

## ABSTRACT

### INTRODUCTION

The bispectral index (BIS) monitoring system is an FDA-approved device to assess the depth of anesthesia. It has been demonstrated that patients who were not sedated, unexpectedly showed a large decrease in their BIS values following paralytic administration. These results suggest that BIS monitors integrate electromyography (EMG) data into their proprietary algorithm.

### OBJECTIVE

The study objective was to determine if the timing of BIS monitoring initiation relative to the paralytic administration affected the BIS values.

### METHODS

IRB approval was obtained for this study, which consisted of nonrandomized convenience sampling. A total of 22 patients participated. The study required two BIS monitors in a bifrontal montage. The first BIS monitor was initiated pre-induction, before muscle relaxant administration, while the second BIS monitor was initiated 5-7 minutes after muscle relaxant administration.

### RESULTS

A Bland-Altman plot showed an average difference between BIS values of -0.32, indicating minimal bias between the two sensors. In a linear mixed model, the mean BIS value and EMG value from the second monitor did not significantly differ from that of the first monitor (BIS: estimated difference 0.32, 95% CI -0.10 to 0.75,  $p=0.142$ ; EMG: estimated difference -0.08, 95% CI -0.32 to 0.15,  $p=0.49$ ).

### CONCLUSIONS

The study suggests no statistical difference related to the timing of initiating BIS monitoring and rocuronium administration. Therefore, BIS monitoring can be initiated before or after muscle relaxant administration.

## BACKGROUND

- The BIS monitoring system is a key technology used to monitor the depth of anesthesia by identifying changes in electrophysiological brain activity.<sup>1</sup>
- Monitoring the depth of anesthesia is critical for any procedure. The incidence of awareness during general anesthesia is around 1 to 2 cases per 1,000 patients (approximately 0.1-0.2%). This rate increases in obstetric cases to 0.4%, and in cardiac cases, it ranges from 1.1% to 1.5%.<sup>2,3,4,5</sup>
- Using a neuromuscular blocking agent (NMBA) during anesthesia leads to a remarkable 16-fold increase in reported instances of awareness compared to cases where NMBAs are not used.<sup>6</sup>
- Studies have suggested that BIS monitors may not be useful in paralyzed patients. In these cases, patients who were paralyzed and not sedated showed a significant decrease in their BIS values after the administration of NMBAs.<sup>7-9</sup>
- The BIS monitor uses a proprietary algorithm to quantify changes in the electroencephalography (EEG) information during anesthesia, outputting a number (0-100) corresponding with a patient's level of consciousness.<sup>1</sup>

