




# Supralabial Site: An Alternative Site for Bispectral Index Monitoring: A Cross-sectional Study

Jitendra K. Dubey<sup>1</sup> Nitesh Goel<sup>1</sup>  Rajiv Chawla<sup>1</sup> Manish Gupta<sup>1</sup> Manoj Bhardwaj<sup>1</sup>

<sup>1</sup>Department of Anaesthesiology and Critical Care, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India

Address for correspondence Jitendra K. Dubey, MD, Department of Anaesthesiology and Critical Care, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi 110085, India (e-mail: jeetdoc11@gmail.com).

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## Abstract

**Background** Bi-spectral index (BIS) has been traditionally used to monitor the depth of anesthesia, with the forehead being the usual site for electrode placement. When the manufacturer-recommended site is itself an operative field or the placement interferes with the surgery, the search for an alternative position of electrode placement is warranted. In our endeavor to do so, we conducted this study to compare BIS scores derived from frontal and supralabial electrode placement.

**Methods** A cross-sectional study was conducted on a group of 50 patients using two BIS Quatro sensors attached to the frontal and supralabial regions of each patient and connected to two different sets of monitors. BIS values, electromyography (EMG) values, and signal quality index (SQI) were noted from both sites every 15 min during the maintenance phase of anesthesia. Collected data were analyzed using the Bland–Altman analysis.

**Results** Data analysis of BIS values showed negative bias at most time points with a minimum negative bias of 0.2 with a limit of agreement of  $-3.67/3.27$  and a maximum negative bias of 1.14 with a limit of agreement of  $-7.61/5.33$ . The overall 95% limit of agreement for pooled BIS data ranged from  $-6.63$  to  $6.1$ .

**Conclusion** BIS sensor placement at the supralabial site can be used as an alternative to the frontal placement in scenarios where the frontal position is the surgical site or is inaccessible during the maintenance of general anesthesia as in neurosurgery with particular emphasis on skin preparation and proper positioning of BIS electrodes to improve the signal quality.

## Keywords

- ▶ supralabial
- ▶ bispectral index
- ▶ intraoperative awareness

## Introduction

Intraoperative awareness is the explicit recall of intraoperative events under general anesthesia when the adequate depth of hypnosis is lacking.<sup>1</sup> The inability to prevent awareness may lead to psychosocial and medicolegal implications. Consequently, it becomes the moral and legal obligation of an anesthesiologist to prevent intraoperative awareness. Postoperatively, these

patients may show sleep disturbances, nightmares, and post-traumatic stress disorder (PTSD).<sup>2,3</sup> Intraoperative awareness can also have far-reaching medicolegal implications. Analysis of an ASA-closed claim project showed that 2% of all claims were attributed to intraoperative awareness.<sup>4</sup> The risk of intraoperative awareness may be minimized by monitoring brain function or maintaining an adequate minimum alveolar concentration of 0.7 or more.<sup>5</sup>

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Numerous devices such as entropy, BIS, narcotrend, and patient state analyzer, have been used to maintain an adequate depth of anesthesia, out of which BIS is one of the most frequently used methods.<sup>6</sup>

BIS is particularly useful in anesthetic titration during neurosurgery as it looks at the very organ being operated upon.<sup>7</sup> BIS being topographically dependent<sup>8</sup> and the difficulty in placement of electrode strip at the manufacturer-recommended site while conducting neurosurgical procedures (when the forehead and the scalp are either the operative site or hidden under the drapes) make for a compelling reason to compare BIS values from different sites and provide an alternate site for BIS electrode placement.

