
2012 Space Radiation Standing Review Panel

Research Plan Review for: *Risk of Acute Radiation Syndromes Due to Solar Particle Events (SPEs)*

Final Report

I. Executive Summary and Overall Evaluation

The 2012 Space Radiation Standing Review Panel (from here on referred to as the SRP) participated in a WebEx/teleconference with representatives from the Human Research Program (HRP) Space Radiation Program Element (SRPE), the National Space Biomedical Research Institute (NSBRI), and the HRP management (list of participants is in Section VII of this report) on February 21, 2013 to review the Research Plan for the Risk of Acute Radiation Syndromes Due to Solar Particle Events (SPEs) in the Human Research Program's (HRP) Integrated Research Plan (IRP Rev. D).

The SRP appreciated the presentations given by the SRPE and the NSBRI and felt the information presented by the NSBRI Center for Acute Radiation Research (CARR) scientists was interesting and of high quality. An overarching issue of significant concern to the SRP was the general direction of research by the NSBRI with the almost exclusive focus on SPE and not on the issues relevant to long-duration spaceflights, such as the Mars missions. This is not to minimize the importance of the questions being asked, however, the space radiation issues (as well as other health and behavioral issues) are complex, multifactorial and require long-term experiments. While SPEs can largely be predicted and the human impact mitigated, and knowledge gained in these studies does apply, it makes sense to focus much more on the Mars and high energy heavy ions (HZE) issues and to do so quickly. It would be unfortunate if exploration missions outside of low-Earth orbit (LEO) were held up for medical-risk issues because the focus in 2013 was on a shorter-term goal with the longer-term issues being secondary or not considered at all.

The SRP noted several areas of concern: tension between the NSBRI Radiation Effects Team Lead and the NASA Chief Scientist of the SRPE; direction for some of the NSBRI work relative to the needs of NASA including animal models, radiation doses, and others; and an apparent disconnect between the NSBRI and NASA space radiation programs. Based on these concerns, the SRP recommends that NASA establish a group to examine, and if needed to restructure, the HRP SRPE and the NSBRI CARR to provide better alignment of the two programs in order to more appropriately meet the needs of NASA.

II. Critique of Gaps and Tasks for the Risk of Acute Radiation Syndromes Due to Solar Particle Events (SPEs)

Gaps and Tasks:

Acute - 1: Determine the dose response for acute effects induced by SPE-like radiation, including synergistic effects arising from other spaceflight factors (microgravity, stress, immune status, bone loss, etc.) that modify and/or enhance the biological response.

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- The SRP thinks this is a relevant gap.
 - The SRP thinks that the targets for closure and the metrics for interim progress are all very appropriate.

Task:

- Center for Acute Radiation Research – PI: Ann Kennedy, Ph.D., University of Pennsylvania
 - In her presentation, Dr. Ann Kennedy, the Director, NSBRI CARR presented data related to LD50 studies using ferrets exposed to protons and gamma-rays. All the ferrets died after doses of 2 Gy for either type of radiation. The SRP does not think the LD50 studies are appropriate (i.e., is death a realistic risk for an SPE?). Ferrets are used essentially exclusively for vomiting studies because they vomit and mice do not. It is unclear why ferrets are being used in this study. Since all the ferrets died after 2 Gy, their sensitivity to radiation does not appear to be relevant to humans.
 - In her presentation, Dr. Kennedy showed the results of several studies where pigs were exposed to doses as high as 25 Gy and the SRP questions whether such doses are relevant to expected astronaut exposures to SPEs. The paper by Hu et al. (Hu et al. Modeling the Acute Health Effects of Astronauts from Exposure to Large Solar Particle Events. Health Physics 96: 465-476, 2009) models skin exposures from the August 1972 worst case scenario as high as 32 Gy/hr for EVA but 2.7 Gy/hr for inside the spacecraft. According to the presentation by Dr. Francis Cucinotta, the SRPE Program Scientist, the astronauts are expected to receive a one-hour warning of incoming SPEs. Thus, it might be expected that most extravehicular activities (EVAs) would be terminated (hopefully) before the proton flux arrived. Thus, it is conceivable that skin doses as high as 20 Gy might happen but may represent the worst-case and not represent the typical risk. The SRP thinks that these studies should move quickly to examine doses that represent a more reasonable case. Along these lines it may be prudent to also examine what endpoints are appropriate for doses in the 5, to maximum 20 gray range. The current endpoints may not be appropriate at the lower total doses expected.
 - Other relative biological effectiveness (RBE) studies were also mentioned during the presentation and it would have been nice to see these results as they could be relevant. However, for some of these studies, protons of energies of 70 and 110 MeV were used. Although such proton energies might be represented during an SPE, it would be important to use proton energies expected inside the spacecraft. Proton energies will be degraded as they are attenuated in the spacecraft shielding and RBE generally increases as proton energy decreases. The SRP is confident that this has been modeled and it would be useful to know what the expected proton energy spectrum inside the spacecraft will be from a typical SPE.
- Rate Effects and Components of Systems Governing Variations in Susceptibility for Carcinogenic and Acute Radiation Risks following Gamma-Ray, Proton, or HZE Irradiation – PI: Joel Bedford, Ph.D., Colorado State University
 - RBE for White Blood Cell (WBC) Counts is interesting data. The SRP does not think the use of an average RBE of 1.1 is correct. The impact of mitigation with hematopoietic growth factors is critical to understanding what might be needed for

