**Fiscal Year:** FY 2017  
**Task Last Updated:** FY 06/27/2017

**PI Name:** Hada, Megumi Ph.D.  
**Project Title:** Computational Model Prediction and Biological Validation using Simplified Mixed Field Exposures for the Development of a GCR Reference Field

**Division Name:** Human Research

**Program/Discipline:** HUMAN RESEARCH--Radiation health

**Joint Agency Name:** TechPort: No

**Human Research Program Elements:** (1) SR: Space Radiation

**Human Research Program Risks:** (1) Cancer: Risk of Radiation Carcinogenesis

**Space Biology Element:** None

**Space Biology Cross-Element Discipline:** None

**Space Biology Special Category:** None

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**Congressional District:** 10

**Comments:**

**Project Type:** GROUND  
**Solicitation:** 2014-15 HERO NNX14ZSA001N-RADIATION, Appendix D: Ground-Based Studies in Space Radiobiology

**Start Date:** 08/26/2016  
**End Date:** 08/25/2018

**No. of Post Docs:** 0  
**No. of PhD Degrees:** 0

**No. of PhD Candidates:** 0  
**No. of Master’s Degrees:** 0

**No. of Master's Candidates:** 0  
**No. of Bachelor’s Degrees:** 0

**No. of Bachelor's Candidates:** 0

**Monitoring Center:** NASA JSC

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**Flight Program:**

**Flight Assignment:**

**Key Personnel Changes/Previous PI:**

**COI Name (Institution):**
- Patel, Zarana Ph.D. (Wyle Laboratories, Inc.)
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- Ponomarev, Artem Ph.D. (Wyle Laboratories, Inc.)
- Shavers, Mark Ph.D. (Wyle Laboratories, Inc.)
- Slaba, Tony Ph.D. (NASA Langley Research Center)

**Grant/Contract No.:** NNX16AR97G

**Performance Goal No.:**

**Performance Goal Text:** This work addresses the need to develop and utilize mixed field irradiation protocols that approximately represent the...
This work addresses the need to develop and utilize mixed field irradiation protocols that approximately represent the shielded tissue environment in space and that can be combined with single-beam studies to validate and further improve cancer risk models. Extensive studies have been carried out on the induction of chromosomal aberrations by low- and high-LET (linear energy transfer) radiation in human lymphocytes, fibroblasts, and epithelial cells exposed in vitro. The results, which are consistent with computational modeling predictions, establish chromosome aberration models as an LET-sensitive tool for predicting damage from single ion exposures. However, there is a lack of data on chromosome aberrations induced by low dose rate chronic exposure and mixed field beams such as those expected in space. These proposed studies will define a simplified mixed field and make model predictions of the effects of dose rate, mixed fields, and shielding on expected biological damage. Chromosome aberration studies at NASA Space Radiation Laboratory (NSRL) will provide the biological validation needed to extend the computational models over a broader range of experimental conditions ((more complicated mixed fields leading up to the galactic cosmic radiation (GCR) simulator)), helping to reduce uncertainties in radiation quality effects and dose-rate dependence in cancer risk models (Cancer-3 and -4). These models can then be used to answer some of the open questions regarding requirements for a full GCR reference field, including particle type and number, energy, dose rate, and delivery order.

### Task Description:

**Research Impact/Earth Benefits:**

This strategy of single and mixed field exposures and varying dose rates along with a well-defined biological assay and established computational models will provide a unique opportunity to develop an intermediate mixed field that can closely approximate the GCR reference field. This represents a critical step towards using the GCR simulator at NSRL to reduce uncertainties in radiation quality effects and dose-rate dependence in cancer risk models.

**Rationale for HRP Directed Research:**

Analysis of chromosome aberrations

Human normal fibroblast cells were irradiated with single of mixed beam of proton, helium, oxygen, titanium, and iron-ions with and without shielding (20 g/cm2 Aluminum and 10 g/cm2 Polyethylene) in NSRL 16C and 17A run at Brookhaven National Laboratory. Beams, energy and dose used are as follows:

- Single beam with shielding: H (344 MeV), He (344 MeV/n), O (450 MeV/n), and Fe (950 MeV/n); 0, 0.5, 1, 5, 10, 20, and 40 cGy with acute and chronic dose rate.
- Single beam without shielding: H (250 MeV), He (250 MeV/n), O (350 MeV/n), and Ti (300 MeV/n); 0, 0.5, 1, 5, 10, 20, and 40 cGy with acute and chronic dose rate.
- Mixed beam with shielding (2 beams combination): H (344 MeV) + Fe (950 MeV/n); 18.03 + 5.64 with acute and chronic dose rate.
- Mixed beam with shielding (4 beams combination): H (344 MeV) + He (344 MeV/n) + O (450 MeV/n) + Fe (950 MeV/n); 9.02 + 3.89 + 4.89 + 2.82, 18.03 + 7.77 + 9.78 + 5.64, 36.06 + 15.54 + 19.56 + 11.28 with acute and chronic dose rate.
- Mixed beam without shielding (4 beams combination): H (250 MeV) + He (250 MeV/n) + O (350 MeV/n) + Ti (300 MeV/n); 10.62 + 3.17 + 1.08 + 0.74, 21.24 + 6.33 + 2.16 + 1.47, 42.48 + 12.66 + 4.32 + 2.94 with acute and chronic dose rate.

