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

Zarana S. Patel¹, Janice L. Huff², and Lisa C. Simonsen³

¹Wyle Science, Technology and Engineering, Houston, TX 77058
²USRA Division of Space Life Sciences, Houston, TX 77058
³NASA Langley, Hampton, VA

INTRODUCTION

Futurist Manned Missions

International Space Station

- ISS-25Characteristics: 395 km, Orbits, 16.7 years, 2-person crew 360 days in planning

Lagrange Points

- Characteristic: ISS-25 currently being formulated near Earth

Near Earth Objects

- Design Reference Mission currently being formulated near Earth

Mars

- 2020 and beyond: Exponential growth, up to 1800 days

The Space Radiation Problem

- Exposures associated with mission planning, for the mission's duration to the Red Planet (before use of any mission planning)

Risk of Radiation Carcinogenesis

- Mobility and mobility risk, major risk for ISS

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

- Possible in-flight risk: 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, vasculature, and lungs

Risk of Acute Radiation Syndromes due to Solar Particle Events

- Protralional effects (nausea, vomiting, anosmia, fatigue, skin injury, and apoplexy of the blood forming organs

Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation

Risk of Degenerative Tissue Effects:

- Effects related to aging, including digestive, respiratory, pulmonary, senescence, endocrine, and immune system abnormalities

Driving Evidence:

- A variety of studies:
  - Radiotherapy, environmental disasters, atomic bomb survivor data, radiation workers

Risk Projections:

- Recent studies suggest there may be dose effects and distinct pathologies at low doses suggesting mechanistic differences

ICRP Recommendations (2012)

Definition of "Threshold Dose":

- Previous ICRP 2010 Report defined a "threshold dose" as an exposure below which clinically significant effects do not occur

- ICRP 2012 Report: "threshold dose" as ED10 (estimated dose for 1% incidence), denoting the amount of radiation that is required to cause a specific, observable effect only if 1% of individuals exposed to radiation

- ED10 effects: just starting to rise above the baseline levels in unirradiated, age-matched controls; occasionally in the range of clinical pathology to an extent which would increase the already high natural incidence or mortality by only 1%.

- ED10 does not apply to biological effects observed at lower doses; it merely defines the dose above which a specific effect becomes clinically apparent in a small percent of individuals.

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

DRIVING EVIDENCE

High Doses > 5 Gy

Radiotherapy Data:

- High doses (≥ 15 Gy exposures) associated with damage to the structures of the brain and to the coronary, cardiac, and other large vessels including marked diffuse fibrotic damage, especially of the pericardium and myocardium, coronary arterial stenosis and aneurysm, microvascular damage and stenosis of the vasculature exposed in patients receiving RT as well as in experimental animals (Little 2013)

- Deterministic effect (tissue reaction)

- Mechanisms involve cell killing or irradiation 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 atrioventricular conduction, micro and macrovascular damage

- Possibly a stochastic reaction

- Mechanisms may involve inflammation and oxidative stress, endothelial dysfunction/vasomotor dysfunction

Low Doses < 0.5 Gy

- Meta-analysis of low dose studies

- Low dose (< 0.5 Gy) associated with systemic effects, microvascular damage

- Possibly a stochastic reaction

- Mechanisms may involve non-targeted effects, kidney dysfunction, microangiopathy, 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

- 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 3.5 Gy and above (data is not statistically significant at lower doses)

Low Dose Confounders & Uncertainties

- Confounding factors in epidemiologic studies include lifestyle and genetic factors, male sex, obesity, and diabetes, high blood pressure, obesity, increased low density lipoprotein cholesterol microvascular damage and increased high density lipoprotein cholesterol plasma levels.

- Risk at lower doses and low dose rates still highly uncertain: existence of threshold dose hypothetic

- There is also a lack of data on dose rate effects

Dose Rate Effects

- Tuberculosis patients in Canadian Fluoroscopy Cohort Study

- E3,707 patients (91% unexposed, 9% ≤0.5 Gy, mean dose=0.79 Gy)

- ERG/Qp is 1.17 for IHD after adjustment for dose fractionation. ERG/Qp is 1.49 for doses <0.5 Gy

- Highest risks were those with lowest fluoroscopy procedures per year

Potential Mechanisms of Radiation-Induced CVD

Risk Mitigation Strategy

- Exercise

- Shielding

- Operations

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

- 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 confounded by lifestyle factors, including intervention and intervention in 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 epidemiology data for lower dose low-LET exposures. Future risk estimates depend on research results describing the quantitative and qualitative differences between GCR and gamma-rays

- Studies of HZE with appropriate animal models are required

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

- The additional morbidity and mortality risks for non-cancer diseases of the cardiovascular system are major concerns because they could increase RER values substantially