National Aeronautics and Space Administration

Mars Mission and Space Radiation Risks

Space Radiation Research and Technologies for Risk Mitigation

Briefing to
NAC HEO/SMD Joint Committee
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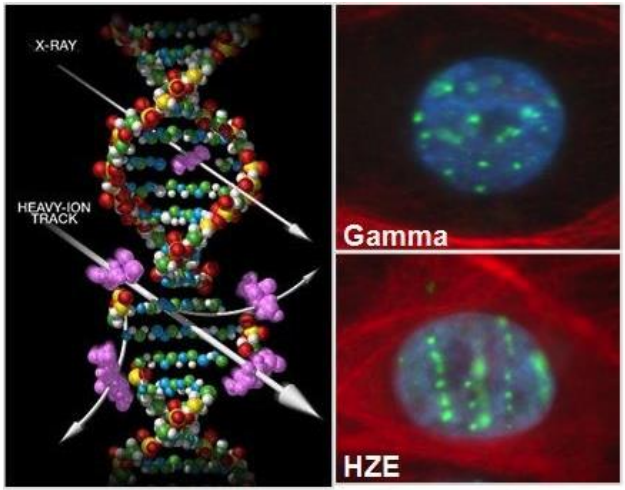
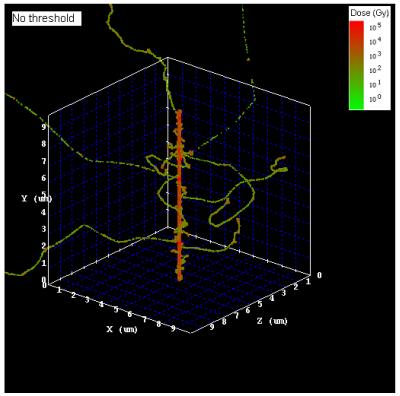
The Space Radiation Problem: The Biological Perspective

- **Interplanetary crews will be exposed to a high LET radiation environment comprised of high-energy protons and heavy ions (HZE's) as well as secondary protons, neutrons, and fragments produced in shielding and tissue**
- **Heavy ions are qualitatively different from X-rays or Gamma-rays:**
  - Densely ionizing along particle track
  - Cause unique damage to biomolecules, cells, and tissues
  - Distinct patterns of DNA damage and distinct profiles of oxidative damage
- **No human data exist to estimate risk from heavy ions found in space**
  - Animal and cellular models with simulated space radiation must be used
- **Synergistic modifiers of risk from other spaceflight factors**

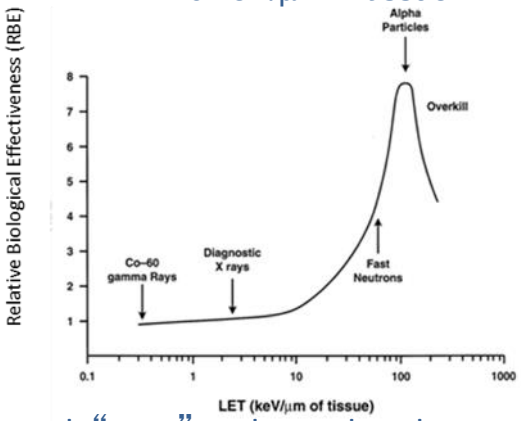


DNA Damage
γH2AX foci in EPC2-hTERT cells.
(Cucinotta & Saganti, Patel & Huff, NASA)

1 GeV/u ^{56}Fe nucleus
LET~150 keV/µm



High LET defined as
LET > 10 keV/µm in tissue



Qualitative differences due to track "core" and correlated tissue damage along a particle path.

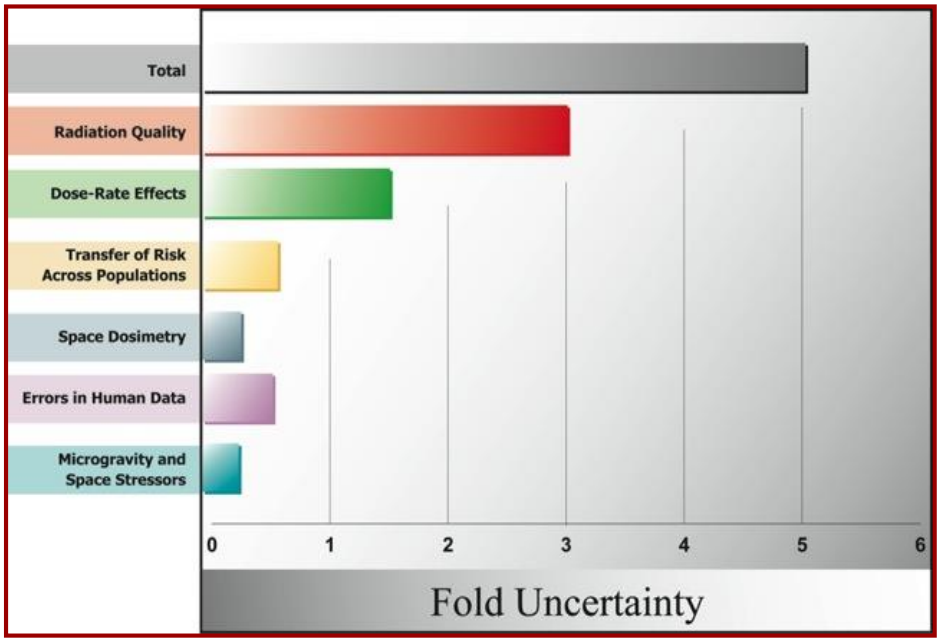
(Plante, I., Ponomarev, A., Cucinotta, F.A., 3D Visualization of the Stochastic Patterns of the Radial Dose in Nano-Volumes by a Monte Carlo Simulation of HZE Ion Track Structure. Radiat. Prot. Dosimetry 143: 156-161, 2011)

Foundation of Space Radiation Radiobiology Research Plan

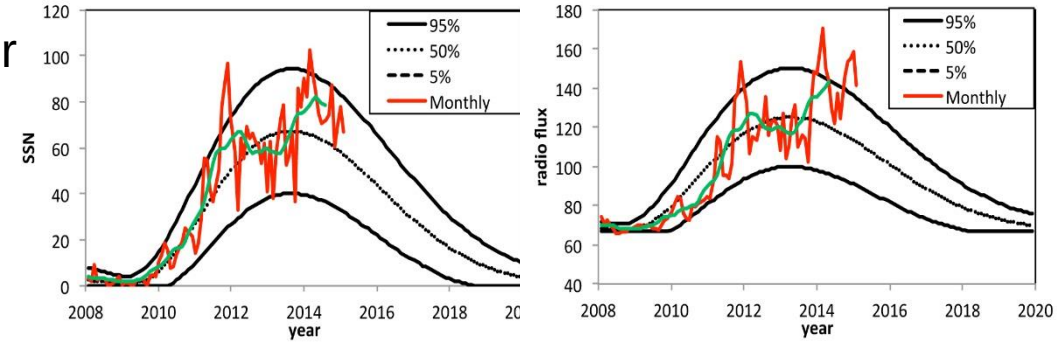
- The Space Radiation Integrated Research Plan is fully documented (http://humanresearchroadmap.nasa.gov/) and updated annually
- External review by National Council on Radiation Protection (NCRP), National Academy of Sciences, and annual Human Research Program (HRP) Standing Review Panels
- Funded research at over 40 US Universities including collaboration with US Department of Energy selected through peer review process
- Seven NASA Specialized Centers of Research
- Space radiation simulated at the NASA Space Radiation Laboratory (NSRL)
- Partnership with NASA's Space Radiation Analysis Group on transition of risk assessment and design tools to operations
- Partnership with National Space Biomedical Research Institute (NSBRI) on acute and cardiovascular risks
- Collaborations with other NASA Programs support an integrated protection strategy across physical and biological solutions

Major Sources of Uncertainty in Estimating Risks for Future Exploration Missions

- **Radiation quality effects on biological damage**
  - Qualitative and quantitative differences between space radiation compared with x-rays or gamma rays
- **Dependence of risk on the dose rates encountered in space**
  - Biology of repair, cell, and tissue regulation
- **Extrapolation from experimental data to humans**
- **Individual radiation sensitivity**
  - Genetic, dietary and healthy worker effects
- **Predicting radiation environment**
  - SPE temporal and size predictions
  - Galactic cosmic ray solar min/max conditions at future time points



Major Uncertainties in Cancer Risk Model
(Durante and Cucinotta, Nature Rev. Cancer, 2008)

