International School on Nuclear Methods for Environmental and Life Science

Report of Contributions

https://indico.jinr.ru/e/nmels18

Contribution ID: **0** Type: **not specified**

RADIOPHARMACEUTICALS IN DIAGNOSTIC AND THERAPEUTIC NUCLEAR MEDICINE

The aim of this lecture is presentation of the basic principles of production and application of radiopharmaceuticals. Radiopharmaceuticals are radioactive labelled substances containing one or more radionuclide(s) suitable for administration to humans and apply either for diagnostic or internal radiation for therapy in nuclear medicine. The radioactive drug will accumulate in target areas in the body. A Single Photon Emission Computed Tomography (SPECT) camera or Positron Emission Tomography (PET) camera are used for detection and image distribution of the radioactivity in the body of the patient.
The lecture will cover following topics: (1) production routes of the main radionuclides produced by cyclotron (fluor-18, carbon-11, iodine-12, iodine-124, copper-64, generators 68Ge/ 68Ga and 82Sr/ 82Rb) and nuclear reactor (iodine-131, 99Mo/ 99mTc); (2) principles of production and quality control of the radiopharmaceuticals and (3) the samples of currently applying radiopharmaceuticals for PET, SPECT and radiotherapy.

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Contribution ID: **1** Type: **not specified**

NUCLEAR TECHNIQUES BASED ON X-RAY AND PROMPT GAMMA-RAY EMISSION FOR THE ANALYSIS OF ENVIRONMENTAL MATERIALS

The distribution of elements in the environment, their concentration and dynamics can be seriously affected by human activities. Environmental pollution occurs through the introduction of various substances in soil, water and atmosphere by anthropogenic activities. Often this pollution produces imbalances in terrestrial and aquatic ecosystems, threatening the health of living beings. The complexity of study of the trace metal migration in the ecosystems requires the application of validated research methods and up-to-date techniques and equipment.
The attractiveness of non-destructive methods and the ability to perform simultaneous multi-elemental determinations has led to an extensive application in research laboratories of accurate, precise and sensitive atomic and nuclear analytical techniques for the investigation of different types of materials (industrial, geological, biological, environmental, etc.). Atomic and nuclear analytical methods, such as neutron activation analysis (NAA), X-ray fluorescence (XRF) and particle-induced X-ray emission (PIXE), play an important role in the frame of instrumental analytical methods, mainly for non-destructive characterization of solid samples. For complex examinations of materials of various matrices or research activities in life sciences, interdisciplinary cooperation is advantageous, mainly involving physicists and chemists, but also, e.g., biologists, medical researchers and material scientists.

X-ray based techniques (XRF, PIXE):

The monitoring of the polluting factors in natural environments requires the use of rapid, accurate and, not least, cheap detection methods. From this point of view, the XRF spectroscopy, using both energy-dispersive (ED-XRF) and wavelength-dispersive (WD-XRF) technique, is very suitable for the analysis of elements of the periodic table between boron (Z = 5) and uranium (Z = 92). XRF technique using stationary or portable ED or WD spectrometers is widely applied for the rapid analysis of the major, minor and trace chemical elements in complex samples for diverse interdisciplinary studies in the laboratory or in the field, with good reproducibility and at low cost.
For the elemental analysis of environmental samples XRF has the advantage of being a rapid and inexpensive method with a simple sample preparation. Quantitative and qualitative analyses are performed without acid digestion processes and a great number of elements can be determined simultaneously in a short time.
XRF and PIXE are two methods very different in terms of their information depth, excitation mechanism, and applied devices. They are based on the ionization of atomic inner shells of a sample/target by a photon (XRF) or charged particle beam (PIXE) entering the target, followed by emission of the characteristic X-rays. The X-rays spectrum is registered by means of an electronic chain based on a high-resolution semiconductor detector. The Z-dependence of the X-ray energy lines in the spectrum, as well as the dependence of the X-ray lines intensities (peak areas) by the element concentrations, allow a qualitative and quantitative determination of the elemental contents in samples. The fundamentals of both techniques in theory and in practice, instrumentation and sample preparation are presented, as well as the problems of matrix correction and secondary effects.
Numerous studies in the life and earth sciences and environmental monitoring on the application of XRF and PIXE techniques to the analysis of natural and environmental samples of various matrices (soils, sediments, fish, aerosols, vegetation, biological samples, food items, etc.) are presented in this course and some papers showing interesting cases in biology, biochemistry, geology, and environmental science are made available to students.
The elements of interest for PIXE in environmental matrices are: Al, Si, P, S, Cl, K, Ca, Ti, V, Cr, Mn, Fe, Ni, Cu, Zn, As, Br, Rb, Sr and Pb.
In order to extent the palette of chemical elements which can be analyzed in environmental samples, including heavy metals, XRF and PIXE can be combined with other atomic and nuclear spec-

