Overview of Space Radiation Health Risks with a Focus on Radiation-Induced Cardiovascular Diseases

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INTRODUCTION

Future Manned Missions

International Space Station
- ISS phase: 2100 to 2300 years; 180 day orbit; 2 person crew 360 days in planning,
- Systems to protect: 3 persons in ISS, 16 persons in 360 day orbit
- Lagrange Points
- Design Reference Mission currently being formulated
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- Mars
- DoD and beyond: Expend crew; up to 1000 days
- Long-term space missions
- Risks exceed NASA Permissible Exposure Limits (PELs) for cancer, and pose significant non-cancer risks

The Space Radiation Problem

- Intra-cranial vasculature can be exposed to a high LET radiation environment containing high-energy cosmic and heavy ions (HZE) as well as secondary protons, neutrons, and fragments produced in shielding and tiles.
- Heavy ions are qualitatively different from low-LET or gamma-rays: high LET, low LET.
- Heavy ions: Denser ionization along particle track
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- No human data to estimate risk from heavy ions in space
- Animal- and cellular models with simulated space radiation must be developed or applied
- Synergistic radiations of risk from other spaceflight factors.

Health Risks from Space Radiation

Risk of Radiation Carcinogenesis
- Mutatory and leukaemia risk: major other for HZE

Risk of Acute (in-flight) & Late Central Nervous System Effects
- Possible in-flight: altered cognitive function including short term memory, reduced motor function, and behavioral changes which may affect performance
- Possible long-term: minimal neurological disorders such as Alzheimer’s disease (AD), dementia, cardiovascular diseases or premature aging

Risk of Cardiovascular Disease and other Depressive Tissue Effects
- Degenerative changes in heart, vessels, and lung
- Diseases related to aging, including degenerative, inflammatory disease, premature senescence, endocrine, and immune system dysfunction

Risk of Acute Radiation Syndromes due to Solar Particles Events
- Prophylactic effects (losses, vomiting, anorexia, and fatigue), skin injury, and depilation of the blood-forming organs

Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation

Risk of Degenerative Tissue Effects:
- High LET: ionic and radiobiological changes
- Caroten irradiated

Other Health Effects:
- Diseases related to aging, including degenerative, inflammatory disease, premature senescence, endocrine, and immune system dysfunction.

Driving Evidence:
- Animal model: radiation workers
- Radiation, environmental disasters, atomic bomb survivors, data, radiation workers, CVD and others
- Data is confounded by lifestyle factors to a larger extent than cancer, especially at low doses

Risk Projections:
- Animal model radiation effects being formulated
- Recent studies suggest there may be low dose effects and distinct pathologies at low doses suggesting mechanistic differences
- Impact of heavy ion largely unknown

ICRP Recommendations (2012)

Definition of “Threshold Dose”:
- Previous ICRP 300 Report defined a “threshold dose” as an exposure below which clinically significant effects do not occur
- The ICRP Threshold Dose (2012): an estimated dose for 1% incidence, denoting the amount of radiation that is required to cause a specific, observable effect only of 1% individuals exposed to radiation.
- An effect starting at a dose above the baseline levels in unirradiated, age-matched controls, e.g., larger number of circulatory diseases, to a dose which would increase the already high natural incidence or mortality by only 1%.
- Dose does not imply that biological effects occur at lower doses; it merely states the dose above which a specified effectiveness clinically apparent in a small percent of individuals.

Moderate Doses 0.5 - 5 Gy

Life Span Study, Clinical, and Occupational Exposures:
- Moderate doses (0.5 – 5 Gy) exposures associated with hypertension, micro and macro vascular damage
- Possibly a stochastic reaction
- Mechanisms may involve inflammation and oxidative stress, endothelial dysfunction/senescence

Low Doses < 0.5 Gy

Meta-Analysis of Low Dose Studies:
- Low doses (< 0.5 Gy) associated with systemic effects, microvascular damage
- Possibly a stochastic reaction
- Mechanisms may involve non-targeted effects, kidney dysfunction, microbiome, senescence
- Controlling effects are large

Although mean cumulative radiation doses were ≤ 0.2 Gy in most of studies, the small numbers of participants exposed at high cumulative doses (≥ 0.5 Gy) drive the observed trends in most cohorts with these higher dose groups

Low Dose Confounders & Uncertainties

- Suggests increased risks for IHD and non-IHD heart diseases
- Data suggest that circulatory disease risk is significantly elevated only for acute or cumulative doses of about 0.5 Gy and above; data is not statistically significant at lower doses

Risk Mitigation Strategy

Potential Mechanisms of Radiation-Induced CVD

Radiation Protection Strategies

DEGEN RISK SUMMARY

- Association between exposure to high doses of low-LET (<5 Gy) radiation during radiotherapy to the chest and increased risk for development of cardiovascular disease at late times post-exposure is clearly established among these higher dose groups
- Effects are considered deterministic, with an associated threshold dose; however recent evidence showing risk at lower doses questions this assumption

Potential Mechanisms of Radiation-Induced CVD

- Tuberculosis patients in Canadian Fluoroscopy Cohort Study
- ERSp/Gy 1.17 for IHD after adjustment for dose fractionation. ERSp/Gy 1.49 for doses ≤5 Gy
- Highest risks were for those with lowest fluoroscopic procedures per year

Potential Mechanisms of Radiation-Induced CVD

- ERSp/Gy 2.30 for IHD after adjustment for dose fractionation. ERSp/Gy 4.51 for doses ≤5 Gy
- Significant exceedance of threshold dose substantially

Potential Mechanisms of Radiation-Induced CVD

- ERSp/Gy 0.40 for IHD after adjustment for dose fractionation. ERSp/Gy 0.95 for doses ≤5 Gy
- Highest risks were for those with highest fluoroscopic procedures per year

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