



University of Naples Federico II

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**PREPARATORY STUDY OF
INVESTIGATIONS INTO BIOLOGICAL
EFFECTS OF RADIATION**

Abstract

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Most of our knowledge on the biological effects of cosmic radiation is based on experiments performed at accelerators. Data from the Bevalac (Berkeley), GSI (Darmstadt), HIMAC (Chiba), and the NASA Space Radiation Laboratory (NSRL) at the Brookhaven National Laboratory (Long Island, NY), provide the basis of our current knowledge of the harmful health effects of energetic heavy nuclei. The results from the experiments are used to define the quality factor of space radiation, both in low-Earth orbit and in deep space. The quality factor is then used to scale our knowledge of radiation risk on Earth to the space environment.

Risk estimates are, however, subject to large uncertainties. The major sources of uncertainty come indeed from the lack of detailed knowledge of the biological effects of energetic heavy ions, especially at low dose and low dose-rate. In some cases, there is evidence for “unique” effects of heavy ions, and these examples challenge the models that use quality factors to scale risk on Earth (low-LET) to those in the deep space (high-LET) environment. NASA has long acknowledged that radiation risk represents the major showstopper for manned exploration and colonization of the Solar system. NSRL in Brookhaven was in fact totally funded by NASA (approximately 34 M\$ for construction, plus 5 M\$/year as running costs) to address some of the open research issues, especially to reduce uncertainties on the risk estimates. NSRL is currently supporting a large research program in the field, and NASA research funds (through NRA and NSCOR programs, for an investment of approximately 36 M\$/year) are attracting top-quality research groups in USA coming from different fields to undertake biological research in the field of space radiation effects. Results flowing from NSRL are certainly contributing to reducing uncertainties and developing effective countermeasures, but it is clear that many questions remain open. Greater involvement of the International community is needed, especially with the goal of developing effective countermeasures before sending a manned mission to Mars, which hopefully will occur in this century.

A *European Accelerator-based space Radiation biology Program* (EARP) has been devised to support safe human exploration of the Solar System and is described herein. *EARP should develop the database and the knowledge required by ESA to accurately predict and to manage efficiently radiation risk for manned interplanetary missions.* The knowledge will be acquired by means of a peer-reviewed, ground-based, and investigator-initiated science research programme. This knowledge should lead to countermeasures to prevent, mitigate, or ameliorate deleterious effects of space radiation. The ultimate goal of EARP should be

- *to allow human colonization of the Moon and exploration of Mars within the year 2020 with acceptable risk from exposure to space radiation*

The research program should provide the essential inputs for

- *risk assessment for exploratory-class missions beyond low-Earth orbit*
- *countermeasures to allow a safe and stable human presence on the moon and planets other than Earth*

The first phase of the EARP (2008-2012) should concentrate on basic research questions, to improve our knowledge of the biological effects of space radiation to reduce the risk uncertainties. During the first phase, we propose to issue either an “open research announcement”, basically investigator-initiated and covering a wide number of research fields of interest for exploration; or, a few “thematic research calls”, with well defined goals and activities to be performed.

For an “open research call”, EARP should give preference to projects with the following characteristics:

- *relevance for protection in interplanetary missions*

- *studies that guarantee a practical impact on radiation risk reduction within a reasonable time frame*
- *existence of a strong competence in Europe*
- *complementarity to NASA programs or, conversely, strong interaction and collaboration with ongoing NASA-supported experimental studies*
- *possible spin-off in hadrontherapy*

For thematic calls, three high-priority research topics were identified:

- *noncancer risk from space radiation exposure*
- *acute effects from solar protons and their mitigation by physical and biomedical countermeasures*
- *combined effects of cosmic radiation and other stressors in space*

Although Europe already has several accelerators with ongoing activities in the field of charged-particle radiobiology, space radiation research has some peculiar characteristics. Requirements are different from studies targeting hadrontherapy (H- and C-ions at energies between 200-400 MeV/n) or radiation protection on Earth where, in addition to γ - or X-rays, studies on charged particles concentrate on slow He-ions (α -particles) or neutrons and their recoils (slow protons). For space radiation research, HZE particles are the most important projectiles. The only European facility that can provide these beams, and has also suitable laboratory infrastructures for the program, is the GSI in Darmstadt (Germany). The SIS accelerator at GSI can presently reach energies around 2 GeV/n for ions from H to U. Additionally the low-energy UNILAC facility at GSI is equipped with a microbeam, which can address the issues of single-ion traversal effects, of particular relevance for space travel.