trometric techniques such as instrumental NAA or atomic absorbtion spectrometry (AAS).

Prompt gamma-ray emission technique (PIGE):

PIXE belongs to the group of Ion Beam Analysis (IBA) techniques which constitute a cluster of analytical techniques that use an ion beam for study of structures and composition of samples belonging to various classes of materials. Particle Induced Gamma-ray Emission (PIGE) is an IBA technique able to determine light elements, such as Li, B, C, F, Na, Mg, Al, P, S, and Cl, besides some heavier elements (e.g. Cr, Mn, Fe, Co, Cu), based on (p,p´γ), (p,γ), (p,αγ) or (p,nγ) nuclear reactions of the projectile particles "p"on target samples. Detection limits are discussed in detail, in comparison with those obtained by PIXE and XRF. Advantages and limitations of each technique are highlighted.
The course presents some applications of IBA techniques, such as: i) simultaneously use of PIXE and PIGE ion beam analytical techniques for the determination of some major, minor and trace elements in selected environmental samples (animal tissues, aquatic plants, bottom sediments, soils), collected from polluted and natural protected areas in Lower Danube basin, Danube Delta and Black Sea; ii) applying IBA techniques for bioaccumulation studies of minerals and toxic elements from environment/substrate to related biological tissues in industrial areas.

Conclusion:

The determination of trace elemental levels in different matrices is a challenge for the entire spectrum of analytical techniques, including nuclear and atomic techniques. Due to the fact that all the employed techniques have own advantages and disadvantages, the choosing of one or another technique is dictated by its sensitivity, type of sample matrix under investigation, the range of chemical elements to be investigated in a single sample, rapidity of analyses (including sample preparation, automatisation, and time of spectra evaluation), cost of instrumentation and level of matrix effects and spectral interferences.
Using a combination of these methods, a large number of microelements could be determined in environmental samples at part-per-million (ppm) level or even less, in the case of INAA. It is worth to mention the great advantage of non-destructivity of samples compared to other atomic spectroscopic analytical techniques, such as AAS.

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CURRENT STATUS AND FUTURE NEEDS OF NUCLEAR ANALYTICAL TECHNIQUES AND THEIR APPLICATIONS

