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 is currently operating, 11 teaspoons 10 years in planning
- Space craft limits for acceptable radiation risk after 10 to 30 years

Lagrange Points
- Missions to Lagrange points currently being formulated
- Celestial body on the opposite side of the solar system

Near Earth Objects
- Design Reference Mission currently being formulated
- Celestial body on the opposite side of the solar system
- Celestial body on the opposite side of the solar system

Mars
- ~200 and beyond, journey times, up to 900 years
- Long time space missions
- Risks exceed NASA Permissible Exposure Limits (PELs) for cancer, and pose significant non-cancer risks

The Space Radiation Problem

- Intracellular effects are well established in high LET radiation, environment composed of high-energy cosmic rays (HECR), as well as secondary protons, neutrons, and fragments produce ionizing and tissue damage
- Heavy ions are qualitatively different from low LET, e.g., protons, neutrons, and heavy ions with large ionization charge

Health Risks from Space Radiation

Risk of Radiation Carcinogenesis
- High-dose and moderate-risk, major organ systems

Risk of Acute (in-flight) and Late Central Nervous System Effects
- Possible in-flight risks: altered cognitive function including short-term memory, reduced motor function, and behavioral changes which may affect performance

Risk of Cardiovascular Disease and Other Degenerative Tissue Effects
- Degenerative changes in the heart, vascular, and other tissues
- Diseases related to aging, including diabetic, respiratory, cardiovascular, endocrine, and immune system dysfunction

Risk of Acute Radiation Syndromes due to Solar Particle Events
- Proximal effects (nausea, vomiting, diarrhea, fatigue, skin injury, and apnea of the blood-forming organs)

Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation

Risk of Degenerative Tissue Effects:
- Cardiovascular disease and neurological changes
- Cardiovascular disease

Other Health Effects:
- Diseases related to aging, including diabetic, respiratory, cardiovascular, endocrine, and immune system dysfunction

DRIVING EVIDENCE

Radiotherapy Data:
- High doses (≥ 5 Gy) exposures associated with damage in the structure of the heart, and to the coronary, cardiac, and other peripheral arteries including reduced arterial stiffness, damage, especially of the pericardium and myocardium, mitral and aortic valve disease, microvascular damage and stenosis of the coronary arteries, and decreased high-density lipoprotein cholesterol plasma levels.
- Risk at lower doses and lower dose rates still highly uncertain; evidence of threshold dose nonexistent.

Meta-Analysis of Low Dose Studies:
- Low doses (≤ 0.5 Gy) associated with systemic effects, microvascular damage
- Possibly a stochastic reaction
- Mechanisms may involve inflammation and oxidative stress, endothelial dysfunction/vasoconstriction
- Moderate doses (0.5 - 5 Gy) exposures associated with atherogenesis, micro and macrovascular damage
- Possibly a stochastic reaction
- Mechanisms may involve inflammation and oxidative stress, endothelial dysfunction/vasoconstriction

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

Low Dose < 0.5 Gy
- Although mean cumulative radiation doses were ≤ 0.2 Gy in most of the 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
- No evidence of 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

Low Dose Confounders & Uncertainties
- Confounding factors in epidemiology studies include lifestyle and genetic factors, male sex, heavy smoking, diabetes, high blood pressure, obesity, increased low density lipoprotein cholesterol, and decreased high-density lipoprotein cholesterol plasma levels.
- Risk at lower doses and low dose rates still highly uncertain; evidence of threshold dose nonexistent.
- There is also a lack of data on dose rate effects
- Subjects are considered determinists, with an associated threshold dose; however recent evidence showing risk at lower doses questions this assumption
- Rotating the radiological image to achieve the radiation damage in the human body (from Franklin and Turrill, 2003)

ICRP Recommendations (2012)
Definition of “Threshold Dose”:
- Previous ICRP 300 report defines a “threshold dose” as an exposure below which clinically significant effects do not occur
- ICRP 2012 redefined “threshold dose” as ED1 (estimated dose for 1% incidence), denoting the amount of radiation that is required to cause a specific, observable effect only 1% of individuals exposed to radiation:
  - ED1 is a value just starting to rise above baseline levels in unirradiated, age-matched, sex-matched, and healthy populations of non-irradiated individuals.
- ICRP’s approach to the threshold dose is not aligned with the current understanding of biological events...
- ED1 is not aligned with biological effects that occur at lower doses; it merely defines the dose above which a specified effectiveness clinically apparent in a small percent 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 accounts for 30-50% of all deaths in most developed countries).

Dose Rate Effects
- Tuberculosis patients in Canadian Fluoroscopx Cohort Study
- 83,707 patients (81% unexposed, 96% <0.5 Gy, mean doses=0.79 Gy)
- ERR/Gy=0.174 for IHD after adjustment for dose fractionation, ERR/Gy=0.149 for doses <0.5 Gy

Risk Mitigation Strategy

DEGEN RISK SUMMARY
- Association between exposure to high doses of low-LET (~1 Gy) radiation during radiation therapy to the chest and increased risk for development of cardiovascular disease at late times post-exposure is clearly established
- Atomic bomb survivor data and analyses of epidemiology data provide evidence for elevation of risk at lower doses than previously identified, with significant risks at doses as low as 0.5 Gy
- Data at low doses is complicated by lifestyle factors, cholesterol intake, and other confounding factors.
- Data at low doses is not well studied and low-dose effects are still highly uncertain.
- There is also a lack of data on dose rate effects
- The additional morbidity and mortality risks for non-cancer diseases of the cardiovascular system are major concerns because they could increase RERD substantially