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RESEARCH PROGRAM OF THE DIVISION OF RADIATION AND RADIOBIOLOGICAL RESEARCH: ITS PERFORMANCE IN 1997 AND THE PROGRAM FOR 1998

Report to the 83rd Session of the Scientific Council of JINR
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1. Scientific research plan for 1997

Major lines of the program in 1997 were concentrated on:

- development of the experimental equipment and measuring techniques;
- improvement of the calculation methods of radiation interaction with matter and radiation transport through the shielding;
- response radiation detector study;
- radiobiological investigation of the regularities and mechanisms of the mutagenic action of ionizing radiation with different LET on pro- and eukaryotic cells;
- investigation of biological effect of low doses of ionizing radiation on human peripheral blood lymphocytes and plant cells;
- development of the biosensor method based on the SOS-lux test.

2. Execution of the 1997 plan

2.1. Radiation researches

Radiation researches were connected with neutron detector study, neutron spectrometry, physical support of the radiobiological experiments at JINR facilities, metrology of dosimetric measurements and development of mathematical models of radiation induced effects.

In accordance with the protocol of the collaboration between the DRRR and Radiation Biophysics Lab of the US National Aeronautics and Space Administration (NASA) it was proposed to *irradiate the biological samples with protons of energies from 1 to 9 GeV for investigation of cytogenetic damages in human lymphocytes and study of oncogenic transformation of mammalian cells*. The design a system of monitoring instruments for physical support of these investigation was begun. The first trial irradiation of lymphocytes was carried out at LHE Synchrophasotron in the end of October 1997. Part of irradiated samples will be mailed to the NASA for chromosome analysis with the FISH technique and RBL transformation analysis, and part of them will be examined in DRRR.

Measurements of the neutron spectra from thick target irradiated with 3,65 GeV protons by the multisphere Bonner spectrometer and the spectra unfolding by the

statistical regularization method were carried out to investigate secondary particle production and yield of neutrons in nucleus-nucleus Interactions. The goal of this investigation is estimation of radioactive waste transmutation cross-sections.

The systematic measurements of the radon-gas concentration in air and water in environment and JINR buildings were continued by the PRASSI radon surveyor and nuclear track detectors from IPCM (Bratislava). It was established that radon-gas does not appeared in any considerable concentration in air of JINR nuclear facilities dwellings and depositories of radioactive isotopes. The levels of radon-gas concentrations in environment were also small.

The works for systematic study and optimization parameters of neutron detectors assemblies for the nuclear safeguards unattended radiation monitoring were finally completed and the main results were published. In the framework of these investigations were done:

1. the experimental optimization of the polyethylene moderators around a thermal neutron detector;
2. the comparative testing of different types gases counters in neutron fields with very high gamma-radiation background (Pu-Be source and ^{60}Co medicine installation with dose rate up to 2 kR/h);
3. the optimization of electronic parameters and shielding of counter.

The improvements of the codes for hadrons and ions interaction with nucleis, thick targets and radiation transport through the shielding (calculations by Monte-Carlo method and numerical solution of kinetic equation) were in progress. The technique and corresponding codes for optimization of detector's set for neutron spectra measurements was developed.

160 individual dosimeters provided by 20 participants of the *IAEA Co-ordinated Research Programme "Intercomparison for Individual Monitoring of External Exposure from Photon Radiation"* was irradiated at the JINR calibration facility. The Programme of the work was implementation of the Operational Quantity $H_p(10)$ for individual monitoring of external exposure from photon radiation by irradiation of personal dosimeters from the participating dosimetry services. Before the irradiation of dosimeters a check of the irradiating laboratories was performed using a thermoluminescence (TL) dosimetry system of the Physikalish-Technische Bundesanstalt (PTB). TL dosimeters were used for the check of the irradiation facilities. They were irradiated on the ISO phantoms in all the positions that were intended to be used during the intercomparison. The check of the irradiating laboratories focused on comparison of $H_p(10)$ values, stated by the irradiating laboratory for TL dosimeter irradiations, and the corresponding TL dosimeter indications, evaluated at PTB. It was concluded that value of our institute (JINR) agrees with PTB value within 1.5%, so that the check demonstrates the conformity of the irradiating facilities at the JINR and the PTB.

