Project Review
“Further Development of Methods, Technologies, Schedule Modes and Delivery of Radiotherapy”
for the period of 2020-2022

Currently a large number of methods have been developed for conducting remote radiotherapy of oncological diseases. One of the most successful and promising among them is proton therapy. The method of proton therapy is the most promising movement of radiation oncology. The effectiveness of proton therapy, compared with standard radiation therapy, is linked to the fact that protons allow the formation of a highly localized radiation dose in a deep-seated tumor with minimal irradiation of normal tissues surrounding the tumor. In the world, about 200 thousand patients have been already treated with this method.

For successful treatment of cancer patients, it is necessary to improve the technology of irradiation with the proton therapy method, first of all, to improve planning irradiation and beam delivery, make more precise determination of the target position, improve possibilities of forming the required dose distribution of the beam in the patient’s tissues, and maximize the biological efficiency of the particle energy trapped in the tumor volume. It is precisely to the solution of these problems that research and development within this topic of the past years have been devoted.

The significant achievements in the field of proton radiotherapy and radiosurgery are the three-dimensional conformal proton radiation therapy technique developed and implemented at JINR as part of these works, in which maximum of the dose distribution most closely corresponds to the shape of the irradiated target. For the treatment of patients with the method of three-dimensional conformal proton therapy, a special radiological department of proton therapy was established in MSCh №9 FMBA in Dubna in 1999. This made it possible in clinical studies conducted at the Phasotron beams of the Laboratory of Nuclear Problems of JINR to irradiate tumors located in the head, neck and chest areas localized near vital organs, irradiation of which is undesirable or unacceptable. The successful solution of this problem was possible due to the fact that all irradiation details were taken into account, new devices were developed - comb filters, which allow forming a beam with the Bragg peak expanded to the required value, figured collimators and compensators (boluses), which make the beam conformal with the target all three directions. In particular, the technology of manufacturing boluses from special wax was implemented with the power of a specialized CNC milling machine.

To implement a more conformal method of dynamic irradiation of a tumor with a wide homogeneous beam, an automated multi-leaf collimator of a proton beam was designed and manufactured. A multi-petal collimator for 33 pairs of plates is under development.

One of the main and crucial components of the three-dimensional conformal proton radiation therapy technique is a simulation and radiation planning system. So far, the MTC has used a planning system developed for this purpose at the Proton Therapy Center in Lom-Linda, USA, and adapted to the phasotron beams. Currently the MTC has basically completed the development of a version of its own similar program, which has already undergone dosimetric verification using the heterogeneous Alderson phantom and radiochromic films, and is currently undergoing clinical testing.

A system that controls the main parameters of the proton beam directly during the therapeutic radiation of patients was established. The proton beams of JINR have already treated about 1300 patients in the period of 2000 - 2019.

Developed methods for improving the "quality assurance" of proton therapy are of great practical importance. It is difficult to overestimate the importance of the development and improvement of detectors for dosimetry of medical proton beams, since it is obvious that one of the main conditions for achieving the desired result in radiotherapy is the correct determination of the dose of ionizing radiation absorbed by the tumor. A very important role is also played by the correct determination of the relative biological effectiveness (RBE) of the proton beam used to irradiate patients, which should be taken into account when planning radiation therapy. In this case, both the physical (microdosimetric) and biological values of RBE were determined. Together with the staff of the Institute of Nuclear Physics (Prague, Czech Republic), the dosimetric calibration of the Rocus-M gamma apparatus was carried out, and background conditions in the proton therapy room №1 were measured. Together with the staff of the Department of Radiation Dosimetry of the Institute of Nuclear Physics (Prague, Czech Republic), the LET spectra of the clinical proton beam of the LNP phasotron were measured using Liulin and Medipix silicon detectors. A lot of work was also done to identify errors that occur when planning exposure in the event that patients have dental metal prostheses in the irradiation area and recommendations were made to minimize them.

It is necessary to emphasize the importance of radiobiological research conducted within the project. Many of them are of great interest, both from a purely scientific and from a practical point of view. In particular, in recent years, the use of the radioprotective effect of laser radiation with a wavelength of 633 nm and 532 nm in radiotherapy has been investigated. A device has been developed and assembled for the radiation protection of biological objects (patent for invention RU 2 428 228 C2). Experiments on the combined effect of ^{60}Co gamma rays and laser radiation on the survival of experimental mice were carried out. Radioepidermite, which is accompanied by a sensation of itching and tension of the skin, is widespread and is a serious problem in people undergoing radiation therapy in the treatment of cancer. The studied patients after irradiation with gamma rays were irradiated with a laser device. Starting from the first day of irradiation with a laser device, the damaged skin of patients gradually began to recover, itching was not observed. When using the laser treatment of the skin of these same patients, radioepidermite was not observed from the first day of the next course of radiation therapy. Laser irradiation also had a preventive effect on the mucous membranes of the oral cavity, pharynx and tongue.

New areas of work in this area should also be noted. Thus, in 2018–2019, joint work was carried out within the framework of the program of cooperation with South Africa (iThemba LABS) on the subject "Neurochemical studies of neurotransmitters in brain tissues after exposure to neutrons, protons and gamma quanta". Work on this topic is focused on the study of radiation effects in the central nervous system - a problem that has been relevant for the past decades mainly because of the increasing use of ionizing radiation in the treatment of brain tumors and the matters of radiation protection of astronauts in long-term space missions outside the Earth's magnetosphere. Without a doubt, work in this area should be continued.

The second direction is to increase the dose released in the tumor volume during proton therapy due to saturation of its cells with heavy metal nanoparticles such as 53I, 64Gd, 78Pt, 79Au, etc. The damage of tumor cells is formed both by the primary and secondary short-range radiation resulting from the interaction of incident particles with nuclei of heavy elements concentrated in tumor cells.

Such induced radiation can be used to increase the target dose during radiation therapy of malignant tumors without increasing the untargeted dose released in healthy tissues.

The decision, made by the team of executors of the project, to continue all these studies for another 3 years is the only correct one. This will allow to continue the clinical testing of the proton therapy method for the treatment of various neoplasms on the JINR phasotron beams. Very important for the development of proton radiotherapy capabilities are the alleged development of computer-controlled equipment for carrying out dynamic proton beam irradiation of deep-seated tumors, including the development of computer-controlled retarder of variable thickness and a full-scale multileaf collimator.

As a result of implementation of the planned work using the developed technical solutions, radiobiological and physical methods, clinical experience that will make it possible to make recommendations on their application in clinical radiology and to determine the direction of further research on JINR medical beams will be gained.

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