TOMSK POLYTECHNIC UNIVERSITY
ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

APPROVED BY

Director of Nuclear Science & Engineering School
_______________ / Oleg Yu. Dolmatov
"25" 06 2020

Course Name: Nuclear and physical technologies and radiopharmaceuticals in diagnostics and therapy

Field of study: Nuclear Science and Technology

Programme name: Nuclear Science and Technology

Specialization: Nuclear medicine

Level of Study: Master Degree Programme

Year of admission: 2020

Semester, year: semester 3, year 2

ECTS: 6

Total Hours: 216

Contact Hours: 64

- **Lectures:** 16
- **Practical experience:** 16
- **Labs:** 32

Self-study: 152

Assessment: Exam

Division: Nuclear Fuel Cycle

Director of Programme _______________ / Vera V. Verkhoturova

Instructor _______________ / Artem G. Naymushin

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Course Name: Nuclear and physical technologies and radiopharmaceuticals in diagnostics and therapy

Course Overview

Course Objectives	The aim of the course is to gain knowledge, skills and experience in the production and use of radioactive isotopes, the synthesis of labeled compounds based on them for nuclear medicine.
Learning Outcomes	**Upon completion of the course, a graduate is expected to acquire the knowledge of:** – calculations in the field of atomic and nuclear physics, the structure of the atomic nucleus and its stability, types and patterns of radioactive decays, the theory of nuclear reactions – general laws, theories and methods for analysis of isotope properties, as well as the possibility to obtain and apply radionuclides in nuclear medicine; – production, isolation, separation and concentration of the required radioactive isotopes with the subsequent synthesis of labeled organic and inorganic compounds for pharmacology – requirements of regulatory documents on special laboratory equipment for the treatment and diagnosis of pathologies using ionizing radiation **Graduates are also expected to develop the following skills:** – to apply knowledge of general laws, theories and methods for analysis of isotope properties, as well as the possibility to obtain and apply radionuclides in nuclear medicine; – to separate and concentrate the required radioactive isotopes with the subsequent synthesis of labeled organic and inorganic compounds for pharmacology – analyze, compare, and search for the requirements of regulatory documents on special laboratory equipment for the treatment and diagnosis of pathologies using ionizing radiation – to perform processing and analysis of data obtained through theoretical, clinical and experimental studies; – to develop and plan the project objectives with account of its basic and alternative implementation options; – to communicate one’s view regarding the obtained experimental and theoretical outcomes based on the general laws of physics and chemistry. – to apply knowledge of the foreign language for the informational search of new technologies of generating radioisotopes and radioisotope-based medications, present one’s scientific outcomes at the social scientific events in the form of presentations and oral reports. – to compile the general activity plan on the specified issue, offer research methods and modes for results processing, conduct scientific research on the generation of radioisotopes and radioisotope-based radiopharmaceutical medications. – to execute the R&D outcomes in the form of articles, papers, scientific reports, and presentations with the use of digital typesetting systems and office software packages.

	Graduates should acquire the practical experience in: – ensuring quality management system control in the production of radioactive isotopes and radiopharmaceuticals – analysis, comparison, and search for the requirements of regulatory documents on special laboratory equipment for the treatment and diagnosis of pathologies using ionizing radiation. – conducting scientific research on the generation of radioisotopes and radioisotope-based radiopharmaceutical medications.
Course Outline	The course is taught using a variety of teaching forms, including lectures, practical experience, laboratory classes, and learners' self-study. The course includes the following obligatory components: – 8 lectures; – 8 practical experiences; – 15 laboratory works; – 9 seminars; – 1 review; – 1 colloquium. **Main sections of the course are as follows:** – Introduction into applied radiation chemistry and nuclear pharmacy – Technologies for producing nuclear reactor radioactive isotopes – Technologies for producing cyclotron accelerator radioactive isotopes – Technologies for the synthesis of radiolabeled inorganic and organic compounds for pharmacology – Methods for quality control of radioactive pharmaceuticals – Production of radioactive pharmaceuticals and medical devices in compliance with regulatory documents The students will achieve learning objectives of the course after a series of lectures on physical-chemical fundamentals of isotopes and radiopharmaceuticals generation, generation of reactor and cyclotron radionuclides, reactor and cyclotron diagnostic and therapeutic radiopharmaceuticals, processes of isotope separation, methods of radiopharmaceuticals quality control. Practical training is organized on the basis of the TPU nuclear research facilities and is arranged in the form of laboratory works: 1. Electrochemical separation of radioactive isotopes Y-90 from Sr-90. 2. Study of the operation of radioactivity control installations. 3. Study of *technetium*-99m *extraction generators.* 4. Study of *sorption generators* of *technetium*-99m. 5. Installations for monitoring radioactivity at the R-7M. 6. Obtaining iodine-123 at the R-7M cyclotron. 7. Obtaining thallium-199 at the R-7M cyclotron. 8. Isotopic exchange of iodine between I2 and NaI in solution. 9. Obtaining diagnostic and therapeutic radioisotope preparations at the IRT-T reactor. 10. Biosynthesis of inulin C-14 at the R-7M cyclotron. 11. Obtaining preparations based on Tc-99 at the IRT-T reactor. 12. Quality control of medicines. 13. Determination of radionuclide and radiochemical purity of the finished product.