For the purpose of this course, we define nuclear analytical techniques (NATs) as those that use nuclear reactions, radioactive decay, or nuclear instrumentation to investigate properties of matter. This definition extends from the well-established radiochemistry, neutron activation analysis (NAA), and prompt-gamma activation analysis (PGAA) to advanced methods at the limits of science and technology, and includes the applications of these techniques to the determination of composition and structure of matter for science and technology.
The broad range of nuclear analytical techniques share a set of advantages over competing methods: (i) highly penetrating probe and response radiation; (ii) independence of chemical state and of analytical blank; (iii) nondestructive character, and (iv) sensitivity. NAA in particular is in regular use worldwide to perform elemental analysis of as many as forty elements in a variety of materials important to industrial process development and control, human health, environmental protection, and cultural heritage. NAA is especially valuable in the case of large samples, complex matrices, solid materials that are difficult to dissolve, and QA/QC. Although NAA is mature, several developing extensions to the method promise greater applicability to the analysis of large ultrapure solids and extremely heterogeneous samples. There is an urgent demand for the determination of ultra-fine particles in environmental studies and an understanding of their health impact. NAT's are and will continue to be applied in studies of atmospheric particulates and the developing field of engineered nanoparticles. The broad elemental coverage and high throughput of NAA have made the technique a dominant one in archaeometry.
Several obstacles stand in the way of further use of NATs. Foremost among them are the decline in the number of research reactors in the developed world. This problem may be partly offset by a number of new research reactors in the developing world but also by new developments in DD and DT neutron generator technology. Higher fluence rates, longer life-time and reduced size of the tubes make them attractive as a source of neutrons for analytical purposes when combined with appropriate moderator/shielding and counting equipment.
New developments in analytical techniques and applications:
Over 200 small and medium charged-particle accelerators are in use in many countries for PIXE and other ion beam analysis techniques. Their applications in materials and life sciences are expanding, especially with microbeam facilities which allow imaging in two or three dimensions (more than 40 operational μ-beam facilities available at this moment). Charged-particle activation analysis (with or without radiochemistry) can be a complementary technique to NAA for the determination of particular elements in different matrices (biological, environmental, and certain technologically advanced materials). In the version of TLA (thin layer activation) this technique is effective for wear and corrosion studies on moving mechanical equipments for industrial applications and the assessment of the performances with time of human prostheses as well.There is a remarkable growth in the number and availability of particle accelerators related to the rapid expansion of diagnostic and therapeutic nuclear medicine procedures, notably positron emission tomography (PET), single-photon emission tomography (SPET), (including hybrid systems with CT or MRI), functional diagnosis, molecular imaging, and metabolic radionuclide therapy. For example, more than ten million tests are made with 99mTc annually in North America alone. The number of qualified and experienced professional nuclear scientists and engineers, in particular radiochemists and radiopharmacists, has not kept pace with this increase, leading to greater risks in these procedures. Analytical techniques based on synchrotron radiation are emerging which can provide qualitative and quantitative information on in-vivo elemental composition, structure, and molecular imaging. As many as ten of the new large facilities are dedicated to the biomedical sciences.
The role of trace elements in health and environmental studies:
NATs are playing a significant role in the three "new epidemics"(WHO 2000) of cancer, cardio-

vascular disease, and diabetes. NATs have a unique role to aid in understanding the mechanism of brain-gut interactions related to satiety and obesity, which appear to be related to the new epidemics, and are in other ways an important health issue in rapidly developing countries. It is noted that a few investigations have commenced involving NATs in the determination of the composition of biological tissues in connection with HIV incidence in sub-Saharan Africa. According with the recommendations of the international and European pharmacopoeia, the quality assurance/control (QA/QC) of labelled compounds and radiopharmaceuticals for human and animal investigations is required making use of sophisticated and sometimes unusual radiochemical and radioanalytical methods of analysis and NATs,. The development of rapid methods of analysis and visualization of radioactive specimens would give a substantial improvement to these technologies. The stability with time of the labelled species and the evaluation of the expiration time is of paramount relevance for the performances of labelled species. Artificially produced radioactive tracers, characterized by short half-life and high specific activity, are finding several applications in the life sciences, in particular in occupational and environmental toxicology, in metallobiochemistry and nanotoxicology as well as in living organisms (cell cultures, plants, animals, and fishes).

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Contribution ID: **3** Type: **not specified**

RADIOACTIVE NUCLIDES IN THE ATMOSPHRE and MEASUREMENT TECHNIQUES FOR FAST ENVIRONMENTAL MAPPING OF CONTAMINATED SITES

Introduction to natural and artificial radionuclide sources in the atmosphere Cosmogenic radionuclides (eg 7Be, 22Na…) and 210Pb from terrestrial origin and their use in global atmospheric models Radioactive aerosols and their diameter, AMAD value, penetration to the lugs, dose assessments Instruments for collecting radioactive nuclides in the atmosphere, collecting substrates, instruments for measuring the air filtes Long range transport of radionuclides in the atmosphere, example of Chernobyl and Fukushima accident Specific measurements in the region of Thessaloniki, Greece and Milano, Italy after the Fukushima accident …FURTHERMORE, a short introduction how we measure in the same air filters trace elements or heavy metals by nuclear techniques eg. XRF and INAA.

