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## **Monitoring Consciousness Using the Bispectral Index™ (BIS™) During Anesthesia**

Second Edition  
Scott D. Kelley, M.D.



# Monitoring Consciousness

## USING THE BISPECTRAL INDEX™ (BIS™) DURING ANESTHESIA

A Pocket Guide for Clinicians

SECOND EDITION

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## LEARNING OBJECTIVES

After reading this guide, the anesthesia clinician will be able to:

- Describe the link between anesthetic effect, EEG signals and the BIS™ Index
- Integrate BIS™ monitoring information during induction, maintenance and emergence
- Identify special situations which can influence BIS monitoring
- Formulate responses to sudden BIS monitoring changes occurring during anesthesia
- Summarize the evidence-based impact of utilizing BIS monitoring during anesthesia care
- Recommend a role for BIS monitoring in a strategy to reduce the risk of awareness
- List resources and pathways to access additional clinical support for BIS monitoring

This resource is intended for educational purposes only. It is not intended to provide comprehensive or patient-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 current product information including the Indications for Use currently provided by the manufacturer. Neither the publisher, author, nor Aspect Medical Systems, Inc. assumes any responsibility for any injury and or damage to persons or property resulting from information provided in this text.

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## EXECUTIVE OVERVIEW AND KEY POINTS

Bispectral Index™ (BIS™) monitoring systems enable anesthesia professionals to access processed EEG information as a measure of the effect of certain anesthetics during the care of patients they select to monitor. The clinical impact of BIS™ monitoring has been demonstrated in a variety of randomized controlled trials that reveal the potential for BIS monitoring to facilitate improvements—including patient safety—in anesthesia care.

Because BIS monitoring may be new to some anesthesia professionals, it is important to recognize the fundamental elements of BIS™ technology and appreciate the linkages between the BIS monitoring information and the clinical status of the patient. Prior to using BIS monitoring information as an adjunct to guide anesthesia care, it is also important to review important situations and limitations that can influence the BIS monitoring number.

A more in-depth discussion of the following key points can be found in this guide:

- **BIS™ Index: A Processed EEG Parameter with Clinical Validation (See Page 5)**
  - The BIS Index is the output from advanced EEG signal analysis offered by Covidien. During signal analysis, multiple characteristics of the EEG are determined. The BIS™ algorithm was developed to quantify the changes in these EEG features that best correlate with drug-induced changes in clinical state.
- **BIS™ Monitoring Clinical Range: A Continuum Concept (See Page 7)**
  - The BIS Index is a dimensionless number scaled to clinical end points as well as specific EEG features. Awake, unsedated individuals typically have BIS values >97.

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With progressive drug-induced sedation, BIS™ numbers decline, and BIS™ values should be interpreted with this continuum in mind. A BIS value of 60 has a high sensitivity for identifying drug-induced unconsciousness. However, in some settings and with some combinations of sedatives and analgesics, unconscious individuals may have BIS values >60. BIS values <30 signify increasing amounts of EEG suppression. A BIS value of 0 represents an isoelectric EEG signal.

- **Using BIS™ Monitoring During General Anesthesia (See Page 11)**

- Administration of general anesthesia involves using anesthetic medications to induce and maintain unconsciousness, and then reducing and/or discontinuing the anesthetics to permit emergence and return of consciousness. Anesthesia professionals should appreciate that in the majority of clinical investigations using BIS monitoring to help guide anesthetic agent dosing, the primary anesthetics were adjusted to maintain BIS values less than 60 during surgery.
- Consideration of BIS monitoring information may be useful in various clinical situations that develop during anesthesia care. Similarly, clinicians should also be prepared to assess and respond to unexpected changes in the BIS values. Ideally, BIS monitoring information should be integrated with other available monitoring information and patient assessment.

- **Special Issues Impacting BIS Monitoring (See Page 18)**

- It is important to understand that several clinical situations can influence the accuracy of the BIS value as an indicator of anesthetic hypnotic effect. Four key areas include: the influence of muscle tone (EMG) from the forehead muscles; electrical and mechanical artifacts



from medical devices; abnormal EEG states; and certain anesthetic agents and adjuvants—which can all lead to elevated BIS values. Serious clinical conditions—which may require prompt response—have been associated with the sudden appearance of low BIS™ values.

- **Clinical Impact of BIS™ Monitoring (See Page 24)**

- A substantial number of randomized controlled trials demonstrate the impact of BIS monitoring-guided anesthesia care on patient outcomes. Compared with standard clinical practice, adjusting primary anesthetic dosing to maintain BIS values within a target range (typically BIS values of 45 to 60 during maintenance) has, with certain anesthetic agents, reduced anesthetic dosing, emergence and recovery times. Use of BIS monitoring to help guide anesthetic administration may also be associated with the reduction of the incidence of awareness with recall in adults during general anesthesia and sedation.

- **BIS Monitoring and Reducing Awareness (See Page 25)**

- Unintended intraoperative awareness may occur in 0.1% to 0.2% of adult patients undergoing general anesthesia. Because of the potential for psychological injury, numerous organizations are supporting efforts to reduce the incidence of awareness. The effectiveness of BIS monitoring has been demonstrated in two prospective trials, and clinicians may wish to consider this evidence in developing patient-specific strategies to avoid awareness.

More recent information and additional clinical, educational and training resources can be accessed at [www.BISeducation.com](http://www.BISeducation.com). If you require clinical information on the use of BIS monitoring, please contact Covidien at (800) 635-5267 option 3 or [www.covidien.com](http://www.covidien.com).

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## Important Information About Using BIS™ Monitoring

BIS monitoring systems are intended for use by healthcare personnel trained in their proper use. They are intended for use on adult and pediatric patients to monitor the state of the brain by data acquisition of EEG signals.

