The ability to judge the depth of anesthesia has been a continuous quest ever since Snow first described 5 stages of ether anesthesia in 1847. Guedel further refined these 5 stages in the 1920s. Guedel’s signs and stages served as the basis for judgment of anesthetic depth until neuromuscular blocking agents gained widespread acceptance. With the advent of neuromuscular relaxants and other adjunctive agents, many of the classic signs and stages described by Snow and Guedel were obliterated.

The incidence of recall and awareness under general anesthesia has been reported to be between 0.2% and 1.6%. Many investigators believe that the incidence of recall is underreported because patients are hesitant to report events of awareness under anesthesia and clinicians may be hesitant to ask patients for evidence of intraoperative awareness. When intraoperative awareness occurs, the patient can have devastating psychological and cognitive effects. Consider this quote from a patient who had an episode of awareness during surgery: “Since my surgery, I have experienced frequent and recurring nightmares. I often wake up in the middle of the night and see my bedroom walls turn red…. I cannot go to bed without [the] nightlight on, and the window blinds must be opened…. At times I have great difficulty remembering things such as finding my way to the airport…. I cannot bear to drive at night…. I forget how to spell the simplest words.”

The development of a monitor to provide reliable, predictable measurement of the anesthetic state of the brain has eluded clinicians for many years. Practitioners commonly rely on vital signs as an indication of the patient’s anesthetic status. Vital signs, however, can be misleading, as they can be influenced by a variety of factors unrelated to the depth of anesthesia. The BIS [bispectral index] monitor (Aspect Medical Systems, Natick, Mass) is, to date, the most effective and the only US Food and Drug Administration–approved monitor to measure the anesthetic state of the central nervous system (CNS). Despite the proven reliability and effectiveness of the BIS monitor, many clinicians are resistant to the implementation of such a device, believing that the incidence of awareness does not justify the cost or that their current practice is adequate without the addition of another monitor. However, the recent attention focused on intraoperative awareness by the media may cause many clinicians to rethink their opinions about the use of the BIS monitor. This article reviews the development of the technology of the BIS monitor, describes the effectiveness and reliability of the BIS monitor in comparison with other frequently used monitors, describes the cost-benefit relationship in the deployment of the BIS monitor, and discusses some possible future uses for the BIS monitor.

**History and development of the BIS monitor**

As early as the 1870s, physiologists were aware of electrical impulse formation in the cortical regions of the brain. Since 1939, anesthesiologists have been aware of changes in the electroencephalogram (EEG) produced by anesthetic agents. Typically, there have been 3 indications for using the EEG to monitor drug effect: (1) for quantification of drug action with CNS activity, (2) for the assessment of metabolic suppression of the CNS by
pharmacological maneuvers, and (3) to monitor for cerebral ischemia during cross-clamping of the carotid artery. 

Because of the labor intensity involved in EEG monitoring, the differing effects on the EEG of different anesthetics, the electrically unfriendly climate in the modern operating room, and the lack of data showing an impact on patient outcomes, the routine use of intraoperative EEG has not been performed. Multiple EEG variables have been evaluated for their relationship to the depth of anesthesia. Information from the standard EEG signal can be digitized to produce what is known as a power spectrum, which integrates data regarding EEG frequency and amplitude. Analysis of the power spectrum has facilitated computation of spectral edge frequency and median power frequency; however, these values were formulated on the basis of the natural awake and sleeping EEG. Therefore, these parameters fail to account for EEG alterations induced by anesthesia, and neither has been shown to be consistently indicative of anesthetic depth. In addition, the power spectrum quantifies power distribution as a function of frequency and ignores information regarding phase. The power spectrum also assumes that the EEG signal formation is a linear process and undervalues the potential for interactions between various components of that signal, a process known as phase coupling that is likely to occur in the CNS. 

The EEG bispectrum is a high-order statistical computation derived from the analog EEG. The bispectrum measures relationships between sinusoidal components of the EEG. A sinusoid has 3 basic parts: frequency, phase angle, and amplitude. Changes in frequency and power alone have been shown to be inconsistent when attempting to measure anesthetic depth. Bispectral analysis incorporates information on power and frequency with the phase coupling information that is more indicative of anesthetic depth not present in other clinical applications of EEG. The BIS uses a combination of EEG subparameters that were selected after analysis of a large database of EEGs to demonstrate specific ranges for varying phases of anesthetic effect (Figure 1). These parameters were then combined to form the optimum configuration for monitoring of the hypnotic state. The BIS is then displayed as a dimensionless number between 0 and 100 (Figure 2), with the lower numbers corresponding to deeper levels of hypnosis. A clinician using the BIS must remember that the BIS measures the response of the CNS to drugs, not the concentration of any one particular drug.