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How can we fast characterize an area if it is high contaminated or not? What about the remediat
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TRACK STRUCTURE MODELLING IN RADIOBIOLOGY AND RADIATION DETECTION

An energetic charged particle (such as a proton or heavier ion) travelling through an absorber, (such as nuclear emulsion) leaves a track of energy deposition events (detected, e.g., by developed grains in the emulsion). Using Poisson statistics of energy deposition in the target (e.g. grain) for its activation, of the radial distribution of delta-ray dose and of action cross section, the Track Structure Theory (TST) was introduced by Robert Katz in 1968 as a theory of RBE and applied in modelling the response of physical and biological detectors after ion irradiation. The ion beam radiation field is specified by the charge Z, speed β (or energy), fluence, and LET of the ion. The detector is represented by radiosensitive elements of size a0 and radiosensitivity D0, its gamma-ray response being represented by c-hit or multi-target expressions. Key to TST is the radial distribution of delta-ray dose (RDD) around the ion path. Radial integration of the RDD folded with the gamma-ray dose response of the physical detector (or cellular line) yields the action cross-section, σ. In its application to radiobiology, four-parameters represent the given cell line (m, D0 , a0 , and σ0). Track Structure Theory enables quantitative and predictive modelling of the response of physical detectors (such as nuclear emulsion, TLDs or alanine) and of in vitro RBE-LET dependences in cellular lines (such as V79, CH3H10T1/2 or HSG) after ion irradiation, to be performed. It has also been used to model carbon beam radiotherapy.
In two lectures, the principles of the Track Structure Theory and its application in radiation dosimetry, radiobiology and radiotherapy, will be outlined.

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Contribution ID: **5** Type: **not specified**

PHYSICS AND TECHNOLOGY OF PROTON RADIOTHERAPY

The basic factor which determines the success of cancer radiotherapy is to deliver the highest possible dose of ionizing radiation (as recommended by the physician) to the tumour volume while sparing the neighbouring critical organs and healthy tissues. Accelerated protons are particularly useful in cancer treatment because of the phenomenon of the Bragg peak, i.e. a rapid increase of energy deposition in tissue the at the end of the proton track. Another advantage of protons is that, due to their well-determined range, the unwanted doses to healthy organs are largely reduced as compared to high energy X-rays used in conventional radiotherapy. This is of particular importance to paediatric patients in whom the probability of later radiation-induced cancer should be minimized.
The two lectures will cover the following topics: (1) proton interactions with matter; (2) accelerators dedicated to proton therapy; (3) methods of beam delivery (4) reference and relative dosimetry of proton beams and (5) Quality Control and verification of proton range in radiotherapy.

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Contribution ID: **6** Type: **not specified**

TRACK MEMBRANES AS A SUCCESSFUL EXAMPLE OF ION-TRACK TECHNOLOGIES APPLICATION: HISTORY AND STATE OF ART

The overwhelming majority of modern productions (from micro- electronics and so-called "high technologies"to biotechnology and medicine) cannot function without the use of membrane technologies which are necessary for obtaining pure liquid and gaseous materials and also for purification and concentration of different solutions and suspensions. The first track etched membranes or so called nuclear filters were created in the USA and the Soviet Union in the early 1970's using ion-track technology. Track etched membranes in contrast to traditional membranes with a network structure have pores in the form of capillaries with a regular usually cylindrical shape. The pore sizes of nuclear filters lie in the range of 0.01-10 micrometers; the pore number reaches values of 105 - 1010 per square centimeter (1-20% of through porosity). The narrow distribution of pores by size is the principle advantage of nuclear filters (no more than 10% from the average diameter). Track etched membranes are manufactured using methods of nuclear physics. At the first stage the thin (8-40 μm) polymer films are either treated with beams of multicharged non-radioactive ions (C, O, N, Ar, Ne, Kr, Xe, Co, etc) accelerated up to energies more than 1 MeV/nucleon at the cyclic or linear accelerators, or by irradiation using U235 fission fragments which are formed by the actions of neutrons in a nuclear reactor. In the second stage the polymer film treated by ion beams or by fission fragments is irradiated by ultraviolet light for formation of polymer defects which appear after film treatment in the first stage. During the final stage the film with numerous tracks is treated by chemical etching and, as a result, the dissolving of track zones, and the appearance of through pores, takes place. Afterwards, the ready product is washed, dried and packed. During last 30 years these filters have been used in large scale processes of water purification, for the needs of microelectronics for manufacturing of modern antiviral vaccines (anti-rabies, anti-influenza, vaccine against encephalitis), for E-coli bacterial analysis of drinking water at water purification plants, for encephalitis immune diagnostics by ELISA method, etc. In the last years these filters were used for manufacturing of apparatus for blood plasmaspheres, for purification of drinking water from microbiological and colloid impurities and for production of infusion filters for safe drug delivery.