A mathematical model was developed to assay the dynamics of the SOS response induction in Escherichia coli bacteria. Expressions for the dynamics of the level of inducing signal for the SOS system after ultraviolet irradiations were derived, describing the early event in the SOS induction. Also, dynamical equation description of the SOS system was proposed to assay the dynamics of induction of various SOS genes, as part of the integrated SOS response.

The DRRR scientists took part in the IRPA regional symposium on radiation protection in neighbouring countries of central Europe (Prague, Czech Republic, 8-12 September 1997).

2.2. Radiobiological researches

Radiobiological investigations were performed on mammalian cells in culture and human lymphocytes, haploid and diploid yeast, bacteria and plant cells.

In experiments with *mammalian cells* the study *of mutagenic effect* of heavy charge particles was continued. The HPRT-mutants, induced by the different doses of accelerated nitrogen ions (^{14}N) with energy of 50 MeV/nucleon have been revealed and separeted from Chinese hamster cells culture (line V-79). LET of ^{14}N-ions was in average 80 keV/μm. It has been noted the increase of period of mutant subclones growth as compared to intact control, that was more for mutant, induced by the dose of 3 Gy. At the same time they were like both spontaneous and γ-induced mutant on this criterium. An increasing of mutant fraction with the slowest growth can be noted only.

The cytogenetical analysis has shown that HPRT-mutants, induced by heavy ions, were distinguished essentially both spontaneous and γ-induced mutants on some parameters. Unlike them the high level of mitotic activity of such mutants has been noted: mitotic index values were 4-11%, that correspond or even exceed to control level. As it has been shown earlier, γ-induced HPRT-mutants were high heterogenious on many cytogenetical parameters and in particular on chromosomal instability. As it was proved all HPRT-mutants, induced by the doses of 1 and 2 Gy of heavy ions, and some mutants, induced by 3 Gy, had the modal number of chromosomes, equal 22, but the most of spontaneous and γ-induced mutants had modal chromosome number equal 21. Chromosomal spectrum were also narrow as compared to them: the cells with such mode put together about 60-80% untill from 30-40 to 80%. The single mutants among ones, induced by the dose of 3 Gy, had modal chromosome number, equal 21 chromosomes, or were tetraploid ones with chromosome number 42-44.

It has been shown earlier among γ-induced mutants the mutants were separated that did not distinguished on chromosomal aberrations level from intact control (the group I) and the mutants with their higher level (the group II). Also unlike spontaneous mutants among γ-induced ones of the group I the mutants appeared at which the chromosomal aberration level was in 2 times less as compared to control (the subgroup Ia). The mutants, induced by the doses of 1 and 2 Gy of ^{14}N, belong to the group I on this parameter, moreover the greater part of them form the subgroup Ia of mutants with lower chromosomal aberrations level. The mutants of the group II were revealed only after irradiation of cell culture by the dose of 3 Gy. Obviously, after heavy ions irradiation the most full value cells survive in general and among the mutants the most stable ones survive in particular.

For the reported period the *study of the stable and unstable chromosomal abberations in human blood lymphocytes* irradiated by γ-rays and accelerated ^{14}N-ions was continued. As it is known, obvious dose dependence of frequency of such unstable aberrations as dicentrics allow to use its as test for biological dosimetry in acute period after radiation. These aberrations are revealed easy by such standart cytological method as metaphase analysis of the whole cell genome by means of usual light microscoping. FISH-method allow to reveal effectively enough the stable aberrations of individual chromosomes (translocations and insertions), using for this purpose the painted chromosome specific probes. The cells with such aberrations can live in irradiated cell population for a long time. That is why this method allows to use the stable chromosomal aberrations as the test for retrospective assessment of radiation doses. The determination of correlation between these methods can be important in practice for making more precise

of radiation doses and also for forecast of their consequencies.

Earlier we have performed FISH-analysis of the chromosome-1 of human lymphocytes after γ-rays and accelerated ^{14}N-ions. At present the aberrations of the chromosome-2 have been studied also and performed summary analysis for both these chromosomes. The chromosome-1 and -2 are the most big ones in human chromosomal set: they are 16.2% of whole genome (Morton N.E. 1991). That is why they are the most targets in the cells for radiation. As for the chromosome-1 the high level of aberrations of the chromosome-2 was observed also. At all doses it was indentical quantitevely to the chromosome-1.

