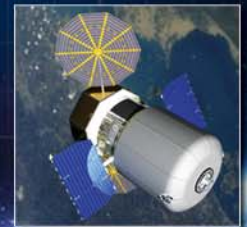


Space Radiation and Risks to Human Health

Janice L. Huff, Ph.D.
Deputy Element Scientist
NASA Space Radiation Program



May 14, 2014





Space Radiation Program Element

*To live and work safely in space
with acceptable risks from radiation*

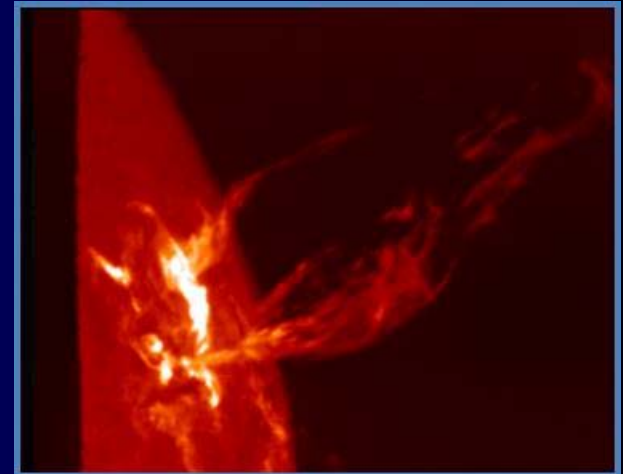
- The space radiation environment poses both **acute & chronic** risks to crew health and safety, with clinically relevant implications for the lifetime of the crew
- “Safely” means that **‘risk limits’** are sufficiently understood, defined, and not exceeded
- Because of unique properties of space radiation, estimating risks from space radiation exposure carries **large uncertainties** that constrain mission planning, with impacts on mission duration, crew selection and development of effective mitigation strategies
- NASA needs to close the knowledge gap on a broad-range of biological questions before radiation protection goals can be met for exploration
- The Human Research Program (HRP), Space Radiation Program Element (SRPE) led by JSC is committed to solving the space radiation problem with the goal of uncertainty reduction in risk estimates for Mars missions (<50%) to support agency goals in vehicle, mission, and crew selection

Space Radiation Environment



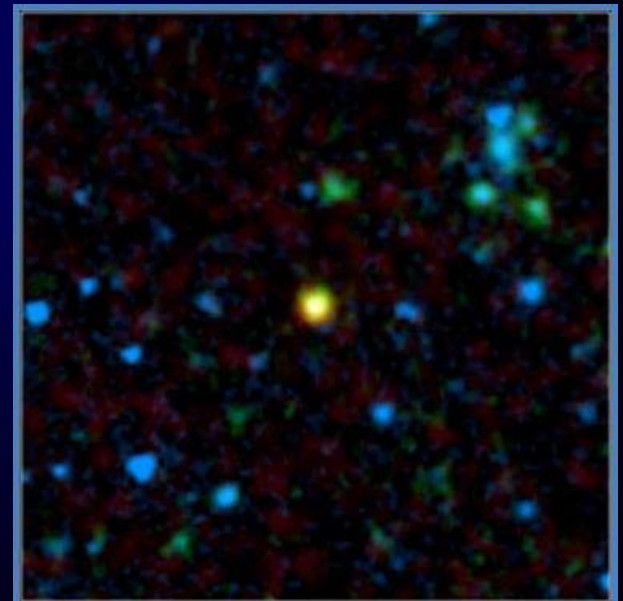
Solar Particle Events (SPE)

- Consist of low to medium energy protons
- Risk of acute radiation effects for unshielded exposure to large event
- Effectively blocked by shielding but optimization required to reduce weight
- Accurate event alert and dosimetry are essential for crew safety
- Improved understanding of radiobiology needed to perform risk model optimization



Galactic Cosmic Rays (GCR)

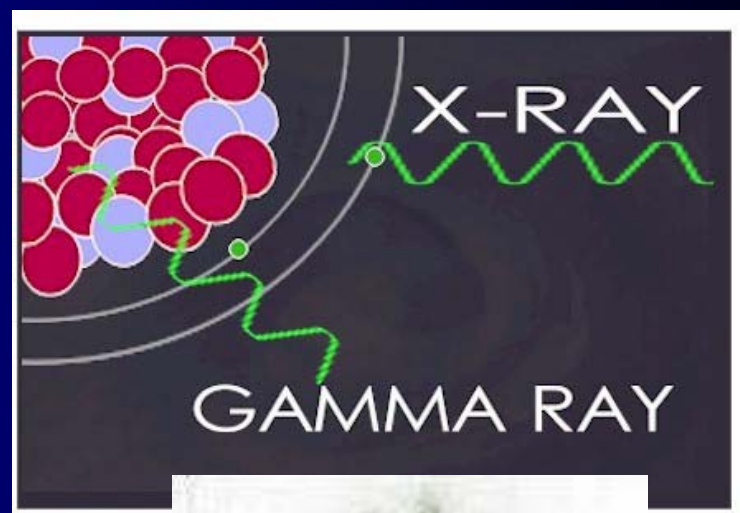
- Penetrating protons and highly charged, energetic atomic nuclei (HZE particles)
- Abundances and energies in space environment understood, but large biological uncertainties limit ability to accurately evaluate risks
- Heavy ions are not effectively shielded (break up into lighter, more penetrating fragments)
- Uncertainties cloud understanding of effectiveness of possible mitigations



Dust-Enshrouded Quasar Spitzer Space Telescope • IRAC • MIPS
Radio: NRAO • VLA
NASA / JPL, Caltech / A. Martínez-Saldaña (Oxford University) sci2005-17a

X-rays and Gamma Radiation

- X-rays are photons (electromagnetic radiations) emitted from electron orbits, such as when an excited orbital electron "falls" back to a lower energy orbit.
- Gamma rays are photons emitted from the nucleus, often as part of radioactive decay
- Considered low linear energy transfer



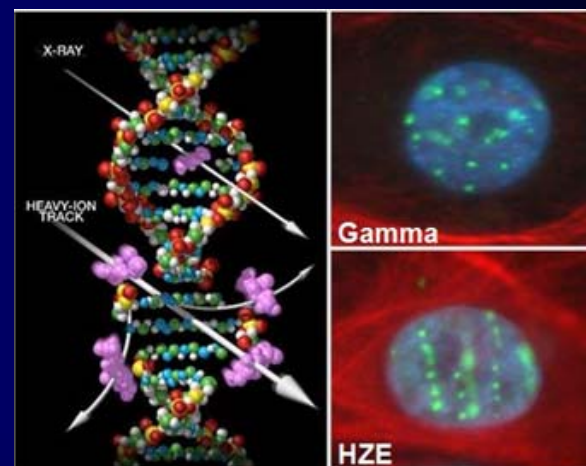


High-LET Radiation

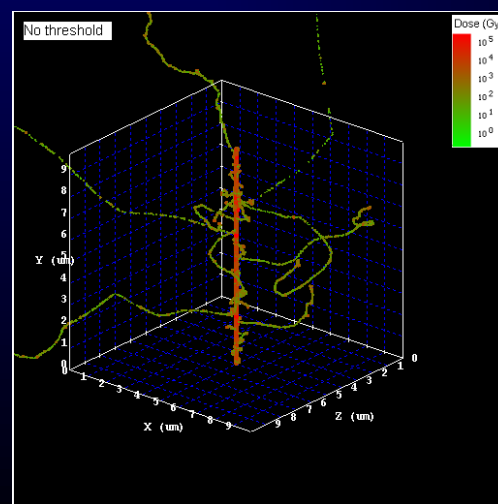
Uncertainty in Radiation Quality

→ Space radiation is composed of high-energy protons and heavy ions (HZE) along with secondary protons, neutrons, and heavy ions produced via interaction with shielding materials

- Linear energy transfer (LET)
 - Energy loss per unit path length as particles pass through matter
- High LET defined as $LET > 10 \text{ keV}/\mu\text{m}$ in tissue
- HZE nuclei traversal causes unique damage to biomolecules, cells, and tissues
- Distinct damage
 - DNA and oxidative damage (ROS) and spatial patterns distinct from terrestrial radiation (x-rays and gamma rays)
- Distinct biological effects and health risks?
- No human data to estimate risk
 - Must use animal and cellular models



γ H2AX foci in EPC2-hTERT cells (Patel and Huff)