**BIS™ technology may be used as an aid in monitoring the effects of certain anesthetic agents; its usage with certain anesthetic agents may be associated with a reduction in primary anesthetic use and a reduction in emergence and recovery time. Use of BIS monitoring to help guide anesthetic administration may be associated with the reduction of the incidence of awareness with recall in adults during general anesthesia and sedation.**

BIS monitoring is a complex technology intended for use as an adjunct to clinical judgment and training. Clinical judgment should always be used when interpreting BIS™ values in conjunction with other available clinical signs. **Reliance on BIS values alone for intraoperative anesthetic management is not recommended.** As with any monitored parameter, artifacts and poor signal quality may lead to inappropriate BIS values. Potential artifacts may be caused by poor skin contact (high impedance), muscle activity or rigidity, head and body motion, sustained eye movements, improper sensor placement and unusual or excessive electrical interference. BIS values should also be interpreted cautiously with certain anesthetic combinations, such as those relying primarily on either ketamine or nitrous oxide/narcotics to produce unconsciousness. Due to limited clinical experience in the following applications, BIS values should be interpreted cautiously in patients with known neurological disorders and those taking other psychoactive medications.

## THE BIS™ INDEX—A CLINICALLY VALIDATED PROCESSED EEG PARAMETER

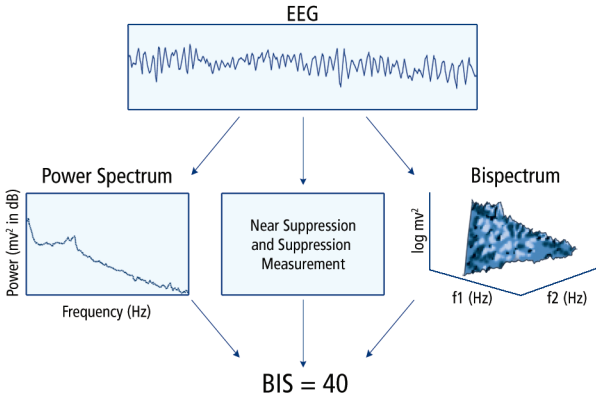
The BIS Index is a processed EEG parameter with extensive validation and demonstrated clinical utility. It is derived utilizing a composite of measures from EEG signal processing techniques including bispectral analysis, power spectral analysis, and time domain analysis. These measures were combined via an algorithm to optimize the correlation between the EEG and the clinical effects of anesthesia, and quantified using the BIS Index range.

In 1996, the U.S. Food and Drug Administration cleared the BIS Index as an aid in monitoring the effects of certain anesthetic agents. In 2003, the Food and Drug Administration cleared an additional indication which states: “Use of BIS™ monitoring to help guide anesthetic administration may be associated with the reduction of the incidence of awareness with recall in adults during general anesthesia and sedation.” The use of BIS monitoring to guide anesthetic administration and monitor patient status is a clinical decision. It is the responsibility of each clinician to make clinical practice decisions that are in the best interest of the patient.

Today, the BIS Index remains the most validated form of consciousness or brain function monitoring used within the clinical context of anesthesia and sedation care. BIS Index values are the result of two particular innovations: bispectral analysis and the BIS™ algorithm.

Bispectral analysis is a 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 yields an additional EEG facet of brain activity.<sup>1</sup>

The BIS™ algorithm was developed to combine the EEG features (bispectral and others) that were highly correlated with sedation/hypnosis in the EEGs from more than 5,000 adult subjects. The four key EEG features that characterized the full spectrum of anesthetic-induced changes were the degree of high-frequency (14 to 30 Hz) activation, the amount of low-frequency synchronization, the presence of nearly suppressed periods within the EEG, and the presence of fully suppressed (i.e., isoelectric, “flatline”) periods within the EEG.<sup>2</sup> The algorithm enables the optimum combination of these EEG features to provide a reliable processed EEG parameter of anesthetic and sedative effect—the BIS™ Index (Figure 1).

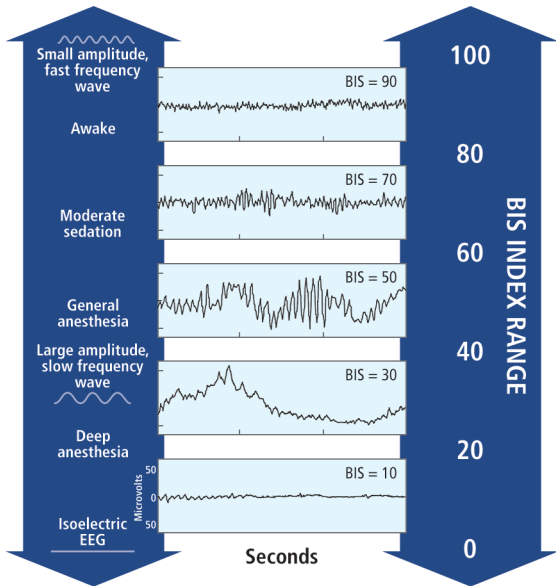


**Figure 1:** The BIS algorithm, developed through statistical modeling, combines the contribution of each of the key EEG features to generate the scaled BIS Index.

## THE BIS™ INDEX: A CONTINUUM

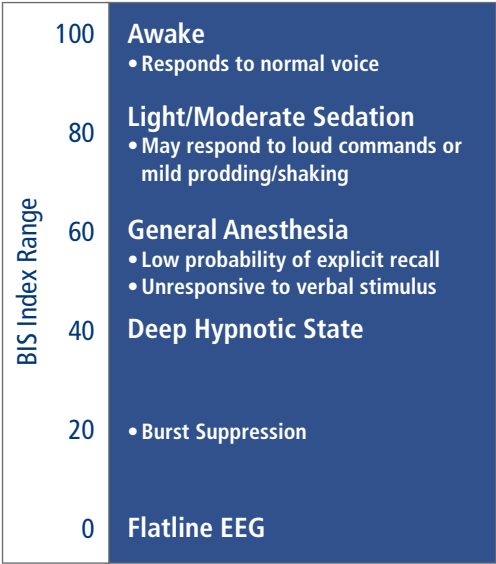
The BIS Index is a number between 0 and 100 scaled to correlate with important clinical end points and EEG states during administration of anesthetic agents (Figure 2).

BIS values near 100 represent an “awake” clinical state while 0 denotes the maximal EEG effect possible (i.e., an isoelectric EEG).



**Figure 2:** The BIS Index is scaled to correlate with important clinical end points during administration of anesthetic agent.

It should be noted that the BIS™ Index range represents a continuum that correlates to the clinical state and expected responses (Figure 3).



**Figure 3:** BIS Index Range: A Continuum of Clinical State and EEG Changes. This chart reflects a general association between clinical state and BIS values. Ranges are based on results from a multicenter study of BIS values involving the administration of specific anesthetic agents. BIS values and ranges assume that the EEG is free of artifacts that can affect its performance. Titration of anesthetics to BIS value ranges should be dependent upon the individual goals established for each patient. These goals and associated BIS value ranges may vary over time and in the context of patient status and treatment plan.

