

Referee report on: Research on the Biological Effect of Heavy Charged Particles with Different Energies - Theme 04 - 9-1077

Scientific merits and intellectual contribution:

Presented notable theme studies of accelerated heavy charged particles are a powerful tool for addressing fundamental issues of modern radiobiology and genetics for solving radiation medicine problems. Radiation therapy with proton and carbon ion beams is one of the most efficient ways of treating hard-to-reach malignant neoplasms — in particular, brain tumors. Report of research and significance in the presented proposal of the project is also innovative in the soundness of the challenge in radiation risk for the interplanetary manned human flights. The concept of radiation for the crew is dangerous under the action of heavy nuclei of the galactic cosmic rays on the central nervous systems structures. This damage is based on two facts: (1) exposure cause changes in the higher integrative functions of the brain – leads to disorders in crew's operational performance; (2) in the simple fact is, that interplanetary flights will be under threat by cosmic radiation and will be not completed with success. The main fields of space radiobiology research call for changes in all experimental systems. The working out new radiation safety standards for space flights is now the future of new experimental design in this research field. The presented theme is based on results from the previous research theme, continues in these studies and wide- spreads them.

The project is based on the insights gained from molecular genetics and applications of resolved problems during the risk estimation. Designed experimental advance requirements, of planned experiments, are real, clear, and are exactly explained in the application form of the funding of the project. The solvers managed to group of precious specialists in the field of molecular radiobiology, radiation genetics, cytogenetics, and physiology. They continue with the specialists from the fields of molecular radiobiological aspects of radiation therapy and the mathematical modeling of radiation based on the induction of radioactive effects. In the end, researchers in the presented group will plan to improve acceleration-based radiobiological experiment procedures, which are the main in the LRB's participation in the design, fabrication, testing, and calibration of nuclear science instruments - the necessary part of such research. In this case, the project meets all the required funding criteria.

Technical feasibility of the project within the proposed timescale:

Modern research of such a problem requires a wide range of the main methods from molecular biology and the methods of condensed matter physics, as it does the Laboratory of radiobiology in the JINR. The project considers all planned participants, experiences of the research group related to planned years are on the excellent level and coordination by the JINR organization is the right choice for evaluating proposed radiobiological studies among all participated institutions. The availability of a wide range of radiation sources at JINR's basic facilities, including heavy ion beams of different energies, offers a unique opportunity for researching in these fields. Special focus will be placed on new ways of increasing the biological effects of radiation therapy with charged particle beams and the analysis of damage to experimental animals' central nervous system to estimate the radiation exposure risk to crews on interplanetary flights and to take into account the possible side effects of the radiation therapy of malignant neoplasms.

The methodology of the proposed project is convincing in showing the main fields of research within the frameworks of the theme as of regularities and mechanisms of molecular, cell, tissue, and system of the human organism damage.

The data collection strategy, potential sources of information, data accessibility and methods of molecular biology, genetics, pharmacology, neurogenesis, morphology, and radioprotection during the research of the heavy charged particles of the induction the damage in genetic

structures of prokaryotic and eukaryotic cells (mammalian and human cells) planned in this project, are really clear and project depicts a developed strategy of meaningful results collection. The authors list the expected results in the next years, which are well formulated and realistic based on the previously reached results.

Compliance of the requested financial resources with the project objectives:

Presented project approach experimental evidence of the radiation damage is formed and contain has the required character and requested funding is realistic for the estimated budget.

Availability of adequate human resources at JINR and in the collaborating institutions:

The human resources of the laboratory are in the good age group with adequate experiences and past achievements in this research field, which were demonstrated by scientific result competences. The investigative model, tools, and methods of the project could resolve this part of the problem and the scientific and technical impacts of this research will require future independent researches based on using JINR's basic facilities. It includes clear overall responsibility of all staff resources for the activities, includes a problem-solving mechanism in the event of assignment experiments between partners including JINR and from the other university or institution, which expressed their interest in the joint studies within the proposed project.

The extent of the project realization is based on the practicable plan for basic and applicative research of all cooperating organizations.

STRENGTHS of the project:

- The veracity of data obtained, and the reliability of conclusions drawn from ground-based studies using model organisms will benefit substantially from accurately simulating combined exposures under heavy ions sources.
- These needs to be delivered in an acute dose regimen, reaching information could be utilized in an integrated fashion to complement and more completely describing the physiological observations.
- The planned timetable, the balance between the time frames and costs, description of the work plan, benefits for JINR arising from this activity are determined clearly.
- The study of the radiation level risk is also meaningful for the use and application of institutional experimental facilities, as it regards obtaining the worldwide level of the research results at JINR.
- No factual errors were found, were no found discriminatory comments. Partners are capable to fulfil tasks from stated periods and the presented proposal is precisely elaborated.

WEAKNESSES of the project:

- The upgrades and constructions of sources could limit the number of JINR-based experiments. A delay in the commissioning of applied research channels at the sources complex may slow down part of the project. But these possible problems don't reduce the quality of the evaluated project.

Within the five usually, limits (Excellent, Very Good, Good, Fair, Poor, and Proposal fail), the evaluation of the project is on an excellent level. The continuation of this topic will generally purvey the solved project criterion, and relevant aspects with the continuation of full financing of the required amount of this theme are recommended.

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