Project Review

“Further Development of Methods, Technologies, Schedule Modes and Delivery of Radiotherapy”

Theme 04-2-1132

The proposed project for reviewing is interdisciplinary, interdepartmental and international, and combines the efforts of JINR LNP MTC researchers and scientists and practitioners of medical institutions of the Russian Federation, as well as research groups from Poland, the Czech Republic, Romania, South Africa and Japan. It is an original project that has no world analogues.

The goal of the project is clearly formulated in the introduction and defined as “conducting biomedical and clinical studies on the basis of the Medical Technical Complex (MTC) of the LNP JINR, studying the effectiveness of hadron therapy of various neoplasms, improving equipment and developing new methods of radiotherapy of oncological patients in phasotron’s medical hadron beams. In our opinion, the provision formulated in this way is a means (instrument) of achieving the main goal, briefly defined in the title of the project.

In their brief summary, the authors of the project describe the fundamental rationale and practical achievements in the field of hadronic therapy of tumors in the world science, as well as the historical and contemporary place of the MTC in the problem. The MTC JINR, due to the vision of V.P. Dzhelepov, was the first in the Soviet Union center of hadron therapy of tumors and today is one of the main methodological centers in the country, providing at the same time the provision of medical care - since 2000 to April 2019, 1287 patients were treated with various nosological forms of cancer.

MTC employees have achieved great success in the field of preserving and developing the technological base to provide comprehensive therapy: hadron and photon therapy for cancer patients. The main work is carried out in the treatment room №1 - universal for proton therapy of tumors of the head, neck and other body parts of patients, as well as the treatment room №6 for gamma therapy. The treatment room №1 was upgraded in accordance with the requirements of precision volumetric conformal proton radiation therapy.

The staff of MTC make a serious contribution to the development of the relatively young scientific discipline “Medical Physics”. They methodologically substantiated and technologically implemented the main stages of pre-radiation preparation and irradiation for 3D conformal proton radiotherapy throughout the entire course of work with patients, from immobilizing the area to be irradiated to computed tomography of tumors in order to compile 3D computer planning of radiation, making individual (for each patient) devices for the beam modulation and implementation of the irradiation treatment plan with verification.

On the basis of international cooperation with scientists from Japan, the Czech Republic, Romania and Poland, adequate dosimetric accompaniment of proton radiation therapy has been provided. Issues ranging from determining the radiation dose absorbed in a tumor and healthy tissue to forming a therapeutic beam, calculation of dose distributions, evaluation of microdosimetric distributions, monitoring of proton beam energy, automation of the irradiation process, calibration of the gamma-therapeutic apparatus based on the recommendations of the IAEA, etc. are successfully resolved. on the device for the implementation of the dynamic method of irradiation of various neoplasms with a proton beam.

The methodological and technological achievements of the MTC staff have been successfully tested clinically. There are examples of successful treatment of cervical cancer, head and neck tumors, brain, vascular tumors, etc.

Research in the field of radiobiology is characterized by the intensive development of the original direction: the use of laser radiation to achieve a radioprotective effect on the effect of gamma radiation and protons. The designed appropriate devices and methods are protected by patents.

Turning to the consideration of planned research and methodological developments, it should be noted that they are a logical continuation and creative development of the above areas.

In general, the main objective of the project for the next period 2020-2022 will be to develop methods of irradiation of patients with a proton beam, providing the highest degree of conformity of the dose field of the irradiated target, which will reduce the dose attributable to healthy tissues and organs, as well as the overall improvement of the effectiveness of therapy.

It is planned to expand the range of localizations available for proton irradiation of nosological forms of cancer.

It is intended to summarize the results of treatment of patients with various diagnoses of brain diseases.

The most important points can be noted.

Testing of the prototype multileaf collimator on the accuracy of the positioning of the plates. Check of operability of electronic control units of the collimator. Creation of test software for automatic aperture setting. Experimental verification on a proton beam. Troubleshooting identified problems.

Development of the project of the computerized system for controlling a dose release. Development of a test unit of the system of automatic control home doses on the basis of the MC Arduino. Testing unit, identify problems in the work.

Continuation of the work to expand the functionality of the three-dimensional planning program of conformal proton radiotherapy developed in the MTC and its clinical testing in irradiation sessions.

Dosimetric calibration of the phasotron proton beam of the LNP, JINR and the ROKUS-M gamma apparatus together with the INP CR, Prague.

