Background: The Bispectral Index (BIS) reportedly reflects anesthetic depth. It is recommended that anesthetic agents should be titrated to maintain the BIS between 40 and 60 arbitrary BIS units during anesthesia. For anesthesia providers to follow this recommendation, the monitor should be predictably affected by different anesthetic agents and have good interpatient and intrapatient reproducibility. The authors hypothesized that when two BISxp® devices (Aspect Medical Systems, Newton, MA) are placed concurrently on the same patient, their readings are concordant throughout the anesthetic period.

Methods: Simultaneous BIS recordings from two BISxp® monitors were obtained during anesthesia at 5-s intervals from 12 participants.

Results: In total 22,860 concurrent paired BIS readings were obtained. For 10.7% of the time, there were sustained periods of 30 s or greater where the readings differed by 10 or more arbitrary BIS units. The regression coefficient (R²) for the two devices was 0.65 (range, 0.35–0.92). There was zero bias between the devices, and the 95% limits of agreement ranged between −18 and +17.

Conclusion: A conflicting anesthetic management was suggested by the simultaneous BIS readings 10.7% of the time. These results suggest that BISxp® does not always provide a reproducible single number. Anesthesia providers should not rely exclusively on the BIS reading when assessing depth of anesthesia.

GENERAL anesthesia is a state of drug-induced unconsciousness during which patients should neither perceive nor recall noxious stimuli. Many patients facing surgery dread the prospect of being awake, in pain, and unable to move as a result of inadequate general anesthesia. A large multicenter study in the United States showed that, despite modern anesthesia techniques, the overall incidence of conscious recall remains approximately 0.1–0.2%. For certain surgeries, such as cardiac surgery, trauma surgery, and obstetric surgery, the incidence of conscious recall approaches 1%.

Conscious recall can lead to extreme anxiety and even post-traumatic stress disorder. Several monitors, including the Bispectral Index® (BIS®; Aspect Medical Systems, Newton, MA), which is based on processed electroencephalographic information, have been developed in an attempt to monitor depth of anesthesia. A recent study suggested that harnessing the information provided by the BIS® monitor decreases the incidence of explicit recall during high-risk surgical procedures from 1% to 0.1%. The American Society of Anesthesiologists and the American Association of Nurse Anesthetists do not currently recommend such monitors as an essential part of routine anesthesia care. Increasingly, pressure is being brought to bear on members of the anesthetic community to adopt into their routine practice a monitor designed to reflect anesthetic depth, such as the BIS® monitor, especially for patients and procedures where the risk of explicit recall is considered to be increased.

When the BIS reading is persistently below 40, it is suggested that the anesthetic plane may be too deep, and when the BIS reading is persistently greater than 60, it is suggested that there is increased risk of explicit recall. It is therefore recommended that anesthetic agents should be titrated to maintain the BIS reading between 40 and 60 arbitrary BIS units (ABUs). For anesthesia providers to follow this recommendation in relation to titrating anesthesia according to ABUs, it is essential that the BIS is affected predictably and similarly by different anesthetic agents and has good interpatient and intrapatient reproducibility. One study suggested that when BIS® electrodes are placed concurrently with different montages, such as one electrode strip on the forehead and the other on the occiput, there is a strong correlation between their readings. Two recent studies, however, showed that when an older version of the BIS® and a BISxp®—the current version of this technology—are placed concurrently, their readings do not always show agreement and are not interchangeable. The manufacturers of the BIS® monitor state on their Web site that "BIS monitoring translates information from the electroencephalograph into a single number that represents each patient’s level of consciousness. This study hypothesized that when two BISxp® electrode strips are placed concurrently on opposite sides of the forehead on the same patient, they reproducibly produce the same single number throughout the anesthetic period."

