patient with breast cancer or in the tumor risk group and in healthy donors.

A distinct decrease in the average H3K9me3 fluorescence intensity was observed in dermal fibroblasts in breast cancer and tumors risk groups.

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γH2AX and 53BP1 as the markers of cell response to DNA damage in cases of patients with breast cancer and people with an increased risk of cancer

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Genome stability is the basis of normal cell activity. In cases of impaired genomic stability there are various pathological conditions of the cells. In a first approximation the emergence of a tumor occurs due to the accumulation of mutations in the genes associated with proliferation or with apoptosis.

This study is focused on features of DNA repair in dermal fibroblasts of patients with breast cancer, people with an increased risk of cancer (with BRCA1 and ATM mutations) and healthy donors. At different time intervals (30 minutes, 1.5 hours, 6 hours and 24 hours) after X-ray irradiation at a dose of 2 Gy cells were stained for the proteins of the cell's response to DNA damage (γH2AX and 53BP1) by means of indirect immunofluorescence. The parameters of local accumulations (foci) of γH2AX and 53BP1, such as their number, area and fluorescence intensity, were studied. It has been shown that there is a slowdown in the cell's response to DNA damage in fibroblasts of cancer patients and cancer risk group.

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Exposure and risk assessment connected to the health and safety of workers in the production of electricity

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The aim of the study is to perform exposure and risk assessment of electromagnetic fields (EMF) at workplaces connected with electricity production according to the requirements of Directive 2013/35/ EU. The study covers the following sets of workplaces:

- Workplaces in power distribution systems (indoor and outdoor distribution systems);
- Workplaces with metalworking machines: lathes, mills, electric welding.

Measurements are made using a frequency non-selective method, based on: "Non-binding guide to good practice for implementing Directive 2013/35/EU Electromagnetic Fields Vol. 1 – Practical guide".

Exposure and risk assessment have been performed by comparing the measured values with action values (ALs) and the exposure limit values (ELVs) according to the requirements of Directive 2013/35/EU, as well as with the reference values adopted by the Council Recommendation 1999/519/EC for persons at "specific risk".

The results of the exposure and risk assessment show the following:

Electric field strength for the power frequency field (50 Hz) does not exceed the high ALs for non-thermal effects; low ALs are not exceeded except for single points in outdoor high voltage substations. In cases where the low ALs for non-thermal effects is exceeded, the reference levels according to Recommendation 1999/519 / EC are exceeded as well.

There are not measured values of the field strength above the reference levels according to Council Recommendation 1999/519/EC at the remaining workplaces.

The results show compliance with the ELVs with respect to the health and sensory effects.

Magnetic flux density values of power frequency fields' do not exceed the ALs for non-thermal effects. Measured values show also compliance with the ELVs for health and sensory effects. The magnetic flux densities do not exceed the reference levels according to Council Recommendation 1999/519/EC.

From the results obtained, it can be concluded that no risk can be expected for the workers' health from the EMFs exposure except for those defined as persons at a specific risk. For persons at a specific risk, appropriate recommendations for the employer have been proposed for health and safety practices at work.

Measurement, exposure and risk assessment of sources of optical radiation in working environment

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The report presents results of measurement, exposure and risk assessment of optical radiation sources in an industrial unit: electric welding, oxygen and plasma cutting machines.

Measurements of the optical radiation parameters are performed over the entire optical range within the scope of Directive 2006/25/EC (transposed in Bulgarian legislation with Ordinance No. 5 /2010). They are made at the level of the exposed eyes and skin of workers having activities or stay in the source area.

The studied sources emit mainly in the ultraviolet (UV) and visible range of the optical spectrum, therefore the applicable exposure limit values (ELVs) correspond to the two ranges.

Although the highest exposure to optical radiation is to the workers who directly handle the source, the exposure and risk assessment refers more to other workers indirectly involved in the activities with sources of optical radiation. The reason is that first group of directly exposed workers is protected by personal protective equipment (PPE) so the radiation does not reach them up to the maximal radiation levels.

The exposure assessment results show an exceeding of the ELVs for the visible and UV range in the vicinity of the electric welding and plasma cutting machine and ELVs for the visible range for the oxygen.

