**Title of the Manuscript**: Protocol-driven prevention of perioperative hypothermia in the pediatric neurosurgical population

**Manuscript Number**: PEDS19-80

***Reviewer 1***

**Comment 1**: The Introduction may be substantially shortened. The authors should describe previous work tying perioperative hypothermia to worse clinical outcomes (eg increased EBL, increased infection rates, increased LOS, etc.).

**Authors’ Response**: Clearer connections made between perioperative hypothermia and worse outcomes; the intro is at least 50% shorter.

**Comment 2**: In addition, the authors should describe their motivation for this study? What was the old process before the study was undertaken? For a QI initiative, there should be baseline data prior to an intervention. 

**Authors’ Response:** See revised introduction / methods:

“At our institution, standard PH prevention for the pediatric neurosurgery service was limited to intermittent use of a radiant warming light (RWL) and the standard placement of a FAW on all patients prior to draping. Though no formal data had been collected about the incidence of PH in our ORs, it was anecdotally obvious that our standard was inadeqate to prevent it. As part of a QI initiative, we wanted to find a set of actions which could effectively prevent PH without imposing an unacceptable ergnomic burden on the OR staff and physicians.

**Methods**

IRB approval was obtained. We designed a non-randomized, controlled, prospective study of 120 pediatric patients at Norton Children’s Hospital. All patients undergoing a neurosurgical procedure between 1 March 2013 and 1 August 2013 were included. In order to reach statistical significance for the patients receiving the new normothermia protocol (NPr), additional patients were added between 1 October 2013 and 1 March 2015. All patients operated by Surgeon 1 received this new NPr (detailed below) and are referred to as the “warming group” (WG). All patients operated by Surgeons 2 and 3 received the institutional standard protocol: many patients received intermittent RWL during preparation, all received a FAW prior to draping. These patients are referred to as the “control group” (CG).”

**Comment 3**: Did the 3 surgeons involved in the study have similar practices? Ie, did one surgeon specialize in craniofacial procedures, spine procedures, etc. over the surgeons? It appears that this is the case if the majority of cases in the control group were craniofacial cases, compared to the experimental group. This adds significant bias to the study.

**Authors’ Response**: In our analysis, it became clear that the window of hypothermic burden occurred early on: while the patient was being prepped for draping. While the surgeons in our group did not subspecialize at the time the data was collected, there were significant variations in case mix. We chose, however, to conduct our analysis within the context of “prep time” – in other words, it isn’t the difference between a VNS case and a synostoses case that was meaningful but instead the fact that for a VNS the prep time is roughly 40 minutes while for a synostoses the prep time averaged over 90 minutes.

**Comment 4**: Did the authors consider a prospective randomized study design to try to ameliorate the bias described above? 

**Authors’ Response**: we did, but felt that the additional complexity would have made this project impossible. Additionally, by analyzing the data with respect to “prep time” we believe that we were able to address the core issue – exposure time -

**Change to Text:** N/A

**Comment 5**: Furthermore, the modalities for measuring temperature in the study via tympanic thermometer and esophageal probe adds variability. 

**Authors’ Response**: We agree that there is variability; however, this was an intentional design of our trial. The most feasible and accurate way to measure temperature in the non-intubated patient is tympanic while the most accurate way to measure temperature overall is esophageal probe (which for obvious reasons cannot be implemented in the pre- and post-operative phases for non-intubated patients). We felt it was most important to preserve intra-phase (i.e. within the preoperative, intraoperative or postoperative) reliability rather mix measurement modalities.

**Change to Text:** N/A

**Comment 6**: Early on, the authors should decide whether their objective is a QI project or a scientific study. Unfortunately, the present submission mixes elements of both. For a QI project, the reason for undertaking this project should be described; baseline data reported; description of an intervention; the method for reaching stakeholder consensus about this intervention; post-intervention results in the form of control charts; analysis of these result and plans for the next iteration of interventions; etc. Ie, the authors should describe the PDSA cycles. On the other hand, a scientific study needs to be much more rigorous as described above. 

