DIVISION OF RADIATION AND RADIOBIOLOGICAL RESEARCH

In 1999, the main lines of the DRRR activity were concentrated on:

— neutron spectrometry and radiation monitoring;
— physical support of radiobiological experiments;
— theoretical modeling of ionizing radiation interaction with matter including interactions with biological structures and shielding calculations;
— investigations of peculiarities and mechanisms of point and structural mutation induction in pro- and eukaryotic cells by radiation with different linear energy transfer (LET);
— problem of low doses of radiation with different LET and sell recovery;
— investigation of «methylene blue — ^{211}At» complex therapy efficiency in melanoma cells.

RADIATION RESEARCHES

Radiation protection conceptual framework of the Cylab cyclotron complex (Slovakia) was developed. The course of feasible study of major radiation protection issues of the complex comprised not only radiation protection of the cyclotron, but also problems related to the safe use of many nuclear and medical technologies. Section of the request for proposal (RFP) of Cylab's design appertaining to radiation protection was prepared in the fullest detail. The radiation protection requirements needed for all nuclear and medical technologies to be used at the complex were specified. The following aspects of radiation protection were considered in all its bearings: criteria of radiation protection design, possible radiation sources, radiation shielding, radiation monitoring, waste management, possible radiation accidents and others.

Attention was given to the use of Monte Carlo method for shielding calculations, radiation detector response study and dosimetric applications. In particular, the depth-dose distribution from a ^{166}Ho skin patch to skin tissue was estimated by the electron-gamma transport simulation. This work was done in frame of collaboration with the INP (Czech Republic) and connected with radionuclide therapy of skin cancers. The neutron spectra of reference fields based on ^{252}Cf in polyethylene spherical moderators were calculated for real geometry. The physical support of the radiobiological experiments was continued [1,2].

Measurements of the neutron spectra generated by 1 GeV protons in the U + Pb + CH_2 assembling in a wide energy range were continued [3,4]. This work was done in collaboration with the LHE for estimation of radioactive waste transmutation cross section. The multisphere spectrometer and the code for neutron spectra unfolding by the statistical regularization method were used. Activation detector's technique for the estimation of the spatial neutron distribution around the assembling was applied. The data of the last experiments with proton energy of 1 and 1.5 GeV have been processed. As a result, the neutron spectra under different angles and estimation of the total neutron yields (for various energy groups) were obtained.

Measurements of the radon-gas concentration in air and water in environment and JINR dwellings were completed [5]. Measurements of radionuclides concentrations in soil near the Balakovo NPP as well as samples of soil and multiyear mosses from Yerevan environs were carried out.

Experimental study of radiation detector characteristics was continued [6]. In the neutron reference fields the characteristics of the personnel dosimeters being used by JINR and Czech Republic as well as the microdosimetric characteristics of the track etch detectors and the thermo-

luminescent detector responses were studied. The data of the LET measurements of the secondary particles generated by 1 GeV proton beams in CR-39 detectors have been processed [7].

RADIOBIOLOGICAL RESEARCH

A data analysis has been conducted on stable and unstable chromosomal aberrations in human blood lymphocytes, induced by scarce and densely ionizing types of radiation (γ rays, 1 GeV protons with LET ~ 0.218 keV/μm, ions ^{14}N with LET ~ 77 keV/μm) [8,9]. Possible mathematical approach has been taken up to compare the data obtained by FISH and standard metaphase methods. The obtained data may serve as evidence for suppositions about various radiosensitivities of different human chromosomes. They testify on a higher frequency of damage of chromosomes 1 and 2 in the human genome.

The question about possibility of extrapolation of the effects induced by high doses of irradiation to the range of low doses and also the problem of induction of adaptive response which is the increasing radioresistance of cells after irradiation with low doses to the following irradiation with higher dose, are the most important aspect of the biological effects of low doses of ionizing radiation. The dose-effect dependence of cytogenetic damage in the dose range 0.1–2 Gy of the single-dose irradiation with Chinese hamster and human melanoma cells in culture had been studied. The nonlinear dependences are shown for the induction of chromosome aberration with dose. The radiosensitivity of cells was maximal at the doses lower than 10 and 20 cGy for melanoma and Chinese hamster cells respectively. This hypersensitivity was followed by increased radioresistance and the reverse dose-effect dependence had taken place at appropriate dose range. It was supposed [10] that this phenomenon reflects induced radioresistance mechanisms at some level of damage and that induced repair processes are more effective and operates at lower doses in melanoma than in Chinese hamster cells. For verification of this hypothesis, a quantitative comparison of induction of adaptive response after double-dose irradiation of these two cell lines was carried out. It was shown that maximal adaptive response was induced at 1 cGy for melanoma cells and 20 cGy for Chinese hamster cells. It can be concluded that the same inducible repair processes are analogous in mechanisms and different in quantitative proportion for different cell types underlying on the base of nonlinear dose-effect curves and induction of the adaptive response.

