



THE MULTI-MODEL ENSEMBLE RISK ASSESSMENT (MERA) PROJECT

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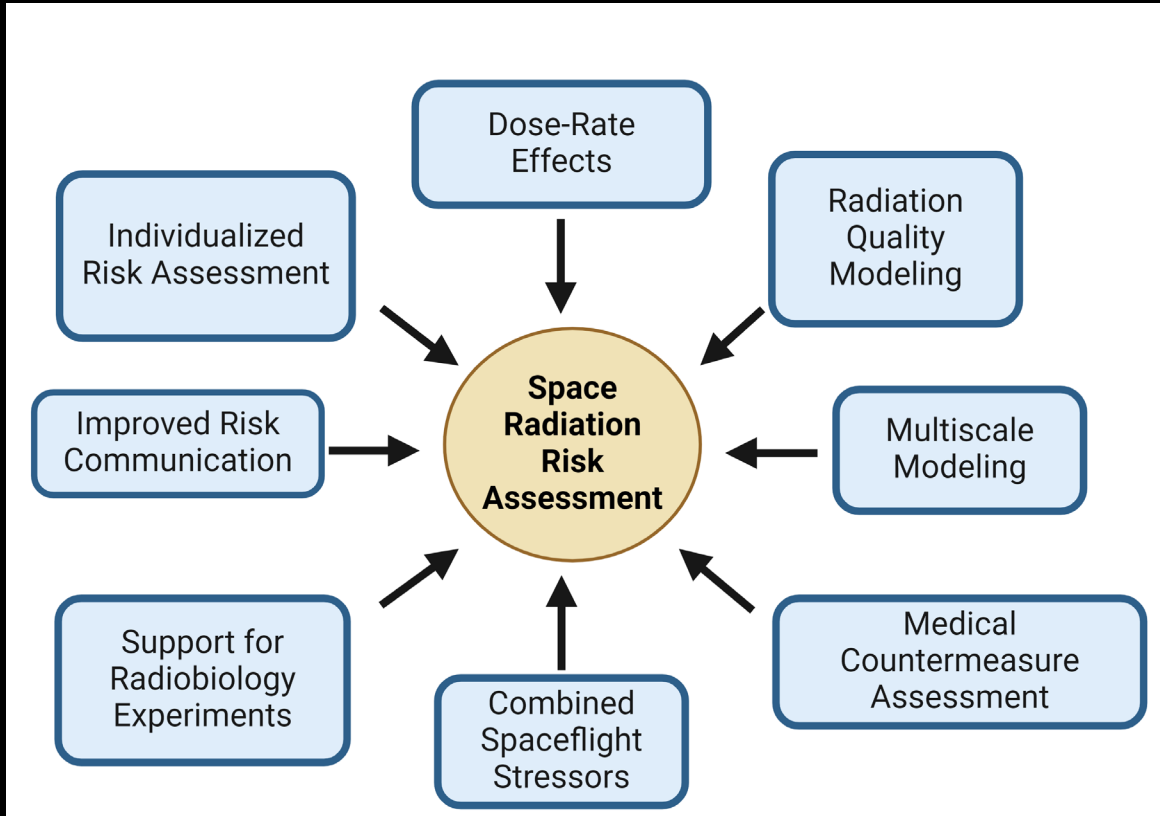
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AMERA Project Goals

To develop robust and accurate tools for evaluating space radiation health risks to support mitigation strategies, informed consent, and operations



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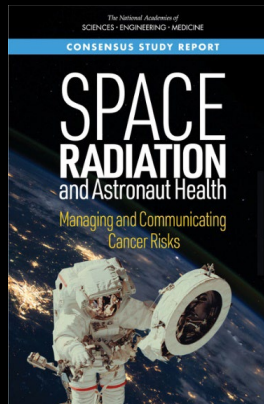
Research activities guided by and aligned with

- Human Research Program (HRP) space radiation element
- Agency roadmaps and gaps
- External advisory panel recommendations

NASEM (2021)

“Space radiation and astronaut health: managing and communicating cancer risks”

<https://www.nap.edu/download/26155>



Main Space Radiation Health Risks

- **Current space radiation risk models are population-based and extrapolate from terrestrial data**
- **Level of evidence in terrestrial data correlates with maturity of risk assessment models**

Acute Radiation Syndromes

LSS, accidental exposures

Cancer

LSS, MPS, INWORKS,
radiotherapy

CVD

LSS, nuclear
workers, radiotherapy

Late CNS

MPS,
radiotherapy

Carcinogenesis

Solid cancers (lung, breast, colon, stomach, esophagus, liver, ovaries, bladder, skin, brain) and leukemias

Cardiovascular Diseases (CVD)