Materials and Methods

We conducted a nonrandomized, prospective, comparative, observational study in patients undergoing...
elective surgery during general anesthesia. Approval was obtained from the institutional review board (Washington University School of Medicine, St. Louis, Missouri), and all patients recruited provided written informed consent. Fourteen patients were enrolled into the study. Two were excluded. One had surgery postponed, and the BISxp® did not provide readings for the other patient. All participants in the study had two BIS Quatro® electrode strips from BISxp® devices placed on each side of their foreheads for the whole duration of their anesthetic, as described in recent studies.10–12 The manner of placement was the same in all the participants (fig. 1). In the last three patients enrolled, we applied three electrode strips. Two were applied as shown in figure 1, and the third was placed on the same side as, parallel to, and just above the left-sided electrode strip. The purpose of this third electrode was to check for intrapatient reproducibility for electrodes placed on the same side of the forehead. Freestanding BISxp® devices were connected to the electrodes. The impedances were measured for each set of electrodes to ensure optimal electrode contact defined as 7.5 kΩ or less as required by the manufacturer. The clocks on the BIS® devices were synchronized to ensure discrepancy of 1 s or less between the clocks, and BIS data—updated every 5 s—were downloaded for analysis to laptop computers.

Anesthesia was administered according to the preference of the attending anesthesiologist. Patients were excluded if they had a history of stroke, dementia, organic brain disease, or carotid bruit or when ketamine—an agent known to induce unusual changes in electroencephalographic activity13—was used as part of the anesthetic technique. A structured questionnaire4 was conducted in the postoperative recovery area and repeated on the first postoperative day in the hospital ward to identify possible episodes of explicit recall of intraoperative events.

The primary outcome measure of the study was the

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* These patients had three Bispectral Index electrode strips affixed to their foreheads and concurrent readings from three BISxp® devices.
ASA = American Society of Anesthesiologist; CABG = coronary artery bypass graft; ORIF = open reduction with internal fixation.
relation of BIS readings between two devices during the course of general anesthesia. Bland-Altman tests of agreement and bias\textsuperscript{14} were used as well as regression coefficients between the BIS recordings. We also performed time-binned analysis where we included only time periods of 30 s (six sequential paired data points) or longer when there were BIS-defined differences in planes of anesthesia between the two BISxp\textsuperscript{®} devices. We analyzed individual data points to establish how many and what percentage of the BIS readings differed by 10\% or by 10 ABUs. We further performed time-binned analysis (for time periods \(\geq 30\) s) as described above to determine whether these differences were sustained or whether they were just sporadic. We did these analyses both for electrodes placed on opposite sides of the forehead (all 12 patients) and for electrodes placed on the same side of the forehead (the last 3 patients).

**Results**

The patients’ characteristics are shown in table 1. All the patients were right-handed. None of the patients included in the study had explicit recall of intraoperative events. From the 12 patients, 22,860 concurrent paired BIS data points were recorded from the electrodes on opposite sides of the forehead. From the last 3 patients, 8,316 concurrent paired BIS data points were recorded from the electrodes on the same side of the forehead.

Overall, there was no bias (\(< 1\)) between the readings from the BIS\textsuperscript{®} electrodes that were placed on opposite sides of the forehead, and the 95\% limits of agreement between them were from \(-18\) to \(+17\) (fig. 2). Correlation (\(R\)) was 0.8, and regression (\(R^2\)) was 0.65. Overall, 30\% of concurrent BIS readings suggested conflicting depths of anesthesia, as defined in previous studies and by the manufacturer of the BIS\textsuperscript{®} (table 2).\textsuperscript{12} The readings

![Bland-Altman plot of 22,860 data points, reflecting the differences between each paired reading from the left- and right-sided forehead BIS\textsuperscript{®} electrodes. There was zero bias between the devices. This means that there was no overall tendency for the BISxp\textsuperscript{®} attached to electrodes on either side of the forehead to read higher than its counterpart, attached to electrodes on the opposite side. The dotted lines show the 95\% limits of agreement between the BISxp\textsuperscript{®} readings. The plot shows the difference between each paired BISxp\textsuperscript{®} reading when the average BISxp\textsuperscript{®} reading ranged between 0 and 100.](http://pubs.asahq.org/anesthesiology/article-pdf/104/2/242/360160/0000542-200602000-00007.pdf)

