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Academy of Sciences of Uzbekistan

NUCLEAR MEDICINE

INTERNATIONAL CONFERENCE

Bukhara, Uzbekistan October 3-5, 2023

BOOK OF ABSTRACTS

CONFERENCE ORGANIZERS:

Academy of Sciences of the Republic of Uzbekistan
Ministry of Health of the Republic of Uzbekistan
Institute of Nuclear Physics of Uzbekistan Academy of Sciences
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Bukhara State University
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Plenary Reports

RESULTS OF THE REFORM OF ONCOLOGICAL AND RADIOLOGICAL SERVICES IN UZBEKISTAN: ACHIEVEMENTS AND HORIZONS

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The Government of Uzbekistan and the President in particular, pays great attention to the field of medicine, especially to the oncological system. For 6 years, 4 presidential decrees on the development of the oncological service have been adopted. As a result of the implementation of these resolutions, a single oncological service has been created in the republic. All 15 regional oncological dispensaries have been transformed into branches of the Republican Center of Oncology and Radiology Also, 228 oncological offices where district oncologists work have been established in all regional medical unities.

9 out of 15 branches have been reconstructed, 3 have been overhauled and 3 have been rebuilt. All oncological institutions are equipped with new, modern diagnostic and therapeutic equipment. In order to improve international cooperation, memorandums were signed with 22 leading foreign clinics. Over the past 5 years, 232 specialists have been improving their qualifications in leading clinics of developed foreign countries at the expense of governmental funds. 13 mobile and 16 stationary mammography devices were purchased for the Bukhara region, 13 more mobile mammography devices were purchased for all regions, and breast cancer screening of women aged 45-65 years is being carried out for the prevention and early detection of breast cancer. Girls aged 9-14 are vaccinated against human papillomavirus with 98% coverage, in order to prevent cervical cancer. Pilot screening of cervical cancer was carried out in Chirchik and Karakalpakstan. It is planned to start screening throughout the Republic. Currently, immunohistochemical laboratories are organized in all branches of the center. RSSPMCOR and its branches have received laparoscopic equipment. Since 2018, 27 types of video laparoscopic minimally invasive operations are being carried out.

2 linear accelerators, 11 gamma and 7 brachytherapy devices have been installed in oncological institutions, and the number of radiation equipment has been increased to 27 devices. Queues have been eliminated, radiosurgery has begun. Electronic medical records and telemedicine have been launched. 5 years ago, 1.2 million US dollars were allocated for antitumor drugs, now almost 10 times more is allocated, i.e. more than 12 million US dollars. The availability of chemotherapeutic drugs improved from 12-15% to 95-98%.

In total, 200 palliative beds have been opened in the branches for the treatment of patients in advanced stages. 2 hospices have been built and are functioning in Urgench and Samarkand, new hospices for the terminally ill and seriously ill are being built in Ferghana and Tashkent. 4 consultants from South Korea, India and Belarus were involved to improve the work of the oncological service. Currently, they are working in cooperation with the specialists of the center. By the decision of the President, a new oncology center with 650 inpatient and 100 outpatient beds is being built on a 5.4-hectare plot of land, which will be commissioned at the end of 2023. Currently, it is planned to purchase equipment for 80 million US dollars as part of the second stage of the loan from the Islamic Development Bank.

FRUITFUL PARTNERSHIP BETWEEN THE INP OF THE ACADEMY OF SCIENCES OF UZBEKISTAN AND THE IBP OF RUSSIA IN THE FIELD OF NUCLEAR MEDICINE

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In December 1972, the President of the Academy of Sciences of the UzSSR A.S. Sadykov and the Chairman of the State Committee for the Use of Atomic Energy of the USSR A.I. Petrosyantc approved a special protocol. The aim - the organization of work in the Institute of Nuclear Physics of the Academy of Sciences of the UzSSR (hereinafter INP) on creating a regional production of radioisotope products for medical and biomedical purposes. The presence of an operating technical base in the INP (the VVR-SM nuclear reactor, as well as the U-150 cyclotron and the radiochemical complex made it possible to organize the production and supply of such products for medical institutions in a short period.

Since January 1973, with the participation of the Institute of Biophysics of the Ministry of Health of the USSR (hereinafter IBP) and some other organizations, has mastered the technology of target irradiation at the VVR-SM reactor and the technology for obtaining the first five radiopharmaceuticals (RP) based on ^{24}Na, ^{32}P, ^{131}I, and for ^{57}Co on the cyclotron U-150 as well. A microbiological laboratory was organized also to monitor the sterility and pyrogenity of RP. The director of the Institute, U.G. Gulyamov, was the head of the work at the INP. At the end of 1974, the first deliveries of RP have been started to medical institutions of Uzbekistan and Kazakhstan, and afterwards to other regions.

In 1976, on the base of the radiochemical complex of the INP a specialized enterprise "Radiopreparat" was created (the first director is M.N. Abdukayumov), which operates to the present time and is successfully developing. The range of isotope products of this enterprise includes ^{99}Mo/^{99m}Tc generators and a number of kits for them, RIA kits, preparations of ^{125}I, ^{131}I, biologically active compounds, labeled ^{32}P and ^{33}P, and others.

By the end of the 1980s several enterprises in the USSR produced in the necessary quantities and were available to medical institutions almost any RPs that were available abroad by that time, as a result of the implementation of measures to carry out new developments and create a new production in Uzbekistan. The level of development of nuclear medicine practically corresponded to the level of developed countries of the world.

It should be especially noted, that it was in the INP that the first in the USSR and almost in parallel with the first in the world (Oak- Ridge, USA) experiments on the creation of the ^{188}W/^{188}Re generator were implemented and published together with the IBP. The head of work at the INP was E.S. Gureev - the Chief of the Laboratory of Nuclear Chemistry. The role of these developments has yet be evaluated in the future, because right now there is a rapid development of radionuclide therapy technologies in the world, where ^{188}Re is a very promising radionuclide. Currently, preclinical and clinical studies of kits for several ^{188}Re-RPs for radionuclide therapy are being conducted in Russia and other countries.

In the future, a number of innovative RFPs and nuclear medicine technologies can be developed in cooperation with our colleagues from Uzbekistan, it is hoped.

POLATOM ON THE MAP OF NUCLEAR MEDICINE

Czajka P.

National Centre for Nuclear Research Radioisotope Centre POLATOM, Warsaw, Poland

National Centre for Nuclear Research Radioisotope Centre POLATOM is located in Otwock-Świerk near Warsaw with direct access to MARIA Nuclear Research Reactor. POLATOM is a Polish producer and distributor of isotope preparations used in medicine, science, industry and environmental protection. It also conducts research and development works. They are of an application nature and concern radiopharmacy, chemistry and nuclear technology as well as such scientific disciplines as radiochemistry, biochemistry, and immunology. The result of the research is the development of own technologies and products.

Development and production of radiopharmaceuticals is positioned as one of the most important branches of POLATOM activities. POLATOM is a renowned manufacturer of *Poltechnet®* *^{99}Mo/^{99m}Tc radionuclide generator* as well as ever-growing line of radiopharmaceutical preparations for ^{99m}Tc labelling including *PoltechColloid*, *PoltechDMSA*, *PoltechDTPA*, *PoltechMBrIDA*, *PoltechMDP*, *PoltechMIBI*, *PoltechRBC* and *Tektrotyd®*, addressing the wide spectrum of diagnostic applications. These are accompanied by a separate line of iodide capsules such as *Iodopol* as well as iodide-based radiopharmaceuticals such as *Hippurate-^{131}I*, *MIBG-^{131}I*, *MIBG-^{123}I*, *Sodium iodide Na^{131}I* solutions for injection. The radiopharmaceutical line of products is completed with *Strontium chloride $^{89}SrCl_2$* solution and radiopharmaceutical precursors: *ItraPol* (^{90}Y) and *LutaPol* (^{177}Lu).

Noteworthy examples of POLATOM's research and development are modern and novelty medicinal substances such as GMP certified *DOTA-TATE* for radiolabelling, GMP grade *PSMA-11* for ^{68}Ga labelling. Moreover, POLATOM provides numerous substances for medical experiments such as *PSMA-T4* and *PSMA-11* for ^{68}Ga labelling, *PSMA-D4* for ^{177}Lu labelling as well as *[Lu-177]Lu-DOTA-TATE* and *[Y-90]Y-DOTA-TATE*.

The most recent advancement of POLATOM's capacity is focused on its Centre for Design and Synthesis of Molecularly Targeted Radiopharmaceuticals which, equipped with cutting-edge technology, enables commercial scale production of cyclotron produced radionuclides such as ^{225}Ac, ^{211}At, ^{64}Cu, ^{67}Cu, ^{89}Zr, ^{68}Ge, ^{68}Ga, ^{18}F, ^{123}I, ^{111}In, ^{43}Sc, ^{44}Sc, ^{47}Sc, further expanding POLATOM's capacity to deliver active pharmaceutical ingredients and radioisotopes for medicinal products research and experimental development in the field of nuclear medicine.

THE CONCEPT OF A BIOMEDICAL PROTON THERAPY CENTER BASED ON A SUPERCONDUCTING COMPACT PROTON CYCLOTRON MSC-230 IN DUBNA

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At the Joint Institute for Nuclear Research (JINR), Dubna, a superconducting proton cyclotron MSC-230 is being created jointly with the NIIEFA (Rosatom State Corporation, St. Petersburg) at the expense of JINR. This cyclotron should provide a current of up to 10 μA at a proton energy of 230 MeV. MSC-230 may become the first model for a series of specialized medical accelerators of this type. The launch of MSC-230 is scheduled for the end of 2024.

The Federal Biomedical Agency (FMBA) of Russia and JINR expressed their intention to participate in the development of a joint concept (and in the future, a project) for the creation of a pilot proton therapy research center on the basis of the existing FMBA medical center in Dubna and on the MSC-230 accelerator being created at JINR. The aims of the center will be investigations and development of modern methods and technologies of beam therapy (protons, neutrons, electrons, gamma), medical technologies and diagnostics for beam therapy, advanced scientific research in the field of radiobiology, experimental irradiation and treatment of patients.

PROPOSAL FOR THE DIGITAL TRACKING CALORIMETER FOR THE PROTON COMPUTED TOMOGRAPHY (PCT) WITHIN THE ARIADNA PROJECT AT JINR

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A new innovation center for experimental and clinical research is beingestablished at JINR. The basic facility of the center will be theMSC-230 proton medical accelerator designed for the proton flashtherapy. We propose to develop and build an imaging detector for protoncomputed tomography (pCT) for the proton therapy treatment planning. Incomparison to the conventional X-ray CT scans the pCT may provide adirect measurement of the distribution of relative stopping power valuesinside the object and thus has a high potential in reducing theuncertainties of the Bragg peak position calculation. The most promisingconcept in this field is a Digital Tracking Calorimeter (DTC) proposedby Bergen pCT collaboration. The DTC is based on several layers ofhigh-granularity silicon pixel sensors and provides both the track andenergy information. Each sensitive layer of our DTC will consist of MICApixel chips being developed for MPD experiment at NICA. Modern read-outelectronics is capable to handle enough data to acquire a single 2Dimage in few seconds making the system fast enough to be used forclinical application.

NEW APPROACHES TO INCREASE THE EFFICIENCY OF RADIOTHERAPY: MATHEMATICAL MODELS AND RADIOBIOLOGICAL EXPERIMENTS

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Distant radiotherapy is an essential part of modern therapy of cancer. Radiation oncologists typically use photon sources (X-rays or gamma-rays). Hadron beams (protons, neutrons and carbon ions) are not so widely available. In contrast to photons and fast neutrons, the depth energy deposition of heavy charged particles has pronounced peak (Bragg peak). On this reason proton therapy has been increasingly used to treat cancer patients in recent years. On the other side, relative biological efficiency (RBE) of protons is comparable with those of photon radiations. Beams of heavy ions with larger RBE are very expensive. This is why the problem of increasing the efficiency of both conventional and proton radiotherapy remains an important issue. Present report provides an overview of current trends in this field, both in relation to theoretical models and ongoing *in vitro* and *in vivo* experiments.

In recent years, there has been an active development of new radiosensitizers based on small molecules, macromolecules, and nanoparticles with different chemical structures. Basic concept of the sensitization of tumor cells to radiation relies on two different approaches. We consider two characteristic examples of each approach.

The first approach is related to the phenomena of physical energy deposition in the process of interaction of radiation with a sensitizer, as a result of which secondary particles are formed with a significantly higher RBE than the original radiation. A well-known example of this approach is neutron capture therapy, when epithermal neutrons with low RBE after interaction with target atoms produce alpha particles and fragments with low range and high RBE. Much less is known about the sensitization of tumor cells or tissues to proton radiation based on similar processes. In recent years, the number of studies devoted to the effect of heavy metal nanoparticles as potential radiosensitizers to photon and proton beams has increased. However, there are a lot of uncertainties in the understanding of experimental data. We developed models suggesting that the effect is most probably based on the clusters of short-range secondary electrons produced after the interaction with primary particle.

The second approach is based on the modification of the biological phenomena which determine the yield of the damage causing cell death (the cell's repair status, oxygenation, the cell cycle phase, the tumor microenvironment, etc.). For example, it was demonstrated in our *in vitro* studies that in the presence of certain DNA synthesis inhibitors the yield of radiation-induced DNA double strand breaks (DSB) was significantly increased due to transformation of non-lethal DNA damage into enzymatic DSB. *In vivo* studies with grafted mouse melanoma tumor and injection of this drug revealed threefold reduction in tumor growth rate during post radiation period as compared to proton irradiation only. The amount of tumor stem cells was also strongly reduced after the application of drug together with proton irradiation. A model explaining the mechanism is also developed in different levels of complexity.

New trends in the radiotherapy research rely on the evolution of the so-called binary methods, where radiation is used together with complementary agent to produce more pronounced damage to the tumor site. This requires development not only the irradiation facilities, but also radiosensitizer delivery systems and, importantly new paradigm of treatment planning. For the latter purpose, a new generation of mathematical models and diagnostic hardware need to be developed.

20 YEARS OF EXPERIENCE IN RADIOIODTHERAPY OF THYROTOXICOSIS. WHEN, HOW, TO WHOM

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Thyrotoxicosis is a syndrome caused by the excessive content of thyroid hormones in the blood and their toxic effect on various organs and tissues. There are three methods of treating thyrotoxicosis: medical - conservative, and radical - surgical and radioiodtherapy. The choice of radial treatment of thyrotoxicosis is determined by: the commitment of specialists and their experience in the use of a particular type of treatment, features of national endocrinological and surgical schools, the possibilities of a specific medical institution, as well as depends on the age of the patient, the severity of the disease, the size and location of the goiter, patient preferences and other factors.

Indications for radioiodtherapy of thyrotoxicosis - increased thyroid hormone production by thyroid gland occurring with clinical thyrotoxicosis syndrome. Criteria for selecting patients: long-term treatment with thyrostatics, intolerance to thyrostatics, relapses after surgical treatment.

Contraindications for radiotherapy are absolute: pregnancy and lactation; relative: urinary incontinence, uncompensated hyperthyroidism, active stage of ophthalmopathy, mental illness, severe somatic diseases requiring emergency therapy and outside care.

The procedure of radioiodtherapy in Russia is carried out according to radiation safety standards in specialized departments equipped with a complex of radiation equipment, air purification and sewage. Medical appointment 131- I must be accompanied by the support of medical physicists and a trained staff of nurses. Work with radiopharmaceuticals should be carried out in accordance with the “Basic Sanitary Rules for Radiation Safety”.

Necessary information for the procedure: previous therapy with thyrostatics and the results of radioiodtherapy or surgical treatment; results of 24-hour accumulation of radioiode by the thyroid gland; the weight of the gland, based on ultrasound determination of the size of the thyroid gland; the presence of nodules in the thyroid gland, their functional activity and cytological examination to exclude malignancy; concomitant diseases. Women of reproductive age should be tested for pregnancy before radiotherapy. After radioiodotherapy of thyrotoxicosis for 6 months, it is recommended not to plan pregnancy. Experience of radioiodotherapy thyrotoxicosis since 2000: total number – 15737 procedures, age from 18 to 78 years, ratio of men: women 1:4, after surgical treatment 24.8%, repeated 5%.

Conclusion. Radioiodtherapy makes it possible to eliminate thyrotoxicosis of various origins with minimal risk when using standard activities and to obtain optimal results with individual dosimetric planning and calculation of the absorbed dose in the thyroid gland of more than 300 Gray.

EFFICIENCY OF RADIOIODINE REMNANT ABLATION IN CASES OF LOCALLY DIFFERENTIATED THYROID CANCER. ORIGINAL CLINICAL TRIAL

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Introduction. The thyroid cancer has increased on the territory of Russia after Chernobyl incidence in 1986, and currently accounts for up to 12,000 newly identified cases. Postoperative radioiodine remnant ablation (RRA) is the second stage of combine treatment of differentiated thyroid cancer, except for the prevalence of pT1aN0M0, with minimal level of TG and AT-TG, according to international guidelines. In the past 20 years a significant number of published practice guidelines for the treatment of this disease. However, the discussion is the amount of medication for administration activity (GBq) ^{131}I, is required for successful RRA.

Aim. Establish the diagnostic and prognostic significance of preliminary studies (US of the neck, radioisotope studies), as well as whole-body scintigraphy after the introduction of therapeutic ^{131}I activity.To evaluate the effectiveness of RRA depending on the degree of hypothyroidism, as the conditions for the preparation and conduct of radionuclide therapy, and by the dynamics of blood thyroglobulin (TG) levels. Establish the dependence of the absorbed dose gradient/administered therapeutic activity (MBq/kg) in thyroid remnants on physiological features, including the level of TSH stimulation.

Materials and Methods. The study analyzed 352 clinical cases of the adulte patients (18-68 y.) after radical surgical treatment (R0) for DTC. In our study, the effectiveness of RRA was compared with certain indicators of specific therapeutic activity ^{131}I (MBq/kg), in groups of patients with different levels of **TSH stimulation: Group 1: 8-29 mMe/ml, n=42; Group 2: ≥ 30 mMe/ml, n=310.**

Results. 1. The effectiveness of RRA in Groups 1 was 89% and in Groups 2 – 86%, does not statistically differ (p>0.05). With TSH stimulation from 8 to 100 mMe/ml within the confidence ranges of specific therapeutic activities in Groups 1 of 36±8.23 MBq/kg and in Groups 2 of 34.5± 9.03 MBq/kg. **2.** Incomplete RRA in both groups was established in 53% of patients who had multiple (3 or more), in 7% of patients who had 2 and in 5.9% of patients who had 1 focus of thyroid remnant according to post-therapeutic scintigraphy of the whole body with 131I. **3.** In order to optimize RRA with thyroid remnants not detected by US, the effective range of specific therapeutic activity of 131I is 30-40 MBq / kg with TSH stimulation of more than 4 nMe/ml and strict adherence to a 14-day low-iodine diet. Then thyroid remnant determined by US (volume ≥ 1 ml), radiometry is recommended with neck SPECT (1200 kBq 131I) and calculation of therapeutic activity, in order to plan D = 300 Gy and reduce the risk of developing radiation sialoadenitis.**4.** RRA revealed at an early stage isolated miliary metastatic lesion of the lung parenchyma in 2 cases (0.56%), with a pre-stimulated TG level of more than 124 ng/ml in the early stages after the surgical stage of treatment. **5.** During the control complex examination with 131I-SVT 6-9 months after the performed RRA, the stimulated TG level of more than 11.9 ng/ml with normal AT-TG indicators and a pathological US may indicate metastatic lesion of the regional lymph nodes of the neck.

STATUS OF PROMETHEUS PROTON THERAPY COMPLEX

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Proton therapy is one of the rapidly developing technologies of conventional radiotherapy. According to the Particle Therapy Co-Operative Group, 312,087 patients worldwide had received proton beam treatment by 2023. In 2016, the first clinical proton center in Russia was launched at the A. Tsyb Medical Radiological Research Center. The Prometheus proton therapy complex was developed by JSC «Protom» and Lebedev Physical Institute of the Russian Academy of Sciences.

The complex is a compact synchrotron with a fixed horizontal beam and an energy of 40 - 250 MeV with an intensity of 2.0E+09 proton/pulse. The proton therapy complex has treated 775 patients by August 2023. Figure 1 presents information on the number of therapy sessions performed.

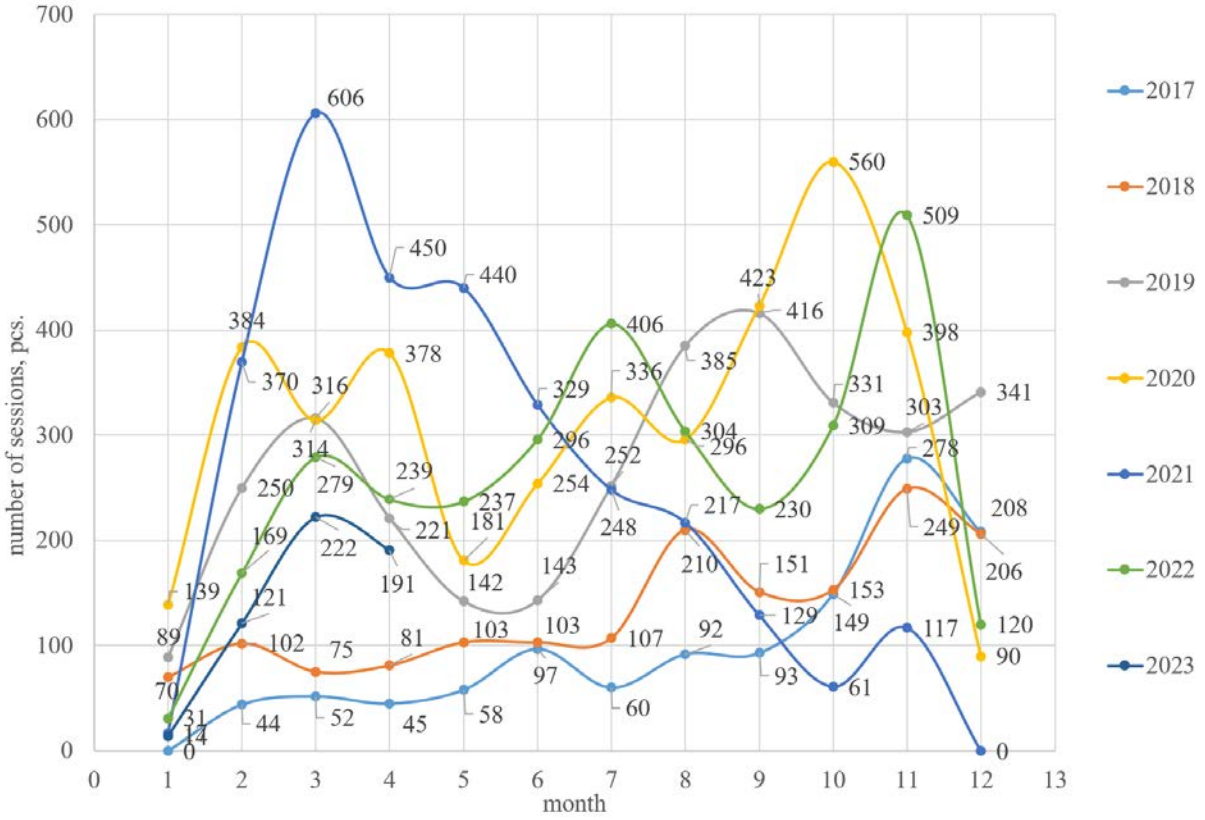

Figure 1. Number of sessions by month

The complex has undergone several major upgrades such as replacement of injector and scanning system of the complex.

PROSPECTS FOR THE DEVELOPMENT OF NUCLEAR MEDICINE IN THE REPUBLIC OF UZBEKISTAN. TECHNICAL CAPABILITIES AND STAFF TRAINING AT SAMSMU

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Nuclear medicine (NM) is one of the most actively developing areas in healthcare in many countries. NM technologies are based on the use of radionuclides (in the form of radiopharmaceuticals) for the diagnosis and treatment of various diseases, as well as for biological (preclinical) studies. Due to the capabilities of molecular imaging, radionuclide diagnostics (RND) methods make it possible to detect diseases with high accuracy and at early stages of their development, and radionuclide therapy (RNT) makes it possible to carry out targeted molecularly directed radiation exposure to tumor and other pathological foci, creating high absorbed doses in them. The Republic of Uzbekistan has unique opportunities in the development of nuclear medicine. The state enterprise "Radiopreparat" (Tashkent) produces a wide range of radiopharmaceuticals (RP) for diagnostics and therapy, fully providing the domestic market with its products and exporting it to the CIS countries, Europe and the USA. Diagnostic drugs are presented in a very wide range. Sets for the ^{99m}Ts generator - Technefor, Technefit, Mezida, Bromesis, Technemag, Technemec, Phosphotech, Pirfotech, Technetril, Pentotech, Karbomek, Medronik, Technoprost (^{99m}Ts-*PSMA-11*) make it possible to perform almost all types of radionuclide diagnostics in oncology, cardiology, as well as in the diagnosis of thyroid diseases. The line of therapeutic drugs provides the capabilities of almost all the main RNT methods used in the world today. Sodium iodide, ^{131}I allow radioiodine therapy (RIT) for thyroid cancer and thyrotoxicosis; samarium oxabifor, ^{153}Sm is a universal drug for bone metastases; ^{177}Lu *PSMA-617* has opened up opportunities for performing modern radioligand therapy for metastatic prostate cancer in Republic of Uzbekistan; ^{131}I MIBG therapy provides unique therapeutic options for neuroblastomas and other neuroendocrine tumors.

Full implementation of the opportunities for the development of nuclear materials in the Republic of Uzbekistan requires the development of a network of nuclear medicine centers, as well as the training of specialists. There are good opportunities at the Samarkand State Medical University (SamSMU), which has the necessary space for the creation of a modern center for radionuclide diagnostics and a radionuclide therapy unit. Currently, the Department of Medical Radiology is training specialists for nuclear medicine. At lectures and seminars, an in-depth study of the principles of action and the basics of the use of radiopharmaceuticals for diagnosis and therapy is carried out, methods for performing procedures for radionuclide diagnostics and therapy are studied. Taking into account the existing opportunities, it is advisable to create a scientific and practical center for theranostics at SamSMU. Working with international involvement is recommended as it allows for the immediate training of our local experts and rapid implementation of emerging technologies.

PET/CT IN THE DIAGNOSIS OF LUNG CANCER

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According to WHO data, lung cancer occupies a leading place in the structure of mortality from oncological diseases, and in terms of the number of newly diagnosed oncological diseases, it shares the first place with breast cancer. The five-year survival rate for this disease is no more than 14.9% for men and 20.8% for women.

In Russia, lung cancer also occupies a leading place in the structure of morbidity and mortality from cancer, especially among the male population.

Over the past decades, the use of PET/CT in the examination and management of patients with lung cancer has expanded significantly.

The ability to combine functional and anatomical information has made it possible to use PET/CT to study various aspects of lung cancer, allowing more accurate staging of the disease and providing useful insights into the characterization of ambiguous pulmonary nodules previously identified on imaging modalities such as chest x-ray or CT.

In addition, numerous studies have shown that the accuracy of PET/CT in some clinical scenarios is higher than that of conventional methods, making PET/CT a valuable non-invasive method for examining patients, both already diagnosed with lung cancer, and at the initial diagnosis.

However, the interpretation of PET/CT results comes with numerous pitfalls and potential artifacts that oncologists, thoracic surgeons, and radiologists need to be aware of.

Nevertheless, in most cases, the PET/CT data obtained allow timely detection of lung cancer, regional and/or distant metastatic lesions, which in turn has a direct impact on patient management and affects overall and disease-free survival.

TRANSARTERIAL RADIOEMBOLIZATION – CLINICAL SCOPE AND PROPOSED IMPLEMENTATION RESULTS IN UZBEKISTAN

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Unresectable locally advanced hepatocellular cancer and unresectable metastases of colorectal cancer pose significant challenges to healthcare systems around the world. According to general estimates, every year the number of these contingents in Uzbekistan increases by seven hundred people, including initially identified cases of neoplasms and progression of previously identified tumors.

Transarterial radioembolization of the liver with microspheres containing radioactive Yttrium-90 is a modern method that significantly improves treatment results for these patient groups.

TARE was initially introduced for unresectable hepatocellular cancer (HCC). For this category, studies have shown an increase in median survival of up to 1.8 years (compared to 8 months with tyrosine kinase inhibitors and PD-1L drugs) and overall survival of up to 5 years. At the same time, the results of TARE in carefully selected groups of patients with metastatic colorectal cancer also indicate the superiority of TARE over many types of systemic drug therapy in terms of overall survival and incidence of adverse events. TARE efficiency is now researched for metastatic ovarian cancer and peritoneal mesothelioma, unresectable locally advanced cancers of the lung, prostate and cervix.

Unresectable HCC is most universally accepted indication for TARE, demonstrating significant superiority in treatment outcomes. At the same time, maximizing the potential of TARE involves careful selection of patients for this group of interventions, taking into account possible alternative options for drug antitumor therapy and possible surgical treatment after TARE (including a bridging strategy for waiting before liver transplantation.

To select patients for these interventions, there is a comprehensive algorithm for analyzing clinical and anamnestic data, which includes both tumor markers and such body characteristics as the type of blood supply in the celiac trunk and the volume of the hepatopulmonary shunt. The development of the method made it possible to specify the predictors of success and low toxicity of the method in multicenter CIRT studies: the absence of previous locoregional treatment, the number and location of nodes (in metastatic treatment), the AST to platelet ratio index, the albumin-bilirubin gradient. It is important to emphasize that the selection of such patients should be carried out in specialized centers and take into account the capabilities and potential effectiveness of alternative therapies.

With current incidence rates (which will increase with effective Uzbekistan efforts to increase population longevity), the use of TARE in Uzbekistan can reduce the cost of treating this category of patients by 10.5-13.4% and save up to 956 years of life over a three-year period for this group.

