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NASA SPACE RADIATION SUMMER SCHOOL FOR RESEARCH

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Abstract

The major goal of NASA's space radiation research is to enable the human exploration of space within acceptable risks. Space radiation from galactic cosmic rays and solar particle events is distinct from common terrestrial forms of radiation because it is composed of very high-energy protons and heavy ions, as well as secondary radiation produced in shielding and tissue. Space radiation risks of concern include carcinogenesis, acute and late risks to the central nervous system, degenerative risks such as heart disease and cataracts, and acute radiation syndromes. As there are no human epidemiological data for these radiation types, risk estimation must be guided by mechanistic understanding based on radiation physics, and on molecular, cellular, tissue, and organismal radiation biology related to cancer, the central nervous system effects and other effects. NASA is working with Brookhaven National Laboratory to learn more about the possible risks to human beings exposed to space radiation. A US\$34-million NASA Space Radiation Laboratory (NSRL) has been established at Brookhaven to study the radiobiological effects using beams of accelerated ions that simulate the cosmic rays found in space, including HZE ions such as 1000 MeV/nucleon Fe ions. Research is performed by investigators throughout the US and abroad. The NASA Space Radiation Summer School (<http://www.dsls.usra.edu/spacerad>) is designed to provide a "pipeline" of multidisciplinary researchers to tackle the challenges. The Summer School is co-sponsored by NASA's Space Radiation Research Program, Brookhaven National Laboratory, and Universities Space Research Association. The three-week course, which has become increasingly competitive, is open to graduate students and postdoctoral fellows with an interest in radiation biology. Foreign nationals and U.S. citizens may apply and past participants have come from around the world. This concentrated program is taught by leading university and national laboratory biologists and physicists actively engaged in NASA space radiation research and BNL experts in heavy ion experimentation and methods. Each "professor" lectures on his/her research specialty with topics ranging from DNA damage/repair, to mutagenesis, epigenetics, signaling, systems biology, carcinogenesis and late degenerative effects following exposure to space radiation, as well as the space radiation environment, physics and biochemistry of charged particle interactions, track structure, dosimetry, accelerator operations and space radiation protection. The Summer School contributes to NASA's research program on the health risks of space radiation, to research in related areas of science (such as mechanisms of carcinogenesis and new developments in heavy particle radiotherapy) and to broadening research and educational collaboration worldwide.

I. SPACE RADIATION AND RISK

When astronauts venture beyond the atmosphere into space, they are exposed to substantially enhanced levels of ionizing radiation from a wide variety of high-energy charged particles. Most of these types of radiation are not experienced on earth and they may act fundamentally differently on biological systems. Space radiation arises primarily from three sources.

-- Firstly, some of the protons and electrons from the solar wind are contained as 'trapped radiation' within the earth's magnetic field.

-- Secondly, solar particle events (SPEs) are composed predominantly of low to medium-energy protons, but include also energetic electrons, alpha particles and heavier nuclei. SPE are injected by the sun into interplanetary space and can be accelerated to near relativistic speeds by the interplanetary shock waves which precede fast coronal mass ejections in the vicinity of solar flare sites.

-- Finally, galactic cosmic rays (GCR) originate from outside the solar system; they consist of atomic nuclei ranging from protons up to uranium travelling at up to relativistic speeds.

As if this weren't enough, in addition, a wide variety of secondary particles, including high energy neutrons and lower-energy nuclear fragments, are produced by interactions of the primary charged particles with matter, such as a spacecraft and human tissue. Although the flux of the GCR is very low, the particles travel close to the speed of light and the heavy elements, such as the abundant iron, produce intense ionization as they pass through matter. In low earth orbit, the Earth's magnetic field provides substantial shielding from the GCR, but they have free access over the polar regions, where the magnetic field lines are open to interplanetary space. In deep space, exposures to astronauts from GCR and SPEs are a critical challenge for space exploration, carrying risks of both delayed and acute health effects.

Most of the components of space radiation are not present on earth and consequently there is no human experience of such exposures on which to base direct estimates of risk for astronauts. For terrestrial human populations, estimates of radiation risk are obtained from epidemiological studies of health effects in large cohorts of people exposed to relevant sparsely ionizing radiations, particularly gamma rays and X-rays, such as from the atomic bombs in Japan and from medical exposures^{1,2}. Cancer has been recognised as the health effect of main concern. Experimental studies have shown, however, that high charge and high energy (HZE) nuclei, such as in GCR, produce both qualitative and quantitative differences in biological effects compared to terrestrial radiation, leading to large uncertainties in predicting exposure outcomes to humans in space, in respect of cancer and also other health effects.

