BIS-Vista™ Occipital Montage in Patients Undergoing Neurosurgical Procedures during Propofol–Remifentanil Anesthesia

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ABSTRACT

Background: Neurosurgical procedures that require a frontal approach could be an impediment for a successful Bispectral Index® (BIS®) frontal sensor placement. The aim of this study was to explore the utility of using the new BIS-Vista™ monitor (Aspect Medical Systems, Newton, MA) for occipital sensor placement in the patients undergoing brain neurosurgical procedures during propofol–remifentanil anesthesia.

Methods: Two BIS® Quatro sensors (Aspect Medical Systems, Newton, MA) mounted on the occipital and frontal regions were connected to two BIS-Vista™ monitors at three anesthesia states: before induction, during anesthesia maintenance, and recovery.

Results: There were significant differences before induction ($P = 0.0002$) and at anesthesia maintenance ($P = 0.0014$) between mean ± SD occipital (83.4 ± 4.8, 66.7 ± 7.2) and frontal (93.1 ± 3.4, 56.9 ± 9.1) BIS-Vista™ values. During anesthesia recovery, there was no difference ($P = 0.7421$) between occipital (54.6 ± 9.3) and frontal (53.1 ± 7.3) BIS-Vista™ values. Bland and Altman analysis revealed a BIS-Vista negative-bias (limits of agreement) of -9.7 ($+1.1$, -20.5) before anesthesia induction, $+9.8$ positive-bias ($+22.8$, -1.7) during anesthesia maintenance, and -0.9 bias ($+10.9$, -12.8) during anesthesia recovery.

Conclusion: We demonstrated that not only the regional limits of agreement are too wide to allow data of the two montages to be used interchangeably but also the variation is a function of anesthetic depth. However, keeping in mind a relatively consistent BIS-Vista™ -10 bias before induction and $+10$ bias during anesthesia maintenance with limits of agreement of approximately ±11 BIS units, approximately double the clinically acceptable less than 10 BIS units level of agreement, BIS-Vista™ off-label occipital montage might be helpful in following a trend of propofol–remifentanil anesthesia in individual cases where frontal access is particularly difficult.

> **What We Already Know about This Topic**
>
> ❖ Bispectral Index (BIS) has been extensively studied with frontal electrodes
> ❖ There is a reasonable agreement between frontal and occipital electrodes montage for BIS using an older algorithm but not with the most recent algorithm
>
> **What This Article Tells Us That Is New**
>
> ❖ In 20 neurosurgical patients, there were large differences between anesthetic effects on BIS using frontal compared with occipital electrodes montage
> ❖ BIS values cannot be used interchangeably between frontal and occipital electrodes montage

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BISPECTRAL analysis is a standard high-order statistical measure of time series analysis first used by oceanographers in the early 1960s to study nonlinearity in ocean waves.[1] The Bispectral Index (BIS) is a processed electroencephalographic parameter quantifying the level of interfrequency phase-coherent synchronization in the signal.[2] The BIS is statistically derived from an empirical database using a complex proprietary algorithm that combines three subparameters into a single metric: BetaRatio, a frequency-domain feature; SynchFastSlow, a bispectral-domain feature; and Burst Suppression, a time–domain feature that consists of two separate algorithms: Burst Suppression Ratio that quantifies the extent of isoelectrical silence and QUAZI suppression index that detects Burst Suppression superimposed on wandering low baseline voltage.[2] None of the BIS disparate descriptors is particular *per se*, because each has a specific range of effect where it performs best. The BIS algorithm allows the different descriptors to dominate sequentially as electroencephalography changes its character.[2] The new BIS-Vista™ monitor version 1.4 (Aspect Medical Systems, Newton, MA) uses a new proprietary algorithm.

