DIVISION OF RADIATION AND RADIOBIOLOGICAL RESEARCH

The scientific programme of DRRR in 2003 in accordance with the first-priority theme of the Topical Plan for JINR Research and International Cooperation was connected with two main directions: radiation investigations at the basic nuclear facilities of JINR and in environment and radiobiological research and radiation genetics. Besides, the «Mitra» project on the development of new radiopharmaceuticals for target therapy of human melanoma was realized in the framework of the theme.

A new fundamental scientific direction, biophysics of photobiological processes, was developed at DRRR. A new department at DRRR structure is being formed now for this purpose. The long-term programme developed together with the physicists from FLNP and VBLHE includes the investigation of photoreceptor membrane structure of visual cells by means of small-angle scattering of neutrons and laser confocal microscopy and the investigation of the impact of heavy charged particles on the lens proteins (crystallins) and isolated retina of an eye. A new theoretical sector for the research in the field of molecular dynamics is established at DRRR as well. In 2003 the theme «Radiation and Radiobiological Investigations at the JINR Basic Facilities and in Environment» was prolonged to 2008.

RADIATION RESEARCH

The radiation research is connected with study of radiation field characteristics at the JINR basic facilities and in environment for different modes of operation, development of the calculation methods for accelerator radiation shields with complex geometries, prognostication of radiation environment at accelerators and around them, estimation of radiation fields that result from the decay of radioactivity induced in accelerator structure and its ancillary components, development of radiation protection systems for designing and upgrading accelerators at JINR and in Member States, study of characteristics of perspective radiation detectors and dosimeters.

The development of radiation protection measures of the Cylab cyclotron complex (Slovakia) was continued. 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: criteria of radiation protection design, possible radiation sources, radiation shielding, skyshine problem, radiation monitoring, waste management, possible radiation accidents and others. The spatial distributions of the neutron effective dose at big distances from the DC-72 building due to skyshine effect are shown in Fig. 1 as an example.

The radiation shielding of the Cylab cyclotron complex was optimized based on the ALARA principle. The comparison between Monte Carlo and phenomenological methods of calculation of neutron effective dose attenuation by concrete shield was conducted for verification of calculation technique [1].

The physics support of the biological experiment with the protons, ^{12}C, ^{24}Mg, ^{40}Ar and ^{56}Fe beams at the LHE Nuclotron was carried out [2]. The new modes of the Nuclotron operation (acceleration of ^{40}Ar and ^{56}Fe) allow extending the range of a linear energy transfer of relativistic nuclei in radiobiological experiments to 200 keV/μm (^{56}Fe nuclei) [3].

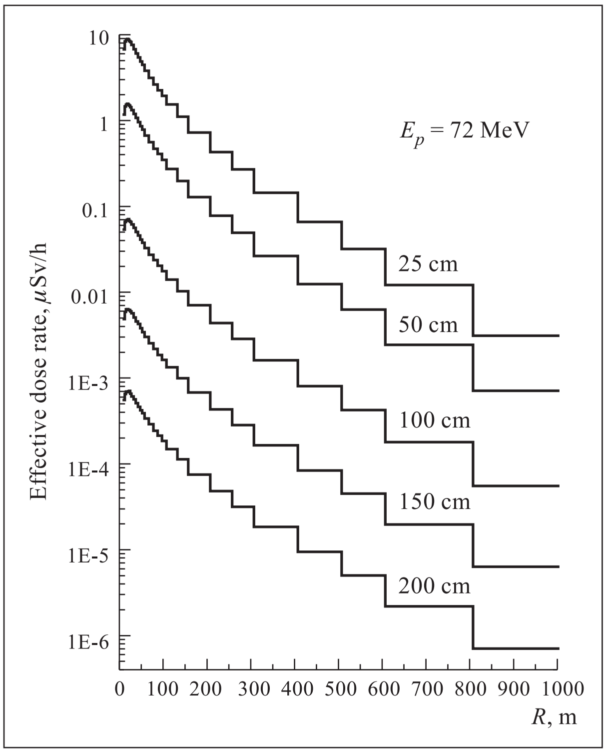

Fig. 1. The spatial distributions of the skyshine-neutron effective dose rate against the thickness of the upper concrete shielding of the DC-72 cyclotron

The measuring instrument of laser light relaxation in pattern during its irradiation was developed for studying the impact of charged particles on the lens proteins (crystallins) aggregation.

The experimental studies of solid-state track detector characteristics were continued in the Nuclotron experiments. Sensitivity of the CR-39 solid-state track detector to heavy nuclei of C, Mg, Ar and Fe with energy 0.5 GeV/nucleon was measured. The dependence of the track size on LET of the particles was obtained as well.

