

CLINICAL EVIDENCE GUIDE

A SAFE AND EFFECTIVE WAY TO OPTIMIZE ANESTHESIA DURING SURGERY

Bispectral Index™ (BIS) Brain Monitoring System

This guide will help you review the clinical evidence that supports the utility of the BIS™ brain monitoring system during surgery to:

- Optimize anesthesia
- Reduce the risk of postoperative delirium
- Reduce the risk of awareness
- Improve emergence and recovery



Medtronic
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3	CHAN 2013	Summary of: Chan MTV, Cheng BCP, Lee TMC, Gin T, CODA Trial Group. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. <i>J Neurosurg Anesthesiol.</i> 2013;25(1):33-42.
4	RADTKE 2013	Summary of: Radtke FM, Franck M, Lendner J, Kruger S, Wernecke KD, Spies CD. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. <i>Br J Anaesth.</i> 2013;110(S1):i98-i105.
5	SIEBER 2010	Summary of: Sieber FE, Zakriya KJ, Gottschalk A, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. <i>Mayo Clin Proc.</i> 2010;85(1):18-26.
6	WHITLOCK 2014	Summary of: Whitlock EL, Torres BA, Lin N, et al. Postoperative delirium in a substudy of cardiothoracic surgical patients in the BAG-RECALL clinical trial. <i>Anesth Analg.</i> 2014;118(4):809-817.
7	NICE 2012	Summary of: National Institute for Health and Care Excellence (NICE). Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M. https://www.nice.org.uk/guidance/dg6 . Published November 2012.
9	PUNJASAWADWONG 2014	Summary of: Punjasawadwong Y, Boonjeungmonkol N, Phongchiewboon A. Bispectral index for improving anaesthetic delivery and postoperative recovery. <i>Cochrane Database Syst Rev.</i> 2014;(6):CD003843.
11	CHIU 2007	Summary of: Chiu CL, Ong G, Majid AA. Impact of bispectral index monitoring on propofol administration in patients undergoing cardiopulmonary bypass. <i>Anaesth Intensive Care.</i> 2007;35(3):342-347.
13	ZHANG 2011	Summary of: Zhang C, Xu L, Ma Y, et al. Bispectral index monitoring prevents awareness during total intravenous anesthesia: a prospective, randomized, double-blinded, multi-center controlled trial. <i>Chin Med J.</i> 2011;124(22):3664-3669.
15	GAN 1997	Summary of: Gan TJ, Glass PS, Windor A, et al. Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. <i>Anesthesiology.</i> 1997;87(4):808-815.
17	KLOPMAN 2011	Summary of: Klopman MA, Sebel PS. Cost-effectiveness of bispectral index monitoring. <i>Curr Opin Anesthesiol.</i> 2011;24(2):177-181.
18	REFERENCES	List of works cited



CHAN 2013

Chan MTV, et al. **BIS-guided anesthesia decreases postoperative delirium and cognitive decline.**
J Neurosurg Anesthesiol. 2013;25(1):33-42.

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STUDY INFORMATION

BACKGROUND	Anesthesia may contribute to long-term cognitive dysfunction after surgery. BIS™ monitoring-guided anesthesia has been shown to reduce the dose of anesthetics.
PURPOSE	To determine whether BIS™ monitoring-guided anesthesia decreases the incidence of postoperative cognitive decline (POCD) and delirium at 3 months in elderly patients undergoing major surgery
METHODS	<ul style="list-style-type: none"> ▪ Randomized controlled trial ▪ Two groups were studied: <ul style="list-style-type: none"> – BIS™ monitoring-guided anesthesia (n=462): Titration of anesthetics to achieve a BIS™ monitoring value of 40 to 60 – Routine care (n=459): BIS™ monitoring value was not made available; anesthetics were titrated according to clinical judgment ▪ POCD was assessed within 1 week before surgery, and 1 week and 3 months after surgery. ▪ Delirium was assessed daily in-hospital starting the morning after surgery.
RESULTS	<p>BIS™ monitoring-guided anesthesia was associated with reduced:</p> <ul style="list-style-type: none"> ▪ Rate of POCD at 3 months (10.2 vs. 14.7%; P=0.02) ▪ Rate of delirium in-hospital (15.6 vs. 24.1%; P=0.01) ▪ End-tidal volatile concentration by 29.7% (P<0.001) ▪ Estimated propofol effect site concentration by 20.7% (P<0.001) ▪ Time to eye opening (10 vs. 15 min; P<0.001) ▪ Time to postanesthesia care unit (PACU) discharge (80 vs. 92 min; P<0.001) ▪ Rate of postoperative infection (16.7 vs. 23.0%; P=0.02) ▪ Duration of time spent with BIS™ monitoring value under a threshold of < 40 (7.2 vs. 22.8 min, P<0.001) <p>Risk factors associated with POCD and delirium were lower intraoperative BIS™ monitoring value, longer time with BIS™ monitoring value < 40, and higher end-tidal volatile concentration.</p>
CONCLUSION	Use of BIS™ monitoring-guided anesthesia minimized episodes of deep sedation, and was associated with decreased incidences of in-hospital delirium and POCD at 3 months compared to routine care. For every 1000 elderly patients undergoing major surgery, BIS™ monitoring-guided anesthesia prevented 83 cases of in-hospital delirium and 23 cases of POCD at 3 months.