BIS is widely used for monitoring the effects of anesthetic–hypnotic drugs and was shown to be a useful monitor in

645

neurosurgery. However, neurosurgical procedures that would require a frontal approach might be an impediment for a successful frontal BIS® sensor placement. The attractive simplicity of a single, easily understood integer value, along with the ease of using the device itself, makes it tempting to propose that the BIS-Vista™ monitor might still serve as an effective monitor when placed on the occipital area. Although Rampil[2] published the general principles of the BIS, and recently Aspect Medical Systems released on the manufacturer's website the general principles of successive BIS algorithms' alterations made during recent years, still to date, the complete details of the proprietary BIS algorithms' core technologies are only incompletely known outside of the manufacturer. Although each release of new BIS algorithms is probably substantially based on sizeable components of the old algorithms, still varied computational algorithms used in each BIS generation cannot be entirely identical, and historical BIS numbers could not be treated as invariant constants. We previously demonstrated substantial bias (limits of agreement) of 7 (+22, −6) BIS units[3] between two simultaneously recorded first generation BIS® A-1000 (version 3.4) and at the time newly introduced BIS®-XP monitor.[3]

Although Shiraishi *et al.*[4] reported a "strong overall" correlation between frontal and occipital montages of the early generation BIS® A-1050 (version 3.3) monitor, still extensive literature in neurology and anesthesia showed that different electroencephalographic montages and their relation to the depth of anesthesia yield different findings.[5,6] Hence, one should not rely on the study of Shiraishi *et al.*[4] and assume that the new software should necessarily perform in an identical manner as earlier algorithms. The aim of our study was to assess the validity of this alternative approach; we compared values obtained from frontal and occipital BIS-Vista™ in patients undergoing brain neurosurgical procedures at three anesthesia states: before induction, during anesthesia maintenance, and recovery.

Materials and Methods

Our report of a prospective controlled consecutive study was prepared in conformity with the guidelines of the "Consolidated Standards of Reporting Trials statement."[7] After the approval of Xuan Wu Hospital, Capital Medical University (Beijing, People's Republic of China) Ethics Committee approval, all patients who agreed to participate in the study gave written informed consent. Exclusion criteria were body mass index less than 18 to more than 24 kg/m^2 or medical conditions that might affect the level of consciousness such as stroke, stupor, or dementia. Twenty patients undergoing scheduled neurosurgical procedures were recruited in the study.

A Quatro sensor (Aspect Medical Systems, Newton, MA) was mounted on the forehead according to the manufacturer's guidelines, with another Quatro sensor mounted ipsilaterally according to Shiraishi *et al.*[4] proposed occipital placement. The occipital process was considered the midline

Fig. 1. Occipital montage of Quatro sensor for the Bispectral Index-Vista™ monitor (Aspect Medical Systems, Newton, MA).

guide point with electrode 1 placed few centimeters cranially, electrodes 2 and 4 placed slanting, and electrode 3 placed laterally (fig. 1). The Quatro sensors were connected to two BIS-Vista™ monitors with the clocks synchronized to the exact "hour: minute: second." The raw electroencephalography signals were band-pass filtered to 2–70 Hz and processed in real time using BIS-Vista™ version 1.4 algorithm. In addition, the BIS-Vista™ monitor calculates the electromyography power in the 70–110 Hz frequency band displayed in decibels. BIS recordings were started after verifying a signal quality index more than 95% and electrodes impedance less than 5 kΩ. With the help of the USB-A port, electroencephalographic variables were digitally collected and stored on a laptop computer once every 5 s for the duration of the study. The smoothing window was set at 15 s. Real-time electroencephalography was analyzed by an electroencephalographer with adequate training in the interpretation of waveforms. BIS values showing sudden high electrocautery or electromyogram artifacts were identified and eliminated in the off-line analysis.

Before induction, BIS-Vista™ was recorded for 10 min while patients relaxed with their eyes closed in a quiet anesthesia induction room with no tactile or verbal communications with the induction room personnel. This averted noise transiently provoking a BIS response.[8] Patients were instructed to remain calm with their eyes closed but not to fall asleep.[9] Patients were also instructed to keep their facial muscles completely relaxed and avoid making any facial expressions as electromyographic activity could spuriously increase the BIS value.[10] For anesthesia induction, a propofol Diprifusor infusion pump (AstraZeneca Pharmaceuticals, Macclesfield, United Kingdom), incorporating Marsh pharmacokinetic model,[11] was started after entry of patients' anthropometric data. Remifentanil 0.1–0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion was started, and rocuronium 600 $\mu g/kg$ was administered for tracheal intubation. The lungs were ventilated mechanically with 40% oxygen in air and adjusted to maintain 30–40 mmHg end-tidal carbon dioxide. We maintained a stable BIS level of approximately 50 *via* propofol target-controlled infusion ±0.2 $\mu g/ml$ rate adjustments, a

level similar to the BIS level of 40–60 used in the previous study.[4] Patients were warmed using a forced hot air blanket to maintain core temperature more than 36°C.

