Space Radiation Future Directions

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Space Radiation Risks

- Risk of Radiation Carcinogenesis
  - Morbidity and mortality risks
- Risk of Acute (In-flight) & Late Central Nervous System Effects from Radiation Exposure
  - Changes in cognition, motor function, behavior and mood, or neurological disorders
- Risk of Cardiovascular Disease and Other Degenerative Tissue Effects
  - Degenerative changes in the CV system and lens
  - Diseases related to aging and immune system dysfunction
- Risk of Acute Radiation Syndromes due to Solar Particle Events
  - Prodromal effects (nausea, vomiting, anorexia, and fatigue)
  - Skin injury
  - Depletion of the blood-forming organs and immune dysfunction

Risks documented in HRP Evidence Books
Assessing cancer risks from space radiation exposure

Exposure of human to charged particles (High-LET) at low dose and low dose rate

Exposure of human to gamma/X rays (low-LET) at high dose and high dose rate

\[ R(\text{High LET, LD, LDR}) = \sum \frac{R(\text{Low LET, HD, HDR}) \times Q(\text{LET, Z, E})}{\text{DDREF(LET, Z, E)}} \]

(Simplified equation)

Exposure of human cells/animals to gamma/X rays (low-LET)

Determine Q(LET, Z, E) and DDREF(LET, Z, E) from cell/animal studies

Exposure of human cells/animals to charged particles (High-LET)
Sources of uncertainties in risk assessment

• Uncertainties in determining the qualitative and quantitative differences between the biological damage induced by space radiation compared to X-rays
• Uncertainties in human epidemiological data including statistical, record keeping, dosimetry, and bias resulting from mis-reporting of cancer deaths
• Uncertainties in transferring radio-epidemiology data to other populations, including cancer rates and survival data in the population of interest for space applications
• Uncertainties in transferring radio-epidemiology data to other radiation types and dose rates of interest to space applications
• Uncertainties in the shape of the dose-response curve at low doses (i.e. linear, linear quadratic) and the possibility of dose thresholds
• Uncertainties associated with extrapolation of experimental data from animals to humans
• Uncertainties associated with individual radiation sensitivity factors, including age, genetic, epigenetic, dietary, and “healthy worker” effects
• Uncertainties in space radiation environmental models, transport codes, geometry models, and dosimetry methods
• Uncertainties associated with predicting SPE occurrence, energy spectrum, and magnitude
• Possible inter-dependence of any of the uncertainties mentioned above

From NASA HRP Evidence Book
Cancer risk projection

Uncertainties in risk projection for terrestrial and space exposures (From Durante and Cucinotta 2008; NASA HRP Evidence Book 2016)
Cancer research focus

- Reducing the uncertainties in risk assessment
- Development of biomedical countermeasures
- Availability of simulated GCR and low dose rate neutron capabilities

GCR is simulated at NSRL with a combination of 33 different particle types and energies

<table>
<thead>
<tr>
<th>Ion</th>
<th>Energy (MeV/n)</th>
<th>Range (cm)</th>
<th>LET (keV/μm)</th>
<th>Dose (mGy)</th>
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</thead>
<tbody>
<tr>
<td>$^1$H</td>
<td>100</td>
<td>0.43</td>
<td>2.59</td>
<td>30.4</td>
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<td>$^3$H</td>
<td>150</td>
<td>0.54</td>
<td>2.29</td>
<td>6.7</td>
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<tr>
<td>$^4$H</td>
<td>250</td>
<td>0.39</td>
<td>2.02</td>
<td>7.4</td>
</tr>
<tr>
<td>$^4$H</td>
<td>1000</td>
<td>0.22</td>
<td>1.79</td>
<td>8.0</td>
</tr>
<tr>
<td>$^4$He</td>
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<td>1.30</td>
<td>1.58</td>
<td>8.7</td>
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<td>1.72</td>
<td>1.39</td>
<td>9.3</td>
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<td>2.26</td>
<td>1.23</td>
<td>10.0</td>
</tr>
<tr>
<td>$^4$He</td>
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<td>2.99</td>
<td>1.09</td>
<td>10.6</td>
</tr>
<tr>
<td>$^5$He</td>
<td>26.9</td>
<td>5.20</td>
<td>0.86</td>
<td>11.2</td>
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<tr>
<td>$^4$H</td>
<td>100.0</td>
<td>7.26</td>
<td>0.73</td>
<td>27.2</td>
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</tbody>
</table>

Low dose rate neutron facility at CSU

Animal Irradiation at Colorado State
Cf-252 Neutrons at 1 mGy/day

2,200 Mice for up to 400 days
Radiation quality effects

Assessing high-LET risks from known low-LET radiation risks through mostly animal studies

- Previously, a single quality factor was used for all cancers.
- Studies have shown that the effectiveness of high-LET radiation can be cancer-type specific.
- Quality factor can now be determined with simulated GCR.

