



Mars Mission and Space Radiation Risks

Space Radiation Research and Technologies for Risk Mitigation

**Briefing to
NAC HEO/SMD Joint Committee
April 7, 2015**

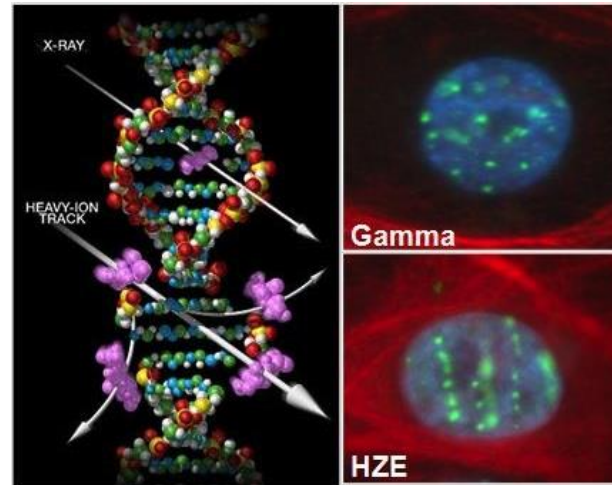
**Lisa C. Simonsen, Ph.D.
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NASA Human Research Program**



The Space Radiation Problem: The Biological Perspective

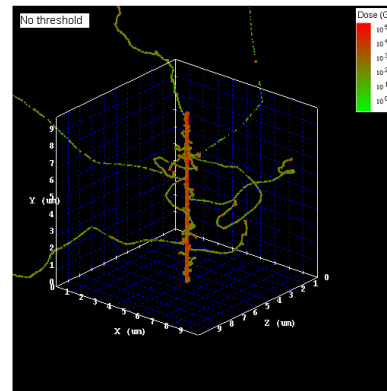


- Interplanetary crews will be exposed to a high LET radiation environment comprised of high-energy protons and heavy ions (HZE's) as well as secondary protons, neutrons, and fragments produced in shielding and tissue
- Heavy ions are qualitatively different from X-rays or Gamma-rays: High LET vs. low LET
 - Densely ionizing along particle track
 - Cause unique damage to biomolecules, cells, and tissues
 - Distinct patterns of DNA damage (mutation spectra, chromosome aberrations) 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 applied or developed
- Synergistic modifiers of risk from other spaceflight factors

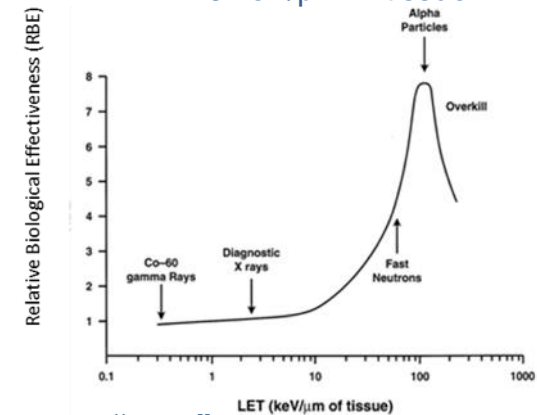


DNA Damage
 γ H2AX foci in EPC2-hTERT cells.
 (Cucinotta & Saganti, Patel & Huff, NASA)

1 GeV/u ^{56}Fe nucleus
 LET $\sim 150 \text{ keV}/\mu\text{m}$



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



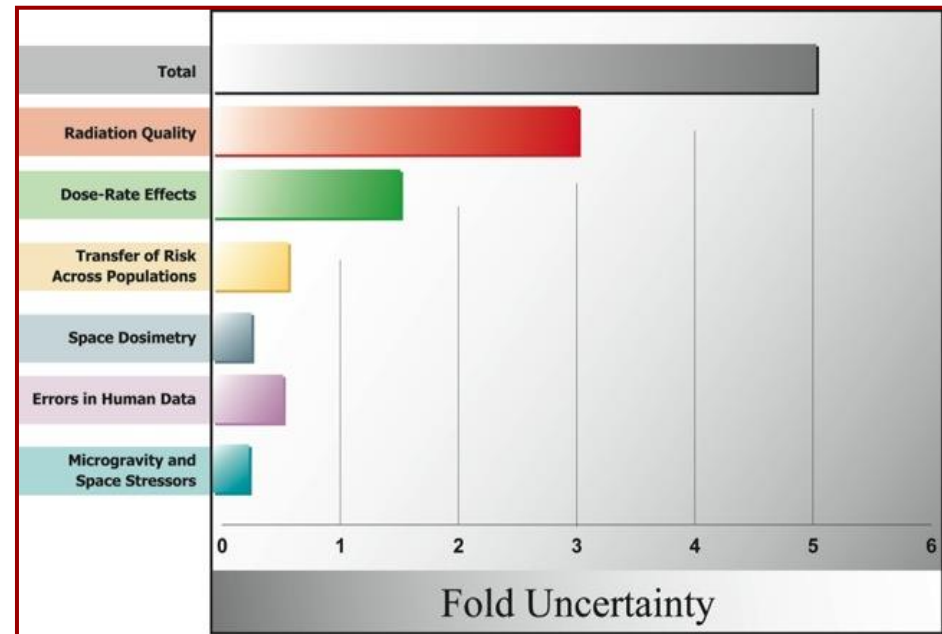
- External review by National Council on Radiation Protection (NCRP), National Academy of Sciences, and HRP Standing Review Panels
- Seven NASA Specialized Centers of Research (NSCOR's)
- Funded research at over 40 US Universities including collaboration with US Department of Energy (DoE)
- Space radiation simulated at the NASA Space Radiation Laboratory (NSRL)
- Partnership with NASA's Space Radiation Analysis Group on transition of risk assessment 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



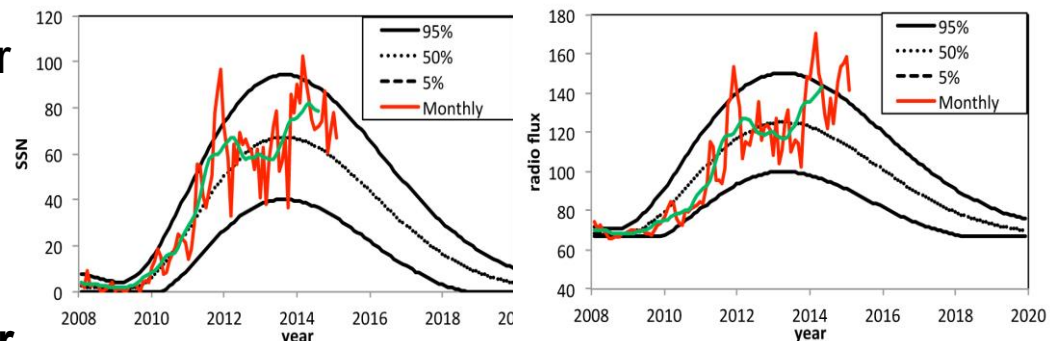
Major Sources of Uncertainty in Estimating Risks from Space Radiation for Exploration Missions