NUCLEAR MEDICINE
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SECTION I

THE USE OF NUCLEAR METHODS IN DISEASE DIAGNOSES

POSSIBILITIES OF NUCLEAR RADIOLOGIC STUDIES IN THE COMPLEX DIAGNOSIS OF HEPATOCELLULAR CANCER

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Relevance. Liver cirrhosis (LC) is one of the most actual questions of hepatology. It is known that the main causes of death in patients with liver cirrhosis are: bleeding from varices of the esophagus and stomach, hepatic encephalopathy, spontaneous bacterial peritonitis and hepatorenal syndrome. Timely diagnosis of liver cirrhosis is currently extremely relevant. The increasing incidence, latent course and severe consequences of this disease makes researchers look for new possibilities of non-invasive diagnostic methods. Modern medical imaging mainly uses complex ultrasound techniques, computed tomography, magnetic resonance imaging and radionuclide studies to establish the diagnosis.

Purpose of the study. To establish the diagnostic efficiency of the applied radiation methods in detecting liver cirrhosis in children.

Material and research methods. The present study included 40 children diagnosed with liver cirrhosis. All of them were examined using echo graphic and computed tomography techniques. To determine the degree of preservation of the function of the organ, all patients underwent a radionuclide study. Changes in liver function were also assessed based on laboratory data. The duration of the disease ranged from 1 to 6 years, averaging 4.1±0.9 years.

Research results. When examining ultrasound in B-mode, 26 (65.0%) children showed pronounced diffuse changes in the liver in the form of an increase in its echogenicity - uniform or focal. The portal vein diameter ranged from 6.5 to 11.2 mm, averaging 8.8 mm. Ultrasound with the connection of Doppler techniques in 32 (80.0%) children showed a significant decrease in the linear velocity of blood flow in the portal vein (less than 15 cm/s) and in 8 (20.0%) children - an increase in the hepatic artery resistance index. SCT with contrasting also assessed the state of the vascular bed. The data of various methods of radiation diagnostics were compared and it was found that in children who, according to the examination in the B-mode, did not have changes in the structure of the liver, CT showed changes in the density characteristics of the parenchyma, and also revealed dilatation of the veins of the stomach and esophagus. According to the results of the radionuclide study, these patients also had a decrease in liver function**.**

Conclusions. Thus, in the diagnosis of liver cirrhosis in children, ultrasound with dopplerography of the portal vein and hepatic veins can be considered the method of choice. To confirm a violation of liver function, radioisotope diagnostics can be used - scintigraphy with technephyte. Computed tomography in cirrhosis for assessing the state of the parenchyma is slightly more informative than ultrasound, so it is more appropriate to conduct it if a volumetric formation is suspected, especially given the high cost of the procedure and the significantly large time costs.

ASSESSMENT OF ORGAN DOSES FROM IODINE-131 IN THYROID USING VOXEL PHANTOMS

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The problem of calculation of organ doses from iodine-131 in thyroid arises in a number of situations: for calculation of health impact of radiation accidents on nuclear power plants, for iodine diagnostics and therapy in nuclear medicine. The problem gets more complicated because of complexity of patient anatomy.

Calculation of radiation doses to patients from iodine-131 incorporated into thyroid was performed. The modern voxel phantoms were used for that purpose. They are freely available in International Commission on Radiological Protection Publication 110. Monte Carlo tools had to be used because phantoms have complex and are inhomogeneous. Data for adult male (AM) and adult female (AF) phantoms were compared with literature results. The discrepancy could be explained by use of different computational codes and approximation of the results. Calculations show that about 97% of effective dose is caused by the dose to thyroid and the remaining 3 % are caused by thymus, which is a part of remainder tissues, oesophagus etc. According to Belarusian national diagnostic protocol activity of 5.6-10 MBq is injected intravenously. The results of the calculations for thyroid activity 5.6 MBq are shown in Table.

Table – Organ doses from iodine-131 distributed in thyroid

Organ	ICRP Publication 56, mSv	Voxel phantom (ICRP 110), mSv		
		AM phantom	AF phantom	averaged
Thyroid	2460	2430	2850	2650
Thymus	0.840	12.9	11.7	12.3
Spleen	0.291	0.238	0.186	0.212
Brain	0.784	0.232	0.382	0.307
Liver	0.263	0.220	0.223	0.221
Skin	0.381	0.214	0.282	0.248
Breast	0.325	0.206	0.479	0.343
Stomach	1.68	0.180	0.132	0.156
Effective dose	109	-	-	72.8

The dose to thyroid is very accurately corresponds to the results of ICRP Publication 56 (currently calculated thyroid dose to AM phantom is lower by 1,5%). Because of various coefficients used for determination of effective dose in ICRP publication 56 (based on ICRP Publication 26 coefficients, where thyroid had weighting coefficient 0.03) and current coefficients (0.04 for thyroid). Because thyroid dominantly contributes to the effective dose, effective dose is caused by this weighting coefficient.

Study shows much larger discrepancy of thymus. Dose to thymus is by about 15 times higher than that calculated using coefficients from ICRP Publication 56. Unfortunately, there was no coefficient for calculation of oesophagus dose in ICPR Publication 56. Other available organs are spleen (dose -22%). Doses to most organs are lower when calculated using voxel phantoms with the exception of thymus and red bone marrow. For organs which lie at a great distance from thyroid (gonads, urinary bladder and uterus) discrepancies reach two orders of magnitude, which can be caused by low statistical power of coefficients calculated in ICRP Publication 56 and by the difference between phantoms used for calculations and voxel phantoms used by us.

USE OF ^{99m}Mo NUCLEUS IN ISOMERIC STATE IN MEDICINE

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The use of the molybdenum-99m (^{99m}Mo) nucleus in an isomeric state enables important medical imaging applications. ^{99m}Mo decays to technetium-99m (99mTc), the most widely used radioisotope in diagnostic nuclear medicine [1]. ^{99m}Mo is typically produced by irradiating ^{98}Mo in a reactor [2]. ^{99m}Mo has a 6 hour half-life, decaying to ^{99m}Tc which emits gamma rays detected for single-photon emission computed tomography (SPECT) [3]. The short half-life minimizes patient radiation exposure [4].

^{99m}Tc is incorporated into radiopharmaceuticals targeting specific organs/tissues for imaging of diseases including cancer, cardiovascular and neurological disorders [5]. SPECT provides detailed 3D organ visualization for diagnosis and disease monitoring [6]. Strict regulations and quality control ensure safe ^{99m}Mo/^{99m}Tc production and use [7].

^{99m}Mo has revolutionized nuclear medicine by enabling better disease diagnosis and care through ^{99m}Tc-based SPECT imaging [8]. Continued research and development are advancing 99mMo production and applications of its decay product ^{99m}Tc in state-of-the-art medical imaging [9].

The use of Mo-99m and its decay product Tc-99m has revolutionized nuclear medicine imaging, enabling healthcare professionals to diagnose and monitor a wide range of diseases with improved accuracy and precision. These imaging techniques play a vital role in clinical decision-making, treatment planning, and patient care.

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THE ROLE OF MICROELEMENTS IN MULTIFOCAL ATHEROSCLEROSIS

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Atherosclerosis is one of the most important problems of modern medicine, primarily due to the undisputed leadership among the causes of death. The first place is occupied by ischemic heart disease, the second - by cerebrovascular diseases, the leading role in the pathogenesis of which is played by atherosclerosis. Atherosclerosis changes the structure and the inner lining of the arteries. In the lesions, lipids, polysaccharides, blood clots accumulate, connective tissue grows, and calcium salts are deposited. All these processes lead to narrowing of the lumen of the vessel and can lead to acute circulatory disorders such as heart attacks and strokes.

Recently, much attention has been paid to the study of the role of macro- and microelements in the development of cardiovascular pathology, since they are part of enzymes, hormones and proteins, and determine the functioning of the entire cardiovascular system.

The significance of elemental imbalance in the development of cardiovascular pathology is ambiguous. The study of chemical elements in the blood and directly in the tissues of organs, where the main chemical reactions take place, makes it possible to understand the mechanisms of development of cardiovascular diseases. The creation of a database of the elemental composition of biological tissues is a new promising direction in cardiology.

The aim of this study is to study the microelement composition of atherosclerotic plaques at various stages of the development of the atherosclerosis process using neutron activation analysis.

Neutron activation analysis is a multi-element method that makes it possible to determine a significant number of elements in various biosubstrates with exceptionally high sensitivity. An important advantage of the method is a simple sample preparation that does not require sample decomposition, no correction for a blank experiment, low sample consumption, high selectivity and exceptionally high productivity. The limits of detection of individual elements reach 1ng/g.

We have studied the microelement composition of four stages of atherosclerotic plaque formation: lipid stain, fibrous plaque, ulcerated plaque and calcification. According to the developed method of neutron activation analysis, the content of 13 elements was determined: bromine, calcium, sodium, selenium, chromium, iron, zinc, cobalt, etc. in the studied samples of atherosclerotic plaques at various stages of the process.The data obtained allowed us to conclude that during the development of atherosclerosis, the content of calcium, selenium, zinc and iron accumulates in plaques. It has been suggested that the role of iron in the pathogenesis of atherosclerosis is associated primarily with the ability to catalyze the formation of free oxygen radicals and cause the oxidation of lipoprotein blood fractions. It is possible that the inability of ferrous iron to oxidize to ferric iron may be related to a potential mechanism for retaining iron in plaques.

The results obtained require more statistical material to elucidate the mechanism of formation of atherosclerotic plaques and determine the role of deficiency, excess or imbalance of elements in the development of atherosclerosis.

SURFACE MODIFICATION OF CARBON NANOTUBES FOR BIOMEDICAL APPLICATIONS

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In 2021-2023, the Uzbek-Indian joint project No. UZB-Ind-2021-77 "CD133 mAbs surface modified carbon nanotubes loaded with survivin siRNA and Paclitaxel for the treatment of non-small cell lung cancer" has been executed in the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan. This project is devoted to creating nanocarriers for target delivery of medications that allows to increase their concentration in certain places and prevent/restrict their accumulation in healthy sites. The targeted transport also allows to increase action time and efficiency of drugs, to decrease their side effects. As a part of the mentioned project, methods of surface modification of carbon nanotubes have been developed. They allow to produce nanocomposites with the following modifications: 1) Nanocarbon-Polyethyleneimine; 2) Carbon nanotube - Paclitaxel, 3) Carbon nanotubes conjugated with CD133 monoclonal antibody; 4) CD133 mAb and Survivin siRNA surface functionalized SWCNT internally loaded Paclitaxel (cf. Fig 1.)

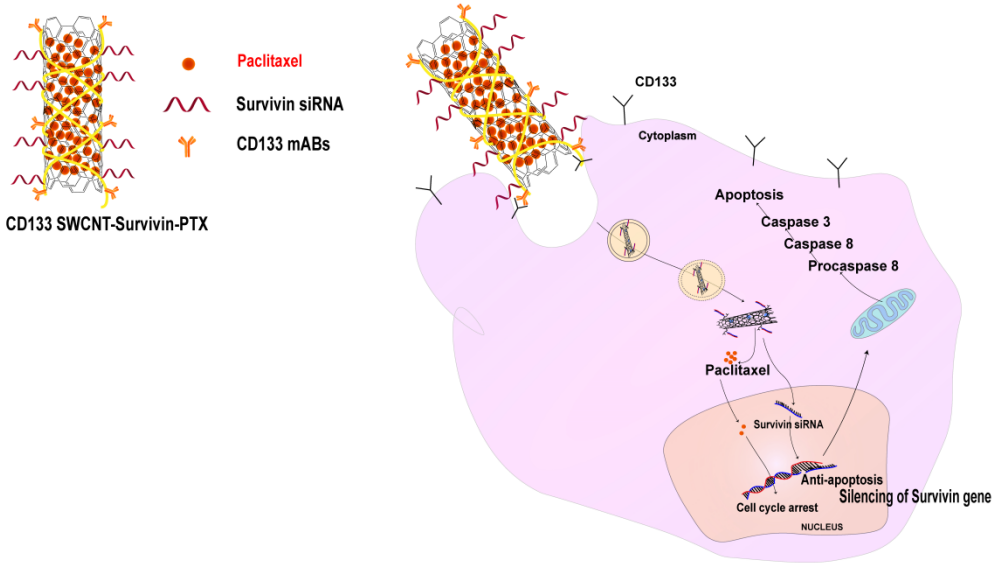

Figure 1. Targeted delivery of CD133-SWCNT-Survivin-PTX formulation (CD133 mAb and Survivin siRNA surface functionalized SWCNT internally loaded Paclitaxel)

NUCLEAR-PHYSICAL METHOD FOR THE EARLY DIAGNOSIS AND PREVENTION OF THYROID DISEASES IN CHILDREN

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By studying the patterns of distribution of macro- and microelements in the human body, it is possible to establish the state of health and microelement status, according to which early diagnosis is performed and a method for preventing most diseases is developed. Studies of the elemental composition of various substrates, organs and tissues of the human body in certain diseases have shown that there is a certain relationship between the elemental composition and various pathological processes. Latest achievements of science have shown that hair is the most suitable and informative biosubstratum, reflecting the patterns of chemical elements distribution in the human body.

This report presents the results of studies on early diagnosis and effective prevention of the most commonly observed disease in children in Uzbekistan - thyroid disease associated with iodine deficiency. Decreased thyroid function can lead to memory and hearing impairment, depression, tooth decay, hair loss, and other symptoms in children.

In the laboratory of “Ecology and Biotechnology” of the Institute of Nuclear Physics of the Uzbekistan Academy of Sciences, hair samples of numerous children were studied, among which a group with a chronic lack of iodine content in the body was identified. To study the macro- and microelement composition of hair samples, we have used a highly sensitive instrumental neutron activation method of analysis, based on a WWR-SM atomic reactor of the Institute of Nuclear Physics of the Academy of Sciences, Uzbekistan. The studied samples were irradiated by neutron flux with a density of $4x10^{13}$ neutron/cm^2 sec.

At present, scientists of Uzbekistan in the field of biology, medicine, chemistry, nuclear physics and food technology have jointly developed a technology for the manufacture of functional products based on natural and edible components, in particular functional cookies saturated with organic iodine. Using instrumental neutron activation analysis, the iodine content in several batches of iodized biscuits was investigated, and the iodine content was determined in the range from 3.6 µg/g to 26.7 µg/g. These values are sufficient to adjust the iodine content in children.

The essence of the method of prevention of thyroid diseases in children, associated with iodine deficiency in the body, is the regular use of functional cookies saturated with organic iodine by a group of children. According to WHO recommendations, the norm of iodine intake is 120 µg per day, and the duration is from 3 to 6 months, depending on the extent of disease. Hair samples from all children in the experimental group have been analyzed at the end of the experiments to confirm the effectiveness of preventive measures.

Preliminary data confirming the authors' idea of a method of early diagnosis and prevention of iodine deficiency related diseases were obtained.

DIAGNOSING CHEST PATHOLOGY WITH ULTRA-LOW-DOSE COMPUTED TOMOGRAPHY, DOSE EQUIVALENT TO CHEST X-RAY RADIOGRAPHY

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Introduction. Digital chest x-ray radiography (CXR) is the imaging modality of first choice for detecting chest pathology. The average effective dose for CXR (posteroanterior and lateral projection) is 0.10 mSv (range: 0.01 to 0.26 mSv). *The objective of this study was to* show that ultralow-dose CT of the chest, below 1 mSv, is feasible for detecting and characterizing a variety of pulmonary and chest diseases. It has also been shown by phantom studies and patient studies that chest CT examinations performed by using ultra–low-dose CT (ULDCT) with doses equivalent to CXR examinations allows for detecting pulmonary nodules with comparable sensitivity as previous standard or low-dose CT techniques. The ULDCT may not only improve detection of pulmonary nodules, but also the diagnosis for a wider range of pathologies.

Methods. For each patient, CXR was performed first, followed by the additional ULDCT. UltraLow-dose CT scan is typically achieved by fixing the tube voltage, lowering the tube current or reducing scan length The field size was adapted individually for each patient. Scanograms were not acquired during this study to save radiation dose. Instead, the start of the scan range was set manually at the gantry using the traditional laser beams. During the scan, real time reconstructions were observed and the scan was stopped using the abort scan button. The scan range was from the lung apex to the full diaphragm. The CT acquisition was performed with breath-hold during inspiration. Scan parameters were helical scan, 80×0.5 mm collimation, 80 kV, 30 mA, and 0.3 seconds rotation time. No iodinated contrast material was used. We investigated the imaging characteristics of lung nodules with a range of 4 to 30 mm in diameter with low (80 kV - doses equivalent to CXR) and standard voltage (120 kV) CT scans.

Results. The tube voltage has an exponential relationship with radiation dose, and thus, lowering the tube voltage can result in a significant decrease in radiation dose, which can be equal to CXR effective dose. Lowing the tube voltage to 80 kV can obtain a high quality and evaluable CT images, while allowing a significant reduction of radiation dose by 32% to 60%. The mean (±SD) perceived confidence for diagnosis was 88±12% with CXR and 98±2% with ULDCT. In all cases with diagnostic difference between CXR and ULDCT, the ULDCT was reported as having higher confidence than CXR. For the entire study group, there were no cases with CXR reported as having higher confidence than ULDCT.

Conclusion. This prospective study shows, in patients referred for CXR for diagnosing chest pathology, that ULDCT performed at an effective dose similar to the dose for CXR, resulted in added value as compared with CXR. Diagnostic yield was caused by pathology that was not seen on CXR but was observed on ULDCT, pathology suspected on CXR that was excluded by ULDCT, and other relevant findings on ULDCT not seen on CXR, with much better perceived confidence for ULDCT as compared with CXR. Current CT techniques allow for acquisitions at a very low effective dose. The effective dose range of 0.011-0.8 mSv for ULDCT will not be a limiting factor for introducing ULDCT of the chest on a broad scale in clinical practice. Our findings suggest that the CT scan with low voltage allows a safe and accurate assessment of lung nodules and other chest pathologies.

BINDING OF COPPER AND YTTRIUM CATIONS BY ACETATE AND PICOLINATE LIGANDS

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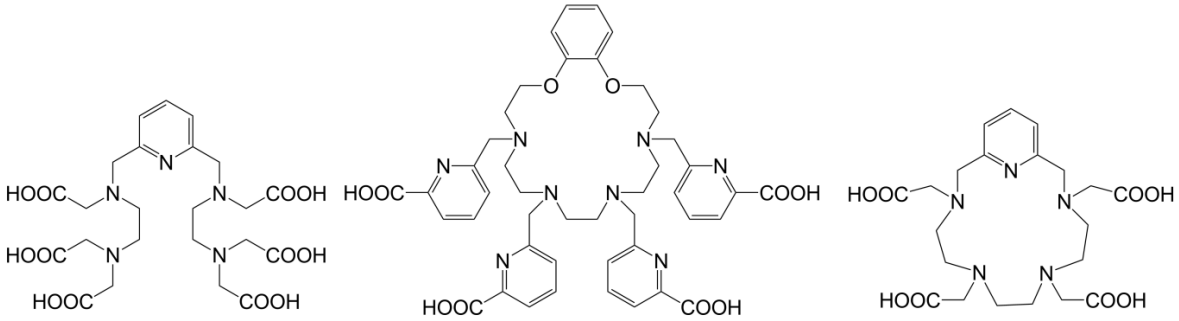
Imaging and therapy of cancer is based on the targeting of the radionuclide to the cell. Isotopes of copper and yttrium have a high potential for use in nuclear medicine. From the point of view of the HSAB theory, Y^{3+} (R=1.02 Å) is hard cation and binds well with hard donor oxygen atoms, while Cu^{2+} (R=0.73 Å) belongs to the borderline cations and exhibits affinity for both hard oxygen atoms and soft nitrogen atoms of amino groups. One of the approaches to improve the binding kinetics and stability of complexes with metal cations is the introduction of acetate and picolinate fragments into the structure of the chelator. Hence, complexes of Cu^{2+} and Y^{3+} with an acyclic ligand L1 containing six acetate groups, as well as with azacrown ethers with picolinate and acetate groups (L2 and L3, respectively) were chosen as objects of study.



L1 **L2** **L3**

In this work, the stability constants of complexes were determined by potentiometric and spectrophotometric titration.

Yttrium-labeled $^{88/90}Y$ complexes and ^{64}Cu complexes with L1-L3 were obtained. TLC was used to determine the efficiency of labeling, the optimal concentrations of ligands, and to analyze the stability of these complexes in the presence of of biologically relevant cations. The stability of studied complexes in 9-fold excess of fetal bovine serum was studied. A stability of the ^{64}Cu-labeled complex with L2 and ^{88}Y-labeled complex with L3 was studied *in vivo*.

The acyclic hexaacetate ligand L1 does not form stable complexes with Cu^{2+}; however, the complex with Y^{3+} turned out to be stable in the fetal bovine serum after 24 h of incubation. At the same time, the tetrapicolinate ligand L2 formed a stable complex with Cu^{2+}: more than 95% of the complex remained unbound to proteins after 24 h. Ligand L3 forms a stable complex with Y^{3+}; in this case, more than 95% of the radionuclide remained in the complex after 24 hours.

Ligand L1 contains six carboxyl groups in structure, the hard donor atoms of which effectively bind hard Y^{3+}. The nitrogen atoms of the picolinate fragments in ligand L2 firmly hold Cu^{2+}. The ligand L3 has a similar structure to the L1, however, L3 is macrocyclic, which has a positive effect on the stability of the complexes formed. The complex of the L3 ligand with Y^{3+} was stable *in vitro* and *in vivo*.

SYNCHROTRON RADIATION APPLICATIONS TOWARDS CLINICAL RADIOTHERAPY, RADIOGRAPHY AND BIOMEDICAL RESEARCH

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Keywords: Synchrotron radiation (SR), X-ray techniques, research infrastructure, medical imaging, beamlines

Purpose: Synchrotron light source is a powerful multi-dimensional, analytical microscope. The main goal of our efforts is to establish a high-profile and a large-scale research infrastructure – an excellent choice of Intellectual Property in Uzbekistan. A synchrotron light source which is a scientific and technological innovation, leads to global collaborations and enhances scientific human resources in the country. This research infrastructure is the key to unlocking the mechanism of renewable energy, new materials which prevents using natural underground resources and creation of true scientific community who works for peace, prosperity, and better quality of life for everyone. Be it physical or virtual, research infrastructures are essential to keep the pace of modernization.

Methods and Materials: Electrons, accelerated to near light speed in a linear particle accelerator and booster ring, whirl around in a large storage ring, creating SR photons that feed beamlines for multiple experimental stations. There are approximately 55 advanced synchrotron light sources in the world, mostly known as Generation III and a successful prototype of Generation IV. SR has important applications in medical imaging, especially in such areas as intravenous coronary angiography, mammography, bronchography, and monochromatic computed tomography. About 30 years ago, the clinical advantages of using synchrotron radiation X-ray beams for radiography, radiotherapy and clinical diagnostics started to be investigated by world known scientists. The synchrotron radiation techniques such as small-angle scattering has been proven to be advantageous for developing potential diagnostic tests. Traditional clinical radiotherapy uses beams of mega-voltage photons for controlling lesions like cancers. This was changed following observations made during studies of the effects of space radiation on astronauts. It was found that very large radiation doses could be tolerated by normal tissue if the dose was given in a very fine beam, roughly the size of a few cells. SR beams being naturally highly collimated down to 25 micrometers using a simple aperture. As knowledge of SR radiobiology research improved, the clinical advantages of this form of radiotherapy became clear. The science of micro-beam radiation therapy was born.

Conclusion: We are working on the conceptual design report (CDR) to build Central Asian Synchrotron Light Source (CASLS) in the territory of Uzbekistan. The main thrust of this CDR is to convince the government of Uzbekistan that its nation's socio-economic development, health, security, scientific and technological prominence in the world would be greatly enhanced by pooling their resources and constructing a multidisciplinary synchrotron light source in the Khorezm-Karakalpak border. We preserved equipment equal to 50 million Euros to build a synchrotron storage ring, which is granted by a European county. We are anticipating a few more grants from European funding.

SUPPRESSION OF THE ACTIVATOR LUMINESCENCE OF $Lu_3Al_5O_{12}$:Pr SCINTILLATOR CRYSTALS BY INITIAL DEFECTS CHARGED BY GAMMA-IRRADIATION

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The global trend in the field of nuclear medical instrumentation in recent years has been caused by the need to improve the quality of diagnostics and create new highly informative (in terms of sensitivity and speed) diagnostic instruments [1]. Optical scintillation crystals are a key part of medical imaging devices for both positron emission tomography (PET) and computed tomography. Single crystals of aluminum lutetium garnet $Lu_3Al_5O_{12}$ (LuAG) activated by praseodymium (Pr^{3+}) ions have high density (6.7 g/cm3), high light output (approximately 20000 photon/MeV) and fast response (20 ns), which favorably distinguishes this material from crystals based on NaI:Tl (3.67 g/cm^3, 230 ns) and bismuth germanate Bi_4Ge3O_{12} (7.13 g/cm^3, 300 ns), traditionally used in the medical diagnostics. The light output decreases due to competing nonradiative recombinations, and the scintillator response can be greatly slowed down due to the localization of free charge carriers at intrinsic and impurity defects. The lacks of the available literature data on imperfection of the crystal matrix of pure LuAG and LuAG:Pr^{3+} activated with praseodymium ions, from which it would be possible to estimate the contribution of nonradiative processes competing with Pr^{3+} emission. In this regard, we studied the absorption spectra, gamma-induced luminescence (GL), thermoluminescence (TSL) and their duration in nominally pure LuAG and in activated LuAG:Pr to reveal the contribution of intrinsic and impurity defects before and after irradiation with ^{60}Co gamma quanta source. The existence of intrinsic F^+ defects (oxygen vacancies that have captured 1 electron) with a characteristic absorption band at 375 nm and impurity Cr^{3+} centers absorbing at 285, 420, 490, and 600 nm in both samples before irradiation is associated with the crystal growth technology and impurity composition. After irradiation with gamma quanta energies of 1.17 and 1.33 MeV at a dose rate of 0.8 Gy/s to a dose of 10^3 Gy at 310 K, the detected increase in the concentration of F^+ and Cr^{4+} centers is due to the additional charging of F centers to neutrality and an increase in the valence of impurity ions to Cr^{4+}. The decrease in the GL light yield by 9% after the accumulation of the dose of 10^3 Gy in LuAG:Pr crystals is due to the capture of charge carriers by intrinsic and impurity defects, which competes with radiative recombination at Pr^{3+} centers. The first broad peak at 340 K in the TSL curves after irradiation to the dose is associated with the release of electronss from shallow trapping levels and radiative recombination with holes at Pr^{4+} luminescence centers. We believe that the intrinsic and impurity defects created during the growth process and the shallow defects generated at gamma irradiation, associated with the appearance of an unstable visible color and the TSL peak at 340 K, are possibly responsible for the recorded decrease in light output and an increase in the intensity of long-term afterglow, which worsen the scintillation characteristics at room temperature. To increase the fast-response and light output, it is recommended either to interrupt the sessions of gamma irradiation (1110 seconds per 24 h) or to raise the operating temperature of the scintillator to 360 K.

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THE REASON FOR THE SLOW RESPONSE OF SCINTILLATION CRYSTALS Lu_2SiO_5:Ce

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Positron emission tomography (PET) is one of the most informative methods of medical imaging used in nuclear medicine for diagnosing oncological, neurological, and cardiological pathologies [1]. The new Lu_2SiO_5:Ce (LSO:Ce) scintillation crystal is very promising, especially for PET, due to its high density (7.4 g/cm^3), light output of more than 30000 photons/MeV, and speed of response (38 ns) [2], which are many times exceed the characteristics of the $Bi_4Ge_3O_{12}$ detector used in existing PET installations [3]. However, the disadvantage of the LSO:Ce crystal is the efficient storage of absorbed energy, which slows down the glow time and reduces the detector light output, which significantly limits its practical application in image visualization systems. This energy of charge carriers captured by structural defects should be released as soon as possible by means of afterglow or thermoluminescence (TSL), when the crystal is heated. The purpose of this study was to elucidate the nature of the centers of slow release of the stored energy through afterglow and TSL. To do this, we studied the correlations between the optical absorption (OA) spectra and the integral thermoluminescence (TL) curves (300–600 K) of Lu_2SiO_5:Ce crystals after ^{60}Co irradiation with gamma-quanta energies of 1.17 and 1.33 MeV at a dose rate of 1.1 Gy/s in the dose range 100–10^4 Gy at 310 K. It was shown that prior to irradiation, the crystal has its own defects caused by the technological process of growing in a nitrogen atmosphere: neutral oxygen vacancies V_O near Lu1-V_{O5} centers with an absorption band of 193 nm, near silicon tetrahedra ≡Si−V_O - 213 nm, Lu1−F^+ −Si - 238 nm, Ce^{3+}/Ce^{4+} - 263 nm, and Ce^{3+}/F - 295 nm centers. After gamma irradiation of the scintillator to a low dose of 100 Gy, the most intense TL peak at 335 K appears, which is associated with electron capture at the Lu1–V_{O5} center, which leads to a decrease in the absorption coefficient of 193 nm band and excites the afterglow at 420 nm band of the Ce1 center by charge transfer mechanism. Irradiation to a high dose of 10^4 Gy reduces the concentration of V_{O5} centers, but does not affect the rest of optical centers. The restoration of the OA 193 nm band and the decrease in the intensity of the 335 K TL peak with increasing exposure time (1, 3, and 10 h) after irradiation at 305 K are associated with the release of electrons from the Lu1-V_{O5} color centers and radiative recombination at the Ce1 centers. Considering the above, it is recommended to thermally treat the scintillator crystal in an oxygen medium to heal V_{O5} and eliminate the intense TL peak at 335 K, which degrades its light output and fast-response by raising the operating temperature to 360 K.

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PRODUCTION AND QUALITY CONTROL OF [^{18}F]FLUORO-DEOXY GLUCOSE FOR POSITRON EMISSION TOMOGRAPHY

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By using of the cyclotron based biomarker generator equipment BG-75 ABT (Louisville, TN, USA) including proton accelerator, chemical production module which combined with quality control system (HPLC, pH-meter), and general controlling center (Human-machine interface) the process of routine production of [^{18}F]FDG for aim of PET-CT is adapted. Single run of equipment intended as personal dose («dose-on-demand») allow to accumulate 18-22 mCi [^{18}F]FDG, that at usual application enough for PET-scanning of the 3 patients. Equipment adapted for synthesis up to 15 doses of radiopharmaceutical per working day. For case of fail, of some quality control parameters (e.g. kryptofix impurity, inorganic [^{18}F]$^{-}$) from automatic quality control system, the appropriate fast manual methods used as alternative and it forward to prevent decay of target radiopharmaceutical.