The risk assessment for workers has taken into account that the risk of exposure of the eye to visible light is high, but exposure to visible radiation is unlikely to occur due to the aversion to bright light and involuntary turning the head away from the source.

This is not the case with exposure to UV radiation, which is invisible to the eye and no natural mechanisms for protection. So, high levels of exposure and risk to the cornea and the lens of the eye are possible.

This means that the risk of exposure to visible optical radiation is high, but the probability of exposure is medium to low. In the ultraviolet range the risk and the likelihood of exposure is high. There is a health risk to persons who are particularly sensitive to exposure to optical radiation as well.

In addition, effects on the health and safety of workers are possible as a result of the interaction between optical radiation and photosensitising substances at the workplace or medications and/or food.

Public concern of electromagnetic exposure in Bulgaria – A case study

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Risk management in the precautionary framework proposed by the World Health Organization (WHO) concerning public health is an interactive process and it encourages the development of new information and understanding, as well as a review of the measures in the context of existing uncertainty. By including a wide range of stakeholders in the process, the framework requires clarification of their interests, as well as transparency about the way of decisions made. The protective framework related to the protection of human beings against electromagnetic fields (EMF) exposures is an upgrading approach that encompasses procedures for managing human health risks that are either known or insecure. The framework assists:

- Development and evaluation of the opportunities to reduce the electromagnetic exposure;
- Choice of action/actions appropriate to the risk under consideration;
- Assessment and supervision of the chosen action/actions.

WHO proposes the "Precautionary Principle/Approach" to be applied for cases when uncertainty of research is great, and when there are serious problems with the implementation of new technologies for which there is insufficient information on their harmful effects.

At the same time, WHO suggests communication strategies to be applied after analyses and evaluation of the exposure to reduce the public concern (EMF Risk Perception… WHO 1998, Risk Perception…ICNIRP 1997, Establishing a Dialogue…WHO 2002).

Here, we would like to present one typical case study of public concern in connection with EMF exposure from base station for mobile communication situated in urban area, and the way how the problem has been solved. Different approaches for exposure assessment have been applied, as follows:

- measuring methods: point measurements; monitoring measurements over a long period of time monitoring for more than 24 hours; spectrum analyses
- analytical methods: exposure assessment through processing data of measurements; and/or evaluation of the safety zones around "sensitive" buildings by calculation/modeling.

A communication strategy with the general population has been chosen and applied on the basis of the analyses of the results of evaluation of the exposure. This communication strategy is specific and proven effective, and it refers to all stakeholders, including administration, mobile operators, local authorities, regional control bodies of the Ministry of Health, and others.

The main purpose of this paper is connected to the methodology of the processes presenting our model for effective solving a problem of public concern connected with EMF exposure.

Keywords: Communication programme, EMF, exposure assessment, risk communication, risk management

Cut–off point values of the estimated central obesity index determined with dual-energy X-ray absorptiometry in diagnosing abdominal obesity in women

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Cushing's syndrome (CS) is associated with weight gain and extreme central, visceral, abdominal obesity. Obesity and especially central, abdominal obesity in CS and non CS abdominal obese with the metabolic syndrome are known risk factors for cardiovascular and metabolic diseases. DXA is considered to be a gold standard method which enables accurate, precise body composition and body fat distribution (BFD) assessment and determines central obesity index (COI) values. Estimated COI (eCOI) is an indicator of central, abdominal obesity, which is the main characteristic of the metabolic syndrome. To date, cut-off point values (CPV) of eCOI have not been provided in order to precisely confirm abdominal obesity in CS and non CS obese and for that reason it is the aim of this study.

Values of eCOI were determined as a ratio of estimated android (eA) and gynoid (eG) tissue percent fat (eCOI=eA/eG) in 3 groups of women: 1st group with CS (n=14), 2nd group of obese women (O) not different according to their age and BMI from group 1 (n=21), and 3rd group of non obese healthy women (C) with normal BMI (n=22). CPV1 was determined of the DXA index of central, abdominal obesity eCOI1, that best differentiated CS with confirmed extreme abdominal obesity and O matched for age, menopausal status, and BMI and CPV2 of eCOI2 that best differentiated group C and O and exclude abdominal obesity, during regular spine and hip scans for osteoporotic risk assessment. Their sensitivity (S), specificity (SP), positive and negative predictive value (PPV and NPV) and diagnostic accuracy (DG) were evaluated. DXA assessment in this study was performed with DXA System Lunar DPX-NT, which uses enCore Windows-XP Professional OS computer.

