Burn Moderate to Severe, Thermal 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*	*2*	*3*	*2*	*2*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes moderate to severe thermal burns resulting from any source of heat that may be present in the spacecraft, whether a result of a failure in heat-emitting equipment used in normal operations, an experiment, a scald from a liquid, or a fire. Moderate to severe burns are often life-threatening and the morbidity/mortality associated with them is directly correlated to the total body surface area that is affected. Specialized burn units are often required for severe burns. There is a separate CLiFF that addresses mild skin burns. The risk largely depends on the engineering safeguards built into the system to mitigate the risk of exposure as well as crew diligence and operational safety measures. There was a significant fire reported during spaceflight on a Mir mission. One crew member suffered a burn which was primarily superficial but did have blistering consistent with a partial thickness burn. Smaller fires have occurred during other space missions. The best case is considered to be partial thickness burns covering less than 20% TBSA, OR full thickness burns covering less than 5% TBSA that meet the following criteria: i) non-circumferential, ii) does not cross a major joint line, iii) is not at risk for permanent impairment of body part function (e.g., extensive burns to hands, face, perinium, genitals). The worst case is a partial thickness burn involving greater than 20% TBSA, full thickness

burns involving greater than 5% TBSA, or burns that meet any of the following criteria: any circumferential burn, anything crossing a major joint line, or threatening to impair body part function or full-thickness skin burns.

2. **Incidence.** It is difficult to calculate the incidence for this condition since the risk is largely dependent on engineering safeguards which can vary with vehicle design. The best data comes from the ISS probability risk assessment (PRA) fire model which calculates the risk that at least one crew member is in a module when a fire event occurs that requires crew response. While this is a poor surrogate for the risk of burns, it is the most reasonable substitute to use since the spaceflight experience with burns is very limited. It is likely that a crewmember would be able to extinguish a fire without being burned. It is also possible that burns could be caused by sources other than fire. The ISS data was normalized to person-years and then adjusted by the American Burn Association repository data to divide the incidence between mild and moderate-severe cases. An Artemis-specific PRA is under development but is not yet available. It is felt that the risk in the Artemis program will be lower than that of ISS because of fewer pieces of experiment equipment and the development of automatic thermal shutoff designs. The best case/worst case probabilities used data from the American Burn Association repository for burns in 2017 that examined fire-related burns that had less than 20% total body surface area and those that presented with greater than 20%. While this does not exactly match the BC/WC definitions, it should provide a good approximation. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. RTDC probabilities are very high given that many serious burns require treatment in specialized burn units that have treatment modalities not available onboard. Since data is not robust for some of the worst-case parameters, subject matter expertise was used as needed. The cause of death in burns can be due to many complications including infections, hypermetabolic syndrome, respiratory failure, etc. In other conditions, complications are left out of duration calculations; however, in this condition the complications are central to the disease process and thus were included as factors that impact duration and Loss of crew life. 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.

6. **Limitations**

- The best data to calculate incidence comes from the ISS probability risk assessment (PRA) fire model which calculates the risk that at least one crew member is in a module when a fire event occurs that requires crew response. While this is a poor surrogate for the risk of burns, it is the most reasonable substitute to use since the spaceflight experience with burns is very limited. It is likely that a crewmember would be able to extinguish a fire without being burned. It is also possible that burns could be caused by other sources than fire.

- There have been several fires in spaceflight such as during the Mir program; however, extensive engineering risk mitigation has been performed to reduce this risk.
- A PRA has not yet been published for Artemis missions. However, it is anticipated that due to the fewer number of experiments on board the risk of fire will be much less than that on ISS. The risk of fire and risk that a crew member is present are surrogates for skin burn and likely significantly overestimate the true risk of burn.
- The ranges of the burns are not consistent with epidemiological data on burns which is typically limited to cohorts based on burn size.
- Small burns to sensitive areas are likely to have an impact on crew function and quality of life metrics but may not impact Loss of crew life directly. It is difficult to represent these patients with the definitions provided.
- The best case definition includes partial thickness burns to less than 20% TBSA. A small partial thickness burn is equivalent to the worst case definition in ICL 21, Mild Thermal burns CLiFF.
- The cause of death in burns can be due to many complications including infections, hypermetabolic syndrome, respiratory failure, etc. In other conditions, complications are left out of duration calculations; however, in this condition the complications are central to the disease process and thus were included as factors that impact duration and Loss of crew life.
- Loss of crew life in a large severe burn without any treatment including even local wound care is extremely difficult to estimate. It is likely very high given the risk of complication, particularly in the spaceflight environment where there are a large number of physiologic stressors. 100% was chosen as a WC maximum
- RTDC and Loss of crew life is likely to vary based on burn location and thus ranges for each are broad.

Reviewed by:

David C. Hilmers