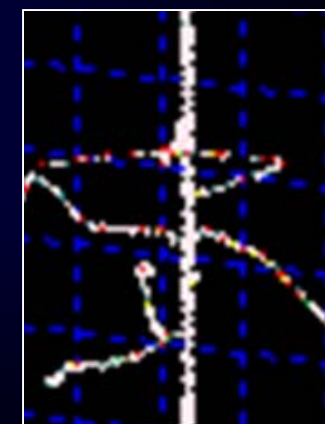
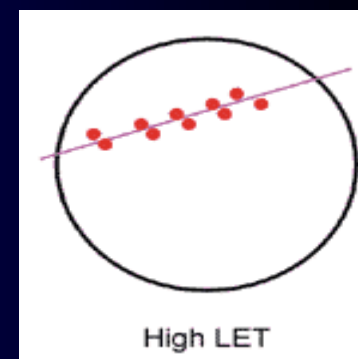
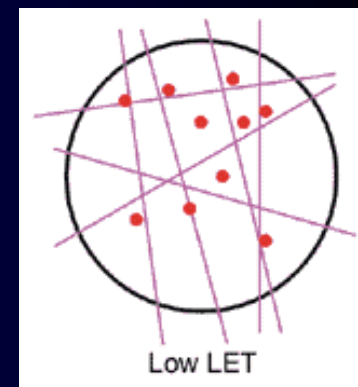


1 GeV/u ^{56}Fe nucleus $LET \sim 150 \text{ keV}/\mu\text{m}$
Qualitative differences due to track “core” and correlated tissue damage along a particle path. (Plante, 2011)



Linear Energy Transfer (LET)

- Radiation dose is the amount of energy per unit of biological material
- The LET is related to Biological Damage
- The average energy locally imparted to a medium by a charged particle of specified energy, per unit distance traversed. Measure of the ion pairs generated/cm of tissue traversed
- Gamma and X-Rays are low-LET and are sparsely ionizing producing uniform ionization across a tissue
- HZE Particle Radiation from GCR are high-LET.
- The localized DNA damage caused by dense ionizations from high-LET radiations is more difficult to repair than the diffuse DNA damage caused by the sparse ionizations from low-LET radiations
- The higher the LET, the higher the Q- quality factor in determining dose equivalent (Sverts, where $1 \text{ Sv} = 100 \text{ rem}$)



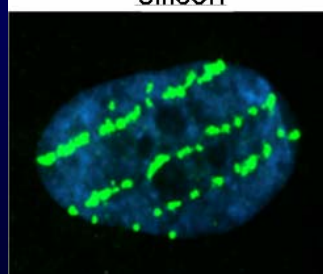
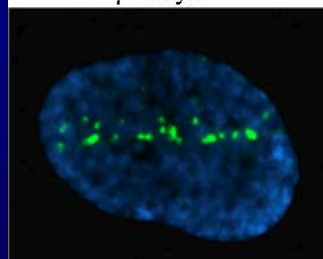
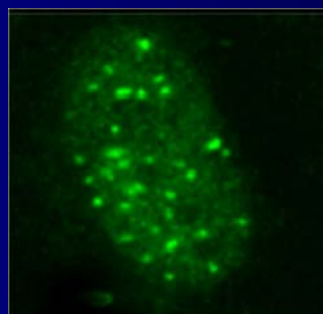
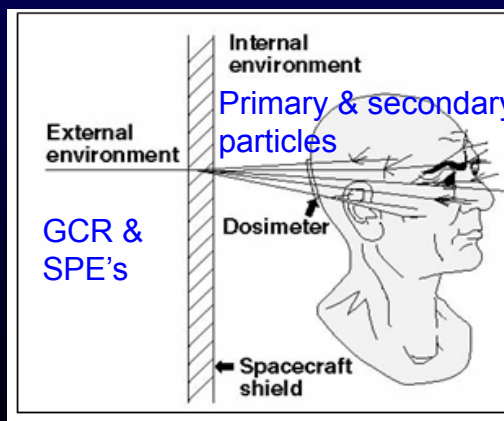
Silicon ion track



The Space Radiation Problem

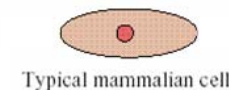
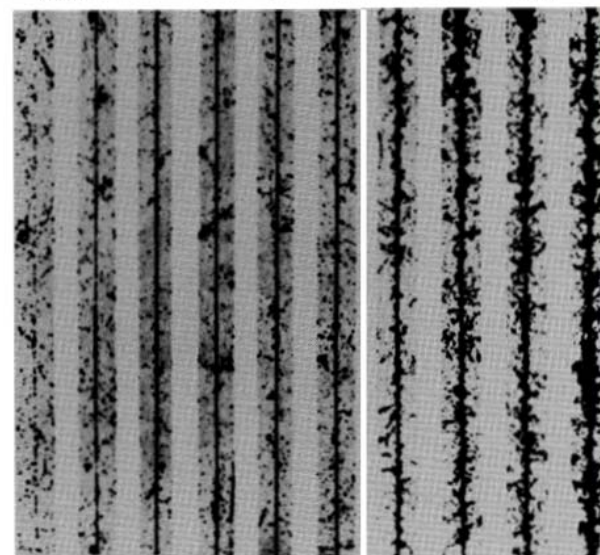
GCR and secondary fragmentation produced by interaction w/ shielding materials

- Unique damage to biomolecules, cells, and tissues occurs from HZE ions
- No human data to estimate risk from heavy ion damage- large uncertainty
- Animal models must be applied or developed to estimate cancer and other risks
- Shielding has excessive costs and will not eliminate galactic cosmic rays (GCR)



Track structure of deposited energy (of what's seen biologically at left)

← Better Biological knowledge → Poor



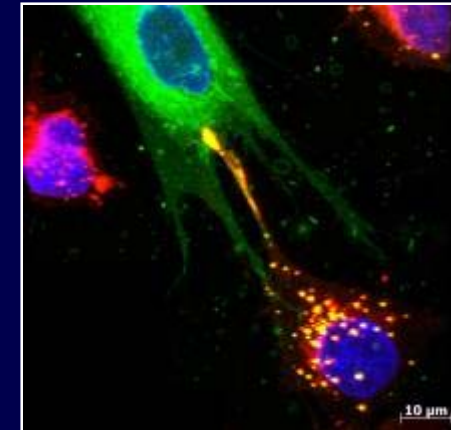
HZE ion traversals in cells and DNA breaks

Single HZE ions in photo-emulsions Leaving visible images

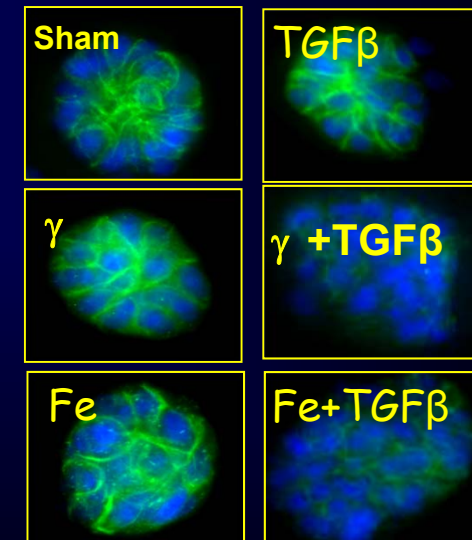
Space Safety Requirements



- Congress has chartered the National Council on Radiation Protection (NCRP) to guide Federal agencies on radiation limits and procedures
 - NCRP guides NASA on astronaut dose limits
- Crew safety
 - limit of 3% fatal cancer risk at 95% Confidence Level
 - prevent radiation sickness during mission
 - new exploration requirements limit Central nervous system (CNS) and Heart disease risks from space radiation
- Mission and Vehicle Requirements
 - shielding, dosimetry, and countermeasures
- NASA programs must follow the ALARA principle to ensure astronauts do not approach dose limits



Cell fusion caused by radiation



Space Radiation in breast cancer formation



Future Manned Missions

International Space Station

- 2013-2020: 6-person crews, 180 days (nominal); 2-person crew 360 days in planning
- Approach limits for acceptable radiation risks after 1 to 3 missions

Lagrange Points

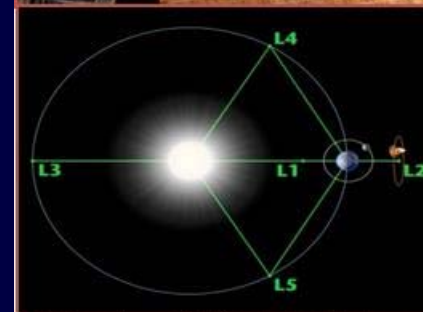
- Design Reference Mission currently being formulated
- Outside Earth's magnetosphere and radiation belts
- Galactic cosmic ray risks are major concern

Near Earth Objects

- Design Reference Mission currently being formulated
- Outside Earth's magnetosphere and radiation belts
- Galactic cosmic ray risks are major concern

Mars

- 2030 and beyond: 6-person crews, up to 1000 days
- Long deep space transit times
- Risks exceed NASA Permissible Exposure Limits (PELs) for cancer, and pose significant non-cancer risks



Integrated Radiation Protection Strategy Enables Human Mars Exploration

Long-Term Commitment across Research and Technology Required...