The following topics will be discussed during the course of the lecture:
1. Main Principle of Track-etched Membrane Technologies
2. Physico-chemical Properties of Track-etched Membranes and Characterization Technologies
3. Track-etched Membrane Filtration Applications and New Concepts to Produce Innovative Polymeric Track-etched Membrane
4. Applications of Track-etched Membrane in Modern Nano-Technologies

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Contribution ID: **7** Type: **not specified**

RADIATION DETECTORS AND MEDICAL IMAGING

Medical imaging technology has dramatically changed healthcare in the past 30 years, by giving doctors a powerful tool to detect and diagnose disease at its earliest and to determine the most appropriate and effective care. Medical imaging is the technique and process of creating visual representations of the interior of a body for clinical analysis and medical intervention, as well as visual representation of the function of some organs or tissues. The progress of well-known techniques like X-ray Computed Tomography (CT), Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) is largely connected with the progress of radiation detectors. The aim of this lecture is to explain the basic principles of operation of the radiation imaging detectors and to present the current status and trends of their development. Particular emphasis will be placed on the novel photon-counting pixel detectors like the ones based on Medipix technology and their potential use in medical application.

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Contribution ID: **9** Type: **not specified**

STATISTICAL TREATMENT OF ENVIRONMENTAL DATA: A STUDY CASE ON PASIVE MOSS BIOMONITORING OF AIR POLUTION IN THE REPUBLIC OF MACEDONIA

We will present results from the application of moss biomonitoring technique to investigate trace elements depositions in the air in the Republic of Macedonia. Since 2002, four moss surveys have been conducted and samples of the terrestrial mosses Homolothecium sericium and Hypnum cupressiforme were collected at 72 sites, evenly distributed over the territory of the country, in accordance with the sampling strategy of the European moss survey program. More then 40 elements on every set of samples, were determined by instrumental epithermal neutron activation analysis, atomic absorption spectrometry and atomic emission spectrometry with inductively coupled plasma.
During the last survey, measurements of the natural radioactivity dose rate were made, at the same locations where the samples were collected and correlation of the measured dose rate and content of some elements in mosses were investigated.
A variety of statistical analysis methods can be performed on the collected data. Different statistical techniques, both in descriptive statistics and inferential statistics are crucial for analyzing the results. Short review of several statistical methods will be given: Fundamental sampling and data description, Estimation problems, Hypothesis testing, Simple and multiple linear regression, Analysis of variance techniques, Correlation analysis, Factor analysis and Nonparametric statistics.
Environmental data can be analysed mostly by descriptive analysis, parametric and non parametric analysis, normality of datasets, Box-Cox transformation etc. Factor analysis can be used to identify and characterize different pollution sources.

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Contribution ID: **10** Type: **not specified**

TRACK ETCHED MEMBRANES BASED NANOTECHNOLOGIES

Among the methods of synthesis of nanostructures in solids currently under development, exhibiting various morphologies and properties, a special place is devoted to so-called nuclear technologies, which include the study of the processes of formation and of the applications of ion (nuclear) tracks. The swift heavy ion technique is based on the unique phenomenon whereby high-energy heavy ions induce latent tracks in materials such as polymers or metals containing a highly disordered zone of about 3-10 nm in diameter. The extremely high volume concentration of tracks in the solid state matrix which is achievable by adjusting the ion fluence, enables the creation of "controlled" nanostructures on the basis of the latent tracks, including the so-called "track membranes"based on polymeric thin films. This is possible because selective etching of the disordered zones in the polymer results in the formation of a set of nano sized or micron sized channels or pores having a high aspect ratio. The hollow track areas can easily be filled with materials of different compositions (metals, semiconductors, biological particles), by, for example, electroplating, electroless deposition and covalent binding. This method of template synthesis has seen wide application in the creation of unique optical, electronic and catalytic structures and nanoscale devices. This nuclear technology was applied to prepare new types of nickel-platinum and nickel-palladium nano-structured electrodes for the production of hydrogen by the electrolysis of water. The logical extension of this work has been the development of cathodes for lithium-ion batteries based on ensembles of nickel and copper nanowires modified by carbon nanotubes. Moreover, the track etched membranes are suitable for the creation of multifunctional membranes for separation processes of liquids and gases. New gas separation membranes based on polymethyl pentane, polyester and polyolefin polymeric films irradiated with heavy ions are applicable for gas separation processes, such as selective isolation of oxygen. Furthermore methods for the reactive sputtering of wide bandgap semiconductors on track-etched polymer films were developed. A range of photocatalytic track membranes were prepared and their physico-chemical and catalytic properties studied. Such new photocatalytic, self-cleaning materials are applicable for organic pollutant degradation and prevention of biofouling on membranes. The development of surface enhanced track membranes as platforms for Raman spectroscopy showed potential for the rapid assessment of water and air quality, on the basis of plasmonic metal coated composite track membranes. Ligand functionalized nanofiber track membrane composites were developed with affinity for toxic metals and are suitable for hydrometallurgical separations. Since the protocols for making these diverse nanomaterials are available at industrial scale, there is a high potential for their rapid commercialization.