Statistical Analysis

Because BIS-Vista™ monitor is recently introduced, an *a priori* sample size power analysis was not possible. Instead, we used data from the first 10 pilot patients in whom the mean anesthesia maintenance frontal BIS-Vista™ values was 55.3 ± 10.2 compared with 67.4 ± 7.2 occipital values. Our interim power analysis paired *t* test ($\alpha = 0.05$) showed that a group size of 12 patients would be required to reveal a statistically significant difference with 90% power. The data of the 10 pilot patients were used in the primary analysis, which might be considered multiple comparisons of the same data. We made no adjustments to the *P* value to account for the interim analysis.

To assess the agreement between frontal and occipital montages, we analyzed the BIS-Vista™ values at three clinically relevant anesthesia states: 10 min before induction, 1 h of anesthesia maintenance, and 20 min of anesthesia recovery of each patient using the statistical method of Bland and Altman.[12] Although frontal sensor placement is the validated standard method for BIS-Vista™ quantifications of anesthetic–hypnotic effects, still Bland and Altman analysis considers both frontal and occipital montages subject to experimental error. Limits of agreement were defined as the bias ±1.96 SD in which 95% of the differences between the two montages are expected to lie.[12] We considered a clinically acceptable level of agreement to be the level of intrapatient reproducibility, where simultaneous bilateral readings would differ by less than 10 BIS units.[13] In that regard, paired measurements we used at each anesthesia state could be considered as repeated measures made on the same individuals. Thus, we further used the "random effects model for repeated measures data" of Myles and Cui[14] to measure agreement with repeated measures of the method of Bland and Altman. This approach does not use all repeated measures made on the same individual, rather mean values of individual patients.

We used repeated measures analysis of variance to compare differences in occipital *versus* frontal values over time (location × time; before induction, during anesthesia maintenance, and recovery). Dunnett's two-sided multiple-comparison *post hoc* test was used to compare BIS-Vista™ values at the three anesthesia states. We used coefficient of determination to assess occipital *versus* frontal correlations. Data were expressed as means ± SD. $P < 0.05$ was considered statistically significant.

Statistical analyses was performed using Number Crunching Statistical System 2007 (NCSS Inc., Kaysville, UT) and StatXact (Cytel Software Corporation, Cambridge, MA).

Results

Patients' characteristics are presented in table 1. Electromyography values were consistently less than 35 dB. There were

Table 1. Patients' Characteristics

Patients' Demographics	
Male/female	12/8
Age (yr)	30.9 ± 8.2
Weight (kg)	61.1 ± 7.4
Height (cm)	168 ± 6
BMI (kg/m²)	21.7 ± 2.4

Values are expressed as means ± SD. n = 20.
BMI = body mass index.

no significant difference ($P = 0.6434$) between the occipital and the frontal electromyography values over time.

There was a significant difference ($P < 0.0001$) between the occipital and the frontal BIS-Vista™ values over time (location × time). Dunnett's two-sided multiple-comparison *post hoc* test revealed significant differences before induction ($P = 0.0002$) and at anesthesia maintenance ($P = 0.0014$) between occipital (83.4 ± 4.8, 66.7 ± 7.2) and frontal (93.1 ± 3.4, 56.9 ± 9.1) values. During anesthesia recovery, there was no difference ($P = 0.7421$) between occipital (54.6 ± 9.3) and frontal (53.1 ± 7.3) values. There was a moderate correlation ($r^2 = 0.671$) during anesthesia maintenance.

Before anesthesia induction, α-wave predominance was more prominent in occipital than in frontal real time electroencephalography, whereas during anesthesia maintenance, an increase in δ and θ low-frequency activities were more evident in frontal than occipital electroencephalography.