- **Radiation quality effects on biological damage**
 - Qualitative and quantitative differences between space radiation compared with x-rays or gamma rays
- **Dependence of risk on dose rates 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 solar events**
 - Temporal and size predictions
- **Predicting galactic cosmic ray solar min/max conditions at future time points**



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

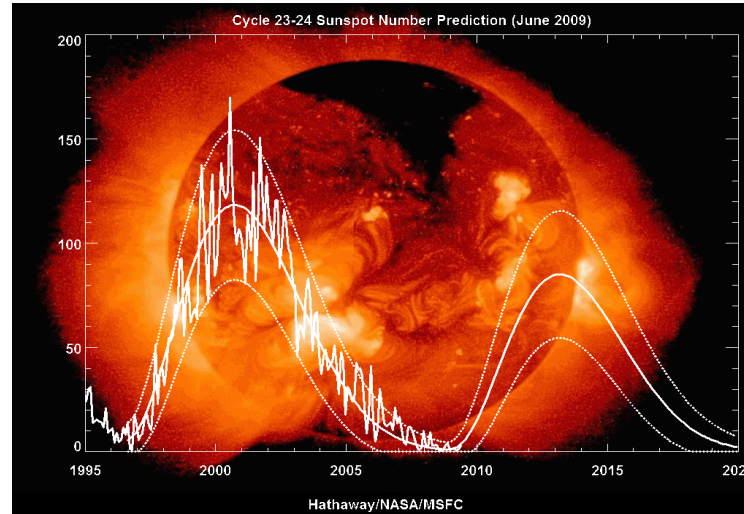


Theory predicts Solar Cycle 25 to be one of the weakest in centuries
(Santos Koos, Lindsey and Badavi, Francis F., NASA-funded research through Old Dominion University Research Foundation)

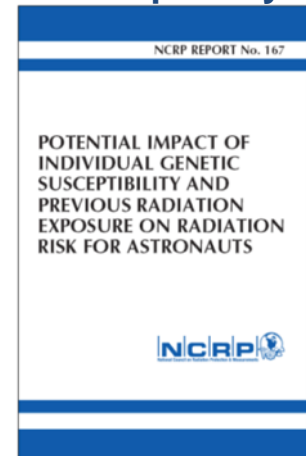
Mitigation Approaches

- **Time in the Solar Cycle**
- **Ability to minimize exposure to SPE's**
- **Radiation Shielding**
 - Amounts and material types
 - Design Optimization
- **Accurate Risk Quantification/ Uncertainty reduction**
- **Crew Selection**
 - Age, gender, lifestyle factors, etc.
 - Individual Sensitivity (genetic factors)
- **Biological Countermeasures (BCMs)**
 - Radioprotectors / Mitigators
- **Biomarkers predictive of radiation induced diseases**
 - Future individualized risk assessment
 - Early detection and prognostic monitoring

Variation of Solar Activity



Individual Susceptibility



(NCRP 2011)

α -lipoic acid

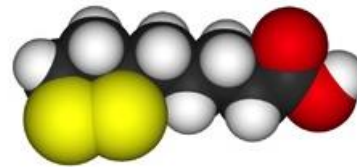
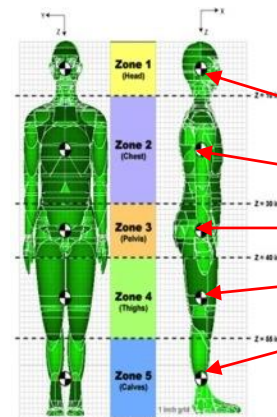


Image credit: Ben Mills

amifostine



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Computerized Anatomical Man
Surfaces & Proposed Zone Definitions

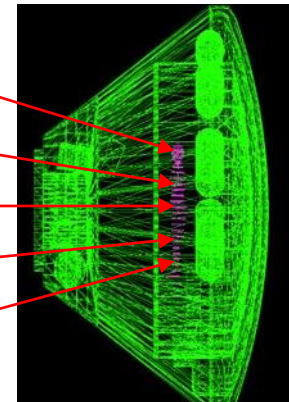


Image courtesy of OLTARIS.nasa.gov

BCM: Pharmaceuticals

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

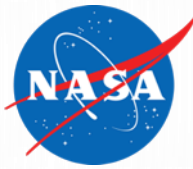


NSRL Beam Line

Images Courtesy of Brookhaven National Laboratory (BNL)