PHARMACOGENETIC AND MORPHOLOGICAL FEATURES OF STOMACH CANCER ON THE BACKGROUND OF UTERINE ENDOMETRIOSIS

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Stomach cancer is one of the most common oncological diseases, occupying a significant place in the structure of morbidity and mortality (V.I. Chissov, V.V. Starinsky, 2002; V.M. Merabishvili, 2011). From stomach cancer in the world annually kills up to 800,000 people. Among the oncological morbidity of the population of the Russian Federation, stomach cancer takes the 2nd place, second only to lung, trachea and bronchial tumors (V.I. Chissov; V.V. Starinsky; B.N. Kovalev; JI.B. Remennik, 2006). According to the Ministry of Health of the Republic of Uzbekistan, gastric cancer ranks second after breast cancer in frequency of occurrence. Unfortunately, in more than 50% of cases, the primary detection of these patients occurs in advanced stages, when their treatment is quite difficult and is in most cases palliative in nature, aimed at some increase in life expectancy and improvement of its quality. (2018 year)

Key words: stomach cancer, morphological features, gastroenterogicial features, endoscopy, cancer of breast, malignancy.

STUDY OF POISONING OF THE ORGANISM WITH FOOD DYES THROUGH MICROELEMENT MONITOR

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Given that food dyes contain various metals and many metals cause poisoning in the body, the experimental study of this problem is considered urgent from a medical point of view.

This report presents the results of an experimental study of the laws of the entry of food dyes into the body organs, accumulation in the organs, and their exit from the body on the example of white laboratory rats. The amount of microelements in the body parts of experimental laboratory rats was carried out by a modern high-sensitivity neutron-activation analysis method. The WWR-SM type nuclear reactor of the Institute of Nuclear Physics of Uzbekistan Academy of Sciences of was used as a source of neutrons.

In the experiments, purebred white laboratory rats were fed with food dyes based on E171-titanium dioxide and E173-aluminum for 90 days, and their accumulation and excretion in body parts were studied.

Food dyes were given to 3 groups of laboratory rats. Group 1 was given orally 500 mg/kg of E 171-titanium dioxide-based food dye to male white laboratory rats for 90 days. The 2nd group was given 75 mg/kg of E 173-aluminum-based food coloring per day. The 3rd group was given 500 mg/kg of food coloring based on titanium dioxide E 171 and 75 mg/kg of food coloring based on aluminum E 173. Compared to the control group, the results obtained in the experimental groups were for titanium: an average of 2.64 μg/g / 0.32 μg/g, which is 8.25 times more, and for aluminum: an average of 3.71 μg/g / 0.51 μg/ A difference of 7.3 times more than was found.

In the next experiment, white laboratory rats fed with the above food dyes were given 5 ml of black sesame oil per day orally for 45 days for the purpose of biological chelation to remove accumulated titanium and aluminum elements from testicles. After detoxification, in the dry mass of testicles of laboratory rats of the 1st group, the neutron activation analysis revealed an average amount of 2.52 μg/g of titanium element residue. In group 2, post-detoxification neutron activation analysis revealed an average of 3.22 μg/g of residual aluminum. In group 3, post-detoxification neutron activation analysis revealed an average of 3.14 μg/g of titanium and an average of 2.88 μg/g of aluminum.

Thus, experimentally, poisoning of the body with food dyes was studied by monitoring microelements, and indicators of accumulation of titanium and aluminum elements in the body organs of laboratory rats were determined.

ADVANCING HEALTHCARE THROUGH TEACHING MEDICAL PHYSICS AT THE NATIONAL UNIVERSITY OF UZBEKISTAN

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Medical physics is a crucial interdisciplinary field that bridges the gap between medicine and physics, playing a vital role in modern healthcare. The integration of medical physics education at the National University of Uzbekistan holds immense potential to enhance medical practices, diagnostics, and treatment strategies those involves ionizing radiation within the country. This thesis explores the significance of teaching medical physics at the university and its potential impact on healthcare advancements.

First step is establishing a strong foundation in Medical Physics by curriculum development and interdissiplinary approaches. This includes designing a comprehensive curriculum encompassing fundamental physics principles and their application in medical contexts. Incorporating specialized courses on radiation physics, imaging techniques, radiation therapy, and nuclear medicine. This is being done with close collaboration with the IAEA by organizing IAEA expert missions and active TC projects taking into account recommendations of the reference [1]. Meanwhile fostering collaboration between physics and medical faculties to encourage cross-disciplinary research and learning with Tashkent Medical Academy and organizing practices in available oncology centers.

Radiological Imaging Techniques are taught, equipping students with knowledge of X-ray, CT scans, MRI, PET, and SPECT imaging modalities and enabling them to understand image acquisition, interpretation, and quality assurance.

Treatment planning and Dosimetry and Quality assurance are studied to advance cancer treatment and radiation therapy [2]. Providing students with insights into treatment planning using radiation therapy techniques, including intensity-modulated radiation therapy (IMRT) and brachytherapy. Training students in optimizing treatment plans for maximum efficacy and minimal side effects and instructing students on accurate radiation dose measurement and delivery verification to ensure precise and safe treatment are key objectives of the program.

To sum up, teaching medical physics at the National University of Uzbekistan presents a unique opportunity to drive advancements in healthcare. By imparting a strong foundation in medical physics principles, the university can contribute to improved diagnostics, safer radiation therapies, and innovative research initiatives. As graduates enter the medical field armed with interdisciplinary knowledge, they have the potential to significantly enhance patient care and contribute to the overall progress of cancer treatment in Uzbekistan.

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APPLICATION OF NUCLEAR REACTORS IN MEDICINE

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Nuclear reactors have found a diverse range of applications in various fields, including medicine. The controlled fission of radioactive elements within nuclear reactors offers a valuable source of radiation for medical purposes. This thesis explores the significant contributions of nuclear reactors to the field of medicine, highlighting their role in diagnostics, therapy, and research.

Nuclear reactors play a pivotal role in providing the necessary isotopes for medical imaging modalities. Application of Nuclear Reactors in Medical Imaging mainly covers Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT).

PET utilizes positron-emitting isotopes, such as fluorine-18 (F-18) and oxygen-15 (O-15), for imaging metabolic processes. Nuclear reactors are used to produce these isotopes through neutron activation of target materials [1, 2].

SPECT employs gamma-emitting isotopes, such as technetium-99m (Tc-99m), for three-dimensional imaging of organs and tissues. Reactor-produced molybdenum-99 (Mo-99) serves as a precursor for Tc-99m, enabling millions of diagnostic procedures globally [3].

Nuclear reactors are essential in delivering targeted radiation therapies for various medical conditions. Application of Nuclear Reactors in Nuclear Medicine Therapies includes Radioiodine Therapy, Yttrium-90 (Y-90) Radiosynovectomy.

Nuclear reactors produce iodine-131 (I-131), used in treating thyroid disorders and thyroid cancer. I-131 selectively accumulates in thyroid tissue, emitting beta radiation that destroys abnormal cells.

Y-90, produced in reactors, is employed in treating painful joint conditions, such as rheumatoid arthritis. Injection of Y-90 into affected joints delivers localized beta radiation, reducing inflammation and pain.

Isotope Production for Research and Diagnosis is also one of thriving applications of nuclear reactors. Reactor-produced Mo-99 undergoes decay to produce Tc-99m, used in a variety of diagnostic imaging procedures. Short half-life of Tc-99m ensures patient safety while providing high-quality images [4]. Moreover, reactors produce isotopes like cobalt-60 (Co-60) for cancer treatment and strontium-89 (Sr-89) for bone pain relief [5].

In conclusion, the application of nuclear reactors in medicine has revolutionized diagnostics, therapies, and research. Their ability to generate isotopes for medical imaging and targeted radiation therapies has significantly improved patient care and outcomes. As technology advances, nuclear reactors will likely continue to play a pivotal role in further enhancing medical practices and contributing to the well-being of patients worldwide.

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CHOICE OF PSMA LIGANDS IN PRE-THERAPY DIAGNOSIS

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Prostate cancer, among oncological diseases, ranks second among men in world practice. One of the main points influencing the tactics of treating a patient is the determination of the prevalence of the process. One of the leading methods for this is PET/CT with PSMA ligands. At the moment, a fairly large number of these ligands already exist and continue to be developed in the world. But in everyday clinical practice, as a rule, there are a small number of them. In the Russian Federation, 18F-PSMA-1007, 68Ga-PSMA-617, 68Ga-PSMA-11, and 99mTc-PSMA are used in clinical practice for the diagnosis. Recently, therapeutic radiopharmaceuticals based on PSMA ligands, in particular, with 177Lu and 225Ac isotopes, have also been actively introduced. In connection with this, an additional task arose for radiologists, the need to select patients for radioligand therapy. A. Tsyb Medical Radiological Research Centre - branch of the National Medical Research Radiological Centre of the Ministry of Health of the Russian Federation (A. Tsy MRRC) started using radiopharmaceuticals for the treatment of metastatic castration-resistant prostate cancer with 177Lu-PSMA and 225Ac-PSMA radiopharmaceuticals. In our clinical practice, we compared a number of diagnostic preparations used for selection for this type of therapy, and when comparing them with each other, we can note the difference between the physical properties of the isotope used and the level of ligand tropism for PSMA receptors. Because of these features, we can observe a certain variability in the visual picture. But when comparing the results of a diagnostic study and post-therapeutic scanning with therapeutic radiopharmaceuticals, we see comparable pictures, where the number of detected foci coincides. When comparing the level of accumulation of diagnostic and therapeutic radiopharmaceuticals, we get a confident correlation of these data.

Considering the above, it can be concluded that when selecting patients for radioligand therapy with PSMA, one can focus on the various available PSMA ligands. But in the future, when performing control studies, it is necessary to give preference to the drug used in the initial selection of the patient. But it's also worth mentioning that a reliable quantification requires running a diagnostic procedure on the same scanner as the original exam or cross-calibrating between different hybrid instruments to minimize quantification inconsistencies and obtain a reliable SUV.

KERMA CALCULATION FOR EXPERIMENTAL IN VITRO GAMMA-IRRADIATION OF HUMAN GLIAL TUMOR SAMPLES

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Nowadays in external radiotherapy, the vast majority of treatments are preferably carried out with high-energy photon beams from accelerators of electrons. However, the treatment by means of medium-energy X-ray beams remains interesting for a certain number of pathologies. The renewed interest is the subject of research such as those concerning the treatment of soft tissue tumors. Studies are also being conducted for additional applications, in particular in the treatment of brain tumors or on innovative systems for the treatment of retinal cancer and age-related macular degeneration [1]. Medium-energy X-rays could also find new therapeutic uses through techniques aimed at increasing the dose delivered during treatment by photoactivation of nanoparticles of heavy metals [2].

As a consequence, various human tissues and biological samples are exposed to photon radiation in a wide-energy range. It is absolutely important quantitative determine the photon radiation effect on these samples.

The photon kerma factors for Gd contrast agent Magnevist, brain, and tissue substitutes were investigated for further experimental in vitro irradiation of human glial tumor samples at 60Co source. To determine the Kerma of the human glial tumor samples and Magnevist used the mass attenuation coefficients depending on the chemical content of the investigated objects for photon energy from 1 keV to 20 MeV. The behavior of the Kerma can be explained due to the linear relation between mass attenuation coefficients and kerma factors.

The present study is useful for photon beam applications in medical practice and for the determination of absorbed doses in researchers of gadolinium neutron-capture therapy [3].

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THE SIGNIFICANCE OF THE MSCT METHOD IN THE CLINIC OF THE BUKHARA STATE MEDICAL INSTITUTE

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Radiation diagnostics is currently developing most rapidly of all medical industries, as it is associated with technological progress. Today, diagnostic studies such as X-ray contrast tomographic (RCT) studies of the coronary vessels of the heart, functional RCT studies of the lungs and neck, abdominal cavity, musculoskeletal system, brain were carried out in the BGMI department of radiology clinic. Features of CT examination. Computed tomography (CT) shows bone structures and organs of the chest very well. It remains the gold standard in the study of abdominal organs due to the greater spatial resolution, that is, it allows you to build three-dimensional reformations of almost any scanning area. CT is usually widely used, scans faster, costs much cheaper and, perhaps, with CT, the patient is less likely to take sedatives or painkillers than with MRI. There are also disadvantages. X-rays are used to form an image during CT examination, therefore it is very important to consider the dose absorbed by the patient per year (it should not exceed 100 mSv). CT uses more contrast media containing elements with a higher atomic number (iodine, barium) than the surrounding tissues. The first generation of CT appeared in 1973. The devices of the second generation were step-by-step: one tube aimed at one detector. Scanning was carried out step by step, making one revolution per layer. One layer of the image was processed for about 4 minutes. In the II generation of CT, a fan type of construction was used. Several detectors were installed on the rotation ring opposite the X-ray tube. The image processing time was 20 seconds. The third generation of CT introduced the concept of spiral computed tomography. The tube and detectors simultaneously performed a complete clockwise rotation in one step of the table, which significantly reduced the study time. The number of detectors has also increased. The processing and reconstruction time has noticeably decreased. The IV generation has 1,088 luminescent sensors located throughout the Gentry ring. Only the X-ray tube rotates. Thanks to this method, the rotation time was reduced to 0.7 s. The V generation is represented by multi-spiral computed tomographs (MSCT) with the possibility of full 3D reconstruction. Spiral scanning technology has significantly reduced the time spent on CT examination and significantly reduced the radiation load on the patient. The fundamental difference between MSCT and spiral tomographs of previous generations is that not one, but two or more rows of detectors are located along the Gentry circle. In 1992, the first 2-slice (2–spiral) MSCT tomographs with two rows of detectors appeared, and in 1998 - 4-slice (4-spiral), with 4 rows of detectors, respectively. The number of revolutions of the X-ray tube was increased from 1 to 2 v s. Thus, 4-spiral MSCTS of the V generation are currently 8 times faster than conventional spiral CT of the IV generation. In 2004-2005, 32-, 64- and 128-slice MSCT tomographs were presented, including those with 2 X-ray tubes. Today, some hospitals already have 320-slice CT scans. These tomographs are a new round in the evolution of X-ray computed tomography. They allow not only to receive images, but also make it possible to observe almost "in real" time the physiological processes taking place in the brain and heart. The results of these studies later formed the basis for the development of devices for emission computed tomography. In our clinic, 2116 studies were performed in 7 months, of which 284 lungs, 133 abdominal cavity, 107 bone system cases. The number of patients is 1836, of which 1011 are rural patients. Of these, 1,132 women, 706 men, 178 patients were re-examined after treatment.

THE PRIMARY ENERGY PARAMETERS OF DOSE ENHANCEMENT AT PHOTON ACTIVATION THERAPY

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Radiation therapy continues as an underlying method for cancer treatment, while precise dose deposition within the targeted tumor with sparing surrounding tissues stays a challenge. This purpose can be achieved by loading the tumor with high-Z elements before radiation therapy. Through quantitative evaluations, we studied the ability of elements with various Z as radiation dose-enhancers:

• Ag in the form of nanoparticles (silver has potent antimicrobial activities via various mechanisms: membrane disruption, apoptosis, and synergy) [1];

• Sm in the form of a pharmacological drug (^{153}Sm preparations have been used for a long time in the radiation therapy of metastases) [1];

• Gd contrast agents, as Magnevist® [2];

• Au nanoparticles are useful for contrast imaging, drug delivery, or radiation therapy enhancement [3];

• Bi metallic nanoparticles having preclinical proofs for theranostic applications [4].

To perform a quantitative evaluation of the radiosensitization effect was determined a parameter called - DEF (dose enhancement factor) [2]. The obtained results prove the possibility of realizing the effect of radiosensitization using kilovoltage X-ray tubes. It should note that low-energy photons with energy ≤ 20 keV are strongly absorbed by biological tissue and will create additional radiation damage without leading to a significant increase in DEF. An increase in DEF is observed when the photon energy is higher than the ionization energy of the K-shell of the atoms, indicating that the photoelectric effect plays a major role in radiosensitization, which is highly energy dependent.

To further optimize the effect of this binary radiation therapy with X-ray it would be interesting to study in more depth the mechanisms of heavy element action at monochromatic irradiation with ideal energy, and time dependency of target agent presence in the tumor to obtain a maximum lethal effect on the cellular scale. It is necessary to correctly estimate the inhomogeneity of the micro-distribution of the absorbed dose in the biological medium formed when atoms of heavy elements are activated by photons.

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CLINICAL USE OF POSITRON EMISSION TOMOGRAPHY FOR RADIOTHERAPY PLANNING IN HEAD-AND-NECK CANCER

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Keywords: Radiotherapy, PET-based contouring, Treatment Planning, Head-and-Neck Cancer.

Purpose: For radiotherapy planning (RTP) of head-and-neck squamous cell carcinoma (HNSCC) 18-Fluoro-deoxyglucose positron emission tomography-computed tomography (FDG PET/CT) image information has shown to provide essential information for reliable and valid target volume delineation. We investigated the potential impact of FDG PET/CT images on three-dimensional conformal radiotherapy planning for patients with HNSCC.

Methods and Materials: 67 patients with HNSCC were planned for RTP using PET/CT device. Each patient underwent CT and FDG-hybrid. Target volume delineation was initially performed on the CT images, and the corresponding FDG-PET data were subsequently used as an overlay to the CT data to define the target volume. A study was performed in which for each patient the gross tumor volume (GTV) was defined based on MRI-CT and on PET-CT data. Three level simultaneous integrated boost plan delivered in 35 fractions with a daily dose of 2 Gy (5 sessions/week) and 70 Gy as the total dose in the high-risk tumor target volume, while the target intermediate- and low-risk tumor volume received a daily dose of 1.8-1.6 Gy, respectively, and 63 Gy-56 Gy as the total dose, respectively. RTP were constructed based on both MRI-CT-GTV and PET-CT-GTV. Dose-volume histograms for the planning target volume (PTV) and organs at risk (OAR) were calculated.

Results:. The GTV was decreased by CT-PET image fusion in 22 patients (33%) and was increased in 16 patients (24%). The median MRI-CT-GTV was 24.8 mL compared with 19.7 mL in the PET-CT-GTV. Occult metastasis was found in 14 patients (21%). In addition, in a significant proportion of patients, more than 20% of the PET-CT-GTV was located outside the MRI-CT-GTV. This suggests that FDG PET/CT may identify tumors that were not detected using standard GTV detection methods.

The D95 was very similar between CT/PET and CT/MRI -generated GTVs and was not significantly different. The differences between the mean and maximum OAR doses were -0.43 ± 1.51 Gy and -0.86 ± 3.13 Gy, respectively. Relatively significant differences were observed in the spinal cord. In the spinal cord using CT/MRI, there was an increase in the number of cases where the maximum dose received exceeded 45 Gy (9 patients).

Conclusion: The tumor volume determined with FDG-PET is on average smaller than with other techniques, but most closely matches the true tumor volume. In patients with HNSCC considered for curative RT, using PET-CT will improve tumor coverage, and in selected patients, will reduce the volume of normal tissues irradiated, and thus toxicity. However, some difficulties are unresolved, including the internal mobility of the GTV, unknown differing set up of patients during CT and PET-FDG. Nevertheless, some tumor regions that are apparent on CT or MRI may not be visualized on PET, and in these cases, the use of PET alone would potentially lead to geographic error.

DETERMINATION OF THE ELEMENTAL COMPOSITION OF THE HAIR BY INAA AND MS-ICP METHODS TO DETERMINE RISK GROUPS FOR VARIOUS DISEASES

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The physiological role of macro and microelements in the human body is grate important. Chemical elements are involved in all biochemical processes in the human body, affect the growth and development of the body, the processes of fertilization, respiration, hematopoiesis, immunogenesis. Determining the content of chemical elements in the human body is the main issue in studying the impact on health of deficiency, excess or redistribution of macro and microelements. It has been established that not only excessive or insufficient intake of certain elements into the body, but also a violation of their ratio affects elemental homeostasis. In this case, the diagnosis of microelementoses is very important, which is associated, first of all, with the quantitative determination of elements in human biosubstrates.

The study of human hair allows you to detect the status of metabolism of microelements in the body. Available data show that the content of microelements in hair reflects the microelement status of the whole body and can serve as an integral index of health status.

Currently, there are various methods of multi-element analysis, each of which has its own advantages and disadvantages. The most promising methods are neutron activation analysis (NAA) and mass spectrometry with inductively coupled plasma (MS-ICP). These methods make it possible to simultaneously determine several tens of microelements in one sample with very low limits of determination, which is very important for studying their mutual influence.

The purpose of these studies is to compare the results of quantitative analysis of hair using these two methods.

The advantage of NAA is that samples can be analyzed without dissolution and special sample preparation, which increases the reliability and accuracy of the determination. Dissolution and mineralization for mass spectrometry inevitably leads to certain losses of some elements. At the same time, elements such as As, Rb, Sr, Ag, Cd, which were difficult to determine by NAA, were determined by MS-ICP. At the same time, NAA makes it possible to determine a number of elements that have various kinds of interference with ICP-MS with lower detection limits.

In general, the results are consistent, taking into account the variability of the samples themselves.

Comparing the results obtained by these methods with reference values, it is possible to draw conclusions about risk groups.

In conclusion, it can be argued that these two methods of analysis complement each other and their combination makes it possible to expand the range of elements to be determined, and their correlation with various diseases makes it possible to identify risk groups for various diseases.

POSITIONAL EMISSION TOMOGRAPHY CAPABILITIES IN COLON TUMOUR DIAGNOSIS AND STAGING

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Introduction. Currently, 1.2 million newly diagnosed patients with colorectal cancer are registered annually in the world. Despite the emergence of new methods for diagnosing cancer of the colon and rectum, a significant percentage of patients continue to be detected in late stages. A significant step in diagnosis was the development and implementation in clinical practice of nuclear medicine methods such as positron emission tomography (PET). The use of this method made it possible to visualize the functional processes occurring under normal conditions, and in the event of cancer, conduct a kind of non-invasive biopsy. PET-CT is more informative in colorectal cancer staging than CT. Sensitivity, specificity, accuracy indicators for stage I are 95%; 96%; 96%, for II - 85%; 98%; 97%, for III - 90%; 95%; 98%, for stage IV - 97%; 97%; 98%, respectively.

Purpose of the study. Improved diagnosis and staging of colon tumors based on positron emission with 18 fluorodeoxyglucose.

Materials and methods. A method of PET-CT of the body was developed during the examination of patients with colorectal cancer. PET-CT studies were performed on a DISCOVERY MI tomograph. Visual evaluation of PET data was carried out using both black-and-white scales (Gray Scale, Invert Gray Scale) and various color scales that allow determining the location of the focus, its contours and dimensions, the intensity of accumulation of FP in them. Semi-quantitative analysis was carried out with the calculation of the standardized radiopharmaceutical capture level (SUV).

Results. A total of 125 patients with a colorectal diseases were examined. According to the peculiarities of the pathological process, all of them were divided into two groups: • Group 1 - patients with verified colon cancer, or with suspected tumor (68 people); • Group 2 - patients after surgery of chemo- and radiation therapy for colon cancer (57 people). The level of tumor localization in the colon in PETCT was determined correctly in all 68 patients. In all patients with colon tumors, an increase in glucose metabolism was determined, which greatly simplified the identification of the area of pathological changes. The mean maximum FDG SUV was 12±2. Of the 68 examined colorectal cancer patients, pathological changes in regional lymph nodes were detected in 15 patients; with all having metastatic lesions. The maximum SUV value was 9, the minimum - up to 4, the average maximum - 6±2. Distant metastasis was found in 12 patients out of 57 examined. In this case, damage to the liver, lymph nodes, peritoneum, bones, lungs, brain occurred in 8 cases. Distant metastases of colon cancer were most often localized in the liver (40.7%). In 34 patients from the second group, no signs of tumor and postoperative complications were found. If a recurrence of the tumor process was suspected in 15 patients from the second group during PET-CT but during further colonoscopy, the recurrence was confirmed only in 2 patients, and anastomositis was established in the remaining 13 patients. Thus, PET-CT made it possible to detect.

Conclusions: The use of PET-CT makes it possible to clarify the stage of the tumor process before surgery treatment and in the postoperative period, after various courses of radiation and chemotherapy, as well as in 28% of cases to change the stage of the disease and, accordingly, the tactics of further treatment.

EXPERIENCE OF MAMMOGRAPHY SCREENING IN THE REPUBLIC OF UZBEKISTAN: FIRST RESULTS AND PROSPECTS

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Background. Breast cancer is one of the leading diseases worldwide. The early detection of breast cancer is the best way to improve survival. Mammography is included in the standard guidelines of all the leading organizations. The procedure is technologically demanding and cost-sensitive. Despite being a standard, it is not practical in many countries, more so in LMIC. The state of Uzbekistan embarked on a massive unique program of mass-level mammography screening starting from one region of the country and expanding to others. Here we report the process of such an establishment and the feasibility of this innovative model.

Methods. Realizing the importance of breast cancer screening, the Republic of Uzbekistan, initiated a pilot project in the Bukhara region. The area is divided into 12 districts. Every district was equipped with a stationary mammography machine in a regional polyclinic and with one mobile van. Personnel was appropriately trained and a selection process was established to invite women for screening. The invitation was sent using the local area's existing municipality residential directory, which contains complete demography details of every individual living in the area. The state has 100 % coverage under the registry. It was targeted to study every woman aged 45-65 starting May 2021. All mammographs are digitally recorded and sent in real-time to a centralized server based at National Republican Cancer Center in Tashkent, Uzbekistan. Reporting is being done at one centralized reading center on the information system platform.

Results. Over a period of two years, 140506 women in the age range of 45-65 underwent mammography screening. Depending on the size of the target group of the district on average 30-60 mammograms were performed per day. A reported preliminary analysis shows the presence of BIRADS 0 in 4495, BIRADS 1 in 78634, BIRADS 2 in 64345, BIRADS 4 IN 4998, BIRADS 5 in 893. All women with BIRADS 4 and 5 were referred to the regional comprehensive cancer center for further evaluation.

A total 7570 patients underwent cytology and 408 underwent core biopsy. Depending on the reports the patients were appropriately managed. A total of 1885 patients were recalled for additional screening due to insufficient technical training of the medical staff. After a year of function, the project was expanded with "Mobile Vans", in the amount of 13 units that were added after 1.5 years.

From January 2023 about 50000 mammograms were additionally performed, taking the total number of screened women to 190506.

Conclusion. Thus, it is feasible to plan and successfully implement a state-owned mass-level mammography screening. This project has the potential of duplication in any part of the world and other organizations can learn from this extensive, wide program.

SPECTRAL X-RAY IMAGING DETECTORS BASED ON DIRECT CONVERSION HR GAAs:CR PIXEL SENSORS

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The report presents the results of R&D in the field of X-ray pixel sensors and spectral X-ray detectors based on chromium-compensated gallium arsenide (HR GaAs: Cr), carried out by the R&D Center “Advanced Technologies in Microelectronics” of Tomsk State University.

It is shown that of HR GaAs: Cr X-ray pixel sensors operating in the photon counting mode is promising candidate for X-ray spectral imaging systems having of spatial resolution up to 30 μm and an energy resolution about 4 keV within 10 – 60 keV energy range at room temperature.

It has been experimentally established that multi-element HR GaAs:Cr X-ray pixel sensors are characterized by radiation hardness about 1.5 MGy at 8–20 MeV beta particle irradiation and more than 1 MGy when irradiated with 12 keV quanta.

The basic principles of material recognition by means of spectral X-ray imaging as well as spectral X-ray images of test objects are given.

Feasibility of spectral X-ray detector application for contrast-enhanced spectral mammography (CESM) as well as for spectral X-ray imaging is discussed.