In the pursuit of a monitor for anesthetic depth, one needs to remember that the anesthetic state is defined by the triad of analgesia, amnesia, and muscle relaxation. Movement, or lack thereof, in response to skin incision has been the traditional mechanism for defining minimum alveolar concentration and also was thought to be indicative of amnesia. However, movement in response to noxious stimuli is now known to be mediated through the spinal cord as opposed to higher brain centers. Volatile agents may, in fact, exert suppressive effects on the spinal cord, whereas hypnotic agents such as propofol and thiopental do not. The BIS monitors the hypnotic state; this accounts for the difference seen in early studies that attempted to correlate BIS with movement and noted variations with different anesthetic techniques. Most of these studies noted that higher BIS numbers did, in fact, correlate with a higher probability of movement. More recent studies have focused on the relationship between BIS and the level of hypnosis and have demonstrated a very good correlation between these parameters.

Although there is good correlation between the BIS and the level of hypnosis, as shown in Figure 2, there are many variables to consider when monitoring the BIS. The index should not be interpreted in a vacuum, but should be looked upon as information to be integrated into the whole of the patient’s anesthetic state. There are normal, genetically determined low-voltage EEG variants among the population that can result in abnormally low BIS values in awake patients; therefore, it is important to obtain baseline values before the induction of anesthesia.

**Figure 1. Schematic depiction of the development of the bispectral index**

EEG indicates electroencephalogram.

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ence of electromyographic artifacts, poor signal quality, and electrical artifacts such as those from electrocautery and forced-air warming units can cause spurious values to be displayed by the BIS monitor. With the administration of ketamine, the BIS may remain high, possibly due to the excitatory actions of ketamine, and, therefore, the BIS monitor is not reliable when used to monitor hypnosis with ketamine.19, 20

Finally, although this is the subject of controversy, there have been studies in which the BIS monitor has not been shown to reflect the hypnotic contribution to the anesthetic by nitrous oxide.21,22

One of the difficulties that had to be overcome in the development of the BIS monitor was the use of traditional EEG electrodes. There are few if any anesthesia practitioners who would go to the trouble of using the skin prep and collodion adhesive involved in the use of standard EEG electrodes. Furthermore, EEG electrodes have to be a low impedance system, thereby ruling out the use of conventional electrocardiogram electrodes. To overcome this problem, a special self-prepping electrode strip that is easily applied (Figure 5) was developed.

The provision of anesthesia has, in recent years, become increasingly safe. Patient outcomes can no longer be measured solely in terms of morbidity and mortality.23 Recent efforts tend to focus on quality of life, patient preferences and satisfaction, psychological well-being, and impact on financial resources.23-25 Potential benefits from the routine use of the BIS monitor include decreased risk of awareness, improved titration of anesthetic agents, and decreased recovery room time (Figure 6). The BIS also gives the anesthetist additional information to consider when selecting drugs for interventions, for example, when making the decision whether to deepen anesthesia with a volatile agent, add more analgesia with an opioid, or use a vasoactive drug.5

Comparison with other monitoring modalities
The aforementioned increase in patient safety in regard to the provision of anesthesia has been largely attributed to improved monitoring. Pulse oximetry, end-tidal gas monitoring, and various monitoring strategies for the detection of myocardial ischemia have been prominently mentioned as reasons for this occurrence. Although as pointed out by Orkin et al,20 much of the improvement occurred during the last 4 decades and largely preceded the introduction of more sophisticated monitoring. In the past, payment from insurance companies for interventions was made retrospectively, and innovative procedures were routinely covered by carriers. However, today much of the cost of medical care is paid for in a prospective manner and by capitated payment. Innovations are not directly covered and, therefore, must have the ability to reduce provider costs through improved

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Figure 2. Bispectral index (BIS) range guidelines

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<tr>
<th>BIS</th>
<th>Awake</th>
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<tbody>
<tr>
<td>100</td>
<td>Light/moderate sedation</td>
</tr>
<tr>
<td>70</td>
<td>Deep sedation</td>
</tr>
<tr>
<td></td>
<td>• Low probability of explicit recall</td>
</tr>
<tr>
<td>60</td>
<td>General anesthesia</td>
</tr>
<tr>
<td></td>
<td>• Low probability of consciousness</td>
</tr>
<tr>
<td>40</td>
<td>Deep hypnotic state</td>
</tr>
<tr>
<td>0</td>
<td>Flat line electroencephalogram</td>
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</tbody>
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(Reproduced with permission from Aspect Medical Systems, Natick, Mass.)