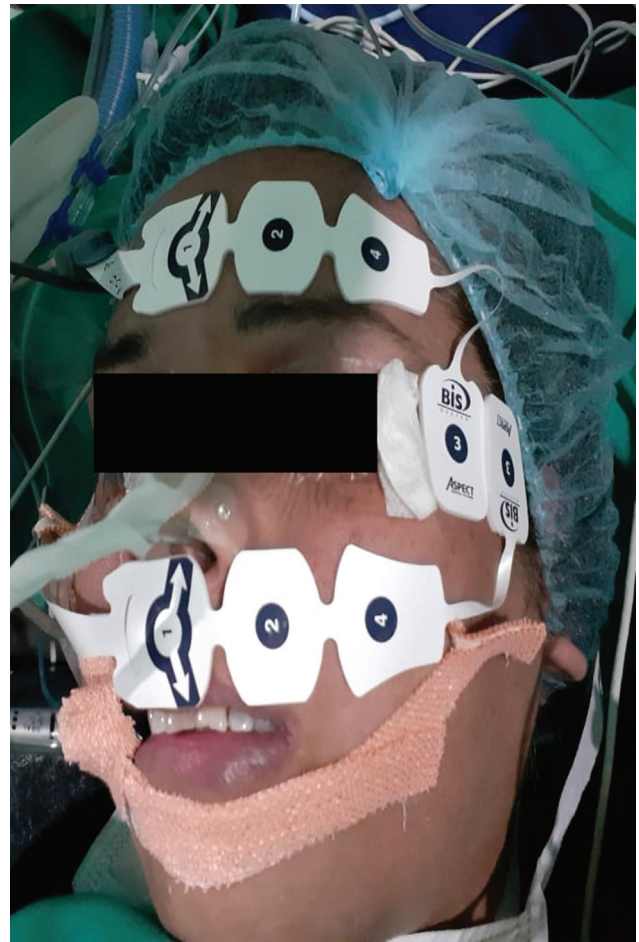
Mandibular, retroauricular, occipital, and nasal sites have been explored as alternatives for BIS placement in previous studies and have shown promising results. Interference with Mayfield pins placement and neuro-navigation remains a limitation of previously studied alternative sites.

This study was planned to evaluate the agreement of intraoperative bispectral index readings from the area of the forehead and supralabial position so that BIS can be effectively utilized in neurosurgical patients.

## Materials and Methods

After approval from the Institutional Review Board, the study was performed on patients undergoing robotic abdominal surgery under general anesthesia in a tertiary care hospital over a period of 1 year from March 2019 to March 2020. Based on previous studies, the sample size was taken as 50. The sample size was calculated based on the study by Lee et al<sup>9</sup> to achieve an  $\alpha$  of 0.05 and a power of 80%. This study was registered with clinicaltrials.gov with ID NCT04252911. Written and informed consent was taken from all patients. Participants were in the age group of 18 to 65 years with no sex bias and had an American Society of Anaesthesiologists (ASA) grading of I-III. Cases having facial deformity, presence of mustache, previous history of neurosurgery, neurological disorders, and patients on psychiatric medications were excluded from the study. Standard ASA monitoring devices were applied to all patients inside the operating room. After securing intravenous access, anesthesia was induced with fentanyl 2  $\mu$ g/kg, propofol 2 mg/kg followed by muscle paralysis with atracurium 0.8 mg/kg. Neuromuscular monitoring was used to guide the timing of intubation.

All patients received an oxygen–sevoflurane gas mixture along with propofol infusion for maintenance of anesthesia. Anesthetic depth was maintained with sevoflurane, and propofol was titrated to maintain the BIS values between 40 and 60 using values from the forehead BIS sensors (BIS™ Quatro sensors, Aspect Medical Systems, Newton, MA, USA). Atracurium was used to maintain muscle paralysis throughout the surgery, followed by reversal with neostigmine 2.5 mg and glycopyrrolate 0.5 mg with neuromuscular monitoring at the end of surgery. Extubation was done once the BIS value was more than 90. Analgesia was maintained



**Fig. 1** Illustration of BIS sensor placement at forehead and supralabial sites. Supralabial electrode 1 at philtrum, electrode 4 on the maxilla, and electrode 3 on the temporal area near electrode 3 of the standard strip. BIS, bispectral index.

additionally using morphine up to 0.1 mg/kg and paracetamol 1 gm intravenously in all patients.