Uncertainties in estimating health risks from GCR are a major limitation to the length of space missions and the evaluation of potential methods of risk mitigation. Radiation risks include carcinogenesis³, degenerative tissue effects such as cataracts⁴ and circulatory diseases^{5,6,7} and acute radiation syndromes⁸. Other risks, such as damage to the CNS, are an additional concern for HZE nuclei⁹. National Aeronautics and Space Administration (NASA) career radiation limits have been based predominantly on fatal cancer risks. For both low Earth orbit (LEO) programmes and for exploration mission planning, an absolute fatal radiation risk of 3% using the quantity Risk of Exposure Induced Death (REID) is used as criteria for NASA career dose limits, which are applied using age- and gender-specific dose-to-risk conversion factors. In order to protect against uncertainties in the risk projections, the upper 95% confidence interval in the risk projection model is applied for these dose limits¹⁰.

The radiation risks are in addition to the many other stresses and hazards of space flight. The health of astronauts is monitored throughout their lives and much has been learnt from their experiences to date, including from many months spent on missions in low earth orbit. For example, the effect of microgravity on the human body produces easily noticeable changes with the depletion of leg muscle and bone density. With respect to radiation, however, because of the very different environment of deep space and the relatively small numbers of who have flown, the human information is far from sufficient to enable prediction of effects on long missions beyond the Earth's magnetosphere. A mission to Mars would involve the crew spending years, rather than months, in deep space. The intense radiation received from sporadic large SPEs could present a threat of acute radiation effects, which need to be minimized to ensure the success of the mission itself. The risks from GCR are mostly of late health effects, but it is within the current bounds of uncertainty that some, such as leukaemia, could present before a return to earth.

II. SPACE RADIATION RESEARCH

Future NASA missions will focus on exploration at greater distances from Earth and extended stays in space. To ensure that these goals are achieved, NASA's astronauts must be able to perform at peak productivity under even the most daunting conditions. NASA's Human Research Program is dedicated to discovering the best methods and technologies to support safe, productive human space travel. NASA scientists within the Space Radiation Program Element (SPRE) are working to study the impact of long-term exposure to space radiation and to develop countermeasures that may help protect crewmembers from these effects. Although information exists to recommend crew exposure limits and spacecraft design requirements for missions in low Earth orbit, there is insufficient knowledge of the health effects of radiation, the space radiation environment, and countermeasure efficacy to provide recommendations on crew exposure limits and design requirements for extended lunar and Mars missions. Thus, a major focus of the SRPE is basic and fundamental research to expand the knowledge base and reduce the uncertainty inherent in current exposure limits and design requirements. Uncertainty reduction for Lunar and Mars missions must occur on a timeline to support agency goals in vehicle, mission, and crew selections.

The multi-centre programme, implemented through interdisciplinary teams at several research facilities, is led by the Johnson Space Center and includes the Langley Research Center and the Ames Research Center. The major goal of NASA's SRPE is to develop the knowledge base required by NASA to accurately

predict and efficiently manage the radiation risk of human spaceflight. The knowledge base has been built over time and continues to be augmented by a peer-reviewed, largely ground-based research program utilizing the NASA Space Radiation Laboratory (NSRL) at the Department of Energy's Brookhaven National Laboratory (BNL) and the Loma Linda University Proton Treatment Center. Experiments performed at these accelerator facilities mimic conditions of the space radiation environment and contribute to the development of risk models, a greater knowledge of the genetic and other consequences of heavy ions to biological systems and better methods of spacecraft shielding. The majority of the research is performed by peer reviewed principal investigators in academia. The intramural and extramural researchers use the NASA Space Radiation Laboratory at Brookhaven to conduct research using accelerator-based simulation of space radiation. Current investigations focus on learning more about the radiation environments that crewmembers will encounter during long-duration missions to the Moon and Mars and the consequent health risks of these unique types of radiation.