Besides that the cytogenetical analysis of the cells on the same preparations was performed by standart metaphase method for an assessment of unstable aberrations of whole genome. Analogical type of dose dependence of the frequencies of chromosomal aberrations was shown for both metaphase and FISH-method of analysis: the linear-quadratic dose dependences were observed after γ-irradiation of the lymphocytes, but after heavy ions they became linear ones.

The analysis of correlation for the aberration frequencies, revealed by these two methods, have shown that after ^{14}N-ions radiation in the range of 1-3 Gy the fractions of total chromosome-1 and -2 aberrations, calculated by FISH-method are in average ~ 0.6 from total number of aberrations, revealed by metaphase method, and it increases to ~ 1.2, when the aberrations of both chromosomes are calculated. It was noted also the increase of these values for the least dose (0.5 Gy) to 1.2-1.3 for the chromosomes-1 and -2 and to 2.4, when their summary aberrations were calculated. These data can be evidence, firstly, about appearence of the chromoso- mes-1 and -2 damages with high frequency after radiation and, secondary, it shows on the big deposit of stable aberrations of these chromosomes in total number of chromosomal damages. So, the fractions of translocations and total number of stable aberrations (translocations and insertions), calculated by FISH-method, from total chromosomal damages, revealed by metaphase method, after irradiation by ^{14}N-ions in the doses more, then 1 Gy, were in average 0.14-0.18 for the chromosomes-1 and -2 and ~ 0.3 for summary calculation for both chromosomes. Moreover, after radiation doses less then 1 Gy these correlation values were higher in 1.5 times then after bigger doses. Besides that the translocation frequency analysed by FISH-method exceeds more then 2 times the 00 frequency of dicentrics after ^{14}N-ions irradiation and almost in 3 times after γ-rays. This circumstance can testify about the possibility to detect lower doses of radiation using test of stable chromosome aberrations.

The study of *genetic effects of low doses of ionizing radiation* was continued in experiments with mammalian cells. The problem of radiobiological action of low ionizing doses is one of the most important and least studies in radiation biology and medicine. The actuality of this problem is conditioned by the necessity of forecasting of genetic risk of low radiation doses. In present time experiment data are accumulated further. They testify to unevenness of extrapolation of high doses action to low doses action. The difficulties of low doses effects estimation are connected to complication of getting of statistically reliable data at low levels of damages, induced by this doses. The most acceptable criterion for estimation of low doses effects is the frequency of genetic damages in cells, characterised by strong quantitative dependence from absorbed dose.

We have investigated the induction of chromosome aberrations in mammalian cell culture (Chinese hamster, V-79) after irradiation by γ-rays of ^{60}Co in doses 10–300 cGy. It is shown, that in the rays 0–20 cGy the linear increase of the number of cells with chromosome aberrations takes place. At the dose 30 cGy the number of cells with aberrant

chromosomes is decreased sharply, sometimes up to the control level, after that increases linearly with dose, but with less inclination, than at 0–20 cGy. In the dose range 0–20 cGy the number of cells with chromosome aberrations calculated for unit of dose is approximately 1.5 times more, than at 30–300 cGy. We suppose that the high radioresistance of cells at doses more than 30 cGy is the consequence of processes of DNA reparation in cells initiated by low radiation doses. The transition of high radiosensibility to induced radioresistance is probably controlled by the same mechanisms as adaptive response.

In experiments with using of *haploid and diploid yeast* the study of *induction of point mutations in eukaryotic cells* has been continued. A tester system, specifically diagnostic for the six possible base - pair substitutions was used to study γ-induced mutagenesis in yeast *Saccharomyces cerevisiae*. Each strain contains a single, unique base - pair substitution at the Cys-22 codon of the CYC1 gene, which codes for iso-1-cytohrom c. Specific base - pair substitutions, which restore the Cys-22 codon can be monitored simply by scoring for reversion to the "*Yc*" phenotype. These strains reverse spontaneously at very low frequencies and exhibit specific patterns of reversion in response to γ-ray. γ-induced mutagenesis showed a preference for GC → AT transitions and GC → TA and AT → TA transversions. The spectrum of γ-radiation - induced base - pair changes doesn't depend on dose from 125 to 1000 Gy. The dose - response dependence features a linear - quadratic function for each of base - pair substitution.

The second task of this research was connected with study of the genetic control of cell cycle arrest on mutagenesis. As known some of RAD genes appear to encode functions that are involved in the cell cycle regulation in response to DNA damage so called checkpoint control. They are monitoring the integrity of the cellular DNA as well as arresting cell cycle progression after damage to allow time for DNA repair; progression without repair is lethal. It is analog of the SOS-system of E. coli.

