Trauma – Severe Head 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*	*2*	*3*	*2*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes the risk of severe head trauma during spaceflight. There is no clear delineation between mild-moderate head trauma (which is the subject of a separate CLiFF) and severe head trauma. There are multiple classification systems that have been used to grade head injury, but one that does not require head imaging (which won't be available onboard) uses the Glasgow Coma Scale (GCS). The GCS is relatively quick and straightforward to administer and thus will be a logical criterion to use operationally. This CLiFF utilizes a cutoff of GCS < 9 post-resuscitation to indicate severe head trauma. Rather than categorizing severe head trauma as "Best Case" or "Worst Case", the definition use two classifications, surgical (category 2) or non-surgical (category 1). Both conditions have severe consequences. Of note, seizures are not considered in this CLiFF as they are the subject of a separate CLiFF. However, it is inevitable that there will be overlap since head trauma is a common cause of seizures, and a seizure can lead to head trauma during convulsions. It is felt that during Artemis missions in which the vehicles are of much smaller size than ISS, the risk of severe head trauma in microgravity is extremely small. Thus, the terrestrial trauma evidence that is used to determine incidence will only be applied during surface operations. Ideally, this would only be applicable to non-EVA surface operations since the

helmet of the EMU protects the head from trauma. However, the current version of IMPACT prevents us from segmenting the mission into surface EVA or non-EVA surface operations. For now, incidence data will apply to all surface operations but not to microgravity operations. There have been reports of mild head trauma during spaceflight, but anecdotally there has been no severe head trauma outside of catastrophic vehicle failures like Challenger and Columbia. For purposes of this CLIFF the category 1 scenario is defined as severe non-surgical TBI (initial GCS < 9) including diffuse axonal injury or other persistent vegetative state. The category 2 scenario is defined as severe surgical TBI (GCS < 9) including epidural hematoma, extensive subdural hematoma, swelling causing risk of imminent herniation, or open skull fracture.

2. **Incidence.** There are spaceflight reports of head trauma, but the descriptions are not detailed enough to determine whether they meet the case definitions of severe head trauma. Anecdotally, it is certain that there have been no occurrences of severe head trauma during spaceflight outside of catastrophic vehicle accidents. Terrestrial data was therefore used to calculate the incidence rate. The best source was felt to be a report from the CDC for 2016/2017 that looked at TBI-related hospitalizations by age, gender, and mechanism of injury. A group age-matched to astronauts was chosen, and mechanisms such as assault and motor vehicle accidents that would not occur in space were removed to improve the accuracy of the incidence estimation. The large sample size results in a small variance which may overestimate the confidence that we have as we apply this data to the spaceflight environment. As mentioned in the section above, the risk of head trauma is considered to be extremely low in microgravity as compared to a partial gravity environment, such as on the lunar or Martian surface. Since MPRAT currently only has the capability to segment the missions between EVA and non-EVA operations, this incidence will be applied to all surface operations, both on EVA and inside the habitat. This will likely lead to a slight overestimate as the EVA helmet will provide protection against severe head trauma. The category 1/category 2 split is based on several terrestrial studies. One series looked at patients presenting with severe TBI to a Swedish hospital. The study noted 75% of patients required surgery. However, the study examined patients with GCS of 4-14 rather than using a cutoff of 9. This figure was used as the maximum rate of category 1 to category 2 (25%). Other studies looked at the rates of DAI (10%) and PVD (2.77%). From these studies the range of category 1 was set at 2.77% to 25% and for category 2 of 75% to 97.23%. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence. However, terrestrial studies provide data where ICU-level care is utilized. This level of care will not be available during spaceflight; therefore, “treated” category 1 and 2 Loss of crew life values are probably underestimates. CP2 minimum times assumes that some patients will have expired immediately upon incurring trauma sufficient to cause severe TBI. RTDC was assumed to be 100% by the Clinical Science Team for all cases, whether category 1 or 2. There is almost no data for untreated TBI, so the assumption was that the Loss of crew life probability is 100%.

3. **Clinical phase data**. I am in agreement with the clinical phase durations 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 durations.

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 constrained by mission segment. The incidence is assumed to be zero during microgravity operations and is only applied during surface operations.

6. **Limitations**

- There are spaceflight reports of head trauma, but none of them appear to meet the definition of severe head trauma. Terrestrial data was therefore used to calculate the incidence rate.
- The overall confidence in the mean incidence value is probably overstated because of the large sample size of the CDC study which results in a very narrow probability distribution.
- This medical condition is constrained by mission segment. The incidence is assumed to be zero during microgravity operations and is only applied during surface operations.
- Estimates of the incidence of head trauma is based on terrestrial studies. However, it is felt that during Artemis missions in which the vehicles are of much smaller size than ISS, the risk of significant head trauma in microgravity is extremely small. Thus, the terrestrial trauma evidence will only be applied during surface operations. Ideally, this would only be applied to non-EVA surface operations since the EMU helmet protects the head from blunt trauma. However, the current version of IMPACT prevents us from segmenting the mission into surface EVA or non-EVA surface operations. For now, incidence data will apply to all surface operations but not to microgravity operations.
- The Loss of crew life probabilities for the category 1 and 2 treated cases are probably underestimates because they were based on studies that showed survival of patients receiving ICU-level care. This level of care will not be available onboard exploration spacecraft.
- Seizures are not considered in this CLiFF as they are the subject of a separate CLiFF. However, it is inevitable that there will be overlap since head trauma is a common cause of seizures, and a seizure may lead to head trauma during convulsions.
- The Loss of crew life probability for the treated Category 1 scenario is based on data with a 3-6 month follow-up period. Data from the same reference (Ashwal et al, 1994, 2014) presented much higher mortality rates for 3- and 5-year follow-up (82% and 95%, respectively). Given the DRM of 210 days, the 3-6-month values will be used to approximate Loss of crew life probability. If DRMs of 3 or more years are used in the future, this Loss of crew life probability should be increased accordingly.
- There is a paucity of data regarding untreated severe TBI presenting with a GCS < 9. There is literature available regarding the treatment interventions needed for TBI, however. Based on the treatment modalities mentioned in the literature, the assumption was made that both untreated scenarios would result in Loss of crew life with a 100% probability.

Reviewed by:

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