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- spaceflight. What might be interesting is doing another challenge after the animals recover their WBC counts to see if there is any loss of reserve such that a second SPE might be worse than a first.
- The SRP thinks the effect of antibiotic therapy is important (e.g. when to administer it- shortly after infection (day 1) or later when symptoms might set in (say day 2 or 3)) to see how mitigation/treatment might matter.

Acute - 2: What quantitative procedures or theoretical models are needed to extrapolate molecular, cellular, or animal results to predict acute radiation risks in astronauts? How can human epidemiology data best support these procedures or models?

- The SRP thinks this is a relevant gap.
- The SRP thinks that the target for closure and the metrics for interim progress are all very appropriate.

Tasks:

- Patterns of Energy Deposition by HZE Particles in Cellular Targets – Task completed
- Space Radiation Risk Assessment Project – PI: Francis Cucinotta, Ph.D., NASA Johnson Space Center
 - No specific comments on the data. Increased use of clinical proton therapy may allow for a late effects database. Single dose experiments may not be representative (was pointed out during presentation) so some of the acute effects may have more consequences after a second SPE on infection and bleeding.
 - The SRP noted the outstanding productivity of Dr. Cucinotta’s team and concluded that the work done with space radiation risk assessment is highly relevant to NASA interests.

Acute - 5: What are the optimal SPE alert and dosimetry technologies? (Closed. Technology maturation transferred to Advanced Exploration Systems)

Tasks:

- Lunar EVA Dosimetry: Design of a Radiation Dosimeter for Astronauts During Lunar Extravehicular Activities – Task completed
- Lunar EVA Dosimetry: Microdosimeter-Dosimeter Instrument – PI: Vincent Pisacane, Ph.D., United States Naval Academy
- Lunar EVA Dosimetry: Small Active Dosimetry System for Lunar Extravehicular Activity Missions: Spacesuit and Tool-Box Applications – Task completed
- Space Radiation Measurement Technologies – PI: Tore Straume, Ph.D., NASA Ames Research Center
- Radiation Alert Immediate Disclosure (RAID) – PI: Eric Krug, Ph.D., Invocon, Inc.
- Lunar EVA Dosimetry: Microdosimeter Instrument (MIDN) System Suitable for Space Flight – Task completed
- Spectroscopic Dosimeter – Task completed
- Tissue-Equivalent Radiation Dosimeter-On-A-Chip – Task completed

Acute - 6: What are the most effective shielding approaches to mitigate acute radiation risks, how do we know, and implement? (Closed. Transferred to Operations)

Tasks:

- Integrated Radiation Analysis and Design Tools – PI: Chris Sandridge, Ph.D., NASA Langley Research Center
- Patterns of Energy Deposition by HZE Particles in Cellular Targets – Task completed
- Space Radiation Risk Assessment Project – PI: Francis Cucinotta, Ph.D., NASA Johnson Space Center

Acute - 7: What are the most effective biomedical or dietary countermeasures to mitigate acute radiation risks?