As BIS™ values decrease below 70, memory function is markedly impaired and the probability of explicit recall decreases dramatically. During sedation care, BIS values >70 may be observed during apparently adequate levels of sedation. At these levels, however, there may be a greater probability of consciousness and potential for recall.<sup>3</sup>

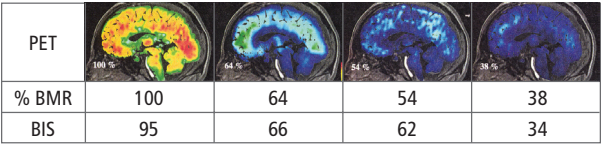
In volunteer studies, a threshold of BIS value <60 has a high sensitivity to reflect unconsciousness. As noted previously, the specificity of this threshold value may be quite dependent upon the anesthetic technique utilized—particularly with the combination of opioid analgesics. Although a continuum of responses may occur around a BIS value of 60, prospective clinical trials have demonstrated that maintaining BIS values in the range of 45 to 60 ensures adequate hypnotic effect during balanced general anesthesia while improving the recovery process.<sup>4</sup> Similarly, in two large prospective trials, maintaining BIS values less than 60 was the clinical strategy associated with reducing the incidence of intraoperative awareness.<sup>5,6</sup>

BIS™ Index values lower than 40 signify a greater effect of the anesthetic on the EEG. At very low BIS values, the degree of EEG suppression is the primary determinant of the BIS value.<sup>7</sup> A BIS value of 0 occurs with detection of an isoelectric EEG signal.

BIS value responses are similar when most, but not all, anesthetic agents are administered in increasing amounts. Specifically, BIS™ monitoring responses to typical hypnotic agents (midazolam, propofol, thiopental, isoflurane) were similar.<sup>8,9</sup> However, halothane has been found to have higher BIS values at an equipotent minimum alveolar concentration dose.<sup>10</sup> Further, BIS value responses to ketamine administration are atypical.<sup>11</sup>

In addition, BIS™ monitoring responses to administration of analgesic agents—including opioid analgesics and nitrous oxide—depend on the level of concomitant stimulation.

BIS™ Index values may reflect the reduced cerebral metabolic rate produced by most hypnotics. A significant correlation between BIS Index values and reduction in whole brain metabolic activity due to increasing anesthetic effect was measured using positron emission tomography (Figure 4).<sup>12</sup> However, factors other than drug administration that can influence brain metabolism (e.g., alterations in temperature or physiologic homeostasis) may also produce changes in the BIS Index.



**Figure 4:** 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 12)

Finally, it is important to note that the BIS value provides a measurement of brain status derived from the EEG, not the concentration of a particular drug. For example, BIS values decrease during natural sleep as well as during administration of an anesthetic agent.<sup>13</sup>



## BIS™ MONITORING DURING TYPICAL GENERAL ANESTHESIA

BIS monitoring provides potentially useful information during each of three phases of a “typical” general anesthetic case:

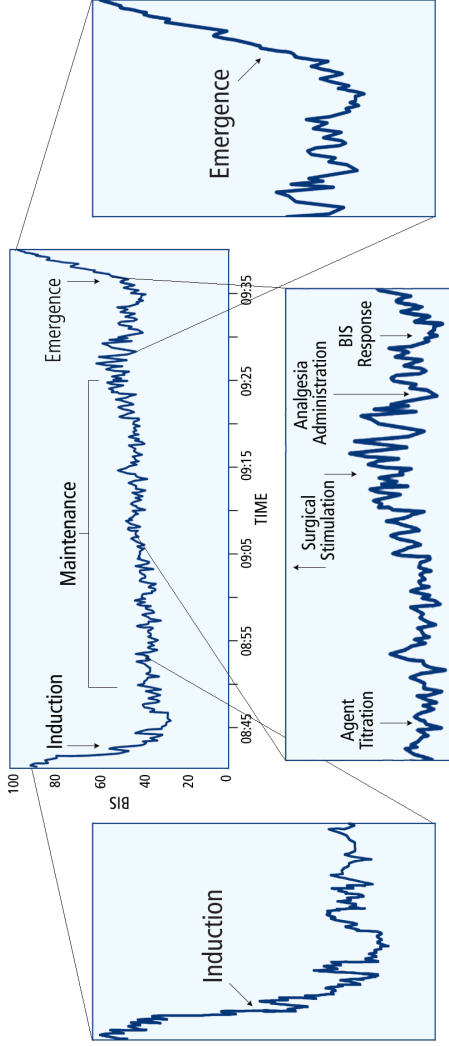
- Induction of anesthesia (and typically airway management)
- Maintenance of anesthesia
- Emergence from anesthesia

BIS™ systems display the BIS™ Index value as a single value, calculated from data gathered over the last 15 to 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. It also allows a value to be determined even if the EEG signal is briefly interrupted. Most BIS systems allow the user to change the smoothing rate to be appropriate to the clinical environment.

A BIS value, while extremely responsive, is not instantaneously altered by changes in clinical status. 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.

Most BIS systems also display a graphical trend—the BIS™ trend (Table 1)—which represents the ongoing calculations of the BIS Index during the case. Table 1 uses the BIS trend to present the information available from BIS monitoring during each of the three phases of a general anesthetic case.

**Table 1:** BIS monitoring during a general anesthetic case.



### BIS™ Monitoring During Induction

- BIS monitoring may be useful to gauge response to intravenous induction dose.<sup>14</sup>

### BIS Monitoring During Maintenance

- In response to noxious stimulation, BIS monitoring responses may be observed either parallel with or independent from hemodynamic responses.<sup>22,23,14</sup>

### BIS Monitoring During Emergence

- 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.