## METHODS

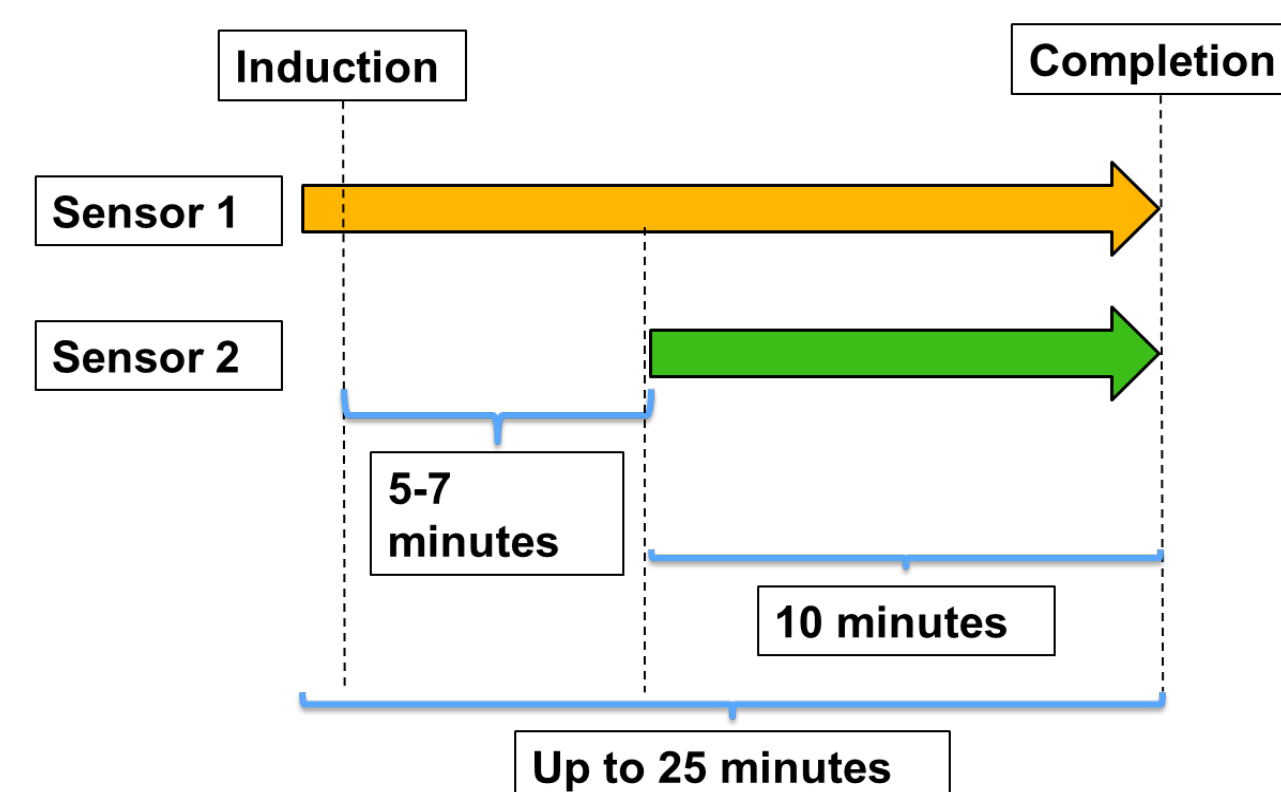
- Prospective, nonrandomized, observational study with convenience sampling in patients undergoing elective cardiac surgery with general anesthesia.
- N = 15-30. The sample size was determined, assuming that a difference of five units or larger between monitors would be considered clinically relevant when monitors are placed before versus after NMBA administration.
- Inclusion criteria: adult patients undergoing elective cardiac surgery with rocuronium administration for muscle relaxation.
- Exclusion criteria: patient refusal, patients under 18 years of age, patients who received ketamine during the study timeframe, emergency procedures, patients with known or suspected carotid or cerebrovascular disease, patients with prior stroke, and skin conditions or anatomy preventing proper sensor placement.
- Values recorded: BIS value, Signal Quality Index (SQI), EMG, EEG Suppression Ratio (SR), and EEG asymmetry. These values were manually transcribed from each monitor.
- Data was analyzed using a linear mixed model in the BlueSky statistics application, considering the nesting of repeated measurements within patients. The dependent variable was the BIS value, and the explanatory variable, monitor, was included as a fixed effect. Time (in seconds) was included as a covariate. A two-tailed  $p<0.05$  was considered statistically significant. Furthermore, the methods of Bland and Altman were utilized to analyze the relationship between each "timed pair" for the 20 patients who completed the study.

## EQUIPMENT



The study utilized two BIS Quatro sensors in a bifrontal montage, two BIS LoC2 modules, two BIS II modules.

## STUDY PROTOCOL



Study protocol: The first BIS monitor was initiated pre-induction, before the NMBA was administered, and BIS readings were collected every 15 seconds during the 25-minute study. The second BIS monitor was started 5 to 7 minutes after administering the NMBA. Thereafter, BIS readings from both monitors were collected every 15 seconds for 10 minutes. The total duration of the study did not exceed 25 minutes.