Accelerated atherosclerosis, ischemic heart disease, and stroke

Neurodegeneration (Late CNS)

*Changes in cognition, motor function, behavior, and neurodegenerative disorders such as **Parkinson's disease**, vascular dementia and Alzheimer's disease*

Scaling Terrestrial Exposures to Space

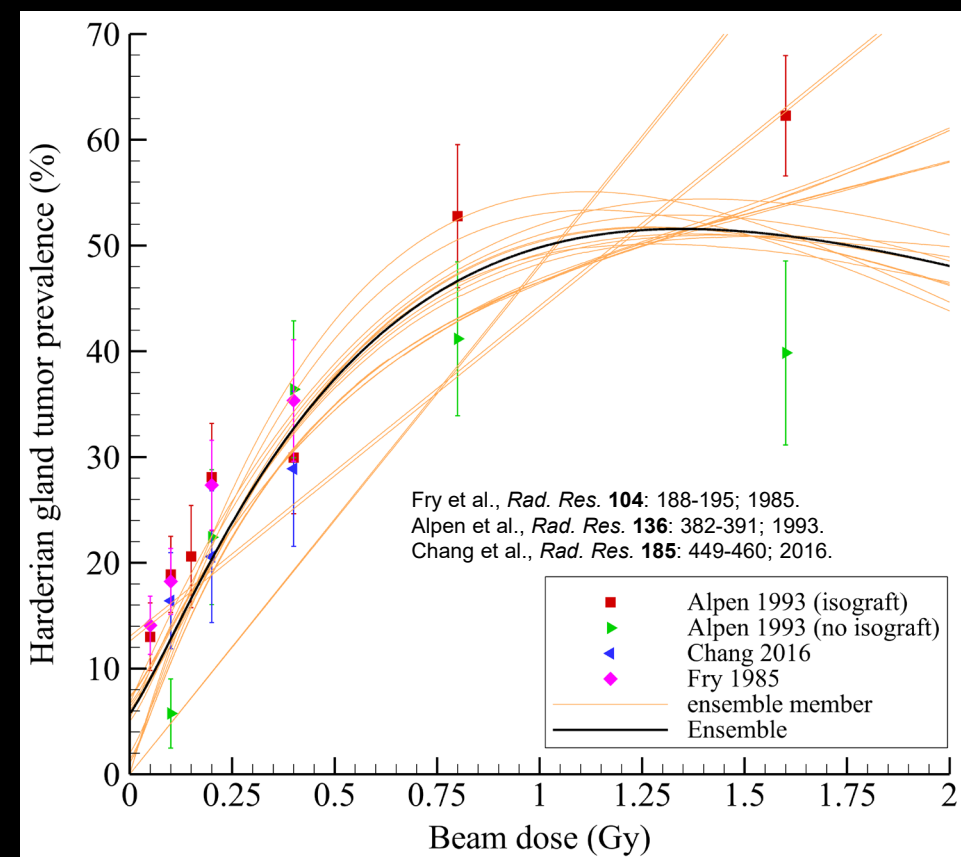
- Address main drivers of uncertainty in cancer risk projections – radiation quality and dose-rate
- Improve capability to extrapolate limited experimental data to complex space radiation environment

Ensemble Dose Response and Quality Factor

- Leveraging existing data sets and empirical dose-response models
- Developing new dose-response models
 - Statistical approach – Xu et al. (in preparation)
 - Microdosimetric approach:
Slaba et al. (in preparation) →
- Robust uncertainty quantification
 - Crespo et al. AMM 95: 734-759; 2021.
- Statistical/objective weighting of ensemble dose response models
- Prepared for GCRsim dose response data

[SESS-92] Analytical Calculation of the Energy Deposition Spectrum and Average Dose to a Spherical Target by Ion Tracks at Impact Parameters", Plante I., F. Poignant, T.C. Slaba. Wednesday at 2:30 pm: Exhibit Hall A -- Posters.

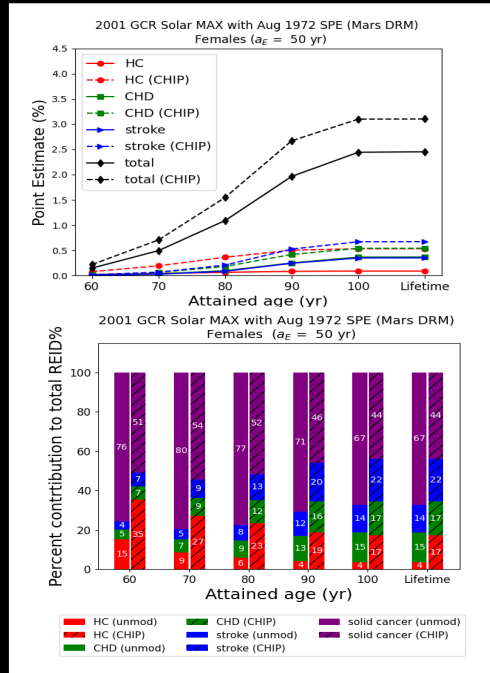
Harderian gland tumor prevalence dose-response for 600 MeV/n ^{56}Fe