**Authors’ Response**

**Change to Text**

***Reviewer 2***

**Comment 1**:  If this was a prospective study, why was it not randomized? What patients received the targeted warming versus those that did not? There would seem to be in the introduction of possible bias here based on preference rather than a true study? Why was it divided by Surgeon? Does this not introduce bias as well? Differences in surgical procedures?

**Authors’ Response**: Similar comments were raised by Reviewer 1 in Comments 2 and 4. Please refer to our answers there.

**Change to Text**: N/A

**Comment 2**: Any difference in outcomes from those that were hypothermic versus those that were normothermic in regards to the parameters concerning such as blood loss, infection, etc.?

**Authors’ Response**: That is certainly an interesting research question which would add further clinical evidence for implementation; however is not a part of our IRB so these variables were not investigated. This investigation was an early phase study to assess whether the protocol was effective in modifying temperature. We are interested investigating variables such as blood loss and infection in the future.

**Change to Text**: N/A

**Comment 3**: What was temperature like in the postoperative period of time? Did the warmed patients devolve to hypothermia?

**Authors’ Response**:

**Change to Text**:

**Comment 4**: What was the extent of the hypothermia encountered by the control group? Did it statistically different from the warmed group?

**Authors’ Response**:

**Change to Text**:

**Comment 5**: The introduction is markedly long and can be shortened significantly. If there are specific issues that they feel strengthen the paper, these should be included in the discussion.

**Authors’ Response**: This comment was also made by Reviewer 1 in Comment 1. Please refer to our answers there.

**Change to Text**: See above.

**Comment 6**: While use the tympanic thermometer when they are ready use a esophageal probe? What is the reliability of the tympanic thermometer? Was there any standardization with core temperature? 

**Authors’ Response**:

**Change to Text**:

**Comment 7**: Were radiant lights used in all ages of patients?

**Authors’ Response**: Yes.

**Change to Text**: N/A

**Comment 8**: For a large pediatric Neurosurgery group, a population study of 120 patients seems like a small number over 2 years. How was it decided to include patients or not into the study? What were the characteristics of the patients who were not included in that two-year period of time? Were patient families consented? Did some refuse?

**Authors’ Response**: All patients scheduled for surgery during this time period were approached for participation in the trial. If the legal guardian refused participation then they were not included.

**Change to Text**: Further description of consent is included in the Methods section. Page 6

**Comment 9**: One of the complications of hypothermia is extended operative time and blood loss. There seem to be a significant decrease in the control group when it came to average operative time?

**Authors’ Response**: This is likely due to a preponderance of tethered cord releases within the control group and represents a study bias that is likely unrelated to the protocol. We discuss this issue within the limitations section.

**Change to Text**: Page 10.

**Comment 10**: How did they define hypothermia? What was the threshold temperature to be considered hypothermic? Was it 36{degree sign}C? Was this threshold chosen prospectively or was this a comparison looking for the highest sensitivity and specificity difference? A 0.23{degree sign}C difference does not seem significant except statistically? Is this difference truly something reportable? 

**Authors’ Response**: We defined hypothermia as per the literature first described by Carl Wunderlich which is still used as the widely accepted standard of practice today. We do feel that this data are still reportable because it shows that our standard practice (CG)

**Change to Text**: N/A

**Comment 11**: I had a difficult time understanding their figures. How did they calculate the mean temperature deficit per patient? Was it time in minutes below threshold? Time in 15 minute increments? This needs to be better defined in the method section as well as depiction in the figures. 

**Authors’ Response**:

**Change to Text**:

**Comment 12**: There was a significant difference in time of operation between the 2 groups. Did they only look at hypothermic burden for one hour in all patients?

**Authors’ Response**:

**Change to Text**:

**Comment 13**: Their formula/calculation of hypothermic burden is very difficult to understand. This needs to be better defined in the method section.