Throughout the measurement range, our limits of agreement were approximately double the clinically acceptable, *a priori* defined, level of agreement of less than 10 BIS units. Bland and Altman analysis revealed a BIS-Vista™ negative-bias (limits of agreement) of −9.7 (+1.1 and −20.5) before anesthesia induction (fig. 2), positive-bias of +9.8 (+22.8 and −1.7) during anesthesia maintenance (fig. 3), and −0.9 bias (+10.9 and −12.8) during anesthesia recovery. During anesthesia recovery up to BIS level of 55, BIS from the occipital signal tends to be greater than frontal, and as the BIS increases more than 55, the *vice-versa* effect occurs (fig. 4). Myles and Cui[14] "random effects model for repeated measures data" approach revealed similar bias, with slightly narrower limits of agreement of −9.7 (+0.7 and −20.1) before anesthesia induction, +9.8 (+21.9 and −0.7) during anesthesia maintenance, and −0.9 (+5.8 and −7.9) considerably narrower limits of agreement during anesthesia recovery.

Discussion

We examined the utility of placing BIS-Vista™ sensor on the occipital area to allow continuous monitoring of clinical situations with an inaccessible frontal montage. Our data confirm that the BIS-Vista™ is a topographically dependent variable. It seems that the general notion that BIS classically collected from frontotemporal montage could be a unique value, representing the best global measurement of the whole
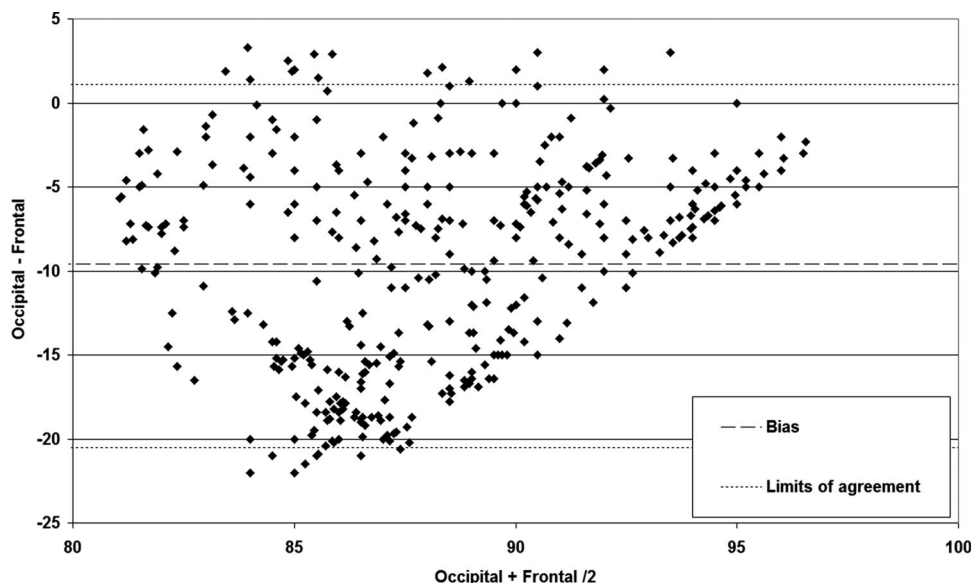
Fig. 2. Bland and Altman scatter plot of the difference between occipital and frontal Bispectral Index-Vista™ values against the mean of the two measurements before anesthesia induction. The *dotted lines* represent the bias and the limits of agreement.

electroencephalographic activity,[4,15] is not entirely valid. BIS-Vista™ frontal montage does not cover all territories changing with anesthesia, rather a restricted monitoring area of the frontal lobe, whereas occipital placement would primarily reflect the unique changes of the occipital territories. As we examined the spatial dependency of BIS-Vista™ monitoring, we clearly documented the regional occipitofrontal differences in BIS-Vista™ values at different stages of anesthesia.