	14. Preparation of premises, equipment and personnel for the production of radiopharmaceuticals at the IRT-T reactor. 15. Preparation of premises, equipment and personnel for the production of radiopharmaceuticals at the R-7M cyclotron. The current assessment allows revealing the quality of learners mastering the course material referring to all sections of the course "Nuclear and Physical Technologies and Radiopharmaceuticals in Diagnostics and Therapy". Seminar is a form of current assessment, which includes one test and one case study report. 9 seminars are planned for the semester. Each seminar is scored with 5 points. In order to assess the current level of knowledge, it is supposed to conduct 1 colloquium in the form of an oral interview. It is necessary to answer on 5 theoretical questions based on the materials of the relevant sections of the discipline. The correct answer to this question is estimated at 2 points. The maximum possible number of points for one colloquium is 10 points. The exam is a final assessment form. The exam purpose is to reveal developed learning outcomes and to determine the degree of correspondence of demonstrated learning outcomes to those expected in the course program. A student is admitted to the exam on condition that all the seminars are completed, all laboratory works are defended and the total score achieved is not less than 44. The structure of an exam paper includes 6 questions and 1 case study report. Each question is given 3 points. The maximum score for the exam is 20. The exam is oral: a student answers the lecturer's questions and presents the results of case study consideration. Additional questions and tasks can be provided by a lecturer at the exam.
Prerequisites (if available)	1. Nuclear Physics. 2. Radiation Physics. 3. Ionizing Radiation Installations. 4. Mathematical Methods for Imaging in Medicine
Course Structure	The course material is divided into six sections. Each section consists of lectures, practical experiences and lab-bases classes. **Section 1. Introduction into applied radiation chemistry and nuclear pharmacy** Basic concepts, goals and objectives of radiochemistry and radiopharmaceuticals (radiochemistry, radiopharmaceutical, radionuclide diagnostics, hyperfixation of a radiopharmaceutical, separation, isolation and concentration of isotopes, etc.). Physicochemical methods used in the isolation, separation and concentration of isotopes (extraction, chromatography, isotope exchange, the Szilard-Chalmers effect, electrochemical separation, etc.). Physical basics of applied radiochemistry. Chemical properties and analysis of radioactive elements. Introduction into nuclear medicine (basic concepts and definitions, physical, chemical and biological basics). Radioactive pharmaceuticals. **Section 2. Technologies for producing nuclear reactor radioactive isotopes** Basic principles of a nuclear reactor. The main mechanisms for producing radioactive isotopes at a nuclear reactor for the purposes of nuclear medicine. Obtaining radioactive isotopes for therapy and diagnostics. Obtaining radioactive isotopes for therapy at the reactor. Obtaining radioactive preparations of palladium-103, samarium-153, tin-117m, rhenium-186, iridium-

