MONITORING LEVEL OF CONSCIOUSNESS DURING ANESTHESIA & SEDATION

A Clinician's Guide to the Bispectral Index®

Scott D. Kelley, M.D.
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This text is intended for educational purposes only. It is not intended to provide any specific clinical practice recommendations for BIS monitoring technology. The clinical choices discussed in this text may or may not be consistent with your own patient requirements, your clinical practice approaches, or guidelines for practice that are endorsed by your institution or practice group. It is the responsibility of each clinician to make his/her own determination regarding clinical practice decisions that are in the best interest of patients. Readers are advised to review the product information including the Indications for Use currently provided by the manufacturer for current recommendations on use. Neither the publisher, editor, or Aspect Medical Systems, Inc. assumes any responsibility for any injury and or damage to persons or property.
CHAPTER 1: INTRODUCTION

The Bispectral Index® (BIS®) is a measure of the effects of anesthesia and sedation on the brain, a new “vital sign” that allows clinicians to deliver anesthesia with more precision and to assess and respond more appropriately to a patient’s changing condition during surgery. As such, it is an important advance in the field of anesthesiology driven by the desire to improve patient care.

BACKGROUND

During the evolution of modern anesthesia practice, patient assessment has undergone gradual change and refinement. Observations of clinical signs such as pupil response, patterns of respiration, quality of the pulse and movement were first augmented by direct measurement of physiologic endpoints including blood pressure, heart rate and respiratory rate and volume. With the development of pulse oximetry and capnography, a precise assessment of ventilatory management could be made. The use of end-tidal agent analysis and peripheral nerve stimulation provided anesthesia clinicians the ability to measure pharmacologic agent concentration and effect, respectively. Today, cardiac function can be evaluated using advanced technologies that range from pulmonary artery catheters and transesophageal echocardiography to new methods of continuous blood pressure and cardiac output monitoring.

Despite the remarkable improvements in assessment of the cardiovascular system during anesthesia, direct determination of the effect of the anesthetic and sedative agent(s) on the central nervous system has remained a challenge. Careful clinical investigation demonstrated that hemodynamic responses do not necessarily provide an accurate representation of the central nervous system responsiveness to anesthetic agents and therefore were unreliable indicators of brain status.¹ In contrast, a technology that would permit independent neurophysiological monitoring of the central nervous system would provide a direct measure of brain status during anesthesia and sedation, allowing clinicians to fine-tune perioperative management and achieve the best possible outcome for each patient. Accurate monitoring and targeting of brain effect, in combination with assessment of clinical signs and traditional monitoring, would permit a more complete approach to adjusting the dosing and mixture of anesthetic, sedative and analgesic agents.
The Bispectral Index (BIS Index) offers the anesthesia professional a direct and accurate method for continuous brain status monitoring throughout the course of anesthetic or sedative administration. Specifically, the BIS Index provides a measurement of the hypnotic effect of anesthesia. It has proven to be accurate and reliable in nearly all patients and clinical settings, and is robust in the presence of the most commonly used anesthetic and sedative agents.2

Development
The development of the BIS Index was driven by a persistent quest for accuracy and clinical utility. The development cycle took nearly 10 years of effort, and required an investment of more than $50 million before a commercial product was brought to market. As a novel technology, the BIS Index required not only validation of principle, but was then subject to rigorous clinical trials to ensure beneficial clinical outcomes during routine use.3-6 The BIS Index has met these challenges in the development and validation process, and after experience with over 6 million patients, it has been proven both practical and useful in clinical care. This proven performance has been followed by rapid global adoption, and utilization of BIS monitoring is having a large positive impact on patient outcomes.

Clinical Benefits
BIS monitoring supports three key elements of anesthesia care:

- Vigilance
- Diagnostic decision-making
- Therapeutic targeting

Vigilance is a cornerstone of anesthesia care, and BIS technology is the first practical neurophysiological monitoring system that provides continuous documentation of central nervous system depression during anesthesia. As such, it functions as an early indicator of changes in brain effect due to anesthetic dosing and delivery.7 BIS monitoring can help answer the question: “Is my patient adequately anesthetized?”
In the operating room, dramatic changes in blood pressure and heart rate are not infrequent and require the anesthesia provider to make rapid diagnostic assessments and timely interventions. BIS monitoring provides new data that can facilitate decision-making and management techniques in many of these situations. BIS monitoring is not a substitute for keen clinical judgment. However, using BIS information as part of their assessment, clinicians can make more informed decisions about the dosing and balance of anesthetic agents and other adjuvant therapies such as analgesics, epidural anesthesia and cardioactive agents, especially in patients at increased risk.

Therapeutic targeting is a clear benefit that results from BIS monitoring. Using this new parameter, the clinician can manage patients within the optimal plane of anesthesia effect, reducing the unwanted occurrence of excessive or inadequate anesthetic effect. Clinical investigations of BIS monitoring during anesthesia have consistently demonstrated an average 25% reduction in intraoperative anesthetic use and a consistent reduction in the time for emergence from general anesthesia. With BIS technology, the question – “Am I overdosing my patient?” – is often quite easy to answer.

Emerging data suggests that subtle differences in anesthetic effect may be associated with patient outcomes days, weeks and even months after surgery. This type of long-term perspective, assessing the impact of anesthesia management, may broaden the scope of positive patient outcomes associated with BIS monitoring beyond the immediate perioperative period.

The use of BIS monitoring is also emerging from a strictly perioperative environment to other clinical areas where sedative use is common. Recent investigations of its use in ICU sedation have demonstrated benefits similar to those achieved in anesthesia care as measured by improvement in drug utilization, improved sedation quality and improved patient outcomes. In clinical research studies, BIS monitoring has also shown early promise as a tool to improve sedation protocols used in areas such as endoscopy and radiology suites, office-based facilities and emergency departments.

**The Clinician’s Guide**

This handbook provides comprehensive information about BIS technology – its ability to refine anesthesia management and its use in clinical practice. The Guide begins with a discussion of brain status monitoring and its evolution into the novel analysis that produced the BIS Index. The handbook continues with a detailed discussion of the integration of this new tool into clinical anesthesia practice, as well as discussion of the use of BIS monitoring in a variety of clinical scenarios. A presentation of special circumstances and evolving applications follow. The appendix offers an easy-to-use quick reference for use of the BIS monitoring system in clinical practice.
REFERENCES


CHAPTER 2: 

**Brain Monitoring with BIS: Technology & Validation**

Since its introduction in 1996, the BIS Index has steadily gained clinical acceptance as a reliable measure of the effects of anesthesia and sedation on the brain. Understandably, many anesthesia providers are curious about the scientific foundation and validation of BIS technology. What exactly is the BIS Index? How is it calculated? Why is it a trustworthy parameter of patient status and anesthetic effect?

**Background**

There is ample evidence that hemodynamic parameters such as blood pressure and heart rate lack acceptable correlation to the adequacy of the anesthetic state, leaving the clinician to infer the state of consciousness from an assessment of cardiovascular system reactivity. A reliable technology that would allow the clinician to monitor brain status directly during anesthesia would greatly assist in patient management. Such a technology would provide a direct measurement of the hypnotic effect of the agent(s) used – reflecting the state of consciousness, level of awareness and ability for memory formation.

**Brain Status Monitoring: EEG-Based Technology**

At the core of brain monitoring technology is the surface electroencephalogram (EEG). This complex physiologic signal is a waveform that represents the sum of all brain activity produced by the cerebral cortex. The normal waveform is notable for two characteristics:

- Small amplitude (20-200 microvolts)
- Variable frequency (0-50 Hz)

![Complex EEG waveform](image)

**Figure 1: Complex EEG waveform**

Waveform is typically analyzed using measures of waveform amplitude (microvolts) and frequency (cycles/second – Hz).
It has been known for decades that the EEG changes in response to the effects of anesthetic and sedative/hypnotic agents. Although individual drugs can induce some unique effects on the EEG, the overall pattern of changes is quite similar for many of these agents. As seen in Figure 2, during general anesthesia, typical EEG changes include:

- An increase in average amplitude (power)
- A decrease in average frequency

These changes become more evident as the EEG waveform frequency patterns move from Beta to Delta – the pattern consistent with deep anesthesia.

The complex EEG waveform can be broken down into its individual components. This data can then be analyzed using a technique called power spectral analysis and displayed as power per frequency component in a “power spectrum” (Figure 3). Power spectral analysis can result in one or more numeric descriptors known as processed EEG parameters.

**Processed EEG Parameters**

Many attempts have been made to utilize power spectral analysis and processed EEG parameters to gauge the effect of anesthesia on the brain. Processed EEG parameters that have been investigated as indicators of anesthetic effects include:

- 95% spectral edge frequency
- Median frequency
- Relative delta power
These parameters are various characteristics that describe the EEG power spectrum. Median frequency and 95% spectral edge frequency (Figure 3) indicate the spectral frequency below which contains either 50% or 95% of the power in the EEG.

Relative delta power describes the percentage of EEG power in the delta band range (0.5-3.5 Hz) relative to the power over the entire EEG frequency spectrum.

Unfortunately, for most anesthetic drugs, the relationship between dosage and changes in EEG power and frequency is not straightforward, so it has been difficult to use traditional processed EEG parameters in a clinically reliable way. A clear challenge for further adoption of the EEG as a reliable indicator of anesthetic effect was to overcome the lack of adequate correlation between anesthetic dose and processed EEG parameters derived from power spectral analysis. With the development of a novel waveform analysis technique, the challenge of using a processed EEG parameter to successfully monitor brain status during anesthesia and sedation has been met.

**THE BIS INDEX – A CLINICALLY-VALIDATED PROCESSED EEG PARAMETER**

The BIS Index is a numerical processed, clinically-validated EEG parameter. Unlike traditional processed EEG parameters derived from power spectral analysis, the BIS Index is derived utilizing a composite of multiple advanced EEG signal processing techniques – including bispectral analysis, power spectral analysis, and time domain analysis. These components were combined to optimize the correlation between the EEG and the clinical effects of anesthesia.

In 1996, the U.S. Food and Drug Administration cleared the BIS Index as an aid in monitoring the hypnotic effect of anesthetics and sedatives. This important milestone was the culmination of the refined application of technology to analysis of the EEG signal within the clinical context of anesthesia and sedation. The BIS Index remains the most clinically-validated form of consciousness monitoring with robust applications across a broad range of anesthetic agents and techniques, and demonstrates validity in nearly all patients. As a result, the BIS Index has emerged as an important tool for anesthesia management.
There are three key elements integral to the BIS technology in monitoring brain status during anesthesia:

- Bispectral Analysis
- BIS Algorithm
- BIS Index

**Bispectral Analysis**
A portion of the cortical EEG reflects changes attributable to harmonic and phase relationships between cortical and subcortical neural generators. These relationships are altered during hypnosis, producing characteristic patterns in the EEG.

Bispectral analysis – and its results, e.g., bicoherence, bispectrum, real triple product – is a sophisticated signal processing methodology that assesses relationships among signal components and captures synchronization within signals like the EEG. By quantifying the correlation between all the frequencies within the signal, bispectral analysis (together with power spectral and cortical EEG analysis) yields an additional EEG descriptor of brain activity during hypnosis.4

**BIS Algorithm**
A key objective in the development of a brain status monitoring technology was to identify EEG features or “descriptors” – bispectral or otherwise – which were highly correlated with sedation/hypnosis induced by the most commonly used anesthetic agents. During development of the BIS Index, these features were identified by analyzing a database of EEGs from more than 5,000 subjects who had received one or more of the most commonly used hypnotic agents and who had been evaluated with simultaneous sedation assessment (Figure 4).5

![Figure 4: BIS algorithm development process –](image)
The key EEG features identified from the database analysis characterized the full spectrum of anesthetic-induced changes and included:

- Degree of beta or high frequency (14-30 Hz) activation
- Amount of low frequency synchronization
- Presence of nearly suppressed periods within the EEG
- Presence of fully suppressed (i.e. isoelectric, “flat line”) periods within the EEG

Multivariate statistical models were used to derive the optimum combination of these EEG features to correlate with clinical endpoints of sedation. From this iterative process, the BIS algorithm that would yield a clinically-tuned, valid processed EEG parameter was developed (Figure 5).

Empirical and statistically-derived, the BIS algorithm is the element within the BIS monitoring system that integrates and combines the EEG features, ensuring accurate interpretation of the EEG signal. This provides a reliable new processed EEG parameter of anesthetic and sedative effect – the BIS Index.

![Figure 5: Schematic diagram of signal processing paths integral to generating a single BIS Index value – Original EEG epochs (following digitization and artifact processing) undergo three primary paths of analysis – Power Spectral Analysis, Bispectral Analysis, and Time-Based Analysis for Suppression/Near-Suppression – to look for key EEG features. The BIS Algorithm, based upon statistical modeling, combines the contribution of each of the identified features to generate the scaled BIS Index.](image)
The BIS Index

The BIS Index is a number between 0 and 100 scaled to correlate with important clinical endpoints during administration of anesthetic agent (Figure 6). BIS values near 100 represent an “awake” clinical state while 0 denotes the maximal EEG effect possible (i.e., an isoelectric EEG).

As the BIS Index value decreases below 70, the probability of explicit recall decreases dramatically. At a BIS Index value of less than 60, a patient has an extremely low probability of consciousness. BIS Index values lower than 40 signify a greater effect of the anesthetic on the EEG. At low BIS values, the degree of EEG suppression is the primary determinant of the BIS value. Prospective clinical trials have demonstrated that maintaining BIS Index values in the range of 40-60 ensures adequate hypnotic effect during general anesthesia while improving the recovery process. During sedation care, BIS Index values > 70 may be observed during adequate levels of sedation but may have a greater probability of consciousness and potential for recall.

The BIS Index provides a direct measurement of brain status, not the concentration of a particular drug. For example, BIS Index values decrease during natural sleep as well as during administration of an anesthetic agent. The decrease produced during the natural process of sleep, however, is not to the degree caused by high doses of propofol, thiopental or volatile anesthetics.

The BIS Index values reflect the reduced cerebral metabolic rate produced by most hypnotics. Using positron emission tomography, a significant correlation between BIS Index values and reduction in whole brain metabolic activity was measured (Figure 7).

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**Figure 6: BIS Index range guidelines**
The BIS Index is a scale from 100 (Awake, responsive to normal voice) to 0 (Representing an isoelectric, flat line EEG). The illustration includes important clinical or EEG milestones that are observed between these two ends of the scale range.

**Figure 7: Correlation of BIS with brain metabolic activity**
Significant correlation is seen between decreasing brain metabolic rate (%BMR = percent of initial whole-brain glucose metabolism measured from PET scan) and increasing anesthetic effect (as measured by decreasing BIS value). [Adapted from Reference 9]
**Validation of the BIS Index**

The accuracy of the BIS Index in assessing hypnotic drug effect on level of consciousness has been validated in a number of studies. These studies investigated:

- Transition into unconsciousness
- Recovery of consciousness
- Consistency of performance

**Assessing the BIS Index in Transition into Unconsciousness**

In a key investigation utilizing common anesthetic agents and combinations (propofol, midazolam, isoflurane, midazolam-alfentanil, propofol-alfentanil, and propofol-nitrous oxide), simultaneous measurements of the BIS Index and assessment of sedation state were obtained.\(^{10}\) In Figure 8, logistic regression curves display the probability of response to voice and the probability of free recall as a function of BIS Index for all agents tested. The overall sigmoid shape of the curve indicates that the BIS Index proved to be a good indicator of hypnotic state. The BIS Index performed as well as (or better than) measured or targeted drug concentration as an indicator of the hypnotic state.

Free recall of word or picture cues is lost when the BIS Index decreases to the 70-75 range, indicating that memory impairment occurs at higher BIS Index values than loss of consciousness. Further investigation has suggested that some memory function – i.e., “learning” memory formation without conscious recall – may occur at lower BIS Index values.\(^{11,12}\)

![Figure 8: BIS response curves showing the probability of measures of consciousness and memory function as BIS decreases – Logistic regression curves demonstrate a sharp reduction in responsiveness (solid line) as BIS decreases below 75. Of note, memory function – assessed by measures of explicit recall (dotted line) – is significantly reduced at BIS values greater than those associated with loss of consciousness. [Adapted from Reference 10]]
This early data has been supported by subsequent investigations that tested the ability of the BIS Index to accurately predict the state of consciousness. In a recent study, the BIS Index had significantly higher prediction probability for level of consciousness when compared to the traditional hemodynamic values of blood pressure and heart rate. More importantly, in this study of volunteers during propofol anesthesia, a BIS Index threshold value of 60 achieved a sensitivity of 99% and a specificity of 81% to predict responsiveness to verbal command, indicative of the accuracy of the BIS Index in the assessment of unconsciousness.

