Exploring Space In Partnership

**Now**
Using the International Space Station

**2020s**
Operating in the Lunar Vicinity

**2030s**
Leaving the Earth-Moon System and Reaching Mars Orbit

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**Phase 0**
Solve exploration mission challenges through research and systems testing on the ISS. Understand if and when lunar resources are available

**Phase 1**
Conduct missions in cislunar space; assemble Deep Space Gateway and Deep Space Transport

**Phase 2**
Complete Deep Space Transport and conduct Mars verification mission

**Phases 3 and 4**
Missions to the Mars system, the surface of Mars

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Advancing technologies, discovery and creating economic opportunities
The goal of HRP is to provide human health and performance coverage on:

- countermeasures
- knowledge
- technologies
- tools

To enable safe, reliable, and productive human space exploration.
Primary Spaceflight Hazards

**Decreased gravity** (incl. gravity transitions, launch/landing loads)
- Musculoskeletal, cardiovascular, sensorimotor, immunology behavior/performance, human factors, clinical medicine

**Isolation/confinement/altered light-dark cycles**
- Behavior/performance, sleep, psychological stress

**Hostile/closed environment** (incl habitability: atmosphere, microbes, dust, configuration, displays/controls)
- Behavior/performance, nutrition, immunology, toxicology, microbiology

**Increased radiation**
- Carcinogenesis, cardiovascular degeneration, behavior/performance, immunology

**Distance from Earth**
- Behavior/performance, autonomy, food systems, clinical medicine
Space Radiation Health Risks

Risk of Radiation Carcinogenesis

- Morbidity and mortality risks for a wide range of cancers (lung, breast, colon, stomach, esophagus, leukemias, liver, ovaries, bladder, skin, and brain)

Risk of Acute (In-flight) & Late Central Nervous System Effects from Radiation Exposure

- Acute and/or late changes in cognition, motor function, behavior and mood, or neurological disorders

Risk Of Cardiovascular Disease and Other Degenerative Tissue Effects From Radiation Exposure

- Cardiovascular disease, stroke, cataracts
- Diseases related to aging, including digestive, respiratory disease, endocrine, and/or immune system dysfunction

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

Risks documented in HRP Evidence Books
Space Radiation Environment

**Solar Particle Events (SPE)**
- Low to medium energy protons with the energy region of most importance to human space flight extending out to a few hundred MeV
- While effectively shielded against to prevent risk of ARS, exposure contributes to inflight and late CNS, Cancer, and Degenerative risks
- **Main challenge**: Optimized storm shelter mass, active dosimetry, operational constraints/forecasting

**Galactic Cosmic Rays (GCR)**
- Highly charged, energetic atomic nuclei (HZE particles) and protons
- Major GCR particle types: H, He, C, O, Ne, Si, Ca, and Fe with broad energy spectra of interest - primarily from ~10 MeV/n to 10,000 MeV/n
- Not effectively shielded (fragment into lighter, penetrating species)
- **Main challenge**: Uncertainty about biological effects limits ability to accurately evaluate risks and countermeasures

**Trapped Radiation (Van Allen Belts)**
- Low to Medium energy protons and electrons
- Effectively mitigated by shielding
- Mainly relevant to ISS and contributes ~40% of dose eq.
- **Main challenge**: Develop accurate dynamic model
Current and Future Missions

**Radiation doses are mission specific:**

- ~Destination and duration
- ~Vehicle and habitat design
- ~Solar conditions

**International Space Station**
- 2013-2024: 6-person crews for 6 months; 2-person crews for 1 year
- Typical exposures: ~50 to 100 mSv (30-60 mGy)

**Lunar Missions: Sortie (30 day) and Lunar Base (1 year)**
- Outside magnetosphere; Protection of planetary surface – larger neutron exposure
- One year missions: ~300 mSv to 400 mSv (100-120 mGy)

**Deep Space Journey**
- Outside Earth’s magnetosphere in free space; No planetary protection; GCR risks major concern
- One year missions: ~500 mSv to 650 mSv (175 mGy-220 mGy)

**Planetary: Mars**
- 2030 and beyond: 6-person crews, up to 3 yrs.
- Long deep space transit times; mixed field environment on Mars
- Estimates for Mars missions: ~ 1000 mSv and 1300 mSv (300 to 450 mGy)
Galactic cosmic rays 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

Distinct biological effects and health risks?