The prognostication of the radiation environment at the SAD installation was continued. The first estimations of the SAD shielding and induced radioactivity of ground were done. The initial radiation situation at different modes of the Phasotron operation and the induced radioactivity of ground in the place of the SAD allocation were measured.

The modification of multisphere neutron spectrometer was carried out for expansion of measurable energy range. A heterogeneous (polyethylene and lead) spherical moderator was developed for this purpose. The real geometry calculation of the neutron detection efficiency of the Russian HEND neutron spectrometer on the basis of stilbene detector (aboard «Mars Odyssey 2001» spacecraft) was started.

RADIOBIOLOGICAL RESEARCH

The study of mutagenic action of radiation with different LET on the human and mammalian cells and microorganisms was continued. The first experiments were performed at the Nuclotron for exposure of the human blood lymphocytes to 1-GeV protons and ^{12}C and ^{24}Mg ions with an energy of $\sim$ 470 MeV/nucleon [4]. Their LET values were 0.218, $\sim$ 12 and 42.7 keV/μm. The dependence of the frequency of aberrant cells on doses was linear after irradiation with all investigated radiation types (Fig. 2). The power dependence of total chromosome aberration on doses was observed after irradiation with protons. It is modified to linear one after exposure to ^{12}C and ^{24}Mg ions. But at their highest doses the effects decrease, which was shown at lower doses for earth radiation depending on their LET. This was a result of mitoses delay of the cells with a great number of chromosome aberrations. The data obtained show that 1-GeV protons do not differ essentially in efficiency from γ-rays and their RBE values are not far from 1. The heavy ions are more effective. At different cytogenetical tests for ^{24}Mg ions the RBE values are 1.4–1.7, the RBE values for ^{12}C ions are 1.2–1.3.

Analysis of chromosome damages in human lymphocytes after exposure to low doses of protons (0.05–0.7 Gy) has shown that the complex nonlinear dependences of the frequency of chromosome aberration formation on doses are observed. Dose–effect dependence curves differ from analogous ones obtained after extrapolation of high dose effects to low dose ones. The «hypersensitivity» of the lymphocytes reveals in ultra-low dose region (0.05–0.1 Gy). The frequency of aberrant cells and total chromosome aberrations were $\sim 4-5$ times greater as compared to effects for corresponding extrapolation curves. The observed effects were a result of chromosome fragmentation and mainly a formation of chromatid and chromosome fragments. Among them the chromatid fragments prevail and their fraction amounted to 70–80% of the total number of fragments. The effects decreased in the region of ~ 0.2 Gy and corresponded to the values of extrapolation curves. At subsequent increase of doses they increase again up to a level at doses of 1 Gy. The data obtained show an incompetence of estimation for influence of sparsely ionizing radiation low doses on the human cells proceeding from extrapolation effect values on the basis of high radiation doses.

The chromosome damages induced by low doses of ^{60}Co irradiation in human peripheral blood lymphocytes have been studied using different cytogenetic assays [5–7]. Despite quantitative differences in the amount of chromosome damages revealed by different methods, all of them have demonstrated complex nonlinear dose dependence of the frequency of aberrant cells. At the dose range of 0.01–0.05 Gy, called hypersensitivity region (HRS), the cells have shown the highest radiosensitivity. HRS peak is completely formed by chromatid aberrations. At a dose of 0.5–1.0 Gy the dose–effect curves become linear with the decreasing slope compared to the initial one by factors of 5 to 10 for different criteria, reflecting the higher radioresistance of cells.

At the low dose range there was found high interdonor variability in the extent and position of HRS peak as well as intradonor variability in two experiments performed on the lymphocytes of the same donor in some time.

So, due to the complex relation of dose and effect, extrapolation of high dose effect to low doses is unreliable, as is biodosimetry at doses below ~ 0.5 Gy, which is also complicated by high inter- and intradonor variability.

Mechanisms underlying HRS may differ from classical model of formation of radiation-induced chromosome damage, as we concluded from the analysis of aberration spectra induced at the low dose range.

The investigations of α and β emitters combined with methylene blue (MTB) application in target diagnostics and therapy of pigmented melanoma are continued. Significant success has been achieved in the investigation of ^{131}I–MTB biodistribution in mice with pigmented melanoma. Gamma-camera imaging as well as direct measuring of radioactivity, accumulated in different organs of mice, shows primary accumulation of the compound in pigmented melanoma and the radioactivity clearance through gastrointestinal and urine systems. Experiments on therapeutic action of ^{131}I–MTB were also carried out. All the results allow concluding ^{131}I–MTB to be suitable for the diagnostics and therapy and open a way for clinical experiments in the nearest future. Experiments with ^{211}At–MTB show inadequate binding stability of the compound. That makes necessary further works in this field.