Acknowledgment

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BUILDING POTENTIAL EXPERTISE IN THE PROCESS OF ESTABLISHING A NUCLEAR MEDICINE DEPARTMENT IN THE NEW CENTRE OF THE REPUBLICAN SPECIALIZED SCIENTIFIC AND PRACTICAL MEDICAL CENTRE FOR ONCOLOGY AND RADIOLOGY

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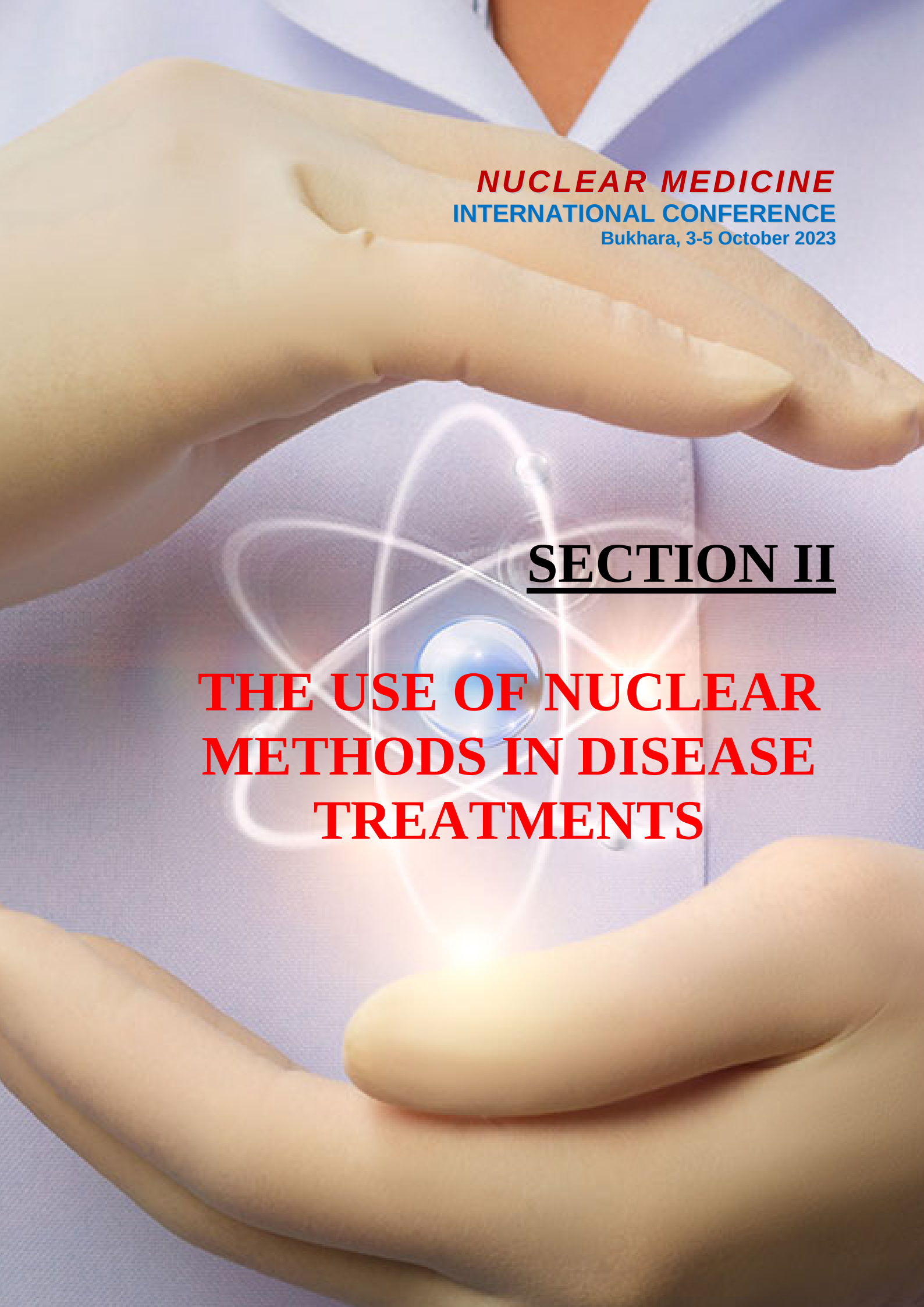
The project "Equipping Oncology Service Institutions of the Republic of Uzbekistan with Modern High-Tech Equipment (Phase II)", with the participation of the Islamic Development Bank, plans to create a scientific and methodological centre for oncology and radiology in the Republic that meets the requirements of international standards. For the first time, a nuclear medicine centre is being established in a State medical institution, which includes both diagnostic and therapeutic aspects of nuclear medicine. The project of the new oncology center consists of three components: firstly, construction of a new modern, internationally integrated building, and secondly, equipping the center with the necessary modernized medical equipment. The coordination structure of the project with IBRD investment is divided into several units: the main project manager or customer is the Ministry of Health of the Republic of Uzbekistan represented by the staff of the Project Implementation Unit, the expert group of the RSSPMCandR consisting of specialists in various fields of oncology, and the international organization - UNOPS implements the marketing service in the form of acquisition of medical and non-medical equipment on the basis of open, transparent tenders. All ongoing project processes should be based on established international standards.

Nuclear medicine of the new oncological center is one of the major and expensive sections of this project, which will carry out scientific-methodological, diagnostic, therapeutic procedures and has a cyclotron with a potential production volume of 18F-based radiopharmaceuticals that will be sufficient to provide PET-CT for the whole region and neighbouring republics. Construction of specialized building for cyclotron and radio-chemical laboratory complex for production of radiopharmaceuticals, treatment rooms with radiopharmaceuticals, PET-CT and SPECT room according to international standards. The purchase of all necessary and modernised equipment, as well as the provision of intellectual support to the local staff enable the new center to join the group of advanced clinics in the region. Implementation of the project includes the following stages: In the first stage: The staff of the Project Implementation Unit of MH R.Uz. and MIP&T R.Uz. together with local and international experts prepared the budget for financing the nuclear center. Second stage: Technical specification of the cyclotron, components of the radiochemical laboratory complex, PET-CT and SPECT was developed. Third stage: Tender bidding and procurement of equipment under UNOPS coordination based on the requirements of customer the staff of the Project Implementation Unit of MH RUz and expert group of RSSPMCandR, based on the criteria of quality, favourable price and principle of equal competition specified in the directive of the organization. Fourth stage: Development of nuclear medicine building design in accordance with the requirements of technical and radiological safety during equipment operation. Fifth stage: Delivery of the equipment to the deployment site, installation, commissioning and start-up of the equipment provided by UNOPS. Intellectual support of local staffs in the form of training in the use of new technologies by equipment suppliers and improvement of experience and qualification with the support of the MH R.Uz. Joint activity and professional fulfillment of their functional duties by all components of the coordinating system of the project, in which all international standards will be observed and the experience of international experts will be used, is the key to the creation of a new modernized scientific and methodological center of oncology and radiology, which will provide the population of the republic with medical services at an internationally recognized level.



NUCLEAR MEDICINE
INTERNATIONAL CONFERENCE
Bukhara, 3-5 October 2023

SECTION II

THE USE OF NUCLEAR METHODS IN DISEASE TREATMENTS

PREPARATION FOR RADIOEMBOLIZATION OF THE LIVER WITH YTTRIUM-90

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In foreign practice, radioembolization of unresectable primary and metastatic malignant neoplasms of the liver has shown promising clinical results. In the Russian Federation, this technique has recently begun to be used in clinical practice and has not yet become widespread.

The application of this technique is based on the anatomical features of the liver, so venous blood from the portal vein normally supplies from 70-75% of the parenchyma. The supply of arterial blood from the hepatic artery accounts for 25-30%. While the arterial blood flow supplies liver neoplasms. This feature allows us to perform selective radioembolization of liver formations, with the least impact on its unaffected parenchyma.

Initial patient selection is based on contrast-enhanced CT or MRI. Patients with inoperable liver masses that do not grow beyond the liver capsule are selected and, as a rule, preference is given to the presence of a unilateral lesion. In radioembolization with ^{90}Y-labeled spheres, one of the main complications, according to the world practice, is radiation-induced pneumonitis (RIP). The implementation of this diagnostic procedure allows us to predict in advance the possibility of developing this complication, as well as to assess in advance the presence of a shunt to other organs. Everywhere, for a preliminary assessment of the distribution of microspheres in the patient's body, the introduction of macro aggregated albumin labeled with the technetium isotope (^{99m}Tc-MAA) into the hepatic artery is used. This procedure evaluates the distribution of ^{99m}Tc-MAA in the liver, the presence and level of pulmonary shunt and shunt to the abdominal region. Traditionally, evaluation of diagnostic radiopharmaceutical (RP) distribution and lung shunt fraction relative to hepatic uptake is calculated from planar scintigraphy (PS) in a whole body mode. On a bilateral scintigram, two-dimensional areas of the lungs and liver are outlined, representing areas of interest. The lung shunt fraction (LSH) is then calculated as the proportion of total lung activity divided by the total amount of lung and liver. The average absorbed dose to the lungs is estimated from the calculated pulmonary shunt and the planned total activity planned for the introduction of ^{90}Y.

The correct conduct of the diagnostic procedure and the interpretation of the results obtained make it possible to assess both the risks of unwanted complications in advance and to preliminarily assess the required maximum therapeutic activity of the therapeutic drug.

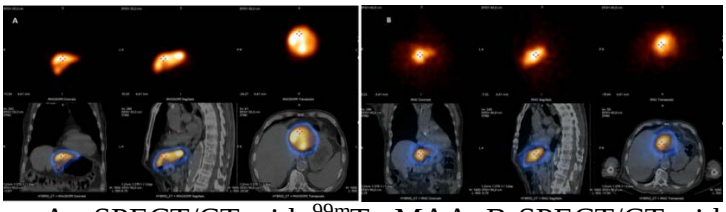

Figure. A - SPECT/CT with ^{99m}Tc-MAA; B-SPECT/CT with ^{90}Y

EFFICIENCY OF RADIOIODINE REMNANT ABLATION IN CASES OF LOCALLY DIFFERENTIATED THYROID CANCER. ORIGINAL CLINICAL TRIAL

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Introduction. The thyroid cancer has increased on the territory of Russia after Chernobyl incidence in 1986, and currently accounts for up to 12,000 newly identified cases. Postoperative radioiodine remnant ablation (RRA) is the second stage of combine treatment of differentiated thyroid cancer, except for the prevalence of pT1aN0M0, with minimal level of TG and AT-TG, according to international guidelines. In the past 20 years a significant number of published practice guidelines for the treatment of this disease. However, the discussion is the amount of medication for administration activity (GBq) ^{131}I, is required for successful RRA.

Aim. Establish the diagnostic and prognostic significance of preliminary studies (US of the neck, radioisotope studies), as well as whole-body scintigraphy after the introduction of therapeutic ^{131}I activity.To evaluate the effectiveness of RRA depending on the degree of hypothyroidism, as the conditions for the preparation and conduct of radionuclide therapy, and by the dynamics of blood thyroglobulin (TG) levels. Establish the dependence of the absorbed dose gradient/administered therapeutic activity (MBq/kg) in thyroid remnants on physiological features, including the level of TSH stimulation.

Materials and methods. The study analyzed 352 clinical cases of the adulte patients (18-68 y.) after radical surgical treatment (R0) for DTC. In our study, the effectiveness of RRA was compared with certain indicators of specific therapeutic activity ^{131}I (MBq/kg), in groups of patients with different levels of TSH stimulation: Group 1: 8-29 mMe/ml, n=42; Group 2: ≥ 30 mMe/ml, n=310.

Results. 1. The effectiveness of RRA in Groups 1 was 89% and in Groups 2 – 86%, does not statistically differ ($p>0.05$). With TSH stimulation from 8 to 100 mMe/ml within the confidence ranges of specific therapeutic activities in Groups 1 of 36±8.23 MBq/kg and in Groups 2 of 34.5± 9.03 MBq/kg. **2.** Incomplete RRA in both groups was established in 53% of patients who had multiple (3 or more), in 7% of patients who had 2 and in 5.9% of patients who had 1 focus of thyroid remnant according to post-therapeutic scintigraphy of the whole body with 131I. **3.** In order to optimize RRA with thyroid remnants not detected by US, the effective range of specific therapeutic activity of 131I is 30-40 MBq / kg with TSH stimulation of more than 4 nMe/ml and strict adherence to a 14-day low-iodine diet. Then thyroid remnant determined by US (volume ≥ 1 ml), radiometry is recommended with neck SPECT (1200 kBq 131I) and calculation of therapeutic activity, in order to plan D = 300 Gy and reduce the risk of developing radiation sialoadenitis.**4.** RRA revealed at an early stage isolated miliary metastatic lesion of the lung parenchyma in 2 cases (0.56%), with a pre-stimulated TG level of more than 124 ng/ml in the early stages after the surgical stage of treatment. **5.** During the control complex examination with 131I-SVT 6-9 months after the performed RRA, the stimulated TG level of more than 11.9 ng/ml with normal AT-TG indicators and a pathological US may indicate metastatic lesion of the regional lymph nodes of the neck.

RADIOEMBOLIZATION OF THE LIVER MICROSPHERES OF RUSSIAN PRODUCTION

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In recent years, there has been an increase in the number of patients with malignant liver tumors. Against this background, there is an active introduction into practice of new methods of treatment, one of which is radioembolization of the liver.

Since 1977, clinical trials of microspheres containing yttrium-90 (^{90}Y) have been actively conducted in the world, and only in 2004 the FDA of USA authorized the clinical use of glass ^{90}Y-microspheres containing for the treatment of hepatocellular cancer and colorectal cancer metastases to the liver.

According to statistics, more than 200 thousand patients with inoperable primary liver cancer and more than 270 thousand patients with inoperable metastatic liver cancer are registered annually in the world for whom radioembolization is the most appropriate treatment method

In Russia, until recently, radioembolization was not used. In 2018, through the efforts of the A.F. Tsyba Medical Radiological Research Center is a branch of the FSBI “NMIC of Radiology” of the Ministry of Health of Russia, the production of domestic glass microspheres containing yttrium–90 radionuclide and albumin microspheres containing rhenium-188 (^{188}Re) was started and work began on their introduction into routine clinical practice.

To date, the A. .F. Tsyba Medical Radiological Research Center is a branch of the FSBI “NMIC of Radiology” of the Ministry of Health of Russia is a reference center for the application and implementation of the method of radioembolization of the liver in Russian Healthcare.

INVESTIGATION AND MODELLING OF RADIOLYSIS OF THERAPEUTIC RADIOPHARMACEUTICALS

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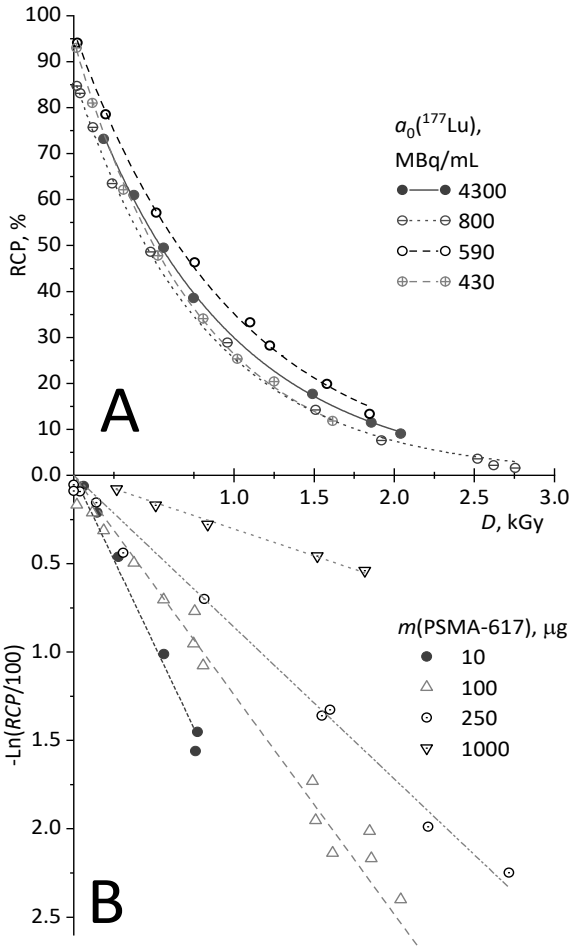
The principal factor influencing the shelf life of therapeutic radiopharmaceuticals is radiolysis of the vector molecule. The development of stable forms of radiopharmaceuticals is critical for their successful deployment in clinical practice. To identify the primary autoradiolysis patterns, the time dependence of the change in radiochemical purity (RCP, %) was explored using HPLC and TLC on [^{177}Lu]Lu-PSMA-617 as an example. Radiolysis of [^{177}Lu]Lu-PSMA-617 was studied in terms of time, radionuclide activity, precursor amount (**Figure**), and preparation volume. The absorbed dose (D, Gy) was found to be the most influential factor on the RCP. The RCP value of the [^{177}Lu]Lu-PSMA-617 preparation was inversely correlated with the absorbed dose and exhibited an exponential relationship. Under various conditions, the lutetium-177 dose factor ψ (Gy·mL·MBq^{-1}) and PSMA-617 concentration-dependent dose constant κ (Gy^{-1}) were evaluated for absorbed-dose estimation using computer modeling, chemical dosimetry, and radiochemical purity monitoring.



External X-ray irradiation was used to simulate the autoradiolysis process using [^{44}Sc]Sc-PSMA-617 samples as a model. Qualitative concordance of the impurity profiles resulting from both external irradiation and autoradiolysis was observed. The preliminary empirical equation linking the radiochemical purity, initial activity, precursor concentration (C_0) and type of radiation (using correction factor $d_{\gamma\to\beta}$) was proposed (see below). Further refinement and application of the discovered dependencies may be useful for forecasting the RCP value at the stage of optimizing the composition of therapeutic radiopharmaceutical finished dosage form.

- In the case of autoradiolysis by radionuclide β-particles,

$$RCP = RCP_0 \cdot e^{-D_\beta \cdot \kappa} = RCP_0 \cdot e^{-\psi a_0 \cdot (1 - e^{-\lambda t}) \cdot [p + q \cdot \ln c_0]}$$

- For external X-ray irradiation,

$$RCP = RCP_0 \cdot e^{-D_\gamma d_{\gamma\to\beta} \cdot \kappa} = RCP_0 \cdot e^{-D_\gamma d_{\gamma\to\beta} \cdot [p + q \cdot \ln c_0]}$$

This research was carried out within the state assignment and financial support of the Federal Medical Biological Agency of Russia (theme No. 122031100121-4, supervisor: A.Larenkov).

RHENIUM-188 SUSPENSION FOR RADIOSYNOVECTOMY, STABILIZED WITH HYALURONIC ACID

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At present, radiosynovectomy is successfully used in the world in the treatment of rheumatoid joint damage accompanied by effusion. Radionuclide therapy for joint diseases is comparable in effectiveness to surgical therapy (72.6% and 75.2% of positive results, respectively), but it is less traumatic and dangerous, much easier to perform and does not require complex and lengthy postoperative rehabilitation. The duration of remission ranges from several months to 4 years. This method consists in the intra-articular administration of a radiopharmaceutical (RPh) containing radionuclides with high β-energy (for example, ^{90}Y, ^{169}Er, ^{166}Ho, ^{186}Re etc.). The therapeutic action of a radionuclide is based on the effect of β-particles on the synovial membrane of the joint. The injected RPh is captured by phagocytosis by the cells of the superficial epithelium of the synovial membrane, thereby exerting a damaging effect. Due to local irradiation of the inflamed synovial membrane of the joint with β-particles, the process of ablation is caused in it, i.e. death of functionally active cells responsible for inflammation. As a result of such exposure, superficial synovial fibrosis usually occurs. Clinically, in cases of a positive result, a decrease in pain and inflammation and, as a result, an improvement in the quality of life of patients is determined.

Aim. In this study ^{188}Re-Sn colloidal solution was synthesized, its properties were studied, and the possibility of using hyaluronic acid to stabilize the particles formed during the synthesis was shown.

Materials and methods. $Na^{188}ReO_4$ was obtained from the domestic ^{188}W/^{188}Re generator "GREN-1" by elution with 0.9% NaCl. Radiochemical purity of rhenium-188 suspension is determined by TLC chromatography on plates with a thin layer of silica gel in acetone. Particle sizes are determined by laser diffraction on LA - 350 (Horiba) with a determination range of 0.1 - 1000 μm.

Results. A colloidal solution of ^{188}Re-Sn is obtained in two stages. At the first stage, rhenium-188 is reduced in an acidic medium, at the second stage, the pH is adjusted with a phosphate buffer solution. To stabilize the colloidal solution, a 0.2% solution of hyaluronic acid is used, due to which the radionuclide is retained in the joint, preventing damage to the periarticular tissue. The optimal conditions for the synthesis of a colloidal solution with a radiochemical purity of more than 90% are found. The average dynamic particle diameter did not exceed 10 μm. The colloidal solution is stable for at least 3 days after its preparation. The possibility of obtaining a lyophilized reagent consisting of 20 mg of tin dichloride dihydrate, 0.2 mg of hyaluronic acid and 10 mg of mannitol was studied. Colloidal particles labeled with radionuclide are homogeneously distributed in the intra-articular space without causing an inflammatory reaction. The bond between the radionuclide and the colloidal particle is quite strong during the entire course of radiosynovectomy, which is determined by the half-life of the radionuclide.

Conclusion. The synthesized colloidal solution is a promising RPh for radiosynovectomy in the treatment of rheumatoid joint damage.

MODELING OF DNA DAMAGE IN MAMMALIAN TUMOR CELL FOR NEUTRON CAPTURE THERAPY

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Boron neutron capture therapy (BNCT) is a promising treatment method for malignant tumors. One of the advantages of this method has been aimed at high effectiveness for targeted sites like tumors while these beams do not have enough radiation effects to damage healthy cells. The application of Monte-Carlo codes latest years has significantly improved the studies of predicting the dose deposition of radiation therapy at both cellular and macroscopic levels. In this study, we focused on calculating the dose deposition of secondary particles resulting from nuclear reactions between various mono-energetic neutrons and ^{10}B nanoparticles with different concentrations. The investigation was conducted in the single-cell model of human glial tumors with ^{10}B nanoparticles with different locations. The resulting absorbed boron dose showed dominance from other particles at lower energetic epithermal neutrons with higher concentrations (Fig. 1). Additionally, we estimated the DNA damage in the two different scenarios of cell geometry with the sphere and ellipsoid for incident and secondary particles using the GEANT4-DNA toolkit. We combined and verified high precision neutron physics with DNAPhysics models. Considering these physics models in the water model for DNA damage as double-strand breaks have been calculated via the DBSCAN clustering algorithm. The findings highlight the importance of precise dose calculations of high LET particles and considering secondary particle effects when evaluating the efficacy of BNCT in tumor treatment.

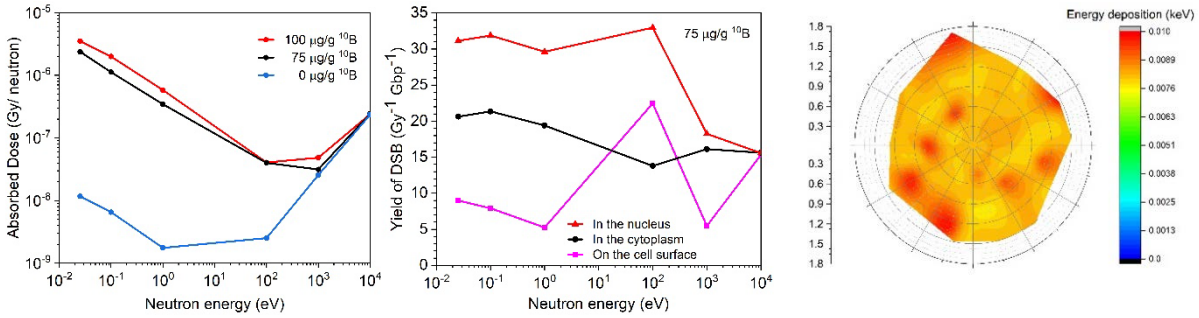

Fig. 1. The total absorbed dose from boron, gamma, neutron beam when with boron nanoparticles in the cytoplasm of the sphere cell is calculated while these values normalized by 50 million events scored on the single simulation (a). A yield of DSB while the amount of DNA damage per gray and Gbp while calculated by the DBSCAN clustering algorithm (b). Angular distribution of ^{7}Li energy deposition calculation (c).

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RADIOBIOLOGY OF AUGER EMITTERS

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Auger emitters, or Auger electron emitters, are radionuclides the decay of which involves the so-called Auger effect. This effect is initiated by a vacancy in the inner electron shell of an atom and results in the relaxation of the atom by a cascade of successive transitions of electrons. The relaxation energy can be released in the form of emission of photons and electrons, so the Auger effect is accompanied by the emission of multiple low-energy electrons.

Auger emitters occupy a special place among other radionuclides and external sources of ionizing radiation in the context of research and interpretation of their radiobiological effects, as well as their potential application as a radiotherapeutic agent in the treatment of malignant tumours. This place is determined by the properties of their radioactive decay involving Auger effect and, as a consequence, by the energy spectrum of emitted radiation, mainly Auger electrons of low energies. The nature of energy deposition in the immediate vicinity of Auger decay, which is characterized by a high local concentration of absorbed energy, leads to the fact that such basic and well-established concepts underlying radiation biology as absorbed dose, linear energy transfer (LET), and relative biological effectiveness (RBE) are at least insufficient and largely inadequate categories for describing the radiobiological effects of Auger emitters and understanding the physical and biomolecular effects of Auger emitters.

Moreover, the high local concentration of absorbed energy causes critical damage to biological structures, mainly DNA, only in the immediate vicinity of the decay point, thus enabling targeted damage to those biomolecules or cells of interest as targets, such as malignant tumour cells and their DNA, while keeping other cells, such as normal tissue cells, intact. It should be kept in mind, however, that such targeted therapy requires a system for selective delivery of Auger emitters to the DNA of the target cells.

Analysis of the results obtained in experiments with a molecular model (synthetic 41-mer oligodeoxynucleotide with incorporated [^{125}I]-dC) allows us to summarise the following main features of induction of DNA breaks due to the decay of radionuclide ^{125}I:

- decay event results in the formation of multiple breaks in both the top (incorporating ^{125}I) and complementary DNA strand, located mainly within 5 base pairs of the [^{125}I]-dC containing nucleotide;
- multiple strand breaks induce the formation of a complex DNA double-strand break with a probability of 0.8 per decay, which is slightly reduced to 0.74 in the presence of the hydroxyl radical interceptor DMSO;
- induction of DNA breaks occurs both due to the absorption of Auger electron energy (radiation mechanism) and due to the neutralization of the multi-charged ^{125}Te ion formed as a result of ^{125}I decay (non-radiation mechanism), with both processes making approximately equal contributions to the overall DNA damage pattern;
- the indirect mechanism of radiation action, associated with the attack of DNA by hydroxyl radicals, makes a minor contribution to the formation of breaks.

SIMULATION OF THE INTERACTION OF PROTON BEAM WITH DELIVERY SYSTEM AND TISSUE EQUIVALENT MEDIA USING MONTE CARLO METHOD

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Interaction of heavy charged particles with matter has led to a number of important discoveries for science and practice. It is a specific type of oncology radiotherapy that uses protons and heavy ions, to achieve highly localized dose deposition, compared to conventional radiotherapy, which uses photons and electrons. To irradiate neoplasms located near radiosensitive structures and organs, it’s necessary to ensure an accurate spatial alignment of the beam with the target in proton therapy sessions. At the same time, the dose drops sharply beyond the boundaries of the target, which makes it possible to irradiate localities that were not previously available for radiation therapy [1]. In this work were demonstrated the capabilities of FLUKA [2] and Geant 4 [3] software packages for simulating the range of proton beams for numerical calculations in the field of dosimetry and radiation therapy. This simulation was performed to evaluate beam properties such as percent depth dose curve, Bragg peak, and distal fall-off, so that, they could be verified with measured data. Based on FLUKA and Geant 4 codes were developed model of virtual experimental setup for proton beam delivery system and calculations of energy deposition of protons.

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RADIOIODINE REFRACTORY THYROID CANCER: MODERN RECOMMENDATIONS

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Radioiodine therapy for differentiated thyroid cancer has been used for a long time, mainly in patients of intermediate and high risk, as well as in the presence of distant metastases. However, about 10–15 % of patients are refractory to radioiodine therapy, which significantly worsens the prognosis. Patients with radioiodine-resistant differentiated thyroid cancer should be treated with targeted drugs, primarily tyrosine kinase inhibitors. The review considers the criteria for refractoriness and the criteria for prescribing targeted therapy, and presents the results of clinical trials of the targeted drugs used. As of today, lenvatinib is the most well-known targeted agent. In particular, in the SELECT trial lenvatinib demonstrated efficacy in terms of progression-free survival and overall survival in patients with radioiodine-refractory differentiated thyroid cancer. As a result, lenvatinib was included in the international and Russian clinical guidelines for the management of this group of patients and recommended as a first-line drug of targeted therapy.

The second most effective drug registered in Russia for this category of patients is sorafenib. The use of sorafenib in progressive differentiated breast cancer was studied as part of the DECISION multicenter study. It has a fundamentally different spectrum of adverse events in contrast to lenvatinib. And this fact should be taken into account when choosing a drug for the 1st line of targeted therapy.

In September 2021, the FDA approved cabozantinib for use in adults and children over 12 years old with locally advanced and metastatic radioiodine refractory differentiated thyroid cancer after disease progression with therapy with other tyrosine kinase inhibitors. The efficacy of the drug was evaluated in the COSMIC-311 study, which demonstrated a significant reduction in the risk of disease progression or death when taking it compared with placebo ($p < 0.0001$). In Russia, cabozantinib for the treatment of progressive radioiodine refractory differentiated thyroid cancer was registered on June 10, 2022. Cabozantinib demonstrates improved survival without progression regardless of the experience of previous therapy (sorafenib, lenvatinib, sorafenib+lenvatinib).

In November 2018, the FDA approved larotrectinib, the first drug specially developed and approved for the treatment of any solid tumors containing NTRK gene mergers, including progressive radioiodine refractory thyroid cancer. It was registered in Russia in July 2022. The features of this drug is that it penetrates the blood-brain barrier and can be used in patients with metastatic brain damage.

In Europe and the USA, pralsetinib or salpercatinib and dobrafenib with trametinib are also used for the treatment of progressive radioiodine refractory thyroid cancer in subsequent lines of targeted therapy. These therapeutic options are not registered in Russia for the treatment of radioiodine refractory differentiated thyroid cancer, but can be used in case the drug is available, given the absence of other therapeutic options as prescribed by the medical commission.

It is widely known that the results obtained in controlled clinical trials are rarely repeated in life, since studies are conducted on selected populations under strictly controlled conditions optimized to demonstrate the effect of the drug. Therefore, real data should be considered as the most important element of monitoring the effectiveness of medicines.

PRINCIPLES OF PET/CT IMAGING FOR PROSTATE CANCER

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Prostate cancer (PC) is the most common male malignancy worldwide and the third most common with regards of mortality. After its diagnosis, precise determination of extent of the disease and follow up scheduling are fundamental steps for both, therapy framing and prognosis. The number, the nature and the sites of lesions offer the basis for a personalized treatment. The earlier the diagnosis of the burden of the disease, the longer the survival of many patients.

Imaging is performed for the detection and characterization of disease to select treatment or guide change in management. Imaging techniques can evaluate anatomic or functional parameters. Anatomic imaging techniques include plain film radiographs, ultrasound, CT and MRI. Functional imaging techniques include radionuclide bone scan, PET/CT, and advanced MRI techniques.

PET/CT is a molecular imaging modality and has been used in the field of prostate cancer for some time. PET/CT uses different radiolabelled tracers to identify and target specific biological pathways with a wide range and an increasing number of applications. Diagnostic accuracy in PET/CT is dependent on the radiotracer used, with different tracers appropriate in different applications. In PC several radiotracers have been trialled, including Choline, Fluciclovine, and prostate-specific membrane antigen (PSMA). PSMA is a transmembrane glycoprotein highly expressed in prostate cancer cells. PSMA expression tends to increase with increased pathological Gleason grade and is thought to be upregulated with the emergence of androgen independence. Nowdays for performing PET/CT in patients with PC 18F and 68Ga labeled ligands have been developed to target PSMA.

Our aim was to emphasize the complementary role of PSMA PET/CT for staging, response monitoring and evaluation of disease recurrence of patients with PC.