Values of eCOI were significantly different among the 3 groups, and were highest in CS ($p<0.0001$). CPV1 of eCOI1 was 0.95 and differentiated the best CS from O with S of 85.71%, SP 57.14%, PPV 50%, NPV 90.91% and DG 67.56%. However, CPV2 value of eCOI2 was 0.87 and differentiated C from O for S of 80.95%, SP of 95.45%, PPV 94.44%, NPV 95.45% and DG 88.37%.

DXA index eCOI discovered extreme central BFD in CS women. Values of eCOI1 lower than 0.87 showed normal body fat distribution and differentiated the best group C from O and eCOI2 CPV2 value of 0.95 differentiated the best extreme central, visceral BFD in CS women from suspect O and C. Values of eCOI2 higher than 0.95 showed abdominal obesity, and could be used as diagnostic DXA index and criterion of extreme central, abdominal obesity in CS and non-CS abdominal obese women in DXA body composition and fat distribution assessment. Determination of eCOI is reliable, practical, fast, with low radiation and acceptable as a routine diagnostic DXA screening procedure for body composition and BFD assessment, during regular spine and hip scans for osteoporotic risk assessment.

Keywords: Cushing syndrome, obese, dual-energy X-ray absorptiometry, obesity index

Computed tomographic diagnostic evaluation of the adrenal and pituitary adenomas in Syndrome and Morbus Cushing

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Cushing syndrome is the clinical manifestation of hypercortisolism. Obese subjects (O) suspected of hypercortisolism first have to be biochemically differentiated from patients with Cushing syndrome with adrenal adenoma (CS) and Morbus Cushing (MC) with pituitary adenoma and adrenal hyperplasia (AH). After the biochemical differentiation of CS and MC, computed tomographic (CT) morphological assessment is necessary by which the localization will be proved and the size of the tumor determined. The aim of this study was to determine diagnostic assessment accuracy of the CT imaging of the adrenal and pituitary adenomas in patients with CS and MC, which were biochemically, clinically and histologically, after surgery, diagnosed.

Adrenal glands were assessed with CT scan in 66 subjects, 36 O suspected for Cushing's, 14 CS and 16 MC. Pituitary CT scan was performed in 16 MC and 11 O. Sensitivity (S), specificity (SP), positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DG) were determined of the CT scan test results in the examined subjects.

Adrenocortical adenomas (CA) were detected by means of CT of the adrenal glands in CS as clearly determined oval, homogenous, unilateral adrenal masses with mean diameter value of 3.42±1.24 cm. CA were found in 13 of 14 CS (S 93%) and in 3 of 36 O patients (SP 91.7%), true positive results were found in 13 CS from total 16 positive (PPV 81.25%), true negative results were found in 33 O of total 34 negative (NPV 97.1%) and DG of 92% as a ratio of the sum of 13 true positive CS and 33 true negative O test results and the sum of all 50 subjects (14 CS and 36 O). In 12 of total 16 MC was found AH (S 75%), and false positive AH was found in 3 of 36 O (SP 91.7%), true positive AH results were found in 12 of total 15 positive (PPV 80%), true negative results of AH were found in 33 O from total 37 negative (NPV 89%) and DG of 86.5%. When comparing all 30 Cushing patients with 36 O, CT scan assessment showed S of 83.33%, SP 91.7%, PPV 89.3%, NPV 86.8% and DG of 87.9%. Pituitary CT scan in MC discovered pituitary microadenomas with S of 56.25%, SP 91%, PPV 90%, NPV 59% and DG of 70%.

Adrenocortical adenomas in CS were detected with high S of 93%, NPV 97.1% and DG of 92% as an oval unilateral adrenal masses and discovered adrenal CT scan as a useful diagnostic procedure in adrenal tumors diagnosis. Bilateral adrenal hyperplasia in MC was determined with low S of 75% as well as PPV of 80% and DG of 86.5%. Low values of the S 56.25%, NPV 59% and DG of 70% of the pituitary CT scans as well as adrenal CT scans in MC indicated the need of previous biochemical differentiation of MC and O in order to exclude adrenal as well as pituitary incidentalomas and also showed the need of more precise MRI investigation of the pituitary gland in MC.