- BIS responses are sensitive to various adjuncts that influence intravenous induction of anesthesia.<sup>15,16</sup>
- During inhalation induction, BIS monitoring reveals interpatient variability of onset time, as well as the effect of other medications or strategies.<sup>17-19</sup>
- BIS monitoring can facilitate different strategies for intubation or placement of airway devices (e.g., laryngeal mask).<sup>20</sup>
- BIS responses during intubation are also important. History of and anticipated difficult intubation are risk factors for intraoperative awareness.<sup>21</sup> Prolonged intubation attempts may result in decreased hypnotic effect from the induction agent without obvious somatic movement.
- Because of these considerations, a good strategy is to implement BIS monitoring along with other standard patient monitors (ECG, blood pressure, SpO<sub>2</sub>, capnography) prior to induction in order to individualize patient care during both induction and airway management.
- Clinical trials demonstrate that adjustment of anesthetic dosing to maintain BIS™ values within a target range of 45 to 60 during maintenance results in improved perioperative recovery patterns as compared with standard anesthesia care.<sup>4,25</sup>
- BIS responses to stimulation may be markedly attenuated in a dose-dependent fashion with opioid administration, e.g., fentanyl or remifentanyl.<sup>26</sup>
- BIS variability—the cyclic oscillation in BIS values during surgery—may be useful to observe. Both short-term BIS variability and BIS-derived EMG activity have been useful in assessing the adequacy of analgesia in surgical patients. In volunteers, opioid analgesia reduced BIS variability.<sup>27-30</sup>
- Abrupt, unexpected changes in the BIS™ trend warrant additional assessment and clinical correlation. (See Tables 4 and 5.)
- BIS trend will reflect the decreasing hypnotic effect when anesthetic agent delivery is reduced or stopped at the end of surgery.
- BIS values during emergence are variable:
  - May increase gradually in response to a reduction in anesthetic dose (e.g., end-tidal agent concentration).
  - May increase rapidly to values >60 prior to return of consciousness, particularly if EMG tone increases substantially.
  - Are typically lower immediately after emergence than at baseline, consistent with residual drug effect.
- With adequate analgesia, a patient may remain unconscious and display BIS values <60 despite low concentration of hypnotic agent until additional stimulation is provided (e.g., oropharyngeal suctioning, positioning).
- High BIS values in an unresponsive patient could result from EMG artifact or from residual NMB effect.

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## **Integrating BIS™ Monitoring Information During Anesthesia Care**

The integration of BIS monitoring with other traditional monitoring has created new paradigms for intraoperative patient assessment and management.<sup>31-33</sup> Table 2 outlines conceptual management strategies based on integration of clinical profile with BIS monitoring data for “balanced” anesthesia techniques utilizing hypnotic and analgesic components. Using the BIS™ value in combination with hemodynamic data and patient assessment can facilitate the rational selection of sedatives, analgesics and autonomic blockers.

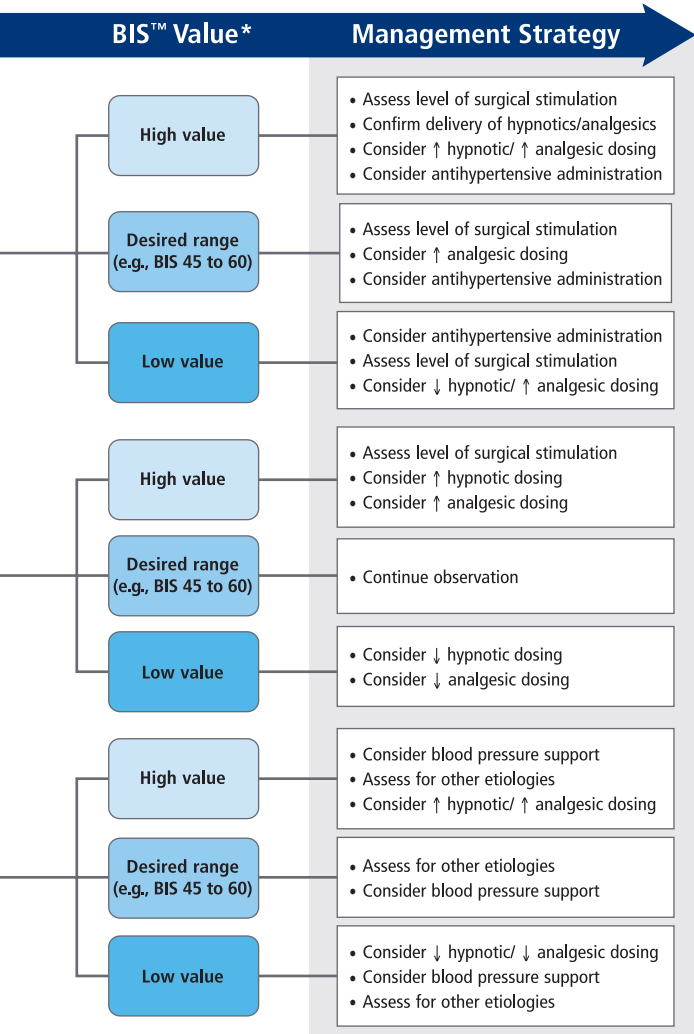
Although a BIS value of 40 to 60 is a typical target during the maintenance phase, the BIS value target range needs to be tailored to the anesthetic technique. For example, during balanced anesthesia including opioid administration to provide adequate analgesia, a target range of 45 to 60 may be very appropriate. However, for anesthesia management that utilizes little or no opioid or analgesic supplementation, increased dosing of the hypnotic agent—typically, a volatile anesthetic—to produce acceptable suppression of a noxious stimulation response (e.g., movement) will result in lower BIS values, commonly in the 25 to 35 range.

Since there is no single anesthetic technique that is appropriate for every patient for every clinical situation, optimum use of BIS monitoring to guide anesthesia care will depend upon the clinical goals of the anesthesia professional. Based on this consideration and agent-specific BIS value responses (discussed in greater detail earlier), it is important to keep in mind that there is no single BIS value or range that can be recommended as appropriate for all patients, conditions and anesthetic techniques.

It is important to emphasize that *reliance on BIS™ monitoring alone for intraoperative anesthetic management is not recommended*. Clinical judgment is crucial when interpreting BIS monitoring 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 is an additional piece of information to be incorporated with other information available for patient assessment.

Table 2: Anesthesia management strategies using the BIS Index.

Physical Signs	Clinical Profile
<ul style="list-style-type: none"><li>• Hypertension</li><li>• Tachycardia</li><li>• Movement</li><li>• Autonomic responses</li></ul>	"Light"
<ul style="list-style-type: none"><li>• Stable hemodynamics</li><li>• No movement/responses</li></ul>	"Adequate"
<ul style="list-style-type: none"><li>• Hemodynamic instability</li><li>• Hypotension</li><li>• Arrhythmia</li></ul>	"Deep"



\*Potential impact of artifact should be considered when interpreting BIS values.