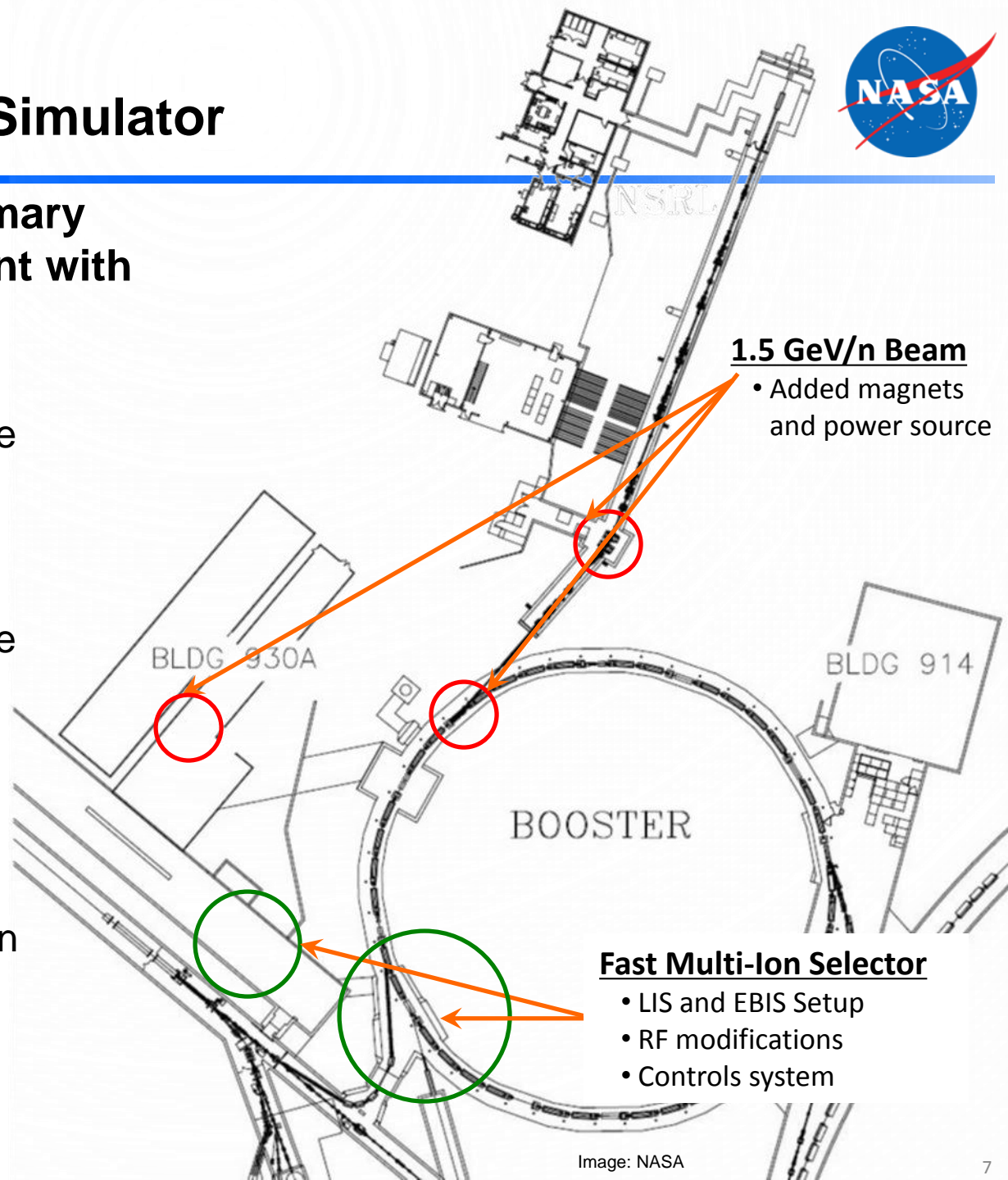
NSRL



NSRL Upgrades: Galactic Cosmic Ray Simulator

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

- Includes a rapidly switchable ion source capable of delivering between 6 to 12 ion species.
- Magnet upgrades enable the delivery of beams at 1.5 GeV/n thus increasing the 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/mm.
- Completion in late 2016.



1.5 GeV/n Beam

- Added magnets and power source

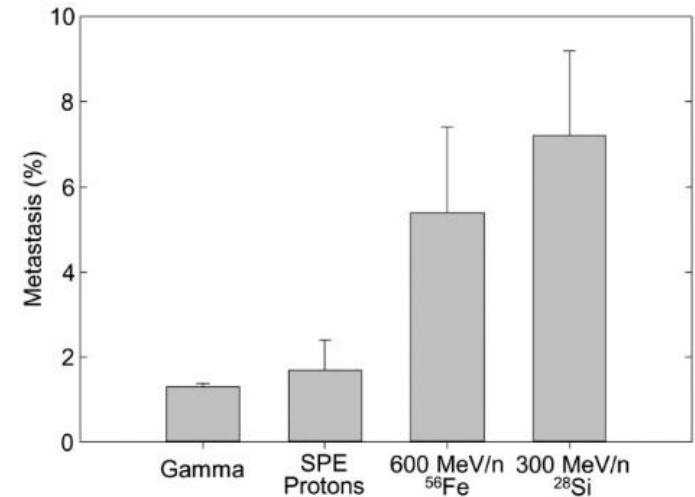
Fast Multi-Ion Selector

- LIS and EBIS Setup
- RF modifications
- Controls system

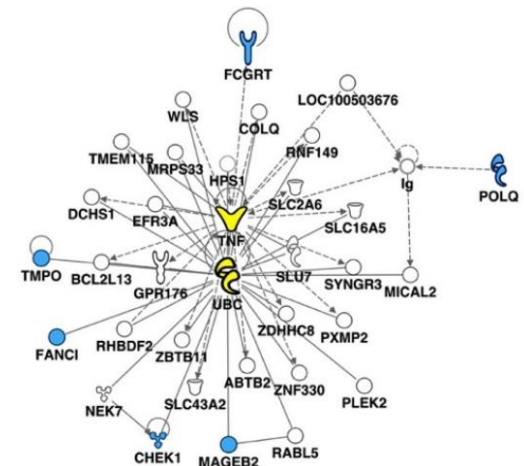
Radiation Carcinogenesis Research Focus



- **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 in carcinogenesis studies 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 on risk estimates
 - Research that will describe the biological basis for sex differences and individual sensitivity on cancer risks
- **Research results support development of an integrated risk model with acceptable uncertainty for exploration missions**
- **Research incorporating 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)



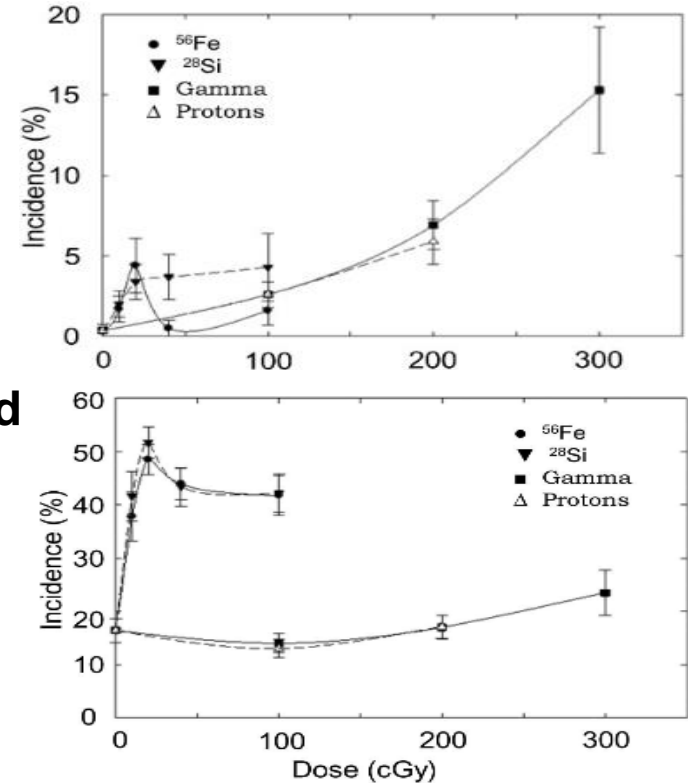
Gene analysis can support the determination of survival outcome of patients with lung cancer
(UTSW NSCOR, PI: J. Minna)