The main finding of our study was a clear topographic distinction of the occipital BIS-Vista™ montage that might provide sensitive but totally different depth of anesthesia indices. Our results provide clear evidence that the occipitofrontal limits of agreement, approximately double the clini-

cally acceptable less than 10 BIS units level of agreement, are too wide to allow data of the two montages to be used interchangeably. Keeping in mind a relatively consistent −10 BIS-Vista™ bias before induction and a +10 bias during anesthesia maintenance with limits of agreement of approximately ±11 BIS units, occipital BIS-Vista™ monitoring might be helpful in following a trend of propofol–remifentanil anesthesia when frontal access is particularly difficult. It would have been very convenient if BIS was independent of the choice of montage, but that does not seem to be the case. In normal awake or anesthetized patients, electroencephalographic activity is not strictly homogeneous across the scalp.[5,6] Thus, our occipitofrontal differences are not particularly surprising, and the extent of the BIS-Vista™ algo-
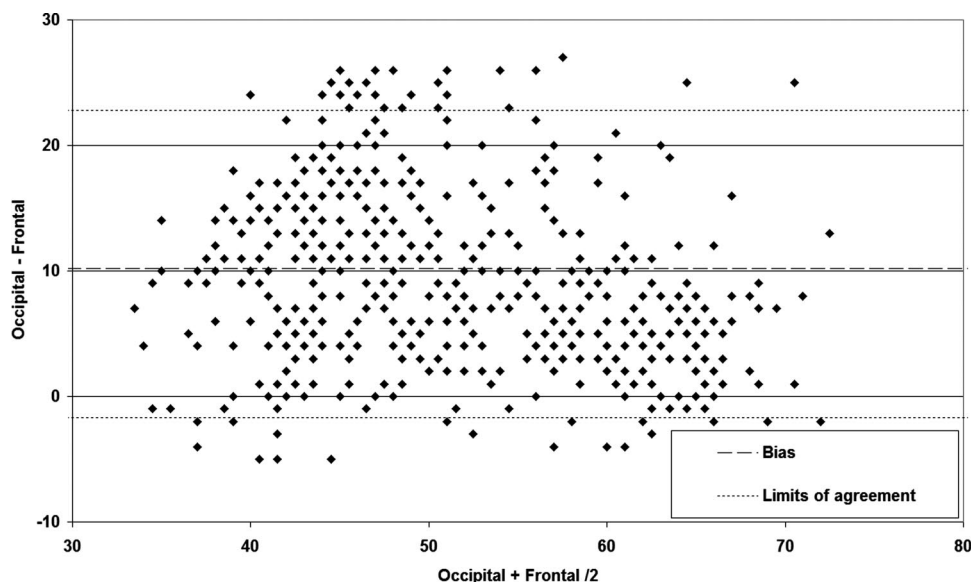
Fig. 3. Bland and Altman scatter plot of the difference between occipital and frontal Bispectral Index-Vista™ values against the mean of the two measurements during anesthesia maintenance. The *dotted lines* represent the bias and the limits of agreement.
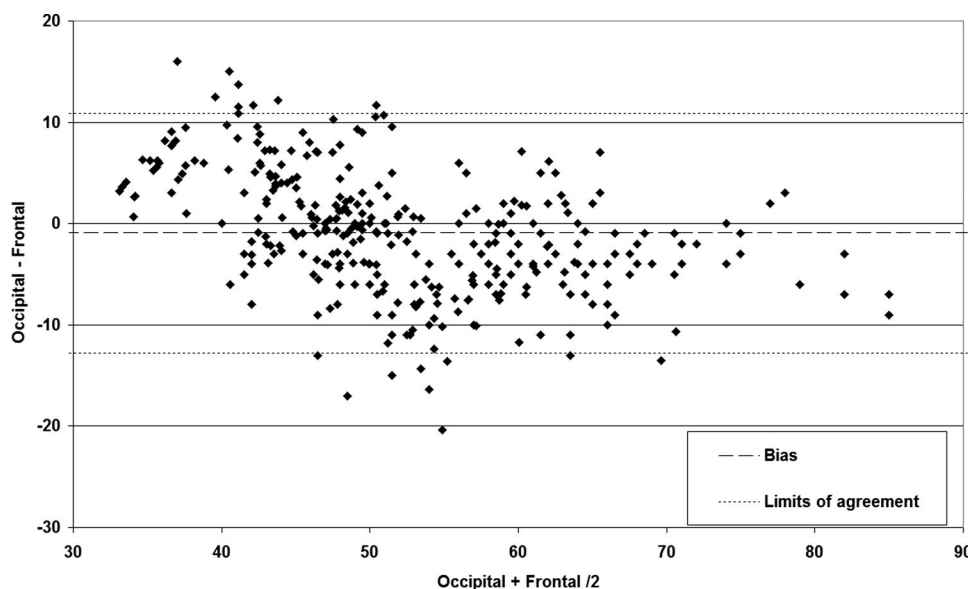
Fig. 4. Bland and Altman scatter plot of the difference between occipital and frontal Bispectral Index-Vista™ values against the mean of the two measurements during anesthesia recovery. The *dotted lines* represent the bias and the limits of agreement.