Taken together, these studies support the accuracy of the BIS Index as a measure of hypnotic state. In particular, they validate the ability of the BIS Index to determine the transition into unconsciousness.

Assessing the BIS Index in Recovery of Consciousness

During anesthesia care, a key imperative is the maintenance of unconsciousness. In this role, the BIS Index has been studied as a indicator of the recovery of consciousness.

Using the isolated forearm technique, accuracy of BIS Index monitoring to predict the return to consciousness following induction of anesthesia was investigated (Figure 9). After a single bolus dose of propofol or thiopental, patients were assessed for consciousness at intervals by asking them to squeeze the investigator’s fingers, and the BIS Index was monitored continuously. Although the intensity and duration of hypnotic effect varied considerably among patients, the recovery of consciousness occurred consistently at a BIS Index value above 60. A BIS Index value < 65 indicated a probability of < 5% that consciousness would return within 50 seconds. Changes in blood pressure and heart rate, in contrast, were poor predictors for the recovery of consciousness.

Despite the response to verbal command, no patient had recall of the episode, thereby confirming the difference in BIS Index values observed for consciousness/responsiveness and the higher BIS Index ranges where free recall was impaired. In addition, this study further validated that a BIS Index value below 60 is an excellent indicator that a patient is unconscious and will have a low probability of free recall.

![Figure 9: Changes in BIS and hemodynamic parameters after induction of anesthesia to produce unconsciousness followed by spontaneous return of consciousness – BIS patterns were more predictive than the hemodynamic measures. [Adapted from Reference 1]]
Assessing Consistency of BIS Index Performance

Crucial to the value of the BIS Index in monitoring brain status is consistency of performance with different anesthetic agents and different patient populations. This consistency is extremely important to anesthesia providers because of the broad range of agents utilized and patient variability.

The consistency of the relationship between the BIS Index value and brain status was tested for the following variables:

- Hypnotic agent
- Patient age

**BIS Index/Hypnotic Agent Relationship**

In the validation studies mentioned earlier, the relationship between the BIS Index and level of clinical response was nearly identical for all hypnotic agents tested or when two anesthetic drugs are combined (Figure 10).\(^{10,14,15}\) Furthermore, during steady state conditions of anesthesia or sedation, the BIS Index is a stable measurement of hypnotic effect and does not vary significantly over time.

**BIS Index/Patient Age Relationship**

Patient age is a strong determinant of the anesthetic dose required to produce a clinical effect. For example, the MAC values for inhalation agents decrease as patient age increases.

In a study of the influence of age on hypnotic dose requirements, the dose of sevoflurane required to achieve hypnotic effect differed markedly among different age groups, and showed the expected decrease in dose required with increasing age (Figure 11A).\(^{16}\)
The BIS Index value displayed a consistent relationship to the sedative effects of sevoflurane across this wide range of age groups — unrelated to dosage (Figure 11B).\textsuperscript{16} Thus, the BIS Index offers a distinct advantage over anesthetic dose monitoring as a tool to measure and manage depth of sedation.

At the other extreme of age, the validation of the BIS Index has been more challenging because of limitations in the ability of an infant or child to respond to sedation scoring scales. As a result, unlike in adult patients or volunteers, there have been no direct comparisons of the BIS Index and a graded sedation scale in pediatric volunteers. However, several clinical studies have explored the relationship between anesthetic dose and the BIS Index value in pediatric patients (Figure 12).\textsuperscript{17,18,19} With multiple measures in each child, a consistent dose-response relationship between the BIS Index value and sevoflurane dose was observed in both age groups.\textsuperscript{17}

\section*{Dynamic Factors Affecting the BIS Index}

The BIS Index value is derived from the preceding 15-30 sec of EEG data. As such, it is a measure of the state immediately prior to the calculation. A similar analogy would be the data provided by pulse oximetry during management of a difficult airway. There is an expected delay in oxygen saturation that results from physiologic processes, and airway difficulty may be clearly evident prior to any changes in saturation. Similarly, increases in saturation will lag behind the restitution of adequate ventilation and oxygenation of the lungs.
Under steady-state conditions (e.g., in a controlled research trial), a BIS Index value predicts subsequent responses to voice command or memory for words. However, the clinical situation during surgery is notably different because of the lack of steady-state conditions. Intraoperative BIS Index values will depend upon a number of variables including:

- Brain concentration of anesthetic
- Level of analgesia
- Surgical stimulation

It must be recognized that brain state, as measured by the BIS Index, changes as a result of these dynamic variables. Nevertheless, the BIS Index is a highly accurate measure of the net effect and responses of the brain to new conditions. It is unable, however, to predict future changes. The effect of these factors and other variables that may influence the BIS Index will be discussed in detail in subsequent chapters.

**SUMMARY**

BIS technology – easy, clinically relevant and useful EEG interpretation – enables practical brain status monitoring. The BIS Index is not just a number. Rather, it is a unique, clinically-validated parameter that allows the clinician to trend changes in the hypnotic state during a case. As seen in Figure 13, during induction, maintenance and emergence, it highlights the important transitions in consciousness and provides valuable patient management data.

![Figure 13: The BIS Index trend during a one-hour surgical procedure conducted with general anesthesia –
During the induction period the rapid decline in BIS parallels the rapid transition from consciousness to unconsciousness. During emergence, the increase in BIS heralds the return to consciousness.](image)

The following chapter provides information about the BIS system and its components.
REFERENCES


The previous chapter reviewed the fundamentals of the BIS Index and its validation as an accurate measure of anesthetic effect. This chapter will present the technology required to allow the continuous monitoring of brain status during anesthesia and sedation using the BIS Index.

**BIS System Components**

The BIS system is comprised of five components (Table 1):

- BIS sensor
- Patient interface cable (PIC)
- Digital signal converter (DSC)
- BIS engine
- Display monitor

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**Table 1: BIS System Components**

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<th>Component</th>
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<td>Captures Raw EEG</td>
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<tr>
<td>Patient Interface Cable</td>
<td>Transmits Raw EEG Signal</td>
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<tr>
<td>Digital Signal Converter</td>
<td>Processes Raw EEG Filters Artifact</td>
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<tr>
<td>BIS Engine</td>
<td>Analyzes EEG Signal Calculates BIS Index Value</td>
</tr>
<tr>
<td>Display Monitor</td>
<td>Displays BIS Index Value Displays Additional Parameters Including SQI, EMG, SR, EEG</td>
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**BIS Sensor**
The BIS sensor is a sophisticated electrode system specifically designed to work with BIS systems. A family of sensors tailored to different clinical applications or different patient sizes is available (Figure 1).

After minimal skin preparation, the single-use sensor is placed on the forehead of the patient with a specific orientation over either the left or right hemisphere. Advanced electrode technology results in low impedance values, allowing reliable capture of raw EEG data and increasing the fidelity of the EEG signal.

BIS systems routinely test sensor impedance to ensure acceptable sensor performance during clinical monitoring.

**Patient Interface Cable (PIC)**
The raw EEG is transmitted from the sensor through the patient interface cable (Figure 2) to the digital signal converter.

**Digital Signal Converter (DSC)**
The digital signal converter (Figure 3) receives, amplifies and digitizes the raw EEG signal for subsequent processing and analysis. In addition, key filters and signal processing steps occur in the DSC to identify and reject certain types of electrical artifact (e.g., electrocautery filters in DSC-XP systems).

The digitized EEG data travels through the DSC cable to the BIS engine.
**BIS Engine**

The BIS engine, the heart of the BIS system, contains the microprocessor responsible for rapid signal processing and computation of the BIS Index.

Some of the steps involved in the analysis of the EEG include multiple methods of artifact detection and processing. Segments of the EEG that are compromised by the presence of artifact are not included in the calculation of the BIS Index.

The BIS Index is made by combining selected EEG features using the BIS algorithm described in Chapter 2. All BIS values are updated every second but reflect a smoothing function set at either 15 or 30 seconds to minimize excessive fluctuations.

**Display Monitor**

All BIS systems are linked to display monitors – either stand-alone BIS monitors (Figure 4) or integrated multiparameter monitors. Common to all display systems is the ability to display a BIS value, BIS trends and important additional data including:

- Signal quality index (SQI)
- Electromyogram/
  High-frequency activity (EMG)
- Suppression ratio (SR)
- EEG waveforms

Signal quality index (SQI) and electromyogram/high-frequency activity (EMG) may be displayed in graphic or digital mode. Suppression ratio (SR) is also available. Details regarding these parameters are discussed in Chapter 8. Finally, EEG waveforms may be displayed on the monitor in real-time.

The display monitor also coordinates a variety of communication alerts and alarms.
CHAPTER 4: USING BIS INDEX MONITORING IN ANESTHESIA PRACTICE

As a clinically-validated, accurate measure of anesthetic effect, the BIS Index adds a new dimension to patient monitoring during anesthesia and sedation. This chapter will discuss how BIS monitoring complements other forms of monitoring and describe how this technology can be used most effectively during all phases of anesthesia care.

INTRODUCTION

Anesthesia practice is one of the safest medical specialties. However, despite significant advances in patient monitoring techniques, most clinicians would agree that patient responses to anesthesia are frequently unpredictable and precise dosing of anesthetics and sedatives remains a challenge.

Much of the uncertainty in anesthesia centers on the fundamental concern of “adequacy of anesthesia.” This concern is justified since the hemodynamic parameters traditionally used to infer adequacy of anesthetic effect have been shown to be unreliable indicators of brain status. Clinical judgment and experience remain the cornerstones for managing uncertainty, and BIS Index monitoring provides valuable additional data that enhances such judgement.

The BIS Index provides a direct measurement of the hypnotic effect of the agent, allowing continuous monitoring of brain activity during anesthesia and sedation. Using this new technology for brain status monitoring substantially facilitates:

- Intraoperative patient assessment
- Dosing and balance of anesthetic agents
- Titration of anesthetic agents
- Patient recovery process
BIS Index monitoring can allow delivery of anesthesia care that is safer, more precise and more pleasant for the patient. Used in combination with assessment of clinical signs and traditional monitoring, BIS monitoring can facilitate balanced hypnotic and analgesic administration, ensuring adequacy of anesthesia. This chapter will demonstrate how BIS monitoring can improve patient safety and comfort by enhancing the quality of anesthesia care in day-to-day anesthesia practice.

**BIS Index Monitoring – Complementing Hemodynamic Indicator Assessment**

As noted in Chapter 2, heart rate and blood pressure are not sensitive to changing levels of consciousness. Consequently, the patient’s hypnotic state cannot be accurately inferred from changes in these vital signs (Figure 1).¹ For example, administration of cardiovascular agents will change blood pressure and/or heart rate, typically without affecting anesthetic depth. A variety of anesthetic adjuvants such as neuromuscular blocking agents, reversal agents, and local anesthetics may have an effect on both cardiovascular reactivity and the anesthetic state but without a direct correlation between the two. Finally, changing levels of surgical stimulation may impact hemodynamics or level of consciousness independently.

Given the shortcomings of using hemodynamics to infer brain state, BIS monitoring can bring unique information to the operating room. BIS monitoring allows anesthesia providers to titrate anesthetics precisely to achieve the desired hypnotic effect while avoiding excessive dosing that can lead to unwanted adverse effects.

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**Considerations in Hemodynamic Monitoring**

Traditional vital signs provide a measure of cardiovascular responses to anesthesia administration and surgical stimulation. While changes in blood pressure and heart rate may correlate with the anesthetic effect in some instances, many factors can interfere with this relationship including:

- **Interaction of multiple anesthetic agents**
- **Unexpected synergistic drug effects**
- **Patient cardiovascular status**
- **Medications that attenuate cardiovascular responses (e.g. antihypertensives)**

Anesthetic dosing which ensures adequacy of anesthesia may produce hemodynamic changes close to acceptable limits of cardiovascular response. This approach is further complicated by the difficulty of measuring the therapeutic window in some patients. In these cases, the anesthesia provider may be unable to discriminate between the dose required to achieve the therapeutic effect (i.e., unconsciousness) and the dose producing undesired cardiovascular effects.
BIS Index Monitoring – Complementing Anesthetic Agent Measurement

Anesthetic agent concentration measurement systems (e.g., end-tidal agent concentration) do not measure anesthetic effect on the target organ, the brain. Thus, these systems cannot identify alterations in expected levels of hypnosis due to pharmacodynamic variability among patients. Rather, the existence of this variability means that identical drug concentrations commonly produce considerably different hypnotic responses among individuals or within the same person at different times.

BIS monitoring continually measures the hypnotic effects of administered anesthetic doses, regardless of pharmacokinetic or pharmacodynamic variability. Using BIS values and responses as a guide allows the anesthesia provider to administer a particular anesthetic agent at the dose required to achieve the desired hypnotic effect in the individual patient.

Figure 1: Brain monitoring with BIS: CNS vs. cardiovascular reactivity during isoflurane and sevoflurane anesthesia – BIS demonstrated a consistent response while a clear agent-based difference was seen with hemodynamic parameters. [Adapted from Reference 1]

Considerations in Anesthetic Agent Measurement

Measurement of end-tidal inhalation agent concentration is an effective method of confirming agent delivery and assessing anesthetic uptake and distribution. The utilization of target plasma concentration systems has also improved the precision of intravenous anesthesia techniques.

Empiric-dosing regimens to maintain end-tidal agent concentration at certain values (e.g., greater than MAC_{awake}) provide useful guidelines during anesthesia care. However, anesthetic dosing using only this measurement does not necessarily consider:

- Known impact of age, gender or metabolic rate on anesthetic requirement
- Individual responses and sensitivity to an agent
- Synergistic interactions among multiple anesthetic agents
- Impact of co-existing disease, or pre-existing alcohol/drug dependence
- Changing requirement due to varying levels of surgical stimulation
BIS Monitoring During Typical General Anesthesia

A “typical” general anesthetic case involves three phases:

- induction of anesthesia (and typically airway management)
- maintenance of anesthesia
- emergence from anesthesia

Monitoring BIS during all phases of anesthesia can assist in evaluating a patient’s current status, and will provide a continuous indicator of the hypnotic state.

Overview: The BIS Trend

As noted in Chapter 3, the BIS system displays a graphical trend – the BIS trend (Figure 2) – which represents the ongoing calculations of the BIS Index during the case. The BIS value itself is displayed as a single value which is calculated from data gathered over the last 15-30 seconds of EEG recording and updated every second. Deriving the BIS Index value from several seconds of EEG data effectively “smooths” the data to prevent excessive fluctuations in BIS values and allows a value to be determined even if the EEG signal is briefly interrupted. When abrupt changes occur in hypnotic state – for example, during induction or rapid emergence – the BIS value may lag behind the observed clinical change by approximately 5 to 10 seconds. A BIS value, while extremely responsive, is not instantaneously altered by changes in clinical status.

Monitoring the BIS trend is particularly useful during surgery. Changing anesthetic dosing to lighten or deepen anesthesia will usually manifest as a slow upward or downward trend, respectively. As seen in Figure 3, for example, a small bolus of propofol will be displayed as a short-lived downward dip in the BIS trend. In contrast, a cortical response caused by intense surgical stimulation is often signaled by large, abrupt increases in the BIS trend. This latter trend change is most likely to occur when the anesthetic technique relies heavily on hypnotic agents but includes little or no opioid analgesia.

Figure 2: BIS trend during a typical general anesthesia procedure

Figure 3: A BIS Index trend showing 2 examples of changes in brain state in response to changing anesthetic and surgical conditions – Administration of a small dose of propofol produces a transient decrease in BIS. Following a period of increased surgical stimulation, the BIS trend displays a “pop” lasting a few minutes.
As noted previously, clinicians should be cautious about using a particular BIS value in isolation as a predictor of patient responsiveness, because arousal responses to pain are not well-correlated with absolute hypnotic effect. However, BIS monitoring will document the cortical EEG reactivity responses associated with stimulation. Further, even allowing for the delay associated with signal processing, surgical stimulation can sometimes produce a rapid increase in BIS values prior to the appearance of other clinical signs such as hypertension or movement, facilitating more timely anesthesia management.