Keywords: Cushing syndrome, CT imaging, adrenal and pituitary adenomas, diagnostic accuracy

Free fatty acid receptors as potential drug targets in therapy and treatment of Type 2 diabetes

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Type 2 diabetes (T2D) is the most common form of *diabetes mellitus*, and condition followed by hyperglycemia and disturbances in fat as well as protein metabolisms. There are many risk factors involved in the development of T2D such as nutrition, the environment and genetics. In 1963, Randle *et al* proposed a vicious "glucose and fatty acid cycle" which include stimulation of hepatic glucose output by fatty acids (FA), potentiation of glucose-stimulated insulin secretion (GSIS) by FAs, and the cellular mechanism whereby high glucose and insulin concentrations inhibit FA oxidation. Fatty acids as an energy fuel in the body, are important as well as biomolecules, particular as free fatty acids (FFAs) and play a key role in various metabolic functions by acting as signaling molecules and regulators or stimulators of biological functions. Recent studies, including lipidomics and pharmacological investigations have been shown that different type of FFAs (short-, medium- and long-chain fatty acids) activated several G-protein coupled receptors (GPCR) and represent important receptors for FFAs termed as FFA1–4. These FFA receptors (FFARs) are mediate various physiological functions, such as peptide hormone secretion and inflammation related conditions and thereby contribute energy homeostasis. Since imbalance in energy homeostasis lead to metabolic disorders, such as obesity and T2D, FFARs are considered to be a potential drug and therapeutic targets in these diseases. Novel findings have been shown that the administration of selective agonists of FFAR1 and FFAR4 improved glucose metabolism and ameliorated systematic metabolic disorders by increasing GSIS as well a direct positive effect on GSIS, while activation of FFAR2 and FFAR3 are linked with metabolic function of saturated fatty acids (SFAs) in anti-inflammation and energy metabolism by reducing inflammation and improvement in insulin sensitivity. This work, presented a recent finding of FFARs physiological as well biological functions and their potential as selective ligands for development as novel drugs to treatment metabolic disorders such as obesity and T2D as well other inflammation related conditions.

Involvement of Caspase–6 in radiation-induced apoptosis

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Aim. The biochemical mechanisms of programmed cellular death, known as apoptosis, in rat thymus lymphocytes upon treatment with ionizing radiation (IR) were studied. The main class of cysteine proteases (caspase family) makes significant and specific contribution to implementation of radiation-induced apoptosis. It involves transduction of apoptotic signal to appropriate cell compartments, and realization of their effectors functions. Caspase–6 is an unique executioner caspase, but it can cleave the initiator caspase–8 leading to its activation; and the list of novel substrates for caspase–6 replenish over the last decade. However, the role of caspase–6 in radiation- induced apoptosis remain to be identified.

Methods. We investigated the effects of ionising radiation (IR) generated by X-ray apparatus RUM-17 (total dose of 1.0 and 7.78 Gy). Animals were sacrificed 3 hr after the exposure, and rat thymus lymphocytes were isolated. The apoptotic cells degree was determined by flow cytometry (Annexin V-FITC and Propidium Iodide fluorescent signals). Caspase–6 activity was measured using chromogenic substrate VEID- *p*NA (ApoTarget™kit). Caspase–8 activity was estimated using chromogenic substrate IETD- *p*NA (ApoTarget™kit).

Results. Flow cytometry analysis revealed the apoptotic stages in rat thymus lymphocytes upon treatment with 1.0 and 7.78 Gy (in 3 hrs after exposure). We observed a dose-dependent increase in caspase–6 activity in thymus lymphocytes under these conditions. During radiation–induced apoptosis, caspase-6 redistributes to the nucleus, cleaves nuclear structural proteins and transcription factors, which leads to the activation of nuclear-mediated pathway of cellular death. Simultaneously caspase-6, which localized to the cytoplasm, directly activates caspase–8, the initiator caspase in the intrinsic apoptosis pathway. Our study revealed the rise of caspase–8 activity in rat thymus lymphocytes after exposure to IR.