Major Findings on Cancer Risk from NSRL

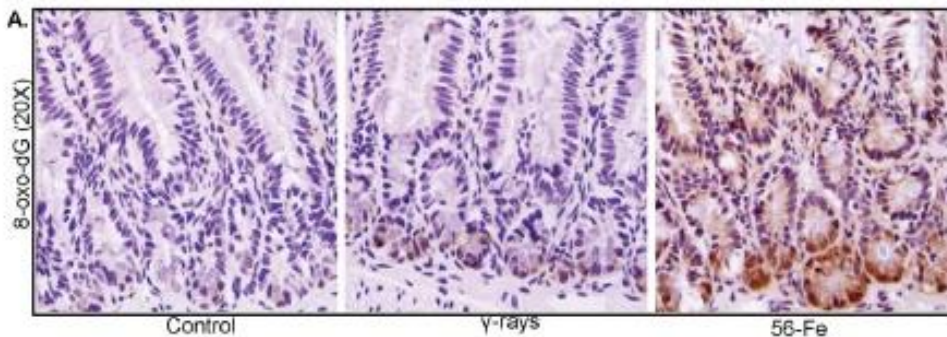


- Evidence for increased aggression of HZE tumors
- Distinct gene expression and metabolomics changes between high and low LET, and between specific ions
- Persistent oxidative stress and inflammatory pathway activation
- Evidence for non-linear response at low dose due to non-targeted effects, which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

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 CNS cognitive, behavioral, and functional changes as well as possible late neurodegenerative conditions
 - Mechanistic basis for observed CNS decrements
 - Establish possibility of dose thresholds for these effects
 - Radiation quality and dose-rate dependencies
- **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**
- **Future systems biology approaches to facilitate extrapolation of CNS effects seen in animal models to possible performance changes in humans**

Eating, sleeping and working in space.



Images courtesy of NASA

Major Findings on CNS Risk from NSRL

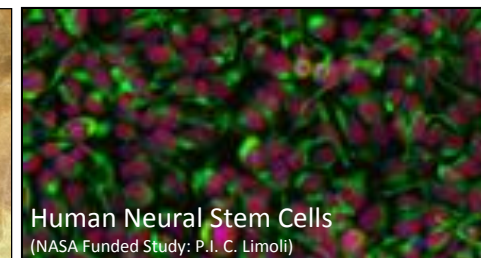
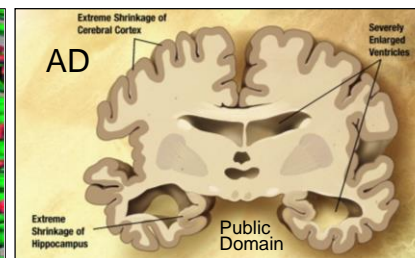
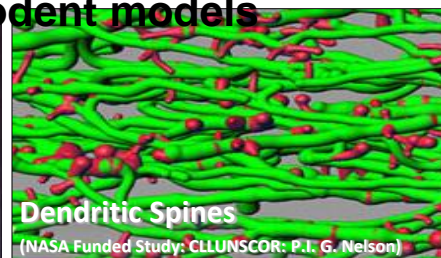


Research with animal models shows important changes to the CNS occur at HZE exposure levels in range of concern to NASA

- NASA studies with rodents 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
- Effects not seen with similar doses of low-LET radiation
 - 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

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; possible limitation in using rodent models



Risk of Cardiovascular Disease from Space Radiation Exposure¹²



- **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**
- **The additional mortality and morbidity risks for non-cancer diseases of the cardiovascular system are major concerns because they could increase REID values substantially**

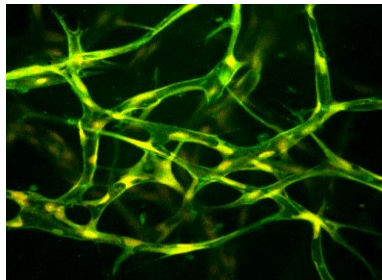


Image courtesy of NASA

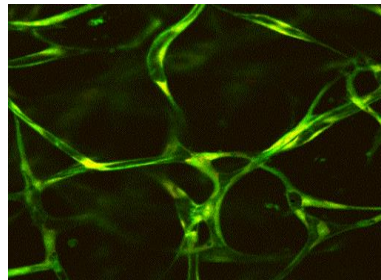
Cardiovascular Disease Research Focus



- **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 and 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**

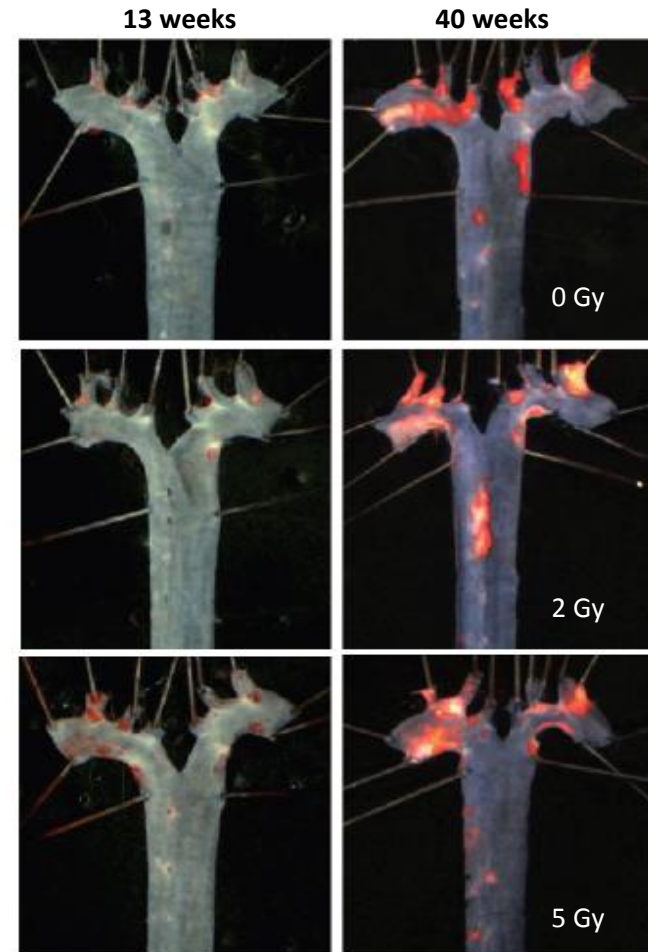


Controls



Iron Irradiated

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



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

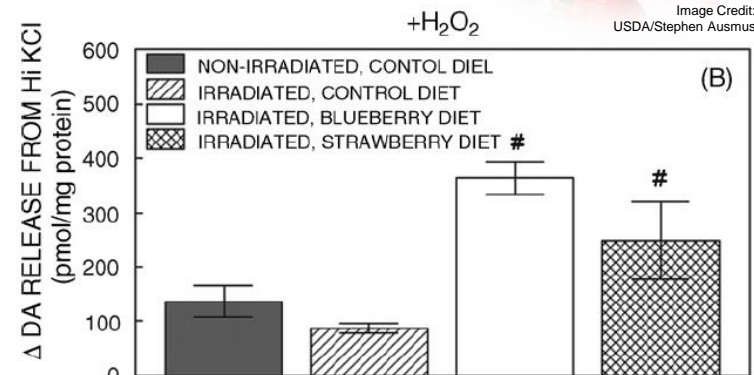
- Protective against many risks (e.g., solid cancers, Leukemia, CNS, cardiovascular)
- Major research emphasis to provide mechanistic basis to identify potential biological countermeasures
- Current studies limited to those providing rigorous scientific rationale for BCM's selected