In all enrolled patients, two BIS strips were used—one on the standard site (forehead) and the other on the study site (supralabial). The supralabial site is just above the upper lip (→ Fig. 1) with electrode 1 at the philtrum, electrode 4 on the maxilla, and electrode 3 on the temporal area near electrode 3 of the standard strip. Each sensor was attached to its own BIS monitor. BIS, signal quality index (SQI), and electromyography (EMG) values were noted from both sites in each patient for comparison. Due to interference and dislodgement of the supralabial BIS strip during bag-mask ventilation, the first value for comparison from both strips was recorded post-intubation. Thereafter, the next recordings were done every 15 min until extubation. Only BIS values with SQI of more than 90 were included in the final statistics.

Bland–Altman analysis was used to assess the agreement between BIS, SQI, and EMG values obtained from frontal and supralabial electrodes at different time points during the surgery. To be clinically relevant, a priori of an acceptable limit of agreement was set as  $-5$  to  $+5$  for BIS. Demographic data were reported as mean  $\pm$  standard deviation (SD).

**Table 1** Demographic data

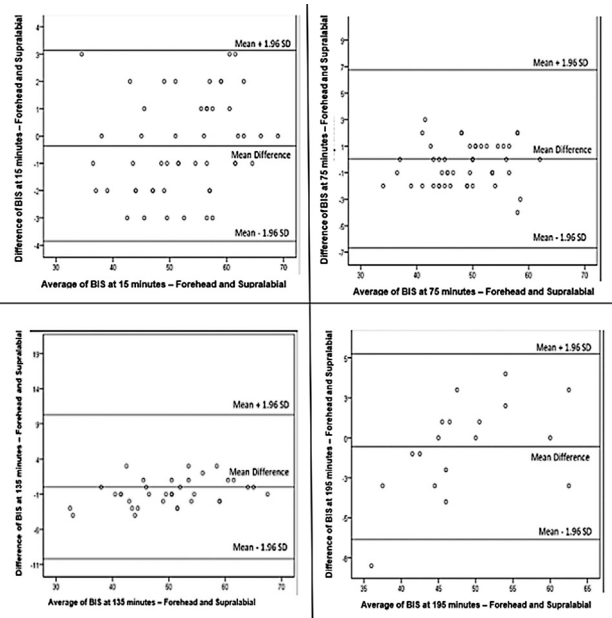
Age (y)	61.38 ± 11.52
Male	42%
Female	58%
Height (m)	1.60 ± 0.09
Weight (kg)	69.06 ± 13.78
BMI (kg/m <sup>2</sup> )	27.07 ± 5.12

Abbreviation: N = 50. Data are presented as mean ± SD for age, height, weight, and BMI, and as a percentage for gender. BMI, body mass index.

## Results

Every patient acted as a test and control for themselves in the study. The mean age was 61 years, with 58% of patients enrolled being female. ►Table 1 shows the demographic profile of patients.

Data analysis of BIS values (►Table 2, ►Fig. 2) showed negative bias at most time points with a minimum negative bias of 0.2 with a limit of agreement of -3.67/3.27 and a maximum negative bias of 1.14 with a limit of agreement of -7.61/5.33. Overall, limits of agreement for BIS ranged from -6.63/6.1 (►Table 3, ►Fig. 3). Analysis of SQI (►Table 4, ►Fig. 4) values showed negative bias at most time points with a minimum negative bias of 0.049 with a limit of agreement of -10.44/10.34 and a maximum negative bias of 2.05 with a limit of agreement of -11.36/7.26. Analysis of EMG values (►Table 5, ►Fig. 5) showed positive



**Fig. 2** Bland-Altman scatter plot comparing BIS obtained from standard frontal and supralabial positions at 15, 75, 135, and 195 minutes. The 95% limit of agreement is ± 1.96 SD. SD, standard deviation.

bias at most time points with a minimum positive bias of 0.024 with a limit of agreement of -3.14/3.18 and a maximum positive bias of 1.1 with a limit of agreement of -5.33/7.53. ►Fig. 2 shows the Bland-Altman plot for limits of agreement for BIS at four different time points. ►Figure 3