Weil et al. 2009
Dose and dose rate effects

• A number of studies have shown hypersensitivity for high-LET radiation at low doses.

• The non-targeted effects have been suggested as an explanation for the super-linear dose response, which potentially increase the risk from previously determined values.

• Low dose rate neutron studies are underway.


Shuryak et al. Rad. Res. 2017
Age and gender effects

- Cancer rates due to radiation exposure are higher in females not only because of female specific organs.
- The life expectancy today is significantly longer than the Japanese after WWII.
- Published million worker study is inclusive of the gender difference in radiation-induced lung cancers.
- Publications have reported higher radio-sensitivity for older people.

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>NCRP Report No. 98</th>
<th>NCRP Report No. 132</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>1.5 Sv</td>
<td>0.7 Sv</td>
</tr>
<tr>
<td>35</td>
<td>2.5</td>
<td>1.0</td>
</tr>
<tr>
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<tr>
<td>55</td>
<td>4.0</td>
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Rate of individuals with clearly increased radiosensitivity rise with age both in healthy individuals and in cancer patients.

https://doi.org/10.1186/s12877-018-0790-y

BMC Geriatrics
Tumor grade/progression/metastasis

- High-LET radiation may induce tumors of different malignancy and latency.
- Proton radiation has been shown to induce cancer progression.
- Simulated microgravity has been reported to increase tumor growth and metastasis.
- Psychological stress experienced in space can potentially affect cancer risks.
Skin cancer

• A number of cohort studies have reported elevated skin cancers among airline pilots. UV exposures during recreational activities are insufficient to explain the increased skin cancer rate.

• Several astronauts have died of melanoma.

• Animal studies have shown potential high RBE values for skin cancer for high-LET radiation.

Cause of death in astronauts

<table>
<thead>
<tr>
<th>Primary Cause of Death among NASA Astronauts as of 12/31/2019</th>
<th>Flyer</th>
<th>Non-Flyer</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Cancer</td>
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<td>2</td>
<td>21</td>
</tr>
<tr>
<td>AML</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Breast</td>
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</tr>
<tr>
<td>Colon</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lymphoma of the Brain</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Melanoma</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Myelodysplastic Syndrome</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Prostate</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Unknown Cancer (Presumed GI)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CVD/Stroke</td>
<td>10</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Accident</td>
<td>6</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Occupational Accident</td>
<td>12</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Illness/Other</td>
<td>7</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Grand Total</td>
<td>56</td>
<td>14</td>
<td>70</td>
</tr>
</tbody>
</table>

Cancer yield in rat skin exposed to electron radiation or argon ions. (Burns et al. Rad. Res. 1993)
Summary of recent findings

• Several findings, including hypersensitivity at low doses of high-LET radiation and effects of other spaceflight factors on tumor progression, can potentially increase the mean value of the cancer risk.

• The quality factor can be different for different cancer types. GCR simulation provides a unique opportunity to experimentally determine the quality factor for GCR exposure and for validating the risk assessment tools based on model calculations.

• A number of other spaceflight factors, including microgravity and immune dysfunction, can potentially affect cancer initiation, promotion and progression.

• Analysis of astronauts’ cancer incidence and cancer mortality data is underway.
Future direction considerations

Historical and projected female 1, 5 and 10-year survival rates by stages of breast cancer

Baseline mortality projections for female breast cancer patients

Potomac Institute Report 2019
Future directions – Potomac Report

• Advanced technologies in early diagnosis of cancer will increase (decrease) the survival (death) rate. Biomarker development for early detections of cancer should be considered.
  • Molecular profiles, omics

• Advancement in treatment of cancer will increase (decrease) the survival (death) rate. Future technologies including molecular therapeutics and drug delivery should be considered.
  • CRISPR/Cas9
  • Synthetic biology

• However, the absolute number of cancer deaths has increased in recent years due to the aging population, which raises the question of updating the radiation protection principles for space travel.
  • Cancer incidence rate instead of mortality rate?
Future directions

• Continue investigations of radiation risks and development of countermeasures.
  • Humanized animal models
  • Tissue on a chip
  • Space vivarium on Gateway and Lunar surface
• Future risk assessment and countermeasures should be individually based.