A study of mutagenic action of ionizing radiation on mammalian cells was continued. Chinese hamster cells (line V79) were irradiated with 1 GeV protons at the LHE Synchrophasotron at doses of 1, 1.5, and 2.5 Gy. HPRT-mutant subclones were revealed and separated from the irradiated cells' culture, their cytogenetic analysis was conducted. An increase of the growth duration of mutants is obtained in comparison to the intact control.

In our earlier study of spontaneous and γ-induced mutants it was distinguished the group-I of mutants which did not differ essentially from the control in the chromosomal aberration level, and the group-II, which had the level of chromosomal damages about 1.5 to 2 times higher. Besides, in contrast to spontaneous mutants among γ-induced group-I mutants those were obtained which had a chromosomal aberration level about 2 times lower than in the control. No difference was observed in the yield of various types of chromosomal aberrations due to proton irradiation in comparison to γ-induced mutants. The obtained data testify that irradiation of mammalian cells with γ rays and high-energy protons may induce stable on cytogenetical parameter types of radiation-induced mutants.

Experiments on the determination of survival and oncogenic transformation regularities of fibroblast cells at the 580 MeV proton irradiation have been started. The curves of survival and frequency of oncogenic transformation for these cells were obtained.

A study of genetic control of checkpoint-regulation in yeast Saccharomyces cerevisiae was continued [11]. Checkpoint mechanisms cause the cell cycle to pause and allow DNA damage repair. In yeast several checkpoint-genes have been identified. Double-mutant strains have been constructed and their radiosensitivity was studied.

A special tester system for detection point mutations after radiation was used. The study of induction of base substitutions in haploid yeast strains by γ irradiation was finished [12]. The γ irradiation induces efficiently all types of the base substitutions. The dose dependence is linear, that differs from those of diploid strains that show linear-quadratic dependence. The base-substitutions spectrum in haploid yeast is the same as in diploid cells. Observation of base-substitution induction by heavy ion in yeast strain was begun. The first experiment with ^{4}He (LET = 20 kev/μm) showed relative biology effectiveness about 2. A study of frameshift induction mutations in yeast was started by using a special test-system based on the reversion tests with a 4-base insertion in the LYS2 gene or a +1T insertion of a stretch of 6T in HOM3 gene.

Studies of regularities in the formation of spontaneous and induced deletion mutations in E.coli bacterial cells were continued [13]. Dose dependence of formation frequency of tonB-trp deletion mutations at γ irradiation is obtained. A series of preliminary experiments has been

conducted on mastering the methods to study the induction process of deletion mutations with heavy ions.

Studies on the regularities of SOS-response in E.coli cells at the ultraviolet light action have been completed [14]. In particular, the influence of visible light (photoreactivation) on the character of kinetic and dose curves of SOS-induction in E.coli cells (uvrA) was investigated [15]. The analysis of these data along with the data obtained earlier concerning UV-induced SOS-response allowed concluding that different molecular events lie in the basis of SOS-system induction. In the region of the 0–2 J/m^2 dose the SOS-signal is most probably caused by gaps, generated in the process of the damaged DNA replication. In the region of 2–10 J/m^2 an interruption of DNA replication may be regarded as a SOS-inducing event. Studies of the influence of umuC-mutations on the SOS-response induced in E.coli cells with UV and γ rays have been finished. It is shown that in both cases the presence of this mutation leads to a 5-time growth of the SOS-induction level. The investigation of the SOS-response was continued on E.coli cells at the heavy ion action. In particular, kinetic curves of SOS-induction in irradiation of wild-type cells with different doses of γ rays and ^{4}He ions with LET = 20 KeV/μm were obtained.

The activities on computer simulation of genetic regulator system of SOS-response in E.coli bacteria have been concluded [16]. They resulted in a model and corresponding differential equations which describe the dynamics of genetic regulation and inducing signal for the regulator SOS-response system after the UV action. Dynamic curves of the SOS-response regulator components after UV irradiation, as well as dose dependence of maximum concentrations of genes recA and sulA production have been calculated and analyzed.