In conclusion, our data suggest the pivotal role of initiator and effector caspases in the complex mechanisms of radiation-induced apoptosis in rat thymus lymphocytes.

Redox-active Ni(II) complexes of 5-tritylbenzene-1,2-diol derivatives with antimycobacterial properties

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Tuberculosis is a widespread infection disease caused by *Mycobacterium tuberculosis*. Nowadays, a cure done by means of multidrug therapy results in the emergence of multidrug resistant tuberculosis. In this connection, there is an urgent need to develop novel antimycobacterial agents, in particular antitubercular ones. Some antimicrobials act *in vivo* as electron transfer agents in the production of radical species or disruption of normal electron transport, it may be suggested that the redox-active metal complexes that are able to affect the electron transport system of cellular respiration can possess a potential for antimycobacterial activity. In this work redox-active Ni(II) complexes with 3-(pyrrolidin-1-ylmethyl)-5-tritylbenzene-1,2-diol (HL^{I}), 3-(piperidin-1-ylmethyl)-5-tritylbenzene-1,2-diol (HL^{II}), 3-(azepan-1-ylmethyl)-5-tritylbenzene-1,2-diol (HL^{III}), 3-(morpholinomethyl)-5-tritylbenzene-1,2-diol (HL^{IV}), 3-((4-methylpiperazin-1-yl)methyl)-5-tritylbenzene-1,2-diol (HL^{V}) were synthesized. According to the elemental analysis, TG/DTA, IR and UV-Vis spectroscopy a general formulae of the complexes is NiL_2 with the *O,N* coordinated ligands forming distorted square-planar coordination cores. The Ni(II) complexes are amorphous, water insoluble non-electrolytes (molar conductivity < 120 $S \cdot cm^2 \cdot mol^{-1}$), stable in water-organic media (a general stability constant $lg\beta = 15 \div 18$). Lipophilicity parameters of these complexes ($lgP_{ow} = 2.9 \div 3.3$) suggest their potential ability for transmembrane transfer. Redox properties of the complexes were evaluated by cyclic voltammetry; first oxidation peak ($E_{pa}^{1} = 0.55 \div 0.63$ V) was taken as a criterion to compare the reducing ability of the compounds. Minimal inhibitory concentration values of the complexes against *M. tuberculosis* are $0.051 \div 0.054$ $umol \times ml^{-1}$ for $Ni(L^{I})_2$ – $Ni(L^{VI})_2$ and 0.025 $umol \times ml^{-1}$ for $Ni(L^{V})_2$. A complicated regularity between antimycobacterial and redox properties of the complexes has been noticed. In this connection, it is significant that the redox potential is a thermodynamic criterion of an electrochemical reaction being possible, while the ability of the redox-active compounds to interact with biomolecules of microorganisms has a more intricate dependence on the structure and physicochemical properties thereof.

Developing a novel approach for ECG classification using modified local binary patterns

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In this paper a novel electrocardiogram (ECG) signals classification approach is proposed based on Local Binary Patterns (LBPs). Although LBP is one of the new and very simple methods used in texture classification but in this paper the method is applied to ECG classification. The training phase consists of applying LBP operator to all different ECG signals individually to extract the reference feature vectors for each class of heart disease. Consequently, each signal is windowed in classification phase and LBP operator is applied to each window and compared with all reference feature vectors. To increase the accuracy of the method two further morphological features are investigated, which are Variance and Mean. The proposed method is applied to eleven different classes of signals selected from MIT-BIH dataset and the average accuracy of 99.76 is obtained. While no signal pre-processing step is required and considering the simplicity and accuracy of the proposed signal classification algorithm, it can be considered as a robust one which is suitable for online ECG classification. Finally, classification accuracy of the proposed algorithm is compared with similar methods to illustrate the capability of the proposed LBP based classification algorithm.