- No human data exist to estimate risk from heavy ions found in space
- Animal and cellular models with simulated space radiation must be used to gain new scientific knowledge
- Potential for additive or synergistic modifiers of risk from other spaceflight factors
GROUND ANALOG: NSRL
NASA Space Radiation Laboratory (NSRL)

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

Medical Building:
- Gamma-ray source
- Long-term labs and animal facilities
- Liaison scientists and administrative support
### Example of NSRL Energy Beams and Characteristics

<table>
<thead>
<tr>
<th>Beam*</th>
<th>Energy, MeV/u</th>
<th>LET, keV/µm</th>
<th>Range in Water, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>protons</td>
<td>50-2500</td>
<td>1.2 - 0.21</td>
<td>2 to &gt;100</td>
</tr>
<tr>
<td>(^4)He</td>
<td>50 - 1200</td>
<td>5 – 0.8</td>
<td>2 to &gt;100</td>
</tr>
<tr>
<td>(^{16})O</td>
<td>50- 1000</td>
<td>80 – 14</td>
<td>0.5 – 80</td>
</tr>
<tr>
<td>(^{20})Ne</td>
<td>50-1000</td>
<td>125 – 22</td>
<td>0.45 – 64</td>
</tr>
<tr>
<td>(^{28})Si</td>
<td>75-1000</td>
<td>179 – 44</td>
<td>0.66 – 46</td>
</tr>
<tr>
<td>(^{37})Cl</td>
<td>100-1000</td>
<td>212 – 64</td>
<td>0.9 – 39</td>
</tr>
<tr>
<td>(^{48})Ti</td>
<td>100-1000</td>
<td>354 – 107</td>
<td>0.8 – 32</td>
</tr>
<tr>
<td>(^{56})Fe</td>
<td>100-1000</td>
<td>495 – 150</td>
<td>0.66 – 27</td>
</tr>
<tr>
<td>Solar particle event simulator</td>
<td>50-2000</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Before final award of selected proposals, the Space Radiation Element will further review the choices of beams and doses to be used in funded research plans.

https://www.bnl.gov/nsrl/
Physics & Biological Challenge: Simulating the Galactic Cosmic Ray Environment

**Challenge:** Define GCR reference environment in terms of NSRL operational and delivery parameters

Current Status: Design and Validation

1. **What?** Define reference tissue environment(s) during exploration missions.
   - Time in solar cycle, shielding, body models
   - What quantities? LET, dose eq, $Z^2/B^2$; energy binning

2. **How?** Determine the best approach to deliver that environment at NSRL. Identify facility, hardware, and software constraints.
   - Beam energies, controls, spill rates, absorbers, low doses & dose rates, operations

3. **Define animal/cell requirements and constraints.**
   - IACUC, cages, sedation, feeding, bedding, lighting, incubators
NSRL Upgrades: Galactic Cosmic Ray Simulator

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

- Magnet upgrades for delivery of beams at 1.5 GeV/n
- Rapidly switchable ion source
- Automated controls
- GCR species will be simulated with high precision in major LET bins ranging between 0.25 - 1,000 keV/µm
- Strategies for chronic exposures
Mixed field proof of concept studies, comparing predicted model outcomes with experimental results, are sought to answer the following questions:

- How many different particles (including particle types and energies) are sufficient to adequately simulate the biological and health consequences of GCR across risk areas? What is the time scale (dose rate and duration) and order of delivery of particle types?

- What mixed radiation field, including protons, helium and heavier nuclei, provides the most stringent tests of model predictions?