Toward Individualized Risk Models

- Develop methodologies to incorporate and evaluate individualized risk factors
- Consideration of clinical tools along with modifiable and non-modifiable risk factors

Clonal Hematopoiesis of Indeterminate Potential (CHIP)



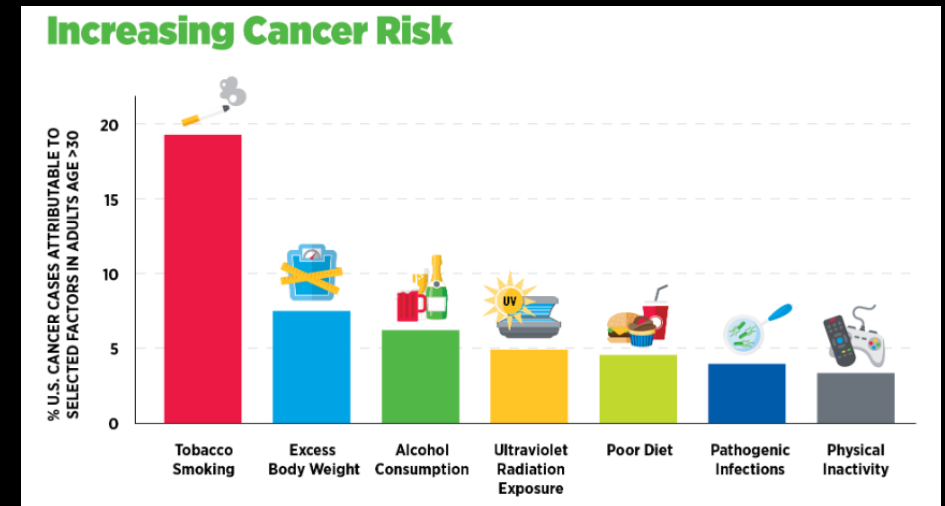
- Common age-related blood condition in older individuals
- Large increase in the total lifetime REID for CHIP carriers compared to average US population
- Identifying individuals with higher risk profiles provides opportunities for tailored interventions

REID – Risk of Exposure Induced Death

"The Effects of Somatic Events on Long Term Health"
 Thursday at 2:45 pm: Grand Ballroom B
 [SESS-103] Clonal Hematopoiesis of Indeterminate Potential and Individual Sensitivity of Space Radiation Health Risks. **C. M. Werneth** and J. L. Huff

Lifestyle Risk Factors

- Investigating how lifestyle risk factors may affect cancer risk
- Examining how data may be incorporated into the NASA Space Cancer Risk Model



[C. M. Werneth, Z. S. Patel, M. S. Thompson, S. R. Blattng, and J. L. Huff. Considering Clonal Hematopoiesis of Indeterminate Potential in Space Radiation Risk Analysis for Hematologic Cancers and Cardiovascular Disease. *Commun Med* 4, 105 (2024)]

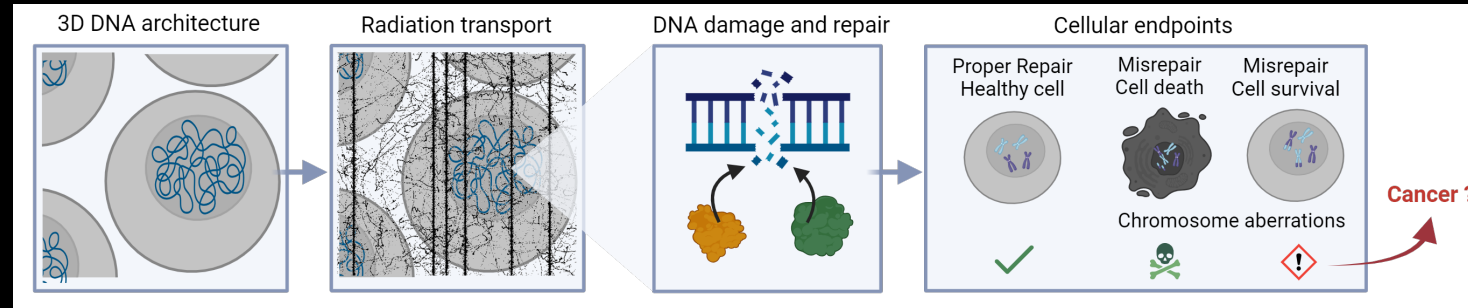
[C. M. Werneth and J. L. Huff (2025), "The Space Radiation Environment and Human Health Risks", In C. Krittanawong (Ed.), *Precision Medicine for Long and Safe Permanence of Humans in Space* (pp. 11 - 44). Academic Press.]