Cyclic oscillation in BIS under steady state conditions may provide an indication of the shifting balance between sensory suppression and sensory stimulation. In volunteer studies, greater BIS variability was observed when sedatives were used alone compared to when alfentanil was used concurrently.

**BIS During The Induction of Anesthesia**

Induction of anesthesia may have individualized goals that are case-specific or patient-specific. In general, however, the overall goal of induction is to produce unconsciousness rapidly, manage the airway in the unconscious patient, and establish adequate anesthesia conditions for surgery. The most common forms of controlling the airway include:

- Endotracheal intubation
- Insertion of a laryngeal mask airway (LMA)

In each of these situations, the production of certain anesthetic conditions related to the airway are ideal, and BIS monitoring can assist the clinician to achieve those conditions.

As seen in Figure 4, the BIS Index trend clearly displays the effects of anesthesia induction in a patient undergoing hernia repair. Close inspection of the left portion of the trend demonstrates rapid decrease of the BIS Index during induction using bolus administration of intravenous hypnotic in preparation for endotracheal intubation.
**BIS Monitoring During Endotracheal Intubation**

During endotracheal intubation, one general goal of the anesthesia provider is to minimize cardiovascular stimulation, thus preventing resultant hypertension and tachycardia. Several strategies are commonly used to blunt the blood pressure and heart rate response including:

- Sufficient dosing of intravenous induction agent (e.g., propofol, thiopental)
- Opioid supplementation (e.g., fentanyl)
- Administration of intravenous or tracheal lidocaine
- Administration of antihypertensives (e.g., esmolol)
- Alternative intubation methods (e.g., fiberoptic intubation)

With the use of these concomitant medications, however, the potential for hypotension during the induction period may also increase.

Several studies have examined the BIS responses during endotracheal intubation to better understand the relationship between cortical CNS and cardiovascular responses. Quite often, a transient increase in BIS value (ΔBIS) can be observed following tracheal intubation or other stimulation. Studies have demonstrated that BIS responses do not directly correlate with the change in blood pressure following laryngoscopy and intubation. Patients with controlled hypertension have demonstrated an exaggerated blood pressure response, while their BIS response was no different than normotensive individuals (Figure 5).

![Figure 5: BIS and mean arterial blood pressure responses to a standardized induction and intubation regimen –](image)

*Of note, patients with well-controlled hypertension demonstrate an exaggerated increase in blood pressure not linked to a different anesthetic response as measured by BIS. [Adapted from Reference 6]*
BIS responses to stimulation associated with laryngoscopy and intubation can be markedly attenuated in a dose-dependent fashion with opioid administration, e.g., fentanyl or remifentanil (Figure 6). In a study focusing on induction of anesthesia in cardiac surgical patients, induction dosing of midazolam and sufentanil was targeted to several BIS values. Targeting the induction to a BIS value of 50 was shown to produce the most stable induction/intubation characteristics. It should be noted that a single BIS value during the induction period is unable to predict subsequent BIS responses to significant stimulation. For example, in one study examining hemodynamic, BIS and awareness responses, BIS values less than 60 prior to intubation did not guarantee a lack of arousal responses following laryngoscopy and intubation. This study did note that BIS Index was an accurate indicator of current clinical state: arousal responses were observed only in patients with high BIS values.

In other settings, particularly in elderly patients or inpatients with significant coexisting illness, a gentle induction technique is sometimes used to minimize perturbation of blood pressure and heart rate. This can be achieved with smaller and/or divided dose administration of induction agent or with low-dose administration of an inhalation agent. During this method of induction, BIS monitoring can measure achievement of the desired hypnotic effect from the various induction protocols.
Clinical Perspective: Unanticipated Difficult Airway

Patient: 58 year-old male, ASA II
Procedure: Intramedullary rodding of femur fracture
Management: Routine monitoring including BIS monitoring

Anesthesia:
  Premedication: Midazolam 2 mg
  Induction Sequence:
   – Fentanyl 150 mcg, propofol 200 mg; BIS noted to be 25
   – Cisatracurium 10 mg after mask ventilation established
   – Difficult laryngoscopy with poor view of cords during three attempts at intubation
   – Ventilation with 100% oxygen via mask
   – Elapsed time 5-6 minutes after initial propofol
     – BP 130/80; HR 84; BIS noted to be 80
   – 50 mg additional propofol given
   – BIS decreased to 40; successful intubation
  Maintenance:
   – Uneventful with isoflurane, N₂O/O₂, hydromorphone
  Recovery:
   – Extubation and immediate postoperative course uneventful
   – Recall limited to arrival at operating room

Discussion

Difficulty with ventilation or intubation are common reasons for the normal sequence of induction to be prolonged. In this case, both the premedication and the initial dose of propofol were generous. However, the 2-3 minute onset of cisatracurium and the prolonged intubation allowed sufficient time for substantial redistribution of the propofol. The anesthetist was appropriately focused on airway management, and supplemental propofol or volatile anesthetic was not being administered during this time.

Routine scanning of the monitors prior to the last intubation attempt showed hemodynamic parameter stability with heart rate and blood pressure readings within normal limits. However, time-linked redistribution of propofol was easily detected by observation of the high BIS value, alerting the provider of the need for more anesthetic. The postoperative visit included questions about the patient’s memory of intraoperative events. He had no memory of intubation, indicating an adequate level of hypnosis was achieved via BIS-titrated propofol administration.

Carl Rosow, M.D.
**BIS Monitoring During LMA Insertion**

In cases involving use of an LMA for airway management, many anesthesia providers aim to limit the period of apnea associated with induction in order to avoid the need for positive pressure ventilation. By observing the BIS trend during initial bolus dosing or incremental injections of an induction agent, the anesthesia provider can adjust dosing to produce unconsciousness while minimizing the likelihood of prolonged apnea. While the BIS trend alone cannot indicate that optimal conditions are present for LMA insertion, BIS monitoring can assist the anesthesia provider in assessing and achieving desired airway management conditions.

**BIS During the Maintenance of Anesthesia**

In most surgical cases, the “maintenance” phase of anesthesia care is the longest. During this intraoperative period, anesthesia care focuses on:

- Maintenance of an adequate anesthetic state
- Maintenance of physiologic homeostasis during surgical events
- Avoidance of potential adverse events
- Preparation for smooth, rapid emergence

BIS monitoring during anesthesia maintenance can help meet these goals of intraoperative care by providing continuous confirmation of hypnotic effect of the agent – for all classes of anesthetics, under most operative conditions and for nearly all types of patients.

By assessing level of consciousness, BIS monitoring can improve intraoperative decision making. For example, observation of the BIS trend can facilitate diagnostic evaluation of unexpected changes in cardiovascular system reactivity, permitting rapid restoration of homeostasis. BIS monitoring can also guide adjustments in anesthesia care – e.g., the addition of an antihypertensive, or an increase in inhalation anesthetic dose. Using BIS information, the anesthesia provider can independently monitor not only cardiovascular responses but central nervous system – specifically, cortical – responses as well.
Maintenance Strategies Using BIS Monitoring

Two important clinical trials have demonstrated that the adjustment of anesthetic delivery to maintain the BIS Index within a bracketed target range during maintenance has resulted in improved perioperative recovery patterns as compared to standard anesthesia care. These studies and several others have highlighted the positive patient outcomes realized when BIS monitoring is combined with assessment of intraoperative hemodynamic data and clinical observations of movement and autonomic response to generate patient management strategies (Figure 7). BIS data can ensure that the key anesthetic goals of hypnosis and analgesia are met throughout the maintenance phase.

The integration of BIS monitoring with other traditional monitoring creates unique opportunities for patient management. Table 1 on the following page outlines conceptual management strategies based on integration of clinical profile with BIS data for “balanced” anesthesia techniques utilizing hypnotic and analgesic components. Using the BIS value in combination with hemodynamic data improves the rational selection of sedatives, analgesics and autonomic blockers in what can otherwise be very confusing clinical situations.

Although a BIS value of 45-60 is a typical target during the maintenance phase, the BIS value target range needs to be tailored to the anesthetic technique. For example, in cases of balanced anesthesia involving sufficient opioid administration to assure adequate analgesia, the typical target range of 45-60 is most appropriate. However, for anesthesia techniques which utilize little or no opioid or analgesic supplementation, increased dosing of the hypnotic agent – typically, the inhalation anesthetic – to produce acceptable suppression of noxious stimulation will result in lower BIS values, typically in the 25-35 range.
Table 1: Anesthesia Management Strategies Using the BIS Index

* Potential impact of artifact should be considered when interpreting BIS values.
As seen in Figure 8, in a patient undergoing hernia repair, a relatively stable BIS trend results from the titration of sevoflurane during maintenance. However, approximately 45 minutes into the case, the BIS trend demonstrated increased variability. Assessment of that data, in combination with other clinical observations established the need for additional opioid analgesia. Following the administration of additional fentanyl, the BIS variability diminished, reflecting an appropriate level of hypnotic effect.

It is important to note that reliance on BIS monitoring alone for intraoperative anesthetic management is not recommended. Clinical judgment is crucial when interpreting BIS data. Patient assessment should include evaluation and correlation of BIS data with hemodynamic and other monitoring data as well as observation of clinical signs. The BIS value should be thought of as an additional piece of information that must be interpreted in the context of all other information available for patient assessment.

**BIS During Emergence from Anesthesia**

The BIS trend documents the decreasing effect of anesthesia when agent delivery is reduced or stopped and the patient enters the emergence phase. Because BIS monitoring provides a real-time measure of level of consciousness, it allows the anesthesia provider to fine-tune titration downward according to individual patient response. BIS monitoring permits reduction in anesthesia dosing in tandem with the decrease in surgical stimulation, promoting a rapid emergence that avoids premature recovery of consciousness as well as delayed emergence from anesthesia.

As seen in Figure 9, in the patient undergoing hernia repair, emergence was heralded by the rapid increase in the BIS Index. BIS monitoring of brain status documented the decreasing anesthetic effect and the increased level of consciousness which correlated with patient eye opening in response to voice command.
**BIS Monitoring During Challenging Emergence**

BIS Index monitoring can be particularly useful in managing anesthesia care during challenging emergence situations including:

- Neurological surgery
- Unexpected prolonged neuromuscular blockade

After neurological procedures such as complex spinal or intracranial surgery, rapid emergence for neurologic assessment followed by postoperative sedation may be required. BIS monitoring allows appropriate titration of anesthetic effect to optimize timing of the assessment, and then helps to guide delivery of appropriate dosing for postoperative sedation.

In rare situations, failure to “emerge” from anesthesia may be a specific complication of neuromuscular blocking agent administration. In situations of excessive effect of succinylcholine (e.g., pseudocholinesterase variants) or accumulation of non-depolarizing agents (e.g., in renal failure patients), a high BIS value without clinical emergence may be an indicator of potential problems with neuromuscular function. In addition, because the management of prolonged neuromuscular block requires postoperative ventilation and sedation, BIS monitoring can provide guidance during that phase as well.

**Responding to BIS Changes During Anesthesia**

When BIS monitoring is used during anesthesia care, it is necessary to note fluctuations in BIS values. However, such fluctuations, like a single fluctuation in blood pressure, are not necessarily clinically significant. However, in some situations, additional assessment is required in response to changes in BIS values.

Changes in the hypnotic state due to changes in dose and/or patterns of agent delivery will produce changes in the BIS value. Normally, if the change in anesthetic dosing was incremental – e.g., slight adjustment in the vaporizer setting or modest changes in intravenous anesthetic infusion dosing – these changes in BIS values are gradual. In contrast, sudden changes would not be expected and would require confirmation and assessment. Tables 2 and 3 present suggestions for this assessment process. Additional discussion of rare situations that may influence the validity of BIS values can be found in Chapter 6.
Responding to a Sudden BIS Increase

- Examine for the presence of artifacts (EMG, electrocautery or high frequency signals).
  - High frequency artifacts including those listed may contaminate the EEG signal and bias the BIS toward a higher value.

- Ensure that anesthetic delivery systems are operating properly so that the intended dose of anesthetic agent is reaching the patient.
  - Changes in vaporizer setting, fresh-gas flow rates, intravenous infusion pump setting, intravenous delivery routes may account for a sudden change in level of anesthetic effect and the resulting BIS value.

- Ensure that the anesthetic dose is sufficient.
  - An abrupt change in the BIS may reflect a new cortical state relative to anesthetic dosing and changes in surgical conditions.

- Assess the current level of surgical stimulation.
  - The BIS may show a transient increase in response to increases in noxious stimulation.

Table 2: BIS increase/high value assessment
Responding to a Sudden BIS Decrease

- Assess for new pharmacologic changes.  
  Bolus administration of intravenous anesthetic, recent changes in inhalation anesthesia, administration of adjuvant agents (beta blockers, alpha2 agonists) can all result in acute decreases in the BIS.

- Assess the current level of surgical stimulation.  
  The BIS may show a decrease in response to decreases in noxious stimulation.

- Consider decrease as possible response to administration of muscle relaxants.  
  In some situations, the BIS will decrease in response to administration of neuromuscular blocking agent, especially if excessive EMG was present prior to giving it.

- Assess for other potential physiologic changes.  
  Profound hypotension, hypothermia, hypoglycemia or anoxia can produce decreases in the brain state activity.

- Assess for emergence from anesthesia.  
  Paradoxical emergence patterns have been described with transient abrupt decreases in the BIS prior to awakening during inhalation anesthesia. The clinical significance of such changes remains unknown.
The BIS Index and Global CNS Function
Since the introduction of more routine cortical EEG monitoring using BIS technology, a variety of clinical reports have noted anecdotal benefits offered by this form of brain monitoring.\textsuperscript{15,16} Although BIS monitoring is not intended to be used for regional ischemia monitoring – for example, during carotid endarterectomy procedures – the relationship of the EEG and BIS to global CNS function does provide an indication of patient response and tolerance to intraoperative conditions. As such, BIS variations may alert the anesthesia and surgical teams to changes in the patient condition which indicate the need for additional evaluation of brain status, including adequacy of perfusion.\textsuperscript{17,18}

REFERENCES


CHAPTER 5:

CLINICAL APPLICATIONS FOR BIS MONITORING

BIS monitoring, although a relatively new adjunct to anesthesia care, can bring proven utility to virtually all surgical cases. This chapter will explore some of clinical applications during which BIS monitoring is of particular value to both patient and provider during delivery of anesthesia care.

The aging of the population and the transition to outpatient surgical procedures will have a growing impact on anesthesia practice. Given these trends, provision of optimum care for the patients of anesthesia providers will become more challenging.

In compelling clinical studies, BIS monitoring has been shown to improve outcomes following anesthesia care. These outcomes include quantitative and qualitative measures of intraoperative anesthesia care in addition to improved speed and quality of recovery. New studies demonstrate the impact of BIS monitoring in strategies designed to reduce perioperative complications. Using BIS technology to monitor the hypnotic effects independently of the hemodynamic effects of anesthesia allows the anesthesia provider to apply appropriate adjuvant therapies or protective strategies with greater confidence.

The clinical applications for BIS Index monitoring can be broadly categorized as patient-related or case-related. Specifically, the potential indications for use of this new monitoring technology can be listed by:

• Patient profile
• Procedure type
• Anesthesia technique
PATIENT PROFILE

BIS monitoring benefits a broad range of patients undergoing general anesthesia. However, for certain challenging patient profiles, the additional data derived from BIS monitoring can be particularly useful in optimizing anesthesia care. These profiles include:

- Elderly patients
- Medically-compromised patients
- Labile patients
- “At risk” patients
- Pediatric patients
- Trauma patients
- Obese patients
- Patients with organ dysfunction

Elderly Patients

Numerous studies have documented a decreased inhalation anesthetic requirement in elderly patients, a fact that may complicate agent dosing. However, because BIS monitoring can consistently trend hypnotic effects of inhalation anesthetics in adults independent of patient age or hemodynamic compromise, this technology offers particular utility in these cases. Specifically, BIS monitoring can confirm desired hypnotic effects at the lower inhalation anesthetic requirement typical for the elderly population. 
Better Correlation

Study Design:
• 41 patients aged 20-85
• Simultaneous measurements of BIS value and systolic blood pressure changes during increasing doses of propofol administration

Outcome/Conclusions:
• Elderly patients displayed greater sensitivity to hypotensive effects of propofol
• Hypnotic effect of propofol as demonstrated by the rate of BIS Index decrease was not affected by age differences
• Reliability of blood pressure as an indicator of the anesthetic effect of propofol is compromised in older patients


Reducing Drug Use and Improving Recovery

Study Design:
• 68 orthopedic surgery inpatients > 60 years
• Isoflurane/fentanyl general anesthesia
• Titration of the isoflurane to BIS target range of 50-60

Outcome/Conclusions:
• BIS monitoring facilitated a 30% decrease in isoflurane use and 26% decrease in time to orientation.

