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-250: Hyperion-764; ISS-Risk: nominal; 2-person crew 30 days in planning

Lagrange Points

- Design Reference Mission currently being formulated
- Slightly different mass but major concern

Near Earth Objects

- Design Reference Mission currently being formulated
- Slight differences in mass but major concern

Marx

- Solar and beyond: Exoplanets crowed, up to 1900 days
- Long-term space missions
- Risks exceed NASA Permissible Exposure Levels (PELs) for cancer, and pose significant non-cancer risks

The Space Radiation Problem

- Intraocular lens is expected to be in a high LET radiation environment composed of high energy cosmic rays (HECRs) as well as secondary protons, neutrons, and fragments produced in shielding and tissue
- High-ons are qualitatively different from 3- to 50-MeV neutrons high LET, low LET
- Primarily impacting along particle track
- Okada’s unique reaction damage to microcirculation, cells, and tissue
- Damage patterns of DNA damage (mutation spectra, chromosome aberrations) and DNA profiles of late damage
- No human data to estimate risk from high-on particle fluence in space
- Animal and cellular models with simulated lesions modelled and/or developed
- Synergistic radiation risk is from other spaceflight factors

Health Risks from Space Radiation

Risk of Radiation Carcinogenesis

- Mobility and mortality risks, major threat for HECRs

Risk of Acute (In Flight) & Late Central Nervous System Effects

- Possible high-flight, altered cognitive function including short term memory, induced motor function, and behavioral changes which may affect performance
- Possible late post-mission deficit, neurological disorders such as Alzheimer’s disease (AD), dementia, cerebrovascular disease and premature aging

Risk of Cardiovascular Disease and Other Degenerative Tissues Effects

- Degenerative changes in the heart, vasculature, and lungs
- Diseases related to aging, including degenerative, inflammatory disease, premature senescence, endocrine, and immune system dysfunction

Risk of Acute Radiation Syndromes due to Solar Particle Events

- Procedural issues (exposure, vomiting, anosmia, fatigue), skin injury, and depilation of the blood forming organs

Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation

Risk of Degenerative Tissue Effects:

- Various types and severity of damage
- Cataract formation

Other Health Effects:

- Diseases related to aging, including degenerative, inflammatory disease, premature senescence, endocrine, and immune system dysfunction

Driving Evidence:

- Age-related increases in incidence of cardiovascular disease in the general population
- Elevated risk of cardiovascular disease associated with known risk factors
- Age and mean cumulative radiation doses were ≤ 0.2 Gy

Risk Projections:

- Clinical studies of short-term reactivity in animal models being formulated
- Recent studies suggested there may be low dose effects and distinct pathologies at low doses suggesting mechanistic differences
- Impact of high-on mass significantly larger

ICRP Recommendations (2012)

Definition of “Threshold Dose”:

- Previous ICRP 103 Report defined a “threshold dose” as an exposure below which clinically significant effects do not occur
- ICRP suggest “threshold dose” as ED1 (estimated dose for 1% incidence), denoting the amount of radiation that is required to cause a specified, observable effect only 1% of individuals exposed to radiation
- ED1 a-effects just starting to rise above the baseline levels in unirradiated, age-matched controls
- ED1 for cardiovascular disease – dose at which incidence of the disease rises
- ED1 does not imply that cardiovascular 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

Radiotherapy Data:

- High doses (>5 Gy exposures) associated with damage to the structures of the heart and coronary artery, and beyond; and other large areas including the development of aortic aneurysms, dilated cardiomyopathy, atrial fibrillation, hypertension, and oxidative stress, endothelial dysfunction/senescence
- Low doses (<0.5 Gy exposure) associated with the development of aortic aneurysms, atrial fibrillation, and hypertension
- Potential mechanisms 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
- Potentially a stochastic reaction
- Mechanisms may involve inflammation and oxidative stress, endothelial dysfunction/senescence

Potential Mechanisms of Radiation

- Cardiovascular 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
- Low dose effect is heterogeneous
- Controlling effects are large

Low Dose Confounders & Uncertainties

- Confounding factors in epidemiological studies include lifestyle and genetic factors, male sex, obesity, and smoking
- High blood pressure, diabetes, obesity, increased low dose exposure may have been confounded by high density (lipoprotein cholesterol) plasma levels
- Risk at lower doses and low dose rates still highly uncertain; existence of threshold dose remains
- There is also a lack of data on dose rate effects

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
- Potentially a stochastic reaction
- Mechanisms may involve inflammation and oxidative stress, endothelial dysfunction/senescence
- Despite robustness of survival data, radiation workers (CVD and others)

Potential Mechanisms of Radiation-Induced CVD

- High dose rates seem to play a role in cardiovascular disease (CVD) response
- High radiation dose rates seem to play a role in cardiovascular disease (CVD) response
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High Dose Rates >5 Gy

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Risk Mitigation Strategy

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DEGEN RISK SUMMARY

- Association between exposure to high doses of low LET (≤0.5 Gy) radiation during recombination to the chest and increased risk for development of cardiovascular disease at late times post-exposure in clearly established
- The observed trend in non-cumulative doses with higher dose groups of the heart, vasculature and lungs
- Diseases related to aging, including degenerative, inflammatory disease, premature senescence, endocrine, and immune system dysfunction
- Age-related increases in incidence of cardiovascular disease in the general population
- Elevated risk of cardiovascular disease associated with known risk factors
- Age and mean cumulative radiation doses were ≤ 0.2 Gy
- Risk Projections:

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Low Dose Effects

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High Dose Effects

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