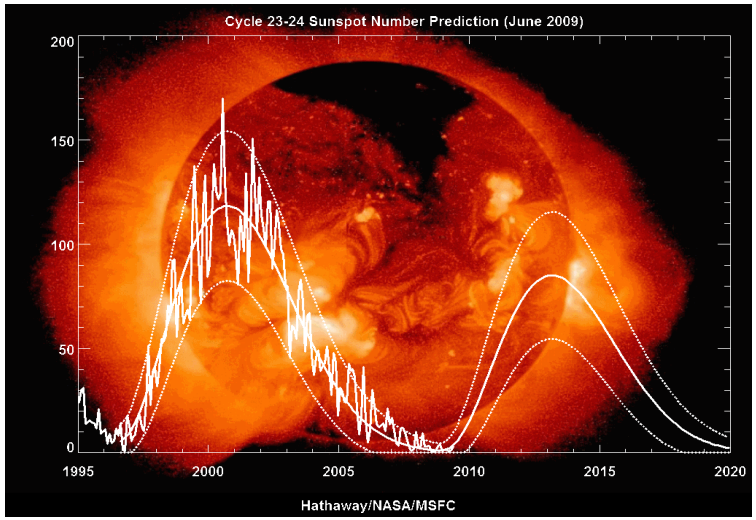


Theory predicts Solar Cycle 25 to be one of the weakest in centuries
(Santos Koos, Lindsey and Badavi, Francis F., NASA-funded research through Old Dominion University Research Foundation)

Mitigation Approaches

- **Time in solar cycle and ability to minimize exposure to SPE's**
- **Accurate risk quantification / uncertainty reduction**
- **Crew Selection**
  - Age, gender, lifestyle factors, etc.
  - Individual Sensitivity (genetic factors)
- **Biomarkers predictive of radiation induced diseases**
  - Future individualized risk assessment
  - Early detection and surveillance
- **Biological Countermeasures**
  - Radioprotectors / Mitigators
- **Radiation Shielding**
  - Amounts and material types
  - Design optimization

Variation of Solar Activity



Individual Susceptibility

(NCRP 2011)

α-lipoic acid

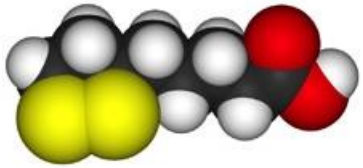
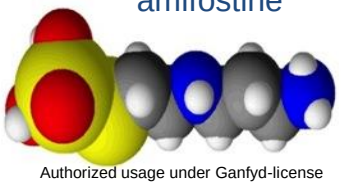


Image credit: Ben Mills

amifostine



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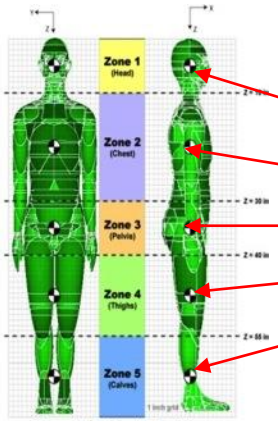
BCM: Pharmaceuticals



Computerized Anatomical Man
Surfaces & Proposed Zone Definitions

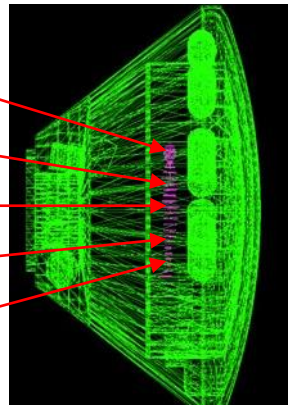
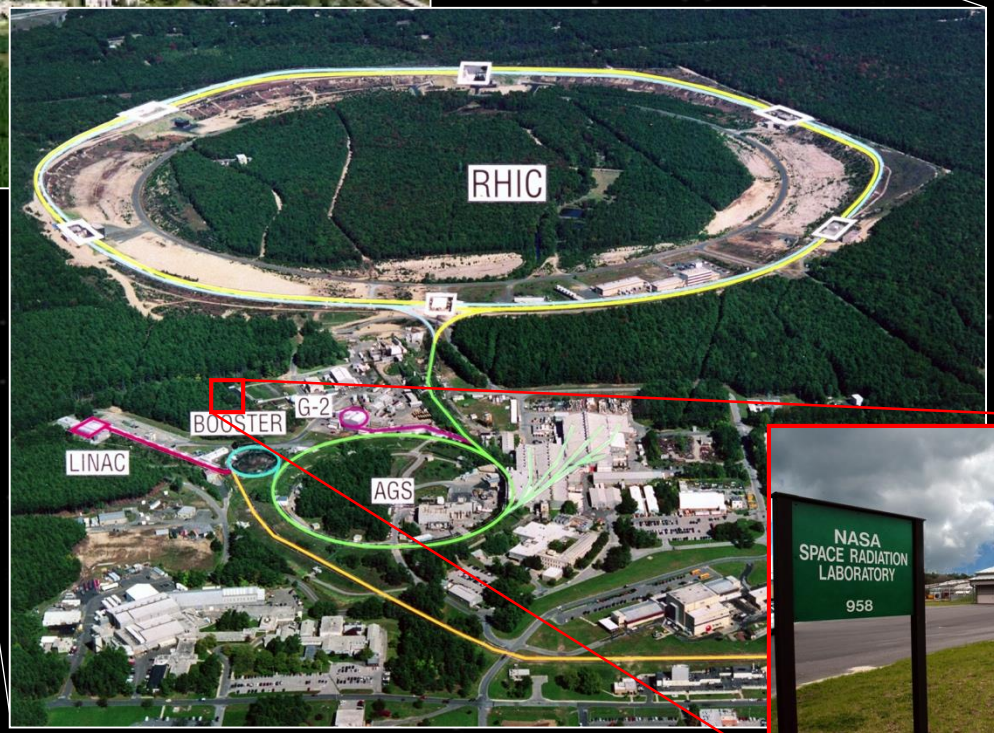


Image courtesy of OLTARIS.nasa.gov

Shield Design and Optimization

NASA Space Radiation Laboratory (NSRL) at Brookhaven National Lab

- Simulates the space radiation environment- high energy ion beams (H^+, Fe, Si, C, O, Cl, Ti, etc.)
- Beam line, target area, dosimetry, biology labs, animal care, scientific, logistic and administrative support
- 3 experimental campaigns per year



NSRL Beam Line

Images Courtesy of Brookhaven National Laboratory (BNL)

NSRL Upgrades: Galactic Cosmic Ray Simulator

Simulation of GCR primary and secondary environment with a mixed field, high-energy capability:

- Rapidly switchable ion source capable of delivering between 6 to 12 ion species.
- Magnet upgrades to deliver ion beams at 1.5 GeV/n (increases range of Fe by 70% from current capabilities.
- GCR species will be simulated with high precision in major LET bins ranging between 0.25-1,000 keV/μm.
- Completion in late 2016.