- Is there an intermediate capability that may provide a similar statistical power for determining the validation of radiation models?
Baseline disease rates  
Excess risk (relative or absolute)  
Excess risk (relative or absolute)

TERRESTRIAL EXPOSURES

EXTRATERRESTRIAL EXPOSURES

LEVELS OF EVIDENCE:
Foundation of evidence used by NASA for research and operational radiation safety.

LATE CNS
Radiotherapy, Million worker data

CVD
Radiotherapy, A-bomb, nuclear workers

CANCER
Radiotherapy, A-bomb, nuclear workers, INWORKS

Acute Radiation Syndromes
A-bomb, accidental exposures
Use **experimental data** from human radiation exposures on Earth (acute, gamma) to:

- Scale to different types of radiation (quality)
- Scale to low dose rates

**Calculate:** Extrapolated risk estimates for other types of radiation exposures

- Carbon ions, protons, x-rays
- Neutrons, alphas
- Alphas, betas, x-ray
- Cosmic rays, solar protons, alphas, neutrons, pions, muons etc.

**Epidemiology data** from human radiation exposures on Earth (acute, gamma)
NASA-Specific Scaling Factors for Risk Assessment

**Scaling factors:**

- Used by NASA and other space agencies in the analysis of cancer risk (and other risks) as a means to evaluate the relative hazards of terrestrial vs. cosmic radiation exposures.
- Rely heavily on biological studies using animal and cell culture models.
Baselining Terrestrially Exposed Populations

2018 US Population
- Mortality, Incidence, Lifespan

US Million Worker Study
- Sex Specific Lung Cancer Study

Japanese Atomic Bomb Survivors
- 1940s Japanese Population
- Lifespan Study Data

Eventually, moving to US cohort as our baseline terrestrially exposed population
Parallelogram Biomedical Model: Common Pathways and Adverse Outcomes

**In Vivo:**
Whole Body Outcomes

**In Vitro:**
Tissues, 3D Organotypic Models, Organoids, Cell Cultures

Common pathways & molecular phenotypes
Surrogate biomarkers
Countermeasures
Computational Modeling/AI

Experimental data provides common pathway insight

Experimental

→ Understanding common pathways across animal models, advanced human cell models, and humans enhances reliability of scaling factors used in risk assessment, supports biomarker identification and allows focusing of countermeasure strategy.
Implementation of the Translational Paradigm

**Standard Internal Mechanisms:**

- Advisory Boards, NRAs, NSCORs, Directed work
RADIATION CARCINOGENESIS
Space Radiation Carcinogenesis Research Portfolio

The Hallmarks of Cancer

- Sustaining proliferative signaling
- Resisting cell death
- Evading growth suppressors
- Inducing angiogenesis
- Activating invasion and metastasis
- Enabling replicative immortality

Emerging Hallmarks and Enabling Characteristics

- Deregulating cellular energetics
- Avoiding immune destruction
- Genome instability and mutation
- Tumor-promoting inflammation

Broad portfolio of research projects focused on understanding the unique biology of HZE ion radiation related to the major cancer development processes.

Includes studies of: DNA damage and repair, ROS, oxidative stress and inflammation, bystander signaling, genomic instability, epigenetics effects, stem cells, role of the microenvironment, omics approaches, biophysical modeling and systems biology.

Hanahan and Weinberg Cell 2011
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

Higher oxidative damage 1 year after $^{56}$Fe exposure in intestinal cells (Datta et al., PLoS ONE 2012)

→ Updates to 2012 NASA Cancer Risk Model based on research findings
Protection and Mitigation Approaches

- **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)
- **Medical Countermeasures (MCMs)**
  - Radioprotectors /mitigators
- **Biomarkers predictive of radiation-induced diseases**
  - Future individualized risk assessment
  - Early detection and prognostic monitoring
Medical Countermeasures