Figure 3. The triad of anesthesia

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(Reproduced with permission from Aspect Medical Systems, Natick, Mass.)
Efficacy studies typically are performed under ideal conditions with narrowly defined study groups.\textsuperscript{24} Effectiveness, on the other hand, refers to benefits to patients in the general population when a technology is used in routine practice.\textsuperscript{24} The BIS monitor has been shown to be both efficacious and effective with no mortality and very low
morbidity. Hypoxemia and coronary ischemia monitoring are commonly used or mandated modalities. However, the commonly used modalities for monitoring for coronary ischemia—automated S-T segment monitoring and monitoring the pulmonary artery pressures—have been shown to have liabilities. The sensitivity of automated S-T segment monitors has been shown to vary between manufacturers; in addition, there is also the possibility of erroneous readings. The pulmonary artery catheter has been widely studied and shown to have no advantage over a regular central venous line in patients with normal left ventricular function. Iberti et al demonstrated a wide range in the understanding among practitioners of the data obtained from the use of pulmonary artery catheters. In addition, the increased cost of caring for patients with pulmonary artery catheters may not be justified for many of the patients in whom these devices are used.

Of all the monitoring devices introduced into clinical practice during the last 25 years, none has gained more rapid acceptance than the pulse oximeter. However, the popularity of the pulse oximeter was not based on prospective studies of the efficacy or cost-effectiveness of this device. One large study done by a group in Denmark found the use of pulse oximetry in the operating room and recovery room led to a higher incidence of hypoxemia being diagnosed, higher rates of supplemental oxygen flow, and longer recovery room stays. Yet, there were no differences in overall outcomes between the monitored group and an unmonitored group. The logical conclusion is, of course, that the routine use of pulse oximetry increases costs without affecting outcome.

In comparison, to date the BIS monitor is used by approximately 650 hospitals nationwide and has been used to monitor more than 1 million anesthetics (personal communication with Peter Sebel, MD, PhD, MBA, April 2000). Cost analysis

Cost analyses of medical technology are usually performed using 1 or more of 4 commonly used methods: cost-minimization, cost-benefit, cost-utility, and cost-effectiveness. Cost-minimization is the comparison of the cost of different technologies without consideration of the outcome. Cost-benefit analysis is a comparison of the benefits obtained from the use of a technology and the overall cost of obtaining and using the technology. Cost-effectiveness analysis evaluates the costs and results of varying technologies to achieve similar outcomes. And finally, cost-utility analysis measures cost against patient preference and patient satisfaction.

Evaluating the BIS monitor by cost-minimization and cost-effectiveness analysis would be difficult, as there are no competing technologies by which the anesthetic state can be monitored. For a cost-utility analysis, it would be difficult, if not impossible, to...
find a patient who, when informed of a monitor that could decrease the likelihood of awareness and facilitate faster emergence, would decline to have such a monitor used during anesthesia, which leaves the cost-benefit analysis as the sole method for cost analysis of the BIS monitor.

Use of BIS monitor was shown in a study by Gan et al\(^7\) to provide not only for earlier extubation of patients (by almost 4 minutes), but also for significantly higher numbers of patients oriented on arrival to the postanesthesia care unit (PACU), resulting in decreased PACU time compared with patients not monitored with a BIS monitor. It has been shown by both computer simulation and in practice that a protocol designed to facilitate rapid emergence from anesthesia results in decreased PACU time and enables some patients in ambulatory settings to fast-track or bypass the phase-I (intensively monitored) PACU, which results in significant savings to both the hospital and the patient.\(^8\)-\(^10\) The BIS monitor was shown to have predictive value, when used in conjunction with desflurane anesthesia, to delineate the patients who could be fast-tracked in the ambulatory setting.\(^39\) Furthermore, it was shown by Johansen and Sigl\(^11\) that the use of the BIS monitor resulted in savings of roughly $80 per patient. These savings were the result of faster time to extubation, exit from the operating room, and faster discharge from PACU.\(^41\)

This article has focused primarily on the use of the BIS monitor in the operating room. In addition to the operating room, the BIS also has shown promise for guiding sedation for patients undergoing endoscopic procedures\(^42\) and for guiding the sedation of patients in the intensive care unit.\(^43\)

From the preceding discussion, it is safe to draw the following conclusions: The BIS monitor is an effective means to monitor the level of hypnosis in patients under anesthesia. In comparison with other commonly used monitoring modalities, the BIS has been shown to have a positive cost-benefit ratio and lower morbidity than more invasive monitoring methods.

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**AUTHOR**

James W. Bard, CRNA, CCRN, BS, is a staff anesthetist employed by The Emory Clinic at Crawford W. Long Hospital in Atlanta, Ga.

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