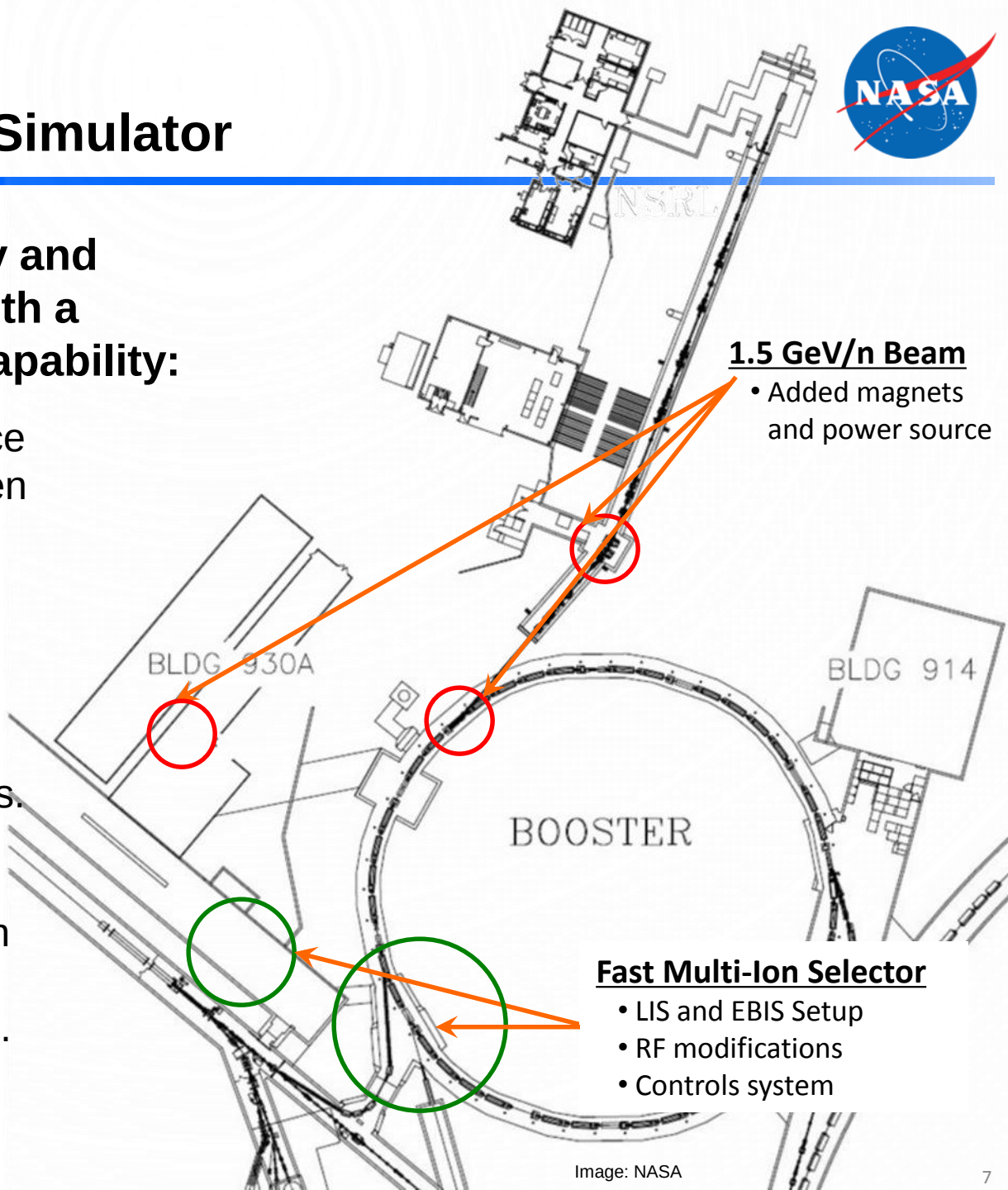
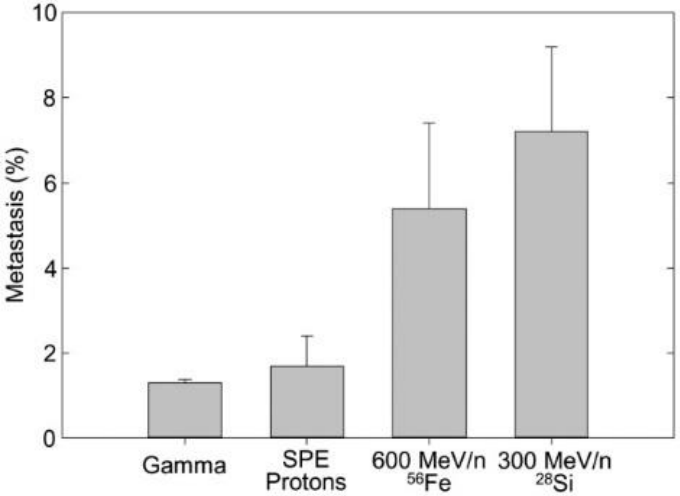


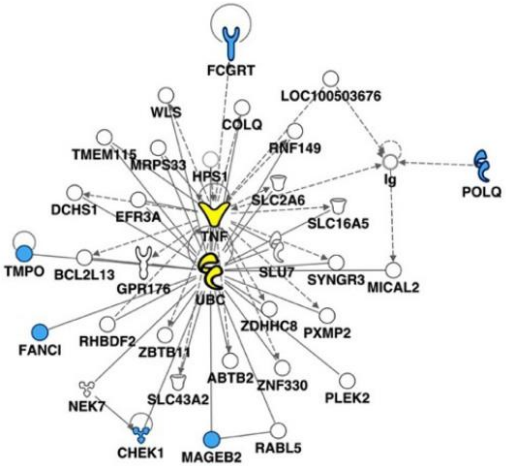
Image: NASA

Radiation Carcinogenesis Research Focus

- **Continued focus on radiation quality and dose-rate effects on cancer processes with goal of reducing uncertainty in risk estimates:**
  - Expand spectrum of ions tested to include light ion component
  - Mechanistic analysis of cancer risk including enhanced aggression observed in HZE tumors
  - Impact of non-targeted effects at low doses
  - Understanding the biological basis for sex differences and individual sensitivity on cancer risks
- **Research results support development of an integrated risk model with acceptable uncertainty in support of meeting PELS for exploration**
- **Research incorporating new integrative "omics" techniques and systems biology approaches**
  - Identification of biomarkers for early disease detection and health monitoring
  - Discovery and validation of biological countermeasures
  - Individualized risk assessment



Greater Incidence (%) of HCC with metastases to the lung with High LET radiation.
(UTMB NSCOR, PI: R. Ullrich)

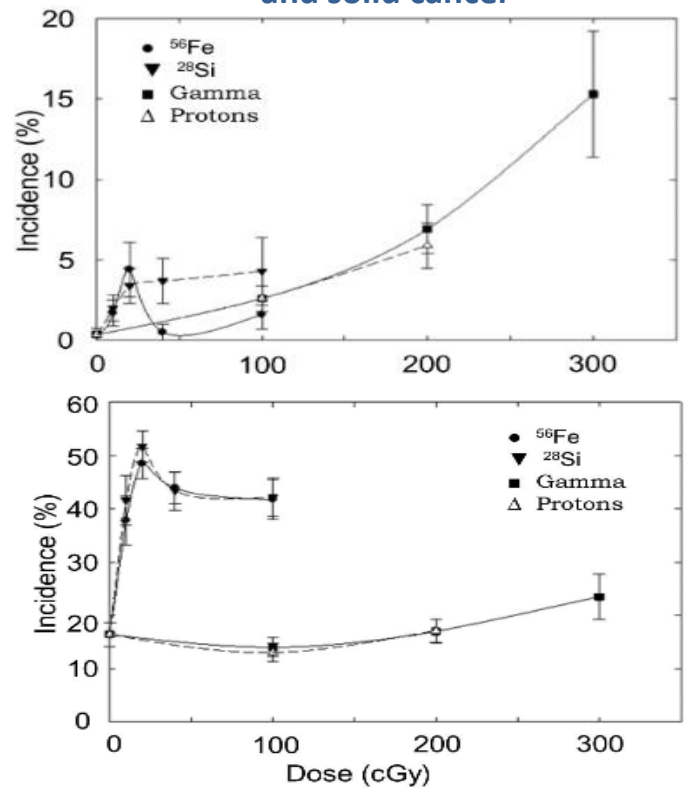


Gene analysis can support the determination of survival outcome of patients with lung cancer
(UTSW NSCOR, PI: J. Minna)

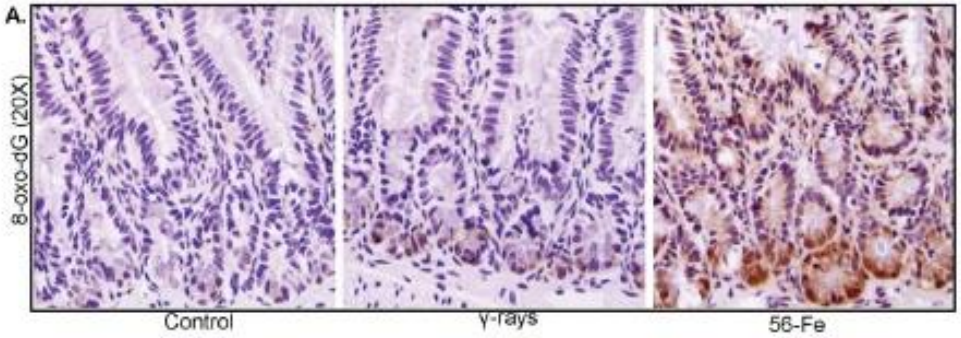
Major Findings on Cancer Risk from NSRL

- A low RBE for HZE-induced Leukemia
- Evidence for increased aggression of HZE tumors
- Persistent oxidative stress and inflammatory pathway activation
- Evidence for non-linear response at low dose due to non-targeted effects, which may confound conventional paradigms and RBE estimates
- Distinct gene expression and metabolomics changes between high and low LET, and between specific ions

Calculation of RBE for leukemia's and solid cancer



(Weil *et al.*, PONE 2014)



Higher oxidative damage 1 year after ^{56}Fe exposure in intestinal cells
(Datta, K., Suman, S., Kallakury, B.V.S., Fornace, A.J., Exposure to Heavy Ion Radiation Induces Persistent Oxidative Stress in Mouse Intestine. Plos One 7: e42224, 2012)

Updates to 2012 NASA Cancer Risk Model included new definitions for radiation quality factors and new tissue weighting factors based on research findings

CNS Research Focus

- **Continued focus on CNS risk definition and characterization**
- **Understanding whether there are significant risks at space relevant exposures**
  - Description of the spectrum and severity of possible in-flight cognitive, behavioral, and functional changes as well as possible late neurodegenerative conditions
  - Mechanistic basis for observed CNS decrements
  - Radiation quality and dose-rate dependencies
  - Establish possibility of dose thresholds for these effects
- **Identification of biomarkers related to early cognitive and behavioral decrements and how they may relate possible late degenerative changes**
- **Research addressing sleep and exercise as countermeasures as well understanding synergistic effects of spaceflight**
- **Current NCRP Committee SC 1-24 "Radiation Exposures in Space and the Potential of Central Nervous System Effects" will provide guidance on future research**

Eating, sleeping and working in space.