**Medically-Compromised Patients**

BIS monitoring is often used in the anesthesia care of patients with significant coexisting disease, such as severe cardiopulmonary disease. Studies have demonstrated that BIS monitoring allows reduction in anesthetic agent dose, thus minimizing the risk of dose-related adverse effects.

### Adequate Hypnosis with Hemodynamic Stability

#### Study Design:
- 30 patients with severe left ventricular inoperable coronary artery disease
- Myocardial gene-transfer therapy via mini-thoracotomy
- Fast-track anesthetic: remifentanil, desflurane, intrathecal opioid
- BIS monitoring: Target range 40-65

#### Outcomes/Conclusions:
- Achievement of intraoperative hemodynamic stability
- Achievement of adequate hypnosis confirmed by BIS monitoring with low concentration of desflurane 2-4% in oxygen
- Achievement of rapid emergence and early tracheal extubation

CLINICAL PERSPECTIVE: INDUCTION MANAGEMENT IN A COMPROMISED PATIENT

Patient: 70 year-old female, 89 kg, ASA III
Cardiac Evaluation: EF = 27%, Global hypokinesis;
No focal perfusion defects
Procedure: Lumbar spinal decompression, fusion, instrumentation (L2-L5)
Management: Routine monitoring, radial arterial line, BIS monitoring
Anesthesia Care:
Premedication: Midazolam 2mg – clinically sedated and BIS = 78
Induction Sequence:
Midazolam 2mg /Fentanyl 100mcg – divided doses during preoxygenation
Propofol 50mg – observed BIS response to BIS~40
Rocuronium 40mg to facilitate endotracheal intubation
Esmolol (20mg) and labetalol (2.5mg) in response to BP 165/80
Maintenance: Fentanyl, Desflurane (titrated to BIS 40-55) in Air/Oxygen
Surgical Duration = 5.25 hours; EBL = 600cc; Crystalloid = 3 Liters
Emergence: Positioned supine, muscle relaxants reversed, successful extubation in OR without difficulty.

Discussion:
BIS monitoring in this case, in conjunction with other monitored parameters and clinical signs, was a valued adjunct in assessing patient responses. In the setting of significant cardiac disease and an ejection fraction of 27%, we aimed for a very gradual induction to minimize the potential for hypotension. A moderate dose of opioid was used to decrease the hemodynamic reactivity. This technique permits a reduction in the dose of other hypnotic agents to minimize myocardial depression. In this particular case, BIS monitoring increased our ability to titrate the other induction agents with more assurance of adequate hypnosis.

This case also had multiple points in which expected changes in hypnotic and analgesic requirements occurred including prone positioning, surgical stimulation, supine positioning, relaxant reversal and extubation. In response to situations which required an increase or reduction in anesthetic effect, BIS values helped guide the dosing of our anesthetic. Decreasing the risk of awareness and recognizing impending arousal states were better achieved with the BIS. In addition, the cumulative effect of titration during this case with use of the BIS monitor helped guide our patient to a fast and more predictable emergence after supine positioning.

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Tulane University School of Medicine
Labile Patients

It is difficult to manage the anesthesia care of patients with unstable hemodynamic profiles in the pre- or intraoperative phase of surgery. The anesthesia provider must respond to rapid changes in blood pressure or heart rate while continuing to deliver the dosage of anesthetic agent required for adequate hypnosis.

BIS monitoring provides an opportunity to measure changes in brain status. This provides two benefits in the management of labile patients, such as those undergoing resection of hemodynamically-active tumors. First, it allows the provider to confidently treat alterations in blood pressure or heart rate without compromising level of hypnosis. Second, it permits the provider to determine if alterations in anesthetic dosage correlate with changes in blood pressure or heart rate. Each of these opportunities may improve anesthesia care for these patients.
**“At Risk” Patients**

BIS monitoring allows the anesthesia provider to monitor the hypnotic effect independently of hemodynamic parameters. This provides exceptional benefits for selected patients deemed at increased risk for perioperative cardiac complications, particularly during application of protective strategies.

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**Study Design:**

- 63 elderly “at risk” patients
- BIS-guided general anesthesia – isoflurane and fentanyl
- Adjuvant beta-blockade (atenolol) therapy administered either perioperatively or intraoperatively

**Outcomes/Conclusions (Table 1):**

- Atenolol administration (compared to standard anesthesia care):
  - Improved hemodynamic stability during emergence
  - Reduced incidence of tachycardia in the immediate postoperative period
  - Reduced isoflurane requirements from 0.40% to 0.25% end-tidal concentration
  - No reports of intraoperative awareness
- BIS monitoring confirmed adequate hypnotic effect at the lower isoflurane dosage

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<tr>
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<th>Control</th>
<th>Periop β-Blockade</th>
<th>Intraop β-Blockade</th>
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<tr>
<td><strong>BIS</strong></td>
<td>54±11</td>
<td>53±10</td>
<td>58±2</td>
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<td><strong>Isoflurane (% ET)</strong></td>
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<td>0.43±0.19</td>
<td>0.25±0.07</td>
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<td><strong>Fentanyl (mcg/kg/hr)</strong></td>
<td>1.8±0.5</td>
<td>1.3±0.2</td>
<td>1.3±0.2</td>
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Table 1: BIS monitoring during adjuvant beta-blockade therapy – Adequate hypnosis is confirmed by BIS monitoring at reduced isoflurane dosage allowed by concurrent beta-adrenergic blockade. [Adapted from Reference 8]

Pediatric Patients

As reviewed previously, the BIS algorithm was developed using EEG data from adults and prospectively evaluated in pediatric clinical studies. Experience to date suggests that BIS monitoring in children can yield benefits similar to those achieved in the adult population (Figure 1).

Study Design:

- 54 ASA I patients: tympanoplasty
  - 27 children (3.5-13 years) / 27 adults (22-72 years)
- Sevoflurane induction; maintenance: sevoflurane and alfentanil
- Clinical assessment and BIS values at key milestones

Outcome/Conclusions:

- BIS correlated with the hypnotic component of anesthesia induced by sevoflurane in children and in adults
- BIS values were comparable in children and adults at each time point during the clinical study (Figure 1)


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BIS: Similar Correlation to Clinical Assessment in Pediatric and Adult Patients

Study Design:

- 54 ASA I patients: tympanoplasty
  - 27 children (3.5-13 years) / 27 adults (22-72 years)
- Sevoflurane induction; maintenance: sevoflurane and alfentanil
- Clinical assessment and BIS values at key milestones

Outcome/Conclusions:

- BIS correlated with the hypnotic component of anesthesia induced by sevoflurane in children and in adults
- BIS values were comparable in children and adults at each time point during the clinical study (Figure 1)
**Study Design:**
- 30 preschool children (1-6 years): tonsillectomy and adenoidectomy
- General anesthesia – sevoflurane with 70% N₂O in oxygen
- Simultaneous measurements of BIS, end-tidal sevoflurane, heart rate and mean arterial pressure

**Outcome/Conclusions (Figure 2):**
- Strongest correlation between BIS and ET-Sevo
  - Pharmacodynamic model with ET-Sevo at which BIS=50: 1.48%
- Weak correlation between sevoflurane and blood pressure, nonsignificant correlation with heart rate
- Findings support the utility of using BIS in children aged more than 1 year to titrate sevoflurane and level of consciousness during anesthesia
- Further, study demonstrates that hemodynamic responses do not correspond with BIS and end-tidal sevoflurane concentration

---

**Figure 2: Pediatric dose-response correlation** – The BIS Index demonstrated a consistent dose-response relationship in infants and children as increasing sevoflurane dose resulted in decreasing BIS values. [Adapted from Reference 10]

**Clinical Perspective: Combined Technique in a Pediatric Patient**

Patient: 14 month-old, 12 kg male child, documented ureteral reflux

Procedure: Bilateral ureteral reimplantation

Anesthesia Care:

- Premed: Midazolam 20 mg PO
- Induction: Inhalation with sevoflurane, nitrous oxide, oxygen
- Regional Technique: Received a lumbar epidural once anesthetized
- Maintenance: General anesthesia with isoflurane in air/oxygen mixture
- Epidural: Intermittent bolus dosing with local anesthetic

Case Management:

It was noted very early in the procedure that BIS values were in the 60-70 range. Several incremental boluses of propofol resulted in prompt reduction of BIS. Isoflurane inspired concentration was increased (from 1.2 – 1.8% end tidal) to achieve target BIS values around 60. Hemodynamic stability, and lack of movement suggested adequate epidural analgesia.

Emergence:

At the conclusion of surgery, isoflurane was discontinued, and the child was awake and ready for extubation within 10 minutes (BIS = 85-90).

**Discussion**

My impression was that BIS facilitated the titration of volatile anesthesia in this child. It seems quite accurate to track the maturational changes in anesthetic requirement previously documented in MAC studies. Of particular note, this child is of the age range where MAC is higher than in older children. The rapid emergence from this concentration of isoflurane also seems consistent with an increased anesthetic requirement. BIS monitoring provided a new perspective of assessment during this combined technique.

William Denman, M.D.
**Study Design:**
- 202 patients (infants - children): inguinal hernia repair, tonsillectomy
- General anesthesia – sevoflurane with 60% N₂O in oxygen
- Caudal block in hernia cases
- Titration to BIS values of 40-60

**Outcome/Conclusions:**
- Impact of BIS monitoring differed between infants and children and varied according to procedure type
  - BIS titration during tonsillectomy reduced sevoflurane use and sped emergence and recovery times
  - BIS titration did not improve recovery time in patients undergoing hernia repair with combined technique
  - BIS titration in children < 6 mos resulted in less sevoflurane administration


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**Study Design:**
- Elective circumcision in 25 infants < 1 year and 24 children
- General anesthesia – sevoflurane in air/oxygen
- Supplemented with regional anesthesia (nerve block)
- Arousal testing by response to auditory stimulus during emergence

**Outcome/Conclusions:**
- In children > 1 year in age, BIS values increased in response to decreases in sevoflurane concentration
- In infants < 1 year in age, BIS values remained stable around 60-65 as sevoflurane was decreased from 0.9% to 0.7% to 0.5%
- BIS response to auditory stimulation was very similar for both groups
- Infants may require very small amounts of anesthetic to maintain unconsciousness in the absence of surgical stimulation

Study Design:

- 41 children (2-14 years): elective, non-neurologic surgery
  – 21 normal children, ASA I-II (control group)
  – 20 children quadriplegic cerebral palsy (profound delay, non-verbal)
- Oral midazolam premedication: 0.5 mg/kg to maximum 15mg
- Inhaled induction: 8% sevoflurane in 66% Nitrous Oxide x 60 sec
- Rocuronium administration; endotracheal intubation
- BIS measured at defined endpoints of anesthesia administration

Outcome/Conclusions (Table 2):

- Children with cerebral palsy demonstrated a similar pattern of BIS value change as observed in normal children during sevoflurane anesthesia
- Absolute BIS values for children with cerebral palsy are lower than those in normal children both while awake and at different end-tidal sevoflurane concentrations
- Seizure history and antiseizure medications may have affected BIS values in cerebral palsy children

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<tr>
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<th>Cerebral Palsy Group BIS Values</th>
<th>Control Group BIS Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedated</td>
<td>91.63±8.05</td>
<td>96.79±2.70*</td>
</tr>
<tr>
<td>Sevoflurane 1%</td>
<td>48.55±12.83</td>
<td>53.88±6.89*</td>
</tr>
<tr>
<td>Sevoflurane 2%</td>
<td>30.43±10.33</td>
<td>32.93±8.21</td>
</tr>
<tr>
<td>Emergence</td>
<td>90.73±11.57</td>
<td>96.45±2.27</td>
</tr>
</tbody>
</table>

*p<0.05 between groups

Table 2: Perioperative Data
BIS values were similar in pattern but lower in children with cerebral palsy as compared to normal children [Adapted from Reference 13]

A frequent challenge is the ongoing resuscitation and stabilization of a trauma patient during the administration of general anesthesia. The increased incidence of hemodynamic instability in this population necessitates use of lower concentrations of anesthetic agents. Concurrently, it is crucial that adequate levels of hypnosis are achieved and sustained. Knowledge of the patient’s current brain status combined with the ability to trend responses to changes in intraoperative anesthetic administration facilitate management of this challenging anesthesia care.
CLINICAL PERSPECTIVE: TRAUMA-RELATED HEMODYNAMIC INSTABILITY DURING ANESTHESIA

Patient: 38 year-old male, ASA 1, auto vs. pedestrian accident resulting in an incomplete traumatic amputation of lower extremity. On arrival to the ED, intravenous lines were placed and four units of un-crossmatched O+ pRBCs were transfused (post transfusion HCT: 24%). He was received in the OR awake and alert complaining of 7/10 pain.

Procedure: BKA left lower extremity

Management: Routine monitors, A-line, BIS; large-bore IV access

Resuscitation (in OR, prior to induction):
- BP 70/40, HR 140, \( S_O2 \) 100%, BIS 98
- Four liters of crystalloid; 4 additional units of blood transfused
- BP 106/58, HR 118; BIS 98

General Anesthesia Care:
- Induction: Rapid sequence induction with etomidate/succinylcholine
  - BP 80/50, HR 120-130, BIS 20-30
- Initial ABG: pH 7.218; \( P_{aO2} \) 370; Lactate 6.5; HCT 9.0
- Maintenance: Sevoflurane 0.5 to 0.9 ET% as tolerated; BIS 40-54
- Rocuronium for NM blockade
- Fentanyl 50mcg boluses (300mcg total) as BP >110 systolic; BIS >50
- Eight additional units of RBCs, plus platelets, cryoprecipitate
- Five additional liters of crystalloid infused

Surgical Duration: 1 hr 35 min; EBL 2000-2500mL; UO: 1050

Transport to ICU: Midazolam 2mg IV prior to transport
- BP 110-120/60, HR 118-126, BIS 48, HCT 28%

Postoperative Assessment (Day 2): Alert awake, remembers anesthesia interview, no memory of events until “awakened in recovery room” (ICU).

Discussion:

During the resuscitative phase of trauma anesthesia sub-MAC concentrations of anesthetics are often administered due to hemodynamic instability. In the trauma patient, the advantages of light anesthesia must be balanced against the risk of awareness. By integrating the BIS with routine monitors in the hemodynamically unstable patient, the anesthetist can better assess the three components of anesthesia (hypnosis, analgesia and areflexia). In this case, as blood pressure and pulse indicated recovery from hypovolemia, the BIS value rose, and additional sevoflurane, fentanyl and then midazolam were administered. The use of the Bispectral Index allowed the anesthetist to maximize the use of analgesics and hypnotics while at the same time minimizing the risk of hemodynamic compromise and minimizing the risk of awareness.

Paul Kammer, CRNA
Obese Patients

Intraoperative anesthesia maintenance in the obese patient population is problematic. Pharmacokinetic characteristics of the agents may be altered due to changes in distribution and clearance patterns. Pharmacodynamic alterations may produce varied responses such as altered sensitivity to respiratory depression. As a result, dosing of intravenous anesthetics and opioids may be more challenging. Similarly, the behavior of inhalation agents will differ from expected norms because of the larger potential uptake into adipose tissues.

Newer anesthetic agents offer an important option for management of obese patients during anesthesia. These agents include:

- Desflurane
- Propofol
- Remifentanil

**Study Design:**
- Laparoscopic gastroplasty in 36 morbidly obese patients
- Anesthetic regimens of desflurane, propofol or isoflurane
- Titration to maintain a BIS of 45-55

**Outcomes/Conclusions:**
- Emergence and extubation time was shortest in the BIS-guided desflurane group

Patients with Organ Dysfunction

Hepatic or renal end-organ disease significantly impacts anesthesia care. Patients with end-stage liver or renal disease exhibit:

- Alterations in anesthesia agent pharmacokinetics
- Alterations in hemodynamics

Pharmacokinetic alterations are prevalent in patients with ESLD or ESRD as the liver and kidneys are responsible for the metabolic clearance and elimination of many intravenous anesthetics, opioids, and neuromuscular blocking agents. These patients differ from the normal population in anesthetic requirements, and routine dosing of common agents may produce abnormal and unpredictable responses.