**Table 2** Limits of agreement for BIS values at different time points

Pair	T (BIS score)	N	Mean difference	95% limits of agreement	
				Mean + 1.96 SD	Mean - 1.96 SD
1	Post intubation	50	-0.2	3.275	-3.675
2	15 min	50	-0.36	3.133	-3.853
3	30 min	50	-0.38	3.001	-3.761
4	45 min	50	0.08	5.149	-4.989
5	60 min	50	-1.14	5.33	-7.61
6	75 min	49	0.041	6.746	-6.664
7	90 min	48	-0.854	5.371	-7.079
8	105 min	47	-0.596	4.743	-5.935
9	120 min	42	0.122	10.402	-10.158
10	135 min	37	0.054	10.301	-10.193
11	150 min	33	0.848	11.438	-9.742
12	165 min	25	-0.2	3.001	-3.401
13	180 min	20	-0.7	2.959	-4.359
14	195 min	18	-0.556	5.236	-6.348
15	210 min	13	-0.308	2.932	-3.548
16	225 min	12	-0.667	3.371	-4.705
17	240 min	10	-0.556	4.997	-6.109

Abbreviations: N, Number of samples at different time points; T, time of recording BIS values.

**Table 3** Overall Bland–Altman analysis for BIS

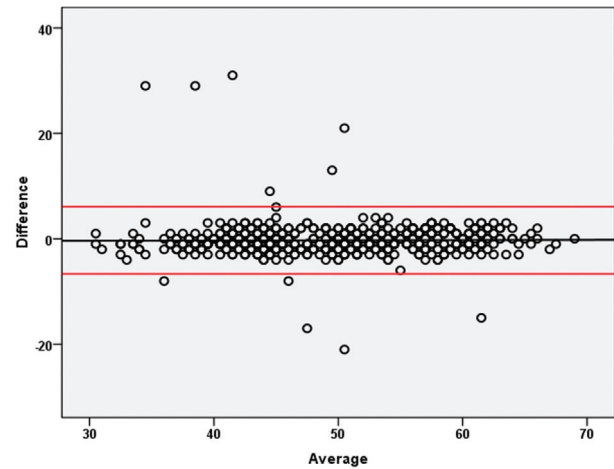
(N = 604)	
Mean difference	−0.266
95% limits of agreement	6.1/− 6.63/6.1
Outside limit (%)	1.8

Abbreviation: N, the total number of samples.

shows a Bland–Altman plot comparing the pooled data of BIS obtained from standard frontal and supralabial positions at all time points.

## Discussion

BIS is a proprietary algorithm that interprets raw electroencephalogram (EEG) data from standard forehead electrodes and provides a dimensionless BIS value ranging from 0 to 100,<sup>10</sup> with 100 representing normal cortical electrical activity and 0 indicating cortical electrical silence. The probability of postoperative recall is very low when BIS is less than 60.<sup>11</sup> Some clinical situations such as neurosurgery make the frontal placement of BIS sensors difficult, our aim was to find an alternative site that served the purpose and did not interfere with the surgical field. We conducted this study to compare and determine the limit of agreement of BIS, SQI, and EMG obtained from frontal and supralabial sites at different time points using the Bland–Altman plot. In our study, we compared the frontal and supra labial BIS/EMG/SQI values every 15 minutes, during the mainte-



**Fig. 3** Bland–Altman plot comparing BIS obtained from standard frontal and supralabial positions at all time points. The 95% limit of agreement is  $\pm 1.96$  SD. SD, standard deviation.