National Aeronautics and
Space Administration



Mission and Architecture Systems Analysis



Near Earth Asteroid Systems

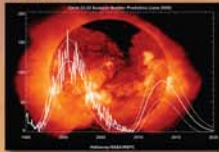
Mars NTV

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



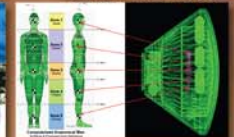
Human Digital Twin

Integrated Radiation Protection System Design and Analysis

Design and
Optimization Tools



Crew Exploration
Vehicle Shield Analysis

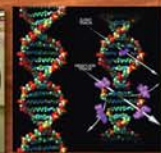


High Energy Nuclear
Physics and Transport

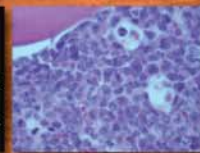
Radiobiology and Biological Countermeasures



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



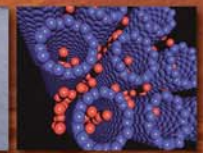
Heavy Ion Testing of
Inflatable Shield Prototype



Water Filled Composite
Shield Sections



Reconfigurable
Personal Shielding



Hydrogen
Storage BNNT

Advances benefit homeland security, cancer therapy, Earth observing and communication satellites, and commercial air safety



Space Radiation Risks

Risk of Radiation Carcinogenesis

- Morbidity and mortality risks
 - Major drivers for PELs and therefore major research emphasis for program



Risk of Acute & Late Central Nervous System Effects from Radiation

Exposure

- Possible in-flight changes in motor function, cognition, and behavior
- Late neurological disorders
 - SRPE aligning with Behavioral Health and Performance Element for possible future collaboration on acute risk monitoring



Risk of Degenerative Tissue or Other Health Effects from Radiation

Exposure

- Degenerative changes in the heart, vasculature, and lens
- Diseases related to aging, including digestive, respiratory disease, premature senescence, endocrine, and immune system dysfunction
 - SRPE monitoring HHC radiation research on heart risks



Risk of Acute Radiation Syndromes due to Solar Particle Events

- Prodromal effects (nausea, vomiting, anorexia, and fatigue), skin injury, and depletion of the blood-forming organs
- Acute radiation syndrome (ARS) from solar particle events (SPE) avoided by
Alert-Dosimetry and Shielding



Foundations of SRP Research Plans

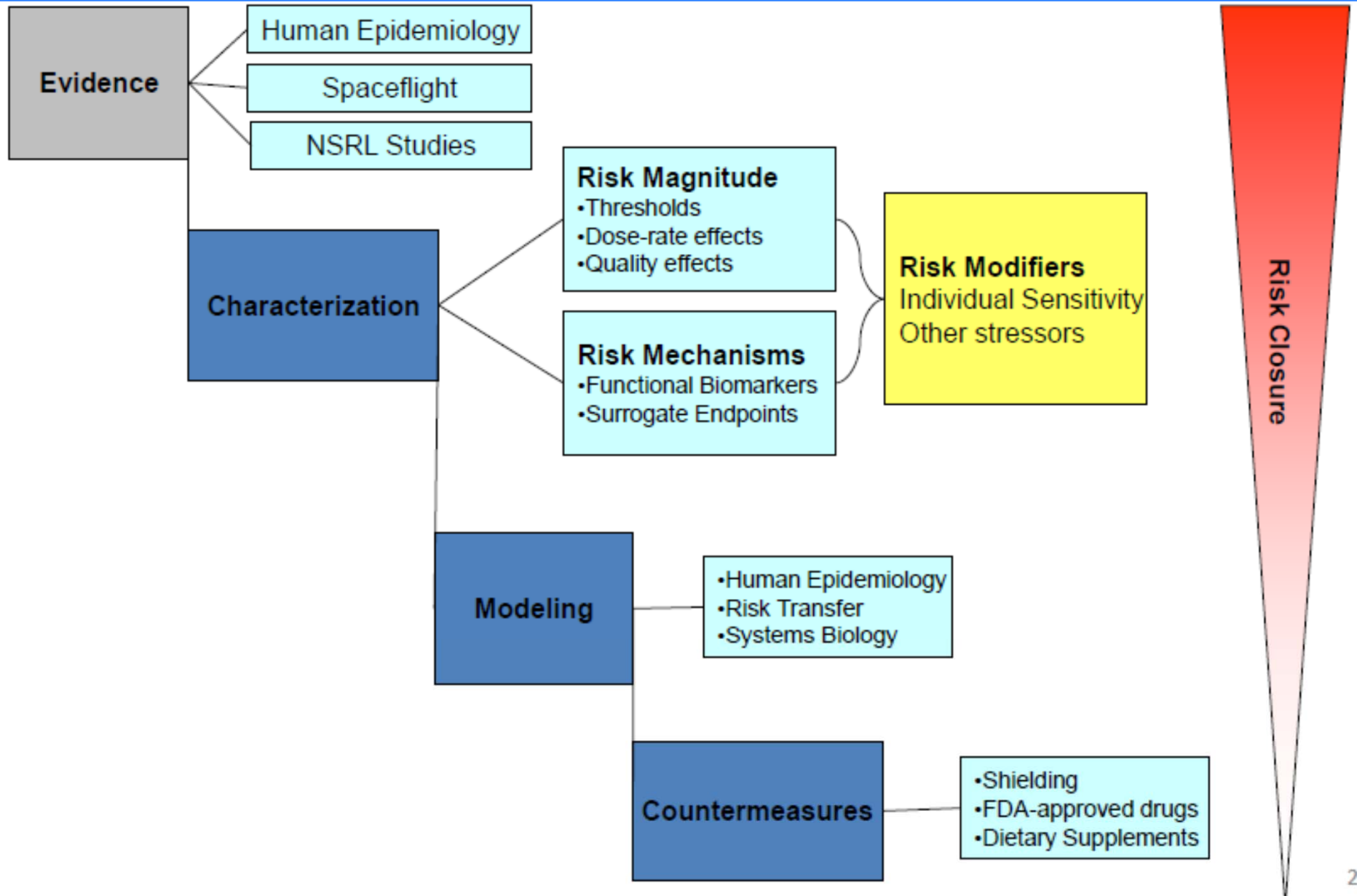


- External review by National Council on Radiation Protection (NCRP), National Academy of Sciences, and standing Radiation Discipline Working Group (RDWG)
- Simulate space radiation at the NASA Space Radiation Laboratory (NSRL)
 - Located at DoE's Brookhaven National Lab (Long Island NY)
- Six NASA Specialized Centers of Research (NSCOR's) studying the biology of space radiation risks
- Broad program of directed research at over 40 US Universities including collaborative research with US Department of Energy (DoE)
- Collaborate with NASA's Science Missions on advanced SPE alert & Mars robotic missions
- Long-term goal to improve knowledge to develop individual risk assessments, countermeasures