Severe hypertension may be present in ESRD, persistent hypotension with increased cardiac output in ESLD. As a result, hemodynamic-based dosing of anesthetic agents requires factoring in these underlying hemodynamic alterations. BIS monitoring allows an independent, patient-specific assessment of the anesthetic effect. Using this technology, the anesthesia provider can assess for abnormal sensitivity to agents and can discriminate between hemodynamic changes related to inadequate anesthesia vs. the underlying end-organ disease. While clinical judgment is still required, BIS monitoring provides additional data to complement traditional monitored parameters.
Study Design:

- 27 consecutive ESRD patients: renal transplant
- 27 ASA I and II patients: various procedures requiring general anesthesia and endotracheal intubation
- Premedication with lorazepam and ranitidine
- Induction: Fentanyl 2mcg/kg and Propofol 0.2mg/kg increments
- Induction endpoints: clinical (dropping of syringe) and objective (BIS=50±5)

Outcome/Conclusions (Table 3):

- Induction dose of propofol greater in ESRD patients
- Despite different propofol dosage requirements, both ESRD and control patients displayed similar hemodynamic responses to induction and intubation

<table>
<thead>
<tr>
<th></th>
<th>ESRD Group</th>
<th>Control Group</th>
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<tbody>
<tr>
<td>Clinical Endpoint</td>
<td>1.42±0.24mg/kg</td>
<td>0.89±0.2mg/kg</td>
</tr>
<tr>
<td>Objective Endpoint</td>
<td>2.03±0.4mg/kg</td>
<td>1.39±0.43mg/kg</td>
</tr>
</tbody>
</table>

Table 3: Perioperative Data
[Adapted from Reference 15]

Since its introduction, BIS monitoring has been utilized successfully to monitor the effects of anesthesia in a wide variety of procedures including:

- Outpatient procedures
- Prolonged surgery
- Cardiac surgery
- Neurosurgery
- Procedures complicated by increased risk of awareness
  - Cardiac surgery
  - Obstetric surgery
  - Trauma surgery
- Remote/Office procedures

From short procedures performed in the ambulatory care unit through major cardiac surgical procedures, BIS monitoring facilitates improved delivery of anesthesia care.

**Outpatient Procedures**

A series of investigations of ambulatory surgical procedures has demonstrated that BIS monitoring in this setting:

- Facilitates maintenance of adequate anesthetic state
- Improves recovery profiles after general anesthesia
  - Increases Phase 1 recovery room bypass
  - Reduces postoperative nausea and vomiting (PONV)

<table>
<thead>
<tr>
<th>Reduced Administration of Volatile Anesthetics</th>
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</table>

**Study Design:**

- 60 female patients undergoing laparoscopic gynecologic procedures
- General anesthesia – desflurane or sevoflurane
- Titration to BIS target value of 60

**Outcomes/Conclusion:**

- BIS monitoring produced 30-38% reduction in volatile agent use
- BIS monitoring produced a 30-35% decrease in the early markers of emergence and recovery

**Study Design:**
- Dedicated outpatient anesthesia facility
- 53 female laparoscopic surgery patients
- General anesthesia – desflurane
- Titration to BIS target value of 60
- Remifentanil or esmolol infusions to provide hemodynamic stability

**Outcomes/Conclusion:**
- Technique produced PACU bypass rates of 78-81%
- Fast-tracked patients recovered quicker
- High degree of patient satisfaction


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**Study Design:**
- 62 female patients undergoing gynecologic outpatient procedures
- General anesthesia – sevoflurane-alfentanil-nitrous oxide
- Randomized to standard care vs. sevoflurane titration to BIS target range of 50-60

**Outcomes/Conclusion (Figure 3):**
- BIS-titrated anesthesia:
  >50% reduction in emesis during recovery

**Prolonged Surgery**

Recovery profiles are affected by various factors that influence anesthetic uptake. These factors include agent dosage, which is of particular concern during lengthy procedures.

**Study Design:**
- 73 patients undergoing prolonged microsurgical procedures
- General anesthesia – sevoflurane, nitrous oxide and opioid
- Randomized to standard practice or titration to BIS target range of 50 ± 5

**Outcomes/Conclusions:**
- Average volatile agent administration decreased by 50%
- 30-50% reduction in awakening, extubation and orientation times


**Cardiac Surgery**

Anesthetic techniques for cardiac surgery vary widely and are affected by:

- Institutional preferences
  - Temperature management during cardiopulmonary bypass
  - Hemodynamic monitoring techniques
  - Timing of extubation
- Procedures
  - Valve vs. coronary artery surgery
  - Cardiopulmonary bypass vs. off-pump procedures
- Patient characteristics
  - Age
  - Coexisting disease

Given the range of variation in anesthesia care, BIS monitoring may offer particular value during cardiac procedures. In one study, a BIS value of 50 has been reported to provide an effective anesthetic effect during induction and endotracheal intubation and achievement of this level of hypnosis was shown to provide control of cardiovascular responses in this population.  

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[19] Decreased Volatile Agent and Faster Recovery

[20]
**Study Design:**
- 40 patients undergoing coronary artery bypass grafting (CABG)
- General anesthesia with TIVA: propofol-remifentanil or sufentanil-midazolam
- BIS-guided titration complementing traditional hemodynamic parameter assessment

**Outcomes/Conclusions:**
- Maintenance of stable hemodynamics more important than the specific technique
- Confirmation of adequate anesthetic effect more important than the specific technique
- BIS monitoring provided confirmation of adequate anesthetic effect

**Study Design:**
- 20 adult patients undergoing surgery with cardiopulmonary bypass
- General anesthesia with variable isoflurane dose and target-controlled fentanyl infusion
- Titration of isoflurane to achieve BIS target value of 55

**Outcomes/Conclusions (Figure 4):**
- Significant reduction in isoflurane dose to achieve target BIS following bypass
- Because surgical stimulation was constant, suggests a reduced anesthetic requirement

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**Study Design:**
- 62 patients: primary CABG procedures
- Preserved left ventricular function (EF > 40%)
- Hypothermic bypass (Temperature = 32.5-33.5°C)
- Intravenous anesthesia: propofol, midazolam, sufentanil
- Randomized: BIS 50 (maintain BIS range 45-55) vs. BIS 40 (maintain BIS range 35-45)
- Achieve BIS ranges by adjusting doses of midazolam and sufentanil

**Outcomes/Conclusions (Table 4):**
- No significant differences in hemodynamic or oxygenation parameters at any time
- No explicit memory during anesthesia in both groups assessed on postoperative day 3
- BIS monitoring of anesthetic effect reduced intraoperative drug use, decreased drug costs and did not increase the risk of intraoperative awareness

<table>
<thead>
<tr>
<th></th>
<th>BIS 50 Group</th>
<th>BIS 40 Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sufentanil Dose</strong></td>
<td>514±99mcg</td>
<td>888 ± 211mcg*</td>
</tr>
<tr>
<td><strong>Midazolam Dose</strong></td>
<td>16.6 ± 3.7 mg</td>
<td>22.4 ± 3.7 mg*</td>
</tr>
<tr>
<td><strong>Cost (Drug/sensor)</strong></td>
<td>$37.50</td>
<td>$50.05*</td>
</tr>
<tr>
<td><strong>Time to Extubation</strong></td>
<td>11.8 ± 3.8</td>
<td>14.3 ± 4.6</td>
</tr>
</tbody>
</table>

*p<0.05 between groups

Table 4: Perioperative Data
Maintaining BIS values at 45-55 allowed reduced intraoperative drug use without increased risk of awareness.[Adapted from Reference 23]

**Study Design:**

- 100 patients undergoing CABG with hypothermic cardiopulmonary bypass
- BIS monitored general anesthesia – sufentanil/propofol
- Computer controlled infusions: stable anesthetic level

**Outcomes/Conclusion:**

- BIS values correlated positively with changes in core body temperature, decreasing by 1.12 units per degree Celsius decline in temperature **Note:** No changes in BIS noted with normothermic cardiopulmonary bypass technique


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**Neurosurgery**

BIS monitoring has proven clinical value in a variety of intracranial and spinal neurosurgical procedures. This technology has been used to facilitate:

- Precise agent titration during “awake” craniotomy for seizure, motor, speech mapping
- Rapid emergence for neurosurgical assessment
- Management of intraoperative “wake up” test
- Optimized anesthetic dosing for blood pressure control

BIS-guided titration of short-acting sedatives and analgesics during “awake” craniotomy allows the provider to appropriately reduce sedative effects during cortical mapping of motor or speech locations around tumors or seizure foci. Because intracranial bleeding or cerebral edema are of great concern in the postoperative neurosurgical patient, BIS-guided titration also allows adjustment of agent administration to ensure rapid emergence and return to consciousness for immediate neurosurgical assessment. Complementing hemodynamic parameter assessment, BIS monitoring guides decision-making regarding choice and titration of anesthetic or antihypertensive agents to tightly manage blood pressure, particularly during induction and emergence.
**Study Design:**

- Case Report: Target-controlled administration of propofol-remifentanil
- Series Report: 7 patients with propofol-remifentanil anesthesia for incision and flap removal prior to awake functional testing

**Outcomes/Conclusions:**

- BIS had better correlation to patient responsiveness than did predicted effect-site drug concentrations


CLINICAL PERSPECTIVE: INTRACRANIAL NEUROSURGICAL PROCEDURE

Patient: 45 year-old male, 96 kg, ASA II
Procedure: Craniotomy for resection of arteriovenous malformation (AVM)
Management: Routine monitoring, arterial line, BIS, somatosensory evoked potentials

Anesthesia Care:

Premedication: Midazolam 2mg in holding area
Preinduction: Marked sedation noted (Initial BIS 88)
  – BIS increased to 95 with stimulation (placement of other monitors)
Induction sequence:
  – Propofol 150mg, fentanyl 200mcg, vecuronium 10mg
  – Endotracheal intubation on first attempt using lighted stylette
Maintenance:
  – Isoflurane 0.2%, fentanyl infusion 2mcg/kg/hr, vecuronium infusion
  – BIS target range of 45-70
  – Additional propofol for placement of headclamp
  – Scalp block with bupivacaine 0.5% with epinephrine 1:200,000

Surgical Duration: 5 hours, 30 minutes
Recovery: Rapid emergence and extubation followed by neurologic examination

Discussion

Neurosurgical patients may demonstrate a marked sensitivity to anesthetics, particularly hypnotic agents. Therefore, it is useful to record a baseline BIS Index, particularly in patients with altered CNS function or those who experience frequent seizures.

During craniotomy procedures, placement of the BIS System sensor is usually possible on the non-operative side of the head. Sensor position may require adjustment for pin placement. The use of clear tape or Tegaderm™ material will help to keep the sensor dry during and after preparation of the field.

This patient remained hemodynamically stable during most of the procedure. While there is little or no pain experienced during brain resection, use of a “scalp block” provides needed analgesia for incision and wound closure.

Monitoring of somatosensory evoked potentials is best achieved with low concentrations of volatile agents. The use of BIS monitoring in this patient allowed for minimal anesthetic agent dosing to allow optimal conditions for cerebral function evaluation. Muscle relaxants were continued and transient increases in EMG (with increased BIS values) can be noted during stimulation.

After resection of the AVM, the surgeon requested rigorous blood pressure control to prevent bleeding and edema. Labetolol and hydralazine were administered during skin closure and the patient emerged promptly without problems.

Irene P. Osborn, M.D.
Study Design:
- 34 children and adolescents undergoing scoliosis surgery
- 2 anesthetic techniques:
  - Low-dose isoflurane, nitrous oxide, fentanyl, midazolam
  - Nitrous oxide, fentanyl, midazolam
- Intraoperative use of neuromuscular blockade and controlled hypotension
- BIS monitoring during anesthesia, and values noted around wake-up test

Outcomes/Conclusions:
- BIS values increased from 72 to 90 during wake-up test
- Explicit auditory recall, without pain, in 6 patients (17.6%)
- Demonstration of BIS utility during complex surgery in which vasoactive medications modified hemodynamic response

**CLINICAL PERSPECTIVES: SPINAL NEUROSURGICAL PROCEDURE**

**Patient:** 62 year-old female, 100 kg, ASA III  
**Procedure:** Cervical laminectomy  
**Management:** Routine monitoring, arterial line, BIS, somatosensory and motor evoked potentials  
**Anesthesia Care:**  
- **Premedication:** Midazolam 1mg, fentanyl 50mcg intravenously  
- **Induction sequence:**  
  - Propofol 100mg, fentanyl 100mcg, vecuronium 8mg  
  - Intubation using LMA-Fastrach™ to place ETT  
- **Maintenance:**  
  - Fentanyl infusion 3mcg/kg/hr, 60% nitrous oxide  
  - Isoflurane 0.3-0.4% during lines and EP monitor placement  
  - After prone positioning, isoflurane discontinued; propofol infusion  
    75-100mcg/kg/min  
  - BIS target range of 45-60  
- **Recovery:**  
  - Emergence and extubation after return to supine position  
  - Ability to follow commands and move extremities noted

**Discussion**

Spine surgery with neurophysiologic monitoring requires occasional adjustment in the anesthetic regimen. This can be complicated by coexisting disease, particularly cardiopulmonary disease.  

In this case, this patient was obese with moderate COPD, hypertension and anxiety disorder. Stenosis of her cervical spine (C4-5) caused upper extremity weakness and numbness but no symptoms on movement. She was taking a number of medications for pain, anxiety and hypertension. BIS monitoring allowed for a smooth induction, as the patient required very little anesthetic but frequent blood pressure support. It is important to note that the BIS system sensor can be used even when prone positioning of the patient is required. The sensor was positioned carefully and padding of the head utilized to avoid injury. Use of BIS monitoring was important in this case as it enabled direct assessment of the level of hypnosis as the anesthetic technique was converted to a nearly total intravenous regimen.  

Motor evoked potentials were elicited producing occasional EEG artifact. Additional narcotic was given when needed, which produced a stable intraoperative course. Upon completion of the laminectomy and fusion the patient was given 3 mg of vecuronium to facilitate wound closure and allow a decrease in the propofol infusion. BIS monitoring allowed for optimal titration of hypnosis while the patient underwent x-rays and was turned into the supine position for a prompt and comfortable awakening.

Irene P. Osborn, MD
Increased Awareness Risk

In routine anesthesia cases, the occurrence of intraoperative awareness has been estimated to occur infrequently: typically in the range of one per thousand cases. Increased risk of intraoperative awareness has been recognized in three distinct clinical settings:

- Cardiac surgery
- Obstetrical surgery
- Trauma surgery

In these patients, clinical concerns about anesthesia tolerance have placed limitations on the type or amount of agent delivered. In several centers, clinicians have used BIS monitoring to ensure adequate anesthetic effect during these types of procedures. While the BIS is not an awareness monitor per se, it can assist the anesthesia provider to accurately assess the risk of intraoperative awareness and recall during these challenging situations.

Cardiac Surgery

The incidence of awareness during general anesthesia with cardiopulmonary bypass has been reported in the 1.5% range in cases utilizing a combination of benzodiazepine, fentanyl and low-dose volatile agent.30

### Study Design:

- Patients undergoing cardiac surgery with cardiopulmonary bypass
- BIS-monitored general anesthesia:
  - Benzodiazepine, fentanyl and low-dose volatile agent31
  - Propofol-sufentanil32

### Outcomes/Conclusions:

- BIS > 70 correlates with increased levels of implicit memory31
- BIS value that correlates with lack of patient response during induction may be useful to identify upper threshold limit for case management32


**Study Design:**
- Case Series:
  - 2 patients with previous documented intraoperative awareness
  - Cardiac surgery with goal of “early” extubation (< 6 hr postoperative)
  - Midazolam, propofol, remifentanil: BIS goal < 40

**Outcomes/Conclusions:**
- Easy titration to achieve BIS goal; no sustained BIS increases
- Achieved goal of early extubation
- No detection of intraoperative awareness


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**Obstetrical Patients**
General anesthesia for emergency cesarean section frequently involves a technique that involves a “light” level of anesthetic effect in order to minimize deleterious effects on the fetus.

