PRE-CURSOR DATA REQUIREMENTS: NORMAL TISSUE INJURY AND FATAL CANCER RISKS FOR HUMAN EXPLORATION OF MARS. Francis A. Cucinotta[1], [1]University of Nevada, Las Vegas, Department of Health Physics and Diagnostic Sciences, Las Vegas NV, 89195, USA. Email: Francis.Cucinotta@UNLV.EDU.

Introduction: Space radiation health risks are an important issue for long-term space missions [1,2]. Central estimates of space radiation induced cancer morbidity and mortality risks for a Mars mission near solar minimum where galactic cosmic ray (GCR) exposures are estimated as 6% and 12%, respectively for average crew demographics [3,4]. Upper 95% confidence levels are above 10% and 20%, respectively for cancer mortality and morbidity [3,4]. For missions near solar maximum GCR risks would be about two times lower, however these missions would involve exposures from solar particle events (SPEs) in addition to GCR. In comparison lifetime risks of automobile fatalities are 1 in 75, of space mission failures 1 in 270 [5], and space radiation fatality on a Mars mission exceeds 1 in 20 with uncertainties suggesting values as high as 1 in 8. Probability of causation estimates [4] suggest most cancers observed in returning crew members would be associated with GCR exposures. Recent studies (Figure 1) suggest that GCR heavy ion induced tumors are more lethal with higher frequencies of metastatic tumors compared to proton or background tumors [6,7]. This qualitative difference for GCR is not accounted for in NASA risk models, and could raise risk estimates by as much as 50% and increase years of life-loss for radiation cancer death from 15 years to more than 20 years [6]. Reducing these uncertainties in risk estimates will require lifespan studies in animal models using ground-based accelerators to similar GCR and SPEs [1-3].

Normal tissue injury is an additional concern for space radiation exposures on long duration missions. These injuries include early effects that would manifest during a mission, and late effects occurring several years after a mission [1]. Tissues with the highest radiosensitivity are ones with the highest cell turnover rates such as the blood forming organ and gastro-intestinal systems, and skin. The accumulation of GCR heavy ion hits to stem cells in these tissues are a major concern. The stem cell hypothesis of GCR damage predicts tissue injury will become manifest when the fraction of stem cells hit by GCR heavy ions approaches or exceeds unity.

Risks to the lens of the eye and central nervous system (CNS) are predicted following exposure to GCR, and increased risk of death due to stroke and heart disease for GCR and SPEs [4,6,8]. Increased incidence of cataracts are associated with very low GCR doses to astronauts on space shuttle and other past mission (Figure 2) [9,10], and there is the possibility that vision impairment could occur for the higher GCR exposures and extended duration of a 30-month Mars mission. Early CNS risks include detriments in memory and cognition, while late CNS risks include advanced onset of Alzheimer's disease and other forms of dementia [11-13].

Precursor Measurements: Space radiation environments and shielding properties en route to Mars and on Mars surface are reasonably well understood [3,4]. However predications of fatality and significant morbidity risks carry large uncertainties. In order to reduce uncertainties in risk estimates and develop mitigation approaches ground-based studies at particle accelerators capable of simulating GCR and SPEs should be used to study the radiobiology of cancer risks, normal tissue injury and CNS effects. Studies with protons and an array of heavy ions of different charge number, kinetic energies, doses, and dose-rates are needed. Studies should employ appropriate human cell culture models, and male and female small animal species with a variety of genetic backgrounds, including the use of genetically engineered mice.

Not all biological time scales in humans can be matched in experimental models. Time scales such as DNA repair, stem cell proliferation, and synapse and neuron integration are readily extrapolated from experimental models to humans with minor adjustments. However, aging of animal models over 2 to 3 years of a deep space mission would be significant. To understand the importance of acute versus chronic exposure, studies with simulated GCR using chronic irradiation proceeding at increasing exposure times from 1, 3, 7, 30 and up to 60 days for low cumulative doses (<1 Gy) should be considered to understand if a limiting slope is achieved as dose-rate is decreased. In order to support the validation of risk prediction models and include potential effects of microgravity on space radiation risks, deep space animal colonies can be considered for exposures outside of the Earth's magnetosphere. Sample sizes of 100 to 200 mice would be needed and replicate experiments standard in biological research. These considerations suggest ground based experiments with simulated space radiation are cost effective and allow for scientifically presise research approaches, while deep space animal experi-

ments would be at a much higher costs with possibly significant limitations in space launch opportunities.

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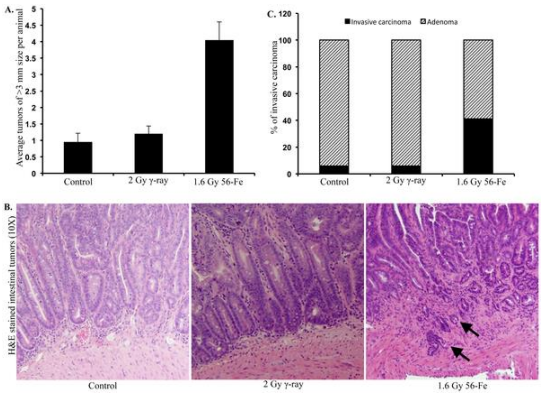

Fig. 1. ^{56}Fe radiation-induced larger and higher-grade intestinal tumors from Datta et al. [7].
A) Compared to γ radiation, exposure to ^{56}Fe radiation led to greater number of tumors whose size was ≥3 mm. B) H&E stained intestinal tumors showing crypt penetration of mucularis mucosa (arrow) indicating invasive adenocarcinoma after ^{56}Fe radiation. Tumors in control and γ irradiated mice were mostly adenomas. C) Percent of invasive adenocarcinoma in control, γ, and ^{56}Fe irradiated tumors.
doi:10.1371/journal.pone.0059295.g003

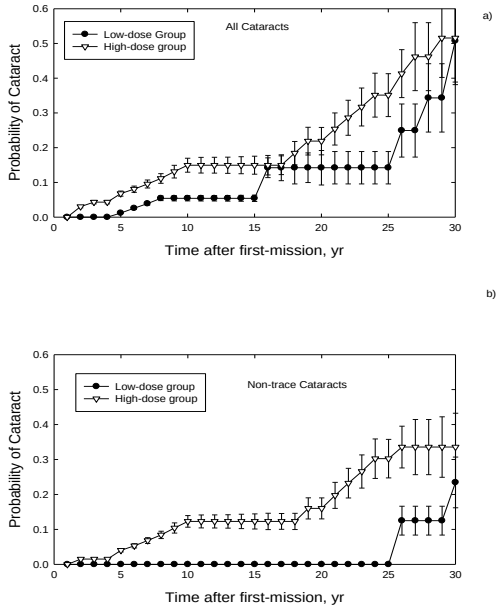

Fig. 2. Probability of cataract observed in astronauts versus time after mission for average lens dose equivalents 30 times less than that of a Mars mission [9]. Top panel show results for all cataracts and bottom panel for vision imparing cataracts. The "high dose" astronaut group has average lens exposures of 45 mSv which is about 30 times less lens dose compared to that of a Mars mission near solar minimum, which suggest vision impairing opacities could occur during a long duration mission with high cumulative exposures.