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## SPECIAL ISSUES IMPACTING BIS™ MONITORING

Numerous prospective trials demonstrate that despite the potential for artifact and other issues, reliable BIS values can be obtained throughout many types of clinical cases.<sup>5,34</sup> However, in certain circumstances, BIS™ values may not be an accurate reflection of the hypnotic state. As noted, BIS monitoring is an adjunct to clinical judgment, not a substitute for it.

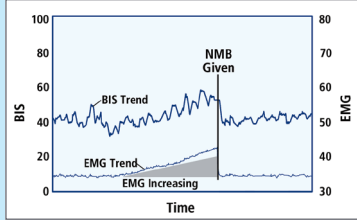
The clinician should be prepared to identify and respond to situations where the underlying EEG signals—and hence the BIS value—may not accurately reflect the clinical endpoints of sedation and hypnosis. For example, BIS values >60 may occur as the result of external artifacts, certain pharmacologic agents, or other unrelated causes rather than reflecting inadequate anesthetic effect and the potential for intraoperative awareness. Similarly, BIS values <40 may develop as a consequence of serious clinical conditions, and not merely from additional anesthetic effect. As mentioned, alterations in physiologic status which reduce brain metabolism may result in decreased BIS values.

A recent review paper provides a comprehensive discussion of the spectrum of possible artifact and clinical conditions which may impact the displayed BIS value.<sup>35</sup> It is important for clinicians to consider these conditions when evaluating unusual BIS values or trend responses. These conditions are augmented with clinical examples in Table 3.



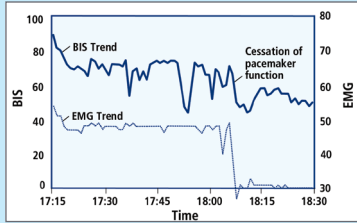
**Table 3:** Reported factors influencing BIS™ values.**EMG Artifact and Neuromuscular Blocking Agents (NMB)**

- Excessive muscle tone from forehead muscles may increase BIS values ("EMG artifact").
- NMB agents reduce EMG activity and may result in BIS decrease.
- During stable anesthesia without EMG artifact, NMB agents have little or no effect on BIS value.

**Medical Devices**

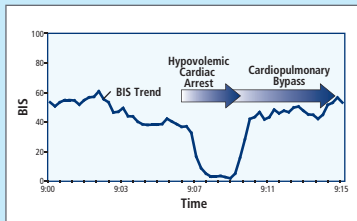
Electromechanical artifact may, under certain conditions, increase BIS values:

- Pacemakers
- Forced-air warmers applied over the head
- Surgical navigation systems (sinus surgery)
- Endoscopic shaver devices (shoulder, sinus surgery)
- Electrocautery

**Serious Clinical Conditions**

The following have been associated with low BIS values during the intra-operative period, presumably because of marked reduction in cerebral metabolism:

- Cardiac arrest, hypovolemia, hypotension
- Cerebral ischemia/hypoperfusion
- Hypoglycemia, hypothermia



**Table 3:** Reported factors influencing BIS™ values (continued).

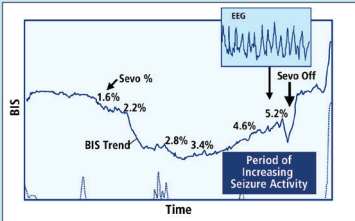
**Abnormal EEG States**

May be associated with low BIS values:

- Postictal state, dementia, cerebral palsy, low voltage EEG
- Severe brain injury, brain death
- Paradoxical arousal or paradoxical delta

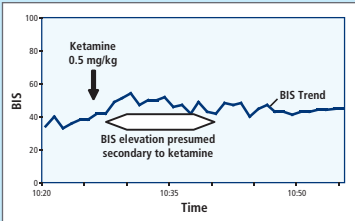
May be associated with increased BIS values:

- Epileptiform EEG activity



**Certain Anesthetic Agents and Adjuvants**

- Ketamine—May transiently increase BIS values due to EEG activation
- Etomidate—Drug-induced myoclonus may transiently increase BIS values
- Halothane—Results in higher BIS values than isoflurane or sevoflurane at equipotent MAC doses
- Isoflurane—Transient paradoxical response to increased dose has been reported
- Nitrous oxide—May have minimal effect on BIS values
- Ephedrine, but not phenylephrine, may increase BIS values



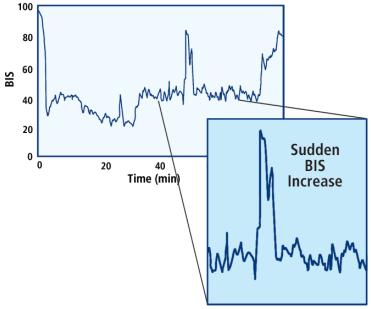
## CLINICAL MANAGEMENT: RESPONDING TO SUDDEN BIS™ VALUE CHANGES

When BIS™ monitoring is used during anesthesia care, fluctuations in BIS values will likely be noted. Such variability, like a single fluctuation in blood pressure, is not necessarily clinically significant. However, specific consideration should be given to sudden BIS value changes or situations where BIS values seem inappropriately high or low.

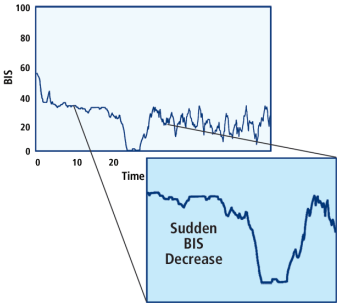
For example, changes in the hypnotic state due to changes in dose and/or patterns of agent delivery will produce changes in the BIS value. Normally, if the change in anesthetic dosing was incremental—e.g., slight adjustment in the vaporizer setting—subsequent changes in BIS values would be gradual. In contrast, a sudden dramatic change would be unexpected and additional assessment would be appropriate.

Tables 4 and 5 present an assessment process for sudden increases or decreases in the BIS value.