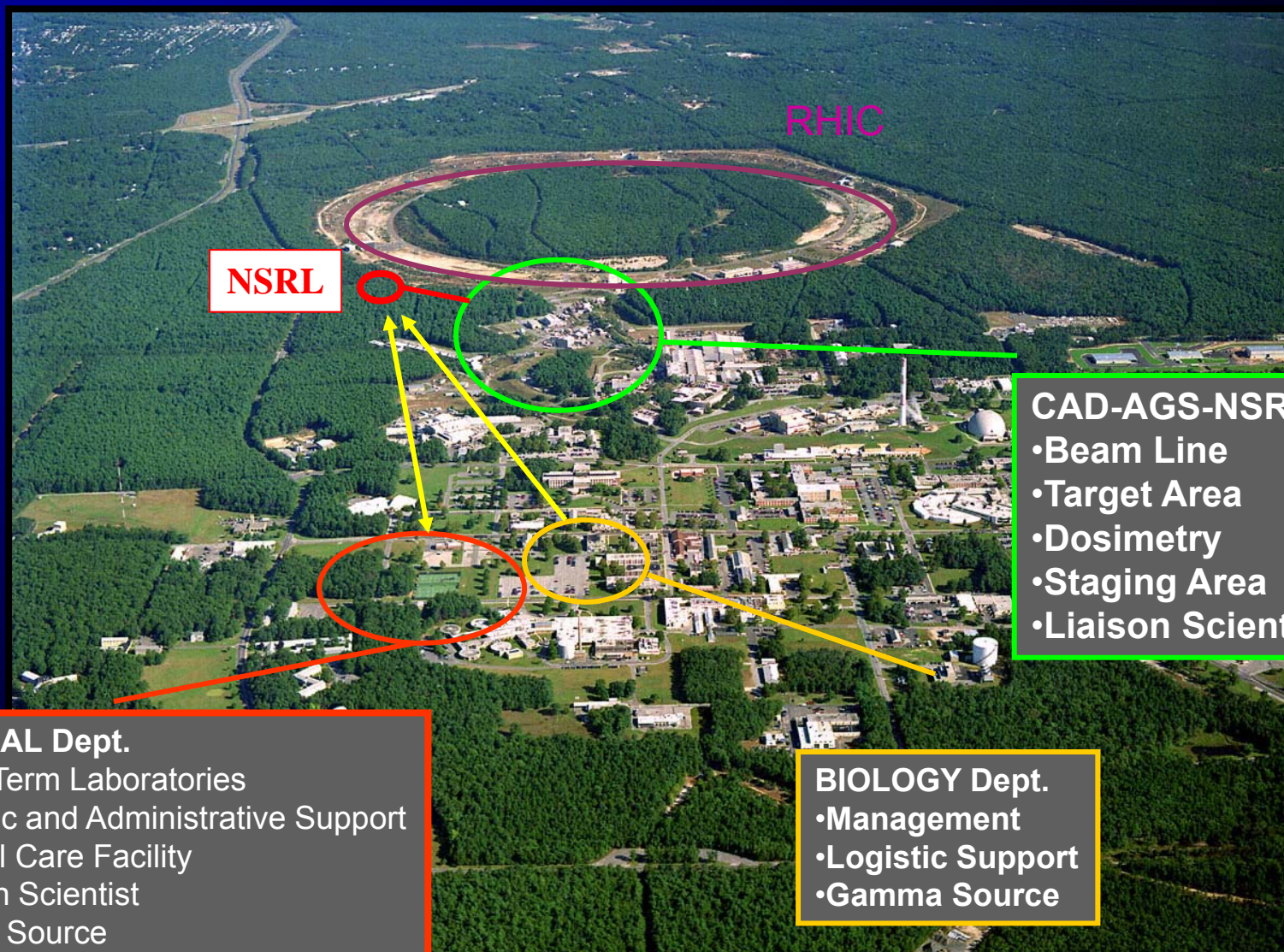


Risk Mitigation Strategy





NASA Space Radiation Lab (NSRL)



NSRL

RHIC

- CAD-AGS-NSRL**
- Beam Line
 - Target Area
 - Dosimetry
 - Staging Area
 - Liaison Scientist

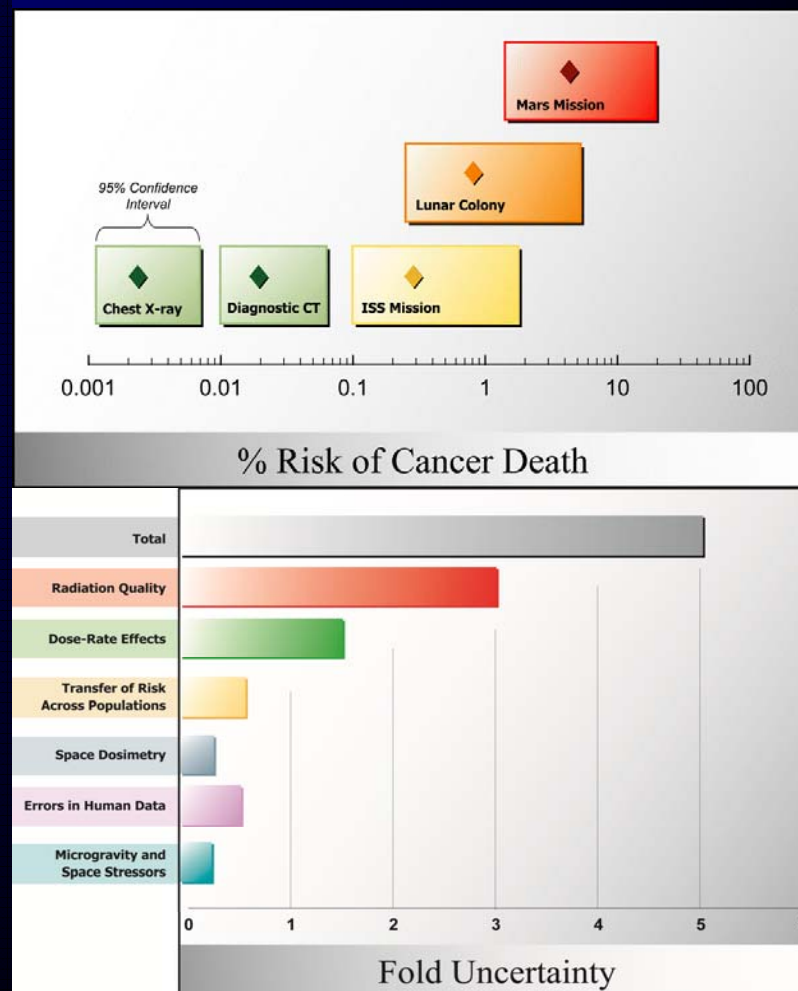
- MEDICAL Dept.**
- Long-Term Laboratories
 - Logistic and Administrative Support
 - Animal Care Facility
 - Liaison Scientist
 - X-Ray Source

- BIOLOGY Dept.**
- Management
 - Logistic Support
 - Gamma Source



Sources of Uncertainty

- Radiation quality effects on biological damage
 - Qualitative and quantitative differences of Space Radiation compared to x-rays
- Dependence of risk on dose-rates in space
 - Biology of DNA repair, cell regulation
- Space dosimetry and organ doses
- Predicting solar particle events
 - Temporal and size predictions
- Extrapolation from experimental data to humans
- Individual radiation-sensitivity
 - Genetic, dietary and “healthy worker” effects



Nature Rev. Cancer (2008)

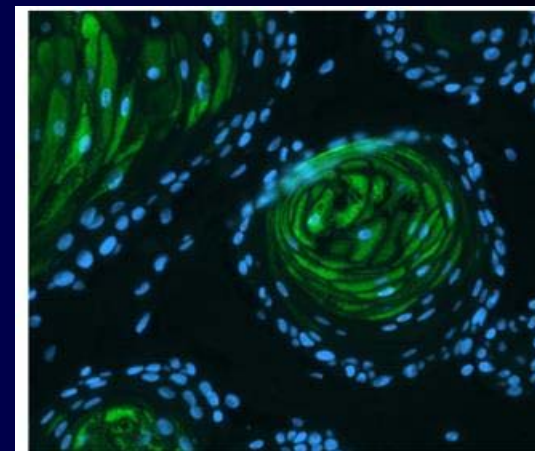


Radiation Carcinogenesis

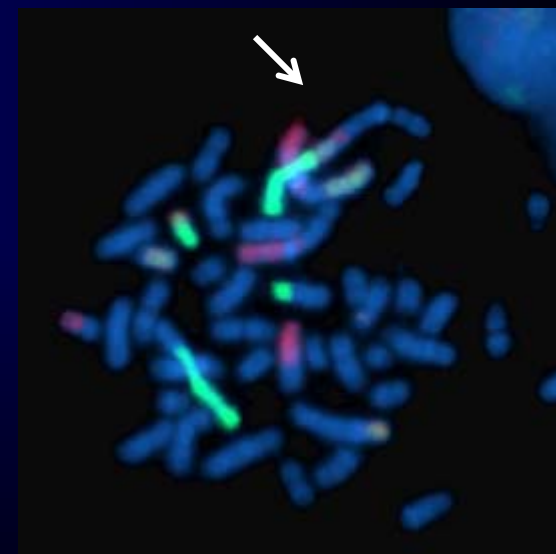
Risk Summary & Research Strategy

Risk of Radiation Carcinogenesis

- Morbidity and mortality risks for a wide variety of cancers [including lung, breast, colon, stomach, esophagus, the blood system (leukemias), liver, bladder, skin, and brain]
- Evidence for space radiation cancer risks are well known and described most recently by:
 - NCRP Reports 132 and 152
 - BEIR VII Report
 - UNSCEAR 2006 Report
- Cancer risk is a major driver for Space Radiation PELs and therefore a major research emphasis of program
- PELs guide mission, vehicle, and crew selection requirements
- The SRPE established a scientific approach that follows a progression of activities designed to feed the development of an integrated risk model **with acceptable uncertainty for exploration missions, followed by activities targeting risk mitigation and monitoring**



