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
- International Space Station (ISS) Risk: 1 person/year 360 days in space

Lagrange Points
- Design Reference Mission currently being formulated
- ISS: 1 person/year 360 days in space

Near Earth Objects
- Design Reference Mission currently being formulated
- Galileo: 1 person/year 360 days in space

Mars
- 2030 and beyond: Exploration crews, up to 1900 days

The Space Radiation Problem

- Intraorbital crews will be exposed to a high LET radiation environment consisting of protons, high-energy cosmic rays (HICR) as well as secondary protons, neutrons, and charged particles.
- Heavy ions are qualitatively different from 3-radiation: high LET, low LET
- Density varying along particle track
- Causes unique damage to genomic material, cells, and tissues
- Damage patterns of DNA damage (mutation spectra, chromosomal aberrations) and detailed profiles of radiation damage
- No human data to estimate risk from high LET in space.
- Animal and cellular models with simulated radiation data must be applied or developed
- Synergistic modifiers of risk for other spaceflight factors

Health Risks from Space Radiation

Risk of Radiation Carcinogenesis
- Evidence and mechanisms require further study for HICR

Risk of Acute (in flight) & Late Central Nervous System Effects
- Possible in-flight effects: altered cognitive function including short term memory, induced motor function, and behavioral changes which may affect performance
- Possible late (post-mission) effects: neurological disorders such as Alzheimer’s Disease (AD), dementia, cerebrovascular disease or premature aging

Risk of Cardiovascular Disease and Other Degenerative Tissue Effects
- Degenerative changes in the heart, vasculature, and lens
- Diseases related to aging, including digestive, respiratory disease, premature senescence, endocrine, and immune system dysfunction

Risk of Acute Radiation Syndromes due to Solar Particle Events
- Proximal effects (tissue, vomiting, anoxia, 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:
- Diseases related to aging, including digestive, respiratory diseases, premature senescence, endocrine, and immune system dysfunction

Driving Evidence:
- Age, sex, lifestyle
- Radiotherapy, environmental disasters, atomic bomb survivor data

Risk Projections:
- All modeling efforts being formulated
- Recent studies suggest there may be late dose effects and distinct pathologies at low dose indicating mechanical differences
- Impact of high dose largely unknown

ICRP Recommendations (2012)

Definition of “Threshold Dose”:
- Previous ICRP 2007 Report defined a “threshold dose” as an exposure below which clinically significant effects do not occur
- ICRP 2012 modified “threshold dose” as ED1 (estimated dose for 1% incidence), denoting the amount of radiation that is required to cause a specific, observable effect only in 1% of individuals exposed to radiation
- ED1 is a reference starting point above the baseline levels in unirradiated, age-matched control populations
- The level of variability—of statistical, disease, and to a degree which would increase above the already high natural incidence or mortality by only 1%.
- ED1 does not imply that biological effects occur at lower doses: it merely defines the dose above which a specified effectiveness clinically apparent in a small percentage of individuals.

≥ 0.5 Gy may lead to approximately 1% of exposed individuals developing the disease in question >10 years after exposure. This is in addition to the high natural incidence rate (circulatory diseases account for 30–50% of all deaths in most developed countries).

DRIVING EVIDENCE

High Doses > 5 Gy

Radiotherapy Data:
- High doses (< 5 Gy exposures) associated with damage to the structures of the brain and to the coronary, cardiac, and other large vessels including impaired afferent sensory damage, especially of the pericardium and myocardium, impaired adhesions, microvascular damage and stenosis of the vascular wall, and bony changes observed in patients receiving RT as well as experimental animals

Moderate Doses 0.5 - 5 Gy

Life Span Study, Clinical, and Occupational Exposures:
- Moderate doses (0.5 - 5 Gy exposures) associated with atherosclerosis, micro and macrovascular damage
- Possibly a stochastic reaction

Low Doses < 0.5 Gy

Meta-Analysis of Low Dose Studies:
- Low doses (< 0.5 Gy) associated with systemic effects, micro and macrovascular damage
- Possibly a stochastic reaction

Low Dose Confounders & Uncertainties
- Confounding factors in epidemiological studies include Lifestyle and genetic factors

Potential Mechanisms of Radiation-Induced CVD

Risk Mitigation Strategy

DEGEN RISK SUMMARY

- Association between exposure to high doses of low-LET (<0.5 Gy) radiation during radiotherapy to the chest and increased risk for development of cardiovascular disease at late times post-exposure is clearly established with these higher dose groups

- Atomic bomb survivor data and analyses of epidemiological data provide evidence for elevation of risk at lower doses than previously identified, with significant risks for doses as low as 0.5 Gy

- Data at low doses is confounded by lifestyle factors, confounding between radiation epidemiology data below 0.5 Gy

- Effects are considered deterministic, with an associated threshold dose; however recent evidence showing risk at lower doses questions this assumption

- Preliminary risk assessment models being formulated based on recent epidemiological data for lower dose low-LET exposures. Future risk estimates depend on research results describing the quantitative and qualitative differences between GRP and Gompertz models

- Studies at HICR with HZC and appropriate animal models are required

- Lack of evidence on radiation quality, disease spectrum, latency and dose rate at low levels of exposures

- The additional mortality and morbidity risks for non-cancerous diseases of the cardiovascular system are major concern because they could increase RED values substantially