**Table 4:** BIS™ monitoring increase/high value assessment.

Responding to a Sudden BIS™ Value Increase	
	
<b>Examine for the presence of artifacts (EMG, electrocautery or high frequency signals)</b>	High frequency artifacts including those listed may contaminate the EEG signal and bias the BIS value toward a higher level.
<b>Ensure that anesthetic delivery systems are operating properly so that the intended dose of anesthetic agent is reaching the patient</b>	Changes in vaporizer setting, fresh-gas flow rates, intravenous infusion pump setting, and intravenous delivery routes may account for a sudden change in level of anesthetic effect and the resulting BIS value.
<b>Ensure that the anesthetic dose is sufficient</b>	An abrupt change in the BIS value may reflect a new cortical state relative to anesthetic dosing and changes in surgical conditions.
<b>Assess the current level of surgical stimulation</b>	The BIS value may show a transient increase in response to increases in noxious stimulation.

**Table 5:** BIS monitoring decrease/low value assessment.

Responding to a Sudden BIS™ Value Decrease	
	
<b>Assess for pharmacologic changes</b>	Bolus administration of intravenous anesthetic, recent changes in inhalation anesthesia, administration of adjuvant agents (beta blockers, $\alpha_2$ agonists) can all result in acute decreases in BIS value.
<b>Assess the current level of surgical stimulation</b>	BIS value may show a decrease in response to decreases in noxious stimulation.
<b>Consider decrease as possible response to administration of muscle relaxants</b>	In some situations, BIS value will decrease in response to administration of neuromuscular blocking agent, especially if excessive EMG was present prior to giving it.
<b>Assess for other potential physiologic changes</b>	Profound hypotension, hypothermia, hypoglycemia or anoxia can produce decreases in the brain state activity.
<b>Assess for emergence from anesthesia</b>	Paradoxical emergence patterns have been described with transient abrupt decreases in BIS value prior to awakening during inhalation anesthesia. The clinical significance of such changes remains unknown.

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## CLINICAL IMPACT OF BIS™ MONITORING

There is a large and growing body of scientific literature on BIS monitoring that can be reviewed by the practitioner to ascertain usage of BIS™ technology for a patient based on the type of anesthetic agent, dosage and individual patient parameters.

To date, at least 25 prospective, randomized clinical investigations have measured the influence of BIS-guided anesthesia care compared with standard practice. In most of these studies, the primary anesthetic was adjusted to maintain BIS values in a “target zone,” typically either 40 to 60 or 45 to 60.

The range of benefits that have been observed in at least one clinical trial with certain anesthetic agents include:

- Reduction in primary anesthetic use<sup>4</sup>
- Reduction in emergence and recovery time<sup>4</sup>
- Improved patient satisfaction<sup>36</sup>
- Decreased incidence of intraoperative awareness and recall<sup>5,6</sup>

The first two benefits above were shown in a study by Gan and co-workers that utilized propofol/alfentanil/nitrous oxide and found that 1) 13% to 23% less hypnotic drug was used; 2) 35% to 40% faster wake up was obtained; 3) 16% faster eligibility for PACU discharge was achieved; and 4) more patients were rated as “excellent-fully oriented” on admission to the PACU (43% vs 23%).<sup>4</sup>

As noted, BIS monitoring is also being recognized as an effective intervention to decrease the incidence of intraoperative awareness – an issue that has taken on new importance in the last several years.<sup>5,6</sup> Using BIS monitoring to reduce intraoperative awareness is discussed in detail in the following section.

## **USING BIS™ MONITORING TO REDUCE INTRAOPERATIVE AWARENESS**

Despite best intentions, a small percentage of patients undergoing general anesthesia regain consciousness unexpectedly and are able to form sufficient memory to recall portions of their intraoperative experience. This section discusses the role that BIS monitoring can play in decreasing the incidence of this adverse event.

### **Intraoperative Awareness During Anesthesia**

In several large-scale prospective investigations, the incidence of intraoperative awareness has been measured to occur during general anesthesia in 0.1% to 0.2% of patients.<sup>37-39</sup>

In 2004, the Joint Commission's Sentinel Event Alert #32 noted that each year, 20,000 to 40,000 patients may become cognizant and have recall of events during surgery.<sup>40</sup>

An overview of various perioperative factors that put patients at increased risk for awareness is presented in Table 6. Presence of some of these risk factors has been reported to increase the relative risk for awareness to nearly 1% of patients.

**Table 6:** Potential risk factors for awareness: an overview.

<b>Patient and Anesthetic History</b>	<ul style="list-style-type: none"><li>• Previous episode of awareness</li><li>• Substance use or abuse</li><li>• Chronic pain patients on high doses of opioids</li><li>• History of or anticipated difficult intubation</li><li>• ASA physical status 4 to 5</li><li>• Limited hemodynamic reserve</li></ul>
<b>Surgical Procedures</b>	<ul style="list-style-type: none"><li>• Cardiac, trauma, emergency surgery</li><li>• Cesarean section</li></ul>
<b>Anesthetic Management</b>	<p>Planned use of:</p> <ul style="list-style-type: none"><li>• Muscle relaxants during maintenance phase</li><li>• Total intravenous anesthesia</li><li>• Nitrous oxide–opioid anesthesia</li><li>• Reduced anesthetic doses during paralysis</li></ul>

The presumed cause of intraoperative awareness is a period of inadequate anesthetic effect resulting from an insufficient anesthetic dose, disruption of anesthetic delivery, or potentially inherent anesthetic resistance.<sup>41</sup> For example, in some clinical situations, administration of very low anesthetic doses may be appropriate in light of hemodynamic compromise or other clinical goals. These doses, however, are associated with a higher frequency of intraoperative awareness.

Patient reports include frightening descriptions of intraoperative awareness, highlighting the potentially horrendous sensations and emotions that may occur if anesthetic effect is inadequate.<sup>42</sup> Patients who experience intraoperative awareness may develop a spectrum of psychological injury ranging from mild, transient symptoms to severe, disabling symptoms consistent with post-traumatic stress disorder.<sup>43</sup>



## ASA Practice Advisory

The Practice Advisory for Intraoperative Awareness and Brain Function Monitoring published in 2006 describes using multiple monitoring modalities—clinical techniques, conventional monitoring and brain function monitoring—to assess anesthetic depth and reduce the likelihood of intraoperative awareness.<sup>21</sup> The Practice Advisory consensus opinion was that “the decision to use a brain function monitor should be made on a case-by-case basis by the individual practitioner for selected patients.” It should be noted that the Practice Advisory also stated that brain monitoring is not routinely indicated for all patients undergoing general anesthesia, and that brain function monitoring currently has the same status as the many other monitoring modalities used in selected situations determined by individual clinicians.