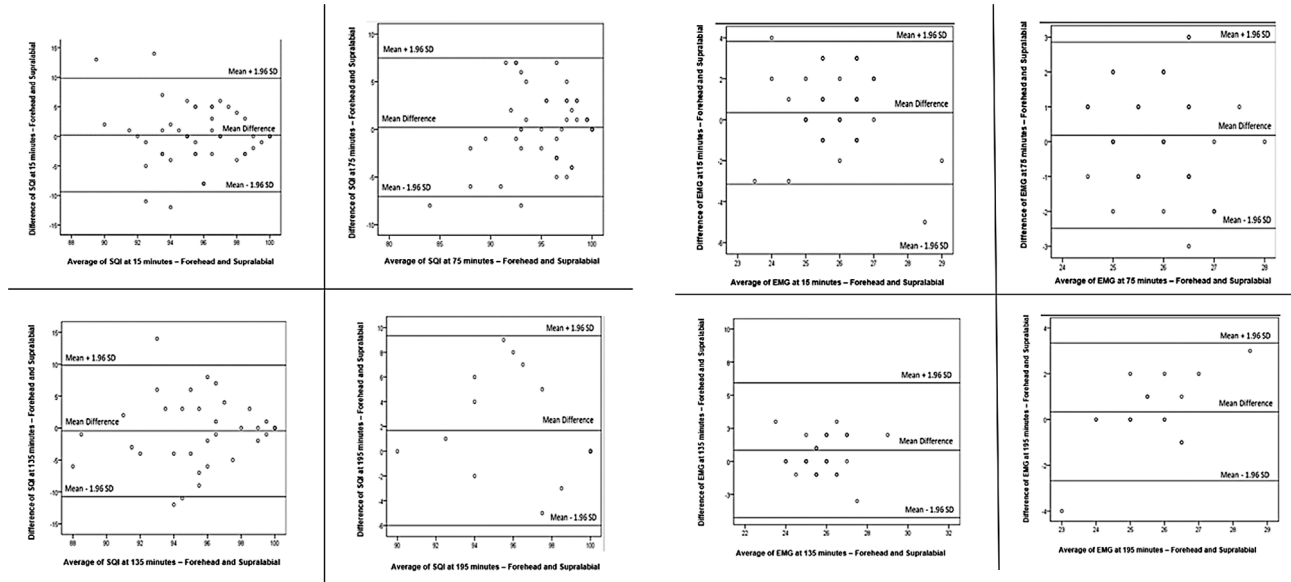
nance phase using the Bland–Altman analysis. Induction and extubation periods were deliberately excluded because previous studies have shown that sudden changes in the BIS score reduced the reliability of alternative sensor placement.<sup>9</sup>

Although there is no source of EEG in the supralabial region, the conduction of electromagnetic wave potential (EEG) from the frontal regions of the brain to adjacent parts might be the reason, we get the BIS values from the said position.<sup>9</sup>

**Table 4** Limits of agreement for SQI values at different time points

Pair	T (SQI)	N	Mean Difference	95% limits of agreement	
				Mean + 1.96 SD	Mean − 1.96 SD
1	Post intubation	50	−0.5	6.362	−7.362
2	15 min	50	0.22	9.816	−9.376
3	30 min	50	−0.34	9.689	−10.369
4	45 min	50	1	8.679	−6.679
5	60 min	50	0.22	10.669	−10.229
6	75 min	49	0.224	7.505	−7.057
7	90 min	48	−0.688	10.474	−11.85
8	105 min	47	0.787	10.971	−9.397
9	120 min	42	−0.049	10.349	−10.447
10	135 min	37	−0.459	9.825	−10.743
11	150 min	33	−0.455	7.861	−8.771
12	165 min	25	2.56	12.825	−7.705
13	180 min	20	−2.05	7.262	−11.362
14	195 min	18	1.667	9.333	−5.999
15	210 min	13	0.077	9.216	−9.062
16	225 min	12	−0.167	8.1	−8.434
17	240 min	10	−1.5	8.964	−11.964

Abbreviations: N, number of samples at different time points; T, time of recording SQI values.



**Fig. 4** Bland–Altman scatter plot comparing SQI obtained from standard frontal and supralabial positions at 15, 75, 135, and 195 minutes. The 95% limit of agreement is  $\pm 1.96$  SD. SD, standard deviation.

**Fig. 5** Bland–Altman scatter plot comparing EMG obtained from standard frontal and supralabial positions at 15, 75, 135, and 195 minutes. The 95% limit of agreement is  $\pm 1.96$  SD. SD, standard deviation.