PSMA-PET/CT can be considered as an alternative to standard imaging of bone and soft tissue for initial staging, the detection of biochemically recurrent disease, and as workup for progression. Patients at high risk of advanced disease are traditionally assessed with a combination of contrast CT of the abdomen and pelvis, primarily to identify nodal metastasis and technetium 99 (Tc99) bone scan. PET/CT, have been shown to be superior in the detection of bony metastasis. Accurate assessment of regional lymph nodes using conventional imaging is poor, with both CT and MRI having a low sensitivity of lymph node metastasis of 42% and 39%, respectively. PET/CT PSMA was compared to conventional imaging (CT and bone scan) and showed higher sensitivity (85% vs. 38%) and specificity (98% vs. 91%) for the detection of a pelvic nodal or distant metastasis. Early detection of biochemical recurrence of PC is important because of the higher rates of curative salvage therapy when treatment is undertaken at low PSA levels. PSMA PET/CT have a high level of accuracy, as it is able to detect recurrence at lower PSA levels than conventional imaging.

PSMA PET/CT has shown unchallengeable results in PC both at initial setting and biochemical failure, reveals more extended disease than expected thus impacting treatment optimization.

MONITORING AND LYMPHOTROPIC CORRECTION OF BRAIN EDEMATO IN PATIENTS WITH SEVERE CRANIO-BRAIN INJURY

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Severe traumatic brain injury (STBI) is the most serious type of brain injury. Mortality in STBI ranges from 41% to 85%. As you know, the skull has clear boundaries, so an increase in brain volume due to fluid accumulation in the interstitium leads to the occurrence of ICH syndrome. Cerebral edema is a pathological process manifested by excessive accumulation of fluid in the cells and intercellular space, as a result of which brain volume increases and intracranial hypertension develops. To date, multislice computed tomography (MSCT) is the main method for emergency diagnosis of patients with STBI.

Purpose of the study: to evaluate the effectiveness of existing methods for monitoring intracranial pressure and the lymphotropic method for correcting intracranial hypertension in patients with severe craniocerebral STBI.

Materials and methods. The study was conducted in the neuroreanimation department of the Bukhara regional branch of the Republican Scientific Center for Emergency Medical Care. The objects of the study were 51 patients with TBI, whose age ranged from 32 to 65 years (mean age was 56.3±3 years), whose clinical and laboratory data were studied. When evaluating neurostatus on the Glasgow Coma Scale (GCS), the average score upon admission to the hospital was 9.3 ± 2.1.For the purpose of anti-edematous therapy in the period from 2019 to 2021, submastoid regional anti-edematous lymphatic therapy was performed in 38 patients with STBI in the intensive complex. The control group consisted of 13 patients who received standard intensive care. Submastoid injections were performed by a doctor. All patients received a single standard of examination, which included: a general blood test, a general urinalysis, a biochemical blood test, a cerebrospinal fluid examination, an examination of the fundus, an MSCT of the brain, and an assessment of the functions of the central nervous system. To achieve this goal, the main parameters of comparison were determined: assessment according to the Glasgow Scale (GCS), MSCT on the first and on days 5-7 of STBI.

Results and discussions. When performing lymphotropic decongestant in combination with standard therapy, the most important criterion for assessing the effectiveness of the therapy was the timing of recovery of the level of consciousness, which was recorded on the Glasgow Scale. Mortality during the first 5-7 days after TBI in the main group was 2 patients. Transfer to the specialized department after 5 days of stay in the intensive care unit took place in all 36 cases, while there was a further improvement in the GCS score to 12.88+1.20, but this was not statistically significant, $p \geq 0.05$. Survival of patients after 5 days of TBI in the main group was 94.8%. To compare the effectiveness of the therapy in the study groups, patients in the control group (n=13) were also divided into three subgroups, similarly to patients in the main group, depending on the number of GCS scores. Mortality during the first five days after TBI in the control group was 5 patients. Transfer to a specialized department after 5 days of stay in the intensive care unit took place in 8 cases, with a further improvement in GCS scores in these patients from 9.97+1.16 points to 12.57+1.03 points. But the survival rate of TBI patients in the control group was 61.6%. Thus, the implementation of lymphotropic decongestant for STBI in the acute period made it possible to effectively influence the course of the pathological process and improve the results of treatment, which is confirmed by significantly better data on GCS, according to MSCT data in dynamics and duration of stay in the intensive care unit in patients of the main group.

Conclusion. Lymphotropic decongestant therapy increases the effectiveness of basic treatment, prevents the progression of cerebral edema in patients with STBI. Monitoring using MSCT allows dynamic objective control of cerebral edema.

USE OF ^{68}GA-PSMA-11 PET/CT IN PATIENTS WITH PROSTATE CANCER

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Objective: The aim of our work is to present the data on this novel, highly promising imaging technique in primary staging and detection of recurrence of prostate cancer.

Methods: 62 patients were examined, 45 with a primary tumor and 17 with a biochemical recurrence of the disease after radical treatment. All patients underwent PET-CT with ^{68}Ga-PSMA-11 according to the whole body protocol. Interpretation of images was carried out visually and quantitatively with the calculation of SULmax.

Results: High focal (24 patients) or diffuse (21 patients) ^{68}Ga-PSMA-11 uptake was found in the parenchyma of the prostate gland in all patients with primary prostate cancer, which corresponded to the tumor focus. In 18 patients, metastases were additionally diagnosed. PET-positive results were obtained in 14 of 17 patients with biochemical relapse. PET-negative results were observed in 3 of 7 patients with low PSA values (less than 1.0 ng / ml). In patients with PSA level more than 1.0 ng/ml PET-positive results were obtained in all cases. Significant correlation was found between the frequency of obtaining PET-positive results and the stage of tumor according to T category.

Conclusions: ^{68}Ga-PSMA-11 PET/CT has a high potential in the work-up of prostate cancer patients, including primary diagnosis, staging and localization of the tumor process in biochemical recurrence. The probability of obtaining PET-positive results in cases of biochemical recurrence is affected by a PSA level above 1 ng/ml and a high stage of the disease according to the T category (T3-T4).

DEVELOPMENT OF A MONITORING SYSTEM FOR A CLINICAL NEUTRON GENERATOR

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In 2019, a project to develop a neutron therapeutic beam facility was launched. The project involves several enterprises of Rosatom State Corporation and Tsyb MRRC and is led by NL Dukhov VNIIA. The main objective of the project is to create a compact unit with the possibility of clinical placement with a 14.1 MeV neutron source for close-focus remote radiotherapy.

One of the tasks in the project was to control the neutron flux of the neutron generator. For this task there are several solutions such as fission chambers, air or gas filled ionisation chambers, scintillation and other detectors. We have made a choice in favour of the fast neutron radiometer based on synthetic diamond produced by Institution «Project Center «ITER». The detector is based on the ^{12}C (n, α_0) ^{9}Be nuclear reaction, and the energy of the α-particle depends on the colliding neutron energy. This dependence allows not only quantitative neutron characteristics to be monitored, but also its qualitative characteristic such as neutron energy. Figure 1 shows an analysis of the NG-24MT operation, where the neutron energy is in red, the flux in blue, and the smoothing by a Gaussian filter with σ = 60 in black.

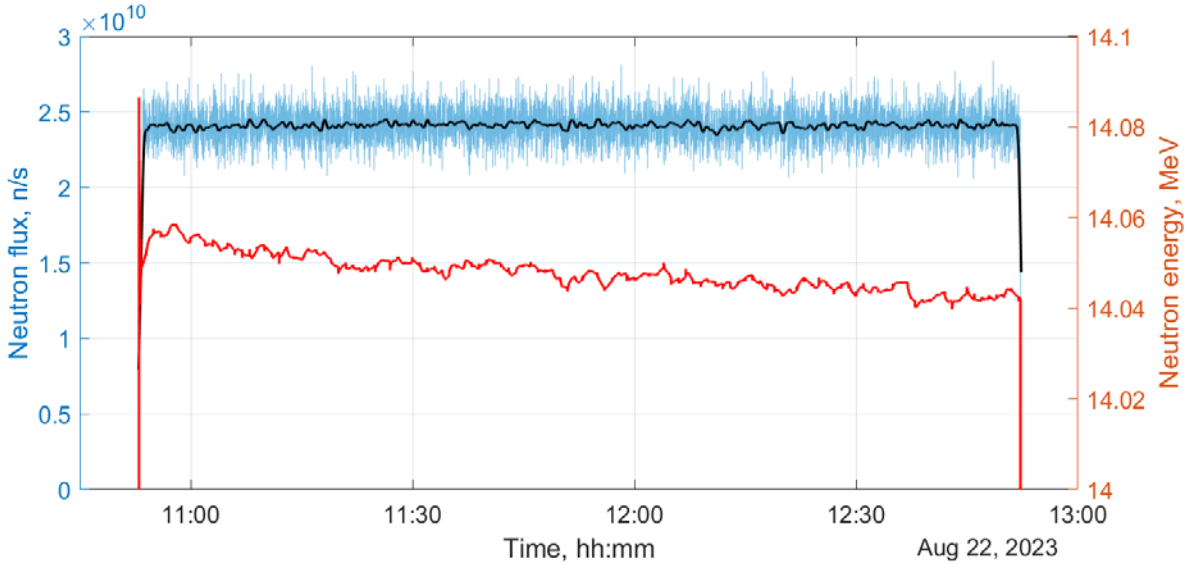

Figure 1: Controlling of the flux and energy of neutron field of the NG-24MT

This neutron generator flux monitoring system can monitor both the flux and the operability and stability of the high-voltage neutron generator equipment. Using the presented detector, we will be able to control the released dose to the patient during the neutron therapy.

RADIONUCLIDE THERAPY IN BONE METASTASES

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Multiple bone metastases are a common variant of progression in such socially significant diseases as prostate cancer, breast cancer, thyroid cancer, and lung cancer. Currently, the possibilities of drug treatment of generalized forms of malignant neoplasms with widespread skeletal lesions have significantly expanded and improved. In many cases, it is possible to achieve long-term stabilization of the disease with minimal clinical symptoms.

There remains a group of patients who, despite effective antitumor therapy, have a pronounced pain syndrome that requires the use of analgesics. These patients may be helped by external beam radiation therapy. Nuclear therapy with bone seeking radiopharmaceuticals is a type of radiation therapy, which can irradiate all the lesions that appear on a bone scan. Radiopharmaceuticals cause persistent pain relief in the majority of patients (70-80%).

Nuclear therapy with bone seeking radiopharmaceuticals is recommended for patients with pain syndrome caused by bone metastases that accumulate bone seeking agents according to a bone scan. Contraindications to the treatment are: unsatisfactory blood counts (a decrease in hemoglobin below 100 g/l, a decrease in the number of platelets below 100 thousand/μl and a decrease in the number of leukocytes below 2.5 thousand/μl), progression of extraosseous tumor foci, the need for cytotoxic antitumor treatment, chemotherapy, some types of targeted therapy, as well as the need for other urgent medical interventions. In Russia, ^{153}Sm-EDTMP and strontium chloride ^{89}Sr are actively used. ^{188}Re zoledronic acid and 188Re-HEDP are at the stage of clinical trials.

In A. Tsyb MRRC, nuclear therapy for bone metastases has been used for more than 20 years; algorithms for prescribing optimal dosages and treatment regimens have been developed. Risk factors of severe hematological adverse events have been identified. The use of strontium chloride, ^{89}Sr in patients with massive bone lesions, in the presence of more than 20 lesions in the bones, leads to the development of persistent, severe thrombocytopenia in some patients. The use of any radiopharmaceuticals with an increased level of AST & ALT in the blood (more than three N) leads to the same complications. Other drugs can be used for any prevalence of bone metastases, but not more than 1 time/2 months. With a good response to treatment, the intervals between courses should be increased. Reduced dosage of ^{153}Sm-EDTMP (0.5 mCi/kg or 30 mCi) achieves the same effect as the standard one (1 mCi/kg) with fewer side effects.

Nuclear therapy with bone seeking radiopharmaceuticals may affect the overall survival of patients. But, to date, there is not enough evidence to recommend this type of treatment with the goal of prolonging life. This type of therapy should not be administered at the expense of the main anticancer treatment. Thus, nuclear medicine is almost never used as a monotherapy. Nuclear therapy works well with all hormonal treatments and many targeted therapies (eg, lung cancer, thyroid cancer), capecitabine chemotherapy, and external beam radiation therapy, with the exception of half-body irradiation and its equivalents. A decrease in blood counts after Nuclear therapy occurs 2-3 weeks after administration, reaches a minimum by the fourth - fifth week, by the seventh to eighth week, as a rule, a complete recovery occurs. These terms must be taken into account when prescribing nuclear therapy and planning cytotoxic treatment after it, so that there is no cumulative effect.

With adequate prescription and following simple recommendations, nuclear therapy is a highly effective and safe method of long-term maintenance of a high level of quality of life with minimal manifestations of pain.

PSMA RADIOLIGAND THERAPY IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER. MRRC EXPERIENCE

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Introduction. Radioligand therapy (RLT) is a new promising method for the treatment of patients with metastatic castration-resistant (mCRPC) with active inclusion of PSMA ligands in all clinically significant pathological foci according to PET-CT data

Purpose of the study. Assess the safety of the use of RLT, select the optimal mode of administration and dosage of the drug for treatment. To evaluate the early response to treatment (biochemical and structural) using ^{177}Lu-PSMA and ^{225}Ac-PSMA in patients with progressive mCRPC

Materials and methods. Data of 37 patients with mCRPC progressing against the background of standard treatment, who received at least 1 course of therapy with ^{177}Lu-PSMA and 18 patients who received ^{225}Ac-PSMA, were selected for the study. Eight patients treated with ^{225}AcPSMA had a previous unsuccessful experience with ^{177}Lu-PSMA. To assess the effectiveness, the PSA level in the patients was measured in dynamics, in the ^{177}Lu-PSMA group, a control PET-CT was performed, in the ^{225}Ac-PSMA group, the structural response was assessed using diffusion-weighted MRI. To assess the safety of therapy, weekly monitoring of the main blood parameters was performed.

Results. As a result of the safety assessment of ^{177}Lu-PSMA, it was found that the drug can be safely used in the dosage range from 5 to 10 GBq, a direct relationship between dosage and the likelihood of adverse events was not identified. ^{225}Ac-PSMA proved to be safe in the dosage range from 6 to 12 MBq. Xerostomia is the most common adverse event after RLT with ^{225}Ac-PSMA, persistent xerostomia was detected in patients who received 9 and 12 MBq. Hematological adverse events were acceptable in all groups, the likelihood of their occurrence being more related to the initial state of the patients and the response to treatment than to the selected radiopharmaceutical or its dosage. With the progression of the disease in patients, a decrease in the level of hemoglobin and the number of platelets in the blood was recorded. ^{225}Ac-PSMA at a dosage of 9MBq was used to treat 2 patients with anemia of the third degree, who underwent red blood cell transfusion to prepare for therapy. After therapy, these patients showed a decrease in the need for repeated transfusions of blood components. No significant effect on renal function was found in any of the groups. In patients with obstructive events caused by the tumor and its metastases, an increase in glomerular filtration rate was observed against the background of a positive response to therapy.

The effectiveness of RLT was high in all groups, somewhat more often in the ^{225}Ac-PSMA group; in most patients, PSA decreased by more than 30%, and a positive structural response was registered as early as 2 months after single cycle of RLT. Unfortunately, the effect of one injection is not stable. In 60% of patients in all groups, PSA levels at the 6-8th week were higher than at the 4th week after administration. Multiple therapy is necessary, but the total number of courses and the interval between them should be determined individually.

Conclusions. RLT is a safe, highly effective treatment for advanced prostate cancer. To improve the results, it is necessary to improve the selection criteria for patients, carefully monitor patients after therapy, identify those who need a second course of RLT after 6 weeks, who can have RLT after 8-12 weeks, and for whom continuation of therapy is inappropriate.

RADIOSYNOVECTOMY FOR KNEE SYNOVITIS WITH RE-188-LABELED ALBUMIN MICROSPHERES. PHASE 1 RESULTS

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Introduction. Synovitis of the knee joints is a common occurrence in rheumatoid, psoriatic arthritis and other diseases. Radiosynovectomy (RSE) - intra-articular administration of radiopharmaceuticals to suppress synovitis is an effective and safe alternative to surgical methods.

Purpose of the study. to study the clinical possibilities of the new Russian radiopharmaceutical "Albumin microspheres 5-10 μm labeled with 188Re" for radiosynovectomy of the knee joints.

Objectives. to study the pharmacokinetics (biodistribution) after a single intra-articular injection in patients using planar scintigraphy and SPECT/CT; Testing increased activity of 370, 555, 740 and 925 MBq with a single injection in one knee joint; Determination of absorbed doses in joints and critical organs; Study of chromosomal aberrations

Materials and methods. The phase 1 study included 20 patients with refractory to standard therapy synovitis of the knee joint (4 groups of 5 people). In the 1st group, 370 MBq was injected intra-articularly, in the 2nd group - 555 MBq each, in the 3rd group - 740 MBq each, in the 4th group - 925 MBq each.

Results.

With intra-articular injection, a high retention of the Re-188 in the joint (97-99% of the administered activity) was noted. Within 2 days, no more than 2% of the administered activity is excreted from the body with urine. Knee scintigraphy and SPECT-CT showed a good distribution of Re-188 in the joint cavity with accumulation in the synovial bursa. The doses of internal irradiation calculated for the knee joint depended on the activity of RFLP introduced into it and ranged from 18 Gy to 74 Gy.

The values of individual radiation loads on risk organs (kidneys, bladder, intestines) turned out to be many times (several tens of times) lower than the critical values presented in the literature, which are allowed during radionuclide therapy. The study of chromosomal aberrations in blood lymphocytes did not reveal significant changes. Side effects in the form of radiosynovitis were noted with the introduction of 925 MBq, in connection with this, it was decided to use the activity of 740 MBq in a further phase 2 study. The phase 2 study is currently ongoing and has shown successful results.

Conclusions.

A phase 1 clinical study showed good tolerability and safety of intra-articular injections of Albumin microspheres 5-10 microns labeled with 188Re, the necessary pharmacokinetics, distribution in the joint cavity without extra-articular distribution, the absence of hematological toxicity and no effect on the chromosomal apparatus. The drug is promising for further research on its use in radiosynovectomy of the knee joints. Phase 2 studies are ongoing. Preliminary results testify to the high efficiency of the method.

PEPTIDE-RECEPTOR RADIONUCLIDE THERAPY. MODERN CAPABILITY AND PERSPECTIVES

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The peptide-receptor radionuclide therapy (PRRT) of radiopharmaceuticals based on somatostatin receptor agonists is radiotargeted against NETs, and is currently active used in foreign clinical practice. The results of the prospective clinical trial NETTER-1 (phase III), showed high response rate, low toxicity and reduced disease progression in patients with inoperable GEP-NETs on the background of conventional treatment with somatostatin drugs. High efficacy of the PRRT method became the basis for its use even in the absence of randomised multicentre controlled trials. To date, sufficient foreign data have been accumulated to confirm the efficacy and safety of PRRT, as evidenced by the positive decision of the Committee for Orphan Medicinal Products of the European Union (COMP EU) dated 25/07/2017. The PRRT is indicated in an adjuvant regimen for the treatment of highly differentiated (G1 and G2 , Ki67 <3% ; grade 2, Ki67 3%-20%) inoperable and metastatic NETs, including adult NETs originating from the upper middle and lower parts of the primary embryonic intestinal tube, including thymus and lung tumours with positive SST_2R status (SST_2R+) and progressing on therapy with somatostatin analogues or other therapies: GEP-NETs, Lung carcinoid, Lung cancer (NET+), NET without primary focus, medullary thyroid cancer, Merkel cell carcinoma, Paragangliomas, Prostate cancer (NET+) Renal cell cancer (NET+). Contraindications to PRRT are: life expectancy less than 6 months, ECOG status 3 - 4; unmanaged urinary tract obstruction or hydronephrosis, urinary retention or high risk of urostasis, myelosuppression, etc. The main diagnostic tracers in foreign clinical practice are: ^{111}In-DTPA-octreotide "Octreoscan" for SPECT/CT, and for PET/CT: ^{68}Ga-DOTA-TATE; ^{68}Ga-DOTA-NOC;68Ga-DOTA-NOC,18F-AlF-NOTA-NOC;68Ga-NOTA-TATE;68Ga-NOTA-NOC. The main radiopharmaceuticals for PPRT of NET at the concept of theranostics are: β/γ emitters (up to 0.95 MeV): ^{131}I-MIBG , ^{177}Lu-DOTA-TATE c 2010 (Lutathera™ / FDA + EMA +), ^{1777}Lu-DOTA-NOC, ^{1777}Lu-DOTA-TOC; β-emitters (up to 2.8 MeV); ^{90}Y-DOTA-TOC from 2003; ^{90}Y-DOTA-TATE from 2005; α-emitters (up to 8.5 MeV) : ^{213}Bi-DOTA-TATE and ^{225}Ac-DOTA-TATE (treatment of paragangliomas). Relative novelty of the PRRT method requires multidisciplinarity in decision making on the appointment of PRRT (endocrinologists, oncologists, radiologists, nuclear medicine physicians et al.), conducting multicentre studies, preparation and methodological recommendations of the PRRT and introduction of this method of radionuclide therapy as a mandatory method of treatment of progressive metastatic NETs on the background of standard treatment.

ANALYSIS OF THE CONTRIBUTIONS OF ^{nat}Gd ISOTOPES TO THE ABSORBED DOSE AT ^{nat}Gd NCT

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An analysis of the literature data has shown that many authors [1, 2] use a greatly simplified version of calculations when calculating the absorbed dose in natural GdNCT. In particular, many authors [3-8]) take into account only the impact (separate or combined) of Auger electrons, internal conversion electrons, gamma radiation and X-ray radiation obtained from estGd during the (n, γ) reaction. Therefore, some authors [6] and [7] believe that in order to damage tumor cells, Gd must be delivered inside the cells. But the authors of R.F. Barth et al. [3, 4] and R.M. Brugger et al. [5], taking into account the large cross section of thermal neutrons and the penetration depth of γ radiation, noted the possibility of killing tumor cells when Gd is outside the tumor cells. Considering the characteristics of secondary particles J.T. Goorley [9] assessed the possibility of using Gd for NCT by dividing them into the following groups: ^{157}GdNCT; ^{159}GdRNT and GdPAT, where RNT is radionuclide therapy, PAT is photon activation therapy. He also noted the non-exclusivity of these three forms of therapy separately. In our opinion, such calculation methods do not sufficiently take into account the nature and characteristics of the epithermal neutron beam itself, which is used to generate the neutron capture reaction. In recent decades, the main progress in NCT has been associated with boron-containing drugs. Because of this, many concepts and calculation models are often transferred to studies with ^{nat}GdNCT. Such a direct transfer is completely unacceptable for ^{nat}GdNCT, since in ^{nat}GdNCT some secondary particles, for example, γ - radiations, have a penetration depth sufficient to knock out the orbital electrons of gadolinium atoms. In this way, knocked-out electrons are successfully used in photon-capture therapy of tumors. Such secondary particles can also cause other reactions. This results in secondary particles with a high linear transfer energy (LET). Therefore, we believe that the model for calculating the absorbed dose for eating GdNCT is many times more complex than for BNCT. Our work presents the results of our research, which shows that, in all models that evaluate the biological effect of tumor tissue damage, a simplified approach is used that evaluates two or three types of radiation. In our opinion, with natural GdNCT, it is necessary to take into account the entire spectrum of all types of radiation absorbed by a biological object. This is also necessary from the point of view that a combination of exposure to two or three types of radiation can give a more powerful damaging effect on tumor tissue, and in the case under consideration, we can talk about a spectrum consisting of several types of radiation that simultaneously affect biological tissue. We carried out a thorough analysis of the literature data and additional own calculations to estimate the secondary particles emitted by gadolinium upon interaction with the epithermal neutrons of the reactor. The results obtained provide valuable corrections to the dosimetric calculations for natural GdNCT.

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MODERN STUDIES TO IMPROVE THE EFFECTIVENESS OF NCT

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Existing preparations for delivering boron to the tumor cannot yet provide the required ratio of tumor/healthy tissue concentration in the treatment of human brain tumors using NCT. M. J. Luderer et al. [1] studied this problem in patients with glioblastoma multiforme (GM) of the brain. The high recurrence rate observed in GM is partly due to the hypoxic mechanism of the tumor. Tumor hypoxia (oxygen starvation) increases metastasis, promotes angiogenesis, and confers resistance to chemotherapy and radiation. In recent years, the latest advances in biology and chemistry have begun to be applied to improve the effectiveness of BNCT in the treatment of human brain tumors. R. Barth et al. [2] proposed molecular targeting of boron delivery agents. Three specific molecular targets were considered and the best therapeutic results were obtained using bioconjugates in combination with intravenous BPA, suggesting that molecular and non-molecular targeting agents should be used together. The issues of an efficient boron delivery system with good effect of permeability and retention (EPR) for BNCT are considered in the work of H. Nakamura [3]. A lipid-based liposomal boron delivery system (LBDS) has been developed. Although LBDS has shown promising effects in mice with colonic tumor implantation, a high dose of liposomes is required to deliver the required amount of boron atoms to the tumor. They found that the number of cations of encapsulated boron clusters affected the formation of liposomes, resulting in highly corrosive liposomes by overcoming osmotic pressure limitations.

Seiji Yasui et al. [4] showed that the currently used BNCT, which usually uses BPA as a boron agent, is effective against melanoma and head/neck (H/N) cancer, but is not always effective against other types of tumors such as glioblastoma. Retrospectively, this can be well explained by the results of transcriptome analysis showing that expression levels of SLC7A5 (encoding the amino acid transporter LAT1: responsible for BPA uptake) are elevated in almost all cases of melanoma and H/N cancer, but not in glioblastoma. To establish a framework, it is necessary to understand: (1) the cellular and molecular mechanisms underlying the cancerous properties of boron uptake, and (2) the intracellular determinants of boron agent pharmacokinetics. Using the cell permeable agent BSH (OKD-002) as an example, the authors demonstrate that the determination of the molecular characteristics of the boron agent makes it possible to create the concept of precision medicine. In the work of S. Miyatake et al. [5] considered these issues with recurrent malignant tumors using the BNCT method on accelerators. It was concluded that BNCT could prolong the survival of patients with recurrent malignant gliomas, especially in high-risk groups.

Also K. Takeuchi et al.[33] evaluated the treatment of high-grade meningiomas using BNCT. Typically, meningiomas are treated with total cranial base excision (CBE), which is particularly challenging and extended surgical excision is often associated with serious complications. It has been shown that BNCT can be a promising therapeutic option for patients with high-grade CBE, and the use of neutron sources based on accelerators is promising.

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ANALYSIS OF NEUTRON NUCLEAR REACTIONS IN ^{nat}Gd FOR ESTIMATION OF ABSORBED DOSE AT ^{nat}GdNCT

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It is known that Gd consists of the following isotopes: ^{152}Gd (0,205%), ^{154}Gd(2,23%), ^{155}Gd(15,1%), ^{156}Gd(20,6%), ^{157}Gd(15,7%), ^{158}Gd(24,5%), ^{160}Gd(21,6%). Irradiation of natural Gd with an epithermal neutron beam from a reactor can produce the following nuclear reactions, with useful yields for Gd NCT: 1) The reaction ^{152}Gd (n, γ) ^{149}Sm has 0.2 nuclear transformations per second. The resulting 149Sm nucleus has a large reaction cross section (n, γ) ~46000 barn. In ^{152}Gd and ^{149}Sm are α-decay nuclei with a half-life of 1.08×10^{14} year and 2.0×10^{15} year, respectively, and the α-decay energy Q_α=2140 keV and Q_α=1869.9 keV [1, 2]; 2) At ^{154}Gd (n,t) ^{152}Eu, in the first excited state, the lifetime is 9.3116 hours and the processes of β^--decay (72%) and electron capture (28%) take place. In the second excited state, the lifetime is 13,537 years and the processes of β^--decay (27,9%) and electron capture (72,1%) take place, with Q_β=1818.8 keV and Q_{EC}=1874.3 keV, respectively. 3) The reaction ^{155}Gd (n, γ) ^{156}Gd has $1,783 \times 10^7$ nuclear transformations per second, in ^{155}Gd (n, α) ^{152}Sm – 14,8 nuclear transformations per second. The reaction energies are 8.54 and 8.33 MeV, respectively. In the reaction ^{155}Gd (n, γ) ^{156}Gd, the outgoing main g-quanta with a relative intensity of ≥100 have the following energies. 4) The ^{156}Gd (n,2n) ^{155}Gd reaction has 19,6 conversions per second. In the ^{156}Gd (n,2n) ^{155}Gd reaction, the stable ^{155}Gd nucleus can also be in an excited state with the excitation of lower levels with energies from 88,97 to 288,187 keV. The excitation is removed by γ-transitions to the ground state. 5) The reaction ^{157}Gd (n, γ) ^{158}Gd has 7.67×10^7 nuclear transformations per second, the reaction ^{157}Gd (n, α) ^{154}Sm has 21,8 nuclear transformations per second and the reaction ^{157}Gd (n,2n) ^{156}Gd has 15.2 nuclear transformations conversions per second. In the reaction ^{157}Gd (n, γ) ^{158}Gd, the outgoing main γ-quanta with relative intensity greater than 100 have the following energies in keV. The output of secondary electrons and X-rays is also observed: 6) The reaction ^{158}Gd (n,2n) ^{157}Gd has 23,8 nuclear transformations per second, respectively, and for the rest these values are negligible. In the reaction ^{158}Gd (n, γ) ^{159}Gd, the ^{159}Gd nucleus is β^--radioactive and has a lifetime of 18,475 hours. In this case, β^--particles are emitted with energies of 970,6 (62,5%), 912,61 (25,4%,), 833,1 keV (0,017%), 622,32 (0.31%) and 607,6 (11,7%) keV, respectively, and γ-rays with energies of 57,99; 137,5; 348,28 and 363,54 keV respectively [1, 2]. In the case of the reaction ^{158}Gd (n,2n) ^{157}Gd, the final nucleus will be in an excited state, with the excitation of the lower levels of ^{157}Gd, then emitting γ - quanta, it goes into the ground state; 7) Also significant are the reactions ^{160}Gd (n, γ) ^{161}Gd with 12,9 and ^{160}Gd (n,p) ^{160}Eu with 0,812 nuclear transformations per second, respectively. From isotopes of ^{nat}Gd, the most interesting for ^{nat}GdNCT are the ^{155}Gd nucleus. In the ^{155}Gd exciting next levels: 60,0106; 86,5464; 105,3106; 107,5804; 117,9981; 121,10; 146,0696; 214,3515; 230,1286; 251,7056 during the decay of which gamma transitions (M1 + E2, E2) have significant γ conversion coefficients, which contribute to the release of secondary electrons of the atom: 9,14; 0,431; 1,95; 362; 2,60E3; 50; 3,4E2; 1,238; 12,6; 3,14; 1,98; 1,17; 1,65; 1,74.