The ASA Practice Advisory aims to help the anesthesia professional develop a clinical strategy to minimize the occurrence of awareness. Such a strategy involves elements of care occurring throughout the perioperative period—preoperative assessment and preparation, intraoperative monitoring and intervention, and postoperative follow-up activities. An overview of the resulting clinical strategy is presented in Table 7. Alternatively, clinicians may wish to implement the algorithm approach presented in Figure 5 to minimize the risk for awareness.

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The Practice Advisory also alerted anesthesia clinicians to recognize that dosing anesthetic agents to achieve certain brain function values in an attempt to prevent intraoperative awareness may conflict with other medical concerns including vital organ function and existing co-morbidity.<sup>21</sup> Similarly, the Joint Commission's Sentinel Event Alert #32 noted that anesthesia professionals must weigh the psychological risks of anesthesia awareness against the physiological risks of excessive anesthesia.<sup>40</sup>

**Table 7:** Clinical strategy to minimize awareness: an overview.

<b>Preoperative Period</b>	<p>Assess risk:</p> <ul style="list-style-type: none"> <li>• Patient</li> <li>• Procedure</li> <li>• Anesthetic technique</li> </ul> <p>Provide informed consent in high-risk situations</p>
<b>Intraoperative Period</b>	<p>Consider premedication to provide amnesia</p> <p>Use multiple modalities to assess anesthetic depth</p> <ul style="list-style-type: none"> <li>• Clinical signs <ul style="list-style-type: none"> <li>– Masked with use of muscle relaxant</li> </ul> </li> <li>• Conventional monitoring <ul style="list-style-type: none"> <li>– BP, HR, end-tidal agent</li> </ul> </li> <li>• Brain function monitoring (e.g., BIS™) <ul style="list-style-type: none"> <li>Consider amnestics for unintended consciousness</li> </ul> </li> </ul>
<b>Postoperative Period</b>	<ul style="list-style-type: none"> <li>• Assess patient reports of awareness</li> <li>• Provide patient with appropriate follow-up care</li> <li>• Report occurrence for quality assurance purposes</li> </ul>

## AVOIDING AWARENESS ALGORITHM

### Preoperative Patient Assessment

- Previous episode of awareness
- Anticipated tolerance to opioids or sedatives
- Known or anticipated difficult airway
- Known or anticipated hemodynamic instability
- Surgical procedure with increased risk for awareness

### Anesthesia Management Plans

- Muscle relaxant use during maintenance phase
- Reduced anesthetic doses during paralysis
- Total intravenous anesthesia
- Nitrous oxide-opioid anesthesia

Does Patient  
Have Risk  
Factors for  
Awareness?

Inform patient of possibility of awareness

YES

Consider prophylactic administration of benzodiazepine

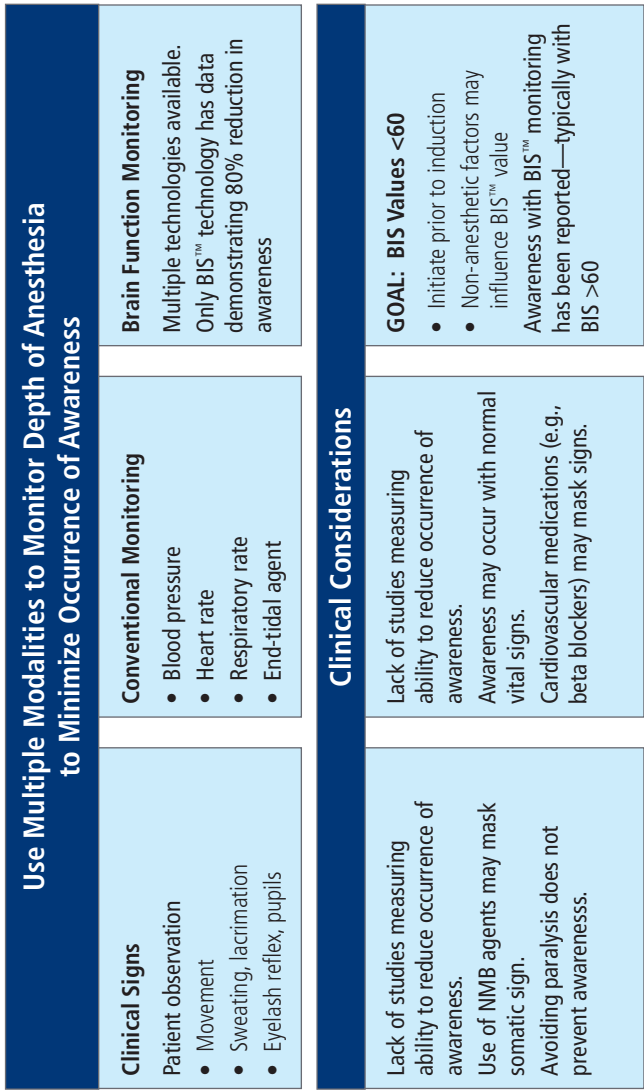
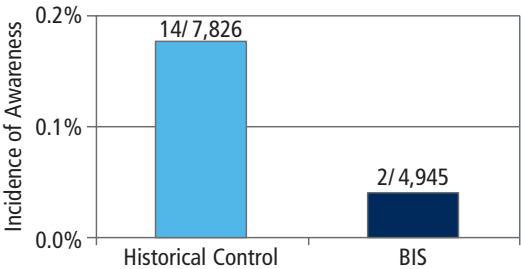


Figure 5: An algorithm approach to avoiding intraoperative awareness.