The Bland–Altman plot is used to describe the agreement between two quantitative measurements by constructing limits of agreement. These statistical limits are calculated by using the mean and the standard deviation of the differences between the two measurements.<sup>12</sup> Limits of agreement help us to analyze if the reading from one site is as reliable and

reproducible as the second. Bland and Altman recommended that 95% of the data points should lie within  $\pm 2$  SD of the mean difference. The difference in BIS values obtained from the frontal and supralabial areas was acceptable at all time points in this study (–Fig. 2). A clinically acceptable limit of agreement has not been defined in any study, but a few studies have recommended it to be  $\pm 10$  BIS units.<sup>13</sup> In this

**Table 5** Limits of agreement for EMG values at different time points

Pair	T (EMG)	N	Mean difference	95% limits of agreement	
				Mean + 1.96 SD	Mean – 1.96 SD
1	Post intubation	50	–0.88	18.969	–20.729
2	15 min	50	0.34	3.829	–3.149
3	30 min	50	0.14	4.119	–3.839
4	45 min	50	0.28	5.131	–4.571
5	60 min	50	0.12	3.352	–3.112
6	75 min	49	0.184	2.857	–2.489
7	90 min	48	0.083	3.462	–3.296
8	105 min	47	0.191	4.625	–4.243
9	120 min	42	0.024	3.189	–3.141
10	135 min	37	0.838	5.93	–4.254
11	150 min	33	–0.03	3.237	–3.297
12	165 min	25	0.28	3.302	–2.742
13	180 min	20	0.25	2.702	–2.202
14	195 min	18	0.333	3.34	–2.674
15	210 min	13	0.231	2.048	–1.586
16	225 min	12	0	5.219	–5.219
17	240 min	10	1.1	7.531	–5.331

Abbreviations: N, number of samples at different time points; T, time of recording EMG values.

study, the level of agreement was within  $\pm 5$  BIS units except at six different time points where the SQI value shows a weak agreement. The overall 95% limits of agreement with the pooled data for BIS were  $-6.63/6.1$ , which is well within the recommended  $\pm 10$  BIS units and very close to our clinically relevant criteria of  $\pm -5$  BIS units.

Historically, studies have shown BIS to be topographically dependent as the EEG activity is not strictly homogenous across the scalp,<sup>8</sup> but studies across the globe have reported alternative BIS electrode placement sites with good correlation and limits of agreement. A study by Lee et al<sup>9</sup> suggests the use of mandibular placement as an alternative to frontal placement during anesthesia maintenance, with a negative bias of  $-1.8$  and a limit of agreement of  $-12.5/9$ . Shiraishi et al<sup>14</sup> found a good correlation between frontal and occipital BIS placements ( $r^2 = 0.96$  at a  $p$ -value of 0.03).

Akavipat et al<sup>15</sup> compared the usual frontal placement of BIS electrodes with postauricular placement in 34 patients scheduled for neurosurgery. The correlation coefficient between frontal and postauricular area electrodes was 0.71 with a  $p$ -value  $< 0.001$ . The overall limit of agreement was  $-12.2/9.2$ , but it improved to  $-9.7/7.4$  if the analysis excluded the BIS values before and after anesthesia. They recommend post auricular placement as a practical alternative to frontal placement.

The use of electrocautery can cause electromagnetic interference, poor signal quality, and affects BIS values. In one of the studies, electrocautery was reported to influence the BIS monitoring in 21% of monitored patients.<sup>16</sup> Matthew et al also stated that there was a significant decrease in the signal quality index during electrocautery use in their study. In our experience, open surgeries show much more electrocautery interference as compared with laparoscopic or robotic surgeries. The most plausible explanation for the decreased interference during robotic surgeries could be the pneumoperitoneum-induced dampening of the electromagnetic field generated from cautery. Thus, we chose to perform our study on patients undergoing robotic surgery for better results.

### Limitation of the Study

Our study was done on robotic surgery patients with the intent of extrapolating the results in neurosurgical patients. Further studies need to be done on neurosurgical patients. As the comparison was done during the maintenance phase of anesthesia, not picking the sudden change in BIS score at the alternate site during induction and emergence remains a limitation of this study.

### Conclusions

Supralabial BIS placement can be used as an alternative where the frontal placement of BIS is not feasible, with

particular emphasis on skin preparation and proper positioning of BIS electrodes to improve the signal quality.

### Funding

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### Conflict of Interest

None declared.

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