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EXACT DETERMINATION OF ABSORBED DOSE IN ^{nat}GdNCT

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The goal of radiation therapy is to create the desired absorbed dose in the volume containing malignant cells while minimizing the absorbed dose in healthy tissue. GdNCT is one of the promising methods of radiation therapy and is based on nuclear reactions in $^{nat.}$Gd. The radiation used in $^{nat.}$GdNCT is a mixed field of complex radiations with high and low linear energy transfer (LET). This field depends on the spatial, spectral, and angular characteristics of the incident neutron radiations, as well as on the geometry and elemental composition of the target. The absorbed dose in GdNCT can be divided into four primary dose components: doses from thermal neutrons, fast neutrons, photons, and natural gadolinium. Problems in neutron radiation dosimetry arise due to the sensitivity of detector devices to radiation. The sensitivity of almost all dosimeters in the complex depends on the neutron energy. Therefore, to estimate the absorbed dose, it is convenient to determine the kerma (K) - a close analog of the absorbed dose. When the secondary charged particles are in equilibrium, the kerma will be equal to the absorbed dose. The advantage of kerma is the possibility of determining it by calculation for a known monoenergetic neutron flux, and for the neutron spectrum. When calculating kerma, all processes that form the absorbed dose in biological tissues are considered. Using the values of partial components of dose estimates in soft biological tissue, one can calculate the value of the total absorbed dose depending on the concentration of natural Gd in the tissue [1, 2]. The total absorbed dose in biological tissue with a Gd-based drug is defined as: $D_{total} = D_n + D_\gamma + D_n^{ppm\,Gd} + D_\gamma^{ppm\,Gd}$. This formula can be written in terms of kermas: $D_{total} = m \cdot t(K_n + K_\gamma) + \rho \cdot t(K_n^{ppm\,Gd} + K_\gamma^{ppm\,Gd})$. As is known, when a flux of epithermal neutrons passes through a substance, the flux decreases depending on the neutron's interaction cross-section. $^{nat.}$Gd has a cross section σ_{Gd} = 46 000 barn. Macroscopic neutron absorption cross section on gadolinium $\Sigma_{Gd} = n\sigma_{Gd}$. To accurately determine the absorbed dose, when planning BNCT and GdNCT, it is also necessary to take into account the effect of attenuation (self-shielding) of the beam in the tumor itself. We have conducted studies to study the influence of this effect on the determination of the absorbed dose in GdNCT [3]. As is known, patients before radiation therapy undergo several tomographic studies with Gd-contrast agents. Since the absorbed dose in GdNCT strongly depends on the concentration of Gd in tumors, therefore, we studied the accumulation of Gd in human brain tumors [4]. It was found that after intravenous injection of Magnevist, trace amounts of gadolinium in various concentrations remain in brain tumors. These concentration values show its correlation with the number of performed tomographic studies. Therefore, the final formula for determining the absorbed dose in the tumor, taking into account the above effects for ^{nat}GdNCT, can be written as follows:

$$D = \left\{\left[(m \times K_n^{tissue}) + (m \times K_\gamma^{tissue}) + (\rho_{Gd} + \Delta\rho_{Gd}) \times K_n^{1\,ppm\,Gd}) + (\rho_{Gd} + \Delta\rho_{Gd} \times K_\gamma^{1\,ppm\,Gd})\right] \times t - \delta\right\} \cdot s$$

where δ is the correction factor to take into account the pharmacokinetics of the drug with Gd, Δρ is the correction to take into account the accumulation of Gd, the coefficient s is to take into account the effect of Gd self-shielding with GdNCT.

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NEW ASPECTS OF THE TREATMENT AND REHABILITATION OF ULCERATIVE COLITIS

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The purpose of the research. Assessment of the effectiveness of the Modulen IBD mixture, which is used for the purpose of nutriciological support in the treatment of patients with ulcerative colitis.

Research material and methods. The study was carried out in the Department of Gastroenterology of the scientific and practical medical center of specialized therapy and medical rehabilitation of the Republic (RIT and TRIATM) in 2020-2022. The study included 48 patients who received both inpatient and outpatient treatment with UC. The median age of patients was 36.8 ± 10.4 years.

All patients are divided into two groups:

* Patients of the main group (30 people) received a mixture of “Modulen IBD” with a volume of 400-600 ml per day for 12-14 days, in addition to basic therapy (5-aminosalicylic acid (5-Ask)) and regular dietary nutrition. The mixture is prescribed in small portions in 2-3 doses between main meals (with the"Siping" method).

* Control group (30 people) patients received only basic drug therapy (5-Ask + glucocorticosteroids (GKS)) and dietary nutrition. Support for nutrition with a mixture of “Modulen IBD” was not carried out.

In the main and control groups, there were no significant differences in gender, age, location of intestinal lesions, severity of the disease, and type of existing nutritional deficiencies.

Research results. Analysis of clinical indications shows that as a result of increased protein loss through the intestine and an active inflammatory process, nutritional deficiencies and associated nutrient and energy deficiencies slow down reparative processes in the mucous membrane of the small and large intestine, and eventually an increase in the remission time of the disease occurs.

The primary group of people with ulcerative colitis had 17 men (56.7%), 13 women (43.3%), and the control group had nearly equal numbers of men and women (14 (46.7% and 16 (53.3%), respectively. The mean age distribution of the primary and control groups is 32.4±5.6 and 34.2±6.8, respectively. In terms of activity level in Truelove and Witts, 2 LA was also significantly active in the group. In the case of the Meyo index, too, 2 La showed the same value in the group 2.

During treatment, activity levels in Truelove and Witts and the Meyo index changed positively in the core group in more patients than in the control group.

In patients with UC, the fecal calprotectin post-treatment rate was much lower in the primary group than in the control group, i.e., before treatment, fecal calprotectin in the primary group decreased 4.2 times the pre-treatment rate (645), while in the control group it decreased 5.1 times (130) from the initial result (668).

Conclusion. Thus, after a course of support for nutrition with a mixture of “Modulen IBD” with the help of additional enteral nutrition in patients with UC, an improvement in nutritional status was noted, which indicates an increase in the body's plastic and energy reserves. Our study shows that the appointment of additional enteral nutrition with a mixture of “Modulen IBD” as part of complex treatment at the stage of UC lamination significantly improves the patient's nutritional status, helps to treat nutritional deficiencies and increases the body's energy and plastic reserves.

STUDY OF RADON-222 CONSENTRATION IN BUKHARA WATERS FOR USE IN RADON THERAPY

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In natural waters there is always an inert, colorless heavy radioactive gas - radon-222. The transfer of radon to water occurs through the soil, either by diffusion, or by surrounding air gases, such as CO_2, CH_4 and ^4He, or by water moving in soil horizons. An increase in the concentration of Rn -222 in natural waters poses a danger to human health on the one hand, and on the other hand it is useful in the treatment of a number of diseases using radon therapy. Therefore, there is a limit on the maximum allowable concentration (MAC) of radon in the waters, adopted by the radiation control authority of each country.

Natural waters with radon-222 concentration ≥185 Bq/l successfully used for the treatment of diseases of the musculoskeletal system, peripheral nervous system, as well as gynecological and urological.

The aim of the proposed work is to study the concentration of radon-222 in various sources of Bukhara for the further use of radon-enriched waters in radon therapy.

To measure the concentration of Rn -222 in water, radon-metric instruments and nuclear solid-state track detectors of the CR -39 type were used. The concentration of Rn-222 in the studied waters was determined by the ratio of the concentration of Rn -222 in the reference water, where the root mean square error was ±25%.

Water samples were taken from taps, wells and natural springs. Water samples from seven shrines of Bukhara were measured: 1. Abdukholik Gijduvony (Gijduvon); 2. Mohammed Arif Ar-Revgariy (Revgari); 3. Khoja Mahmud Anzhir Fagnaviy (Vobkent); 4. Khoja Azizona (Shofirkon); 5. Bobo As-Samosy (Kogon); 6. Said Amir al Sukhoriy (Sukhor); 7. Bahauddin Nakshbandi (Hinduvan), as well as from the sanatorium Sitorai Mohi-Khosa, Zhuizar and Issiksuv.

The concentration of Rn -222 from the tap of Bukhari was 3.84 Bq/l. In the sacred springs and sanatoriums of Bukhara, the concentration of Rn -222 is in the range of 3.1-12 Bq/l, which does not exceed the maximum allowable concentration of Rn -222 in water of 60 Bq/l kg, established in the norm NRB RUz.

However, high concentrations of radon-222 up to 500 Bq/l and more were found in the well waters of Kyzylkum (Navoi), adjacent to Bukhara.

OPTIMIZATION OF RADIATION THERAPY IN THE COMPLEX TREATMENT OF MALIGNANT TUMORS OF THE HEAD AND NECK IN THE DEPARTMENT OF RADIOTHERAPY RSPMCO&R

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In most cases (about 60-70%), patients with oral and oropharyngeal cancer start treatment at a locally advanced stage of the disease.

After the installation of linear accelerators (Elekta Infinity and Elekta Sinergy) in the Oncology center and gamma therapeutic devices (Terabalt with 3D planning system) in all other 12 centers, the approach to the treatment of this pathology has radically changed. Previously, there were 5 units of cobalt devices with a 2D planning system in the whole country.

To choose the right treatment program for head and neck cancer, it is necessary to have a reliable idea not only about the features of the primary tumor, but also about the characteristics of the cervical lymph nodes. Thus, a thorough examination of the cervical lymph nodes in patients suffering from malignant tumors of the head and neck (computed X-ray tomography, magnetic resonance imaging, lymphoscintigraphy with the use of tumorotropic drugs) is absolutely mandatory when deciding on adequate treatment tactics.

Oropharyngeal cancer.Remote irradiation at SOD 66-70 Gy is sufficient to provide local control of oropharyngeal cancer T1–2 in 90% of cases. To destroy waste products classified as T3 and T4, the total focal dose should be increased to 76 Gy and higher. Of course, part of this radiation load must be provided by local access either by an electron beam on linear electron accelerators, or by brachytherapy with iridium 192 implants. If there is no lesion of the cervical lymph nodes, then remote irradiation is brought to 45-50 Gy.

In other oncopathologies, where the risk organs are close and it is difficult to achieve the desired result with the help of remote radiotherapy and there are metastases in the lymph nodes, it is not possible to bring the dose up to 65-75 Gy, a combination of remote irradiation and brachytherapy is used, with the help of iridium 192 implants or locally irradiated with an electron beam.

According to R.T. Meoz Mendez et al., for cancer of the pharyngeal walls, standard fractionation up to 70-75 g should be used after 7-7.5 weeks. This leads to local control of tumors of category T1 – in 91% of cases, T2 – in 73%, T3 – in 61%, T4 – in 37%. In addition, the surgical component increases the localization frequency at T1 – up to 100%, T2 – 78%, T3 – 71%, T4 – 41%.

According to G.E. Laramore et al., the following algorithm is the most suitable for the treatment of oropharyngeal cancer: T1N0M0 – surgery or radiation therapy SOD 66-70 Gy; T2N0M0 – surgery or radiation therapy (65-72 Gy); T3N0M0 – resection + postoperative irradiation (50-60 Gy).

APPLICATION OF 4D PLANNING IN BRACHYTHERAPY FOR CERVICAL AND RECTAL CANCER

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The main method of treatment for locally advanced cancer of the cervix and rectum is combined radiation therapy. Properly performed radiation treatment is the key to increasing the life expectancy of patients and improving the quality of life. Improving methods of combined radiation therapy is an important task in the treatment of cancer of the cervix and rectum. Unconditional progress in the development of brachytherapy is associated with the use of CT-MR tomograms in modern planning of intracavitary therapy, which makes it possible to accurately calculate doses for the tumor itself, the cervix, rectum, tumor infiltration zones and risk organs.

Objective of the study. to improve methods for planning the calculation of doses for the tumor, critical organs and organs at risk.

Materials and methods. for researching 18 cervix cancer patients with intracavity treatment after radiation therapy were collected. All patients who received course of radiation therapy on all small pelvis to the total general dose 44-46 Gr, in the subsegment were directed to a brachytherapy course. All patients underwent a full course of brachytherapy by using 4D planning the total general dose on tumour and uterine cervix was brought to 30-35 Gr at the same time organs at risk (bladder and rectum) received the minimum maximum permissible dose.

A group of patients with rectal cancer (17 patients) at the first stage underwent a course of radiation therapy to the entire small pelvis up to SOD=46Gy while taking Capecitabine chemotherapy tablets. At the second stage, the course of brachytherapy SOD 15-20Gy, up to the total total dose per formation zone up to SOD=60Gy. Radiation therapy was carried out in 3D mode for the entire pelvis. Brachytherapy was performed on patients in 4D mode, i.e. with MSCT topometry, contouring and planning at each patient position.

All patients had a histologically confirmed diagnosis. All patients with the third stage of the process.

After the end of therapy, the regression of the primary tumor ranged from 60 to 100%. At the same time, the isodose load on risk organs did not exceed the tolerable values. The expected complications of radiation therapy were minimized.

Results. thus the further development of technologies in this direction of real time planning in brachytherapy, corrected by images of MSCT-planning in real time, taking into account the physiological changes of the patient in order to improve the visualisation of the target, increase the possibility of dose delivery to the tumour, leads to increase of the effectiveness of radiation treatment. It also made possible to bring the total focal dose on the residual tumours to the maximum permissible dose, taking into account the radiation load on critical organs during each laying. As s results, complete tumour regression was achieved over the entire course of combined radiation therapy, while maintaining dose limits on the bladder and rectum.

PRECLINICAL PET/CT OF PROLONGED TUMOR GROWTH AFTER ^{177}Lu-PSMA TREATMENT IN XENOGRAFT MODEL OF HUMAN PROSTATIC CANCER

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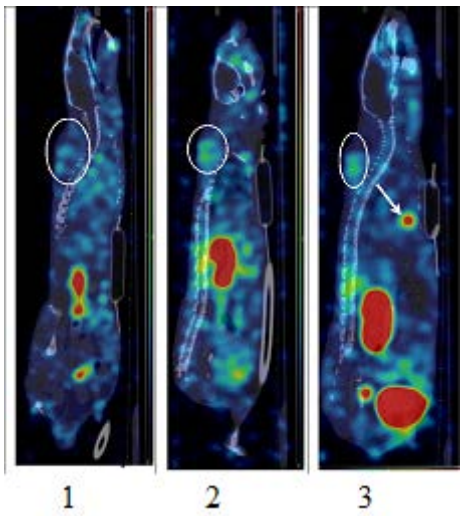
Background. New treatment methods of castration-resistant prostate cancer with radionuclide therapy are needed. New methods will optimize personalized strategy for radionuclide therapy of metastatic castrate-resistant prostate cancer using low molecular weight ligands to PSMA labeled with lutetium-177.

Aims. To define the long-term effects and effectiveness of the treatment experimental animals with PET imaging to refine the research strategy.

Materials and methods. The study was performed in nu/nu male mice with PSMA-expressing 22Rv1 prostate cancer xenografts. PET/CT study with ^{18}F-PSMA-1007 was used to confirm the tumor regrowth after a single injection of 9.2 MBq [^{177}Lu]Lu-PSMA I&T, which is equivalent to minimal human therapeutic dose 28.6 MBq/kg.

Results. PET imaging with ^{18}F-PSMA-1007 showed the possibility of prolonged 22Rv1 tumor regrowth after a single therapeutic dose.



PET scans of a mouse with prolonged growth of 22Rv1 tumor. 1 – 55 min; 2 – 2.5h.; 3 – 3h. In the circle – tumor 22Rv1. Arrow – hyperfixation of radiopharmaceutical ^{18}F-PSMA-1007 in tumor metastatic area.

Conclusions. The study confirmed the short period of the observed therapeutic effect after a single injection of 9.2 MBq [^{177}Lu]Lu-PSMA I&T. The tumor regrowth in 2.5 months after the reduction of 22Rv1 xenografts to a non-palpable state was confirmed by PET/CT with ^{18}F-PSMA-1007.

EVALUATION OF THE EFFECTIVENESS OF ADJUVANT RADIATION THERAPY FOR BREAST CANCER IN HYPOFRACTIONATION MODE

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The relevance of the problem. Breast cancer is the most common malignant disease in women in the Republic of Uzbekistan. In 2022, 4407 new cases were registered, which is 24.4% in the structure of the incidence of malignant neoplasms in women [Tillyashaykhov M.N., 2023]. Currently, the main negative aspect of postoperative radiation is the duration of the course of radiotherapy, which is 5-6 weeks, taking into account pre-radiation preparation.

The purpose of the study. Evaluation of the effectiveness of adjuvant radiation therapy in hypofractionation mode in patients with operable breast cancer.

Material and methods of research. The object of the study was the medical documentation of 120 patients with stage I–IIIA breast cancer who received adjuvant radiation treatment in the radiotherapy department of the RSSPMCO&R of the Ministry of Health of the Republic of Uzbekistan from 2020 to 2023. All patients were divided into two groups: basic (hypofractionated radiation therapy (HFLT) and control (traditional course of LT).

Results and discussion. In the experimental and control groups, the frequency of local relapses (in the irradiation zone) during postoperative radiation therapy of breast cancer in the mode of 2.66 Gy/16 Fr/42.5 Gy was comparatively studied. In the main group, relapse was observed in 3 (5.0%) patients, whereas in patients receiving traditional radiation, relapse was observed in 5 patients (8.3%). Median follow-up was 2.3 years and 2.4 years in the HFLT and TLT groups, respectively ($p = 0.75$). Five cases of relapses (62.5%) were of the invasive morphological type, and 3 (37.5%) were intracurrent carcinomas. Although the differences in the rates of recurrence and their types did not have statistical significance, the indicators of recurrence were significantly higher in late stage III – 6 cases than in stage II (4 cases), the established difference was statistically significant.

Conclusion. Analysis of the results of the treatment study showed that during the follow-up period, the indicators of local and ipsilateral recurrence of breast cancer were the same in both groups. There were no characteristic clinical features of the growth of recurrent tumors depending on the volume of radiation exposure. The attractiveness of HFLT lies in the fact that the time and costs of treating patients are reduced, locoregional relapses are reduced, the load on the equipment is reduced.

CLINICAL USE OF POSITRON EMISSION TOMOGRAPHY FOR RADIOTHERAPY PLANNING IN HEAD-AND-NECK CANCER

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Keywords: Radiotherapy, PET-based contouring, Treatment Planning, Head-and-Neck Cancer.

Purpose. For radiotherapy planning (RTP) of head-and-neck squamous cell carcinoma (HNSCC) 18-Fluoro-deoxyglucose positron emission tomography-computed tomography (FDG PET/CT) image information has shown to provide essential information for reliable and valid target volume delineation. We investigated the potential impact of FDG PET/CT images on three-dimensional conformal radiotherapy planning for patients with HNSCC.

Methods and Materials. 67 patients with HNSCC were planned for RTP using PET/CT device. Each patient underwent CT and FDG-hybrid. Target volume delineation was initially performed on the CT images, and the corresponding FDG-PET data were subsequently used as an overlay to the CT data to define the target volume. A study was performed in which for each patient the gross tumor volume (GTV) was defined based on MRI-CT and on PET-CT data. Three level simultaneous integrated boost plan delivered in 35 fractions with a daily dose of 2 Gy (5 sessions/week) and 70 Gy as the total dose in the high-risk tumor target volume, while the target intermediate- and low-risk tumor volume received a daily dose of 1.8-1.6 Gy, respectively, and 63 Gy-56 Gy as the total dose, respectively. RTP were constructed based on both MRI-CT-GTV and PET-CT-GTV. Dose-volume histograms for the planning target volume (PTV) and organs at risk (OAR) were calculated.

Results. The GTV was decreased by CT-PET image fusion in 22 patients (33%) and was increased in 16 patients (24%). The median MRI-CT-GTV was 24.8 mL compared with 19.7 mL in the PET-CT-GTV. Occult metastasis was found in 14 patients (21%). In addition, in a significant proportion of patients, more than 20% of the PET-CT-GTV was located outside the MRI-CT-GTV. This suggests that FDG PET/CT may identify tumors that were not detected using standard GTV detection methods.

The D95 was very similar between CT/PET and CT/MRI -generated GTVs and was not significantly different. The differences between the mean and maximum OAR doses were -0.43 ± 1.51 Gy and -0.86 ± 3.13 Gy, respectively. Relatively significant differences were observed in the spinal cord. In the spinal cord using CT/MRI, there was an increase in the number of cases where the maximum dose received exceeded 45 Gy (9 patients).

Conclusion. The tumor volume determined with FDG-PET is on average smaller than with other techniques, but most closely matches the true tumor volume. In patients with HNSCC considered for curative RT, using PET-CT will improve tumor coverage, and in selected patients, will reduce the volume of normal tissues irradiated, and thus toxicity. However, some difficulties are unresolved, including the internal mobility of the GTV, unknown differing set up of patients during CT and PET-FDG. Nevertheless, some tumor regions that are apparent on CT or MRI may not be visualized on PET, and in these cases, the use of PET alone would potentially lead to geographic error.

THE APPLICATION OF RADIONUCLIDES IN THE DIAGNOSIS AND TREATMENT OF VARIOUS ONCOLOGICAL DISEASES

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In the private multi-profile Nano Medical Clinic, from 2020 to September 2023, 300 patients with differentiated thyroid cancer following total thyroidectomy were treated with radioiodine therapy using NaJ-131. Among these patients, 220 (73%) exhibited complete remission of differentiated thyroid cancer (DTC) after the initial iodine ablation course, as evidenced by background radioiodine uptake on scintigraphy, clear neck ultrasound (US), and serum thyroglobulin levels below 10 ng/ml. The cumulative total dose of NaJ-131 ranged from 3000 to 3800 MBq. Among the remaining 55 (18%) patients with regional lymph node metastases in the neck, a second and third course of NaJ-131 radioiodine therapy was required to achieve a positive treatment outcome. The cumulative total dose of NaJ-131 ranged from 6000 to 7500 MBq. In 25 (9%) patients with distant metastases, 3-4 courses of radioiodine therapy were administered, with a cumulative total dose of NaJ-131 ranging from 11500 to 13500 MBq. The interval between radioiodine therapy courses was 2-3 months. In the group with distant metastases, 7 (2%) patients experienced a fatal outcome. The three-year survival rate for all DTC patients was 98%.

During the same period, 170 patients with oncological diseases and bone metastases were treated with radionuclide therapy using Sm153 oxibifor. Almost all patients experienced a 50% reduction in pain syndrome after the course of radionuclide therapy. The dose of Sm153 was administered at 40 MBq per kilogram of body weight, with an average cumulative total dose of 2500 MBq. Among 130 (76%) patients who underwent two therapy courses with a 2-month interval, regression of bone metastases with pain relief was observed. However, in 40 (24%) patients, progression of bone metastases with increased pain syndrome was noted even after 3-4 therapy courses, primarily among patients with prostate and breast cancer. A fatal outcome occurred in 27 (16%) patients. The three-year survival rate for all patients with bone metastases was 84%.

Starting from October 2022, our clinic-initiated treatment with radionuclide Lu177 PSMA in patients with stage 3-4 prostate cancer metastases. To date, 35 patients with prostate cancer have undergone this treatment. Among them, 32 (91%) patients exhibited a positive response after four courses of Lu177 PSMA treatment, characterized by the absence of pain syndrome, normalization of PSA levels, and a return to social life. The average cumulative total dose administered ranged from 4500 to 5000 MBq, with an interval between courses of 5 to 6 weeks. Three 3 (9%) patients experienced a fatal outcome due to metastasis progression and pain syndrome

MEASURES TO IMPROVE ONCOLOGICAL CARE IN UZBEKISTAN

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The purpose of the study. Organization of measures to improve oncological care in the regions of the republic through regular visits of highly qualified specialists from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology.

Materials and methods. 10 working groups (highly qualified specialists) from the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology were formed and sent to regions of our republic to increase the knowledge of general practitioners and doctors of other specialties in the field of oncology, increase oncological alertness of the population, improve preventive measures and early detection.

Results. Since 2017 it was formed 10 visiting groups from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. A detailed schedule of targeted visits was developed, indicating the date and name of the area, and a plan of all activities, specifying the goals and objectives for each specialist from the working group. For timely and effective execution of the tasks, all the necessary information on the visits was presented on the procedures that were sent to all regional government, district/city medical associations of the republic, and accordingly to all branches of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. During the year, every month each group went for 3-days to each region, according to the approved schedule. On the first and second day the doctors of the visiting group organized lectures, “master classes” and patient consultations in the regional branches of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, and the third day was devoted to work in rural medical centers lectures for general practitioners and patient consultations. Moreover, specialists from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology appeared in regional media, where a special role was assigned to the healthy lifestyle promotion, primary and secondary prevention of oncological diseases.

Conclusion. Regular visits of highly qualified specialists to the regions of the Republic of Uzbekistan contributes primarily to the population knowledge expansion in the field of oncology, as well as to the increase of oncological alertness of primary care doctors.

IMPROVEMENT OF ONCOLOGICAL CARE IN UZBEKISTAN: RESULTS OF THE ACTIVITIES

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The purpose of the study. Improvement of oncological care in the regions of the republic through regular visits of highly qualified specialists from the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology.

Materials and methods. It was formed 10 working groups for visits to the regions. Each group consisted of 3 highly qualified doctors from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. A detailed schedule of targeted visits was developed, including the date and name of the area, and a plan of all events (lectures, master classes, trainings, consultations, operations) and specifying the goals and objectives for each specialist from the working group. During the year, every month each group performed a 3-day visit to each region, according to the approved schedule.

Results. Over the last 6 years, it was performed 1,398 visits to the regions, including: 332 visits were carried out in 2017, 346 in 2018, 472 in 2019, 105 in 2021, 143 in 2022 and 72 in 2023. In 2020, there were no regional visits due to the global COVID-19 pandemic. The number of specialists who visited remote regions of the country in 2017 was 358; in 2018 – 733, in 2019 – 1189, in 2021 – 164, in 2022 – 184 and in 2023 - 113. Totally there were organized 3,415 lectures and master classes over the past period. In 2017, 9889 regional specialists participated in lectures and master classes, in 2018 – 12286, in 2019 - 12530, in 2021 – 8821, in 2022 – 10134 and in 2023 - 5896. During the visits over the last 6 years, 45 453 people were examined and 42122 patients were provided with specialized medical care: in 2017 – 6700, in 2018 – 9092, in 2018 – 17335 and in 2021 – 2839, in 2022 – 6156 and in 2023 - 1422. Moreover, 27,609 patients were provided with qualified care in outpatient settings and 14,498 patients – in a hospital setting.

Conclusion. It can be concluded that over the last 6 years, according to the approved schedule, there were almost 1400 visits of specialists from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, 3415 lectures and master classes and more than 40,000 patients received specialized care. Every year there was an increase in the number of regional visits and examined patients. Due to traffic restrictions and COVID-19 pandemic, the number of visits and examined patients decreased in 2020 and 2021.

ONCOLOGICAL SERVICE IN UZBEKISTAN: HIGHLY QUALIFIED MEDICAL CARE TO THE POPULATION IN THE REGIONS

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The purpose of the study. Improvement of oncological care to the population in the regions of the republic through regular visits of highly qualified specialists from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology and providing specialized medical care.

Materials and methods. It was created 10 working groups for visits to the regions. Each group consisted of 3 highly qualified doctors from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. Moreover, it was formed detailed schedule of visits indicating the date and name of the district and a plan of all with clarification of goals and objectives for each specialist from the working group.

Results. Starting from 2017 to 2023 there were organized 1,398 visits to the regions. Specialized medical care was provided to 42,122 patients. More then 27,000 (65.5%) patients were treated on an outpatient basis and 14,498 (34.4%) - in hospitals. Totally, it was performed 776 surgical interventions by specialists from working groups over the last period, of which: in 2017 – 218 (28.1%), in 2018 – 169 (21.8%), in 2019 – 138 (17.8%), in 2021 – 53 (6.8%), in 2022 – 198 (25.5%) and in 2023 – 80 (10.3%). Totally it was performed 330 (42.5%) high–tech operations: in 2017 – 82 (24.8), in 2018 – 68 (24.8%), in 2019 – 46 (13.9%), in 2021 - 20 (6.1%), in 2022 – 114 (34.5%) and in 2023 – 50 (15.1%). It was noted that if in 2016 the number of visits advisory polyclinic of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology were 58 188, in 2017 - 54796, in 2022 – up to 44609, in 2020 – up to 43677 and in 2021 – 49620. Over the last 6 years, the number of visits to the outpatient polyclinic of Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology has decreased by 17.3%.

Conclusion. In conclusion, it should be noted that in the republic there was an annual increase of regional visits of specialists from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. Moreover, 776 surgical interventions were performed, of which more than 40% were high-tech. In turn, all the above measures have led to a decrease the number of patients (by 17% over the past 6 years) to the outpatient polyclinic of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology.

WAYS TO INCREASE ONCOLOGICAL ALERTNESS OF DOCTORS AND ONCOLOGICAL LITERACY OF THE POPULATION IN UZBEKISTAN

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The purpose of the study. The purpose of this study was to organize events to improve oncological care to the population of the republic through the regular regional visits of highly qualified specialists from the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology.

Materials and methods. It was created 10 working groups from the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (consisting of 3 highly qualified doctors) to improve the knowledge of doctors, awareness of the population, and the availability of specialized care in remote regions,.

Results. Since 2017, every month each group performed 3-day visit to each region, according to the approved schedule. On the first and second day doctors organized lectures, master classes and trainings for both doctors and the entire population. Totally it was performed 3415 lectures and master classes in the regions of the republic over the last period. Moreover, specialists from Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology appeared in regional media, where a special role was assigned to the promotion of a healthy lifestyle, primary and secondary prevention of oncological diseases. There were 773 speeches in the media, of which: on television – 284 (36.7%), on radio – 47 (6.1%), in newspapers and magazines – 214 (27.7%) and on websites - 228 (29.5%).