The combined effect of low-dose ionising radiation and chemical agents on seeds of higher plants (plantain Plantago Major) in the area of the Balakovo Nuclear Power Plant (NPP), Saratov region was studied [17]. The subjects of the studies were the antioxidant status, mitotic activity and chromosome material damage in meristem cells of plantain seedling apex. The data were analysed with the account of results in radionuclide and chemical contamination determination, and simulation of the gaseous flux exhaust of inert gases from NPP. The research demonstrated that the delay in sprouting and the number of not sprouted seeds in populations correlated with the chromosome damage yield in the first mitosis of meristem cells, in case the damage was large, both at the radiation action and at the effects of chemical agents. In these populations the level of chromosome aberrations was 3–4 times higher than the control level.The analysis of chromosome aberration yield and the quantity of proliferating cells in the apex in the first mitosis showed that the action of the ionising radiation lead to classical dependence of these values on the fixation time, while the combined action with chemical agents detained and arrested the cell division. The decrease in the mean values on the quantity of dividing cells in the apex was observed in populations subjected to the effect of radioactive fallout from NPP and chemical agents. These processes affected the normal growth of the plant root, studied in some populations. The study of the antioxidant status demonstrated its decrease by 2–3 times in populations situated mostly on the wind direction from NPP.

The analysis of the results in dose–effect relationship studies has been carried out on the cell and organism level, with the aim to obtain more precise data on the risk coefficient at low doses [18]. The results are represented by two contrasting groups of dose dependence on effect. Both types of dependence are described by the equation solutions of an assumed unified protective mechanism, which comprises two components: constitutive and adaptive or inducible ones. The latest data analysis of the downwards concave dependence curves shows a considerable underestimation of radiation risk in all types of cancer, except leukemia, for a number of critical groups in a population, at low doses comparing to the ICRP recommendations.

The series of experiments had been finished for the purpose of quantitative comparison between degrees of damage of normal Chinese hamster cells and human melanoma tumor cells in vitro treatment with free astatine-211 and ^{211}At-labelled methylene blue (MTB) [19]. The results of experiments confirmed our preliminary data that the efficiency of ^{211}At-labelled MTB on melanoma cells was one order higher than on Chinese hamster cells. Also it was shown the same efficiency of ^{211}At in ionic form for both cell lines.

This means that ^{211}At-MTB is selectively accumulated in pigmented tumor cell, which prove this compound to be clinically effective in radiotherapy of disseminated melanoma accompanied by minimal damage of normal tissues.

RADIATION PROTECTION

The radiation monitoring for occupational exposure at JINR nuclear facilities was carried out in 1999 by the automatic systems of radiation control (ASRC) and by portable instruments. The radiation field investigations in dwellings around the cyclotron U-400M were continued. The organizational and technical measures on radiation protection ensured inexceeding of planned doses.

The regular environmental monitoring of soil, plants (grass), water from the river basins in Dubna vicinity, water-supply system and water effluents of enterprises con-

firms that the environmental radiation pollution around JINR area remain constant during a long time and contains the natural radioactivity and products of global fallout only. Any contribution to radioactive pollution of the environment from the JINR nuclear facilities was not found.

In 1999, the Individual Dosimetry Service maintained dose control to 1816 persons, including 77 visitors, under individual monitoring. Their number decreased by 72 persons as compared with 1998. The yearly individual doses to the personnel did not exceed 21 mSv/yr. The highest values of the average individual dose per year among the JINR Laboratories are at FLNP and DRRR — 2 mSv/yr. The exceeding of the control levels of doses at the Laboratories and the dose limits was not observed in 1999 as well.

EDUCATIONAL ACTIVITY

The second run of the 9-weeks IAEA Regional post-graduate educational course on radiation protection was held in JINR in autumn 1999. The course was opened to 25 young specialists from the IAEA Member States in East Europe and West Asia region. The course was organized on the basis of DRRR and the University Centre. The course consisted of 125 lectures, 17 laboratory exercises, and 10 scientific visits. The main part of the lectures and all practices were given by the specialists from DRRR. As the course result the listeners were awarded by the IAEA certificates. Taking into account the high level of the course organization and experience accumulated in JINR it was proposed by the IAEA to prolong the effective cooperation in this field on the permanent basis.

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