




## pBIC in analgesia management: sensitivity vs. specificity

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### Introduction

We read with great interest the article published by Uno et al. that suggested the use of electroencephalographic bicoherence (pBIC) as a better indicator of intraoperative analgesia than standard hemodynamic monitoring [1]. Despite the intriguing data, there are concerns in their study design and data presentation that warrant further discussion.

First, the high sensitivity and very low specificity of pBIC, may limit its practical application as a reliable indicator for analgesia monitoring. The peak heights of pBIC are affected by various factors including drugs, noxious stimuli, and hemodynamic changes [2, 3]. Synthetic opioids like fentanyl have shown variable effects on pBIC based on age of the patient and type of surgery [2, 4]. Surgery type can affect delta arousal responses and pBIC-low changes and is more pronounced in surgical procedures involving the body cavity compared to procedures involving the body surface [2]. In addition, EEG alpha power, which corresponds with pBIC-high changes, can vary significantly based on factors such as age, gender, and type of surgery [2]. In fact, a high percentage of female participants (93%) primarily in gynecological procedures (77.8%) limits the generalizability of the study. The low specificity of pBIC is further evident by the fact that 47 (32.4%) instances of fentanyl administration did not correlate with the pBIC percentage drop and were excluded from the data analysis [1]. The dynamic nature of the pain,

generated by distributed network of stimuli, rather than an isolated pain cortex [5], poses a challenge in the clinical application of the bicoherence as a reliable indicator of analgesia during surgery.

Second, the study does not provide details about the amount of fentanyl used by the patients. The fentanyl doses listed in the study abstract and anesthetic protocol are not only contradictory but against the standard clinical practices. The abstract states that 5 µg/kg of fentanyl was administered prior to the surgical incision, while the anesthetic protocol states that 2 g/kg was given before the start of the surgery with additional unknown number of 1 g/kg boluses to maintain the height of the pBIC [1]. Similarly, the intraoperative minimum dose of 50 g fentanyl seems to be a typographical or formatting error, creating confusion about the fentanyl dose used in the study and needs further clarification. Regardless of the dosing discrepancies, the fentanyl dose used in the study is significantly higher compared to standard clinical practices [6]. In addition, there is published evidence that higher fentanyl doses reduce the minimum alveolar concentration requirements for inhalation anesthetics like sevoflurane [7]. Failure to adjust sevoflurane dose based on the amount of fentanyl given to the patients would have resulted in deeply anesthetized patient, failing to hemodynamically and physically respond to noxious surgical stimuli.

Finally, the study does not include a control group to establish the superiority of pBIC for monitoring adequate analgesia and/or total opioid consumption. The authors used changes in hemodynamic parameters as a comparison to establish the superior efficacy of pBIC. However, the study does not discuss in detail the protocol used for accurately measuring the hemodynamic changes. The heart rate and systolic blood pressure were recorded 5 min before and after fentanyl administration for both pBIC high and low [1]. By default, operating room monitors are programmed to repeat blood pressures every 5–15 min. It is not clear if the

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study actively obtained the hemodynamic parameters corresponding to the timing of fentanyl dosing. There is a strong possibility that lack of difference in hemodynamic changes result from non-corresponding measurements collected from anesthesia record. Given that hemodynamic responses can be influenced by many factors other than analgesic adequacy, a robust and strict protocol for hemodynamic monitoring is warranted to effectively use it for comparison against pBIC.

In conclusion, we congratulate the authors for publishing an interesting paper. However, the present data suggest that pBIC may have limitations in terms of specificity and general applicability across diverse patient populations and surgical procedures. Future studies with more rigorous designs are necessary to establish whether pBIC can reliably monitor analgesia during surgery and improve upon current standard practices.

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## Declarations

**Conflict of interest** None.

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