Conclusion. Regular visits of highly qualified specialists to the regions of the Republic of Uzbekistan contributes primarily to the good oncological awareness of the population, as well as to the increase of oncological alertness of primary care doctors.

WAYS TO IMPROVE DOCTORS SKILLS BY CARRYING OUT REGULAR VISITS TO THE REGIONS

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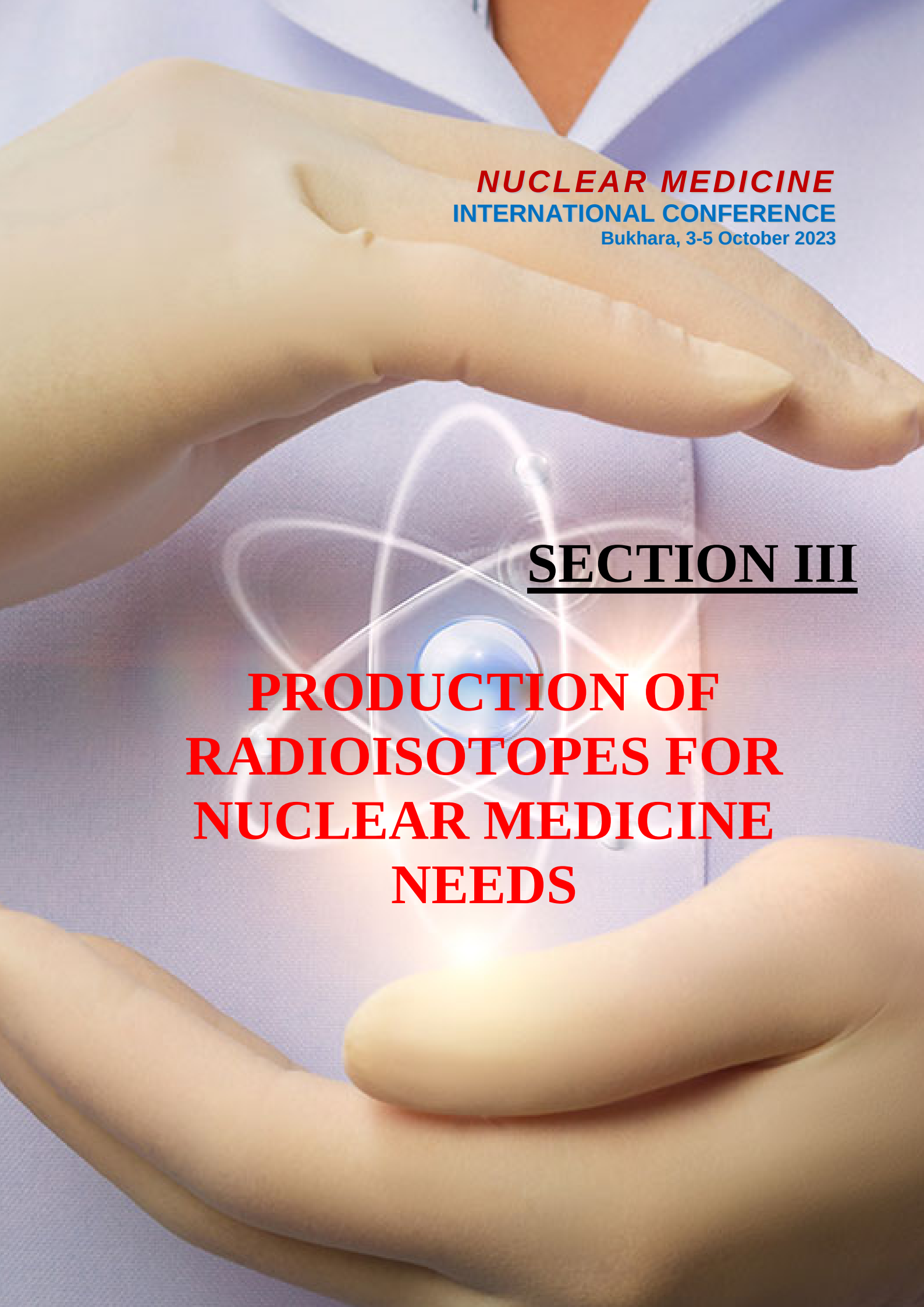
The purpose of the study. Professional development of oncologists by studing them in leading clinics of the world, exchange of experience with leading foreign specialists, conducting regular visits of mobile groups of highly qualified specialists to the regions of the country.

Materials and methods. According to the decree of the Government of the Republic of Uzbekistan, starting from 2017, the state allocates finance for professional development and exchange of experience of specialists both throughout the republic and abroad.

Results. Over the last 6 years, 780 specialists from various regions of the republic have improved their qualifications in the the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology: 130 (16.7%) specialists in 2017, 86 (11.0%) in 2018, 53 (6.8%) in 2019, 38 (4.9%) in 2020, 60 (7.7%) in 2021, 190 (24.4%) in 2022.) and 223 (28.6%) in 2023 specialists. Almost 400 highly qualified specialists from leading foreign clinics were invited to exchange experience and conduct master classes: 55 (14,1%) in 2017, 66 (16,9%) in 2018, 60 (15,4%) in 2019, 54 (13,8%) in 2020, 68 (17,4%) in 2021 and 87 (22.3%) in 2022. Moreover, it was noted that 232 young specialists of oncological institutions of the republic have completed advanced training courses in leading foreign medical clinics at the expense of the state budget: 41 (17.7%) specialists in 2017, 55 (23.7%) in 2018, 40 (17.2%) in 2019, 22 (9.5%) in 2021 and 74 (31.9%) in 2022.

Conclusion. As a result of the work carried out to improve the qualification of doctors and exchange experience, over the last few years, it was implemented modern and high-tech diagnostic and treatment methods, including immunohistochemical diagnostic methods, minimally invasive surgical interventions, radiation therapy methods (including stereotactic radiation therapy), immunotherapy, targeted therapy and others in the oncological service throughout the republic.



SECTION III

PRODUCTION OF RADIOISOTOPES FOR NUCLEAR MEDICINE NEEDS

RADIOCHEMICAL RESEARCH ON THE PRODUCTION OF RADIOISOTOPIC PRODUCTS AT INSTITUTE OF NUCLEAR PHYSICS OF UZBEKISTAN ACADEMY OF SCIENCES

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Radioactive isotopes are widely used in different spheres of science, technology and medicine. Radioactive isotopes are an effective and, in some cases, an irreplaceable tool in solving various scientific and industrial problems. In many countries of the world the problems of production and application of radioactive isotopes is given great attention [1]. At present the application of radioactive isotopes and other methods of nuclear technology at industry and medicine are more important than use of nuclear energy as a source of energy [2].

Currently, radioisotopes are obtained in nuclear reactors on nuclear reaction (n, gamma) constitute ~ 50% of the nomenclature and ~ 40% of total activity of all radioactive preparations. The advantage of nuclear reactors for production of radioactive isotopes provides the following opportunities:

- Long time irradiation;
- Ability to load big volume of target materials into the irradiation channels;
- Simultaneous irradiation of many and various targets.

For many years, the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan has been constantly working on the development and production of radioisotope products. Much attention is paid to obtaining finished products in the form of a radiopharmaceutical. The basic ones for obtaining radioisotope products at the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan are the radiochemical laboratory, the research nuclear reactor WWR-MS, the U-150 charged particle accelerator as well as “Radiopreparat” and “Tezlatgich” manufacturing enterprises.

The problems of production radioactive isotopes and many other problems of the nuclear science are bound up with decision radiochemical tasks and planning radiochemical investigations. The table below summarizes the main methods of radiochemical research and applied radiochemistry and their share of participation in total research worldwide.

Table. Basic methods of radiochemical investigations

Method	The share, %
Extraction	40-45
Ion exchange chromatography	20-22
Chromatography on inorganic sorbents	8-10
Extraction chromatography	8-10
Adsorption	3-5
Sublimation	3-5
Others	Less than 5

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PRODUCTION OF ^{44}Sc WITH ^{44}Ti/^{44}Sc GENERATOR FOR RADIOPHARMACEUTICAL PURPOSES

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Radionuclide ^{68}Ga (T½ = 67.71 min, β+ - 90%), derived from the ^{68}Ge/^{68}Ga radionuclide generator, has now become the most actively used of the metal radionuclides for the synthesis of radiopharmaceuticals (RPs) for PET. Nevertheless, a number of studies have shown that, in tandem with therapeutic radionuclides ^{177}Lu, ^{225}Ac, and ^{90}Y, it is preferable to use a diagnostic radionuclide with a longer half-life and similar physicochemical characteristics. This radionuclide is scandium-44. ^{44}Sc (T½ = 3.97 h, β+ - 94.3 %) is an actively investigated and promising radionuclide for PET-radiopharmaceuticals. ^{44}Sc can be produced in the cyclotron (^{44}Ca(p,n)^{44}Sc) or from a radionuclide generator (^{44}Ti/^{44}Sc). The cyclotron method is preferred, but in the absence of a cyclotron-radiochemical complex, the ^{44}Ti/^{44}Sc generator becomes a convenient (and, in fact, the only) alternative.

As part of the development of the ^{44}Sc-RPs concept, a ^{44}Ti/^{44}Sc generator (based on a solid-phase Aliquat-336 extractant) was developed at the Burnazyan FMBC to produce scandium-44 directly at the application site in the absence of a cyclotron. The generator prototype with a 50 MBq of ^{44}Ti activity (Ø2.1 mm ×150 mm column) demonstrated a high separation efficiency of ^{44}Ti and ^{44}Sc during one and a half years of active use (more than 200 elutions). The yield of ^{44}Sc in 1 mL of eluate (solution of 0.1 M oxalic acid in 0.2 M hydrochloric acid) was 89 ± 7 %. The breakthrough of ^{44}Ti did not exceed 1.7×10^{-6} % (with an average value of 6.3×10^{-7} %). The high concentration of oxalic acid in the generator eluate had a negative effect on the incorporation of ^{44}Sc into the structure of the vector molecules. Therefore, several additional eluate post-processing methods were considered.

The most efficient and convenient method of post-processing the generator eluate using strong cation-exchange (SCX) resins was found to produce solutions of scandium-44 in the medium of pharmaceutically acceptable sodium/ammonium acetate (0.75-1.0 mol/L, pH 4.5), which can be directly used in the synthesis of various tracers. A high ^{44}Sc desorption in sodium/ammonium acetate solution was found for DOWEX 50W×8 (Bio-rad), Chromafix HR-XC (MACHEREY-NAGEL), MP-50 (Bio-Rad), Bond Elut SCX (Agilent) and Chromabond PSA (MACHEREY-NAGEL) resins. The use of SCX in acetate buffer resulted in up to 80% of scandium-44 activity in 1 mL, giving more than 98% of radiochemical conversion when synthesized in the presence of 5 nmol of different DOTA/DOTAGA-conjugated precursors.

The possibility of using salts of other carboxylic acids (such as sodium succinate, sodium lactate, sodium pyruvate, sodium malate, sodium alpha-hydroxy-iso-butyrate, and sodium propionate) to desorb scandium-44 from SCX, as well as their influence on the incorporation of scandium-44 into the structure of vector molecules, were also studied.

Stability and functional suitability of scandium-44 preparations obtained using developed technology (e.g. [^{44}Sc]Sc-DOTAGA-PSMA-617) were evaluated in comparison with lutetium-177 and actinium-225 preparations.

This research was carried out within the state assignment and financial support of the Federal Medical Biological Agency of Russia (theme No. 122031100121-4, supervisor: A.Larenkov).

TERBIUM RADIOISOTOPES PRODUCTION FOR NUCLEAR MEDICINE APPLICATIONS

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Terbium radioisotopes with mass numbers 149, 152, 155 and 161 are of great interest for nuclear medicine due to a favorable combination of nuclear characteristics and the ability to form stable coordination compounds. The presence of several isotopes with different types of emitted radiation makes terbium a promising tool for theranostics. However, the production of terbium isotopes is associated with significant difficulties. The methods of production of all four isotopes were implemented in National Research Center "Kurchatov Institute". Alpha-emitter ^{149}Tb was obtained by irradiating ^{151}Eu targets with helium-3 ions at the U-150 cyclotron. Irradiation of the same targets with α-particles makes it possible to produce activities of the positron emitter ^{152}Tb sufficient for clinical use. For ^{155}Tb, a method was proposed for production via intermediate isolation of ^{155}Dy. This radionuclide can be obtained by irradiating ^{nat}Gd with α-particles. The use of enriched ^{155}Gd makes it possible to increase the radioisotope purity of the product. To obtain a β-emitter ^{161}Tb without a carrier, a traditional method was used - irradiation of ^{160}Gd with thermal neutrons in a reactor. To isolate terbium isotopes from irradiated targets, radiochemical procedures based on the application of extraction-chromatographic sorbents have been developed.

The work was supported by the Ministry of Science and Higher Education of the Russian Federation (grant agreement No. 075-15-2021-1360).

RADIOPHARMACEUTICALS PRODUCTION EXPERIENCE IN ACCORDANCE WITH GMP STANDARDS

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The Institute of Nuclear Physics of the Ministry of Energy of the Republic of Kazakhstan has been producing radioisotope products using its basic facilities, such as a nuclear research reactor WWR-K and U-150M, Cyclone-30 cyclotrons for more than 30 years and it is also the first manufacturer of radiopharmaceutical products in the Kazakhstan to introduce GMP standards into production practice.

The paper presents the experience in the production of radiopharmaceuticals with ^{131}I, ^{18}F isotopes and ^{99}Mo/^{99m}Tc generators based on (n, gamma) ^{99}Mo, as well as the advantages and disadvantages of production under GMP conditions.

PRODUCTION OF $^{68}GaCl_3$ FROM ENRICHED ^{68}Zn-TARGET IN MC-30 & FORMULATION OF [^{68}Ga]Ga-PSMA-11 & [^{68}Ga]Ga-DOTA-TATE RADIOPHARMACEUTICALS

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Gallium-68 ($t_{1/2}$ = 67.8 min, E_γ = 511 keV and 1077 keV) is a potential PET radioisotope having favourable properties for radiolabeling with various biomolecules like DOTA-TATE, PSMA-11, Exendin-4, CXCR4, FAPI etc. It is widely used as PET isotope mainly for prostate cancer and neuroendocrine tumors imaging. At present, the supply of ^{68}Ga for medical imaging is primarily based on the costly ^{68}Ge/^{68}Ga generator. The present trend is to produce ^{68}Ga directly from enriched ^{68}Zn. The aim of this work is direct production of ^{68}Ga from electroplated ^{68}Zn target via ^{68}Zn(p, n)^{68}Ga transformation in DAE MC-30, Kolkata. Enriched ^{68}Zn solid targets (approx.100µm thickness) were prepared by electrodeposition technique for production of ^{68}Ga. The enriched ^{68}Zn were irradiated with 15MeV proton beam in the MC-30 at 35-50 µA beam current for 30-60 minutes. After irradiation, the solid target mounted on a target carrier system (rabbit) was transported to the receiving hotcell from the irradiation station via an automated pneumatic transfer system without any manual intervention for further radiochemical processing. The ^{68}Ga was separated from the target, resulted in a very dilute HCl solution. All the operations were carried out remotely using the computer operated chemistry modules installed inside the processing hotcell. The $^{68}GaCl_3$ was labelled with PSMA-11& DOTA-TATE ligands to formulate [68Ga]Ga-PSMA-11 & [68Ga]Ga-DOTA-TATE radiopharmaceuticals. The Gallium-68 chloride was evaluated by performing physico-chemical test such as radionuclidic purity determination by HPGe detector to detect the radioactivity of 68/67Ga. The Radionuclidic purity of ^{68}Ga was found to be 99.90-99.99%. The co-produced ^{65}Zn was not detectable. The iron content was less than 3ppm. The Radio Chemical Purity of ^{68}Ga-PSMA-11& ^{68}Ga-DOTA-TATE were >98% and >95%, respectively.

RADIOCHEMISTRY FOR NUCLEAR MEDICINE AND LOW-BACKGROUND EXPERIMENTS

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Radioactive isotopes are used in many areas of science and industry, and their use in nuclear medicine occupies a special place. On the one hand, during the rare process studying the low-background materials with the level of radionuclide content of μBq/kg - mBq/kg are needed. On the other hand, radioactive preparations for nuclear medicine have specific activities of 10^{19} Bq/kg and higher.

Despite of huge difference in the values of specific activity, the tasks in these areas overlap in many ways. We deal with very long-lived radionuclides in low-background measurements, and in nuclear medicine with the short-lived ones. As a result, the separation task is the same - the separation of macroquantities of radionuclides from macroquantities (target, low-background material).

Our department successfully develops these two directions. First of all, chromatographic methods of separation are taken as a basis. The countercurrent method of supplying eluents and the reverse scheme of the radionuclide generators are actively used. The methods for the ultrapure salts preparation are being developed, including salts used as basis for eluting solutions. Highly efficient sorbent-solution systems for elements separation, pure reagents and chemical vessel materials are being sought.

The report reveals the above topics on the examples of the radionuclide generators based on reverse-tandem schemes (^{68}Ge→^{68}Ga, ^{44}Ti→^{44}Sc, ^{172}Hf→^{172}Lu) and the production of low-background materials (^{82}Se).

THE USE OF CHITOSAN SORBENTS FOR OBTAINING Cs-131 BIOPOLYMER GRANULES FOR NUCLEAR MEDICINE

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The radionuclides ^{125}I ($T_{1/2}$=60 d; E_γ=28 keV), ^{103}Pd ($T_{1/2}$=17 d; E_γ=21 keV) and ^{131}Cs ($T_{1/2}$=9.8 d, E_γ=31 keV) have been successfully used in modern brachytherapy of the Germany, Israel and USA, respectively. But nuclear medicine experts from American company "IsoRayMedical" (www.isoray.com) have given their preference to ^{131}Cs than to ^{125}I and ^{103}Pd, because of its shorter half-life and higher X- ray energy. One of radionuclides will be fixed into titanium capsules for implanting into tumor body. The X-rays of radionuclide effectively destroyed cancer cells, while undamaging nearby healthy tissue and thereby reducing negative side effects. The implementation and application of the ^{131}Cs radionuclides in titanium capsules are related with some technical difficulties and unavailability of high-tech equipment in our conditions.

The aim of this study was to elaboration the obtaining technique of the ^{131}Cs and to creation the spherical biopolymer X-emitters on the base of ^{131}Cs radionuclide and chitosan sorbent.

The ^{131}Cs is a daughter radionuclide of the ^{131}Ba parent radionuclide, which produced through the $^{130}Ba(n, \gamma)^{131}Ba$ reaction, after irradiation 140 hour 3 gr of the BaO at the nuclear reactor WWR-SM of INP of AS RUz . To selection of the Cs-131 from huge radioactive barium solution there were elaborated the radiochemical method of separation of the ^{131}Cs under microwave radiation.

The chitosan and its derivatives are used widely in nuclear medicine and pharmaceutical industry because of its following properties: biodegradable, biocompatible, acceleration of wound healing, reduction of blood cholesterol level and inhibition of tumor cells. The sorption efficiency of chitosan solution to ions of ^{131}Cs was studied without modified additives originally. The results of tests as show the maximal values of sorption of the ^{131}Cs ions by chitosan sorbent without modification did not exceed 36%. To increase sorption efficiency, the chitosan solution has been modified by additives of potassium ferrocyanide and chlorides of transitive metals. The used chitosan – has been synthesized from cocoons of a silkworm and was presented by a Research Center of Chemistry and Physics of Polymers of National University of Uzbekistan. On basis of the $^{131}CsCl$ ions and chitosan sorbent with modify additives there were created the X-ray biopolymer granules that having biocompatible and biodegradable properties. For creation X-ray granules were elaborated a double-layer bath technique with xylene and alkali solution. The angular distribution of dose activity of the granules was measured in the air, water and the biological tissue by using universal dosimeter FH-40LG Eberline. The results of measurements showed that the angular distribution γ-rays from granules were distributed identical in all directions. The received granules have been crosslinking with glutar-aldehyde solution for forming hardness and hermetic spheres. The diameters and radioactivity of the granules can be regulated within 0.5±0.05 – 1.0±0.1 mm and $(0.74–2.22)\cdot10^8$ Bq/granule respectively.

PREPARATION AND STUDY OF THE STABILITY OF THE PHARMACEUTICAL COMPOSITION [PSMA-617] AND THE RADIOPHARMACEUTICAL [^{177}Lu]-PSMA-617 FOR THE TREATMENT OF PROSTATE CANCER

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Today, one of the most common types of malignant diseases in men and the fifth leading cause of death from cancer worldwide is prostate cancer [1]. According to the GLOBOCAN 2020 estimate, more than 1.4 million patients were diagnosed with prostate cancer in 2020, resulting in 375,304 associated deaths worldwide [2]. To reduce the mortality rate of patients with prostate cancer, early screening and diagnosis is necessary, followed by therapy with radiopharmaceuticals specific to prostate tumor cells. Among such promising preparations are [^{177}Lu]-PSMA-617, labeled with the radionuclide lutetium-177, without a carrier [3]. The successful use of radiopharmaceutical [^{177}Lu]-PSMA-617 in the clinical treatment of prostate cancer with encouraging therapeutic efficacy is shown by the results [1, 4-7].

This work is devoted to the study of the conditions for the synthesis of a pharmaceutical composition (PhC) [PSMA-617] with optimization of the amount of the PSMA-617 ligand peptide and the substance «Lutetium chloride (^{177}LuCI$_3$) with ^{177}Lu, carrier free» with a specific activity close to the theoretical production of the State Enterprise «Radiopreparat» and pH of the reaction mixture for obtaining radiopharmaceuticals «[^{177}Lu]-PSMA-617, labeled with lutetium-177, carrier free». The amount of the PSMA-617 ligand peptide varied from 10 to 100 μg, and ascorbic acid 50-55 mg/ml was used as a buffering agent and antioxidant.

The results of the studies showed that during the synthesis of the radiopharmaceutical «[^{177}Lu]-PSMA-617 labeled with lutetium-177, carrier free» containing the PSMA-617 ligand peptide 48 nmol, the amount of the added ^{177}Lu radionuclide should not exceed 300 mCi, where the radiochemical purity is ≥ 98.7±0.3%.

The study of the stability of PhC [PSMA-617] was carried out by synthesizing the radiopharmaceutical «[^{177}Lu]-PSMA-617 labeled with lutetium-177, carrier free» from stored PhC [PSMA-617] with storage conditions of 3-5 ^{0}C from 1 to 6 months. The results of the studies showed that after 1 month of storage of PhC [PSMA-617] RCP was 99.6%, and after 6 months it was above 97.5% and did not decrease by more than 2.0%, which is outside the requirements of Ph.

A research of the stability of the radiopharmaceutical «[^{177}Lu]-PSMA-617 labeled with lutetium-177, carrier free» synthesized from PhC [PSMA-617] for 7 days both in physiological NaCI solution and in human serum under normal conditions showed that the radiochemical the purity of the radiopharmaceutical «[^{177}Lu]-PSMA-617, labeled with lutetium-177, carrier free» decreased to 95%.

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EVALUATION OF CLINICAL-DOSIMETRIC AND PHARMACOKINETIC PROPERTIES OF THE RADIOPHARMACEUTICAL PREPARATION “SAMARIUM, ^{153}Sm OXABIFOR” IN THE TREATMENT OF BONE METASTASES

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At present in Uzbekistan much attention is paid to the development of experimental research on obtaining radionuclides and radiopharmaceuticals for their use for diagnostic and therapeutic purposes in oncology clinics. Among such radiopharmaceuticals is "Samarium, ^{153}Sm oxabifor", which is successfully used in specialized clinics of the Republic of Uzbekistan as a therapeutic agent for the treatment of cancer patients with bone metastases. The necessity of development of technologies for production of radionuclide ^{153}Sm in Uzbekistan is conditioned by the fact that with the development of technology and improvement of domestic radiotherapeutic techniques of the Republic, the need to improve the quality of drug standards laid down in foreign certified pharmacopeial description becomes obvious. In radionuclide therapy the problem of clinical dosimetry is inseparably connected with pharmacokinetics, since the peculiarities of distribution, accumulation and excretion of radionuclides have on the formation of absorbed doses not less, and sometimes even more influence than their nuclear-physical properties.

"Samarium, ^{153}Sm oxabifor", as well as other osteotropic drugs, most intensively accumulates in metastatic foci, areas of inflammation, places of former fractures. After intravenous administration, in bone tissue is usually fixed from 50 to 80% (in rare cases - up to 90%) of the drug entered into the body. The therapeutic effect of samarium oxabifor, ^{153}Sm is determined by its β-radiation. To determine the clinical-dosimetric and pharmacokinetic properties of the drug, dosimetric control and skeletal bone scanning were performed immediately after drug administration (6 and 24 hours later). The results of this work have been implemented in production at SE "Radiopreparat" of Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan as the form of technology for production of radiopharmaceutical preparation "Samarium, ^{153}Sm oxabifor». At present time products, manufactured by this technology, are successfully used in medical clinics of the Republic of Uzbekistan and supplied to foreign clinics.

EXPERIENCE IN THE PRODUCTION OF ^{18}F-PSMA AT THE INSTITUTE OF NUCLEAR PHYSICS

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Fluoro-PSMA (^{18}F-PSMA) is a radiopharmaceutical that is an inhibitor of prostate-specific membrane antigen (PSMA) and is used in the diagnosis of prostate tumors. ^{18}F-PSMA is characterized by less urinary excretion (compared to other PSMA-targeted tracers), and therefore better visualization of the prostate.

Experiments are being carried out at the Institute of Nuclear Physics to obtain ^{18}F-PSMA using the IBA Synthera+ synthesis module. For the production of the ^{18}F isotope by the reaction ^{18}O(p,n)^{18}F, the IBA Cyclone 30 cyclotron is used.

The paper presents the results of experiments on the production and quality control of ^{18}F-PSMA. During the experiments, three experimental series of ^{18}F-PSMA were obtained.

ORGANIZATION OF QUALITY CONTROL IN THE PRODUCTION OF RADIOPHARMACEUTICAL IN GMP CONDITIONS

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The paper presents the experience of organizing quality control in the production of radiopharmaceuticals at the Institute of Nuclear Physics of the Ministry of Energy of the Republic of Kazakhstan.

The production site currently produces the following radiopharmaceuticals:

- "Fluorodeoxyglucose ^{18}F, solution for injection";
- “Sodium pertechnetate ^{99m}Tc, solution for injection” from ^{99}Mo/^{99m}Tc generator;
- "Sodium iodide ^{131}I, oral solution".

Quality control includes: incoming quality control of initial and packaging materials; technological control; quality control of the finished product.

Particular attention is paid to equipment qualification, validation and verification of analytical methods.

ALPHA-PARTICLE INDUCED REACTIONS AS ROUTES FOR PERSPECTIVE MEDICAL RADIONUCLIDES ^{169}Yb, ^{167}Tm, ^{165,160}Er, ^{161}Ho, ^{140}Nd PRODUCTION

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New advances in targeted drug delivery expand the range of radionuclides used in nuclear medicine, in particular for theranostic approach and Auger electron therapy. New radiopharmaceuticals require well-studied methods for producing radionuclides without a carrier.

This work is devoted to medically relevant rare earth radionuclides production in reactions induced by alpha-particles. They were studied by activation stacked foils with thin layers of $^{141}Pr_8O_{11}$, $^{nat}Er_2O_3$, $^{nat}Dy_2O_3$, $^{165}Ho_2O_3$. Reactions' products were determined by gamma-spectrometry and cross sections were found. Yields calculations allowed to consider reactions as a method of medical nuclides production in comparison with other routes.

All of studied nuclides (Table 1) decay by electronic capture and are considered as agents for Auger electron therapy. Some of the nuclides are already or have been used in medicine but in different types of diagnostics.

Alpha-particle induced reactions are less often considered as a way to produce medical isotopes. However, in some cases, such reactions make it possible to obtain isotopes indirectly, for example, ^{nat}Dy(α,x) ^{161}Er→^{161}Ho and ^{165}Ho(α,4n)^{165}Tm→^{165}Er. Two-stage chemical isolation with indirect production increase the radiochemical purity of the final product.

Table 1. Medical rare earth nuclides, studied production routes and their possible applications in medicine

Nuclide, $T_{1/2}$	Studied production routes	Possible applications
^{140}Nd 3.37 d	^{141}Pr(α,5n)^{140}Pm→^{140}Nd	Auger therapy, *in vivo* generator ^{140}Pr for long term PET.
^{160}Er 28.58 h	^{nat}Dy(α,x)^{160}Er	Auger therapy.
^{161}Ho 2.48 h	^{nat}Dy(α,x) ^{161}Er→^{161}Ho	Auger therapy.
^{165}Er 10.36 h	^{165}Ho(α,4n)^{165}Tm→^{165}Er ^{nat}Er(α,x)^{165}Yb→^{165}Tm→^{165}Er	Auger therapy, diagnostics by multiwire proportional cameras.
^{167}Tm 9.25 d	^{165}Ho(α,2n)^{167}Tm ^{nat}Er(α,x)^{167}Yb→^{167}Tm	Auger therapy, SPECT.
^{169}Yb 32.018 d	^{nat}Er(α,x)^{169}Yb	Auger therapy, brachytherapy.

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METHOD FOR REGENERATION OF YTTERBIUM ENRICHED IN YTTERBIUM-176 FROM WASTE SOLUTIONS OF IRRADIATED SAMPLES OF YTTERBIUM-176

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Today, the modern developed oncological direction without radionuclide therapy, where radioactive pharmaceutical preparations (RP) are used for targeted, i.e. targeted effect on tumor tissues. The main active ingredients of these preparations are radionuclides with certain nuclear-physical characteristics.

One of the promising radionuclides in recent years in targeted radionuclide therapy is the lutetium-177 radionuclide with high specific activity, which has optimal nuclear physical characteristics with an average half-life ($T_{1/2}$ = 6.7 days) and an acceptable energy of β-particles (maximum 0.5 MeV), which allows you to destroy small tumors and metastases without affecting healthy tissues, as well as soft accompanying γ-radiation with sufficient energy for imaging. To date, in world practice, the lutetium-177 radionuclide with a high specific activity close to theoretical is obtained by irradiating ytterbium targets enriched (with an enrichment degree >96%) with a stable isotope of ytterbium-176.