Measurement of radiation dose beyond the proton beams generated by the passive method using collimators, compensators and ridge filters with the phasotron proton beam LNP, JINR as well as using active scanning beam generated by the gantry in the proton therapy center in Prague.

Continued research to determine the forms of fibroblast cell death depending on the dose of ionizing radiation.

The study of the mechanisms of functional and neurochemical disorders in the central nervous system under the action of radiation with different linear energy transfer. The study of neurochemical and behavioral effects after exposure to ionizing radiation, widely used in radiation therapy in ground-based experiments on the modeling of the biological effects of cosmic radiation. Studying the effect of radiation from different LET on the functions of glutamate and GABA receptors.

The development of new methods for assessing the effectiveness of the cytotoxic effect of nanoparticles on tumor cells. Effects will be evaluated using various microscopy techniques (optical microscopy and fluorescence microscopy).

Measurement of background conditions in the cabin for proton therapy.

Verification of the radiotherapy systems for planning proton beam irradiation. Measurements of spatial dose distributions using radiochromic films and other detectors in various phantoms, including the heterogeneous Alderson phantom.

The study of the lethal effects of laser radiation with a wavelength of 532 nm on the survival of fibroblast cells.

Obtaining an integrated assessment of the state of the central nervous system when exposed to different types of ionizing radiation based on a comprehensive analysis of neurochemical indicators of the brain and behavioral characteristics of laboratory animals. Search and study of drugs with neuroprotective effects against radiation-induced effects in the central nervous system. Investigation of the dose dependences of the functional response of the brain in various combinations of radiation factor and pharmaceutical preparations. The study of molecular mechanisms of radiation exposure in cultures of neuron-like cells.

Combined γ-ray and proton beam irradiation of tumor cells with metal nanoparticles. Identification of effective combinations and differences in the radiobiological action of gamma rays, proton beams and metal nanoparticles.

Completion of the development and implementation of algorithms for the work of a three-dimensional program for planning conformal proton radiotherapy for the method of dynamic irradiation of deeply located targets with a wide uniform beam. Tests and refinement of the program.

Establishing patterns of induction of functional disorders in the workings of the brain structures under the action of ionizing radiation used in radiation therapy. The use of computer simulation techniques to analyze the results of experimental studies on the effects of ionizing radiation on the central nervous system. Establishing patterns of influence of different doses of pharmaceuticals with neuroprotective effects during irradiation; formulating concepts of their practical application in order to minimize the negative effects of radiation during radiation therapy and for the radiation protection of astronauts in long-range space flights.

As a result of the project on the basis of fundamental research and analysis of the results of previous work, practical recommendations will be given for further improvement and optimization of methods of radiation proton therapy and combined proton-photon therapy for tumor diseases. In addition, it is expected to gain new fundamental knowledge in the field of radiobiology.

There are no comments on the submitted schedule of works on the draft, as well as on form № 26 and № 29. It is necessary to correct the date of the project execution in form № 24.

In order to discuss the content of the project, in our opinion, it should be noted that it does not reflect the great contribution of the MTC staff to the development of space radiobiology. It is known that the phasotron and Rocus-M are working on the irradiation of various biological objects on the orders of LRB researchers. Much attention is paid to the effect of proton radiation on the central nervous system, which is critical, according to some authors, for the action of corpuscular radiation. Given these assumptions, it would be extremely interesting to summarize the unique clinical results on the effect of proton radiation on the neurological status of patients with irradiation of the brain.

The secondary radiation of the phasotron, having in its spectrum neutrons of various energies, photons and secondary protons, can be used to simulate radiation in the cabin of a spacecraft and to conduct corresponding radiobiological experiments. It was necessary to mention a series of experiments on the passage of protons through concrete protection.

Given the general orientation of the team on the treatment of oncological diseases, it is advisable, in our opinion, to begin work on experimental oncology as applied to the capabilities of the MTC.

Summarizing the content of the review, a number of provisions should be noted.

The scientific team of MTC LNP JINR, together with domestic and foreign partners, carried out a fundamental substantiation of practically significant problems in the field of hadron therapy of oncological diseases.

The presence in the MTC of a unique irradiation base and highly qualified personnel makes it possible to successfully solve the most complex tasks in the field of radiation therapy and related areas of radiobiology, including space radiobiology and astrobiology.

I recommend to support the project “Further development of methods, technologies, schedule modes and delivery of radiotherapy”, theme 04-2-1132.

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