Images courtesy of NASA

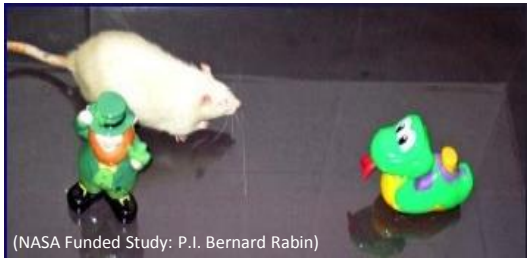
Major Findings on CNS Risk from NSRL

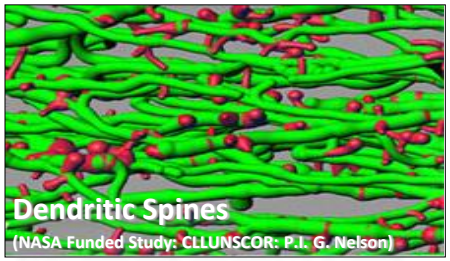
Research with animal models shows important changes to the CNS occur at HZE exposure levels in range of concern to NASA

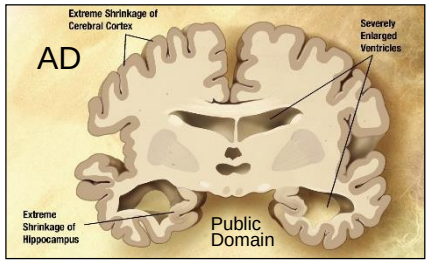
- Rodent studies show HZE induced cognitive and performance deficits in behavioral tasks including those that rely on the hippocampus and prefrontal cortex
- Associated with changes in neurogenesis, oxidative stress, apoptosis, inflammation, neuronal structure and synaptic plasticity
- Decrements dependent on radiation dose and quality as well as on age of animal at time of exposure; complex dose responses observed
- Studies using transgenic mice prone to develop pathologies reflective of Alzheimer's disease show low dose of GCR accelerates time of appearance and related molecular biomarkers
- Effects not seen with similar doses of low-LET radiation

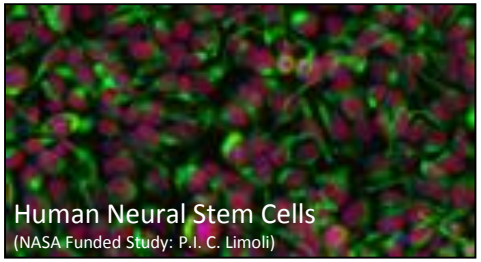
Significance of these results on the morbidity to astronauts has not been elucidated

- Lack of human epidemiology data to form the basis for risk assessment for CNS effects
- Major uncertainty in how to extrapolate results from animals to humans









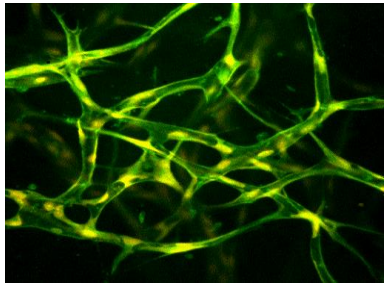
Risk of Cardiovascular Disease from Space Radiation Exposure

Image courtesy of NASA

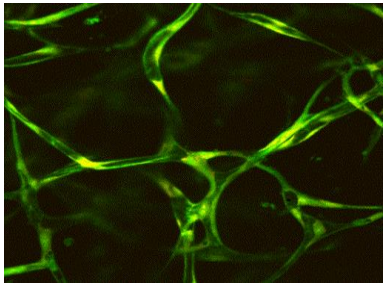
- **Well documented that exposure to high doses of low-LET (>5 Gy) radiation during radiotherapy to the chest is associated with increased risk of cardiovascular disease later in life**
- **Recent studies of atomic bomb survivor data and epidemiology data from occupational and medical exposures provide evidence for elevation of risk at doses as low as 0.5 Gy**
  - Data at low doses is confounded by life-style factors, clouding interpretation of epidemiology
  - Effects are considered deterministic, with an associated threshold dose; however recent evidence showing risk at lower doses questions this assumption
- **Preliminary risk assessment models are being formulated based on recent epidemiology data for lower dose low-LET exposures — future risk estimates will depend on high LET research results**
- **Additional mortality and morbidity risks for non-cancer diseases of the cardiovascular system are of concern because they could increase REID values**

Cardiovascular Disease Research Focus

- **Current research is focused on understanding and quantifying the risk of cardiovascular disease at space relevant exposures:**
  - Establishing whether a dose threshold exists
  - Qualitative differences between GCR and gamma-rays to establishment of RBEs
  - Influence of dose-rate
- **Identify disease spectrum and latency for low dose rates of heavy ions**
  - Necessity for life span studies in an appropriate animal models
  - Reflective of healthy lifestyle factors (never-smokers, normal weight, diet) consistent with astronaut corps
- **Identify and validate surrogate biomarkers for radiation induced disease endpoints**
- **Future studies will address impact of individual sensitivity and other spaceflight stressors**

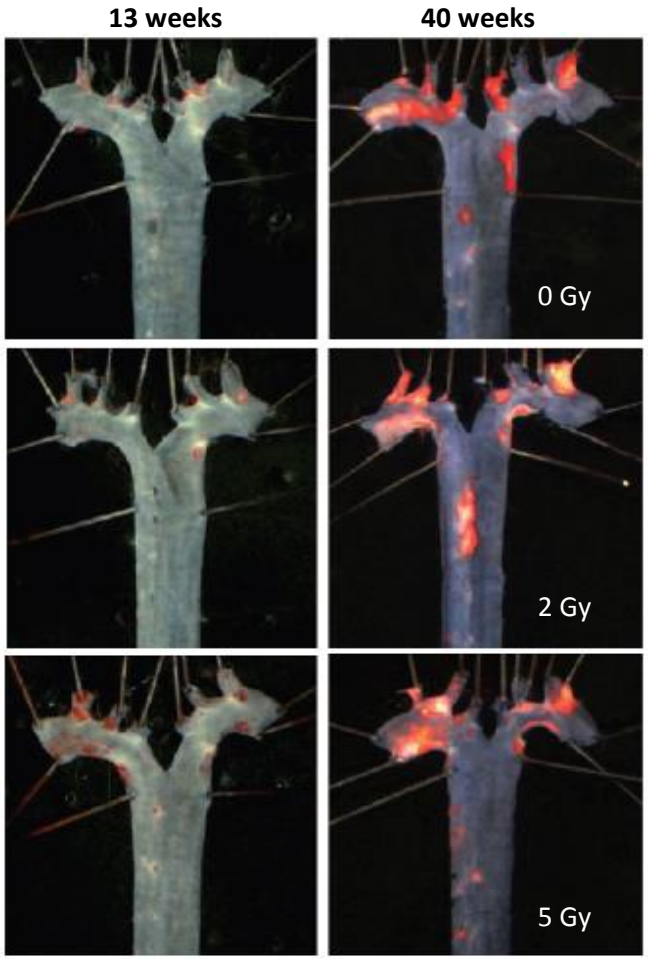


Controls



Iron Irradiated

Vasculature damage: μm of vessel per cell after protons or Fe
(PI-C. Geard Columbia U)



Aortic lesions in apoE-/- mice after ^{56}Fe irradiation

(Yu, T., Parks, B.W., Yu, S., Srivastava, R., Gupta, K., Xing, W., Khaled, S., Chang, P.Y., Kabarowski, J.H., Kucik, D.F., Iron-Ion Radiation Accelerates Atherosclerosis in Apolipoprotein E-Deficient Mice. Rad. Res. 175: 766-773, 2011)

Biological Countermeasures Research (BCM)

Targets for biological countermeasures are not well understood.