Cell invasion in 3-D organotypic cell model
(Patel and Huff)



Complex chromosome damage
following SR exposure (Hada)

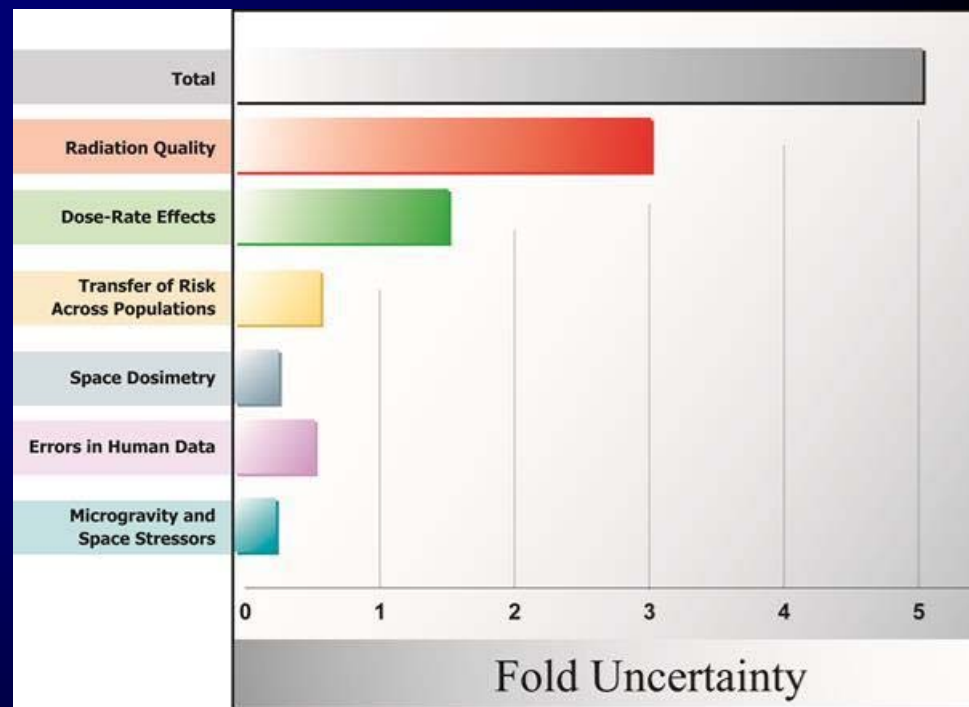


Radiation Carcinogenesis

Research Strategy

Sources of Uncertainty in Cancer Risk Estimates:

- Radiation quality effects on biological damage
- Dose-rates effects
 - Biology of DNA repair, cell regulation
- Space dosimetry and organ doses
- Solar particle events prediction – timing and size
- Extrapolation from experimental data to humans
- Individual radiation-sensitivity
 - Genetic, dietary and “healthy worker” effects



Cucinotta et al., Nat Rev Cancer 2008

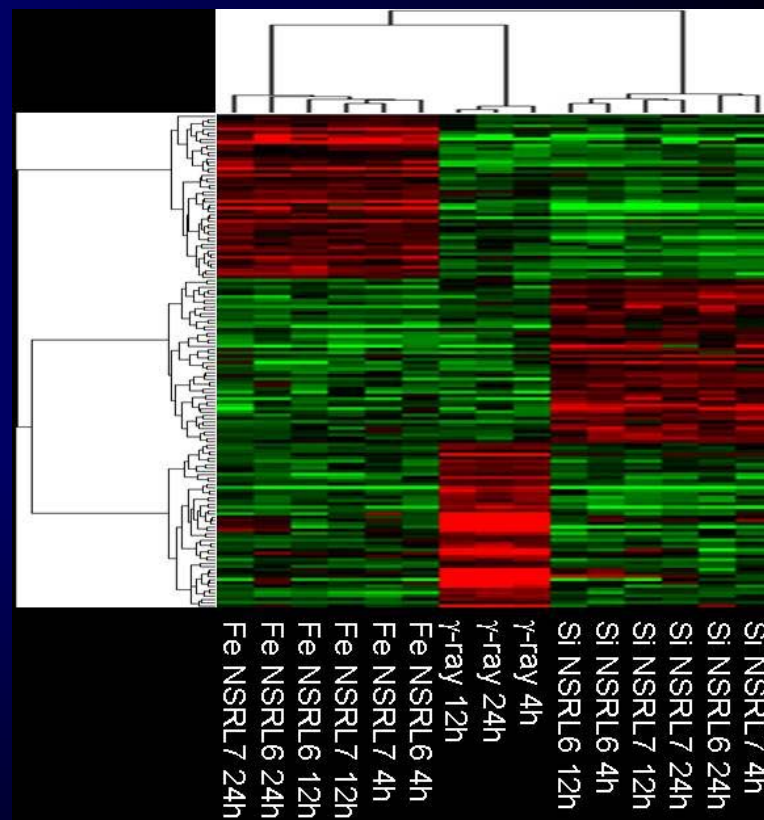
→ Research to reduce uncertainties in risk projection models are expected to increase NASA's ability to select crew, extend mission duration, and reduce cost through possible reductions in shielding requirements



Major Findings on Cancer Risk from NSRL

First experiments at NSRL were in Oct, 2003 and many publications are in preparation. Findings to date include:

- A low RBE for Leukemia from Iron due to high efficiency of apoptosis
- A high RBE for solid cancer is emerging
- Major differences in signaling pathways between high and low LET and high and low dose



Acute and Late CNS Risks

Risk Summary



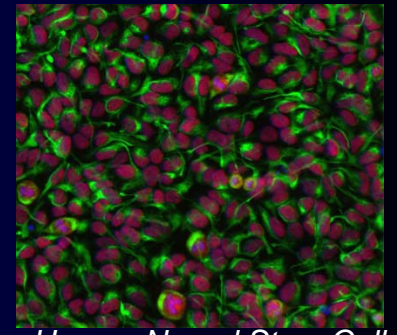
The Acute CNS risks include altered cognitive function including short-term memory, reduced motor function, and behavioral changes, which may affect performance and human health.

- The NCRP recommends that all clinically significant acute risks must be avoided
- Further development of evidence base for acute and late CNS risks required to define areas of significant concern and establish limits

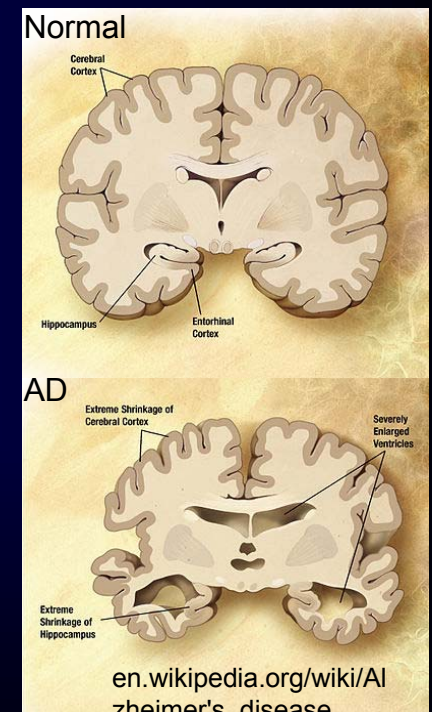
→ SRPE in process of aligning with Behavioral Health and Performance Element for possible future collaboration on CNS Acute risk monitoring

The Late CNS risks are possible neurological disorders such as Alzheimer's disease (AD), dementia, cerebrovascular disease or premature aging.