BCM Research

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

New Work

- NSBRI CSRR will consider countermeasures against acute and degenerative tissue effects
- 2014 NSCOR solicited for research addressing sleep and exercise as possible modifiers of acute inflight CNS radiation effects
- Systems Biology Approaches for integration of large “omics” datasets to support identification and validation of biological countermeasures
- GCR simulator at NSRL essential for mixed field validation



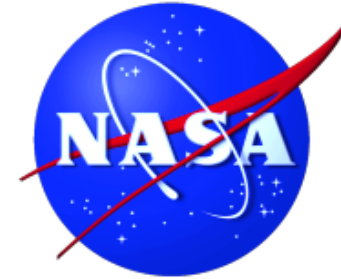
Both blueberry and strawberry diets significantly protected against the effects of radiation on dopamine release compared to controls.

(Shukitt-Hale, et. al 2007)

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

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



The 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. Configuration Managed.
- Methodologies and data bases shared with NASA Cancer Risk Assessment Model and Operations



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OLTARIS
On-Line Tool for
the Assessment of
Radiation In Space

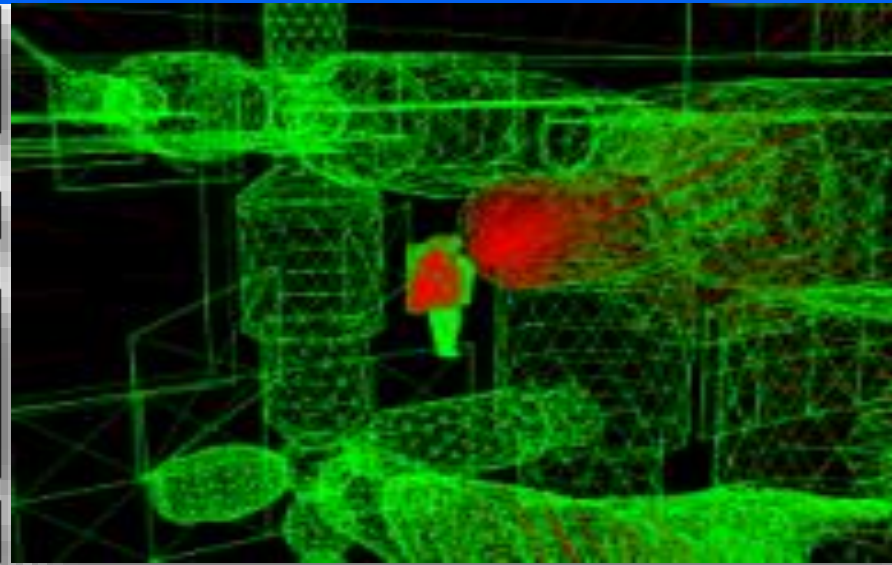
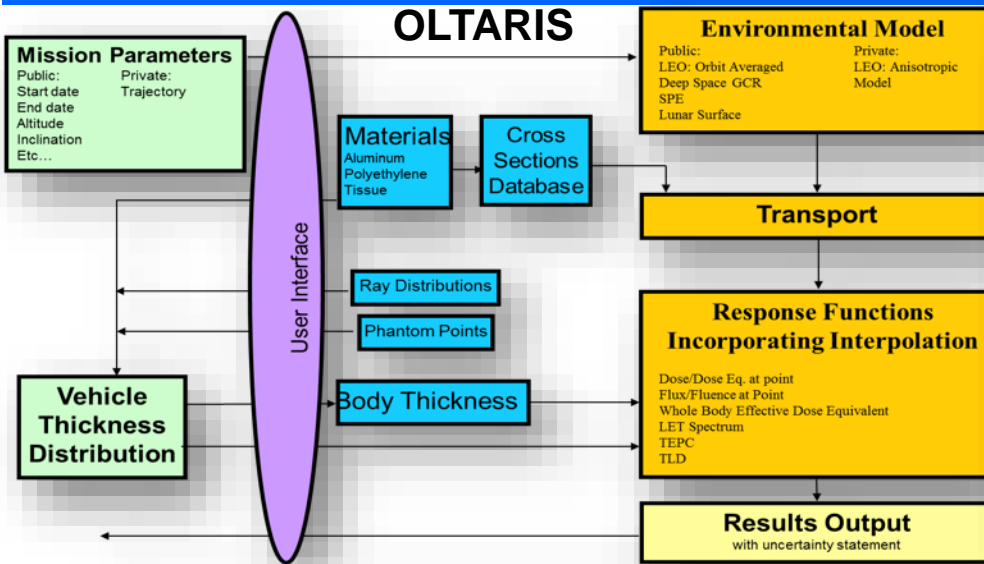


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<https://oltaris.nasa.gov>

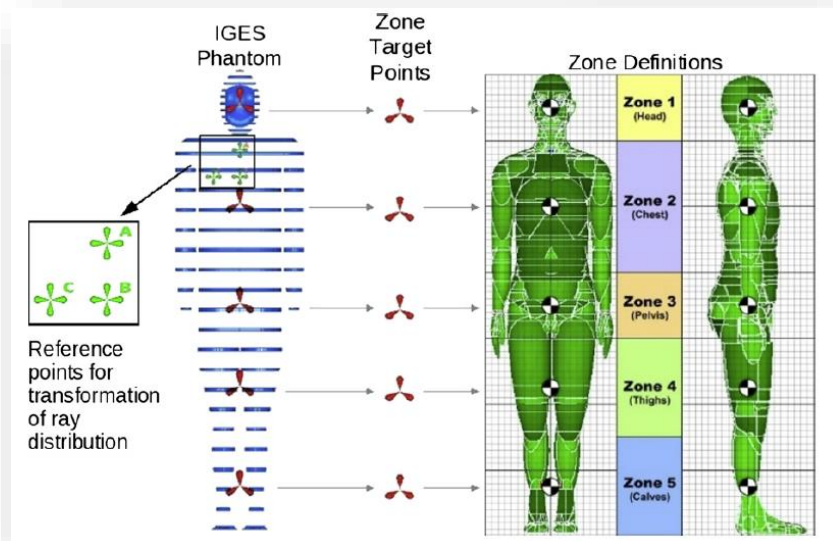
- Access provided to industry and government customers:
 - NASA: HRP, AES, STMD, Mission Operations
 - MSL RAD Science Team
 - Boeing, ATK, SpaceX, Bigelow Aerospace
 - Universities
- Supports development of GCR Simulator Requirements at NSRL