- The SRP thinks this is a relevant gap.
- The SRP thinks that the target for closure and the metrics for interim progress are all very appropriate.

Tasks:

- Center for Acute Radiation Research – PI: Ann Kennedy, Ph.D., University of Pennsylvania
- Effect of Deep Space Radiation on Human Hematopoietic Stem and Progenitor Cell Function – Task completed

Acute - 8: How can Probabilistic risk assessment be applied to SPE risk evaluations for EVA, and combined EVA+IVA exposures?

- The SRP agrees with the need to study the sub-acute, sub-clinical, and long-term effects, including empiric observations, some mechanism studies and impact of mitigation in preparation for longer flights.
- The SRP thinks that the target for closure and the metrics for interim progress are all very appropriate.

Tasks:

- Space Radiation Risk Assessment Project – PI: Francis Cucinotta, Ph.D., NASA Johnson Space Center

Acute - 4: What are the probabilities of hereditary, fertility, and sterility effects from space radiation?

- The SRP thinks this is a relevant gap.
- The SRP thinks that the target for closure and the metrics for interim progress are all very appropriate.

III. Discussion on the strengths and weaknesses of the IRP and identify remedies for the weaknesses, including answering these questions:

Is the Risk addressed in a comprehensive manner?

- The SRP thinks that the Risk is addressed in a comprehensive manner.

Are there obvious areas of potential integration across disciplines that are not addressed?

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- The SRP thinks that central nervous system effects would impact crew response to other acute effects so that a “formulaic” use of mitigators might be developed based on a dose and not waiting to see effect.

IV. Evaluation of the progress in the IRP Rev. D since the 2011 SRP meeting.

The SRP thinks that substantial progress has been made in the CNS, Degenerative, and Cancer risks since last year, but there is concern about the progress of the Acute risk, specifically that it is extraneous and that the doses used are not relevant to space radiation.

IV. Additional Comments

An overarching issue that the SRP is concerned about is the tension between the SRPE Program Scientist and the NSBRI. The SRP thinks that it will help the overall research program significantly if efforts are made to smooth things out and clear up possible misunderstandings. The excellence and dedication of the investigators at NASA and the NSBRI are not an issue. In addition to the concern of the focus on SPE, the idea of not working on mitigation until the mechanisms of injury are understood raised concern for a few reasons: 1) The practice of medicine, which much of this is, does not wait for a full understanding of a medical condition before treatment is undertaken. Not that understanding isn’t critical but wise empiricism is useful and often solves much of the practical problem. 2) Some of the radiation-related illnesses can be treated with current therapies that have been developed for routine medical conditions, for example treating infection, bleeding and coagulopathy in cancer treatment, and seeing how the known treatments work early on may well direct the research.

Nonetheless, separating the majority of the Acute risk from the SRPE (as it currently is) is creating a scission of experience and expertise, and may compromise the success and credibility of NASA’s research on the acute risks. The SRP would suggest that some major course correction be considered now and since the NSBRI is a cooperative agreement, that the home agency (NASA HRP) play a substantial part in its directions. This approach does not detract from the quality of research but can help focus on the priorities, which may change more rapidly than a five-year funding cycle. It is possible that better coordination between the NASA SRPE and the NSBRI Radiation Effects Team may be necessary since it seems that the work that was funded by the NSBRI does not fit into the overall needs of NASA

The SRP is aware that these comments may be out of the purview of the SRP, but we feel that this can be readily modified and that the questions for the exploration missions outside of LEO can include those of the SPE more readily than the other way around.

Lastly, the SRP thinks that a review of the type expected by NASA for programs that are complex and multi-faceted is extremely difficult to conduct in a WebEx/teleconference format. While that format is ideal for providing information to the group, when discussions and evaluations of experimental efficacy and design are required, face-to-face meetings provide a much better opportunity for assessment and discussion. It is recommended that in the future

such review panels occur in a face-to-face format as much as possible.