- AD is fatal, with mean time from early stages to death approx. 8 yrs
- Inclusion in the overall acceptable REID probability for space missions if AD risk established



Human Neural Stem Cells
C.Limoli, UC Irvine



CNS Risks from Galactic Cosmic Rays



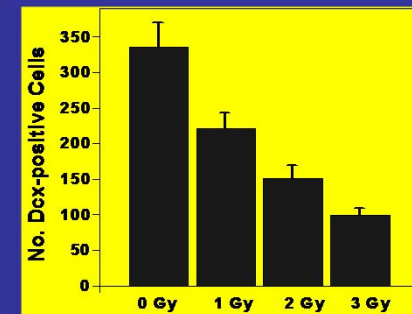
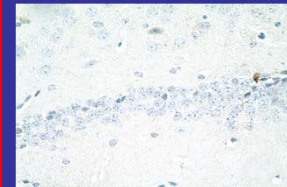
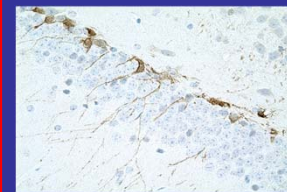
- In-flight acute performance changes and late effects similar to Alzheimer's disease are a concern for GCR
- Retinal flashes observed by Apollo astronauts suggests single heavy nuclei can disrupt brain function
- Central nervous system (CNS) damage by x-rays is not observed except at very high doses
- NASA research on performance of animals is establishing threshold doses for acute CNS risks
 - **studies have quantified rate of neuronal degeneration, plaque formation and changes in dopamine function related to late CNS risks**
- Studies will be extended to other GCR components to establish acute CNS Permissible Exposure Limits, and to derive a risk limitation approach to neurological disorders



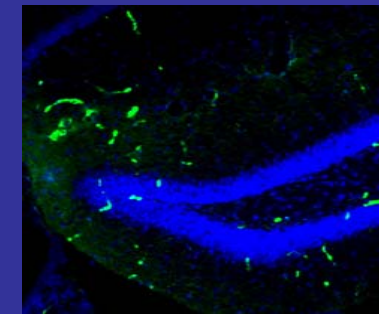
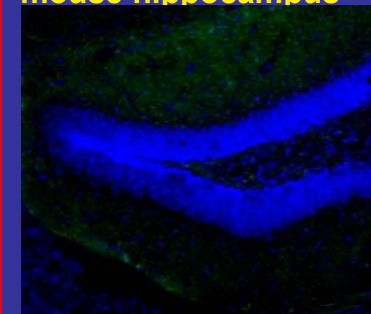
CNS Acute



CNS Late



Reduction in number of neurons (neurodegeneration) for increasing Iron doses in mouse hippocampus



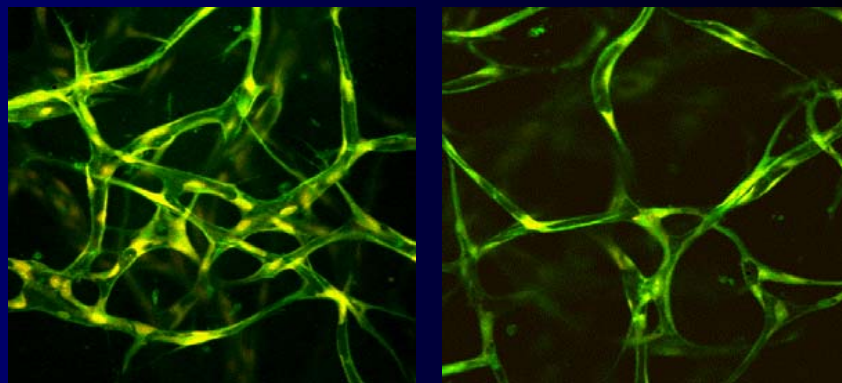
Oxidative Stress (Lipid peroxidation:4-Hydroxynonenal) is Increased in Mouse Hippocampus 9 Months After 2 Gy of ⁵⁶Fe Irradiation



Radiation and Non-Cancer Effects

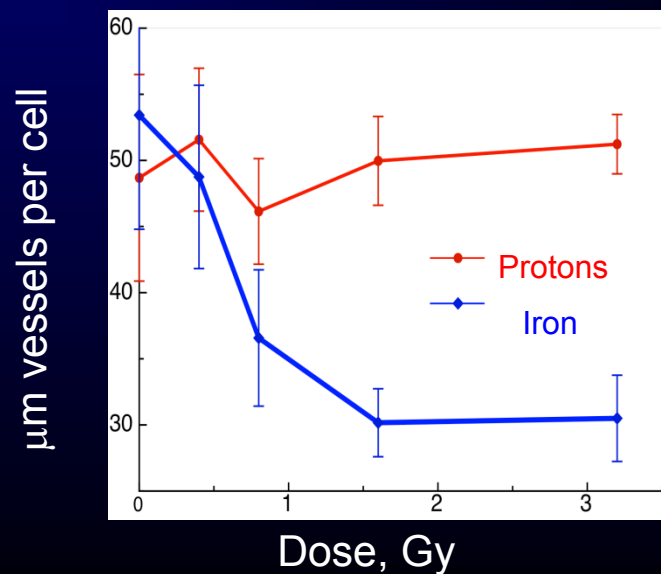
- Early Acute risks are very unlikely:
 - Low or modest dose-rates for SPE's insufficient for risk of early death
 - SPE doses are greatly reduced by tissue or vehicle shielding
- Radiation induced Late Non-Cancer risks are well known at high doses and recently a concern at doses below 1 Sv (100 rem)
 - Significant Heart disease in Japanese Survivors and several patient and Reactor Worker Studies
 - Dose threshold is possible making risk unlikely for ISS Missions (<0.2 Sv) ; however a concern for Mars or lunar missions due to higher GCR and SPE dose
 - Qualitative differences between GCR and gamma-rays are a major concern

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



Controls

Iron Irradiated



Degenerative Risks

Risk Summary



Risk of Degenerative Tissue Effects:

- Cardiovascular and circulatory changes
- Cataract formation

Other Health Effects:

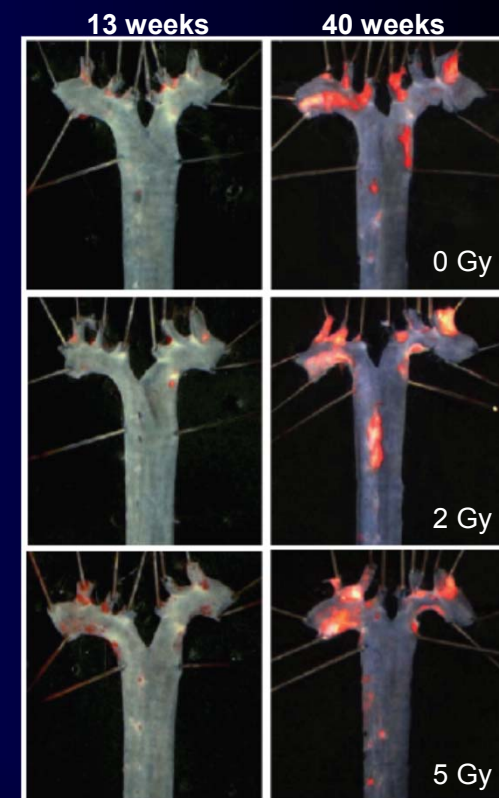
- Diseases related to aging, including digestive, respiratory disease, premature senescence, endocrine, and immune system dysfunction

Driving Evidence:

- Astronaut data (cataracts)
- Radiotherapy, environmental disasters, and atomic bomb survivor data
 - Data is confounded by life-style factors to larger extent than cancer
- Most prior work focused on high dose effects, high fat diets or other protocols that are atypical for astronauts

Risk Projections:

- Preliminary risk assessment models being formulated
- Current exposure limits set as dose thresholds; recent studies suggest there may be low dose and dose-rate effects