We identified at least three additional checkpoint genes. Mutations in genes CDC28, SRM8 and SRM12 increase the sensitivity of yeast cells to ionizing radiation and are involved in epistatic interactions with a mutations in a well known checkpoint genes RAD9, RAD24 and RAD53 . It is known that disruption of the checkpoint control mechanism is accompanied by increased rates of chromosome loss. We found that mutation cdc28-srm decrease stability of chromosomes. The frequency of spontaneous gene conversion in mutant cells was found to be about one order of magnitude higher than in wild type cells, however there was no difference between cdc28-srm mutant and non-mutant strains as regards the frequencies of spontaneous point mutations.

The study of *deletion induction mutations in bacteria* was started by using a special test-system that based on the two flanked genes TonB (the resistance to bacteriophage T1 or f80vir and colicine V and B) and tryptophane auxotroph. The optimal conditions for measurements of TonB mutant were chosen. The initial experiment with g-radiation has been started.

In experiments with *Lux-test bacterial cell* the dependence of the light output on the incubation time of DNA repairs wild type cells after UV- and g-irradiation has been studied. The kinetics of the light output reflects the SOS response of cells on the damage of DNA which is induced by radiation. It was shown that the kinetics of the light output depends strongly on the temperature of incubation. The temperature 30^0 C is more optimal for realization of the bioluminescent reaction. The stabilization of temperature conditions during the measurements is very important for the reproductivity of results. The growth conditions influence on the light output of irradiated suspension. The difference of kinetics

for the samples with and without shaking reflects in a longer Lag-phase of the samples without shaking. The kinetics of growth of cells under various conditions differ after irradiation with different doses. The new repair deficient strains were constructed using cell transformation. SOS response depends strongly on the repair genotype of the bacterial cells. The umuC mutant is more sensitive to UV- and g-radiation than DNA repair wild type cells. A higher SOS response than in DNA repair wild type cells after low doses of UV can be observed in two repair deficient mutants: AB1886 (uvrA) and TK610 (uvrA umuC) cells. The photoreactivation effect in uvrA mutant and in DNA repair wild type cells was studied. It was shown that the ability of the uvrA mutant to photoreactivation depends on the UV dose. Such an effect was not seen in experiments with the wild type cells.

In experiment with *plant cells* the *influence of low doses of g-radiation* has been studied. Pea seeds (*Pisum sativa*) were exposed to g-radiation (^{60}Co, dose 7Gy) at different dose rates (from 0.3cGy/h to 19.1 cGy/h). Mitotic activity, number of cells with chromosomal aberrations (CA) and adaptive response (acute dose 50 Gy) in first mitosis anaphases of the meristematic cells of rootlets were examined. At dose 7cGy the radiation hormesis was identified at the dose rate 1.2cGy/h. At dose rate 19.1cGy/h damaging effect and decrease in the mitotic activity were observed. At the increasing of the dose rate the adaptive response is better expressed. The level of the adaptive response correlates with the radioresistance of the seeds. It was shown that the adaptive response is absent at the dose rates corresponded to the radiation hormesis.

Radiobiological experiment with radionuclides has been started for the reporting period. As known, *targeted radiotherapy* is defined as a treatment selectively directed at a particular tissue, most often neoplastic, by using either radioisotope exhibiting a high affinity with this tissue or a compound with such affinity used as a carrier for a suitable radioisotope. It is known a high affinity ob methylene blue (MTB) to melanin synthesized in the tumour cell of pigmented melanoma. The effects of ^{211}At-MTB on the survival of human melanoma cells in vitro were investigated. ^{211}At is an α-particle emitter characterised by $T_{1/2}$=7,2h., LET=99kev/mkm and maximum RBE. It is shown that efficiency of ^{211}At-MTB is the order higher than the efficiennncy off nonorganic ^{211}At.