The space radiation research is performed throughout the United States and abroad and in cooperation with other governmental agencies, as well as with non-profit and commercial entities. In addition to the intramural research performed in laboratories at NASA's field centres, a large number of extramural project grants are awarded to individual principle investigators and special awards are made for NASA Specialized Centers of Research (NSCORs), which differ from individual grants in that they incorporate a number of complementary research projects that focus on a single research area. Listings and details of past and current awards are available for inspection at <https://taskbook.nasaprs.com/Publication/index.cfm>. At present about 76 awards are listed as active in 2012. The awards reflect that NASA has identified the following health concerns as its highest research priorities: risk of radiation carcinogenesis from space radiation – increased risk of cancers; risk of acute or late central nervous system effects from space radiation – changes in motor function and behaviour or neurological disorders; risk of degenerative tissue or other health effects from space radiation – other degenerative tissue defects such as cataracts, circulatory diseases, and digestive diseases; acute radiation risks from space radiation – prodromal risks, significant skin injury, or death from a major solar event or combination solar/galactic cosmic ray event that jeopardizes crew and mission survival. This research is also expected to provide a substantial contribution to the scientific basis for eventual development of biological countermeasures

to these risks as appropriate. Because there are no human epidemiological data for these types of radiation, risk estimation must be derived from mechanistic understanding based on radiation physics, and on molecular, cellular, tissue, and organismal radiation biology related to cancer and other diseases.

III. SPACE RADIATION SUMMER SCHOOL

The above multidisciplinary research commitment requires the involvement of a wide range of highly-specialized scientific expertise within NASA and academia. The NASA Space Radiation Summer School (NSRSS) held annually at the U.S. Department of Energy's (DOE's) Brookhaven National Laboratory is designed to provide a "pipeline" of researchers to tackle these challenges of harmful radiation exposure to humans who will travel on space exploration missions. It is based at BNL and co-sponsored by NASA's Space Radiation Research Program, Brookhaven National Laboratory, and the Universities Space Research Association. The three-week course has been offered each summer for the past nine years through an internationally open and increasingly competitive application process.

The Summer School takes place at BNL, on Long Island some 100 kilometres from the city of New York, so that the students can benefit directly from using the NASA Space Radiation Laboratory (NSRL), where most of NASA's charged-particle radiobiology research is carried out by visiting research teams with local expert support from BNL staff. NSRL, a \$34-million facility, jointly managed during a four-year construction project by the DOE's Office of Science and NASA's Johnson Space Center, is one of the few places in the world that can simulate the harsh cosmic and solar radiation environment found in space. The facility, opened in 2003, employs beams of heavy ions extracted from Brookhaven's Booster accelerator, the best in the United States for radiobiology studies. The NASA Space Radiation Laboratory features its own beam line dedicated to radiobiology research (Fig. 1), as well as state-of-the-art specimen-preparation areas.

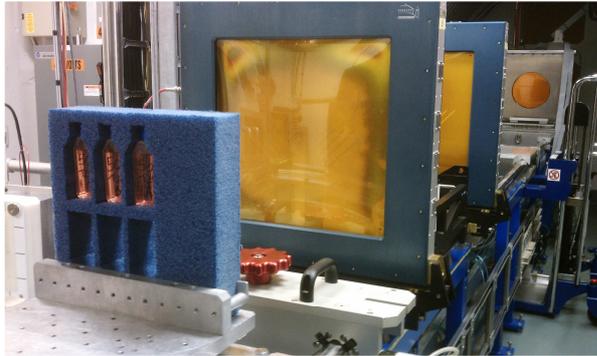


Fig. 1: The NSRL beam-line with tissue culture flasks in position for irradiation with HZE ions.

Protons and heavy ions, accelerated to energies up to 1 GeV/nucleon, are delivered to the experimental area to study the physical interactions and the biological effects. Of particular interest are Fe ions because this is the most abundant ion species from GCR in the space environment apart from the much lighter protons and He nuclei. Dedicated radiobiology and physics experiments are conducted at NSRL three to four times per year, for three to four weeks per run.