**American Association for Cancer Research Cancer Progress Report 2022*

[*cancerprogressreport.aacr.org/wp-content/uploads/sites/2/2022/09/AACR_CPR_2022.pdf](https://cancerprogressreport.aacr.org/wp-content/uploads/sites/2/2022/09/AACR_CPR_2022.pdf)

Track Structure and Biophysical Modeling

- **Computational models to simulate initial damage, repair processes, and intermediate surrogate endpoints**
- **Improve capability to extrapolate limited experimental data to complex space radiation environment**



DNA Damage

- Updated the radiation transport algorithm of RITRACKS (Relativistic Ion Tracks) and the radiation chemistry to simulate DNA damage by HZE ions
- Modeling effects of DNA compaction and epigenetics

[Plante I, West DW, Weeks J, Risca VI. Simulation of Radiation-Induced DNA Damage and Protection by Histones Using the Code RITRACKS. BioTech (Basel). 2024]

[SESS-88] SIMULATION OF RADIATION-INDUCED DNA DAMAGE WITH THE CODE RITRACKS **I. Plante**, H. Canaj, A. Scorteia, A. B. Clerkin, J. Rendleman, Devany W. West, J. Weeks, V. I. Risca. Tuesday 2:30pm Exhibit Hall A Posters

[SESS-624] MAPPING HIGH- AND LOW-LET RADIATION-INDUCED DNA DAMAGE ON THE HUMAN GENOME H. Canaj, A. Scorteia, A. B. Clerkin, J. Rendleman, D. W. West, **I. Plante**, V. I. Risca ., Friday 11:00am Grand Ballroom B

Chromosome Aberrations & Cell Survival

- New classification of simple and complex exchanges in RITCARD to account for partial staining and fragment detection thresholds reproducing experimental results well
- Model of cell survival to understand the fate of cells following exposure to HZE ions

[Poignant F, Pariset E, Plante I, Ponomarev AL, Evain T, Viger L, Slaba TC, Blattnig SR, Costes SV. DNA break clustering as a predictor of cell death across various radiation qualities: influence of cell size, cell asymmetry, and beam orientation. Integr Biol (Camb). 2024]

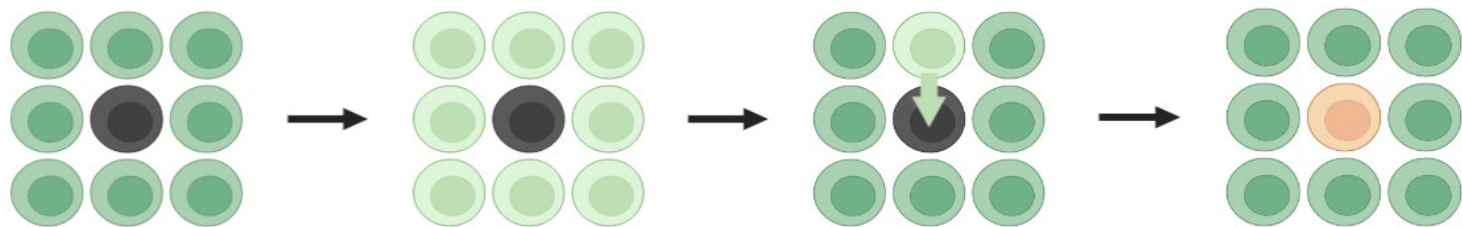
[SESS-60] EFFECT OF FLUORESCENCE IN SITU HYBRIDIZATION PARTIAL STAINING AND DETECTION THRESHOLD ON CHROMOSOME ABERRATION COUNTING: A SIMULATION STUDY **F. Poignant**, I. Plante, J. L. Huff, T. C. Slaba Tuesday 4:30pm Exhibit Hall A Posters