3. Proposals for 1998-2000 are:

Radiation researches in the frame of the program will be connected with the following directions:

a) *Neutron spectrometry.* It is propose to take part in measurement of the neutron spectra (in energy range from 10^{-8} up to hundreds MeV) generated in thick target by the high-energy protons. These measurements will be performing by the multisphere Bonner spectrometer and activation detectors' technique. The unfolding of the neutron spectra from the spectrometer readings will be carrying out by the statistical regularization method. The improvement of the code for neutron spectra unfolding is planned.

b) Shielding Studies. It is planned to carry out shielding experiments at the U-400M cyclotron. Investigation of mixed radiation fields behind shield of proton and heavy ion accelerators at the JINR with application to verify shielding calculation methods. Integral and differential quantities of the fields will be measured. In the frame work of the programm it is also intended: to develop methods and calculate neutron production (neutron yields, angular and energy distributions) generated by heavy ions in thick targets with application to radiation protection.

c) Physical Support of Radiobiological Experiments and Physical Modeling of Radiation Induced Damage. It is proposed to develop and design a system of monitoring instruments for physical support of the radiobiological investigations on the beams of particles with various LET. These systems will be created at JINR accelerators (first of all, at LHE synchrophasotron) and will include the beam monitors (ionization chambers, scintillation counters, etc.), the instruments for beam compositions and lateral distributions study. This work is especially important in view of settlement in 1997 of the agreement on the collaboration between DRRR and Radiation Biophysics Lab NASA. It is planned to irradiate the biological samples with protons of energies from 1 to 9 GeV for investigation of cytogenetic damages in human lymphocytes and study of oncogenic transformation of mammalian cells. It is also planned to carry out modeling of the radiobiological effects obtained in experiments which are planned at the JINR (see chapter "Radiobiological Research"). Methods of micro- and nanodosimetry will be developed and used.

d*) Response Detectors Study.* It is planned: to study the response of individual dosimeters in reference neutron fields developed at the JINR to investigateresponses of thermoluminescence detectors, nuclear track detectors and bubble damage neutron detectors. The DRRR will be continue the works in the frame of the IAEA Coordinated Research Program on intercomparison for Individual Monitoring of External Exposure from Photon Radiation.

The main objectives of the **Radiobiological research** will be connected with:

- study of the peculiarities and mechanisms of mutation induction in mammalian cells, stable chromosomal aberrations in human lymphocytes using FISH technique,
- induction of point mutations in haploid and diploid yeast, deletion mutations in bacteria under the radiation with different LET;
- investigation of biological effect on mammalian and plant cells under low doses of ionizing radiation;
- the development of methods for target therapy of pigmented melanoma by using complex "methylthyonin chloride - alpha-emitters".

a) Mutagenic Action on Mammalian Cells. The goal of planed investigations are the study of peculiarities mutation induction in mammalian cells exposed to radiation with broad region of LET, RBE assessment by the criteria of mutation induction, study of molecular nature of mutations in cells exposed to radiation with different LET. The objects of investigations are peripheral blood lymphocytes of human beings and V79 line, B11-d-ii-FaF28431 clone of Chinese hamsters cell cultures. An important part of the project is concerned with the research on peripheral blood lymphocytes of human beings for the analysis of stable chromosomal aberrations induction using FISH-method. The peculiarities of induced mutations in HGPRT locus of Chinese hamster cells are going to be studied.

b) Mutagenic Action of Radiation on Yeast Cells. The objective of this research is the estimation of point mutation induction in eukaryotic cells. A new test system for detection each of the six base-pair substitutions in Saccharomyces cerevisiae will be used in experiments. The role of *cdc28-srm* mutation in *Saccharomyces cerevisiae* radiation mutagenesis will be studied.

c) Determination of Deletion Mutations in E.coli Cells. The objective of this work is connected with research of peculiarities of deletion mutants induction in bacteria by ionizing radiation with different LET. The program of the research includes the following

directions: investigations of forward mutants induction in bacteria irradiated with γ-rays and heavy ions; the study of deletion mutant induction in bacteria irradiated with γ-rays and heavy ions; blot-analysis of the mutant clones induced by γ-rays and heavy ions; investigations of deletion mutant induction in repair deficient cells.

d) Biological Effects of Low-dose Exposure. The biological effects of low-dose exposure will be investigated in the frame of the program. We assume to perform investigations on genetic consequences under low doses irradiation action on plant cells and mammalian cells (Chinese hamster). By the cytogenetic criteria the effectiveness of the influence of low doses will be taken into account.