Application to participate in the Summer School is open to graduate students, postdoctoral fellows, and faculty with an interest in radiation biology. Both foreign nationals and U.S. citizens may apply. Due to the intense nature of the course, applicants must demonstrate oral and written proficiency in the English language. All selected students must satisfy BNL and DOE safety and security requirements in order to be admitted. Each year, high quality applications are received from around the world, some from those already involved in study or research on the radiation biology or physics of high-energy particles in the context of space exposure, including several already active in NASA laboratories or NASA-funded external projects or in the context of particle radiotherapy. Other applicants are new to the field, but have a keen interest to enter it to expand their knowledge and put it to practical application. The maximum number of students selected is limited to about 18 per year (Fig. 2), to allow optimum use of the facilities at BNL and to ensure maximum interaction amongst the students and with the faculty.



Fig. 2: Summer School 2012, students and a few members of faculty.

Successful applicants have been of many nationalities and from very many different institutes in North America and most other continents. For example, successful students in 2011 and 2012 originated from the USA, Bulgaria, Canada, Egypt, Germany, India, Italy, Japan, Pakistan, Poland, Portugal and the United Kingdom. Applications were received also from Bangladesh, Belarus, Brazil, China, Ecuador, France, Hungary, Ireland, Malaysia, Morocco, Nigeria, Philippines, Romania, Russia, Slovenia, Spain, Sweden and Thailand. Participation in the residential Summer School is at no cost to the students; all needs are provided, including travel within the USA for those based there or from landing at the nearby airports for those from abroad. The annual call for applications is placed annually on the USRA website, and adverted elsewhere, in about November with a closing date in early February for the Summer School to commence in late May and continue into June. The 2013 Summer School is planned for student arrivals at BNL on Wednesday 29 May and to end on Friday 22 June.

This concentrated program is taught by about 30 leading university and national laboratory biologists and physicists, mostly actively engaged in NASA space radiation research, and additional BNL experts in heavy ion experimentation and techniques. Each “professor” lectures on his/her research specialty, with topics including DNA damage and repair, genotoxicity, cell cycle checkpoints and apoptosis, mutagenesis, genomic instability, epigenetics, cell and tissue signaling, immune response, neurodegeneration, systems biology, cataractogenesis, cardiovascular disease and the relationship of these processes to carcinogenesis, late degenerative effects (including cataracts and cardiovascular disease) and acute effects following exposure to space radiation, as well as the space radiation environment, microgravity, physics and biochemistry of charged particle interactions, track structure, dosimetry, accelerator operations and space radiation protection.

The Summer School course starts with a few induction days for administrative procedures and

completion of BNL safety and security training necessary for access to BNL computers, laboratories and accelerators. This is followed by 3 full weeks of intense instruction and practice. The main elements of the schedule are lectures from expert faculty members invited in specifically for the purpose, practical sessions in the cell biology laboratories and on the NSRL beam line with HZE particles, homework exercises and problem solving sessions, team presentations utilizing the experimental results that have been obtained and preparation and submission by each student of a mock proposal for beam time at NSRL. The schedules and faculty lists for recent Summer Schools are available at <http://spaceradiation.usra.edu/>.

The selected students are from many different backgrounds and have followed many different programs of study to reach the point at which they are accepted for this course. For example the biologists are likely to have a limited understanding of the fundamentals of physics and even if they have studied this science beyond high school level they may well have encountered only Newtonian mechanics! Similarly the physicists are not likely to have studied much cell biology. So before they begin to hear the complex topics listed above, they given a crash introduction to the key basics of radiation physics and cell biology.

As well as the physicists, biologists and chemists, the students in recent years have also studied for first degrees in medicine, mathematics, veterinary science and many of the branches of engineering and many have already completed higher degrees. Some of the students are part-way through their PhD course, others are post-docs and a few further along their careers are accepted as 'auditors'. Despite their formidable list of qualifications, the students are very willing to accept the value of brief revision of the basics and this provides a way in which they can all test their strengths and weaknesses in a relaxed and non-challenging environment and learn to complement each other's strengths. They are encouraged to work together to solve the problems set and in this way the teamwork, which plays an important part in the later practical work on the accelerator and in the laboratory, is established.

The students are all provided with accommodation on the Brookhaven site and stay in the hostels or apartments. They are supplied with three mini-vans, with drivers allocated from amongst those students carrying US driving licences. The vans are needed primarily for movement around the large Brookhaven site and also for dining out in the evening when the joys of the local food on site begin to pale. They may also be used to access public transport for excursions into New York or to reach the beaches of Long Island. The wine estates with their sampling, as well as the shopping

outlets of Long Island, also provide popular destinations for light relief during the first weekend and earlier parts of the time at BNL, before the intensity of the course becomes all encompassing. These social excursions add to the bonding that makes the group ready to move forward together.