The study of induction of different type mutations by ionizing radiation in yeast *Saccharomyces cerevisiae* as model of eucariotic cells was continued. A new method was developed to test extended deletions on plasmid bearing a cluster of yeast genes (two negative selection markers, the CAN1 and CYH2 genes, and three positive selection markers, the URA3, TRP1, and LEU2 genes). We suppose to use this system for investigation of efficiency of deletion production on ionizing radiation with different physical characteristics.

The study of genetic control of DNA damage-induced arrest of cell cycle progression, named checkpoint control, was continued along with the Institute of Molecular Genetics, RAN (Moscow) [8]. We have studied interactions between checkpoint genes RAD17 and RAD53. Epistatic interactions between these genes in respect of γ-ray sensitivity are shown. So RAD17 and RAD53 genes act in the same pathway determining the sensitivity of yeast cells to radiation.

DRRR and the University of Perugia (Italy) started the investigation of involvement of checkpoint control and DNA polymerases δ and ε in spontaneous and induced mutagenesis in nondivided cells.

Analysis of genetic characteristics of SRM genes was continued. We have investigated the effect of srm mutations on induced mitochondrial rho-mutagenesis.

A study of charged particles influence on the lens proteins – crystallins was started. As was previously shown, the analysis of kinetics of UV-light-induced photoaggregation of proteins is an effective way to

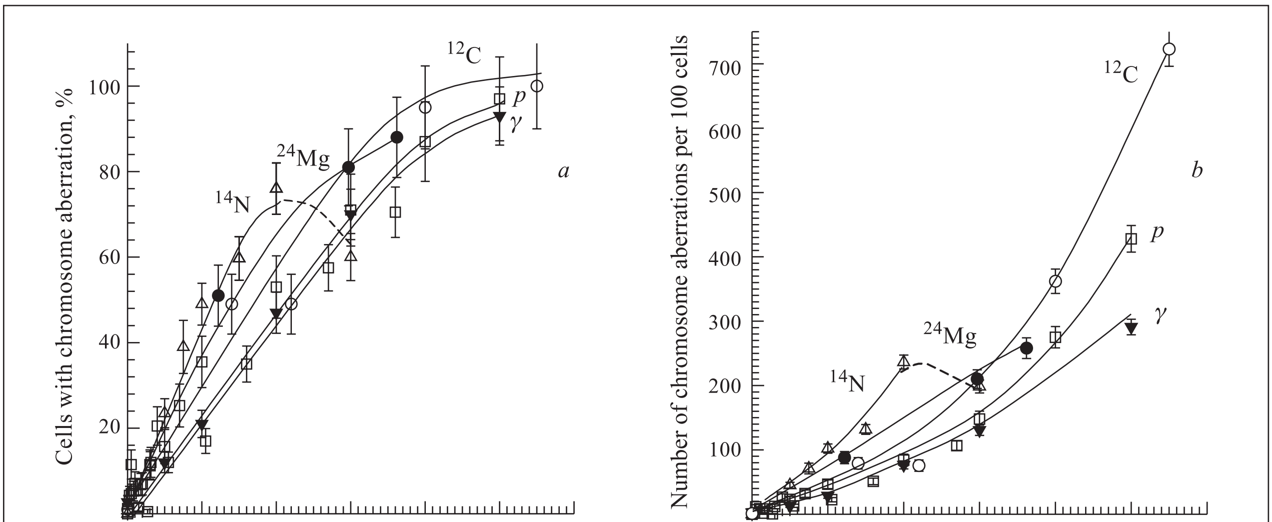

Fig. 2. The dependences of frequency of aberrant cells of human blood lymphocytes (*a*) and of the total number of chromosome aberrations (*b*) on absorbed dose at irradiation with ^{60}Co γ-rays (▼), protons (□) ,^{12}C (○), ^{14}N (△) and ^{24}Mg (●) nuclei