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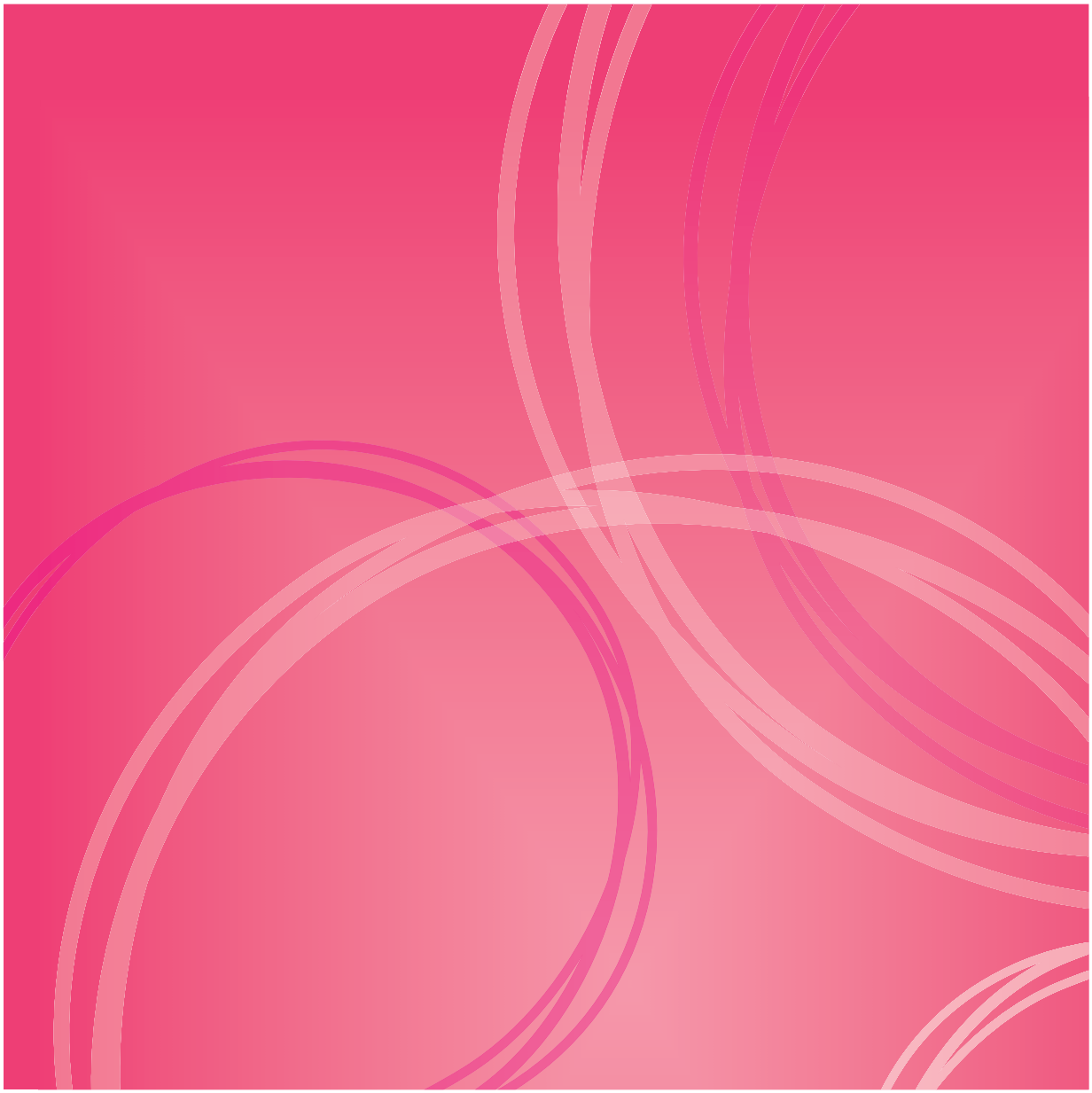

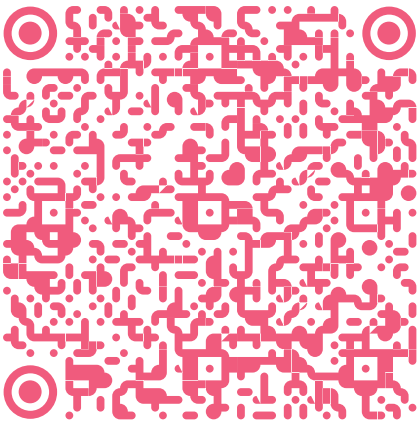

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