Author’s response to reviews

Title: False elevation in Entropy but not in PSI during general anesthesia: A case report

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Author’s response to reviews:

Authors’ response to reviewers’ comments

Reviewer reports:
Stefano Romagnoli (Reviewer 1): Thank you for the opportunity to review the paper by Young Sung Kim and co-workers. I have read the manuscript with great interest. Please find below my comments and suggestions:

Answer: Thank you very much for your kind review and recommendations. The edits that were made based on your recommendations are written in blue in the main manuscript.

Abstract:
- Despite adequate anesthesia, entropy made the two kinds of wrong decisions. The first was due to the effect of EMG and the second was misleading due to the hammer during surgery.

- How can the author state that anesthesia level was "adequate"? How can the author state that the hammer caused SE abnormal increase? The author are probably right but I suggest them blunting the statement.

Answer: The sentence was revised based on your recommendations.
“Despite the absence of other abnormal events, the entropy data led to two types of incorrect decisions. The first was owing to the effect of the EMG and the second was misleading during the surgeon’s hammering.”

- Hemodynamic instability should be included among the side effects of too deep anesthesia level.

Answer: The sentence was revised based on your recommendations.

“deep anesthesia may give rise to not only cardiovascular and respiratory function impairment, but also hemodynamic instability, an increased risk of delayed emergence, post-operative nausea and vomiting, and other post-operative complications”

- "named Root in Korea" … please delete "in Korea"

Answer: I deleted that phrase in the sentence. (page2 line23)

- "Root is a complex monitoring" .. please replace "complex" with "multi-parametric"

Answer: The sentence was revised based on your recommendation.

Root is a multi-parametric monitoring and connectivity platform

- Please delete the following "in their 2016's official brochure (SedLine ver 2.1 vs 2.0)."

Answer: I deleted that phrase in the sentence. (page 3 line 7)

- Replace the term "old" with "previous".

Answer: I replaced those terms based on your recommendation.

(page 3 line 5, page 3 line 8)

- I would like to suggest the authors to replace the term "FALSE" with "UNUSUAL OR ABNORMAL". You could use "FALSE" just in the discussion.
Answer: I replaced those terms based on your recommendation.

(Title, page2 line 18, page 5 line 4, page 6 line 19, Legends for figure 2,3)

- Provide information about: informed consent to publish the case and Ethical Committee authorization.

Answer: The contents have been revised with references to case reports recently published in BMC Anesthesiology.

(page 10 line 1)

“Ethics approval and consent to participate

Written informed consent was obtained from the patient for the publication of this case report. The consent form will be provided upon request.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report. The consent form will be provided upon request.”

- "EEG monitoring techniques have markedly evolved since 1996.". A REF is necessary to support the statement.

Answer: I provided its reference and revised it into a detailed sentence.

(page6 line2) EEG monitoring techniques have markedly evolved since the introduction of BIS monitoring in 1996 [16]

- One MAJOR aspect that should be considered and included in the discussion is the following:

  o Whether the operators learn to "read" the EEG trace, similarly as they commonly do with EKG trace, the probability to be deviated by the NUMBER (pEEG) is less likelihood.

Answer: I think it is difficult to come to a conclusion based on what matters more. I fully agree with your suggestion. I added the contents to the discussion. I think that the meaning of the answer may seem ambiguous, but I would like to ask you to understand and accept it.
Nevertheless, this has several advantages. To the best of our knowledge, there are no reports of artifacts that occur only one side while assessing two monitors at the same time. Moreover, it is uncommon for two types of artifacts to be observed during a short period of time. The relatively low frequency of constant hammering in our second situation is differentiated to other reports of EEG interferences with surgical devices. Although the probability to be deviated by the EEG score is less likely, the wrong anesthetic depth may give rise to critical complications. Therefore, we think the impact of our findings is not weak.”

- Finally, English should be improved. If the authors are to resubmit this manuscript, it should be reviewed by someone who is well versed in the English language.

Answer: I apologize if the English was not fluent, making the paper difficult to comprehend.

Prior to submission, the original manuscript had already undergone an English language editing process (Editage; www.editage.co.kr, www.cactusglobal.com). This revision will undergo the same process prior to resubmission

Francesco Barbani (Reviewer 2): Thank you for the chance to review such an interesting contribution from Young Sung Kim and co-worker. The manuscript gives the opportunity to focus on EEG monitoring and its potential pitfalls during every day clinical scenarios; I read it with great interest and curiosity. Despite these monitors give us the opportunity to deliver to each patient exactly the best anesthesia depth, in order to prevent adverse events from under or over administration, the case here reported underline the perception that EEG monitoring systems should be used being aware of possible artifacts of signal sampling, being able as anesthesia providers, to correctly detect, avoid and interpret them.