Radiation Tools for Design, Analysis, and Optimization

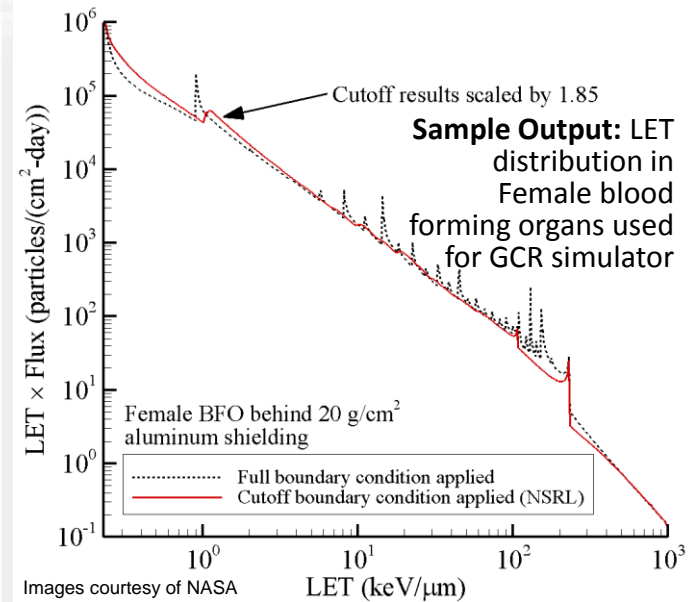


Design Tool Models, Databases, and Interfaces

ISS Shield Distribution for EVA



Human Body Phantoms to Position in Vehicles

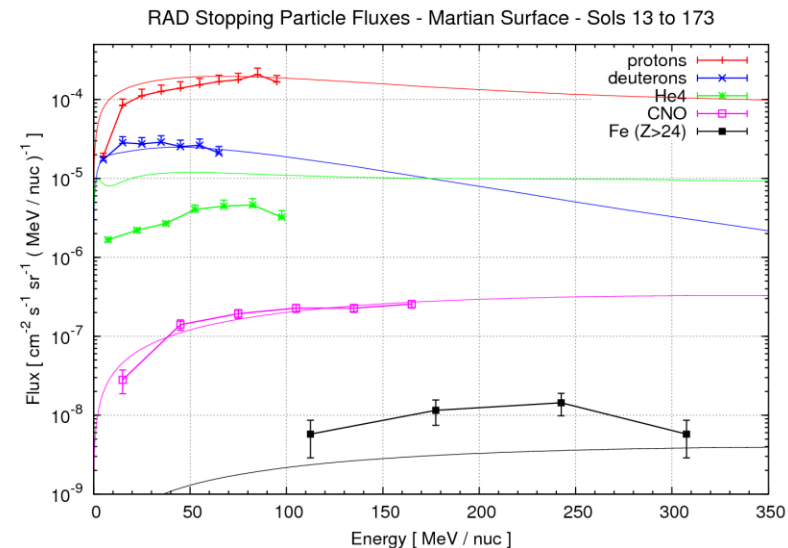
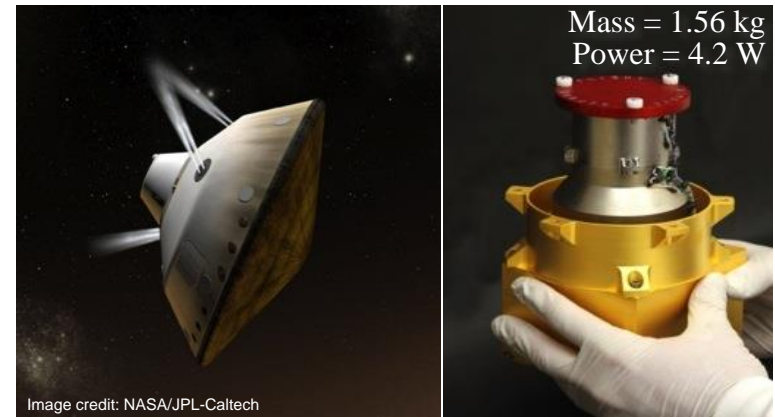


Space Radiation Transport Codes



- **HZETRN 2015 Release (December 2015)**
 - Includes 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
- **Quantification of mixed field environment on Mars important to understanding radiobiological risks as well as for shield optimization**
- **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 $\Phi = 627$ MV (MSL RAD)

Mitigation of Galactic Cosmic Rays: STMD GCR Thick Shield Project



Problem Being Addressed:

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

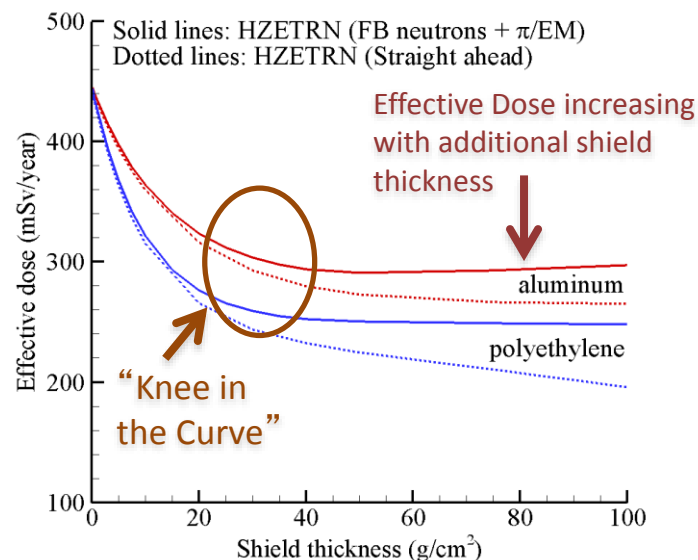
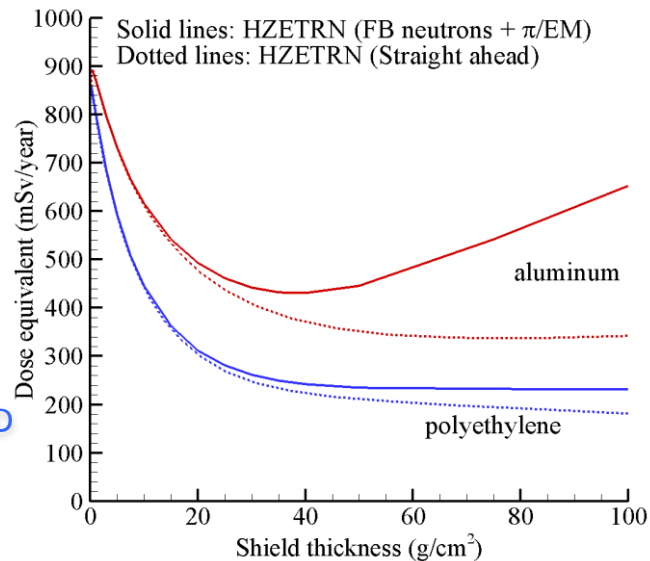
Project:

Establish first shield thickness requirements for exploration taking passive shielding out of design trade space. 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.