Although GSI is recommended as the principle centre for the future ESA-supported ground-based program, it is unlikely that a single facility will be able to host the entire European program. The involvement of a second facility is recommended, especially in the particle energy range 20-100 MeV/n which is not covered by the SIS and UNILAC accelerators at GSI. GANIL, in France, has the potential to be a second support facility for the program. GANIL provides beams of light and heavy ions with energy up to 95 MeV/n and has recently invested in an excellent support radiobiology laboratory (LARIA) available to external users.

The available experimental supporting infrastructure in GSI and GANIL are excellent. However, they may be insufficient to host a large scientific program involving several research groups. For instance, the NASA Space Radiation Health Program is currently funding over 70 research programs, with a load of 100-200 external investigators and approximately 1,000 beam hours at the Brookhaven National Laboratory per year. Even assuming that the European program will be smaller than that of the US, support within the facilities in terms of rooms, office, and laboratory space for external users appears insufficient. It will be necessary to allocate some resources, perhaps around 20% of the budget, to local support at the facilities, in term of materials and manpower to assist external users in preparing their experiments according to the local regulations for safety etc. In addition, the animal facilities at GSI and GANIL should be improved to accommodate external users willing to perform in vivo experiments, which are certainly very relevant for the program.

Several new medical accelerator facilities are currently under construction in Europe. Most of the beamtime will be used for therapy, and as a consequence it is unlikely that any of them will have beamtime available for space radiation research. However, ESA should follow the progress of the new facilities, especially considering that experiments involving patients treated with protons or heavy-ions can be an important source of information for the space radiation program. A special opportunity for future ground-based space radiation research is offered by the Facility for Anti-proton and Ion Research (FAIR), the new synchrotron currently under construction at GSI with a

price tag now fixed at 1187 M€. FAIR will be the largest world accelerator for nuclear physics, and a beamline dedicated to radiation biophysics is already planned, under the supervision of the same group running the biophysics program at GSI since many years. FAIR will start operation in 2012 with very high energy (around 10 GeV/n) heavy-ion beams, state-of-the-art technologies for beam delivery and dosimetry, new support infrastructures, and significant levels of beamtime available for space research. *A formal expression of interest from ESA to the FAIR steering committee to be included among the “observers” is strongly recommended.*

Finally, the roadmap to reach the EARP goals can be summarized as follows:

- *to support a ground-based radiobiology program using, in the first phase, high-energy charged particle beams at SIS- GSI (Germany) and LARIA-GANIL (France)*
- *in phase-II, to exploit the capabilities of the new FAIR accelerator at GSI*
- *to create a strong link between ESA-EARP and NASA-SRHP in order to develop common strategies and to reach common goals*
- *in phase-III, to test results and predictions of EARP in spaceflight experiments, including robotic precursor missions*

Most research topics relevant for space radioprotection are also important for charged-particle cancer therapy (hadrontherapy). Although the type of exposure is very different in therapy (partial-body, high-dose, fractionated irradiation) and space travel (whole-body, low-dose, chronic exposure), many open questions are the same: for instance, carcinogenesis is a concern both for astronauts involved in long-term missions and for patients cured in young age (secondary tumors); individual sensitivity is a major issue both for crew member selection and individualization of treatment planning; radioprotectors are useful both in space travel and during the therapy course; and so on. Hadrontherapy may represent a major spin-off of space radiation research in the field of public health. Because Europe is leader in the field of hadrontherapy, emphasis should be given to research topics of interest for both disciplines.