**Study Design:**
- 24 female patients undergoing emergency cesarean section
- Induction – thiopental and succinylcholine
- BIS monitoring during “light” general anesthesia – low concentration of volatile agent in 50% nitrous oxide

**Outcomes/Conclusions:**
- BIS frequently > 60 during “light” general anesthesia
- High BIS values associated with increased risk of explicit memory and conscious recall
- BIS monitoring can indicate need for other strategies such as reassurance, communication, appropriate tone in the operating room

**Study Design:**
- 20 ASA I parturients: general anesthesia for elective caesarean section
- Premedication: oral ranitidine and sodium citrate
- Rapid sequence induction: thiopentone 4-5 mg/kg; succinylcholine 2 mg/kg
- Maintenance:
  - Before delivery: nitrous oxide 50% in oxygen; inspired isoflurane 1.0-1.5%
  - After delivery: nitrous oxide 66% in oxygen; morphine 0.1-0.2mg/kg; isoflurane 0.75%.
- Anesthesiologists blinded to BIS values

**Outcome/Conclusions:**
- Median BIS value at intubation: 60 (Range 52-70)
- Median BIS value at skin incision: 70
  (Interquartile Range = 62-68)
- End-tidal isoflurane at skin incision: 0.62 ± 0.04%
- Median BIS value at uterine incision: 60 (Range 52-70)

**Trauma Patients**
The rate of recall during trauma surgery has been reported to be increased depending on the severity of injury and the ability to deliver anesthetic agents.

**Recall and Learning During Trauma Cases**

<table>
<thead>
<tr>
<th>Study Design:</th>
</tr>
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<tbody>
<tr>
<td>• Trauma surgery</td>
</tr>
<tr>
<td>• BIS monitoring during general anesthesia – isoflurane and fentanyl</td>
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<thead>
<tr>
<th>Outcomes/Conclusions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Average BIS value – 54 (adequate anesthesia)</td>
</tr>
<tr>
<td>• 1/96 patients had auditory recall</td>
</tr>
<tr>
<td>• No evidence of explicit memory formation</td>
</tr>
<tr>
<td>• BIS value range 40-60 – small percent of patients had implicit memory (evidence of learning without free recall), suggesting some auditory processing</td>
</tr>
</tbody>
</table>


**Intraoperative Awareness During Routine Anesthesia**

As stated previously, the incidence of awareness is quite low – in the range of 0.1-0.2%.29 Despite this low incidence, it is a major source of patient dissatisfaction following anesthesia.37 In addition, the occurrence of unintentional awareness can have significant personal and long-term consequences.38,39 Although some authors have postulated it may potentially increase the incidence, other investigators have initiated a prospective, randomized trial to measure the effect of BIS monitoring on the incidence of intraoperative awareness.40,41
Procedures in Remote and Office Locations

One of the recent changes in anesthesia practice has been a greater utilization of anesthesia care outside of the traditional operating room environment. Anesthesia providers are asked more often now to provide anesthesia and/or sedation/analgesia to patients undergoing diagnostic or therapeutic procedures throughout the hospital environment. Frequently, the administration of anesthesia in remote or office locations will be associated with a different model of recovery care than that used in the Post Anesthesia Care Unit.

Study Design:
- Office-based surgical procedures
- BIS monitored general anesthesia – propofol-ketamine\(^{42}\) or desflurane vs. propofol techniques\(^{43}\)
- Target BIS range – 55-65

Outcomes/Conclusion:
- BIS monitoring facilitated decreased dosing of the anesthetic, improving recovery profiles and enabling fast-track management in office-based anesthesia
- Anesthesia techniques tailored to minimize the incidence of nausea and vomiting


Anesthesia Techniques
There is a wide variety of anesthetic approaches utilized by anesthesia providers including:

- Sedation management and Monitored Anesthesia Care (MAC)
- Intravenous-based anesthesia
- Combined regional-general anesthesia
- Nitrous-narcotic anesthesia
- Adjuvant therapies
- Hypotensive anesthesia
- Closed-loop anesthesia

As indicated above, multiple agents and adjuvants are often utilized during the course of a single surgical procedure. Despite this diversity, however, it has been demonstrated that the clinical utility of BIS monitoring is not compromised by the choice of primary anesthetic agent, or by the addition of supplemental agents or anesthetic adjuvants. In fact, BIS monitoring allows the provider to accurately assess combined agent effect on the hypnotic state.

Sedation Management and Monitored Anesthesia Care
Frequently, anesthesia professionals provide sedative and analgesic agents to supplement intraoperative conditions during local anesthesia infiltration (e.g., breast biopsy procedures, hernia repairs) or during procedures utilizing regional anesthesia (e.g., spinal or epidural blockade, plexus nerve blocks). Investigations in these clinical settings have generally supported the accuracy and clinical ability of BIS to objectively measure sedation effect. Initial studies reported the correlation of BIS with sedation score during MAC procedures and in volunteers receiving propofol during epidural anesthesia.44,45 Subsequently, similar results were reported in patients being sedated with either propofol or midazolam.46,47 Most recently, BIS was utilized as a measure in a comparative study of sevoflurane, midazolam, and propofol as sedative agents during local or regional anesthesia.48 Despite BIS decreasing during clinical sedation, the authors noted significant variability and overlap in BIS values at various sedation levels. Although the clinical prediction of BIS was less during sevoflurane use (compared with propofol), the prediction probability was much greater than either hemodynamic measures or end-tidal sevoflurane concentration.
Intravenous-Based Anesthesia

Unlike end-tidal monitoring with volatile anesthetics, there is no technology to provide a rapid measurement of drug concentration during intravenous anesthetic techniques. Further, there is potentially a 3-5 fold interpatient variability in the response to most intravenous agents. Because BIS monitoring provides direct feedback on patient response to IV-based anesthesia, it allows individual dosing adjustments.

Study Design:
- Short gynecological procedures
- BIS-guided vs. standard practice propofol administration (target-controlled infusion)

Outcomes/Conclusion:
- BIS monitoring allowed better targeting of propofol and resulted in a more consistent level of sedative effect
- Improved intraoperative anesthesia care noted with BIS monitoring: less movement and implicit memory

CLINICAL PERSPECTIVE: TOTAL INTRAVENOUS ANESTHESIA

Patient: 49 year-old female, 55 kg, ASA II
Medical History: Anxiety disorder; newly diagnosed pelvic mass
Procedure: TAH/BSO & Pelvic Lymph Node Sampling
Management: General ET anesthesia, routine monitoring, BIS monitoring

Anesthesia Care:
Premedication: Midazolam 2mg; initial BIS in OR 94
Induction Sequence:
– Sufentanil 1mcg/kg during preoxygenation; propofol 300 mcg/kg/min x
  3 minutes to BIS ~45; vecuronium 7mg to facilitate ET intubation
Maintenance:
– Propofol infusion variable (Range 100 to 90 to 50mcg/kg/min);
  titrated to BIS
– Sufentanil infusion: .45mcg/kg/hr first hour; 0.3mcg/kg/hr until fascia closed
– Vecuronium: intermittent administration to maintain TOF=1-2 twitches
– Ventilated with oxygen in air (F\textsubscript{1}O\textsubscript{2} = 0.5; End-tidal CO\textsubscript{2} = 32-35 mmHg)
– Anti-emetic prophylaxis: ondansetron 4mg/metoclopramide 10mg

Surgical Duration: 2.5 hr; EBL=200 mL; crystalloid=3000mL; urine output: 225mL
Recovery: Extubated in OR at case conclusion; transferred to PACU with
supplemental oxygen; postoperative pain management initiated in PACU
with PCA-morphine

Discussion
Utilizing a TIVA technique can be challenging during a laparotomy procedure
particularly as case length increases. The potential variability in patient responses to
fixed-dose infusion regimens can produce large swings in emergence time.
In this case, BIS monitoring allowed incremental adjustments of the propofol
infusion to maintain adequate but not excessive effect. Sufentanil dosing was based
upon our clinical experience to facilitate good hemodynamic control during the
procedure, rapid emergence without respiratory depression, and then a planned
transition to PCA-morphine in the postoperative period.

BIS monitoring is clearly an important contributor to increasing the utility of TIVA
techniques in a wider range of patients.
Vlad Frenk, M.D.
Brigham & Women’s Hospital
Combined Regional-General Anesthesia

Major abdominal, thoracic or extremity surgery may benefit from regional techniques to enhance postoperative analgesia, but these procedures may also require general anesthesia. Clinical investigation has demonstrated that BIS monitoring provides a unique perspective on anesthetic management when combined techniques are utilized. Better assessment of the anesthetic interactions within a combined technique should reduce the potential for hypotension.

**Reduced Anesthetic Requirement**

**Study Design:**

- Prospective study of 30 patients with random assignment:
  - Combined epidural (15 mL of 2% lidocaine via an epidural catheter)/ general anesthesia
  - General anesthesia – sevoflurane (with control for systemic lidocaine absorption)

- Minimum alveolar concentration of sevoflurane to achieve a BIS of 50 (MAC_{BIS50}) was measured

**Outcomes/Conclusions (Figure 5):**

- Epidural anesthesia reduced MAC_{BIS50} by 34% (not as result of systemic lidocaine absorption)

- Two viable hypotheses:
  - Neuroaxial blockade causes reduction of tonic spinal signaling to the brain – a component of wakefulness
  - Rostral spread of local anesthetic has direct sedating effect

- BIS monitoring documents adequate depth of anesthesia with significantly reduced concentration of volatile agent during a combined technique

![Figure 5: Measured sevoflurane dose required to achieve BIS target value of 50 during various anesthetic regimens – In the setting of epidural blockade, sevoflurane dose was reduced by 34% documenting the strong interaction in combined technique.](adapted-from-reference-50)

CLINICAL PERSPECTIVE: COMBINED ANESTHESIA TECHNIQUE

Patient: 37 year-old female, ASA I
Procedure: Donor nephrectomy
Management: Routine monitoring including BIS monitoring

Anesthesia Care – Combined Technique:

Thoracic epidural anesthesia (Level:T8-T9)
  Test Dose: appropriate sensory change documented
  Maintenance: 2% lidocaine 5mL bolus every 90 minutes

General Anesthesia:

Induction:
  – Propofol 1.5mg/kg
  – Fentanyl 1mcg/kg prior to intubation

Maintenance:
  – Propofol 80-90mcg/kg/min
    (titrated to BIS of 48-55)
  – Controlled ventilation with air/oxygen mixture

Surgical Duration: 2 hours, 45 minutes

Discussion

Patients undergoing open nephrectomy procedures may benefit from epidural analgesia in the postoperative period. In anticipation of this, a combined anesthesia technique which includes epidural anesthesia may be appropriate.

In this case, intraoperative anesthetic management included placement of an epidural catheter for delivery of local anesthesia via intermittent bolus technique. General anesthesia maintenance was accomplished with propofol infusion. BIS monitoring provided a direct measure of the anesthetic effect of the agent and allowed dosing titration.

Intraoperative blood pressure and heart rate were clinically acceptable throughout the procedure and no evidence of inadequate surgical anesthesia such as movement or hypertension was noted. Crystalloid volume therapy was generous as per routine protocol for donor management. Stable hemodynamics and excellent urine output were followed by excellent renal transplant function in the recipient. With the epidural catheter in place, transition to postoperative analgesia infusion was easily accomplished in the PACU.

Scott Kelley, M.D.
**Study Design:**
- 50 ASA I-II patients (20-65 years)
- Procedure: total abdominal hysterectomy
- General anesthesia technique, all patients:
  - Induction: propofol 1.5mg/kg
  - Alfentanil infusion (target concentration = 100ng/ml)
  - Isoflurane (automated delivery to EEG SEF = 17.5 Hz)
- Epidural technique (n = 25):
  - Lumbar epidural catheter
  - Local anesthesia: 0.5% bupivacaine

**Outcome/Conclusions:**
- Epidural blockade reduced isoflurane requirement by 21%
  - End-tidal isoflurane concentration:
    - GA: 0.91 ± 0.24
    - Combined technique: 0.72 ± 0.22
- BIS values slightly higher in control group
  - BIS:
    - GA: 50±5
    - Combined technique: 54 ± 6
- Reduced isoflurane dosing associated with more rapid emergence in combined technique group
- Hypotension, requiring treatment, more common in combined technique
- Authors caution against further reduction in isoflurane dosing to manage hypotension

Nitrous-Narcotic Anesthesia

BIS monitoring has been evaluated during nitrous oxide-opioid anesthetic technique for accuracy in determining adequacy of anesthesia.

**BIS Responses During Nitrous-Narcotic Anesthesia**

**Study Design:**

- Nitrous oxide-remifentanil anesthesia
- Remifentanil dosing per assessment of hypertension, tachycardia, autonomic signs or movement as indicators of inadequate anesthesia
- BIS values during transitions from adequate to inadequate anesthesia state were determined

**Outcomes/Conclusion:**

- BIS median value during adequate anesthesia – 47
- BIS median value during inadequate anesthesia – 62


The case trend illustrated in Figure 6 displays the BIS response during the induction and early maintenance period of an abdominal procedure initiated with a nitrous-narcotic technique. The initial trend showed significant sedation from midazolam premedication and then decrease from induction with propofol. Of special note is the BIS response observed following surgical incision that was not reflected in hemodynamic measures, and which prompted administration of isoflurane.

**Figure 6: BIS trend during the initial time period of a “nitrous-narcotic anesthesia”**

Anesthetic regimen involved propofol induction, fentanyl dose of 15 mcg/kg and 70% nitrous oxide. Despite stable hemodynamics, BIS response to surgical incision and dissection prompted the addition of 0.3% isoflurane to reduce BIS value.
Adjuvant Therapies

Anesthetic adjuvants such as some antihypertensives and, as cited previously, beta-blockers (e.g., esmolol), can vary anesthesia requirements. By measuring consciousness as a specific endpoint, BIS monitoring enables the provider to see the total effect of all medications in each individual patient.

**Study Design:**
- 50 patients
- General anesthesia – propofol
- Concurrent clonidine administration

**Outcomes/Conclusion:**
- BIS monitoring allowed 20% reduction in propofol dosing to maintain the same anesthetic effect

Study Design:
• 20 patients
• General anesthesia – propofol/alfentanil
• Impact of esmolol infusion on BIS and EEG-suppression measured

Outcomes/Conclusion (Figure 7):
• Esmolol infusion produced 40% decrease in BIS and resulted in increased EEG suppression
• Hysteresis of onset and offset of EEG effects measured
• Demonstrates a potentiation of anesthetic effect by esmolol

Figure 7: Changes in BIS values during antihypertensive infusion –
During stable intravenous-based anesthesia, initiation of esmolol infusion produced a rapid BIS decrease that persisted for several minutes following termination of the infusion.

[Adapted from Reference 54]

Study Design:
- 50 patients, randomized, double-blind
- Primary anesthetic: propofol – TCI to effect-site = 4mcg/ml
- 6 minutes after propofol infusion:
  - Esmolol (1mg/kg then 250mcg/kg/min) or saline (control)
- Isolated forearm technique prior to vecuronium administration
- Intubation responses: BIS, Gross Movement, MAP, HR

Outcome/Conclusion (Table 5):
- Esmolol treatment attenuated hemodynamic, gross motor and BIS arousal responses to laryngoscopy and intubation
- Esmolol may produce clinically significant antinociceptive effect

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<tr>
<th>Movement</th>
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<th>Control Group</th>
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<td>23±14%</td>
<td>45±19%</td>
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Table 5: Intubation Responses – Esmolol attenuated BIS responses as well as changes in mean arterial pressure and heart rate. [Adapted from Reference 55]

**Study Design:**
- 54 patients: total abdominal hysterectomy
- Anesthesia: propofol, nitrous oxide, vecuronium
  - Control group: normal saline infusion
  - Magnesium group: 50mg/kg bolus then 8mg/kg/hr
  - End-Point: propofol infusion rate to maintain normal MAP/HR
- BIS Comparison: 20 additional patients, 10/group
  - Control group: propofol infusion at 160mcg/kg/min
  - Magnesium group: 50mg/kg bolus then 8mg/kg/hr; propofol at 80 mcg/kg/min
  - End-Point: BIS value during steady-state infusion

**Outcome/Conclusions:**
- Magnesium reduced propofol requirement based upon hemodynamic response, but reduced propofol dose is associated with increased BIS values
- Hemodynamic Titration:
  - Propofol requirement significantly less during magnesium infusion (81±13 vs. 167±47mcg/kg.min)
- BIS Comparison:
  - BIS values significantly greater during magnesium infusion (58±7 vs. 41±4)
- Potentially, magnesium could:
  - augment anesthetic effect of propofol
  - enhance hypotensive effect of propofol
  - have inherent anesthetic and analgesic effect (not measured by BIS)

Hypotensive Anesthesia

Hypotensive anesthesia has been employed for a number of years as a strategy to reduce intraoperative blood loss and the requirement for allogenic transfusion. This has particular applicability in:

- Orthopedic surgery (spine, hip revision)
- Urologic procedures
- ENT procedures

There have been many descriptions of the techniques used to obtain deliberate hypotension. The use of potent medications to directly lower blood pressure obscures the clinician’s view of hypnotic state. In these cases, BIS Index monitoring provides a means of assessment that is patient-, procedure-, and drug-independent. It therefore provides an accurate, direct measure of anesthetic effect.