Human → Human with Scaling Factors from Model Systems

Human and Animal In Vitro, Animal In Vivo → Predictions in Human

Agents with known human profiles → Assess NASA-specific drug usage

Human Epidemiology
Human Biomedical Data
Human Omics

Common Pathways and Adverse Outcomes in Human and Animal Model Systems

Drug repositioning and off-label use of known drugs, animal model data on disease outcome, validate using common pathways and FDA animal rule as required
GCR-Specific Countermeasures

Requirements driven by mission operations:

• Conservative prophylactic use; no designer drugs, must demonstrate proven long-term use, minimal side effects
• FDA approved, FDA Off-label, FDA IND Status drugs
• Dietary supplements, neutraceuticals

Biological countermeasure criteria:

• Mechanism of action well known; independent of sex
• Chronic administration (potentially up to 3 years)
• Easily self administered (e.g. oral, inhaled)
• No contraindications with other drugs
• Long shelf-life

Categories of Potential Agents:

• Cross-risk agents targeting common pathways (ex. anti-inflammatory agents)
• Radioprotective/mitigating agents targeting early damage and acute effects; potential for cross-over to late effects
Radiation Carcinogenesis Research Focus

- Discovery and validation of medical countermeasures
- Development of an integrated risk model with acceptable uncertainty in support of meeting PELS for exploration
- Continued focus on radiation quality and dose-rate effects on cancer processes with goal of reducing uncertainty in risk estimates
  - Understanding the biological basis for sex differences and individual sensitivity on cancer risks
  - Mechanistic analysis of cancer risk including enhanced aggression observed in HZE tumors
  - Impact of non-targeted effects at low doses
- Research incorporating new integrative “omics” techniques and systems biology approaches
  - Identification of biomarkers for early disease detection and health monitoring

Greater Incidence (%) of hepatocellular carcinoma with metastases to the lung with high-LET radiation. (Ullrich et al.)

Gene analysis can support the determination of survival outcome of patients with lung cancer. (Minna et al.)
RADIATION-INDUCED ACUTE AND LATE CNS EFFECTS
Central Nervous System Radiation Injury

- NASA studies reveal effects in hippocampus, neostratum, and pre-frontal cortex
- Cognitive tests in rats/mice show detriments at doses to 10 mGy (1 rad) at early times after exposure
- Associated with neuronal degeneration, oxidative stress, apoptosis, inflammation, and changes in dopamine function
- Low doses of GCR alter the creation of new neurons in rodents, disrupting “new memory” and cognition
- New evidence for GCR acceleration of AD pathology in susceptible mouse model
- Interdependency of multiple neural cell types for normal function (supporting glia and vasculature)

**Acute:** Disruptions in Learning/Cognition & possibly Mood/Stress

**Late:** Degenerative diseases such as AD

**How do these changes translate to inflight risks to humans?**

**How do other inflight cognitive risks impact these processes?**

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Image adapted from Petrik, Lagace & Eisch 2012
Persistent CNS cell structure and organization, tissue level composition, function and homeostasis, genetic and epigenetic regulation and animal cognitive behavior are altered/impaired at doses as low as 5 cGy in a charged particle specific pattern.

- **Gene Expression**
  - Oxidative Stress Markers
  - Physiological Markers

- **Neuron Structure**
  - Cell Properties

- **Neurogenesis**

- **Electrophysiological Properties**

- **Behavioral Performance**

- **Neurodegenerative Disease Markers**

Altered levels of growth factors, proteins, neurotransmitters & receptors, microRNAs, redox enzymes, immediate early genes, cytokines, gene methylation patterns.

Dendritic tree complexity, spine/synapse number persistently reduced in mice and rats at space relevant doses. Astrocyte and microglia activation. Transmitter vesicle fusion reduced.

The number of newly-born neurons and glia are persistently reduced and differentiation patterns altered.

Intrinsic membrane properties, excitability, synaptic plasticity and strengthening impaired in mouse hippocampus and cortex.

Behaviors in multiple models indicate impairments in several memory types, reaction time, attentiveness, learning and anxiety.

