Radiation and Radiobiological Research

08-9-1015-96/2008

Priority:	1
Status:	Data taking

Radiation and Radiobiological Investigations at the JINR Basic Facilities and in the Envitonment

Leader from JINR: E. Krasavin, V. Aleinikov

Participating countries and international organizations: Armenia, Belarus, CERN, Czech Republic, Germany, Hungary, JINR, Mongolia, Poland, Russia, Slovak Republic, Ukraine, the USA.

As a result of experiments on the Nuclotron accelerator, in the frame of theme 1015, new data concerning the genetic action of heavy ions with Z=4–12 were obtained. A tendency of increasing the number of chromosome lesions after ^{12}C ion irradiation comparing 1 GeV proton (LET~0.218 keV/μm) was observed. ^{24}Mg ions (LET~10 and 40 keV/μm) caused a much more pronounced effect. Chromosome fragmentation and alteration of correlation between different types of chromosome damage took place because of increasing intrachromosome aberrations. The coefficients of relative genetic efficiency on the criterion of chromosome aberration were determined for lymphocytes exposed to 500 MeV/nuclon charged particles.

The first experiments in the new field of investigation concerned with the mechanisms of cataract formation induced by heavy ions were conducted. Particularly, kinetics of aggregation of crystallines after helium ions (500 MeV/nuclon) irradiation has been studied. This year, the investigation of the structure of protein molecules with mathematical methods of the molecular dynamics was started in newly founded theoretical DRRR sector. Work on experimental basis of clinical application of pharmaceutical preparation “methilen blue–^{131}I” in the frame of the project “Mitra” was finished. The results were sent to clinic for the further examination.

The results obtained for the heavy charged particles action on genetic apparatus of cells and protein molecules of eye lens reveal an important role of cluster lesions of DNA and protein structures. The investigation of single and double strand breaks of DNA is necessary for further study of genetic effects of heavy ions. For this aim, the new method “comet-assay” has been developed in the DRRR. In order to define the character of DNA-damage induction, the experiments with lymphocytes irradiated by γ-rays were performed.

Cytogenetic effects of low doses of ionizing radiation (γ-rays and heavy ions) in mammalian cells as well as in normal and tumor human cells were studied. Non-linear dependence of chromosome damage at low doses was revealed characterized by hypersensitivity (HS) followed by induced radioresistance (IRR). For the investigation of the mechanisms underlying the HS and IRR new molecular approaches have to be found. It is necessary to continue the investigation in these directions with the Nuclotron heavy ion beams.

Radiation research will be continued in the following main directions:

- study of radiation fields at the JINR basic installations;
- prognostication of radiation environment around the SAD and CyLab complex in Slovakia;
- physics support of the biological experiments at the Nuclotron.

The Expected Results in 2004:

- The determination of the features of DNA-damage induction in human cells by accelerated heavy ions;
- The receiving of new data, concerning kinetics of crystalline aggregation of eye lens after heavy charged particle exposure;
- The clinical testing of the radiopharmaceutical preparation “methilen blue–^{131}I” developed for target radiotherapy of human pigment melanoma.

08-2-1035-2001/2006

Priority of the project:	1
Status:	R&D

Further Development of Methods and Instrumentation for Radiotherapy and Associated Diagnostics with JINR Hadron Beams

Leader from JINR: G. Mytsin

Participating countries and international organizations: Bulgaria, Russia, Czech Republic.

The main goal of the theme is to carry out medico-biological and clinical investigations on cancer treatment using seven-compartment Medico-Technical Complex of DLNP JINR, to improve equipment and instrumentation, and to develop new techniques for treatment of cancer with medical hadron beams from the JINR Phasotron and for associated diagnostics.

One of the promising ways to increase the efficiency of radiotherapy is to use new types of radiation, such as heavy charged particles and high-energy neutrons, produced at modern accelerators. These particles show pronounced advantages in the space distribution of the dose absorbed and favourable changes in some of their biological effects (relative biological efficiency and oxygen ratio).

During the last 50 years about 38000 patients were treated with heavy charged particle beams (more than 34000 of them with protons) all over the world in more than 30 centres. The results of these clinical trials have clearly showed that hadron therapy is a very powerful method of treating malignant and some other diseases and in many cases it is the only one possible way to help a patient. So, by the end of the last century specialised hospital based centres for proton therapy with dedicated accelerators were made and put into operation. At present, there are more than 20 new projects of such centres in the world at different stages of realization.

At the same time, the technique of the proton beam delivery, irradiation and fixation of a patient is the field of further investigation. The main goal of this research is to increase the conformity of irradiation, which will result in spearing of healthy tissues and higher efficiency of treatment.

First investigations on proton therapy in the DLNP JINR were initiated by professor Dzelepov and were started in 1967. To the date, a Medico-Technical Complex (MTC) based on 660 MeV proton Phasotron were constructed and now it is currently being put into operation. It will allow tumour treatment with wide and narrow beams of protons, negative pions, high-energy neutrons, and with their combinations. MTC includes seven treatment rooms (Fig.1).