Closed-Loop Anesthesia

One of the most innovative applications for BIS monitoring has been as an integral element – i.e., the “controller” – during the delivery of anesthesia via closed-loop control of agent dosing.

Note: Closed-loop systems are not commercially available at this time.
Study Design:
• Prospective and randomized investigation
• Orthopedic procedures
• BIS-monitored closed-loop anesthetic agent delivery

Outcomes/Conclusions (Figure 8):
• Compared to standard practice, BIS monitoring resulted in better intraoperative conditions and postoperative recovery characteristics

REFERENCES


INTRODUCTION
Most signal artifact in waveforms such as the ECG, $S_pO_2$, or arterial blood pressure are easier to detect than artifact within the electroencephalogram waveform. Indeed, with the variable frequency and amplitude of the EEG waveform, the presence of certain types of artifact may be extremely difficult to recognize visually.

BIS monitoring systems utilize a variety of signal analysis methods to detect and reduce extraneous artifacts that contaminate the EEG. In fact, many of the improvements in the BIS system over the past decade have been in the area of artifact processing. With the development and release of the BIS-XP system, the performance and reliability of BIS have been substantially improved, especially in the presence of electrocautery artifacts.

Despite these improvements, however, artifact produced by some non-EEG signals can potentially interfere with the ability of the BIS system to render an accurate BIS value. Given this potential for artifact contamination, the clinician must identify situations where the underlying EEG signal – and hence the BIS value – may not accurately reflect the clinical endpoints of sedation and hypnosis.
Inaccurate calculation of BIS values due to artifact contamination of the EEG signal may be due to:

- Electromyogram (muscle) activity
- EEG variants/signal analysis
  - Paradoxical Delta phenomenon
  - Small amplitude EEG
  - Epileptiform activity
  - Missed near-suppression
- High frequency artifacts
- “Abnormal” brain
- Pharmacologic responses
  - Nitrous oxide
  - Ketamine
  - Etomidate

Each of these situations is discussed in the following sections.

**BIS and the Electromyogram (EMG)**

The most frequent source of EEG contamination in sedated and lightly anesthetized patients is the electromyogram (EMG). This contamination results from increased tone of the frontalis muscle of the forehead that lies beneath the BIS sensor. Typically, significant EMG activity is present during awake states and during emergence from anesthesia (Figure 1).

The frequency spectrum of endogenous EMG activity partially overlaps with the frequency spectrum of the awake EEG. In order to maximize the sensitivity of BIS to detect wakefulness, these high frequency signals are analyzed by the BIS processing system. As a result, in the presence of significant EMG activity, calculated BIS values may tend to be higher – in a range that normally may indicate the potential for inadequate anesthesia – than would actually reflect the true hypnotic state of the patient.¹
As in all clinical situations, it is important that patient care decisions not be based solely upon the displayed BIS value but rather upon complete clinical assessment of the patient. During intraoperative anesthesia situations where EMG is biasing BIS to a higher value, administration of either increased anesthetic or a muscle relaxant can produce a significant decrease in EMG.

In Figure 2, an example of the influence of EMG on the BIS value is demonstrated, as is the prompt resolution of the bias that occurs following administration of a neuromuscular blocking agent (NMB). It is important to recognize that although significant EMG contamination may elevate the BIS value while the patient remains unconscious, muscle relaxants have no direct effect on the hypnotic level.²

As noted, appearance of high frequency facial EMG activity commonly occurs during awakening and, in fact, has been incorporated in experimental “depth of anesthesia” monitors.³ During emergence from anesthesia, BIS will usually increase in conjunction with this increased EMG activity, although the presence of EMG is not required for BIS to track the return of consciousness.⁴

Although EMG activity can sometimes be seen in the raw EEG trace, typically it is more difficult to discern. Therefore, in situations with the potential for EMG contamination, it is important to note the amount of activity generated by EMG. BIS systems display an EMG parameter that shows total power of electrical activity seen in the frequency bandwidth of 70-110 Hz. When the EMG power exceeds 50 dB, there is greater potential for EMG contamination of the underlying EEG signal.

To further address the problem of EMG contamination, Aspect Medical Systems developed the BIS-XP platform. This system uses dual-channel EEG processing, making it more resistant to the effects of EMG. The potential for spurious BIS values is reduced when using the XP platform; however, it is not eliminated entirely.
BIS AND EEG VARIANTS/SIGNAL ANALYSIS

Two challenges to any EEG-based assessment of the level of consciousness are the presence of EEG variant activity and the recognition of anesthesia-induced EEG effects. Specifically, these challenges are presented by:

- Paradoxical Delta Phenomenon
- Small amplitude EEG
- Epileptiform activity
- Missed near-suppression

Paradoxical Delta Phenomenon

In a small percentage of patients, a paradoxical response develops in the EEG during a lightening of anesthesia effect or in response to surgical stimulation. This phenomenon, known as “paradoxical arousal” or “paradoxical delta,” is characterized by a slowing of the EEG, with large delta waves. In response to this unusual EEG slowing, the BIS value decreases suddenly.

In Figure 3, a raw EEG epoch is displayed showing a characteristic pattern during such an episode. In a review of over 1,900 cases, paradoxical delta patterns—which produced variations in the BIS trend similar to what is displayed in Figure 3—occurred more often during inhalation anesthesia (2.6%) and in patients younger than 18 years of age (4.3%). During the episodes of paradoxical arousal, average BIS values reached a nadir of 32. Of note, the BIS values before and after the episode were 61 and 72, respectively, consistent with the appearance of this response during decreasing anesthesia effect.

Small Amplitude EEG

In a single case-report, an awake individual had a very low BIS value. This was presumed to be the result of EEG variant activity—specifically, a congenital, extremely small amplitude EEG.
**Epileptiform Activity**

The occurrence of epileptiform activity, for example, during the administration of high concentrations of sevoflurane anesthesia, can also lead to temporal increases in BIS values.\(^{10,11}\) In one report, BIS values were appropriately low during administration of high concentrations of sevoflurane. However, with the development of epileptiform activity, BIS values increased abruptly during the epileptic discharge, corresponding to increases in cerebral blood flow (and presumably glucose metabolism) measured with PET scanning.\(^{12}\) The case illustrated in Figure 4 demonstrates the onset of epileptiform activity following increased sevoflurane administration and the resultant increase in BIS value. Also of note is the transient dip in BIS following discontinuation of sevoflurane and cessation of seizure activity. In situations of concern regarding sevoflurane administration, unexpected increases in BIS, particularly following an increase in the administered dose, should prompt a rapid inspection of the raw EEG to assess for the presence of epileptiform activity.

**Missed Near-Suppression**

In a small number of patients, early BIS systems had difficulty detecting the presence of nearly suppressed EEG. i.e., “near suppression.” Because near-suppression is one of the core features of increasing anesthetic effect identified by the BIS system, episodes of missed near-suppression resulted in BIS values greater than the apparent level of anesthetic effect.

The development of the BIS-XP platform has also addressed the problem of missed near-suppression. BIS-XP platforms include additional signal processing features that detect this particular EEG state.
A variety of medical devices generate high-frequency signals that can contaminate the EEG signal. If this extraneous artifact is not detected, the inclusion of the high-frequency signal could lead to errors in the calculation of BIS. Some of the devices that have been reported, in rare settings, to produce artifact and resultant inaccuracy of the BIS are listed in Table 1.

For an external device with the potential to generate artifact, proximity to the BIS sensor or to the DSC (digital signal converter – see Chapter 3) increases the risk of EEG signal contamination and effects on BIS values. Therefore, it is critical to consider the physical location of such devices in relation to BIS system components. To confirm artifact in situations where an external device may be interfering with BIS, temporary cessation of the device usage (if appropriate) may reveal a characteristic pattern of interference.\textsuperscript{13,14}

A few important external sources of artifact noted in Table 1 include:

- Pacemakers
- Medical/surgical devices
- Electrocautery devices

**Pacemakers**

Typically, signals emitted from pacemakers have a high amplitude and regular pattern. As a result, they are readily identified as artifact by BIS systems and are not processed as EEG.

In some situations, the programmed pacing rate and current causes the extraneous paced signal to be interpreted as an EEG signal. The presence of this artifact influences the BIS value.
**Medical/Surgical Devices**

Medical/surgical devices that generate high-frequency electrical or mechanical signals may produce artifacts within the measured EEG. Such devices include:

- Fluid and forced air-warming devices
- Intravenous administration devices
- Mechanical surgical instruments
- Cardiopulmonary bypass machine

**Electrocautery Devices**

In many situations, the electrical signature of an electrocautery device is recognized as non-physiological and is not processed with the EEG data. However, these devices can generate a variety of electrical artifacts that may affect BIS as well as other patient monitoring systems used in the operating room. In situations of prolonged electrocautery, there may be a reduction in the amount of artifact-free EEG available for analysis and calculation of BIS.

In addition to addressing the problems of EMG contamination and missed near-suppression, the BIS-XP platform includes significant filtering mechanisms designed to filter out electrical artifact produced by electrocautery use. Clinical trials of the BIS-XP system have demonstrated a marked improvement in availability of BIS values and resistance to electrocautery contamination during cardiac surgical procedures.

**BIS and the “Abnormal” Brain**

Some anesthesia providers have appropriately expressed concern about the accuracy and reliability of the BIS Index in patients who have abnormal brain structure or function as the result of injury or disease. This would include patients with clear evidence of CNS disease such as prior cerebral vascular accident with residual neurologic impairment. It would also include patients with systemic illness who may have neurologic implications, for example, those with encephalopathy complicating hepatic or renal disease. Because of limited clinical experience using BIS technology with such patients, BIS values should be interpreted cautiously in patients with known neurological disorders. For example, one case series reported response to command at lower BIS values (50-70) in patients while undergoing tumor resection during awake craniotomy. All of these patients were taking anticonvulsant medication. Similarly, awakening (eye opening) has been observed at low BIS values during the postictal recovery phase of ECT procedures. One approach advocated by two authors is to obtain a baseline BIS value prior to induction of anesthesia to determine whether abnormal CNS status may impact the reliability of the BIS Index.
BIS and Pharmacologic Responses

Nitrous Oxide
The BIS Index is sensitive to the clinical pattern of administration and the relative dosing of nitrous oxide and other anesthetic agents. For example, as a sole agent administered for sedation, nitrous oxide appears to have little sedative effect at concentrations of up to 50%, and the BIS value similarly is unaffected. In one volunteer study, however, administration of 70% nitrous oxide did produce unconsciousness but without a change in BIS value.

The intraoperative addition of nitrous oxide to inhalation anesthesia has had variable effect on BIS values. One study reported a dose-dependent decrease in BIS when 20-60% nitrous oxide was administered, while another found no change in BIS with addition of 50% nitrous oxide. In studies with intravenous balanced techniques (propofol/remifentanil or midazolam/fentanyl), the addition of 70% nitrous oxide did not alter BIS with or without surgical stimulation.

In a study focusing on the response to laryngoscopy, nitrous oxide administration prevented the movement response but not a hemodynamic response, without changing BIS. Thus, the effect of nitrous oxide per se seems to be non-linear with respect to hypnosis, and the contribution to the anesthetic state may be via its potent analgesic effects.

Ketamine
Ketamine, an intravenous anesthetic of unique chemical and pharmacodynamic characteristics, continues to play a valuable role in the care of a small number of patients. One of the expected physiologic effects of ketamine is the activation of the EEG (increase in high frequency activity). Thus, following administration of a clinically effective dose of ketamine (e.g., 0.25 – 0.5 mg/kg), BIS values may remain high, despite onset of significant sedation.

The timing of administration of ketamine is also important. When a dissociative dose of ketamine is administered in the setting of propofol-induced sedation, it has no acute effect on BIS, but minimizes the increase in BIS in response to profound stimulation. Several reports have described the successful use and clinical utility of BIS during intravenous techniques involving ketamine administration (i.e., dose administration < 1 mg/kg) with simultaneous propofol administration.
**Etomidate**

Etomidate, another intravenous anesthetic agent, also has a unique pharmacodynamic profile. Anesthesia induction with etomidate frequently results in skeletal muscle excitation (i.e., myoclonus, tremor, fasciculations). This clinical effect may result in the presence of high EMG activity and thus an increased BIS during the period of musculoskeletal excitement. However, following induction (or with the onset of neuromuscular blocking agent activity), BIS will reflect the hypnotic state of most patients. The ability of the BIS Index to reflect the sedative effect of etomidate during induction and allow effective titration of an etomidate infusion has been reported.27

**Clinical Management**

In Chapter 4 (refer to Table 2, Page 4-14 and Table 3, Page 4-15), specific consideration regarding response to sudden BIS changes or situations where BIS seems inappropriately high or low were discussed. In general, an orderly process should be followed (Table 2).

In clinical situations where artifact seems likely to have influenced the BIS value, the anesthesia provider should review all of the data collected by the BIS monitoring system. For example, as seen in Figure 5 and Figure 6, additional data provided by the EMG trend display can be used to evaluate increasing BIS values.

---

**Table 2: Recommended process to respond to sudden BIS changes or situations where BIS seems inappropriately high or low.**

---

**Figure 5: BIS Trend and Impact of EMG Tone**

BIS response during a 65 min procedure performed under general anesthesia (propofol induction, sevoflurane-nitrous oxide-fentanyl maintenance) is shown. Thirty-five minutes after induction, BIS values show a significant increase to a range > 60, suggesting possible inadequate anesthesia. However, the increase in the EMG parameter was apparent on trend review, likely from endogenous muscle tone. Because anesthetic delivery was confirmed, hemodynamic parameters were stable and clinical assessment had not changed, no change was made in anesthetic dosing during the 10 minutes prior to anesthetic discontinuation for emergence.
Where there is concern regarding the accuracy of the currently displayed BIS value, a simple strategy facilitates a rapid determination of the potential for artifact:

- Assess the signal quality index (SQI)
- Assess the EMG activity measure
- Assess the real-time EEG

The BIS system continuously calculates a signal quality index (SQI) to reflect the amount of quality EEG data entering the BIS system over the previous minute and provides that data on the display monitor. In situations of extraneous artifact correctly detected by the BIS processing system, the SQI will decline rapidly.

Many, but not all extraneous artifacts have been reported to be associated with increased “EMG” activity as measured by the BIS system. Because the EMG parameter displayed in BIS systems utilize a high-frequency spectral window (70-110 Hz), many electromechanical devices may generate an artifact that is apparent within the EMG parameter.

Figure 6: Evaluating acute changes in BIS values –

In the left panel, a sudden BIS spike raises question of adequacy of anesthesia effect during a head and neck procedure. The right panel shows the same BIS trend with simultaneous display of the EMG trend showing the link of increased EMG power (light trace) with artifactual increase in displayed BIS value. The changes in EMG activity were associated with mechanical motion at the surgical site, presumably transmitted to the BIS sensor.
Figure 7 demonstrates an example of a pacemaker-induced artifact associated with “increased EMG” activity. In contrast, a recent report of high BIS values associated with a mechanical surgical shaving device did not note an increase in EMG activity.