![Bland-Altman plot of 22,860 data points, reflecting the differences between each paired reading from the left- and right-sided forehead BIS\textsuperscript{®} electrodes. There was zero bias between the devices. This means that there was no overall tendency for the BISxp\textsuperscript{®} attached to electrodes on either side of the forehead to read higher than its counterpart, attached to electrodes on the opposite side. The dotted lines show the 95\% limits of agreement between the BISxp\textsuperscript{®} readings. The plot shows the difference between each paired BISxp\textsuperscript{®} reading when the average BISxp\textsuperscript{®} reading ranged between 0 and 100.](http://pubs.asahq.org/anesthesiology/article-pdf/104/2/242/360160/0000542-200602000-00007.pdf)
from electrodes that were placed on the same side of the forehead had a bias of $-2.8$, and $95\%$ limits of agreement between them were from $-17$ to $+11$. Thirty-two percent of these concurrent readings suggested conflicting depths of anesthesia. The correlation ($R$) was $0.83$, and the regression ($R^2$) was $0.68$.

With time-binned (six sequential paired data points) analysis, $10.7\%$ of the time, the simultaneous readings of the BISxp® devices from electrodes on opposite sides of the forehead suggested sustained ($\geq 30$ s) differences in depth of anesthesia (table 3). From the electrodes that were placed on the same side of the forehead, $14\%$ of the time, the simultaneous BIS readings suggested sustained ($\geq 30$ s) differences in depth of anesthesia (table 3). The BIS readings from electrodes on opposite sides of the forehead differed by 10 or more arbitrary BIS units. Figures 3 and 4 show photographic examples of concurrent BIS trends in 2 of the patients. One of the photographs shows sustained differences between the BIS readings for a portion of the anesthetic period, and the other shows an example of good agreement between the readings for a portion of the anesthetic period. Figure 5 shows the concurrent BIS trends over time for each of the 12 patients for the whole anesthetic period.

**Discussion**

An ideal monitor of anesthetic depth should be affected similarly and predictably by different anesthetic drugs and should reproducibly reflect anesthetic depth in different patient populations. An ideal monitor should...
display good interpatient and intrapatient reliability.\textsuperscript{15,16} The results of the current study suggest that the BISxp\textsuperscript{®} did not consistently display intrapatient reproducibility in the patients that we studied.

If the BIS readings were consistently divergent, this could suggest technical error. However, for much of the time, the readings were concordant. In addition, the BIS reading was displayed as a solid number, signal quality index was always good, and the impedance was acceptable (≤ 7.5 kΩ). These are criteria by which the manufacturer recommends that the reliability of the BIS reading may be judged. We initially suspected that the differences between the devices could represent lateralization: The BIS may be different when obtained from right- and left-sided electrodes. However, the results from the patients that had electrodes placed on the same side also showed inconsistent intrapatient reproducibility. There was no discernable overall hemispheric bias, although all of our patients were right-handed. The BIS has been shown to be affected by organic brain disease.\textsuperscript{17,18} It is unlikely that the inconsistent intrapatient reproducibility was attributable to unrecognized, unilateral brain pathology, because we excluded any patients with neurologic disease by careful preoperative history and physical examination. Moreover, with all the patients, there were sustained periods of discordance between the BISxp readings (table 3 and fig. 5). It is improbable that all the patients had unrecognized unilateral brain pathology.

One of the patients, patient 5 (table 2), had results that were strikingly different from the rest of the patients. The BIS readings showed the greatest discordance, and there was bias between the BIS readings. One explanation for this discordance is that there was artifact or a technical error. However, as with all of the patients, there was no evidence of technical error. The signal quality index was consistently good for both BIS readings, yielding solid BIS numbers, and the impedance was acceptable. The discrepancies between traces could hypothetically be reflective of occult unilateral brain pathology, which may be a potential source of discrepant hemispheric BIS readings. This explanation is not likely for this patient. A magnetic resonance imaging scan of the head revealed no organic brain injury. In addition, the discordance was not consistent or sustained; for part of the anesthetic period, the two BIS readings were reproducible for this patient (fig. 5). There are reportedly four components parameters that are combined to provide a composite BIS index.\textsuperscript{19} Suppression is not weighed heavily in the BIS index until it exceeds 40%.\textsuperscript{19} The differences between the BISxp\textsuperscript{®} in the suppression ratio readings may have contributed to the simultaneous and sustained discordant traces. The extent of discordance in this patient is concerning.
Differences between monitoring devices may be statistically significant but clinically unimportant. Although 30% of the concurrent BIS readings suggested different depths of anesthesia as defined by the manufacturer, this does not necessarily mean that 30% of the time the two monitors displayed clinically relevant divergence. This could be reflective either of sporadic differences between the simultaneous BIS readings or of small differences between the readings. We therefore analyzed the data for fixed differences between the readings (> 10% and > 10 ABUs) and we determined the proportion of simultaneous BIS readings that differed uninterruptedly for at least 30 s. When only 30-s uninterrupted periods (six sequential BIS readings on each device) were in-