Chromosome samples were collected in the first mitosis after exposure (total 119 samples). Analysis of chromosome aberrations (CA) with 3-color fluorescent in situ hybridization (FISH) chromosome painting methods has been progressing and currently about 40% of samples analysis has completed. Preliminary results show: 1) Shielding fully blocked the 56Fe beam. The 344.1 MeV proton beam punched through the shield with roughly 250 MeV remaining. Although shielding blocked 100% of the primary 56Fe beam, chromosome aberrations were observed behind the shielding from the secondary exposure.

- 2) Chronic exposure induced less chromosome aberrations than acute exposure with proton beam without shielding, but more chromosome aberrations than acute exposure in with shielding. Chronic exposure induced more chromosome aberrations than acute exposure in Ti-ions but no difference in acute and chronic exposure in Fe-ions with shielding.

3) Proton and Fe ion mixed exposure with shielding induced more damage than additive of two single exposures.

**Updates to RITRACKS**

Several changes were made in the code RITRACKS (Relativistic Ion Tracks) to simulate mixed beams and galactic cosmic rays (GCR). More specifically, the code is currently able to simulate stochastic track by multiple beams of particles of various ion types, energies and dose/fluence specified by the user. Another sub-program was included in RITRACKS to simulate beams representative of the GCR environment. By using known GCR fluence spectra, the code generates sample of ions at various energies impacting a given surface during a specific time frame (e.g., the tracks impacting a 10 micro m nucleus during a 3-years mission).

Dose-rate was added later in RITRACKS. Specifically, the time intervals (begin and end) of a given ion type are added in the input parameters. The time intervals can be separated and/or overlapping. All these parameters are entered in various graphic user interfaces (GUI).

Using the parameters, the tracks are simulated as usual. In the visualization interface, it is now possible to select the individual tracks to display.

The time-dependent differential and cumulative voxel dose map is calculated. The differential voxel dose map will be used for future dose-rate effect studies.

A new GUI was added to display the time of creation of each particle in the beam.

For additional validations, changes in the code to generate statistics for individual tracks are in progress.

Beams calculations

Calculations of the input parameters were made for the beams after shielding for the ion types used in the experiments of...
this project.
The calculation part was implemented in the new cluster for parallel calculations, as a part of the simulation code BDSTracks.

BDSTracks

Calculations of chromosome aberrations by acute fields are in progress.

The size of the simulated irradiated volume was chosen to ensure that at least one or more ion track is present on average (see below), so that the nucleus has a reasonable probability to be hit by a secondary electron. Incidentally, the larger the box size is, the more realistic the radiation field is for the broad beam at a given fluence; however, it is advantageous to reduce the box size at higher doses to reduce simulation time.

A field of spatially distributed double strand breaks (DSBs) produces DNA fragments after an acute radiation, which, in the CA part of the code, are allowed to rejoin via a stochastic process that picks DSBs at random and either restitutes them properly or creates a CA, or leaves them unrejoined. Herein, we simulate fragment-size distributions produced by both the amorphous and stochastic tracks. Specifically, we focus on the difference in the shape of this distribution generated by the two track models.

Among several calculations, the algorithm counts the number of intact chromosomes, which are used for a proper normalization of the fragment-size distribution. We calculate the yields of deletions and dose-response curves for simple and complex exchanges for several ions of energies varying from 1 MeV/u to 1,000 MeV/u using the amorphous and stochastic tracks, and compared the results to the experimental data.

Bibliography Type: Description: (Last Updated: 06/28/2018)

Abstracts for Journals and Proceedings

Abstracts for Journals and Proceedings

Abstracts for Journals and Proceedings

Abstracts for Journals and Proceedings

Abstracts for Journals and Proceedings

Abstracts for Journals and Proceedings

Awards
Hada M, Cacao EE, Saganti P. "First award to Megumi Hada for the poster presentation 'A recent study of chromosome aberrations induced by targeted and non-targeted effects in human fibroblasts' at 5th International Symposium on Space Radiation and Particle Therapy, Suzhou, China, May 24-26, 2017." May-2017

Significant Media Coverage