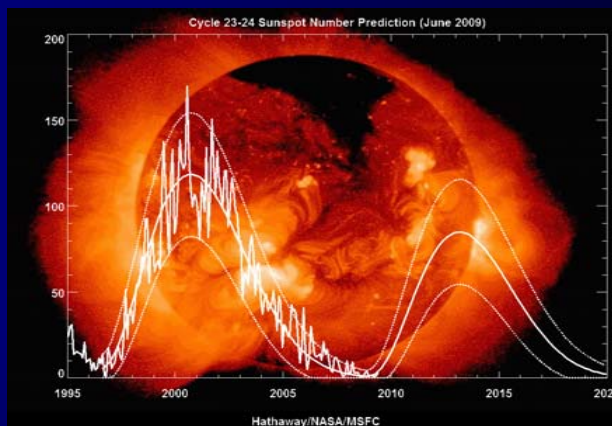
Aortic lesions in apoE^{-/-} mice after ⁵⁶Fe irradiation (Kucik et al., Rad Res 2011)



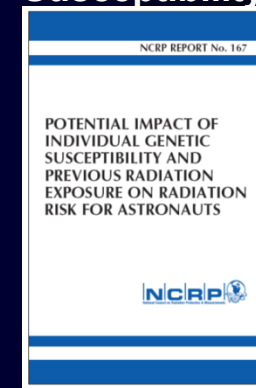
Mitigation Approaches

Variation of Solar Activity

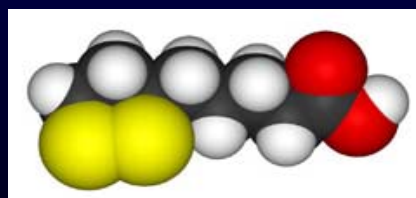
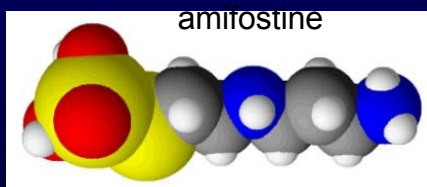
- Time in the Solar Cycle
- Radiation Shielding
 - Amounts and material types
 - Design Optimization
- Accurate Risk Quantification / Uncertainty reduction
- Crew Selection
 - Age, gender, lifestyle factors, etc,
 - Individual Sensitivity (genetic factors)
- Biological Countermeasures (BCMs)
 - Radioprotectors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



Individual Susceptibility

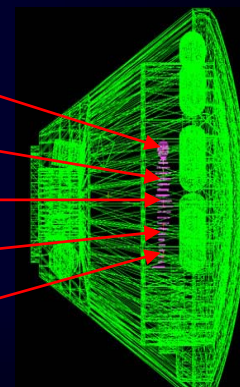
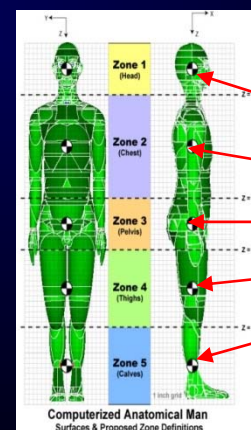


Shield Design and Optimization



α -lipoic acid

BCM: Pharmaceuticals





Summary

Space radiation is a major challenge to exploration:

- Risks are high limiting mission length or crew selection
- Large mission cost to protect against risks and uncertainties
- New findings may change current assumptions

NASA approach to solve these problems:

- Probabilistic risk assessment framework for ISS and Exploration Trade Studies
- Ground-based research focused on uncertainty reduction at NASA Space Radiation Laboratory (NSRL)
- Collaborative research with DoE, and ESA
- Ongoing external reviews by authoritative bodies
- Well defined deliverables to Cx, ISS, and CHMO



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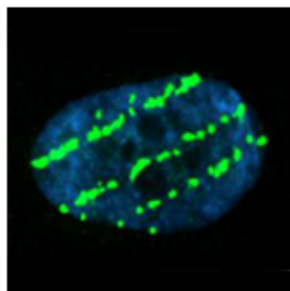
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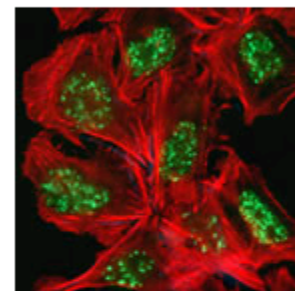
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Thank You!

As seen through the Hubble telescope, thousands of stars are forming in the cloud of gas and dust known as the Orion nebula. More than 3,000 stars of various sizes appear in this image. Some of them have never been seen in visible light.



BACK-UP SLIDES



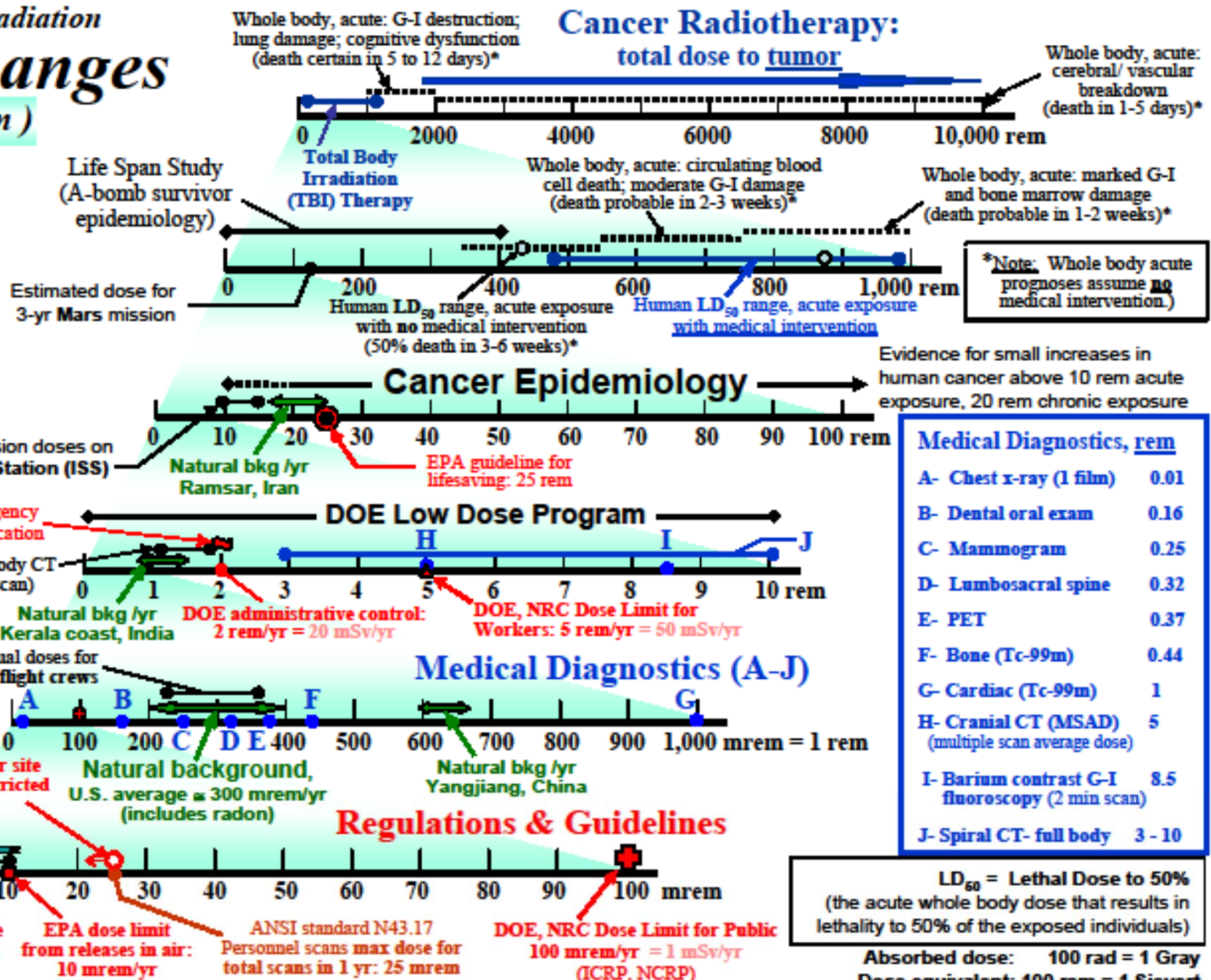
Physical Quantities

- HZE = High charge (Z) and energy (E) nuclei (ions)
- Fluence (F) = number of particles per unit area ($\#/cm^2$)
- Linear energy transfer (LET) = rate of energy loss per unit distance in bulk matter (keV per micron)
- Range = average distance traveled before ion stops
- Absorption cross section = probability of nuclear reaction expressed as an Area
 - Dose (D) = Energy absorbed in bulk matter $D = F \times LET$ (1 Gy = 100 rad)
- Relative Biological Effectiveness (RBE) = ratio of doses of ions to gamma rays to produce Equal biological effect
- Quality Factor (Q) = committee assigned value of RBE for human radiation protection
- Dose Equivalent (H) = $D \times Q$ (1 Sv = 100 rem) (*organ shielding*)
- Risk = *model quantity can not be measured*

Ionizing Radiation Dose Ranges (Rem)



Office of Science
U.S. DEPARTMENT OF ENERGY



*Note: Whole body acute prognoses assume no medical intervention.