rithm is able to identify these local variations might be of interest for some potential clinical applications.

One would expect a certain degree of inherent BIS discrepancy manifesting even at the same electrode location (ideally the frontal location), which would give us a sense of the best limits of agreement we can hope for. A recent study[13] assessing the intrapatient reproducibility of 2 BIS®-XP (version not specified) monitors symmetrically mounted on the forehead showed that simultaneous BIS recordings were concordant only 94% of the time, and for 6% of the time, there were sustained periods of more than or equal to 30 s where simultaneous readings differed by more than 10 BIS units.[13] This would probably define the best BIS values we would expect frontal/occipital locations could possibly agree.

Our results do not concur with two previous studies that considered the first-generation BIS® monitors as a topographically "independent" variable.[4,15] Shiraishi *et al.*[4] reported a "strong overall" agreement ($r^2 = 0.961$), between BIS® A-1050 (version 3.3) recorded from frontal and occipital areas.[4] Similarly, Glass *et al.*[15] reported that BIS® A-1000 (versions 2.0 and 3.0) recorded from frontocentral montage provided "similar" results to a bifrontal montage.[15] However, unlike our study design neither study separately analyzed the different stages of anesthesia (before induction, during anesthesia maintenance, and recovery). They provided no scatter plots or Bland and Altman analysis comparing the magnitude of agreement between BIS values derived from different electrode montages. Glass *et al.*[15] used the pooled data of four different anesthetic regimens (propofol, midazolam, isoflurane, and alfentanil) in healthy volunteers experiencing no surgical stimulation. The authors of both studies[4,15] provided no justification or rationalization for why BIS monitoring could possibly be topographically independent, despite the fact that their results and its logical interpretations[4,15] are in sharp contrast to a body of literature

showing a very clear pattern of distinctive topographic electroencephalographic variations in anesthetized patients.[5,6]

Kochs *et al.*[6] demonstrated, in a leading study, that topographic representation of intraoperative electroencephalographic responses to surgical stimulation are not homogeneously distributed. Thus, it would be expected that different montages might give sensitive but different depth of anesthesia indices.[6] With low-dose isoflurane, surgical stimulation resulted in predominate frontal "δ shift"; an increase in δ activity termed "reverse arousal phenomena."[6] The authors believe that afferent nociceptive stimuli during anesthesia arise from the midbrain structures and propagate to mainly frontal cortical areas. Frontal electroencephalographic responses would mostly reflect these afferent signal transmissions.[6]

In that regard, it is important to mention that BIS-Vista™ was designed to detect anesthetic-induced frontal alterations in electroencephalography[2] and was neither designed nor validated for detecting the type of electroencephalographic changes that occur in the occipital region. Although the standard electroencephalography itself is well understood and characterized in various topographic regions, the BIS remains in part, a "black box" as the proprietary nature of the algorithm makes it difficult to evaluate scientifically the suitability of the BIS-Vista™ for applications beyond those for which it was designed and validated. We can only speculate on regional electroencephalographic changes that resulted in the occipitofrontal BIS-Vista™ differences at different stages of anesthesia.