# BIS™ Monitoring and Awareness: Evidence

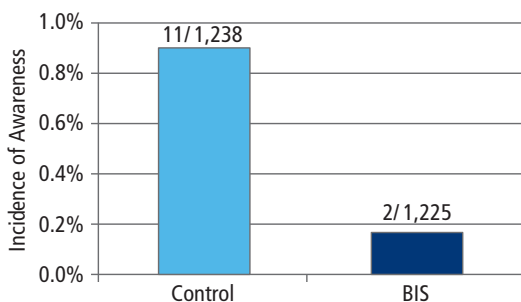
To date, the addition of BIS monitoring is the only monitoring intervention shown by scientific evidence to reduce intra-operative awareness. Two large, prospective trials have both found an approximate 80% reduction in the incidence of awareness when using BIS monitoring in addition to other routine monitors.<sup>5,6</sup> In addition to these two large trials, other reports of BIS monitoring and intraoperative awareness have appeared in the literature. These include a small randomized controlled trial,<sup>44</sup> a large cohort observational study,<sup>37</sup> as well as several case reports.<sup>45-48</sup>

The two large prospective trials provide a clinical management framework for effectively using BIS monitoring. In one investigation, the anesthesia staff was instructed to maintain BIS™ values within a range of 40 to 60, and to avoid values greater than 60 during induction and maintenance.<sup>5</sup> This management resulted in significant benefit: only two patients in the 4,945 treated patients reported awareness, representing a 77% reduction compared to the investigators' prior study (Figure 6).



**Figure 6:** BIS monitoring reduced awareness by 77% in routine patients undergoing relaxant general anesthesia.<sup>5</sup>

In the other randomized trial involving patients at increased risk for awareness, BIS™ monitoring was initiated prior to induction, and the delivery of anesthetics was titrated to maintain BIS™ values between 40 to 60 from laryngoscopy until wound closure.<sup>6</sup> This care resulted in an 82% reduction in the incidence of awareness (Figure 7).



**Figure 7:** BIS monitoring reduced awareness by 82% in patients at increased risk for awareness.<sup>6</sup>

In each study, two episodes of awareness were reported in patients despite the use of BIS monitoring. All four cases of awareness occurred during periods of significant noxious stimulation (e.g., intubation, median sternotomy) and were associated with BIS values near or greater than 60. These cases highlight the need for the anesthesia professional to be particularly vigilant to BIS value responses to noxious stimulation and to be prepared to intervene promptly when BIS values exceed 60 for some time.

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## Intraoperative Awareness and Anesthesia Practice

In addition to the ASA, professional societies from around the world have addressed the specific topic of brain monitoring to prevent awareness. The American Association of Nurse Anesthetists,<sup>49</sup> the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland<sup>50</sup> and the Australian and New Zealand College of Anesthetists<sup>51</sup> emphasize that brain function monitors be considered for use and/or available in clinical situations that place a patient at increased risk for awareness. For example, the AANA's 2006 Position Statement advised that "brain function monitoring, if available, should be considered particularly in situations where the risk of intraoperative awareness is increased."<sup>49</sup> These statements augment the opinions of ASA members: 69% of ASA members surveyed in the Practice Advisory agreed or strongly agreed with the statement: "Brain function monitors are valuable and should be used to reduce the risk of intraoperative awareness for patients with conditions that may place them at risk for intraoperative awareness."

It should be appreciated that other patients, without recognized risk factors, will experience awareness due to unanticipated or unrecognized intraoperative events. It is important to remember the clinical evidence demonstrating the efficacy of BIS™ monitoring in this situation as well.<sup>5</sup>



## THE EVOLVING ROLE OF BRAIN FUNCTION MONITORING

Despite remarkable improvements in the assessment of the cardiovascular and respiratory systems during anesthesia, determination of the effect of anesthetic agents on the central nervous system had remained a challenge. Now, technologies that permit routine neurophysiologic monitoring of the central nervous system provide a direct measure of anesthetic effect during anesthesia.<sup>52</sup> Combining brain function monitoring with traditional monitoring and assessment of clinical signs, can provide the anesthesia professional a more complete approach to optimizing the selection and/or dosing of anesthetic and adjuvant agents for each patient.

Concerns regarding the consequences of both inadequate and excessive anesthetic effect have increased in the last few years. As noted previously, inadequate anesthetic effect is the primary etiology of unintentional intraoperative awareness.<sup>41</sup> This adverse event was discussed in detail in the previous section.

Excessive anesthetic effect also has consequences. In some situations, excessive anesthetic effect may result in cardiovascular depression, and very rarely, cardiac arrest.<sup>53</sup> More recently, new concerns about other consequences of excessive anesthetic effect have appeared. Exposure to high doses of volatile anesthetic is a risk for acute transient epileptiform changes in the EEG.<sup>54</sup> In addition, excessive anesthetic effect has been associated with adverse long-term outcome.<sup>55,56</sup>

The ability of brain function monitoring to allow the anesthesia professional to monitor patient-specific anesthetic effect is important. Avoidance of excessive anesthetic effect reduces the occurrence of prolonged recovery and delayed orientation.<sup>4,36,57</sup>

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As future investigations and clinical experience establish the potential short-term and long-term risks of excessive anesthetic effect, it may become important for anesthesia professionals to better modulate patient exposure to anesthesia. Given the increasing recognition of consequences of excessive—as well as inadequate—anesthetic effect, it is likely that more anesthesia clinicians will integrate brain function monitoring into overall anesthesia management.

## SUMMARY

This pocket guide discussed how BIS™ brain function monitoring can be used most effectively during the different phases of anesthesia care. It is important for anesthesia professionals to fully appreciate the applications, limitations and special considerations for use of BIS™ monitoring.

During the past decade, BIS monitoring has been utilized in the care of more than 18 million patients with a well documented safety and efficacy record. As a result, BIS monitoring is well established as a useful device within the anesthesia professional's realm.

Evidence in the literature documents patient benefits in the area of safety and in the quality of anesthesia care resulting from the use of BIS monitoring. These clinical investigations provide an evidence-based rationale for incorporation of BIS monitoring as a tool to facilitate intraoperative management with certain anesthetic agents.

Depending upon the specific patient characteristics, surgical procedure and planned anesthetic technique, utilization of BIS monitoring may be a very appropriate decision. However, the decision to use BIS monitoring should be made on a case-by-case basis by the individual practitioner.

As clinical experience and investigation continue, anesthesia clinicians are encouraged to stay current with available literature regarding the use, benefits and limitations of BIS monitoring to guide patient care. Additional clinical information and other educational resources can be accessed at [www.BISeducation.com](http://www.BISeducation.com). Clinical support is also available via telephone (USA Toll Free: 800.635-5267, option 3) and email ([HQTSWEB@Covidien.com](mailto:HQTSWEB@Covidien.com)).

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