- Protective against many risks (solid cancers, leukemia, CNS, CVD)
- Major research emphasis to provide mechanistic basis to identify potential BCM's
- Current studies limited to those with rigorous scientific rationale for BCM's selected

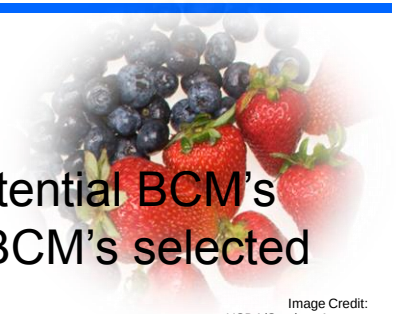
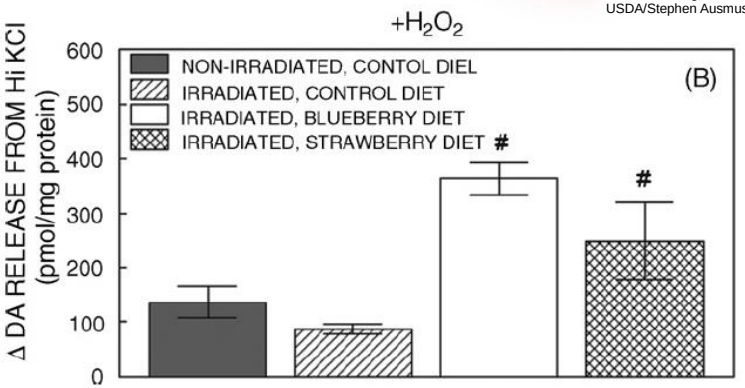


Image Credit: USDA/Stephen Ausmus

BCM Research

- Studies targeting major cancer pathways (TGF-Beta, Telomerase, p53, etc.)
- Studies of anti-inflammatory / anti-oxidants on cancer and CNS endpoints
- Clinical therapies against acute syndromes: myeloid growth factors (Neupogen, Neulasta), anti-nausea drugs (Zofran), steroid creams, and antibiotics



Both blueberry and strawberry diets significantly protected against the effects of radiation on dopamine release compared to controls.
(Shukitt-Hale, et. al 2007)

New Work

- NSBRI CSRR considers BCMs against acute and degenerative tissue effects
- 2014 NRA/NSCOR solicited for research addressing sleep and exercise as possible modifiers of acute inflight CNS radiation effects
- 2015 NRA included Special Research Topic on Biological Countermeasure Studies
- GCR simulator at NSRL essential for mixed field validation

Biological Countermeasures Development: Collaborative Opportunities

NASA is member of Informal Working Group of government agencies established to share information on aspects pertaining to radiological/nuclear terrorism: Radiation Bioterrorism Research and Training (RABRAT)

Much of "other Agency" work focused on protection from acute radiation syndromes

However, largest risks for NASA are late effects

- Acute countermeasures against bioterrorism/nuclear accidents largely prevent cell death after irradiation
- These BCM's have potential to increase yield of mutant cells survival with increased risk of cancer

NCI/NIH and BARDA are expressing interest in low dose/dose-rate late effects opening possibility of increased collaborative studies

National Institute of Allergy and Infectious Diseases

Radiation Tools for Design, Analysis, and Optimization

Integrated Radiation Shielding Design Tool Project *maintains an engineering tool set of current best practices, databases, and state-of-the-art methodologies to evaluate and optimize human systems such as spacecraft, spacesuits, rovers, and habitats.*

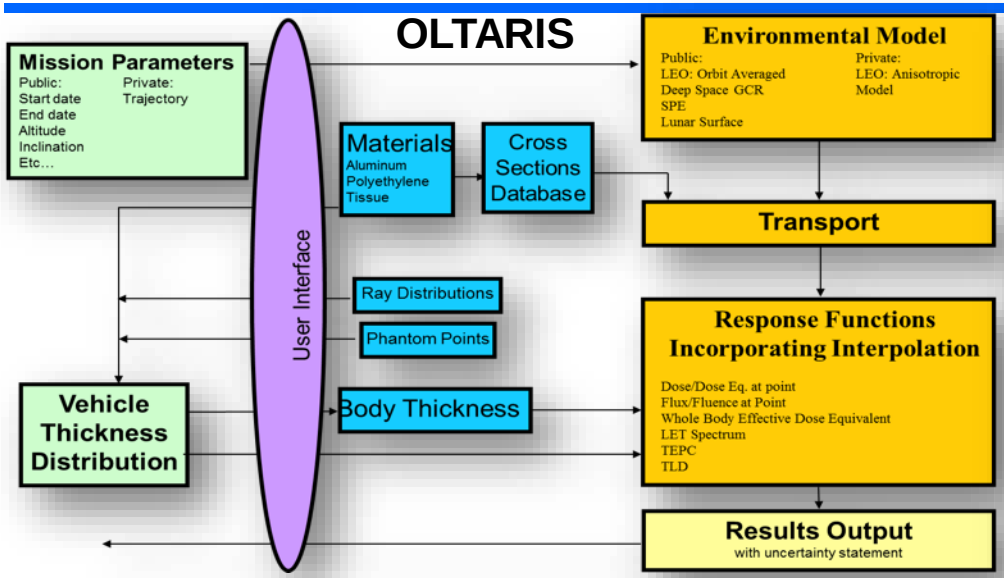
- Supports verification of radiation vehicle design requirements and adherence to ALARA (as low as reasonable achievable) requirements
- Incorporates most recent research results into computational models that are made available to radiation community
- Follows NASA Software Development and Verification and Validation (V&V) processes and is Configuration Managed.
- Methodologies and data bases shared with NASA Cancer Risk Assessment Model and Operations

https://oltaris.nasa.gov

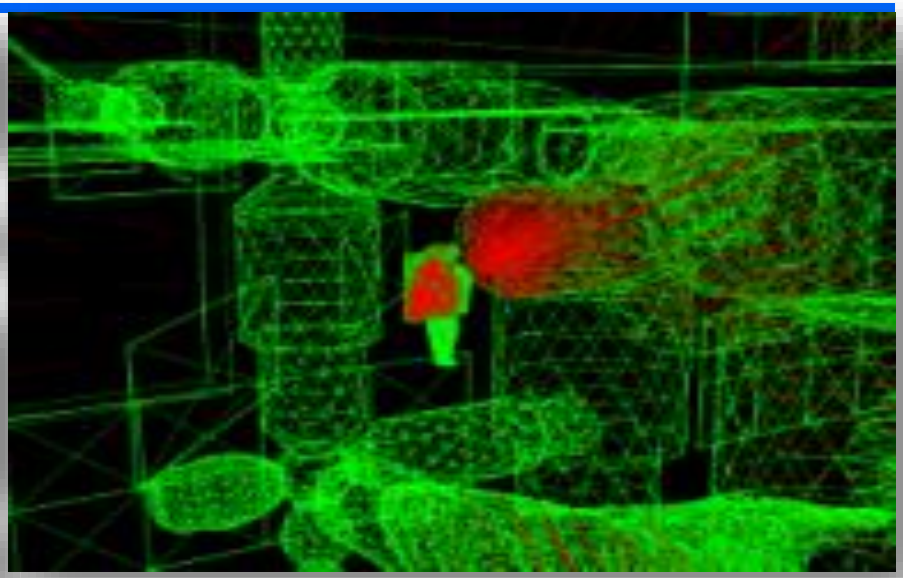
- Access provided to industry and government customers:
  - NASA: HRP, AES, STMD, Mission Operations
  - MSL RAD Science Team
  - Boeing, ATK, SpaceX, Bigelow Aerospace
  - Universities

- Supports development of GCR Simulator Requirements at NSRL

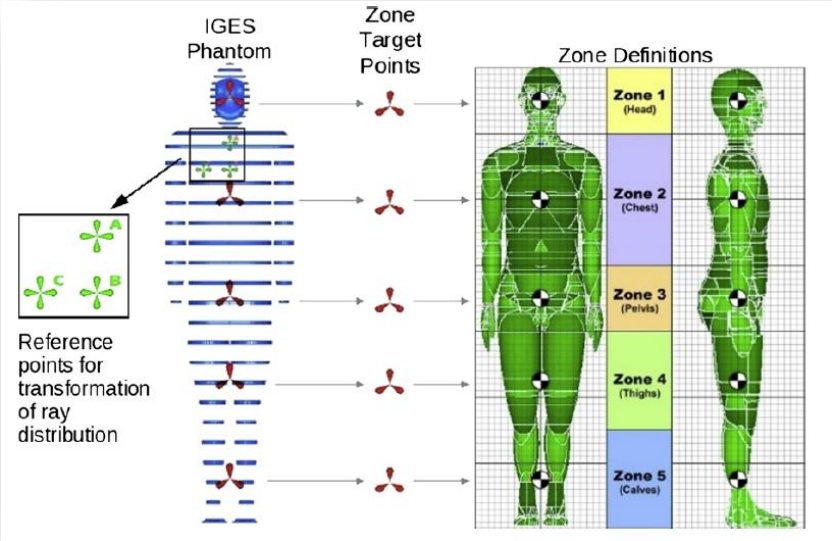
Radiation Tools for Design, Analysis, and Optimization



