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-2016: Hyperbaric (H2) & vacuum (V) effects; 2 person crew 360 days in pressurized habitat

Lagrange Points

• Design Reference Mission currently being formulated

Near Earth Objects

• Design Reference Mission currently being formulated

Mars

• 300 and beyond; exploration crews, up to 1900 days

DRIVING EVIDENCE

The Space Radiation Problem

Interdependency will always be prevalent in a high LET radiation environment compared to low energy cosmic and heavy ions (HZE) as well as secondary protons, neutrons, and fragments produced in shielding and tissue.

High Doses > 5 Gy

Radiotherapy Data:

• High doses (> 5 Gy exposures) associated with damage to the structures of the heart and to the coronary, cardiac, and other large arteries including related arterial diseases, damage of the microcirculation, and increased microvascular damage and stiffness of the peripheral vessels and arteries. However, some of these effects are only observed in patients receiving RT as well as in experimental animals (Dutil et al. 2011).

• 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/sclerosis

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, myocardial infarction, mortality

• Confounding 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.

DEGEN RISK SUMMARY

• Association between exposure to high doses of low-LET (<5 Gy) radiation during radiotether therapy to the chest and increased risk for development of cardiovascular disease at late times post-exposure is clearly established.

• Atomic bomb survivors 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, leading interpretations of 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

Potential Mechanisms of Radiation-Induced CVD

Risk Mitigation Strategy

Low Dose Confounders & Uncertainties

• Confounding factors in epidemiology studies include lifestyle, race, sex, body mass index, age, hypertension, diabetes, high blood pressure, obesity, increased low density lipoprotein cholesterol, and decreased high density lipoprotein cholesterol plasma levels; however little is known about the role of spaceflight factors.

• Risk at lower doses and low dose rates still highly uncertain: existence of threshold dose remains unclear

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

Risk Transfer

Characterization

Evidence

Modeling

Risk Mitigation

Other terms

Countermeasures

Potential Mechanisms of Radiation-Induced Moderate and Low Doses

Health Risks from Space Radiation

Risk of Radiation Carcinogenesis

• Dose and dose rate effects, major driver for PELs

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

• Possible in flight: altered cognitive function including short term memory, reduced motor function, and behavioral changes which may affect performance

• Possible low dose (baseline): neurologic disorders such as Alzheimer’s disease (AD), dementia, cardiovascular disease or premature aging

Risk of Cardiovascular Disease and Other Degenerative Tissue Effects

• Degenerative changes in the heart, vasculature, and lens

• Diseases related aging, including degenerative, respiratory disease, premature senescence, endocrine, and immune system dysfunction

Risk of Acute Radiation Syndromes due to Solar Particle Events

• Prognostic factors (toxins, vomiting, anorexia, and fatigue), skin injury, and depression of the blood forming organs

Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation

Risk of Degenerative Tissue Effects:

• Dose, dose rate, and possibly radiation quality

Other Health Effects:

• Diseases related to aging, including digestive, respiratory disease, premature senescence, endocrine, and immune system dysfunction

Driving Evidence:

• Animal data

• Radiation therapy, environmental disasters, atomic bomb survivors data, radiation workers, CV disease and others

• Data is confounded by lifestyle factors to a larger extent than cancer, especially for dose

Risk Projections:

• Recent predictions or models being formulated

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

• Impact of heavy ion data largely unknown

ICRP Recommendations (2012)

Definition of “Threshold Dose”:

• Previous ICRP 2000 Report defined a ‘threshold dose’ as an exposure below which clinically significant effects do not occur.

• ICRP 2012 defined a ‘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 effects just starting to rise above the baseline levels in unirradiated, age-matched controls. The addition of a threshold dose to a dose which already has a baseline incidence or mortality by only 1%

• ED1 dose not applicable to biological effects occurring at lower doses, it merely defines the dose above which a specified effectiveness clinically apparent in a small percent of individuals.

• Low Doses (<0.5 Gy) may lead to approximately 1% 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).