## BIS SENSORS PLACEMENT

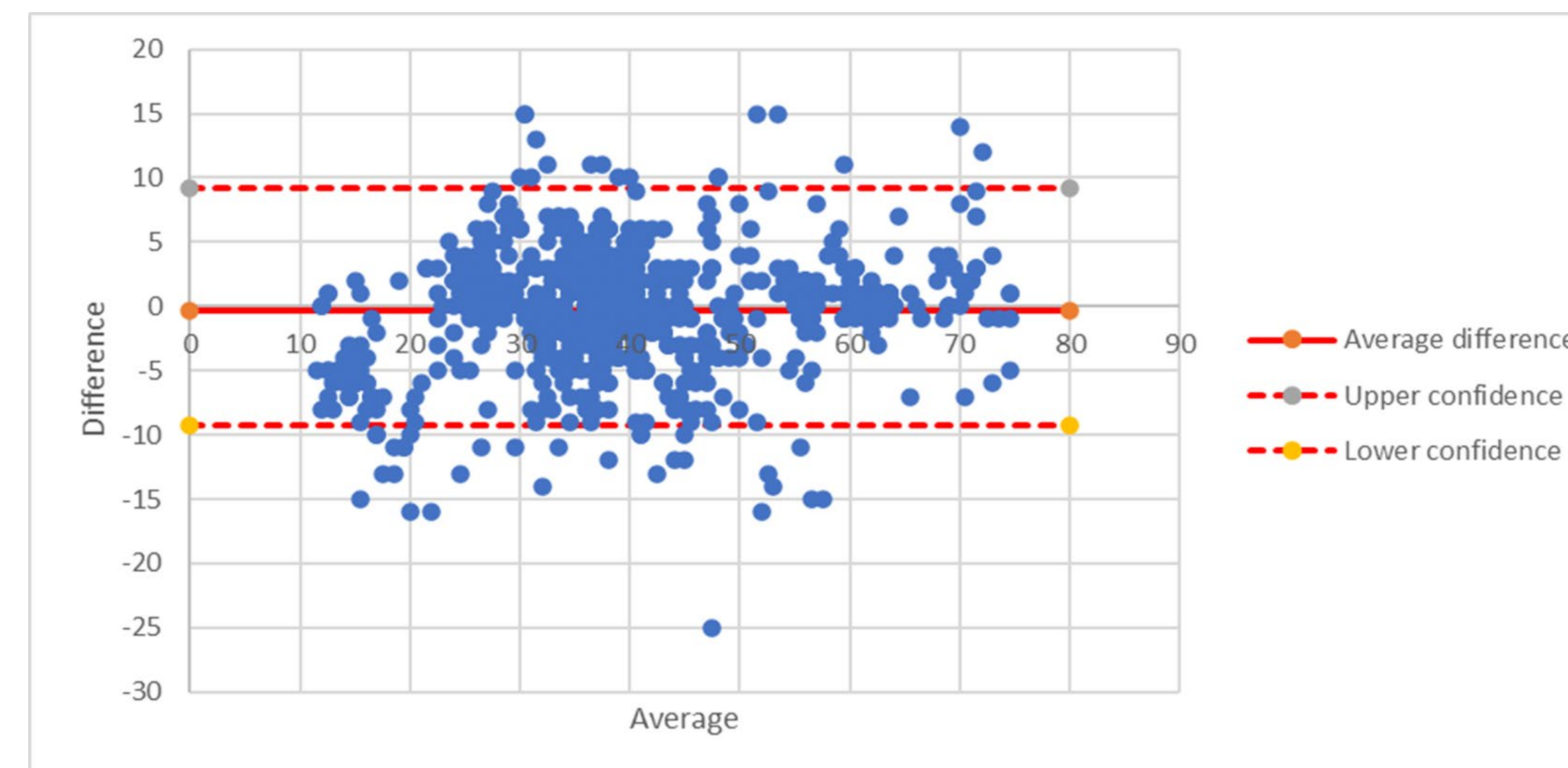


Bifrontal montage of BIS sensors.

## RESULTS

- A total of 22 patients participated in the study.
- Two subjects were excluded due to using a different paralytic and a sensor failure.
- The linear mixed model, the mean BIS value and EMG value from the second monitor did not significantly differ from the first monitor (for BIS: estimated difference 0.32, 95% CI -0.10 to 0.75,  $p=0.142$ ; for EMG: estimated difference -0.08, 95% CI -0.32 to 0.15,  $p=0.49$ ).
- Results from the Bland-Altman plot (known as the difference plot) showed an average difference between BIS values of -0.32, indicating minimal bias between the two sensors. The standard deviation of the values was 4.70, with upper and lower limits (95% confidence intervals) of 8.90 and -9.54, respectively. The SQI value remained high throughout the study period, implying that the corresponding BIS values are reliable.

## BLAND-ALTMAN PLOT



A Bland-Altman plot of the difference in BIS values against the mean of the two measurements (pre-induction BIS value from the first monitor and post-induction BIS value from the second monitor). The horizontal solid red line is the average measurement difference between the two BIS values; the checkered line is the 95% confidence interval.

## DISCUSSION

- Although the BIS system is commonly used to monitor the depth of sedation and anesthesia, several studies have shown that EMG activity can falsely increase the BIS value. Furthermore, the BIS value decreases following the administration of both depolarizing and nondepolarizing NMBAs.<sup>1,14,15</sup>
- The positioning of the BIS sensor on the forehead exposes it to potential contamination or interference from EMG of the frontalis muscle in the BIS calculation. There is an overlap between the frequency bands of EEG and EMG signals. This could pose a problem if the BIS algorithm misinterprets the suppression of EMG activity following the administration of a neuromuscular blocking drug as a sign of deeper anesthesia.<sup>13,14,16</sup>
- Our study showed no significant difference in BIS values before and after NMBA administration. Initiation of BIS monitoring after paralysis, which eliminated exposure to initial EMG activity, did not lead to a different dataset and/or a more precise evaluation of patient sedation depth.

## LIMITATIONS

- This study's limitations include convenience sampling, which may introduce bias to the results. Additionally, the data from the two BIS monitor recordings were manually entered into a digital spreadsheet, risking recording errors. A possible limitation is also using diverse induction agents, but the study reflects common practical settings.

## CONCLUSIONS

- The timing of initiating BIS monitoring does not influence the BIS value in relation to administration of muscle relaxant.
- Acquiring a "baseline" BIS value is not indicated.

## ABSTRACT & REFERENCES