Room 1 is intended for proton irradiation of deep seated complex-shape tumours in the region of head, neck, and thorax. For this room topometric X-ray and proton tomographs combined with a therapeutic chair were designed and constructed. This ensures high value of reproducibility of the patient positioning during topometry and irradiation. The technique and instrumentation for 3D conformal proton irradiation of intracranial targets have been developed for this room and now are implemented in the treatment sessions.

Room 2 has been used for proton radiotherapy of gynaecological diseases. 36 patients with uterine cervix cancer were successfully treated here. The 5-year survival was about 83% without any significant complications caused by the radiation treatment.

Room 3 allows so-called “shoot-through” irradiation of small intracranial targets, such as normal and tumour-affected pituitary gland, and arterovenous malformations with a narrow 660 MeV proton beam.

A negative pion beam of energy 30–80 MeV is delivered to room 4. This beam combines advantages of dose field distribution and of favourable biological effects to the cancer cells.
Room 5 is intended both for proton and high energy neutron irradiation of large hypoxic tumours.

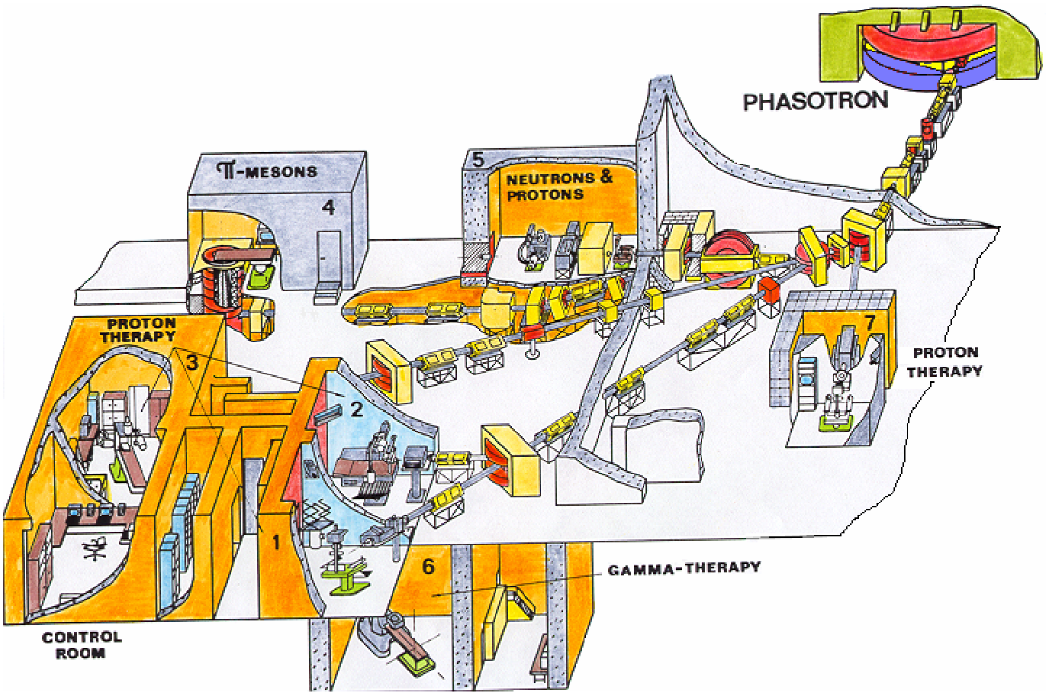

Fig.1. Medico-technical complex of DLNP JINR for hadron therapy of cancer patients.

Room 6 accommodates standard Co-60 therapeutic unit Rokus-M for external irradiation which is used in combined treatment methods.

Room 7 is designed for proton radiotherapy of eye tumours. With a proton beam it is possible to form dose fields satisfying to an eye tumour of any possible size and location with high dose gradient at the border tumour — normal tissue.

A single-ring positron emission tomograph (PET) has been constructed to evaluate changes in biophysical and biochemical processes in patient organs during the course of fractionated treatment and possibly to control the coincidence of a dose field and a tumour volume.

The most important achievement in the plan of organization of wide treatment of cancer patients with the JINR Phasotron beams was inauguration of a specialized onco-radiological department for 25 beds in the Dubna Hospital in 1999. It allowed us to start regular irradiation of patients in MTC. It is planned to treat up to 90–100 patients during 2003.

The following development and upgrading work is planned for the period of 2003–2009 to implement the research programme and to provide competitive results: design and upgrading of equipment for new proton beam delivery techniques, patient poisoning and treatment verification to improve the conformity of irradiation; development of various types of detectors and investigation of their sensitivity to increase the clinical dosimetry accuracy of medical hadron beams; improvement and upgrading of the automated control system for diagnostic procedures, treatment planning, accumulation of information, and treatment of cancer patients with medical beams from the JINR Phasotron.

It is planned also to carry out the molecular biological investigations to study the DNA lesions underlying the gene mutations induced by ionising radiation of different LET in animal and human cells. In future the results of the investigations will allow us to develop the genetic monitoring of oncological patients undergoing a course of radiotherapy with the JINR Phasotron medical beams.

Fulfilment of the programme will yield estimates of the proton therapy efficiency for some malignant tumours, practical recommendations on the choice of optimum radiation treatment of patients and on further development of methods for radiotherapy with beams of heavy nuclear particles, new tested means and techniques for treatment of patients with these beams, and accompanying diagnostics of the hadron radiotherapy.