Fig. 5. Figure showing the concurrent BISxp® trends from all 12 patients from the electrodes placed on opposite sides of the forehead during the whole anesthetic period. BIS values are shown on the y-axis, and time course is shown on the x-axis. The right forehead sensor is displayed by the solid line, and the left is displayed by the dotted line.
cluded, 10.7% of the time, the BISxp® devices suggested different anesthetic planes from each other, which would suggest different anesthetic management. With the criteria of a difference between simultaneous BIS readings of at least 10 ABUs sustained for at least 30 s, the readings were concordant 94% of the time. This could be interpreted in two ways. On the one hand, the broad agreement between the BISxp® monitors 94% of the time may be perceived as encouraging. On the other hand, if an accurate BIS reading is considered important in guiding appropriate anesthesia, the 6% sustained (> 30 s) and meaningful (> 10 ABUs) difference between two concurrent BIS readings may be concerning. The graphs showing the concurrent BIS trends in each patient (fig. 5) show that the extent of concordance differed among patients and that for most patients, there were periods when the simultaneous BIS trends were discordant.

In the B-Aware study, one of the patients reportedly experienced explicit recall from a period during surgery when the BIS readings were in the range of 55–59 ABUs.4 The authors explain, "This episode suggests that awareness can arise when the BIS is at the upper limit of the recommended (40–60) range."4 They suggest that a response to this might be to ensure that the BIS is below 55 ABUs if awareness is to be avoided in most cases.4 Another group of investigators has suggested that a consistently low BIS reading (≤ 45 ABUs) is associated with adverse long-term outcome.20 If the findings of these studies are applied to routine anesthetic practice, providers should strive to maintain the BIS within a very narrow range of 10 (45–55) ABUs. The results of our study suggest that the BISxp® may lack the accuracy and reproducibility (tables 2–4) to be able to achieve this. If the target for the BIS number is 45–55 ABUs and we aim for the middle of that range (50 ABUs), a deviation of a mere 5 ABUs in either direction will take the reading out of the desired range. From our results, when two BISxp® are placed simultaneously, if one BIS reading is 50 ABUs, the other would read 45 ABUs or less or 55 ABUs or greater approximately 17% of the time (≥ 10% discordance sustained for ≥ 30 s).

There have been several recent studies that have suggested that using BIS® during general anesthesia may decrease the incidence of explicit recall.4,7 Although there has been some criticism of these studies base on methodologic issues, it is conceivable that BIS monitoring reduces explicit recall despite the inconsistency of its intrapatient reproducibility. The presence of any monitor designed to alert the anesthesia provider to the problem of explicit recall may heighten vigilance and decrease the likelihood of explicit recall. Also, these monitors may be helpful in critical situations such as when no volatile anesthetic agent is being delivered or when an intravenous anesthetic infusion has run out. Although the BIS, a processed electroencephalograph, is only a surrogate marker of consciousness, it may be more reliable in this regard than other surrogates, such as volatile anesthetic concentration. Further research is needed to address this.

In summary, the results of this study suggest that the BISxp® does not consistently display intrapatient reproducibility. These results are at variance with the manufacturer’s claim that the BIS® monitor provides a reproducible and “reliable single number that represents each patient’s level of consciousness.” The results of this study reinforce the sentiment expressed on the Aspect Medical Web site: “Clinical judgment should always be used when interpreting the BIS in conjunction with other available clinical signs. Reliance on the BIS alone for intraoperative anesthetic management is not recommended.”

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References