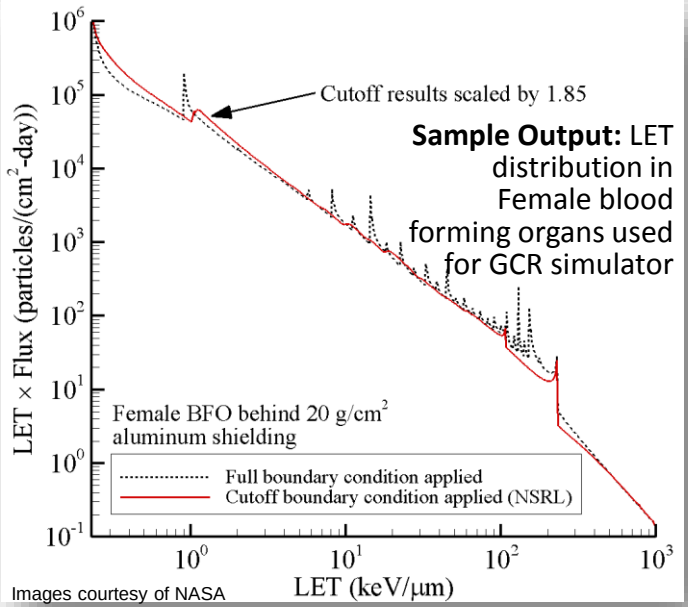
Design Tool Models, Databases, and Interfaces



ISS Shield Distribution for EVA



Human Body Phantoms to Position in Vehicles

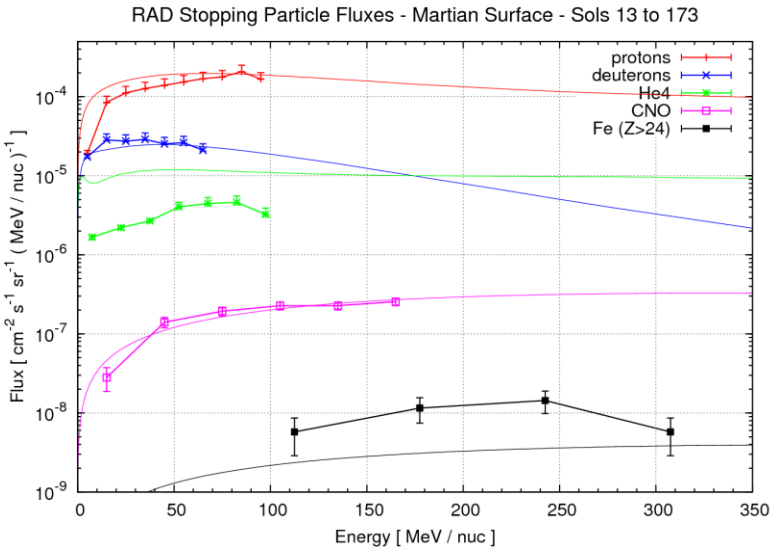


Images courtesy of NASA

Space Radiation Transport Codes

- **Quantification of mixed field environment within spacecraft and on Mars important to understanding radiobiological risks as well as for shield optimization**
- **HZETRN 2015 Release (December 2015)**
  - Updates Include transport of multiple additional particle types: pions, muons, electrons, positrons and photons important thick shields including Mars atmosphere and ISS
  - Addition of 2D/3D transport procedures for neutrons and light ions
- **Extensive verification and validation continues**
  - Comparisons to measurements in Earth's atmosphere and ISS
  - Comparisons with Monte Carlo transport models
- **MSL RAD measurements being evaluated using NASA radiation models for validation of GCR, SPE, and atmospheric models as well transport methods and nuclear models**
  - Initial validation with RAD measurements in good agreement
  - Areas where models potentially need improvement have been identified

Mars Science Laboratory RAD



Measured fluxes (symbols) are compared to OLTARIS simulations (thin lines) assuming atmospheric shielding of 18.6 g/cm2 and a solar modulation parameter of Φ = 627 MV (MSL RAD)

Images courtesy D.M. Hassler, MSL RAD PI: Southwest Research Institute

STMD Game Changing GCR Thick Shield Project: Mitigation of Galactic Cosmic Rays

Problem Statement:

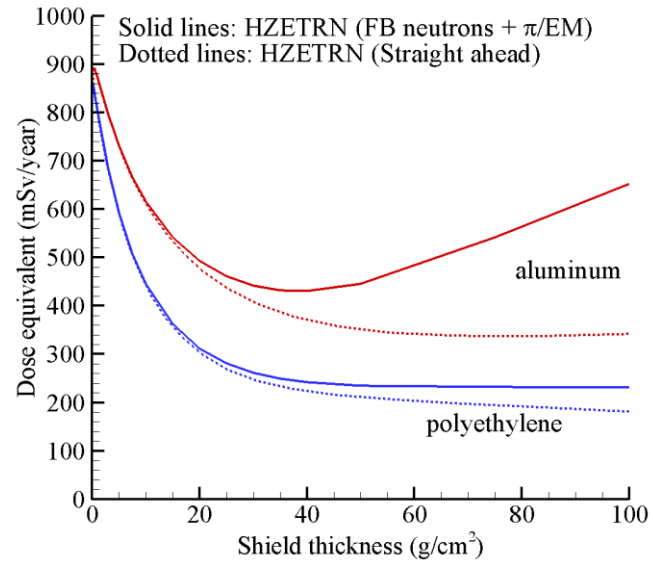
- Cost/mass effective radiation shield solutions against galactic cosmic radiation to enable NASA's exploration DRMs beyond LEO do not exist

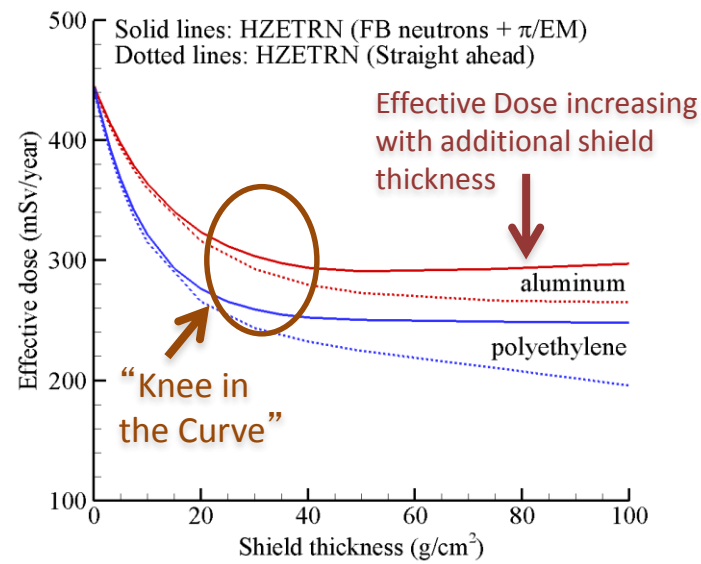
Project:

- Establish first shield thickness requirements for exploration which removes passive shielding from design trade space. (STMD FY15 Project)
- Validate multi-purpose GCR thick shielding material systems and technologies that offset the mass and volume penalties of parasitic shielding by performing other mission essential functions.

Why now?