Multiscale Modeling of Cancer and Medical Countermeasures

Key Biological Events for Evolution of Cancer*

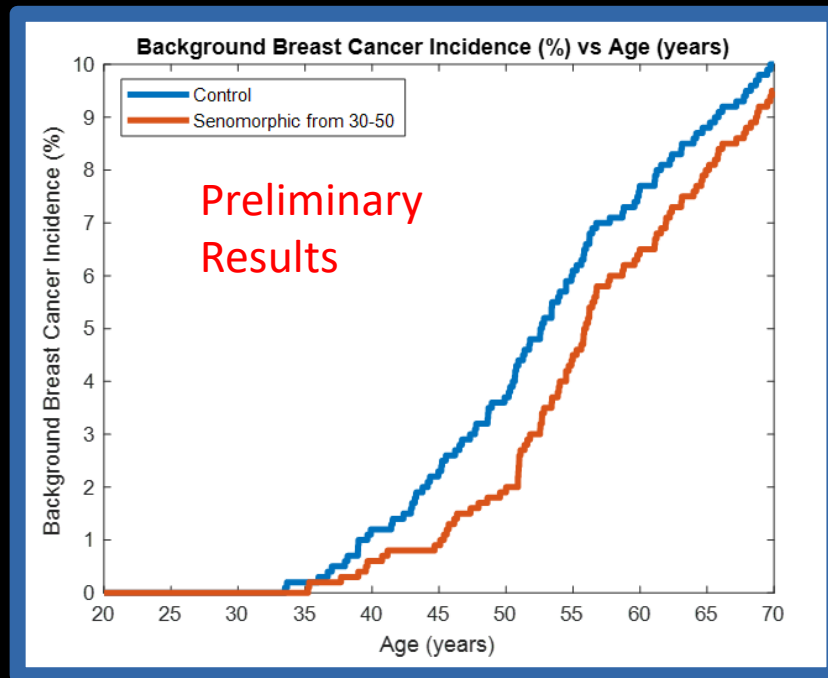
Spontaneous and radiation induced mutations	Deregulated signaling pathways	Inflammation	Growth of preneoplastic lesions	Tumor Growth	Cancer
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Clonal Expansion Models of Background- and Radiation Induced Cancer



Biophysical Modeling Can Inform
Model Parameters for Clonal
Expansion Models:
For example: Cell Survival

- Modified Costes[†] cellular automata model to perform preliminary sensitivity analysis of Senolytic and Senomorphic Drugs
- J. Bailey, C.M. Werneth, and J.L. Huff, "Incorporating Senotherapeutics in Cellular Automata Model of Breast Cancer", August 2024



Combined Spaceflight Hazards and CNS

- Evaluate combined risks for multiple spaceflight hazards on CVD using human data
- Investigate potential for CNS hazard due to space radiation exposure using human terrestrial data

Spaceflight Combined Stressor Risk Assessment



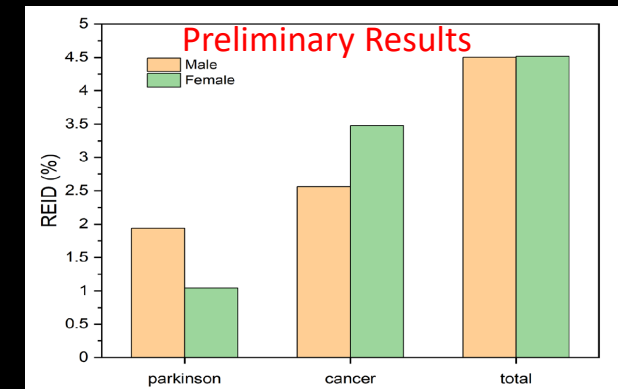
Examples of Earth-based Exposures with Cardiovascular Disease Impacts

- Multiple spaceflight hazards may contribute to CVD and other SR risks, however data to estimate these risks is limited
- Utilize population data from exposure to Earth-based “equivalent stressors”
- Proof of concept - Systematic review and meta-analysis to evaluate relationship between space-like sleep deficiencies and CVD

[SESS-50] META-ANALYSIS OF SLEEP DURATION AND THE RISK OF CARDIOVASCULAR DISEASE RELEVANT FOR SPACEFLIGHT **R.J. Reynolds**, J. Butler, S. Blattnig, R. Norman, C. Werneth, E. Flynn-Evans, Z. Patel, and J.L. Huff. Wednesday 9:15am Grand Ballroom B

Million Person Study evaluation of late CNS adverse outcomes

- Large number of workers who received both low and high linear energy transfer exposures
- Cohorts being evaluated for dementia and cognitive decrements
- Linkage between career exposures and recorded diagnoses, neuropsychological test scores, and mortality



“Epidemiology, What We Know and How Can We Use It” Tuesday at 2:45 pm Grand Ballroom B

[SESS-68] RADIATION-INDUCED PARKINSON’S DISEASE: EVALUATING THE LEVEL OF EVIDENCE AND RECOMMENDING FUTURE WORK M. Beavers, **S. Blattnig**, J.D. Boice Jr, E. Cekanaviciute, S. V. Costes, L. Dauer, C. Davis, D. Iacono, K. Miller, G. Nelson, M. K. O’Banion, S. Tolmachev Tuesday 3:30pm Grand Ballroom B