However, please find below my comments and questions:

Thank you very much for your kind review and recommendations. The edits that were made based on your recommendations are written in red in the main manuscript.

Major Comments:

Section "Background":

Row n. 49-50 "We report the FALSE elevation on Entropy of…”
Since there is not a Gold Standard EEG monitoring system I would suggest to blunt the term "false".

Answer: I changed the term from “false” to “unusual.”

(page 3 line 12) We report unusual elevations in Entropy using the Datex-Ohmeda monitor, but not in the PSI derived from SedLine data, which is included in the data from the Masimo Root monitor used during general anesthesia.

Section "Case presentation":

Row 52-54 "The patient did not complain of recall in the postoperative period"

This is an interesting topic that you should further explain or investigate: did you explicitly investigate the occurrence of recall? What kind of method or interview did you choose to do that? What was the result from the "Brice Interview" or similar investigations coming from literature? (Brice DD, Hetherington RR, Utting JE. A simple study of awareness and dreaming during anaesthesia. Br J Anaesth 1970; 42: 535-42).

Given that awareness during surgery and recall are some of the main reasons to use EEG monitoring, but not the only, I would suggest that before than sentencing "false elevation of Entropy" this topic should be assessed in depth and not briefly explained in a few words sentence.

Answer: I fully agree with your opinion. In our center, when awareness or recall is suspected, we ask the patient several questions similar to those from the Brice interview - the last thing they recall happening before falling asleep, the first thing they recall happening after awakening, the dream content while asleep, and any feelings of discomfort.

(page 5 line 17) “There were no specific events that occurred during the remaining intraoperative period. The patient did not complain of recall in the postoperative period. Upon discharge from the PACU, the last memories the patient had prior to sleep were the events of the surgical time-out just after entering the operating room. The first memory the patient had after awakening was the instruction from the medical staff to open her eyes in the recovery room. The patient did not dream during surgery. Mild surgical pain and dry mouth were the only discomforts the patient complained of in the recovery room.”

Figures 2 and 3

In both of these pictures you properly underline and show to the reader the quality of EEG signals sampled with the Masimo's device but, at the same time, there is no way to assess quality
sampling from Datex's monitoring. Since you are reporting a potentially false elevation of a computed parameter (State Entropy and Response Entropy vs SedLine) it is fundamental to assess quality of signal sampling and graphic wave representation shown on the monitoring screen.

What I want to underline is: if I use to double check cardiac frequency on EKG signal quality, the same I would do in the case of anesthesia depth (RE/SE or BIS…) and EEG signal and waves.

Answer: I agree with your opinion. However, at that time, I did not think to save those data. I tried to record data as much as possible, but it is a pity that the raw EEG data is missing. I added these limitations to the discussion.

(page 7 line 20) “There are some limitations in our case report. First, as shown in Figure 1, the position of the Entropy sensor was higher than that of the SedLine sensor on the forehead. Prior to attaching the SedLine sensor, the Entropy sensor was properly placed. However, in order to attach the SedLine sensor in its place, we had to shift the Entropy sensor up. Although the unusual elevation of entropy accompanied by an EMG elevation was observed even before the Entropy sensor moved, their different positions are associated with the limitation in an exact comparison between the two EEG monitors. Second, we only provided the trend and values from Entropy and not the raw EEG data from Entropy. To assess the quality of the EEG signal, we should have checked the raw EEG data from the Datex Ohmeda monitor, in addition to the Masimo monitor”

Minor Comment:

Figure 1

You show the position of EEG electrodes on patient's forehead; well, their positions are slightly different and maybe they could simultaneously assess different brain areas? Moreover, why did you set Entropy's electrodes so high on forehead, almost on patient's hair? No pictures of signal's sampling are shown, did you check EEG sampling quality before starting the procedure? Masimo's electrodes, on the contrary, seems to be very well positioned and probably on the best situation to sample data.

Answer: You are correct. The Entropy sensor had been properly placed until the placement of the SedLine sensor. When attaching the SedLine sensor, I had already suspected the Entropy score was strange, so I replaced the entropy sensor with a SedLine sensor. (page 7 line 20)