**Authors’ Response**:

**Change to Text**:

**Comment 14**: Because of the poor methodology it is unclear how to view the results. Better defining how this is truly significant needs to be delineated.

**Authors’ Response**:

**Change to Text**:

***Reviewer 3***

**Comment 1**: The introduction is overly long and should focus on scientific question that is being addressed. At the end of the introduction, the authors should state the study question being addressed. 

**Authors’ Response**: The introduction has been significantly shortened. We have added the sentence: “We aimed to test the efficacy of an evidence-based protocol addressing maintenance of normothermia in the pediatric neurosurgical population.” at the end of the introduction.

**Change to Text**: Page 1, 2

**Comment 2**: The manuscript has multiple examples of incomplete sentences and poor grammar. It should be edited for clarity.

**Authors’ Response**: Our apologies. We have edited the manuscript for brevity and proper grammar in the revision.

**Change to Text**: Multiple changes, please refer to track changes.

**Comment 3**: Some of the conclusions drawn, such as the cost and burden on the OR staff, are not supported by the data and should be omitted.

**Authors’ Response**: The sentence: “Only limited resources were required for implementation at a low cost; staff comfort was not significantly affected – though this data was not explicitly collected, only rarely was OR staff behavior affected and complaints were minimal.” has been removed from the conclusion section.

**Change to Text**: Page 10

**Comment 4**: A limitations section should be included in the discussion.

**Authors’ Response**: This has been added at the end of the discussion section.

**Change to Text**: Page 9

***Reviewer 4***

**Comment 1**: The Introduction should be condensed to 3-4 paragraphs. The statement "there are no standard protocols" should be revised to "no published standard protocols" as many children's hospitals surgical teams implemented pan-OR protocols to prevent hypothermia years ago. 

**Authors’ Response**: The introduction has been significantly shortened. The sentence referenced has been changed to read: “Despite well-documented risks, there are currently no published, validated protocols for reducing the burden of PH in the pediatric neurosurgical population.”

**Change to Text**: Page 1, paragraph 1

**Comment 2**: What was the rational for implementing the protocol by surgeon rather than randomization? Certain types of cases and age groups are more prone to hypothermia, and thus randomizing across 3 surgeons would decrease confounding factors and increase generalizability to other institutions. 

**Authors’ Response**: Similar comments were raised by Reviewer 1 in Comments 2 and 4. Please refer to our answers there.

**Change to Text**: See above.

**Comment 3**: Please provide the range of ages and other factors. 

**Authors’ Response**: We have included demographic information in Table 1. Perhaps, we are not following what the reviewer is commenting on here. Please clarify if so.

**Change to Text**: N/A

**Comment 4**: The "hypothermic burden" should be described in the Methods, and the Results in the Results.

**Authors’ Response**: Agree. We have moved any statistical definitions originally placed in the results section to the methods section.

**Change to Text**: Page 7

**Comment 5**: It would greatly increase the impact of this study to acquire a subsequent randomized cohort across all surgeons to remove the surgeon-specific characteristics, and to show the protocol works without the pre-operative warming. It would also be important to look at outcomes aside from temperature such as time in PACU, infection rate, or other metrics used in the hypothermia literature. Other outcomes would change the focus from "number-chasing", a frequent criticism of such protocols, to one that demonstrates improved patient care. This would also clarify if the increased OR time is due to the warming protocol or other surgeon/case-specific differences.

**Authors’ Response**: Agreed

**Change to Text**: Please see the limitations section. Page 10,

***Editor-in-Chief***

**Comment 1**: Your manuscript has been carefully reviewed, and as you can see, the Reviewers' comments are somewhat mixed. I would, however, entertain a revision if you can answer their many helpful suggestions. Please note that major revisions will be required, and even with those, I cannot fully guarantee acceptance in the journal. In addition, your revised manuscript may undergo re-review. 

**Authors’ Response**: Thank you for the editors’ feedback. We appreciate the opportunity to revise our manuscript.

**Change to Text**: N/A