Focus of
New STMD
Game
Changing
Project in
FY15

Why now?

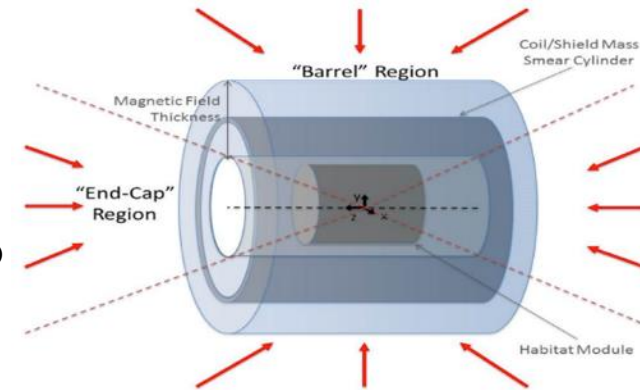
New analytical evidence of minimum in dose equivalent at depths important to shield design allowing for optimization. NASA radiation facility upgrades allows experimental validation of thick shield approaches.



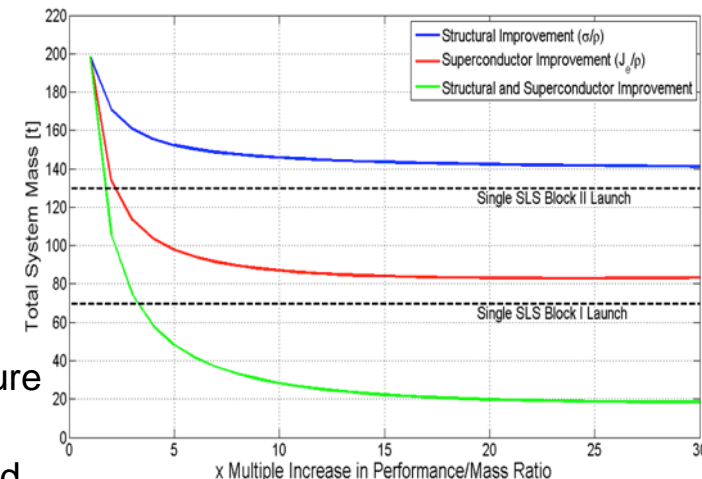
STMD: Active Radiation Shielding Concepts



- 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. Other potential problems were also identified.
- NASA early innovation programs continue to fund high-risk, high pay-off ideas to advance active shield technologies and concepts
- Recent improvements in superconducting technology motivated a reevaluation of active shielding concepts using superconducting magnets through a collaborative effort:
 - 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., Blattinig, 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

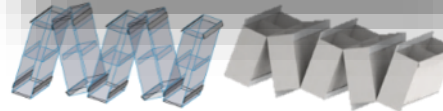
Approach:

- Design concepts utilizing onboard mass (water, equipment, consumables, waste, etc.)
- Evaluate radiation protection
- Fabricate of prototypes
- Perform operational evaluations

Concepts developed:

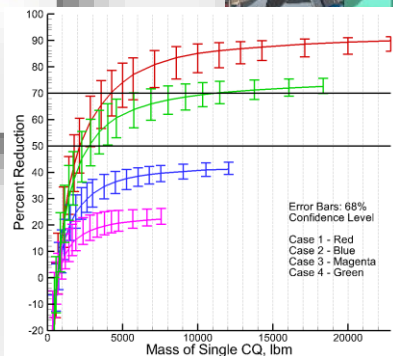
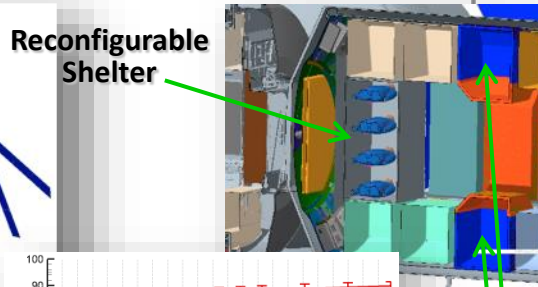
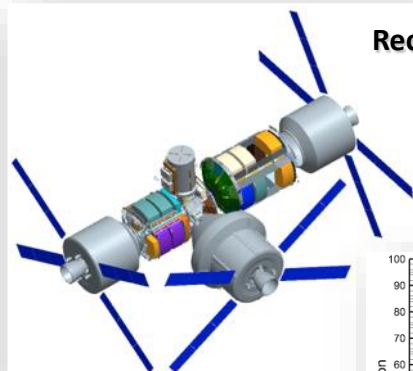
- Water walls and pantries in the crew quarters
- Reconfigurable logistics concepts
- Wearable vests and augmented sleep restraints