Fig. 3: Summer School 2011, students with NASA astronaut Michael Barratt, MD, MS.

Apart from the direct benefit of the advanced scientific and technical content of the course, the advantages of such a Summer School include providing the field of radiation research with a group of young scientists who are given the opportunity to see a career path ahead of them, having seen role models whom they can emulate. The Faculty who are invited to deliver the lectures and interact with the students are specialists who have achieved a high measure of success themselves. Their names and reputations are often well known to the students by virtue of their publications and books. The students enjoy their chance of access to these people not only at the end of their lectures but also informally over meals, refreshments or at occasional barbeques laid on in the evening. In recent years, they have also had the opportunity to hear at first hand, and discuss, the experiences of an astronaut as guest speaker at the final banquet (Fig. 3).

The final week of the course is very arduous. Each student has to prepare and present an application to Brookhaven for Beam Time, as if they were proposing a real experiment. They have to fill in all the appropriate paper work explaining and justifying the proposal and specifying its logistics, including all the formal documentation needed as if they were going to transport their live rodents or cells to Brookhaven for radiation and have all the necessary support materials available. The proposals are reviewed by appropriate faculty, who provide verbal feedback on the strengths of each proposal and potential improvements, after its

presentation. Initially this is seen by the students as rather a daunting exercise, but it keeps them asking questions throughout of all the personnel they come across and it provides valuable experience to assist their principal investigators in future applications and for their aspirations to become principal investigators themselves.

As well as the individual beam time proposal, the students in each assigned team have to present the results of the experiments they have undertaken during the course in as novel and exciting a way as they can in a notional scientific context. It is within this endeavour that the true ability of this gifted group of students can be demonstrated. With all the electronic wizardry available to this generation they manage to produce presentations which are beyond all expectations. We were assured by one group this year that they had been 'up all night' filming!

The final day of the Summer School ends on a high note with the drama of the students' team presentations and the subsequent awards of their Certificates of Achievement. The students feel they have made 'friends for life' and, perhaps more importantly, they have found colleagues and research collaborators for life, who will meet up at many subsequent meetings at venues around the world. The shared experience and close co-operation over the three and a half weeks sets the foundation for a professional international multidisciplinary network to enhance their common areas of research and appreciation of other areas, within the bounds of space radiation, radiation therapy, health, basic science and well beyond. One recent student has been heard to say on several occasions since, that it was 'the best three weeks of my life!' 'I got three great research ideas just in the last week of the program', said another¹¹.

For quality control and guidance for the planning of subsequent Summer Schools, as soon as the students have returned home they are sent a questionnaire to obtain their evaluations of the quality, content and depth of each lecture and of the effectiveness of course

activities. The feedback has been very positive and the students provide a range of additional useful comments.

III. CONCLUSION

The Summer School contributes to NASA's research program on the health risks of space radiation, to research in related areas of science (such as mechanisms of carcinogenesis and new developments in heavy particle radiotherapy) and to broadening research and educational collaboration worldwide.

This paper has focused on radiation risks from heavy particles in space, but much of the underlying radiobiology research has relevance also on earth for new modalities of radiation treatment of cancer. Radiotherapy has become increasingly effective with advances in the ability to identify accurately the tumour margins and use the precision of charged particle beams to target the tumour while sparing normal tissue. Additional radiobiological advantages can be achieved by using the intense ionizations of high-energy heavy particles, such as carbon ions, to treat resistant tumours. Proton therapy is now widely available and heavier-ion treatment facilities are already in use or under development in several countries.

The Summer Schools over the past nine years have provided invaluable advanced training in space radiation radiobiology to about 150 young researchers from NASA's own laboratories, from NASA-funded academic groups throughout the USA and abroad and from other institutes concerned with basic radiobiology and the effects of radiation for prevention of risk or for medical treatment. Some of the students have subsequently progressed to become principal investigators in their institutes. Additionally the Summer Schools have contributed significantly to professional networking within the US and internationally. It is intended that the 10th NSRSS, to be held in May/June 2013, will continue in the same vein. Application forms will be on the USRA website in November 2012 (<http://spaceradiation.usra.edu/nsrss/>).

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