Deposition of disease-related proteins (Aβ, tau), altered protein turnover system, neuroinflammation markers and general accelerated aging patterns.
Major Findings on CNS Risk from NSRL

Research with animal models shows that 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 (adaptive remodeling/strengthening)
- Decrement are dependent on radiation dose and quality as well as on age of animal at time of exposure or testing; complex dose responses observed
- Studies using transgenic mice prone to develop pathologies reflective of Alzheimer’s disease show that low dose of GCR accelerates time of appearance and related molecular biomarkers
- Effects are not seen with similar doses of low-LET radiation (outcome measure dependent)

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

- Lack of human epidemiology data at low doses and high-LET to form the basis for risk assessment for CNS effects
- Major uncertainty in how to extrapolate results from animals to humans and establish “significance”
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**
• Identification of **biomarkers** related to early cognitive and behavioral decrements and relationship to 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**
RADIATION-INDUCED CARDIOVASCULAR DISEASE
“DEGEN” Risk Overview

**Risk of Cardiovascular Effects:**
- Cardiac and vascular pathologies
- Cerebrovascular events

**Other Degenerative Tissue Health Effects:**
- Cataract formation
- Diseases related to aging, including digestive, respiratory disease, premature senescence, endocrine, and immune system dysfunction

**Driving Evidence:**
- Astronaut data (cataracts)
- Radiotherapy, environmental disasters, atomic bomb survivor data, radiation workers (CVD and others)
  - Data is **confounded by life-style factors** to larger extent than cancer, especially at low doses
  - Effects are **considered deterministic** (threshold dose); recent evidence showing risk at lower doses questions this assumption

→ Additional mortality and morbidity risks for non-cancer diseases of the cardiovascular system are of concern because they could increase total calculated risk values.
Main types of cardiovascular disease:

- **Congenital heart disease.** Includes a range of abnormalities in heart structure or function that are present at birth. Such conditions could potentially be caused by irradiation of the fetus but obstetric irradiation is carefully controlled.

- **Cardiac valve diseases.** Include a variety of abnormalities to the heart valves including mitral stenosis and tricuspid regurgitation.

- **Hypertrophic cardiomyopathy.** Increased muscle density in the heart leading to less effective pumping of the blood.

- **Cardiac Arrhythmias.** Abnormally slow (bradycardia) or fast (tachycardia) beating of the heart often attributable to abnormalities in the electrical signaling that co-ordinates the beating of the four chambers of the heart.

- **Pericarditis.** Inflammation of the pericardium, the membrane that surrounds the heart, most frequently attributable to infectious agents but also well established to be caused by high doses of radiation.

- **Coronary heart disease/congestive heart disease.** Obstruction of the blood flow in the heart due to narrowing of cardiac vessels restricting blood and oxygen supply to the heart. In a mild form, this leads to **angina** where the reduced blood flow leads to discomfort. When blockage is severe, **myocardial infarction (heart attack)** occurs leading to acute heart failure.

- **Stroke.** Interruption of the blood supply to the brain due to blockage or rupture of vessels. Loss of blood and oxygen to areas can lead to cell death and consequently permanent brain dysfunction. Two majors forms of stroke are recognized, ischemic stroke caused by blockage due to blood clots forming locally (**thrombotic stroke**) or fragments from distant clots lodging in the brain vasculature (**embolic stroke**).

→ The circulatory diseases subtypes that are considered to be affected by radiation exposure appear in bold text.
Driving Evidence

Space Relevant Doses

< 0.5 Gy
- Systemic effects?
- Non-targeted effects, kidney dysfunction, monocyte killing?

0.5 - 5 Gy
- Atherosclerosis; micro and microvasculature damage
- Endothelial dysfunction; inflammation and oxidative stress

> 5 Gy
- Cell killing and inactivation
- Tissue damage and functional impairment

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Fig. 6. Hypothetical mechanisms of radiogenic CVD. Solid arrows represent the inflammation theory. Dashed arrows represent hypotheses discussed here.
Hamada 2014
Fig. 6. Hypothetical mechanisms of radiogenic CVD. Solid arrows represent the inflammation theory. Dashed arrows represent hypotheses discussed here.