[SESS-22] RISK MODEL DEVELOPMENT FOR RADIATION-INDUCED PARKINSON’S DISEASE AND CONSEQUENCE FOR SPACE EXPLORATION **I. Plante**, S.R. Blattnig, M. Mumma, R.B. Norman, J.L. Huff Tuesday 4:30pm Exhibit Hall A Posters

GCRsim and Space Environment Modeling

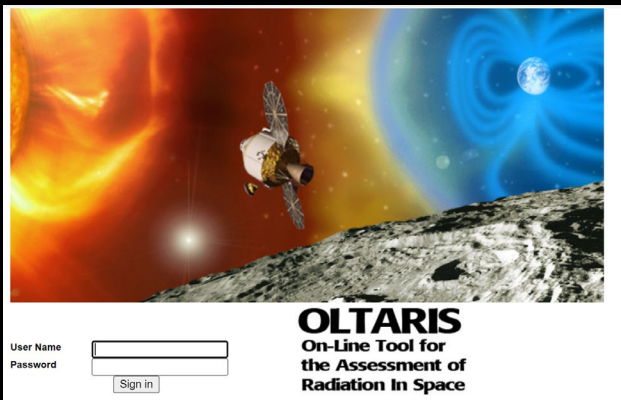
- Validation of GCRsim (and SPESim) for multiple experimental platforms at NSRL
- Provide GCR environmental prediction capabilities for space-based experimental platforms

NASA Space Radiation Laboratory Brookhaven, NY



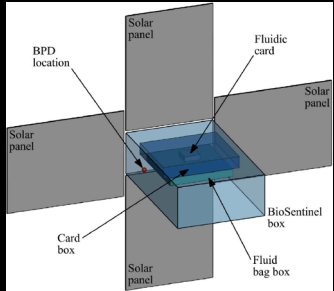
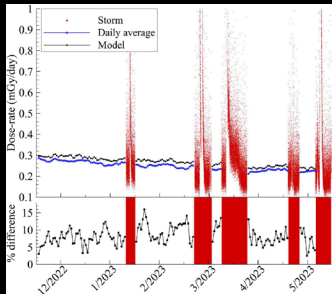
Space Health Impacts for the NASA Experience (SHINE) @ NSRL
<https://www.nasa.gov/hrp/radiation/shine/>

Online Tool for the Assessment of Radiation in Space



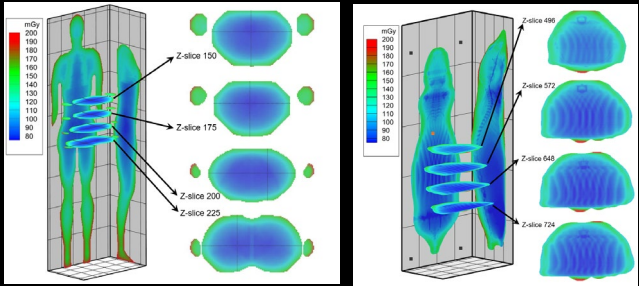
GCRsim is intended simulate radiation environment as seen by astronauts in deep space

Modeling GCR environment



[Rahmanian S, Slaba TC, George S, Braby LA, Bhattacharya S, Tore Straume, Santa Maria SR. Galactic cosmic ray environment predictions for the NASA BioSentinel Mission, part 2: Post-mission validation. Life Sciences in Space Research. 2024, In press.]

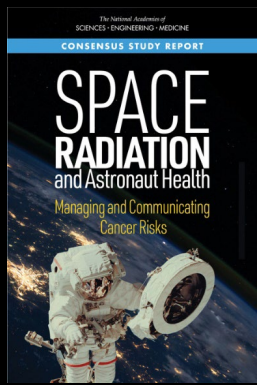
SPESim Verification in a Rat Model



SPE simulation at NSRL to generate an internal dose profile in a rat model similar to what might be seen in humans in space behind shielding