Reconfigurable Logistics



Water Walls

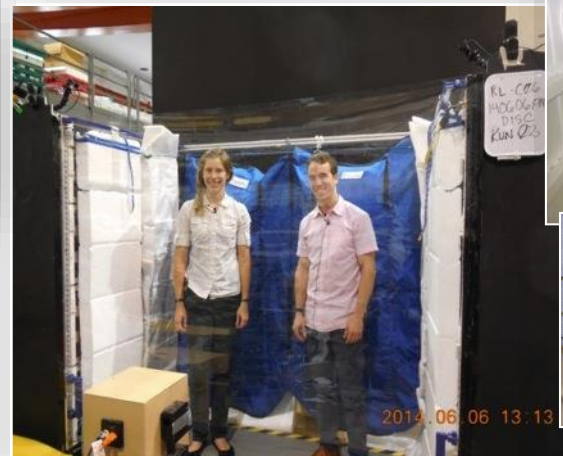
Radiation Protection Analyses



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

Crew Quarter

Operational Testing

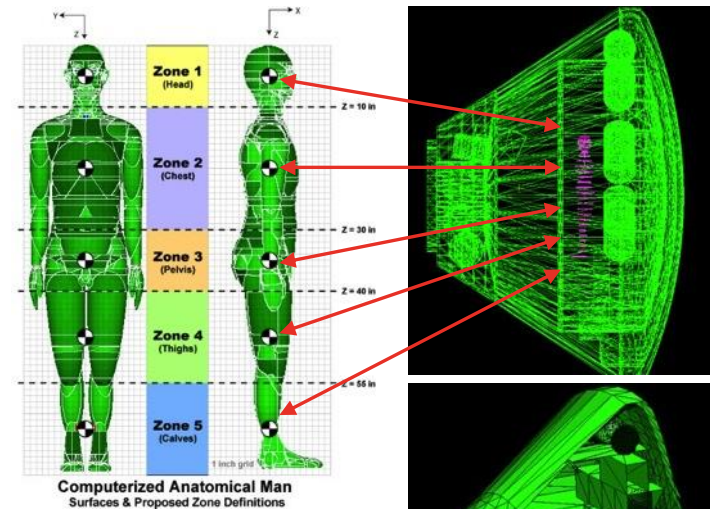


Vehicle Optimization for Improved Protection



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

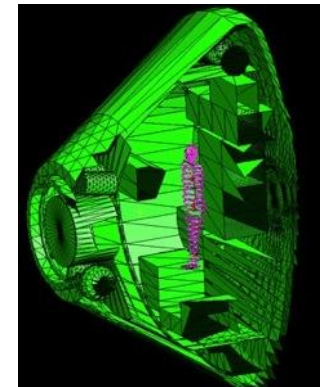
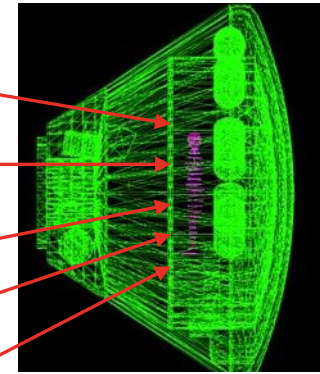
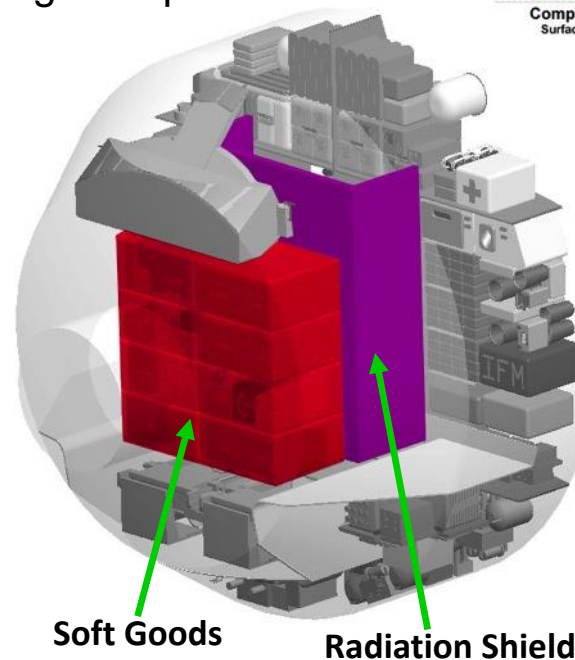


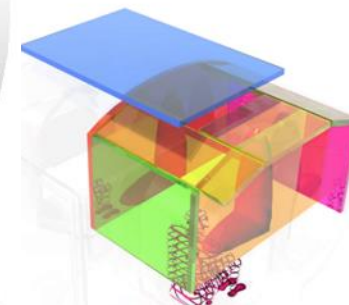
Image credit: OLTARIS.nasa.gov

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

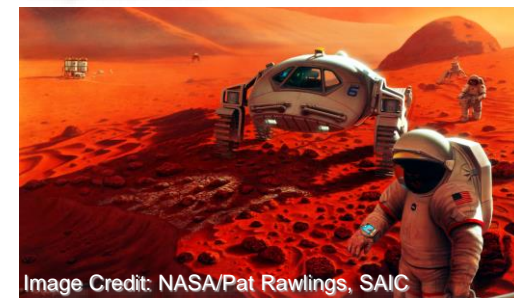
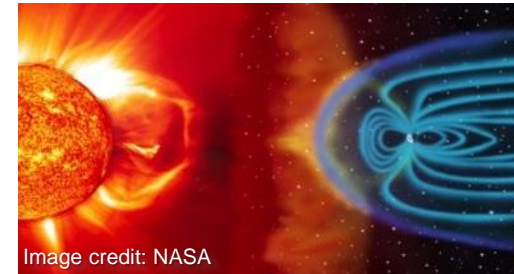


Space radiation is a major challenge to exploration:

- Risks are high limiting mission length and/or crew selection
- Large mission cost to protect against risks and uncertainties
- New findings expected to change overall risk posture

NASA approach to solve these problems:

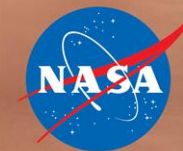
- Established pool of high quality external investigators making significant progress on closing the knowledge gap on a broad-range of biological questions
- Ground-based research focused on uncertainty and risk reduction at NASA Space Radiation Laboratory (NSRL)
- Ongoing/extensive external reviews of our HRP Space Radiation Research Plan by authoritative bodies
- Probabilistic risk assessment framework and validated tool sets supporting Exploration Trade Studies and verification of requirements
- HEOMD and SMD collaborations on research to improve SPE alert, monitoring, and forecasting
- Recent investments in SPE forecasting, SPE shield maturation, and GCR shielding technologies



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

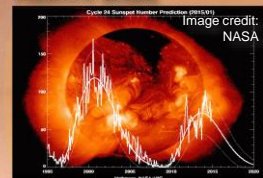
Mars MTV-02

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

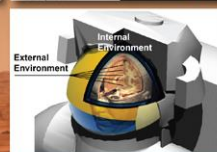
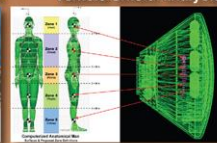
Integrated Radiation Protection System Design and Analysis

Design and Optimization Tools



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

Crew Exploration Vehicle Shield Analysis



High Energy Nuclear Physics and Transport

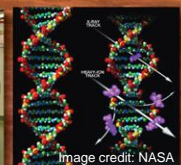
Radiobiology and Biological Countermeasures



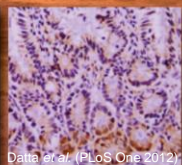
NASA Space Radiation Lab at Brookhaven National Laboratory



Image credit: BNL



X-ray vs. Heavy ion Track Damage to DNA



Data et al. (PLoS One 2012) Leukemia induction with GCR — Mouse Model

Innovative Multi-Purpose Shield Solutions



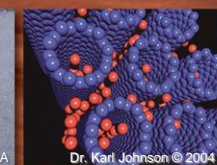
Heavy Ion Testing of Inflatable Shield Prototype



Water Filled Composite Shield Sections



Reconfigurable Personal Shielding



Hydrogen Storage BNNT

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