	192, phosphorus-32. Nuclear reactions for obtaining 89Sr. Obtaining tin-117m and accompanying nuclear reactions. Technologies for producing molybdenum-99. Methods and technologies for obtaining technetium-99m. Radioisotope generators Mo-99 / Tc-99m, W-188 / Re-188, Sr-90 / Y-90 and their types (Chromatographic, sublimation, extraction). **Section 3. Technologies for producing cyclotron accelerator radioactive isotopes** Basic operation principles of accelerators (cyclotron, betatron, etc.). Types of targets and devices for their irradiation, target cooling systems. The peculiarities of the production of radioactive isotopes at accelerators. Obtaining radionuclides at charged particle accelerators. Process control sensors and logistics. Methods of obtaining thallium-201, thallium-199, gallium-68, fluorine-18, iodine-123. Obtaining radionuclides emitting positrons. Scheme of obtaining labeled preparations based on ultra-short-lived isotopes. Generators of positron-emitting radionuclides. **Section 4. Technologies for the synthesis of radiolabeled inorganic and organic compounds for pharmacology** Methods of obtaining radioactive pharmaceuticals "Thallium chloride, Tl-201", "Diethyldithiocarbamate, Tl-199", Biosynthesis of inulin C-14, Biosynthesis of fructose C-14, "Sodium iodide, I-123" and "O-iodohydippurate, I-123", "m-iodobenzylguanidine, I-123". Obtaining thiophosphamide labeled with P-32 and S-35. Producing 15- (p-iodophenyl) -3-methylpentadecanoic acid labeled with iodine-123 and the preparation. Biosynthesis of vitamin B-12 labeled with Co-60. Isotope exchange synthesis of labeled thiourea. Preparation and use of drugs based on Tc-99. **Section 5. Methods for quality control of radioactive pharmaceuticals** Quality control methods for radioactive pharmaceuticals. Conducting of alpha, beta and gamma radiometric measurements. Processing of radioactivity measurement results. Determination of the authenticity of radionuclides. Determination of volumetric activity. Determination of molar activity. Method for determining the pH value. Determination of radiochemical and radionuclide purity. Determination of impurities in the final product. Conducting of microbiological analysis. **Section 6. Production of radioactive pharmaceuticals and medical devices in compliance with regulatory documents** Production of radiopharmaceuticals in accordance with GMP drug production and quality control rules. Quality assurance in the production of radiopharmaceuticals. Production of active pharmaceutical ingredients, including stages to reduce the content of impurities. Basic requirements and organization of drug production. Basic requirements for premises and equipment according to GMP. Methods for organizing the production of sterile medicines. Requirements and types of production of radiopharmaceuticals.
Facilities and Equipment	1. Lecture room with multimedia equipment (projector, PC): 634050, Tomsk, Lenina Ave., 2, building 10, room 125A. 2. Laboratory 31 located at the Research Nuclear Reactor IRT-T TPU). 3. Laboratory for radioactive substances technologies (cyclotron of TPU).
Grading Policy	In accordance with TPU assessment system we use: - Current assessment which is performed on a regular basis during the semester by scoring the quality of mastering the theoretical material and the results of practical activities (tests, tasks, problem solving). Max score for current assessment is 80 points.

	- Course final assessment (exam) is performed at the end of the semester. Max score for course final assessment is 20 points. The final score is determined by summing the scores of the current assessment during the semester and exam score at the end of the semester. Maximum overall score corresponds to 100 points, min pass score is 55 points.
Course Policy	Class attendance will be taken into consideration when evaluating students' participation in the course. Students are expected to be actively engaged in class discussions on the assigned reading materials. All classes are obligatory to visit. Medical allowance to work with radiation is required. Students should pass briefing about electrical, work and radiation safety in laboratories of Nuclear Science and Engineering School.
Teaching Aids and Resources	**Compulsory reading:** 1. Editorial: Innovative Radiopharmaceuticals in Oncology and Neurology / Jacques Barbet, Nicolas Arlicot, Marie-Hélène Gaugler [and etc.] // Frontiers in Medicine. - Vol. 3, Article 74. — P. 1 - 3. — URL: https://www.frontiersin.org/articles/10.3389/fmed.2016.00074/full (дата обращения: 04.03.2020). — Режим доступа: свободный доступ из сети Интернет. - Текст : электронный. 2. Practical Clinical Oncology / editors L. Hanna, T. Crosby, F. Macbeth. – 2 th ed. – Cambridge: Cambridge University Press, 2015. – 338 p. - Текст: электронный // Cambridge University Press. – URL: https://www.cambridge.org/core/books/practical-clinical-oncology/66F869C03F6901256B1B7EDFFE816B83#fndtn-contents (дата обращения: 20.09.2020). – Режим доступа: по подписке. **Additional reading:** 3. Мурогов, В. М. Nuclear technology: history, state and technical challenges of nuclear power development : монография / В. М. Мурогов. — М. : ИНФРА-М, 2019. — 123 с. - ISBN 978-5-16-107748-1. - Текст : электронный // Znanium.com : электронно-библиотечная система. — URL: https://znanium.com/catalog/product/1022694 (дата обращения: 12.03.2020). — Режим доступа: по подписке. 4. Innovative medicine: basic research and development / editors Kazuwa Nakao; Nagahiro Minato; Shinji Uemoto. – New York: Springer Open, 2015, 330 p. - Текст: электронный // SpringerLink. – URL: https://www.springer.com/gp/book/9784431556503 (дата обращения: 20.09.2020). – Режим доступа: по подписке.
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