- New analytical evidence of minimum in dose equivalent at depths important to shield design allowing for optimization
- NASA radiation facility upgrades allows experimental validation of thick shield approaches.
- Supports Exploration Trade Studies

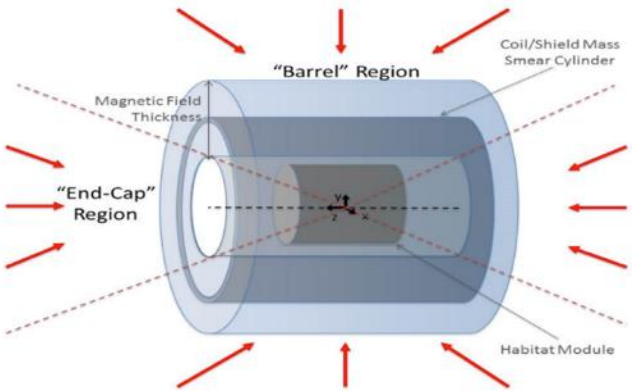




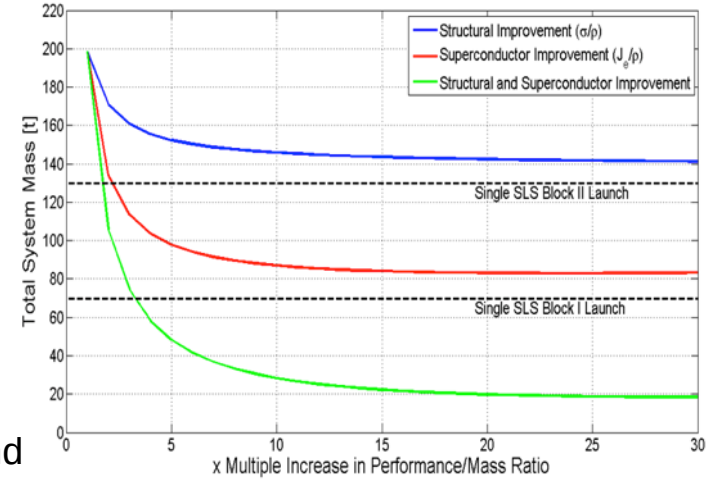
NASA calculated graphs: Blattnig, S.R., Slaba, T.C., Bahadori, A.A., Norman, R.B., Clowdsley, M.S., Impact of Recent Transport Code Updates on Vehicle Design and Optimization Strategies. Human Research Program Investigators Workshop. Galveston TX, 2014.

STMD NIAC: Active Radiation Shielding Concepts

- **NASA early innovation programs continue to fund high-risk, high pay-off ideas to advance active shield technologies and concepts**
- **Evaluations of potential active radiation shielding concepts include mini-magnetospheres, electrostatic shielding, and confined magnetic fields using superconducting magnets**
- **Parametric studies have traditionally indicated that active concepts require too much power and/or structural mass to be credible in a system context as well as other potential problems (safety and reliability).**
- **Recent improvements in superconducting technology motivated a reevaluation of active shielding concepts using superconducting magnets:**
  - ESA Active Radiation Shield for Space Exploration Missions project
  - NIAC Radiation Protection and Architecture Utilizing High Temperature Superconducting Magnets project
  - Study concluded that dramatic improvements in superconducting and structural technologies are needed to enable concept
- **Investment in analytical tools for accurate sizing and evaluation as well as periodic trade studies in a systems construct are warranted as technologies advance**



Model Geometry and Mass Locations



Structural (Strength/Mass Ratio) and Superconductor (Current/Mass Ratio) Performance Improvements Effects on System Mass for 2m Field Thickness and 150 mSv Exposure Limit Design

(Washburn, S.A., Blattnig, S.R., Singlettery, R.C., Westover, S.C., Active Magnetic Radiation Shielding System Analysis and Key Technologies. Life Sci. Space Res. 4: 22-34, 2015)

Solar Particle Event Storm Shelter Technology Maturation (AES)

Goal: Minimal Mass Shield Concepts

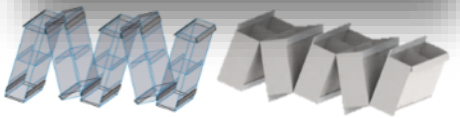
Approach:

- Design concepts utilizing onboard mass (water, equipment, consumables, waste, etc.) and evaluate radiation protection properties
- Fabricate prototypes
- Perform operational assessments

Concepts developed:

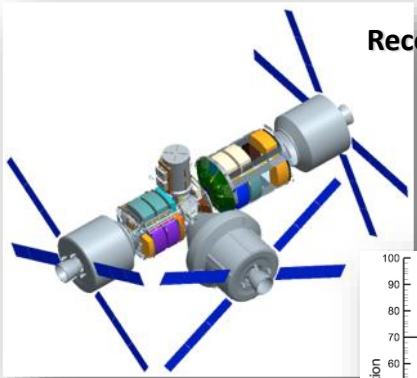
- Water walls and pantries in the crew quarters
- Reconfigurable logistics concepts
- Wearable vests and augmented sleep restraints

Reconfigurable Logistics

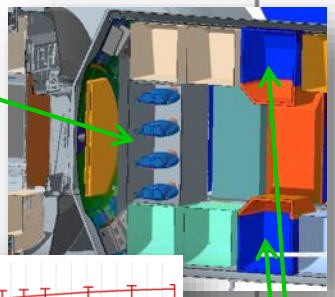


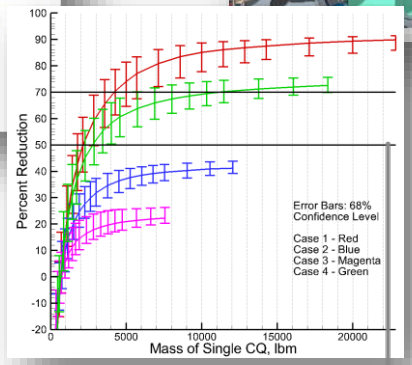
Water Walls

Radiation Protection Analyses

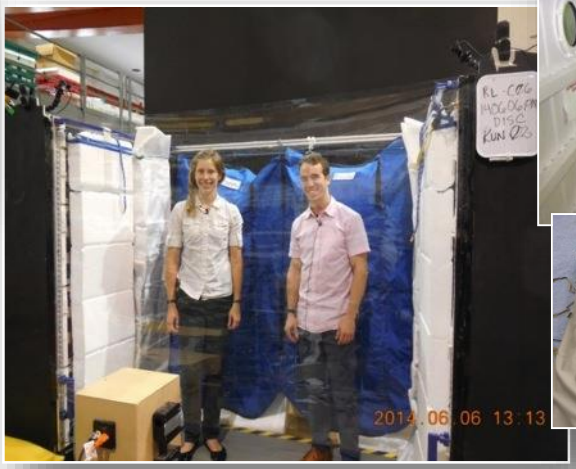


Multiple versions analyzed in realistic vehicle architecture to identify options requiring least parasitic mass.





Operational Testing

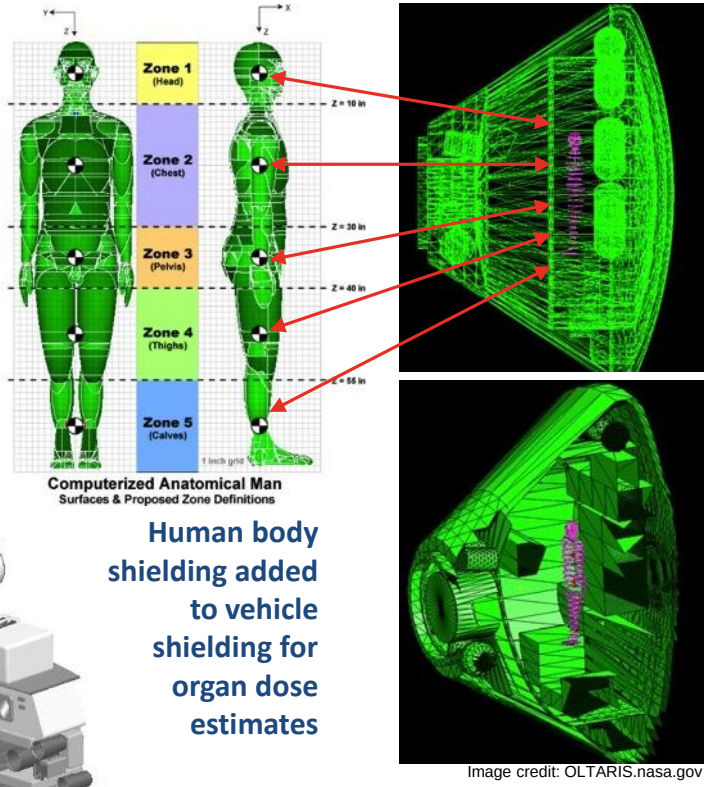


Images courtesy of NASA, used with permission

Vehicle Optimization for Improved Protection

Optimization Tools utilized to Meet Vehicle Design Requirements

- Current mission modeling and computational capabilities support the rapid evaluation of astronaut exposure for multiple vehicle configurations through all design phases (PDR, CDR, Phase C/D simulations, and Ops).
- Vehicles requiring minimal parasitic mass for radiation protection can be designed through the optimal placement of vehicle systems, cargo, and consumables.
- Requirements for additional shielding or improved shield materials can then be optimized.