e) Radiobiological experiments with high energy protons. Inaccording with the agreement between DRRR and Radiation Biophysics Laboratory (RBL) NASA Johnson Space Center (Houston, USA) the radiobiological experiments in the study of cytogenetic damages in human lymphocytes and oncogenic transformation of mammalian cells after proton irradiation with energies from 1 to 9 GeV are planned. Part of these fixed samples will be mailed to RBL for chromosome analysis with FISH technique, and part of these samples will be examined in DRRR. Data from these samples will be compared and shared between RBL and DRRR.

f) The development of methods for target therapy of tumors. As known, the pigmented melanoma cells contains the specified pigment melanin having the high selective affinity to methylen blue. This make a possibility to transport different alpha-emitters into tumor cells without damage of the normal cells. Taking it into account the technique on theconstruction of different complexes of "methylen blue - alpha-emitters" will be developed. The testing of this selective method in vitro and invivo will be carry out by using the normal and tumor cells.

4. International cooperation

The work under the project will be done in close collaboration with specialists from Austria, Bulgaria, Czech, Germany, Mongolia, Poland, Romania, Slovakia, Yugoslavia, CIS countries and Russian scientific Institutes. The profitable collaboration between the NASA and the JINR has a great role for international co-operation in the frame work of this project. DRRR maintains extensive contacts with IAEA.

5. Scientific meetings

In cooperation with UNESCO and different Institutes of Russia the International Symposium of Biochemistry, Radiation and Space Biology on the 90-th anniversary of the Academician N.M.Sissakian was held in Moscow and Dubna from 22 to 25 January 1997. There was a plenary meeting of Presidium of Russian Academy of Sciences before opening the Symposium. The scientific program of the Symposium included three sessions: biochemistry, radiobiology, space biology and medicine on which were presented about 70 reports.

The International Conference on Nuclear Medicine Problems and First Congress of Russian Society of Nuclear Medicine was conducted on July 9-12, 1997 in Dubna by Russian Society of Nuclear Medicine and JINR. The scientific program was to cover the following major topics:

- radionuclide methods in clinical diagnostics and therapy;
- methodological problems of application of radionuclide and other methods (NMR, USN, etc.) of diagnostics and treatment;
- problems of radiopharmaceutics, radiochemistry, and radiopharmaceuticals quality control;
- practical organization of nuclear medicine;
- nuclear medical equipment and dosimetry;
- training and professional level increase.

The exhibition of up-to-date nuclear medical equipment and preparations manufactured by Russian and world leading companies was held during the Congress.

The International Workshop "The basic JINR nuclear facilities, nuclear medicine and radiobiology" was held in Dubna on 1-2 December 1997.The goal of the workshop was to discuss the opportunities of medical radionuclides and new perspective radiopharmaceutical preparations productions on base of the JINR nuclear and radiochemistry facilities. The specialists from CERN, Poland, Czech, Hungary and various scientific organizations of Russia were attracted for the discussion. As a result of the workshop the memorandum was accepted. The main purposes of the memorandum are:

- to establish the Programme Advisory Committee on Nuclear Medicine and Radiobiology at the JINR;
- to join efforts of the JINR specialists in oder to develop and produce a new radiopharmaceutical preparations (RP) in the frame of the special research project;
- to develop together with Institute of Medical and Biological Problem investigation on space medicine;
- to develop the cooperation between CERN and JINR (including ESI);
- to make more active the works on produce of RP based on ^{211}At - methylen blue.

6. JINR University Center

In 1997 year the process of student training in the University Center on the specialty "Radiobiology" (holder of the chair Prof. E.A.Krasavin) was successful. Three students were graduated from the chair in the early 1997. Eight of specialists graduated the chair since 1991 have been working as staff mambers of the DRRR and two are post graduate school students.

7. Administrative activity

Personnel. As of 01.01.98 the total personnels of the DRRR are 87, including the direction staff 11.

Finance. Funding of research in the field of radiation and radiobiological research in 1998 is shown in table 1. The DRRR share in the JINR budget is 1.4%. The annual extra-budgetary resources will depend on grants (RFFR, ISTC, ISF, etc.) received by the research groups.

Table 1. Financing DRRR in 1998.

Area	Financing plan (k$US)
08-9-1015-96/2000 (I-st priority)	282.1
Infrastructure	70.4
Total:	352.5

8. Conclusion

The realization of the program makes the JINR reach the world's level of radiation monitoring and in some fields of radiation protection even to surpass such world level. It will also receive the basic experimental and theoretical data which can be used for the estimations of risk involved with ionizing radiation.