LD₅₀ = Lethal Dose to 50%
(the acute whole body dose that results in lethality to 50% of the exposed individuals)

Absorbed dose: 100 rad = 1 Gray
Dose equivalent: 100 rem = 1 Sievert
100 mrem = 1 mSv

(1 rem = 1 rad for x- and gamma-rays)

Note: This chart was constructed with the intention of providing a simple, uncluttered, "order-of-magnitude" reference for radiation quantities of interest to scientists, managers, and the general public. In that spirit, most quantities were expressed in the more commonly used radiation protection unit, the rem (or Sievert, 2nd page), and medical doses are not in "effective" dose. It is acknowledged that the decision to use one set of units does not address everyone's needs. (NRC—US Nuclear Regulatory Commission; EPA—US Environmental Protection Agency)
Disclaimer: Neither the United States Government nor any agency thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information disclosed.

Chart compiled by NF Matting, Office of Science, DOE/BER "Orders of Magnitude" revised August 2005



Syndrome	Dose*	Prodromal Stage	Latent Stage	Manifest Illness Stage	Recovery
Hematopoietic (Bone Marrow)	> 0.7 Gy (> 70 rads) <i>(mild symptoms may occur as low as 0.3 Gy or 30 rads)</i>	<ul style="list-style-type: none"> • Symptoms are anorexia, nausea and vomiting. • Onset occurs 1 hour to 2 days after exposure. • Stage lasts for minutes to days. 	<ul style="list-style-type: none"> • Stem cells in bone marrow are dying, although patient may appear and feel well. • Stage lasts 1 to 6 weeks. 	<ul style="list-style-type: none"> • Symptoms are anorexia, fever, and malaise. • Drop in all blood cell counts occurs for several weeks. • Primary cause of death is infection and hemorrhage. • Survival decreases with increasing dose. • Most deaths occur within a few months after exposure. 	<ul style="list-style-type: none"> • in most cases, bone marrow cells will begin to repopulate the marrow. • There should be full recovery for a large percentage of individuals from a few weeks up to two years after exposure. • death may occur in some individuals at 1.2 Gy (120 rads). • the LD50/60† is about 2.5 to 5 Gy (250 to 500 rads)
Gastrointestinal (GI)	> 10 Gy (> 1000 rads) <i>(some symptoms may occur as low as 6 Gy or 600 rads)</i>	<ul style="list-style-type: none"> • Symptoms are anorexia, severe nausea, vomiting, cramps, and diarrhea. • Onset occurs within a few hours after exposure. • Stage lasts about 2 days. 	<ul style="list-style-type: none"> • Stem cells in bone marrow and cells lining GI tract are dying, although patient may appear and feel well. • Stage lasts less than 1 week. 	<ul style="list-style-type: none"> • Symptoms are malaise, anorexia, severe diarrhea, fever, dehydration, and electrolyte imbalance. • Death is due to infection, dehydration, and electrolyte imbalance. • Death occurs within 2 weeks of exposure. 	<ul style="list-style-type: none"> • the LD100‡ is about 10 Gy (1000 rads)
Cardiovascular (CV)/ Central Nervous System (CNS)	> 50 Gy (5000 rads) <i>(some symptoms may occur as low as 20 Gy or 2000 rads)</i>	<ul style="list-style-type: none"> • Symptoms are extreme nervousness and confusion; severe nausea, vomiting, and watery diarrhea; loss of consciousness; and burning sensations of the skin. • Onset occurs within minutes of exposure. • Stage lasts for minutes to hours. 	<ul style="list-style-type: none"> • Patient may return to partial functionality. • Stage may last for hours but often is less. 	<ul style="list-style-type: none"> • Symptoms are return of watery diarrhea, convulsions, and coma. • Onset occurs 5 to 6 hours after exposure. • Death occurs within 3 days of exposure. 	<ul style="list-style-type: none"> • No recovery is expected.

* The absorbed doses quoted here are "gamma equivalent" values. Neutrons or protons generally produce the same effects as gamma, beta, or X-rays but at lower doses. If the patient has been exposed to neutrons or protons, consult radiation experts on how to interpret the dose.

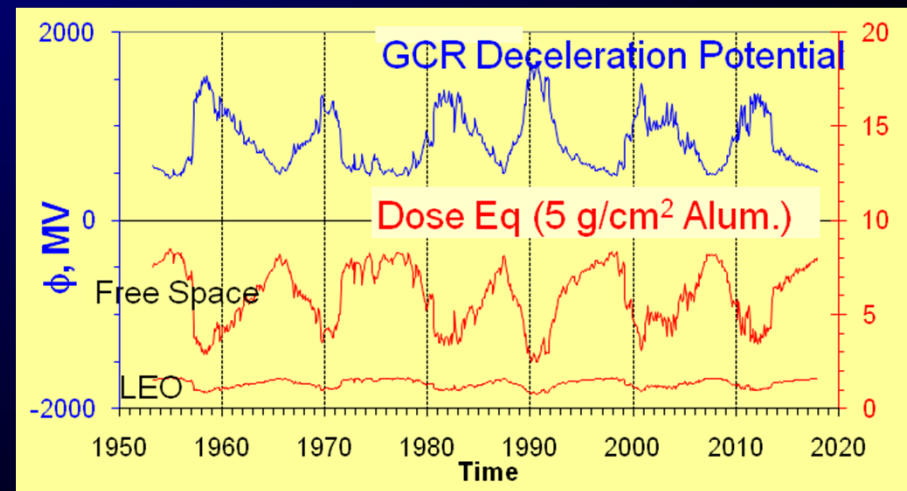
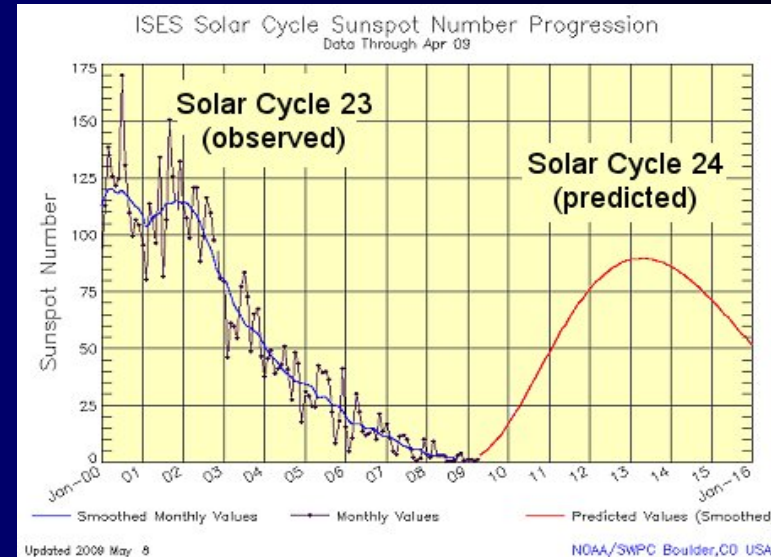
† The LD50/60 is the dose necessary to kill 50% of the exposed population in 60 days.

‡ The LD100 is the dose necessary to kill 100% of the exposed population



Solar Cycle Effects

- The solar cycle is approximately 11-years in length, however variations in length of ± 2 y can occur
 - Doses from SPEs are highest at solar maximum when solar activity is highest
 - Doses from GCR are highest at solar minimum when the solar wind is strongest
- Each cycle will have varying modulation conditions and number and sizes of SPE
- The prediction of solar conditions temporal patterns are uncertain for future solar cycles





Value Of Uncertainty Reduction:

Cost of research to reduce uncertainties 2-fold, much less than cost of shielding in space or reducing mission length