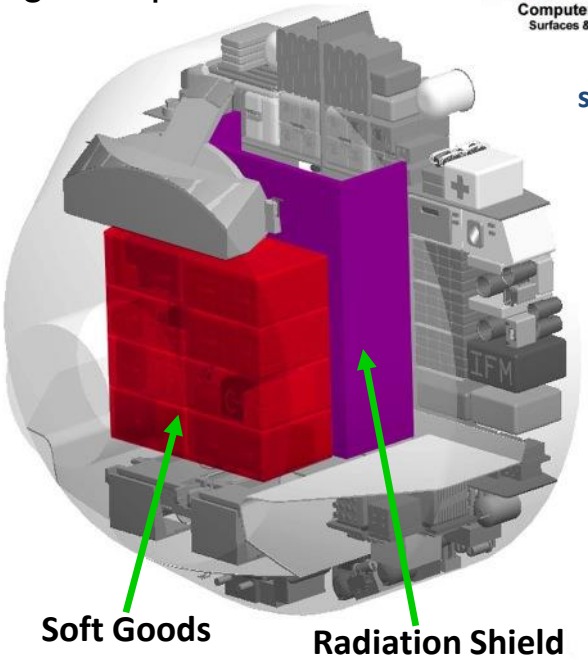


Human body shielding added to vehicle shielding for organ dose estimates

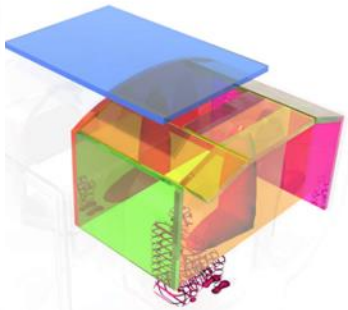
Image credit: OLTARIS.nasa.gov

Constellation Crew Exploration Vehicle (CEV)

- Early in the design process, the need for parasitic shielding for SPEs was minimized by moving soft goods to cover the thinly shielded regions.
- As design matured, a solution requiring no parasitic mass was identified.



Lunar Rover Concept



SPE protection: Radiator water and reconfigurable shielding minimum mass analysis to meet requirement

Images credit: NASA

Summary
Radiation Protection Research and Technology

Space radiation is a major challenge to exploration

- Risks impact mission length and/or crew selection
- Significant shield mass to protect against risks and uncertainties
- New findings and technology advancements expected to change overall risk posture

NASA approach to solve these problems

- Established pool of high quality external investigators making significant progress on closing the knowledge gap on a broad-range of biological questions
- Perform extensive peer reviewed research focused on uncertainty and risk reduction at NASA Space Radiation Laboratory
- Ongoing/extensive external reviews of our HRP Space Radiation Research Plan by authoritative bodies
- 2014 NCRP Commentary No. 23 “Radiation Protection for Space Activities” confirms our research strategy and emphasis
- Probabilistic risk assessment framework and validated tool sets supporting Exploration Missions and shield design optimization
- Recent Agency investments in SPE alert, monitoring and forecasting, SPE shield maturation, and GCR shielding technologies
- HEOMD and SMD collaborations supporting our understanding of the space radiation environment and operational monitoring

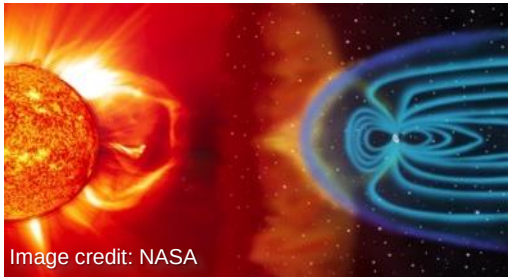


Image credit: NASA

Image credit: Brookhaven National Laboratory (BNL)

Image credit: NASA

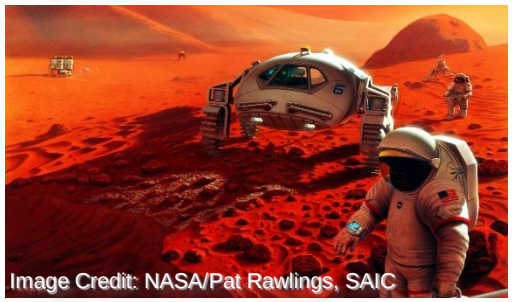


Image Credit: NASA/Pat Rawlings, SAIC

Integrated Radiation Protection Strategy Enables Human Mars Exploration

Integration across Research and Technology Required…

National Aeronautics and Space Administration

Mission and Architecture Systems Analysis

Near Earth Asteroid Systems

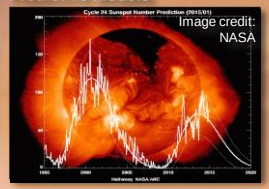
Mars MTV-02

In-situ Resource Utilization

Active Shielding Concepts

Environmental Modeling, Monitoring, and Prediction

Predictive Models



Precursor Data — MSL RAD

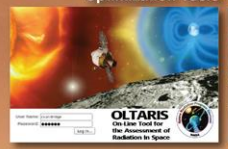
On-board Dosimetry– ISS TEPC

Crew Selection and Operations

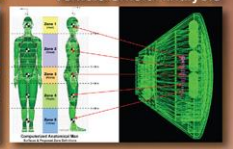
Individualized Risk Assessment

Integrated Radiation Protection System Design and Analysis

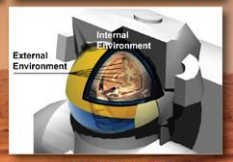
Design and Optimization Tools



Crew Exploration Vehicle Shield Analysis



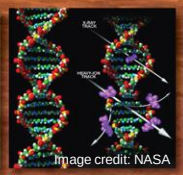
Images credit: OLTARIS.nasa.gov (top) and NASA (lower)



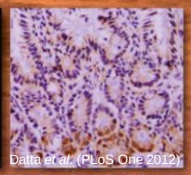
High Energy Nuclear Physics and Transport

Radiobiology and Biological Countermeasures

NASA Space Radiation Lab at Brookhaven National Laboratory

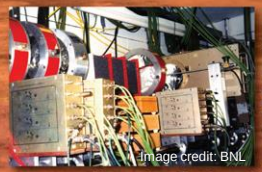


X-ray vs. Heavy ion Track Damage to DNA



Leukemia induction with GCR — Mouse Model

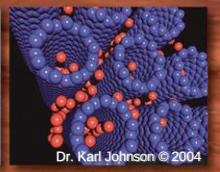
Innovative Multi-Purpose Shield Solutions



Heavy Ion Testing of Inflatable Shield Prototype

Water Filled Composite Shield Sections

Reconfigurable Personal Shielding



Hydrogen Storage BNNT

Background Image credit: NASA

Overview of Mars Mission Crew Health Risks

- **Mission And Crew Health Risks Are Associated With Any Human Space Mission**
  - Briefing is focused on space exploration crew health risks associated with space radiation
- **Exploration Health Risks Have Been Identified, And Medical Standards Are In Place To Protect Crew Health And Safety**
  - Further investigation and development is required for some areas, but this work will likely be completed well before a Mars mission launches
- **There Are No Crew Health Risks At This Time That Are Considered "mission-stoppers" for a Human Mission to Mars**
  - The Agency will accept some level of crew health risk for a Mars mission, but that risk will continue to be reduced through research and testing
- **The Most Challenging Medical Standard To Meet For A Mars Mission Is That Associated With The Risk Of Radiation-induced Cancer**
  - Research and technology development as part of NASA's integrated radiation protection portfolio will help to minimize this long-term crew health risk

ACRONYM LIST: Human Research Program

- AES – Advanced Exploration Systems
- ALARA – as low as reasonable achievable
- BCM – Biological Countermeasures
- CDR – Critical Design Review
- CEV – Crewed Exploration Vehicle
- CNS – Central Nervous System
- CSRR – Center for Space Radiation Research
- DRM – Design Reference Missions
- GCR – Galactic Cosmic Radiation
- HCC – Hepatocellular Carcinoma
- HEOMD – Human Exploration and Operations Mission Directorate
- HRP – Human Research Program
- HZE – High charge (Z) and energy
- HZETRN – High charge & energy transport code
- ISS – International Space Station
- IV&V – Independent Verification and Validation
- JSC – Johnson Space Center
- LEO – Low Earth Orbit
- LET – Linear Energy Transfer
- MSL RAD – Mars Science Laboratory Radiation Detector
- NCRP – National Council on Radiation Protection
- NSBRI – National Space Biomedical Research Institute
- NSCOR – NASA Specialized Center of Research
- NSRL – NASA Radiation Laboratory
- PDR – Preliminary Design Review
- REID – Risk of Exposure Induced Death
- RBE – Relative Biological Effectiveness
- SMD – Science Mission Directorate
- SPE – Solar Particle Event
- SRPE – Space Radiation Program Element
- STMD – Space Technology Mission Directorate
- V&V – Verification and Validation