In our study, we demonstrated an occipital bias of approximately −10 BIS before anesthesia induction. This we can infer to the well-documented posterior α waves predominance, compared with frontal regions, in awake relaxed with eyes closed state seen in our study patients.[5,16] Furthermore, Bianchi *et al.*[17] using spectral and bispectral analysis showed

that, in basal awake relaxed with eyes closed conditions, spontaneous α rhythms are generated by two totally independent oscillators in the occipital and frontal regions.[17]

At deeper propofol levels, observations of anesthesia-induced electroencephalographic changes were summarized by the term "frontal predominance" describing a clear sustained frontal increase in β activity as excitation of the frontal cortical regions becomes manifest.[16,18] This is eventually superseded by marked increases in the δ and θ low-frequency activities migrating anteriorly in a topographic pattern of "anteriorization."[5] This was demonstrated in earlier generation BIS® monitors during anesthesia maintenance.[19,20] Hall and Lockwood[19] using BIS® A-1000 (version 2.51) in patients undergoing a variety of anesthetic regimes demonstrated that data generated from the central locations were approximately +13 BIS units higher than those derived from the frontal locations. Similarly, Pandin *et al.*[20] demonstrated, in patients receiving graded increases in propofol target controlled infusion, that BIS® A-1000 (version 3.12) exhibited consistently central/frontal bias of +12 and parietal/frontal bias of +25 BIS units.[20] This is in accordance with our study results of a consistent occipital/frontal bias of +10 BIS units. They also found weak frontal–central correlation ($r^2 = 0.374$) and moderate frontal–parietal correlation ($r^2 = 0.66$),[20] which was also comparable with our moderate frontal/occipital correlation ($r^2 = 0.671$) during anesthesia maintenance.

In addition, at propofol anesthesia maintenance, there is considerable loss of coherence with significant uncoupling of anterior from the posterior regions within each hemisphere.[5] This strongly implies that deep anesthesia depends on some "anterior" critical system structure, plausibly comprising the orbital, superior frontal, anterior cingulated, and parahippocampal gyri.[5] This suggests different anterior and posterior electroencephalographic derivations.[16] Our consistent occipital bias of +10 BIS with deepening of propofol–remifentanil anesthesia probably arises from the BIS-Vista™ SynchFastSlow descriptor at occipital regions being less capable of detecting and displaying a mainly anterior region event, of decrease in the cortical generators of α and β activities with a simultaneous shift toward generators of δ and θ activities.[16]

Propofol anesthesia-specific electroencephalographic changes associated with return of consciousness are basically a gradual reversal of those occurring with loss of consciousness. Emergence is preceded by generalized loss of power in δ and θ activities and continual reduction of "frontal predominance."[16] Anterior–posterior coherence increases, as regional interactions are resumed.[5] At these levels, BetaRatio descriptors detect the graduated β-wave reappearance, as SynchFastSlow descriptors lose their predominance with the graduated decrease of δ activity.[18] Interestingly, during anesthesia recovery up to BIS 55, BIS from the occipital signal tends to be greater than frontal, and as the BIS increases more than 55, the *vice-versa* effect occurs. This "emergence" trend should be carefully taken into consideration during the crit-

ical phase of anesthesia recovery, because the occipital BIS-Vista will probably not recover to more than BIS 88.

Myles and Cui[14] "random effects model for repeated measures data" approach revealed similar bias, with slightly narrower limits of agreement before anesthesia induction and maintenance, with narrower limits of agreement during anesthesia recovery. This validated our approach of including equal durations from the 20 study patients would eliminate, to a great extent, the effect of repeated measurements on the Bland and Altman analysis.

Electromyographic activities are artifact signals that occur within the frequency "range of interest" of the bispectrum. Electromyograpgy (30–300 Hz) could simulate the BetaRatio electroencephalography (30–47 Hz) that would be construed by the BIS-Vista™ algorithm as electroencephalographic activity and assigned a spuriously high BIS value.[10] However, in our study, occipital and frontal electromyographic values were consistently less than the cutoff point of 35 dB,[21] clearly indicating that high electromyographic activity did not confound our study results.

The current results provide evidence that BIS-Vista™ is a topographically dependent variable in patients receiving propofol–remifentanil anesthesia. Not only the regional limits of agreement are too wide to allow data of the two montages to be used interchangeably but also the variation is a function of anesthetic depth. However, keeping in mind a relatively consistent BIS-Vista™ −10 bias before induction and a +10 bias during anesthesia maintenance with limits of agreement of approximately ±11 BIS units, BIS-Vista™ off-label occipital montage might be helpful in following a trend of propofol–remifentanil anesthesia when frontal access is particularly difficult.

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