Hamada 2014
Overall, there is still a paucity of experimental data related to radiation-induced heart diseases and other degenerative tissue diseases at low doses:

- Identify **disease spectrum and latency** for low dose heavy ions
- Establish **dose thresholds** for heavy ions and mixed fields
- Evaluate **qualitative differences** between GCR and gamma-rays to establish RBEs
- Evaluate effect of **dose-rate**
- Identify and validate **surrogate biomarkers** for radiation-induced disease endpoints
- Evaluate **medical countermeasures** for risk mitigation
- Address impact of **individual sensitivity, gender, and other spaceflight stressors** on risk levels
CVD / LATE CNS Research Approach

**CVD** → **COMMON PATHWAYS** (e.g. vascular dysfunction, inflammation, oxidative stress, metabolic dysfunction, accelerated aging) → **Late CNS**

- **Traditional Risk Factors** (e.g. Framingham factors, apoE, etc.)
- **Radiation-Sensitive Disease Biomarkers** (e.g. troponin, CRP, growth factors, imaging data, CAC, amyloid, cognitive tests, metabolomics/proteomics)
- **Clinical Standard-of-Care Practices** (e.g. diet, exercise, aspirin, statins)

**Validation in Animals with HZE**

**Recommendations for clinical guidelines with CMs, PELs, Combined Risk Model with Cancer**

**DELIVERABLES**

Human research (top-down) approach
Dose Limits for Short-Term or Career Non-Cancer Effects (in mGy-Eq or mGy)

- Relative Biological Effectiveness (RBEs) for specific risks are distinct
- The Gray-Equivalent quantity is used to limit non-cancer effects
- The RBE for CNS non-cancer effects is largely unknown; the linear energy transfer (LET)-based radiation quality factor for cancer risk estimates, Q(L), is used for CNS effects

<table>
<thead>
<tr>
<th>Organ</th>
<th>30 day limit</th>
<th>1 Year Limit</th>
<th>Career</th>
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<tbody>
<tr>
<td>Lens*</td>
<td>1000 mGy-Eq</td>
<td>2000 mGy-Eq</td>
<td>4000 mGy-Eq</td>
</tr>
<tr>
<td>Skin</td>
<td>1500</td>
<td>3000</td>
<td>6000</td>
</tr>
<tr>
<td>BFO</td>
<td>250</td>
<td>500</td>
<td>N/A</td>
</tr>
<tr>
<td>Circulatory System**</td>
<td>250</td>
<td>500</td>
<td>1000</td>
</tr>
<tr>
<td>CNS***</td>
<td>500</td>
<td>1000</td>
<td>1500</td>
</tr>
<tr>
<td>CNS*** (Z≥10)</td>
<td>-</td>
<td>100 mGy</td>
<td>250 mGy</td>
</tr>
</tbody>
</table>

* Lens limits are intended to prevent early (< 5 yr) severe cataracts (e.g., from a solar particle event). An additional cataract risk exists at lower doses from cosmic rays for sub-clinical cataracts, which may progress to severe types after long latency (> 5 yr) and are not preventable by existing mitigation measures; however, they are deemed an acceptable risk to the program.

** Circulatory system doses calculated as average over heart muscle and adjacent arteries.

*** CNS limits should be calculated at the hippocampus.
Major Challenges

• 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

Research solicitations focused on understanding and quantifying these uncertainties to increase safe days in space and identify/validate biomarkers and countermeasures for risk mitigation.
https://www.nasa.gov/hrp/elements/radiation
Thank You

A cluster of massive stars NGC 3603 seen with the Hubble Space Telescope.

Credits: NASA/U. Virginia/INAF, Bologna, Italy/USRA/Ames/STScI/AURA