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-26: 2006–2009: 14 months (218 people)
- MARS Sample Return Mission: 360 days
- MARS Exploration Mission: 1–3 years
- EVA mission: 6–24 hours
- Lagrange Points
- L1/L2: Sun-Earth intervals currently being formulated
- Design Reference Mission (DRM): 360 days
- Near Earth Objects
- Design Reference Mission currently being formulated
- Large # of cells in a single organism may lead to approximately 1% of exposed individuals

Risk Modifiers

Design Reference Mission currently being formulated
- Galactic cosmic ray risks are major concern
- 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

Medical countermeasures

DRIVING EVIDENCE

The Space Radiation Problem

- Interrelated stressors will activate a high LET radiation environment consisting of charged particles and high energy cosmic rays (HEDCR) as well as secondary protons, neutrons, and fragments produced in shielding and tissue
- Heavy ions are qualitatively different from 3°-rays or Gammas; high-LET, low LET
  - Dose linearity along particle track
  - Damage to DNA, genome, cells, and tissue
  - Damage to DNA (mutation, chromosome aberrations) and cellular profiles of radiation damage
  - No hard data to estimate risk from heavy ions found in space
  - Animal and cellular models with simulated space radiations must be applied or developed
  - Synergistic nonlinear of risk with other spaceflight factors

Health Risks from Space Radiation

Risk of Radiation Carcinogenesis
- Tumors and organ-related cancers, major concern for HEDCR

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

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

Risk of Acute Radiation Syndromes due to Solar Particle Events
- Protracted effects (anosmia, otorhinolaryngologic, skin injury, and apnea of the breathing function)

Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation

Risk of Degenerative Tissue Effects:
- Cardiovascular disease and other degenerative disorders
- Cataract formation

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

Driving Evidence:
- Cancer mortality
- Radiation-induced, environmental, atomic bomb survivors, CVD and others
- Data is contributed to lifestyle factors to a greater extent than cancer, especially in late dose

Risk Projections:
- Last line of defense models being formulated
- Recent studies suggest there may be late dose effects and distinct pathologies at low to high dose suggesting mechanistic differences
- Impacts of heavy ions largely unknown

ICRP Recommendations (2012)

Definition of “Threshold Dose”:
- Previous ICRP 30/1959 Report defined a threshold dose at an exposure below which clinically significant effects do not occur
- ICRP 103 defined a “threshold dose” as ED1 (estimated dose for 1% incidence); extending the amount of radiation that is required to cause a specific, observable effect only 1% of individuals exposed to radiation
  - ED1 – effects just starting to rise above the baseline levels in unirradiated, age-matched controls
  - ED2 – effective levels of radiation that would increase the overall incidence of cardiovascular diseases, to a degree which would increase the already high natural incidence by no more than 1%.
  - ED0 does not apply to whether effects occur at lower doses; it merely sets the dose above which an effect is detectable clinically apparent in a small percentage of individuals

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 natural incidence rate (circulatory diseases account for about 30–50% of all deaths in most developed countries).

High Doses > 5 Gy

Radiotherapy Data:
- High doses (≥ 5 Gy exposures) associated with damage to the structures of the heart to and the coronary, cardiac, and other large arteries including myocardial infarction, tissue damage, especially of the peripheral and myocardial, resulting in distal adhesions, microvascular damage and sclerosis of the vascular wall
- Deterministic effect (tissue reaction)
- Mechanisms involve cell killing or inactivation of large # of cells – functional impairment

Moderate Doses 0.5 - 5 Gy

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/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, monocytic activation, T-cell response
- Conflating effects are large

Still, there is conflicting data even at moderate dose ranges
- The results of these 11 studies have not been published in a sufficiently uniform format to permit a formal heterogeneity test but still clear that there is substantial heterogeneity between them
- Other challenges for these types of analyses include disability, incidence, and etiologic pathogenesis of pathologies/cause of death

Low Dose Confounders & Uncertainties

- Although mean cumulative radiation doses were ≤ 0.2 Gy in most 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
- The additional mortality and morbidity risks for non-cancer diseases of the cardiovascular system are major concerns because they could increase RVD values substantially

Dose Rate Effects
- Tuberculosis patients in Canadian Fluoroscopy Cohort Study
  - 83,707 patients (31% unexposed, 96% ≤ 0.5 Gy, mean dose=0.79 Gy)

Potential Mechanisms of Radiation-Induced CVD

Potential Mechanisms for Exposures at Moderate Doses

Risk Mitigation Strategy

EVIDENCE

Radiation Risk

Risk Characterization

Risk Mitigation

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