In addition to assessment of the SQI and EMG parameters, inspection of the current, real-time EEG directly recorded (and displayed on the monitor) may assist in the assessment of the patient and current anesthetic effect. The EEG tracing may reveal a clearly contaminated appearance thus facilitating the determination that artifact may be affecting the calculation of the BIS. However, some subtle artifacts may not be apparent in the assessment of the EEG recording from the monitor screen.
In situations where the BIS value seems discordant with another clinical parameter, EEG assessment can facilitate clinical assessment of the adequacy of anesthetic effect. Because BIS values in the range of 30-60 are frequently maintained during the maintenance period of anesthesia, typical EEG waveform patterns (Figure 8) will be seen frequently and, with experience, are easily recognized. It is important to note that no single pattern of EEG waveform will always be observed at each BIS value.

Figure 8: Representative EEG tracings associated with maintenance BIS range – Each panel shows a typical EEG tracing that may be observed during maintenance period of general anesthesia. In general, these tracings show characteristic changes of increasing amplitude, decreasing frequency and then emerging EEG suppression with deepening of anesthetic effect and decreasing BIS value.

The variety of special situations reviewed in this chapter are important reminders to anesthesia clinicians about the need to always consider BIS an additional parameter used in their assessment and management of patients under their care. No single monitoring parameter (whether BIS or another vital sign) should be used alone or in isolation to determine patient care. This chapter has attempted to review all of the known potential limitations or artifacts that may compromise the accuracy of BIS information. Prudent clinicians will recognize these potential limitations and use BIS in an appropriate manner to guide care – not as the sole source of information.
CHAPTER 6 • SPECIAL CIRCUMSTANCES

REFERENCES


**CHAPTER 7: BIS – EVOLVING ROLES AND NEW CHALLENGES**

While BIS monitoring has been used most extensively as an adjunct to anesthesia care, this practical technique for measuring brain status clearly has broader potential applications. The use of BIS monitoring can provide important – or even critical – brain status data that can significantly improve patient care and treatment outcomes in a variety of clinical settings.

**Introduction**

Real-time quantitative assessment of brain status is now an integral component of clinical anesthesia practice, enabling providers to make more informed decisions about patient management during anesthesia and sedation. However, this empiric measure of the effects of anesthetics provides information about brain status that may be of clinical value in applications outside of surgical anesthesia including:

- ICU sedation monitoring and management
- Compassionate end-of-life sedation
- Procedural sedation applications
- Neurological EEG assessment

In addition, the role of BIS monitoring continues to be explored and defined within the advancing field of anesthesiology. Recent investigations highlight the potential for BIS monitoring to both further improve anesthetic delivery and optimize intraoperative patient management.
**Evolving Roles**

**ICU Sedation Monitoring and Management**
Numerous studies have shown significant correlation between the BIS Index and the most commonly used clinical sedation rating scales – Ramsay Sedation Score, Sedation Agitation Scale, Richmond Agitation Score, COMFORT Scale, Glasgow Coma Score – but without the subjectivity and limitations that accompany such observational measures of sedation.\(^1\) As a result, BIS monitoring has been explored as a technology to facilitate sedation management and comfort care in the ICU environment.

BIS monitoring is currently most often used for evaluation of:
- Patients on mechanical ventilation
- Patients in barbiturate-induced coma
- Patients undergoing neuromuscular blockade
- Patients undergoing bedside procedures\(^2\)\(^-\)\(^4\)

**Compassionate End-of-Life Sedation**
There have been several reports describing successful use of BIS monitoring in selected patients receiving sedation during compassionate end of life care.\(^5\) As a measure of sedative effect, BIS monitoring can aid clinicians in sedative dosing decisions to maintain the desired goals of patient comfort. This approach may offer significant reassurance to both the patient’s family and ICU staff providing care during a difficult time.

**Procedural Sedation Applications**
Sedation and analgesia are administered by a variety of health care professionals in a range of settings to patients undergoing diagnostic or therapeutic procedures. BIS is being studied for the potential benefits this technology can bring to those patients.\(^6\)\(^-\)\(^7\)
Neurological Assessment

The BIS Index has been shown to correlate closely with the reductions in global cerebral metabolic rate produced by anesthetics. As reviewed in Chapter 2, in a study of volunteers receiving graded doses of anesthetics, positron emission tomography (PET) revealed a significant, direct correlation between decreases in the BIS Index and reduction in whole-brain metabolic activity (Figure 1).

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Figure 1: Correlation of BIS with Brain Metabolic Activity –
Significant correlation is seen between decreasing brain metabolic rate (%BMR = percent of initial whole-brain glucose metabolism measured from PET scan) and increasing anesthetic effect (as measured by decreasing BIS value). [Adapted from Reference 8]

This research concerning the BIS Index – as a unique processed EEG parameter – also suggests that reductions in cerebral metabolism caused by other factors will result in decreases in BIS. For example, in the operating room, physiologic changes known to impact cerebral metabolic activity – e.g., cardiac arrest, hypothermia – have been characterized by changes in BIS. A clear limitation of the BIS system, however, relates to its derivation from unilateral, frontal-lobe EEG signals. Clinicians must decide whether the capability and limitations of BIS monitoring may be appropriately utilized as a more encompassing and revealing measure of brain function.

The established link between cerebral metabolic activity and BIS values can provide revealing insights into brain function. In a recent study comparing baseline (awake) BIS values in patients with Alzheimer’s disease and multi-infarct dementia to an age-matched control group, a significant proportion of the neurologically-impaired group showed BIS values less than 93 at baseline. These abnormally low values might be expected in patients with a disease process that impairs cerebral function and memory. This observation suggests:

- Intraoperative BIS values (as a measure of anesthetic effect) must be interpreted more cautiously in these patients
- BIS technology may become useful for assessment of neurological impairment

Brain Status Monitoring During Critical Events

In the perioperative setting, several reports have described how BIS monitoring was utilized to provide reassuring confirmation of brain activity during critical events including cardiac arrest and resuscitation. In some of these reports, the link between BIS Index values and cerebral function has been an important component of patient care decisions.
**Study Design:**
- 50 year-old female; post major gynecologic procedure
- Cardiac arrest in PACU secondary to electrolyte disorders
- CPR with rapid intubation; continued for 30 minutes without success
- Evaluation of brain status with BIS prior to termination of CPR

**Outcome/Conclusions:**
- Termination of resuscitation efforts had been discussed due to concern regarding possible brain damage
- Assessment with BIS revealed BIS Index > 90
- CPR continued with successful restoration of cardiac rhythm after 5 minutes
- Patient recovered with no neurological injury

## Decrease in BIS: Alterations in Pharmacokinetics Prior to Hemodynamic Crisis

### Study Design:
- 70 year-old female: elective AAA repair
- TIVA Anesthesia: propofol and alfentanil
- Routine monitoring supplemented with BIS
- Initial course: stable hemodynamics; BIS approximately 35

### Outcome / Conclusions:
- Aortic graft inserted with cross-clamp time of 60 minutes
- Immediately after unclamping, rapid decrease in BIS from 35 to 20
- HR/MAP stable for 10 min, then severe hypotension
- Occult venous bleeding discovered, but hemostasis not possible
- Measured propofol concentration increased rapidly, presumably secondary to hemorrhage-induced alterations in pharmacokinetics
- Authors suggest that sudden, unexplained decreases in BIS should prompt assessment for factors that could alter anesthetic disposition and effect, including hypovolemia

**Study Design:**

- 69 year-old male undergoing LVAD removal 6 days after CABG for MI
- Abnormal lab values: ↑prothrombin/activate partial thromboplastin times (patient heparinized); ↓platelets; ↑BUN/↓Creatinine
- Separation from cardiopulmonary bypass successful on first attempt with moderate inotropic support
- BIS decreased precipitously: 50-60 range to < 10
- BIS remained < 15 for case duration

**Outcome/Conclusions:**

- Despite heparinization, cerebral embolus was suspected and CT imaging confirmed extensive cerebral infarction
- In this case, extensive cortical injury was apparent; small infarcts, or non-cortical infarcts may not register with decreased BIS
- BIS decreases are not specific for cerebral infarction
- A sustained and marked decrease in the BIS Index in a suspicious clinical context may warrant additional assessment

BIS in Anesthesia: New Challenges

“Closed-loop” Anesthesia Delivery

As discussed in Chapter 5, there is considerable research interest in the use of a “closed-loop” (automated) anesthesia delivery system. Several publications have appeared demonstrating the technical feasibility of this approach, and at least one study has shown that a closed-loop system may provide a more consistent outcome.22,23

Such closed-loop systems are presently only being used in clinical research. However, the ability of BIS to function as the monitoring element in these delivery systems supports the utility of this parameter for tracking anesthetic hypnotic effect.

Intraoperative Management: New Questions

Because BIS provides a measure of anesthetic effect on the brain, research will be required to further elucidate the potential links between BIS-defined anesthetic state and other indicators of patient safety.

In a novel investigation,24 intraoperative anesthetic level (as recorded by blinded BIS values) was a significant factor associated with mortality at one year following non-cardiac surgery. Of note, one-year mortality rates were higher in patients with low intraoperative BIS values, particularly in elderly patients. This finding suggests that many factors, including co-existing disease, age, and total anesthetic exposure may need to be considered as important risk factors for surgical patients.

BIS: Current Status and Future Direction

BIS is the first practical EEG parameter introduced specifically to measure the effects of anesthetics and sedatives on the brain and consciousness. BIS provides a practical tool to integrate the variables of routine anesthesia practice – anesthetic dose, drug interactions, and surgical stimulation – into a new measure of patient response. BIS monitoring enables clinicians to assess these effects separately from cardiovascular responses, enhancing the targeting of anesthesia care to individual patient requirements. Most importantly, substantial clinical research (resulting in more than 1,000 articles, abstracts and chapters) and routine experience in more than 6 million patients have demonstrated that anesthesia management that integrates BIS monitoring with other traditional vital signs and clinical judgment improves patient outcomes.

As experience with BIS monitoring technology grows and the technology becomes increasingly integrated in anesthesia care and sedation management, new applications for its use will continue to evolve. All new technologies have limitations. The challenge and the opportunity ahead is to realize fully the potential of BIS monitoring in the wide variety of clinical settings where it has the potential to enhance clinical decision-making, improve patient outcomes, and provide greater insight into brain function.
REFERENCES


The BIS system consists of (Figure 1):

- Sensor
- Patient interface cable (PIC)
- Digital signal converter (DSC)
- Monitor/module

The following sections provide information on the handling and operation of each component.

**SENSOR**
There are a variety of sensors (Figure 2). Each sensor terminates in a tab which allows connection to the patient interface cable.

Correct application technique of the sensors is described on the following pages.
**Quatro Sensor**

The Quatro sensor incorporates 4 circular areas which need to be positioned accurately on the patient’s forehead (Figure 3).

Sensor application should be done in the following sequence:

- Determine which temple area is to be used for sensor attachment.
- Orient the sensor so that circle 3 can be secured to that temple area and the sensor can be applied on forehead at an angle.
- Remove backing and position circle 1 approximately 2 inches above the nose.
- Position circle 4 above and adjacent to the eyebrow.
- Position circle 3 on either temple area between the corner of the eye and the hairline in a vertical fashion.
- Press edges of sensors to assure adhesion.
- Press circles firmly for 5 seconds to assure proper contact.
- Insert sensor tab into patient interface cable.

![Figure 3: Quatro Sensor Placement](image)
**Pediatric Sensor**

The Pediatric sensor is designed for better fit on smaller patients. The sensor incorporates 3 circular areas which need to be positioned accurately on the patient’s head (Figure 4).

Sensor application should be done in the following sequence:

- Determine which temple area is to be used for sensor attachment.
- Orient the sensor so that circle 3 can be secured to that temple area.
- Remove backing and position circle 1 approximately 1.5 inches above the nose in the center of the forehead.
- Position circle 3 on either temple area between the corner of the eye and the hairline in a vertical fashion.
- Press edges of the sensor to ensure adhesion.
- Press circles firmly for 5 seconds to assure proper contact.
- Insert sensor tab into patient interface cable.

**Standard Sensor**

The Standard sensor incorporates 3 circular areas which need to be positioned accurately on the patient’s head (Figure 5).

Sensor application should be done in the following sequence:

- Determine which temple area is to be used for sensor attachment.
- Orient the sensor so that Circle 3 can be secured to that temple area.
- Remove backing and apply Circle 1 to center of forehead, approximately 1.5 inches above bridge of nose.
- Apply circle 3 to temple area, between corner of eye and hairline in a vertical fashion.
- Press edges of the sensor to ensure adhesion.
- Press circles firmly for 5 seconds to assure proper contact.
- Insert sensor tab into patient interface cable.
**Patient Interface Cable (PIC)**
The patient interface cable (PIC) connects the sensor to the digital signal convertor.

To connect the sensor to the PIC (Figure 6A):
- Orient sensor tab with blank side up.
- Insert tab into PIC connector and advance until audible click is heard.

To disconnect the sensor from the PIC (Figure 6B):
- Press release button on PIC connector.
- Retract sensor tab.

**Digital Signal Converter (DSC)**
The digital signal converter includes an attachment clip to secure the DSC near the patient’s head. The converter also incorporates:
- Pigtail with PIC connector
- Monitor interface cable

To connect the PIC to the DSC pigtail (Figure 7):
- Inspect pin configuration and align the two connectors properly.
- Insert the PIC into the DSC pigtail.

The monitor interface cable provides the connection between the DSC and the monitor.
**Monitor/Module**

To connect the monitor interface cable to the DSC port on the front of the monitor (Figure 8):

- Inspect pin configuration and align monitor interface cable properly with the DSC port.
- Insert the monitor interface cable firmly into the DSC port.

In a modular configuration, the monitor interface cable attaches the same way to the DSC port on the module.

The monitor front panel on the A-2000 incorporates the controls required for operation of the BIS System and the BIS trend display screen.
Front Panel Controls (Figure 9)

Silence Key (1)
- Toggles alarms off and on.

Review Keys (2)
- Provide access to Review mode to inspect data logged during the case (BIS Index log).

Menu/Exit Key (3)
- Provides access to Setup Menu.
- Allows exit from menus or review mode.
- Terminates certain diagnostic procedures (e.g., sensor check)
- Signals “No” answer to questions.

Up and Down Arrow Keys (4)
- Allow access to various menu selections.
- Increase and decrease values.
- Vary reporting intervals in BIS log display.

Select Key (5)
- Allows access to options within menu selection.
- Confirms entries.
- Signals “Yes” answer to questions.
**BIS Trend Display Screen**
The BIS Trend Display Screen (Figure 10) consists of four regions:

- BIS Index numeric region (1)
- Signal quality region (2)
- Message region (3)
- Graphic display region (4)

**BIS Index Numeric Region (Figure 11)**

- Displays current BIS Index value.
  - Solid number indicates good signal quality
  - Outlined number indicates signal quality less than 50%
  - Absence of number indicates loss of signal
- Displays alarm silence icon when silence key is pressed.
- Displays battery icon when monitor is operating on battery power.
**Signal Quality Region (Figure 12)**

- Displays Setup Menu when Menu/Exit key is pressed.
- Displays instructions when in Review mode.
- Displays signal quality information in all other modes:
  - Signal quality index Bar Graph
    - Scaled from 0 to 100 in increments of 10.
    - 100 indicates optimal signal.
  - Electromyograph (EMG) Bar Graph
    - Indicates power (in decibels) from muscle activity or high-frequency artifacts.
  - Electroencephalogram (EEG) Waveform Display
    - Displays EEG waveform.
  - Suppression Ratio (SR) Number
    - Indicates percentage of time over last 63-second period that the EEG signal is in suppressed (isoelectric) state.

**Message Region (Figure 13)**

- Displays text which indicates status and error messages.
Graphic Display Region (Figure 14)

- Trends BIS as graph over 1 hour period.
  - BIS Range on left axis
  - BIS displayed above left corner of graph
- Trends graphs of optional secondary variable.
  - Secondary variable on right axis
  - Variable name displayed above right corner of graph
  - Optional variables include:
    - Suppression Ratio (SR)
    - EMG
    - Signal quality index (SQI)
- Displays instructions and status during sensor check procedure
- Alternate data displays include:
  - EEG waveform
  - BIS log-numeric table
  - Density spectral array (DSA)
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Anesthesia Management Strategies Using the BIS Index

* Potential impact of artifact should be considered when interpreting BIS values.
Awake
- Responds to normal voice

Burst Suppression

General Anesthesia
- Low probability of explicit recall
- Unresponsive to verbal stimulus

Deep Hypnotic State
- Burst Suppression

Flat Line EEG

BIS INDEX RANGE

BIS Index