As a rule, the cost of highly enriched stable isotopes is very high. In addition, the availability of highly enriched stable isotopes is not always possible. In this regard, when obtaining the ^{177}Lu radionuclide carrier free by irradiating neutrons from a nuclear reactor enriched in ^{176}Yb, it is very important to develop a technology for the regeneration of ^{176}Yb from spent irradiated targets, in which the loss of the raw material-target ^{176}Yb was minimal.

In this work, a procedure is presented for the recovery of gram quantities of ytterbium enriched in the yttebium-176 isotope in the form of chloride with a high radiochemical yield while ensuring high chemical purity.

The technology of regeneration of spent irradiated samples of ytterbium-176 consists in collecting the accumulated spent solutions of irradiated ytterbium-176 after carrying out cycles of extraction of the lutetium radionuclide: acetic acid solution of amalgam-ytterbium-176, solutions of the fraction with ^{176}Yb-α-HIBA, after isolating the target fractions of the radionuclide ^{177}Lu , acidified with HCI solution to pH=2,5.

Then, the acidified solution was passed through a chromatographic column filled with D-2-EHPA/fluoroplast-4 solid extractant in a ratio of 1:2; the chromatographic column was washed with three column volumes at the same rate with a diluted HCI solution. After that, ^{176}Yb was eluted from the chromatographic column with a 6.0 M HCI solution at a rate of 2.0 ml/min from bottom to top, and the resulting ^{176}Yb solution was evaporated to a dry residue on a rotary evaporator at a temperature of 80 ^{0}C. The dry residue was calcined in a muffle furnace to decompose ytterbium (III) crystalline hydrate. As a result, ^{176}Yb in the form of chloride with a chemical yield of more than 97% was obtained.

SEPARATION OF GERMANIUM-68 RADIONUCLIDE FROM GALLIUM CYCLOTRON TARGET

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^{68}Ge-^{68}Ga generator system is widely used in positron emission tomography (PET). Radionuclide ^{68}Ge ($T_{1/2}$=271 d) decays to ^{68}Ga ($T_{1/2}$=68.1 min) by electron capture, and ^{68}Ga emits positrons with a branching ratio of 90% and weak γ-rays. The short-lived radionuclide ^{68}Ga (half-life of 68 minutes) is useful in a variety of biomedical applications, e.g., in bone imaging and soft-tissue tumor imaging. The parent radionuclide ^{68}Ge is used as sealed source to calibrate PET systems.

The large-scale production of ^{68}Ge (100-1000 mCi) is currently limited to proton accelerators of high current such as the BNL 200-MeV LINAC (BLIP facility) and the LANL 800-MeV LAMPF. The BLIP facility makes use of the ^{69}Ga(p,2n) reaction with a metallic gallium target of natural abundance. In this case the use of natural Ga targets contained in an electron beam welded Nb capsule is the most favorable target material. Typical irradiation yields are 470 mCi from a 4 week irradiation. At LAMPF, ^{68}Ge is produced by proton spallation of a RbBr target with an effective cross section of ~20mb. In this case the typical yield is on the order of 1 Ci per run.

The Germanium-68 can be produced with both ^{66}Zn(α,2n)^{68}Ge and ^{69}Ga(p,2n) ^{68}Ge nuclear reactions in small cyclotrons. Several target materials based on natural gallium compounds have been proposed. Irradiation of gallium as oxide Ga_2O_3 prohibits the use of high particle currents since absorbed energy dissipation is inadequate and such targets deteriorate. The use of binary alloys of Ga-Ag, Ga-Cu and especially Ga-Ni is the most favorable technical approach to decide the problem of production of germanium-68 in classical cyclotron.[5-7] In this case the typical yield is in the range of tens of mCi per run.

After dissolution of the target ^{68}Ge can be separated from target gallium by distillation, chromatography or solvent extraction. The solvent extraction using carbon tetrachloride is one of the most widely used methods for ^{68}Ge separation. However this process requires several steps and application of special equipment for separation of ^{68}Ge. On the contrary radiochemical separation by extraction chromatography method permits ^{68}Ge radionuclide to be separated from target in one step with using only one chromatographic column. It should be noted that the extraction chromatography method at the same time enables a deep purification and separation of the desired radionuclide to be accomplished from macroamounts of the starting elements of the target(Ga, Zn) and radionuclides which formed as a result of nuclear reactions (α,xn; p,xn).

In the present report the method using the extraction chromatography method was developed for separation of carrier-free ^{68}Ge from a proton bombarded gallium cyclotron target. The extraction of carrier-free ^{68}Ge from the mixed solutions of HCl + H_2SO_4 and HCl + HNO_3 by benzene, toluene, xylene and carbon tetrachloride was studied. The extraction-chromatographic method for separation of carrier-free ^{68}Ge from a proton bombarded gallium-nickel cyclotron target was developed.

UTILIZATION OF THE REVERSE-TANDEM SCHEME OF THE RADIONUCLIDE GENERATOR FOR PRODUCTION OF ^{90}Y

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The use of radionuclides with different emitting types with the same targeting vectors is known as theranostics. In theranostics concept the radionuclides of the same element (^{131}I/^{124,122}I, ^{67}Cu/^{62}Cu, ^{47}Sc/^{44}Sc) or analogous elements ((^{225}Ac, ^{177}Lu, ^{90}Y)/(^{111}In, ^{68}Ga, ^{44}Sc)) are used. Yttrium has two isotopes suitable for this concept. The diagnostic component ^{86}Y ($T_{1/2}$ = 14.74 h) is used for therapy planning and for evaluation the biodistribution of radiopharmaceuticals with ^{90}Y [1, 2]. The therapeutic component of the pair ^{90}Y is obtained mainly through the radionuclide generator ^{90}Sr ($T_{1/2}$=28.91 y) → ^{90}Y. There are several schemes of the radionuclide generator ^{90}Sr→^{90}Y based on electrochemical separation [3], supported liquid membrane (SLM) technique [4], ion exchange [5] and extraction chromatography [6].

In this study, a scheme of the radionuclide generator ^{90}Sr→^{90}Y with a reverse elution scheme is proposed. The scheme is based on cation exchange resin Dowex 50×8 and solution of 0.1 M CH_3COOH / 0.5 M CH_3COONH_4. The generator resulted a high yield of the daughter radionuclide ^{90}Y ~ 70% with content of ^{90}Sr < $4\cdot10^{-3}$%. To develop the generator, the distribution coefficients K_d of the Sr(II) and Y(III) pair were determined in the system of ion exchange resins Dowex 50×8 and Dowex 1×8 - a mixture of acetic acid and ammonium acetate.

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CONTROL AND CALIBRATION RADIONUCLIDE SOURCES FOR NUCLEAR MEDICINE

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Ionizing radiation is actively used in medicine for both diagnosis and therapy. Currently, nuclear medicine has stepped quite far and there is a huge list of various kinds of devices related to the use and measurement of ionizing radiation. Diagnostics is extremely important in medicine. Recently, instrumentation in the field of Nuclear Medicine has been rapidly developing. PET/CT and SPECT/CT tomographic diagnostics are spreading all over the world. A prerequisite for the high–quality operation of this equipment is calibration and periodic (daily) monitoring. For these purposes, specially designed radionuclide sources on Na-22, Co-57, Ge-68 are used. Noteworthy are the shape and materials from which these sources (phantoms) are made due to the specifics of their application.

A wide range of radiopharmaceuticals (RFP) is used for the treatment of oncological diseases. Dose calibrators are used to measure the activity of RFP before injection to patients. As well as diagnostic equipment, this technique requires monitoring and calibration. Specially developed sources based on Co-57, Co-60, Ba-133 and Cs-137 radionuclides allow calibration across the entire energy spectrum, which, in turn, will allow high-quality measurements of the activity of various radionuclides used in nuclear medicine.

This presentation provides a range of products, control, calibration and reference sources that provide high-quality measurements for Nuclear Medicine and their features due to the specifics of the application.

FEATURES AND PRACTICAL ASPECTS OF RADIOCHEMICAL PURITY DETERMINATION OF THERAPEUTIC RADIOPHARMACEUTICALS

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Receptor-specific radionuclide therapy directed against primary cancer as well as distant metastases is now recognized as an effective and reasonable method of treatment for various oncological diseases. Among the already used and actively developed therapeutic radiopharmaceuticals (RPs), the vast majority are based on β-emitting rare earth element (REE) radionuclides: ^{47}Sc, ^{90}Y, ^{149}/^{164}Tb, ^{153}Sm, ^{159}Gd, ^{166}Ho, ^{169}Er, $^{170/172}$Tm, ^{175}Yb, ^{177}Lu, etc. (and for some of them, there are true theranostic pairs–$^{43/44}$Sc, ^{86}Y, $^{152/155}$Tb, ^{167}Tm - for radionuclide diagnostics). A critical point in both the development and production of such RPs is the reliable control of the presence of radiochemical impurities, with the content of unbound radionuclides being the highest. This is caused by higher requirements to radiochemical purity (RCP) of therapeutic preparations in comparison with diagnostic preparations.

Radiochemical purity is one of the main criteria for the quality of RPs used in clinical practice. The choice and routine use of a particular method of RCP analysis in the quality control of RPs in a healthcare organization is entirely left to that organization. However, measurements performed as part of quality control are often based on detection parameters specific to a particular analytical system. When analyzing literature data on the synthesis, pharmaceutical development, preclinical and clinical studies of the same RPs by different groups of researchers, it is possible to pay attention to the significant differences in the presented results of the determination of the RCH value. The difficulty in comparing the results is primarily owing to the choice of different analysis methods. Often, the analysis performed by a single, even pharmacopoeial method, may indicate a high RCP of the RP and its suitability for clinical use, while analysis by a more precise and detailed method will establish that the actual RCP is below any permissible limits.

In this work, the chromatographic behavior of clinically used radionuclides ^{44}Sc, ^{90}Y, ^{153}Sm, ^{177}Lu, as well as ^{88}Y, ^{152}Eu, ^{166m}Ho, ^{170}Tm (as model radionuclides), and their complexes with vector molecules PSMA-617/I&T and DOTA-TOC/TATE/NOC were investigated in order to determine suitable chromatographic separation parameters for radiochemical purity analysis. The study was carried out using radio-THC and radio-HPLC methods with different combinations of eluents and stationary phases. The influence of the method and analysis parameters on the detection efficiency of various radiochemical impurities (unbound forms of radionuclides, products of thermolysis, and radiolysis of the vector molecule), and the determination of RCP in general were demonstrated. Among the various investigated systems for the analysis of these RPs, the TLC system using SG/Cellulose-plates on an aluminum support and MeCN:H2O mixture (1:1) as a solvent should be especially emphasized. In this system, the retention factor (Rf) of the ionic form was 0. For complexes of radionuclides with DOTA-TATE, PSMA-617/I&T molecules for all the mentioned REE radionuclides Rf was 0.3-0.4; 0.7-0.8 and 0.75-0.85, respectively (with FWHM, which allows to achieve a tap of high resolution (> 4σ) in a short time (8-10 min)).

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RESULTS OF THE DEVELOPMENT AND APPLICATION OF A CLUSTER OF METHODS FOR ESTIMATIONS THE DOSES OF INTERNAL EXPOSURE TO FOCI AND ORGANS AT RISK IN PRECLINICAL/CLINICAL TRIALS OF RADIOPHARMACEUTICALS

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The cluster of specialized software tools and digital data bases was developed, registered on the State level, and implemented for estimating the doses of internal exposure to foci and organs at risk during preclinical/clinical trials of radiopharmaceuticals. The software tools and corresponding dosimetric and nuclear physical data bases make it possible to estimate the absorbed doses of internal irradiation normalized to the accumulated radiopharmaceuticals' activity (Gy/(MBq×h) in foci and organs of the human body and/or experimental animals. Mathematical phantoms of human and various laboratory animals with different body weights, organs and tissues, as well as data on the spectra of corpuscular and quantum radiation of various radionuclides (more than 300 radionuclides - at the user's choice) are using for internal radiation dose estimations. A special software allows to perform dose estimations for biostructures with non-standard shapes (for example, tumors, microstructures of organs etc). The cluster of methods developed was used for determination of individual doses of internal irradiation of foci and organs of risk during clinical trials of the following therapeutic radiopharmaceuticals: a) ^{177}Lu-DOTA-PSMA for radioligand therapy of metastatic castrate-resistant prostate cancer; b)^{188}Re albumin microspheres 5-10 μm for radiosynovectomy in the local treatment of chronic inflammatory diseases of the joints, c)^{188}Re albumin microspheres 20-40 μm for intra-arterial radionuclide embolization in the treatment of inoperable liver cancer. The results of determination of radiopharmaceuticals' absolute activities in the body of patients during dynamic SPECT/CT scanning were verified by measurements using physical phantoms of humans with different body weights and with various standard activities of radionuclides distributed inside the phantoms. It has been established that internal radiation doses increase with an increase in the administered radiopharmaceuticals' activity, however, with the same administered activity, the doses of internal irradiation of foci decrease significantly with an increase in the volumes of foci. This means that radionuclide therapy must be planned individually, based not on the preliminary determined standard activity of radiopharmaceuticals (in GBq), but on the basis of the doses of internal irradiation of foci (in Gy). Individual absorbed doses in organs at risk also vary greatly between different patients and between different critical organs. It was found that doses of internal irradiation of organs at risk are many times less than "commonly applied dose constraints" in radiotherapy.

DEVELOPMENT OF THE COMPOSITION OF SUPPOSITORIES BASED ON CLARY SAGE

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Abstract. Suppositories occupy an important place among the dosage forms, and recently there has been an increase in the interest of clinicians in their use. The use of suppositories can reduce the level of allergic reactions, prolong the therapeutic effect, especially in the focus of inflammation, increase the rate of absorption of the drug and in some cases reduce the dose.

Materials and methods. Vaginal suppositories are often used in the treatment of inflammatory gynecological diseases. Intravaginal administration of medicines in the treatment of bacterial, fungal, trichomonas, chlamydia, viral and other mixed urogenital infections provides a direct effect on the focus of the inflammatory process. The main attention in the treatment of gynecological inflammatory diseases is paid to the widespread use of antimicrobials.

Results. The Department of Pharmacology and Clinical Pharmacology of the Bukhara State Medical Institute has developed a technology for obtaining a thick extract of clary sage (TECS). Pharmacological and microbiological studies have proven its high antimicrobial activity, the presence of pronounced anti-inflammatory and reparative properties. This paper reports the results of experimental studies on the development of the composition of suppositories, where this substance is recommended as an active pharmaceutical ingredient. To justify the choice of a carrier for vaginal suppositories, suppositories were made on hydrophobic and hydrophilic bases – a mixture of PEO, cocoa butter and solid fat. Suppositories were prepared by generally accepted technological methods and in appearance and pharmacotechnological parameters met the requirements of the GF. Studies on the antimicrobial activity of samples of suppositories with TECS were carried out by the method of diffusion into agar, which is generally accepted in microbiological practice. The results of a microbiological study show that the greatest antimicrobial activity is observed in suppositories prepared on the basis of PEO-1500:PEO-400 in a ratio of 9:1. The developed composition exhibits pronounced antimicrobial activity in relation to strains of Staphylococcus aureus and Bacillus subtilis. Taking into account the data obtained, it was necessary to conduct biopharmaceutical studies for the final selection of the rational composition of the carrier of vaginal suppositories with TECS, since the processes of release and distribution of active substances can significantly depend on pharmaceutical factors, among which the influence of the carrier base is important. To study the ability of the suppository base to release TECS, experiments were conducted in vitro by diffusion into an agar gel based on the formation of a colored zone, which appears as a result of the interaction of the active substance (flavonoids) with a reagent 1% solution of iron (III) chloride.

Conclusion. Analyzing the results obtained, it is possible to draw conclusions about the advantage of a polyethylene oxide base. The difference in the release of phenolic compounds with the studied lipophilic bases: solid fat and cocoa butter is insignificant. As a comparison drug, suppositories with propolis on a polyethylene oxide basis, manufactured by Apipol-Farma (Poland), were used. Thus, it is shown that a mixture of polyethylene oxide bases is a rational carrier of a thick extract of nutmeg sage in the form of suppositories.

DEVELOPMENT OF A TECHNOLOGY FOR OBTAINING A SUBSTANCE BASED ON THE LIGAND POTASSIUM-SODIUM SALT OF 1-HYDROETHYLENEDIPHOSPHONIC ACID WITH DIVALENT TIN, FOR THE PREPARATION DIAGNOSTIC KIT OF GENERATOR TECHNETIUM-99m

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The problem of timely and accurate diagnosis has been and remains one of the main problems of clinical medicine. To solve this problem, a symbiosis of natural and exact sciences is used, such as radionuclide diagnostics or diagnostic nuclear medicine. Modern nuclear medicine is characterized by a multitude of diagnostic and therapeutic methods that objectively provide the physician with unique, alternative-free possibilities. In nuclear medicine, one of the most demanded diagnostics is the diagnosis of skeletal diseases. To diagnose these diseases, the most sensitive and specific method is scintigraphy with osteotropic radiopharmaceuticals. The method is based on the introduction into the patient's body of a radiopharmaceutical tropic to bone tissue, with subsequent registration of its distribution and accumulation in the skeleton. Bisphosphonates occupy a special place among such compounds, which are used in the detection and therapy of any skeletal pathology. Bisphosphonates have a high affinity for bone hydroxyapatite crystals, which makes it possible to obtain the most information from the investigated area of the human body [1-5].

This work is devoted to the study of the formation of the complex of potassium-sodium salt of 1-hydroethylenediphosphonic acid (HEDP) with the radionuclide technetium-99m (HEDP ^{99m}Tc), by selecting the optimal ratios of the basic substance - potassium-sodium salt of 1-hydroethylenediphosphonic acid and reducing agent - divalent tin (Sn^{2+}) in solution with different pH. Also in this work the kinetics of formation of complex (HEDP ^{99m}Tc) - potassium-sodium salt of 1-hydroethylenediphosphonic acid (HEDP) with radionuclide technetium-99m and shelf life of HEDP(Sn) were studied.

The efficiency of formation of stable HEDP^{99m}Tc complex in substances with Sn^{2+} 0.3 mg/mL and HEDP 2.5 mg/mL and solution pH 5.0±0.1 after 20 minutes after addition of radioactive $^{99m}TcO_4^-$ to the substance was determined, and it was more than 99.5 %. The stability of the HEDP (Sn) substance stored from 1 to 12 months by obtaining HEDP^{99m}Tc - radiopharmaceutical was determined, and it was 12 months.

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A METHOD OF OBTAINING A SUBSTANCE BASED ON A LIGAND OF METHYLENE DIPHOSPHONIC ACID (MDP) WITH DIVALENT TIN FOR THE PREPARATION DIAGNOSTIC KIT TO GENERATOR TECHNETIUM-99m

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In nuclear medicine, one of the most requested diagnostics is the diagnosis of skeletal diseases. It should be noted that metastatic lesions of the skeleton are detected in more than 60% of patients with breast, lung, prostate, and colon cancer. For the diagnosis of these diseases, the most sensitive and specific method is scintigraphy with osteotropic radiopharmaceuticals. The method is based on the introduction into the patient's body of a tropic radiopharmaceutical, to bone tissue, and its subsequent registration during distribution and accumulation in the skeleton. Among these compounds, a special place is occupied by bisphosphonates used in the detection and treatment of any pathology of the skeleton.

After the discovery of Tc-99m-labeled polyphosphate for bone imaging in 1971, a number of pyrophosphate- and biphosphonate-labeled Tc-99m compounds were introduced for bone imaging by G. Subramanian and others [1-4]. The agents that have received the widest clinical application include complexes of polyphosphate, hydroxyethylidene diphosphonate (HEDP) and methylenediphosphonate with Tc-99m.

This work is devoted to the study of the formation of complex ($MDP^{99m}Tc$) - methylenediphosphonic acid (MDP) with technetium-99m radionuclide by selecting the optimal ratios of the basic substance methylenediphosphonic acid and reducing agent divalent tin (Sn^{2+}), in solution with different pH, as well as studying the kinetics of complex formation ($MDP^{99m}Tc$) - methylenediphosphonic acid (MDP) with technetium-99m radionuclide, and storage time of MDP(Sn) substance.

As a result, the optimal ratios of the active ingredient methylenediphosphonic acid (ligand) and reducing agent divalent tin (Sn^{2+}) in the preparation of the substance MDP(Sn) were determined by obtaining the radiopharmaceutical preparation MDP ^{99m}Tc, used in medical practice for the detection of bone metastases. The effects of the concentration of the reducing agent Sn^{2+} and ligand complexing agent on the complex formation efficiency of MDP ^{99m}Tc in solutions at 0.8-1.15 mg/mL and 7.0-12.0 mg/mL, respectively, and pH of the medium 4.0-7.0 were studied.

The efficiency of formation of stable complex of MDP ^{99m}Tc in substances with Sn^{2+} 0.95 mg/mL and MDP 10.0 mg/mL and pH of solution 6.0±0.1 after 20 minutes after addition of radioactive $^{99м}TcO_4^-$ to the substance was determined, it was more than 99.5 %. The stability of MDP(Sn) substance stored for 1 to 12 months was determined by obtaining MDP ^{99m}Tc radiopharmaceutical, which was 12 months.

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PREPARATION AND STUDY OF THE STABILITY OF THE PHARMACEUTICAL COMPOSITION [PSMA-11] AND THE RADIOPHARMACEUTICAL «[^{99m}Tc]-PSMA-11 LABELED WITH THE RADIONUCLIDE ^{99m}Tc» FOR THE DIAGNOSIS OF PROSTATE CANCER

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In recent years, the most common malignant tumors among men is prostate cancer, which on average accounts for 20% of all cases of malignant neoplasms [1]. In this regard, for early and precise detection of these diseases in modern nuclear medicine, positron emission tomography (PET) with targeted prostate-specific membrane antigen (PSMA) has become an essential part of the work of this field. However, in many countries, access patients requiring PET examinations is often limited, either due to the high cost of PET procedures or due to limited availability of the country's nuclear centers. In this regard, one of the important clinical problems of modern medicine is the early detection and visualization of relapses after prostatectomy, primary and metastatic prostate cancer, which will subsequently help timely decision-making on the exact targeted therapy of this disease. For this purpose, an expensive ^{68}Ga-HBED-CC-PSMA (PSMA-11) PET/CT diagnostic method is currently used in clinical settings, which is not available to the general population. In recent studies [2-3], it was demonstrated that the ^{99m}Tc-labeled PSMA inhibitor [^{99m}Tc]Tc-MIP1404, which allows SPECT scanning, detects PSMA-positive lesions with high sensitivity in patients with biochemical recurrence of PCa (70 and 77% of those examined, respectively).

Thus, based on economic considerations, it is required to develop a technology for obtaining a radiopharmaceutical based on the PSMA-11 ligand peptide labeled with the ^{99m}Tc radionuclide, which allows registration on SPECT/CT to provide inexpensive medical support to all segments of the population, especially those in need of social protection of patients.

The present work is devoted to the study of the synthesis of a pharmaceutical composition (PhC) with the peptide-ligand of PSMA-11, with optimization of the amount of the peptide-ligand of PSMA-11, reducing agent, sodium pertechnetate ($Na^{99m}TcO_4$) from the ^{99m}Tc Generator, and the pH of the reaction mixture for obtaining radiopharmaceuticals «[^{99m}Tc]-PSMA-11 labeled with technetium-99m» with the highest possible radiochemical yield (RCY) and radiochemical purity (RCP). Also studied the stability of the synthesized PhC [PSMA-11] and radiopharmaceutical «[^{99m}Tc]-PSMA-11 labeled with technetium-99m» in 0.9% NaCl solution and human serum.

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SEPARATION OF RADIONUCLIDE OF ^{177}Lu, CARRIER FREE FROM MACRO-QUANTITIES OF YTTERBIUM BY ELECTROLYSIS AND ION-EXCHANGE CHROMATOGRAPHY METHODS

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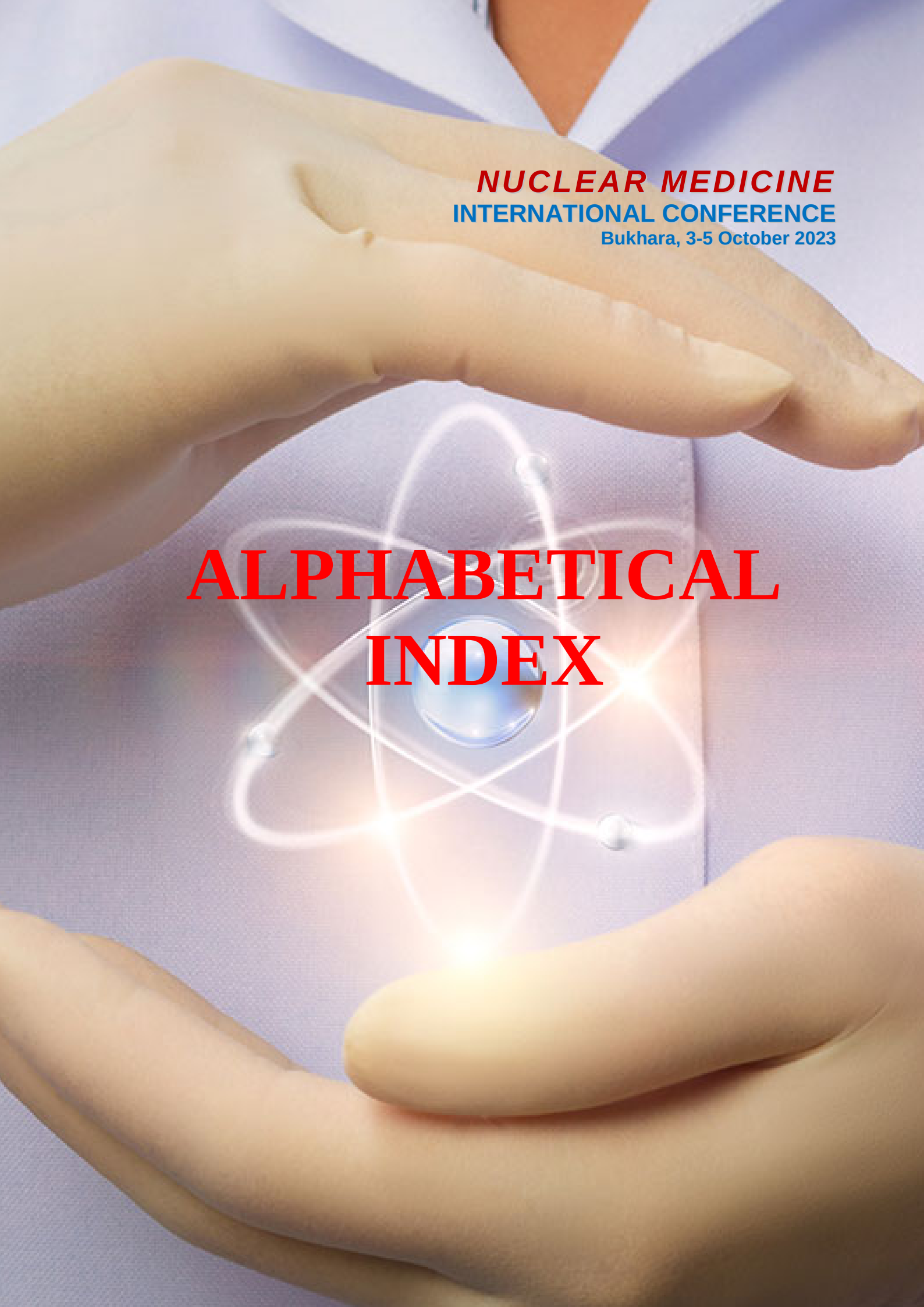
The problem of separating ^{177}Lu and ytterbium radionuclides is associated with the need to obtain a radionuclide of ^{177}Lu carrier free of high purity suitable for the synthesis of radiopharmaceuticals used in peptide receptor radionuclide therapy (PRRT). The concentrations of PRRT compounds in the composition of the radiopharmaceutical are extremely low and amount to several micrograms. Therefore, in order to obtain a high yield in the labeling reaction, the initial solutions of radionuclides in the ideal case should not contain impurities of other elements and stable isotopes of the target radionuclide. In this case, labeling reactions, as a rule, are realized by means of bifunctional chelating agents (BCA), which are attached to the molecules of a biologically active compound on the one hand and, on the other hand, have chelating groups capable of binding metal cations.

This paper presents the results of experiments on the separation of the radionuclide of lutetium-177 carrier free, from gram amounts of the target material of ytterbium-176. The process of separating gram amounts of target material of ytterbium-176 consists in separating the main amounts of ytterbium-176 by electrolytic reduction of $^{175,176}Yb^{3+}/Yb^{0}$ on a mercury cathode with subsequent purification from residual amounts of ytterbium-176 by the ion-exchange - chromatographic method.

The results of the obtained of the radionuclide ^{177}Lu carrier free, with sequential purification by electrolytic and ion-exchange chromatography are shown in the table.

Names of characteristics	**Result**
Sample of the irradiated material according to Yb-176	1,0 g
Initial activity of Lutetium-177	7,3 Ci
Initial activity of ytterbium-175	1,6 Ci
Precipitation $^{175,176}Yb^{3+} \longrightarrow Yb^{0}$ on a mercury cathode, %	1,58 Ci 99,0
The amount of the finished product ^{177}Lu after electrolysis and ion-exchange chromatographic purification	6,79 Ci
Radiochemical yield of the finish product, %	≥ 93
Radiochemical purity, %	≥99,9%
Specific activity, Ci/mg	≥ 92

Thus, the proposed method for obtaining the radionuclide ^{177}Lu, carrier free in the form of chloride, by electrolytic reduction of ytterbium ions $^{175,176}Yb^{3+}/Yb^{0}$ on a mercury cathode and post-purification by ion-exchange chromatography, provides for the rapid production of ^{177}Lu carrier free, in accessible large quantities, of high specific activity, near to theoretical with high radiochemical, radionuclide purity in the form of chloride, conformance to the requirements of the pharmaceutical standard for the synthesis of radiopharmaceuticals with labeling on protein bases. The method is implemented in production, and conformance to the requirements of Ph. Eur. "Lutetium (^{177}Lu) Solution for labeling with the radioactive isotope ^{177}Lu".



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