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Contribution ID: **11** Type: **not specified**

RADIOBIOLOGICAL RESEARCH AT JINR ACCELERATORS AND MODELLING OF RADIATION-INDUCED DISORDERS IN CENTRAL NERVOUS SYSTEM

JINR accelerators provide extensive capacity for multifaceted radiobiological research concerning basic problems of radiation genetics, molecular radiobiology, and radiation physiology, as well as a wide spectrum of practical issues, the most challenging ones being space radiobiology with special reference to manned interplanetary missions and the use of charged particles for the treatment of malignant tumors. Possible acute and delayed risks to the central nervous system (CNS) are accepted now as the most concerning in these fields. The aim of this lecture is to explain approaches for solving the problem of radiation-induced disorders in CNS. Particular emphasis will be given on principal difference of biological action between low-linear energy transfer (LET) radiation (X rays or gamma-rays) and high LET radiation (protons and heavy charged ions). Current progress in the experimental physiological and molecular biological studies in conjunction with theoretical results obtained by computer modelling techniques will be reviewed.

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Contribution ID: **12** Type: **not specified**

CONTENT OF HEAVY METALS IN ECOSYSTEM MONTENEGRIN COAST AS A RESULT OF ENVIRONMENTAL POLLUTION

Anthropogenic seawater pollution with heavy metals has significantly increased in past decades. These pollutants aim to integrate in bottom sediments, making sediments in ecosystems in areas with constant inflow of heavy metals highly contaminated.
Currently, in the country and abroad, numerous investigations focused on analysis of environmental protection and improvement, particularly water as a sensitive and limited resource, is being conducted. One of main environmental tasks is water quality monitoring, i.e. monitoring of the possible presence of harmful substances as well as determining their concentrations in water. Monitoring of marine environment trace metals pollution, which represent a basis for the control of pollution of the marine environment is usually limited by performance and detection limits of the existing analytical techniques, but also by the general lack of interest, since rivers and oceans have for quite some time been used for disposal of various wastes.
In recent decades anthropogenic activities (agricultural, urban and industrial) have led to increased pollution of marine ecosystems, especially in the bays. As a consequence of these actions, pollutants get into the water and often cause irreversible changes in marine ecosystem. Beside these pollutants, heavy metals are of the major concern due to their persistence and bio-accumulative nature. Heavy metals can be introduced into the aquatic environment and accumulate in sediments by disposal of liquid effluents, chemical lichgates and runoff originating from domestic, industrial and agricultural activities, as well as atmospheric deposition.
Therefore, investigations of the south-eastern Adriatic marine environment quality have been intensified in the last decade monitoring sea water, biota and sediment quality related to heavy metals pollution along the Montenegrin coastal area.

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Contribution ID: **13** Type: **not specified**

SOURCES AND TRANSFER OF RADIONUCLIDES IN THE TERRESTRIAL ENVIRONMENT

Natural and anthropogenic sources of radionuclides in the terrestrial environment. Importance of chemical speciation of radionuclides for their distribution in terrestrial ecosystems and their transfer in food chains. Influence of precipitation chemistry on

the fate of airborne radionuclides in the terrestrial environment. Relative contributions

of 137Cs and 239-240Pu from atmospheric nuclear weapons tests and the Chernobyl reactor accident as evident from field studies in Norway.

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