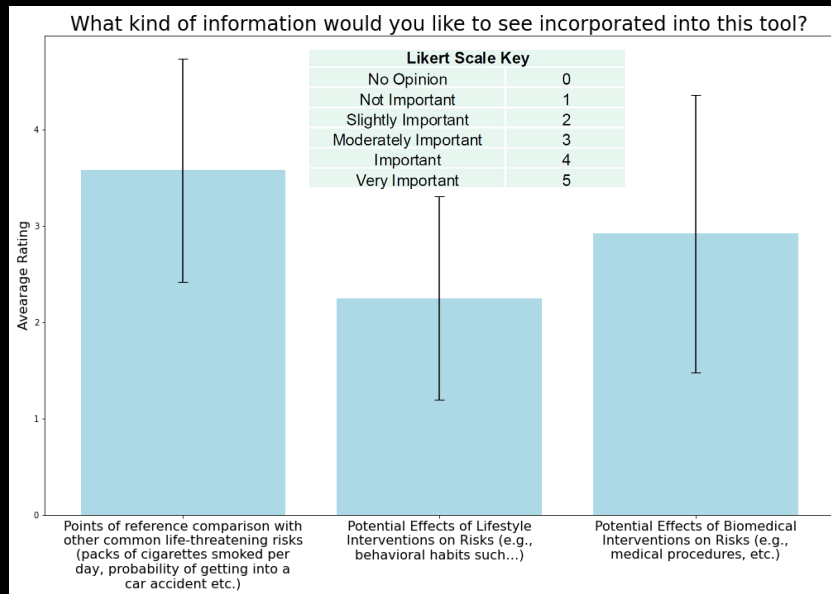
Risk Communication

- **Space radiation induced health risks must be effectively communicated to a diverse audience of stakeholders**
- The need for more effective communications was highlighted in recent NASEM report 



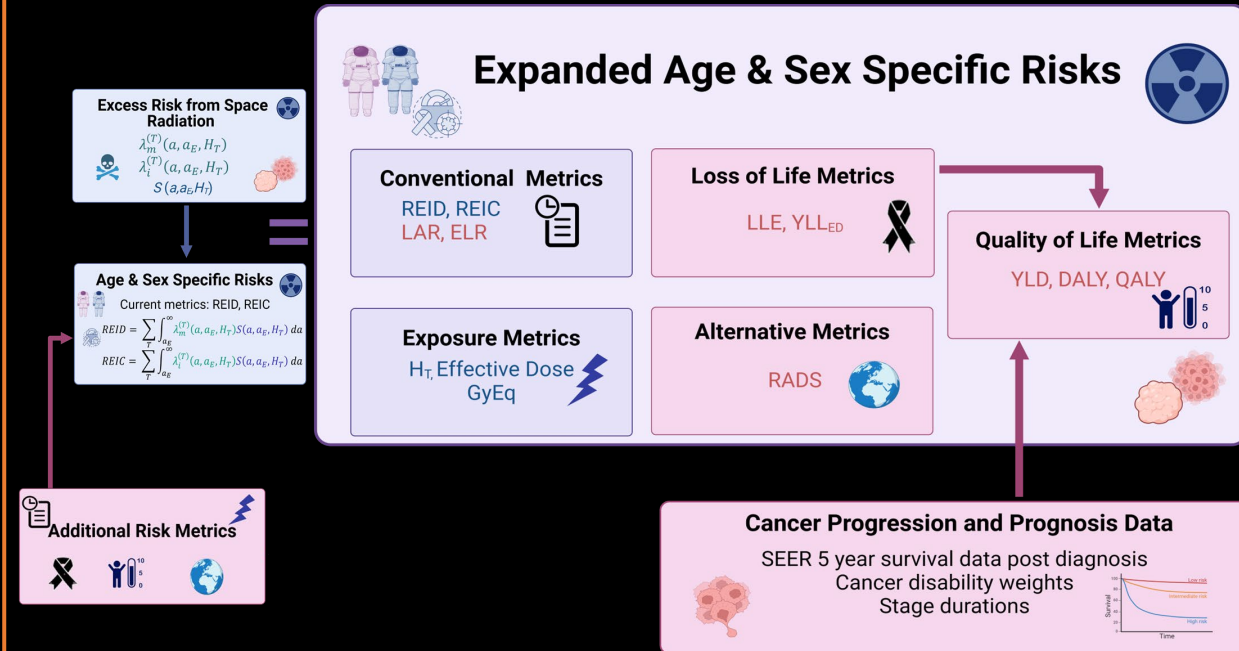
➤ NASA flight surgeons survey

Goal to better understand key information that stakeholders need to make decisions regarding radiation exposure risks



[SESS-55] A NASA Flight Surgeon Survey for Space Radiation Risk Communication **R. W. Ghatas**, R. J. Daiker, C. M. Werneth, S. R. Blattnig, R. B. Norman. Wednesday 2,30pm Exhibit Hall A - Posters

➤ Additional risk metrics will be added to the MERA framework



[SESS-64] AN ENHANCED MULTI-METRIC AND INDIVIDUALIZED APPROACH TO IMPROVE SPACE RADIATION RISK COMMUNICATION **S. Rahmanian**, C. Werneth, T. Slaba, J. Huff. Wednesday 2:30pm Exhibit Hall A - Posters