VI. 2012 Space Radiation SRP Research Plan Review (WebEx): Statement of Task for the Risk of Acute Radiation Syndromes Due to Solar Particle Events (SPEs)

The 2012 Space Radiation Standing Review Panel (SRP) is chartered by the Human Research Program (HRP) Chief Scientist. The purpose of the SRP is to review the Space Radiation Element and the National Space Biomedical Research Institute (NSBRI) section of the HRP's Integrated Research Plan, Revision D (IRP Rev. D) which is located on the Human Research Roadmap (HRR) website (<http://humanresearchroadmap.nasa.gov/>). Your report will be provided to the HRP Chief Scientist.

The 2012 Space Radiation SRP is charged (to the fullest extent practicable) to:

1. Evaluate the ability of the IRP Rev. D to satisfactorily address the Risk by answering the following questions:
 - A. Have the proper Gaps been identified to address the Risk?
 - i) Are all the Gaps relevant?
 - ii) Are any Gaps missing?
 - B. Has the appropriate target for closure for the Gaps been identified?
 - i) Are the interim stages appropriate to close the Gaps?
 - C. Have the proper Tasks been identified to fill the Gaps?
 - i) Are the Tasks relevant?
 - ii) Are any Tasks missing?
2. Identify the strengths and weaknesses of the IRP Rev. D, *and* identify remedies for the weaknesses, including answering these questions:
 - A. Is the Risk addressed in a comprehensive manner?
 - B. Are there obvious areas of potential integration across disciplines that are not addressed?
3. Please evaluate the progress in the IRP Rev. D since your 2011 SRP meeting.
4. Please comment on any important issues that are not covered in #1, #2, or #3 above. If a charge addendum is provided, please address each of the questions as fully as possible.

Additional Information Regarding This Review:

1. Expect to receive review materials at least four weeks prior to the WebEx conference call.
2. Participate in a WebEx conference call on February 21, 2013.
 - A. Discuss the 2012 Space Radiation SRP Statement of Task and address questions about the SRP process.
 - B. Receive presentations from the NSBRI.
 - C. Participate in a question and answers session.

D. Attend Element or Project presentations, question and answer session, and briefing.

3. Prepare a draft final report (within one month of the WebEx/teleconference) that contains a detailed evaluation of the current IRP specifically addressing items #1, #2, #3, and #4 of the SRP charge. The draft final report will be sent to the HRP Chief Scientist and he will forward it to the NSBRI for their review. The NSBRI and the HRP Chief Scientist will have 10 business days to review the draft final report and identify any misunderstandings or errors of fact and then provide official feedback to the SRP. The SRP will have 10 business days to address any issues and finalize the 2012 SRP Final Report. The 2012 SRP Final Report will be submitted to the HRP Chief Scientist and copies will be provided to the NSBRI and the Space Radiation Element and also made available to the other HRP Elements. The 2012 SRP Final Report will be made available on the Human Research Roadmap public website (<http://humanresearchroadmap.nasa.gov/>).

VII. 2012 Space Radiation SRP Research Plan Review WebEx/Teleconference Participants

SRP Members:

Gayle Woloschak, Ph.D. (chair) – Northwestern University
Norman Coleman, M.D. – National Institutes of Health
Colin Hill, Ph.D. – University of Southern California
George Iliakis, Ph.D. – University of Duisburg-Essen Medical School
Christina Meyers, Ph.D. – M.D. Anderson Cancer Center
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NASA Headquarters (HQ):

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Janice Huff, Ph.D.
Sarah Lumpkins, Ph.D.
Lisa Simonsen
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Lisa Stephenson
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National Space Biomedical Research Institute (NSBRI):

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Jeff Chancellor
Scott Graham, Ph.D.
Ann Kennedy D.Sc. - Director, NSBRI Center of Acute Radiation Research

NASA Research and Education Support Services (NRESS):

Tiffin Ross-Shepard

VIII. 2012 Space Radiation Standing Review Panel Roster

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