reveal the differences between them. Using this approach, we were able to discover the different behavior of recombinant normal and amino-arm truncated βA3-crystallins with respect to UV-light-induced photoaggregation. Now we have observed the latent radiation defects of crystallins. The preliminary results of our first experiments with accelerated helium ions (500 MeV/nucleon) have shown that the irradiation of bovine βL-crystallin with relative low doses of helium ions (8.2 Gy) does not induce detectable changes of light scattering of protein solution. However, the comparison of kinetics of UV-light-induced photoaggregation of helium ions irradiated and control, nonirradiated βL-crystallin samples demonstrates that the irradiated βL-crystallin is more sensitive to photoaggregation than the nonirradiated one. In contrast to UV-light-induced photoaggregation results, the study of aggregation induced by heating at 60 °C did not show any difference between irradiated and nonirradiated samples of helium ions. Also, we did not reveal any differences between the samples using Na-SDS electrophoresis technique both at normal and reducing conditions (150 mM DTT). One can propose that the irradiation of bovine βL-crystallin with relative low doses of accelerated helium ions induces the latent radiation defects in the native structure of protein. The changes are probably in the tiny dimerization of βL-crystallin molecules. Actually, the gel-filtration profile (Sephacryl S200) demonstrates slightly wider peak of helium-ion irradiated βL-crystallin in comparison with control, nonirradiated one. Thus, the UV-light-induced photoaggregation revealed the latent defect of βL-crystallin irradiated with rather low doses of accelerated helium ions as it was in case of recombinant genetically modified amino-arm truncated βA3-crystallin.

An analysis of stochastic radiobiological effects of low-dose exposure of different biological objects has been carried out on the basis of the two-protection reaction model. The model leans upon the accepted scheme of the principal stochastic radiobiological process and uncontradictorily describes accessible data. The analysis shows that the yield of initial damages, in such structures as DNA, follows the linear no-threshold (LNT) relationship dose–effect. The resulting effect also follows the LNT relationship, provided that there is no reparation process or its suppress. The action of inducible or adaptive protective mechanisms, having restricted possibilities, leads to nonlinear relationship dose–effect. The power of nonlinearity is determined by the nature of the biological object, degree of damage, exposure conditions and level of the spontaneous effect.

The estimation of the excess of the relative risk (ERR) of cancer mortality for adult residents of contaminated regions of Belarus as a result of the Chernobyl accident, has been carried out on the basis of the two-protection reaction (TPR) model. With such an estimation the testing of the model was founded on the data of cancer mortality for survivors of Hiroshima and Nagasaki at low doses. The estimation of ERR has been carried out on the basis of accumulated doses for adult residents of contaminated regions. The results show that the ERR of cancer mortality as a result of the Chernobyl accident is about 5–6% during the whole life. This value is sometimes larger than the value calculated on the basis of International Commission for Radiological Protection's recommendations.

RADIATION PROTECTION

The radiation monitoring for occupational exposure at JINR's nuclear facilities was carried out by the automatic systems of radiation control (ASRC) and by portable instruments.

In 2003 the individual dosimetry service maintained dose control to 1662 persons, including 52 visitors. The average individual yearly dose at JINR was 1.5 mSv. The maximum individual yearly dose was at FLNP (1.9 mSv).

The regular environmental monitoring of soil, plants and water from the river basins in the Dubna vicinity confirmed the conclusion: the environmental radiation pollution around the JINR has remained constant for a long time and is due to natural radioactivity and products of global fallout only. Any contribution to radioactivity pollution of the environment from JINR nuclear facilities was not found.

The exceeding of planned personal doses at JINR was not observed in 2003. The level of radiation protection and control at JINR corresponded to the federal rules and regularities, which was confirmed by regular inspections.

INTERNATIONAL COLLOQUIUM. EDUCATIONAL ACTIVITY

The 2nd International COSPAR Colloquium «Radiation Safety of Manned Mars Mission» took place in Dubna on 28 September – 2 October. It was organized by the Russian Academy of Sciences (the Scientific Council of RAS on radiobiology and SRC RF – Institute for Biomedical Problems), the Joint Institute for Nuclear Research and the Branch of the Skobeltsyn Institute of Nuclear Physics MSU. More than 100 physicists and radiobiologists from Russia, JINR, many European countries and the USA participated in the Colloquium. The main scientific objects of the Colloquium were:

- the radiation environment on the lane Earth–Mars–Earth and on the Martian surface;
- the radiobiological effects of the astronauts exposure (substantiation of the space radiation protection rules);
- the physical and methodical aspects of the radiation protection of the Mars mission crew.

The COSPAR Working Group meeting took place within two days after the Colloquium end.

Forty-six students in sum are studying now on specialty «Radiation Protection of People and Environment» at the chair «Biophysics» of the International University «Dubna». Besides the present specialization «Radiation Biophysics», a new specialization «Biophysics of Photobiological Processes» was established at the chair in 2003.

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