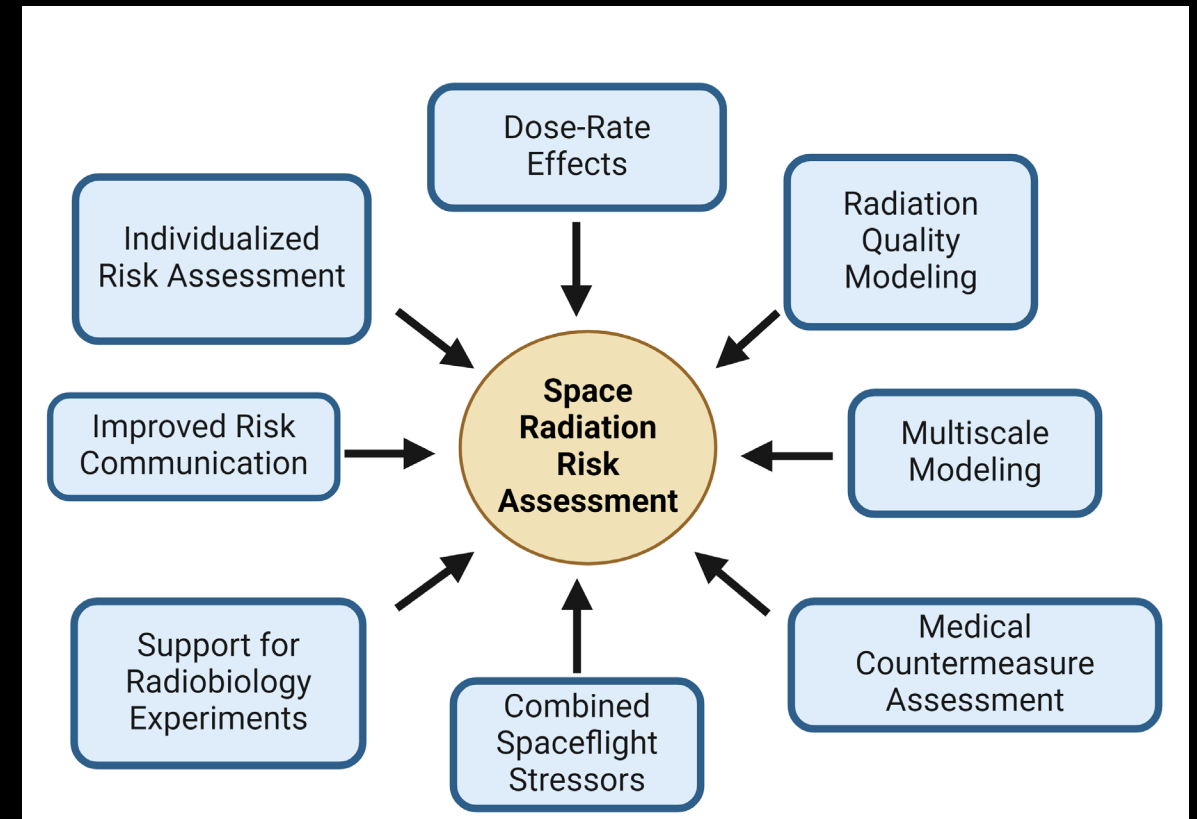
Summary

AMERA Goal: To develop robust and accurate tools for evaluating space radiation health risks to support mitigation strategies, informed consent, and operations

Research activities guided by and aligned with

- HRP space radiation element
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- External advisory panel recommendations

Ongoing and future work



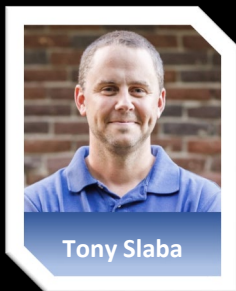
Created in <https://BioRender.com>

The MERA Team



Janice Huff

MERA Project Scientist
Individual risk assessment



Tony Slaba

Cancer ensemble risk model
Galactic cosmic ray simulator design



Charles
Werneth

*Medical countermeasure &
Mitigation assessment*
Biologically-based risk models



Steve Blattnig

CVD risk models
Late CNS risk assessment
Combined spaceflight risks



Xiaojing Xu
(Sharon)

Dose response modeling
Risk Modeling



Ryan Norman

MERA Project Manager
Lung cancer



Martha
Cloudsley

MERA Project Manager
Engineering design



Floriane
Poignant

Chromosome aberration modeling
Track structure & biophysics



Shirin
Rahmanian

Risk communication
Radiation transport



Ianik Plante

Track structure & biophysics
CVD clinical prediction models
CNS risk modeling



Rania Ghatas

Risk communication
survey



Ronald Daiker

Risk communication
survey



Sean Kenny

Uncertainty analysis



Luis Crespo

Uncertainty analysis



Robert Reynolds

Combined spaceflight risks



Francesca Luoni

Cancer Risk Model

Chris Sandridge

*OLTARIS - On-Line Tool for the Assessment of
Radiation in Space*