Acute Radiation Syndrome CLIFF Peer Review

1. *Strength of evidence presented in CLIFF in modeling the characteristics and mission impact of this medical condition within the spaceflight environment?*

   Score: 2

   Grading Scale:

   4 - Confident

   3 - Somewhat confident

   2 – Neutral

   1 – Somewhat unconfident

   0 – Not confident

2. How confident are you that these data accurately represent the spaceflight environment?	*Tables 1, 2* *Composite Incidence and Level of Confidence*	*Table 3, 4 BC/WC* *Loss of Crew and probability*	*Table 4 - Clinical Phase 1, 2 durations* *Table 5 – CP 2 Loss of Crew*	*Table 4 – RTDC %* *Table 6 – RTDC Loss of Crew*	*Table 4 – Loss of Crew Life %* *Table 7 – Loss of Crew Life, Loss of Crew*	*Table 8 – TI*
Score	*2*	*3*	*2*	*2*	*2*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes the risk of acute radiation syndrome (ARS) during exploration mission outside the earth's protective magnetosphere. The two types of radiation that are encountered during lunar and Martian missions are galactic cosmic radiation (GCR) and solar particle events (SPE's). Of the two, SPE's present the highest risk for multi-organ injury, especially to blood forming organs (BFO's). The symptoms of ARS can range from relatively mild nausea and fatigue to severe diarrhea, central nervous symptoms, and death. Monitoring of SPE's has only been possible for the past 55-60 years, and the only missions during which astronauts left low earth orbit were during Apollo. Thus, there are a number of uncertainties associated with modelling the risks of ARS. There is little data to predict when and how often SPE's will occur. They tend to occur more frequently during periods of high solar activity. Secondly, it is unclear what dose of radiation will cause ARS as estimates vary widely, and there may be some individual variation in sensitivity to radiation among astronauts. It is also unknown how the length of exposure increases the risk of ARS. Does peak dose matter more than average dose over time? The dose of radiation is dependent upon the shielding from the structure of the spacecraft. This is an engineering issue whose resolution depends on the vehicle or habitat design. Finally, for EVA crewmembers who may be

outside the vehicle or habitat during an SPE event, operational considerations such as the amount of warning that can be given to at-risk crewmembers and the amount of time that it takes to return to the airlock are important. The best case is a single exposure dose exposure exceeding the NASA 30 day exposure limit of 250 mGy but less than 500 mGy to blood forming organs. The worst case is defined as a single exposure dose exceeding 500 mGy to blood forming organs.

2. **Incidence.** There have been no documented cases of ARS during manned spaceflight. The only extra-terrestrial missions were during the Apollo program. Analog and terrestrial data does not reflect the radiation environment encountered by astronauts on exploration missions. Therefore, incidence is based on historical SPE occurrences, assumptions about the shielding to be used on future spacecraft, and modelling of the damage caused by such events on blood-forming organs. The incidence was derived by making an assumption that the shielding on future vehicles will be a minimum of 20 g/cm^-2 or greater in order to comply with the 30d NASA limit of 250 mGy, based on the 1989 SPE. It is assumed that all EVA crewmembers will have sufficient warning to return to the safety of the vehicle. A probability of 1 was assigned to reflect that all astronauts onboard would be affected if such an event occurred. Given these assumptions, a fixed incidence of 0.01 events per year (once per 100 years) that would exceed the 250 mGy threshold was derived from historical modelling of SPE. The best case/worst case probabilities are based on the percentage of recorded events that potentially are energetic enough to cause a dose of 500 mGy to BFO's (about 10%), giving a BC/WC split of 90%/10%. The clinical phase durations, return to definitive care (RTDC) and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. Given the shielding that is anticipated and the extraordinarily low probability of an event causing a 500 mGy exposure, the RTDC and Loss of crew life probabilities were considered to be zero. The probability density curve that was derived appears to be a reasonable representation of the data presented.

3. **Clinical phase data**. I am in agreement with the clinical phase 1 duration entered in this CLIFF. This data was compiled by a team of expert clinicians, and I was involved in the discussions leading to the calculation of the clinical phase duration. CP2 was supported by terrestrial evidence.

4. **Task impairment**. The analysis was performed and reviewed by a separate team of expert clinicians. I am aware of the methods that were used but did not directly participate in the discussions.

5. **Dependence on mission phase or duration of mission**. This medical condition is not dependent on mission phase, but the incidence will be affected by solar activity, especially during solar maximums.

6. **Limitations**

- Risk of ARS in flight is dependent on the rate of SPE which is difficult if not impossible to predict at this time. Only historical data can be used. The rate of SPE varies widely over the solar cycle.
- Models that calculate exposed radiation dose while a crew member is on EVA assume that the crew member was on EVA for the entirety of the SPE. Not only are these events often >24 hours in length, operationally a crew member would be immediately evacuated to shielding upon recognition of an SPE. We have assumed that crewmembers on EVA will have sufficient warning to return to the vehicle. Thus, all crewmembers are affected equally.

- There are a number of uncertainties associated with modelling the risks of ARS. It is unclear what dose of radiation will cause ARS as estimates vary widely, and there may be some individual variation in sensitivity to radiation among astronauts. It is also unknown how the length of exposure increases the risk of ARS. Does peak dose matter more than average dose over time?
- The designs for lunar habitats and landers have not been finalized; thus, the density of shielding that will protect a crew member within a spacecraft or habitat cannot be determined. We assumed this to be at least 20g/cm^3 in order to comply with NASA standards for 30-day radiation exposure.
- Most terrestrial literature on high dose radiation is limited to gamma rays which behave differently than the protons and other large particles seen in SPE and is therefore not useful for exploration missions.
- Our best case and worst-case definitions are based on exposure to blood forming organs such as bone marrow. Protons penetrate less deeply into tissue and thus the effective dose of radiation of a crew members skin is likely to be at least an order of magnitude higher than that of the bone marrow. The definition of this condition does not capture skin injury during SPE.
- The assumption is made that no severe symptoms of ARS will occur. This is based on the fact that no recorded SPE has been sufficiently energetic to cause severe symptoms,

Reviewed by:

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