RADTKE 2013

Radtke FM, et al. **Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction.** *Br J Anaesth.* 2013;110(S1):i98-i105.

STUDY INFORMATION

BACKGROUND	Postoperative delirium is common in elderly patients and associated with adverse patient outcomes. Anesthetic technique is a potentially modifiable risk factor in the development of delirium through BIS™ monitoring-guided anesthetic titration.
PURPOSE	To assess whether BIS™ monitoring-guided anesthesia reduces the incidence of postoperative delirium in elderly patients undergoing noncardiac surgery expected to last at least 60 minutes
METHODS	<ul style="list-style-type: none"> ▪ Randomized controlled trial ▪ Two groups were studied: <ul style="list-style-type: none"> – BIS™ monitoring-guided anesthesia (n=575): Titration of anesthetics to achieve a BIS™ monitoring value of 40 to 60 – Routine care (n=580): BIS™ monitoring value was not made available; anesthetics were titrated according to clinical judgment ▪ Delirium was assessed twice daily in-hospital for 7 days.
RESULTS	<ul style="list-style-type: none"> ▪ BIS™ monitoring-guided anesthesia was associated with: <ul style="list-style-type: none"> – Lower incidence of delirium (16.7 vs. 21.4%; P=0.036) – Trend toward lower incidence of POCD at 7 days (18.1 vs. 23.9%; P=0.062) – Lower average number of BIS™ monitoring values < 20 (3.7 vs. 5.6; P=0.04) ▪ Delirium was associated with increased mortality after 3 months (OR=2.05; P=0.015). ▪ Percentage of episodes of BIS™ monitoring value < 20 was an independent predictor of delirium (OR=1.027; P=0.006). ▪ Mean average BIS™ monitoring values in both groups did not differ, and were below the prespecified target range of 40 to 60.
CONCLUSION	BIS™ monitoring-guided anesthesia was associated with a decrease in the incidence of delirium in elderly noncardiac surgery patients compared to routine care, potentially by preventing extremely deep sedation (BIS™ monitoring value < 20).

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SIEBER 2010

Sieber FE, et al. **Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair.** *Mayo Clin Proc.* 2010;85(1):18-26.

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STUDY INFORMATION

BACKGROUND	Postoperative delirium can persist and is associated with poor patient outcomes in elderly patients. Anesthetic technique is a potentially modifiable risk factor in the development of delirium through BIS™ monitoring-guided anesthetic titration.
PURPOSE	To compare the prevalence of delirium between deep and light BIS™ monitoring-guided propofol sedation in elderly patients undergoing hip fracture repair with spinal anesthesia
METHODS	<ul style="list-style-type: none"> ▪ Randomized controlled trial ▪ Two groups were studied: <ul style="list-style-type: none"> – Deep sedation (n=57): BIS™ monitoring-guided titration of propofol to achieve a BIS™ monitoring value of approximately 50 – Light sedation (n=57): BIS™ monitoring-guided titration of propofol to achieve a BIS™ monitoring value of ≥ 80 ▪ Delirium was assessed starting on the second postoperative day through hospital discharge.
RESULTS	<ul style="list-style-type: none"> ▪ Light sedation was associated with: <ul style="list-style-type: none"> – Lower incidence of delirium (19 vs. 40%; P=0.02) – Shorter duration of delirium (0.5 vs. 1.4 days; P=0.01) – Lower propofol dose (2.5 vs. 10.2 mg/kg; P<0.001) – Greater use (19 vs. 5%; P=0.04) and dose (5.53 vs. 1.26 mg/kg; P=0.02) of midazolam ▪ Deep sedation was identified as a predictor of delirium.
CONCLUSION	<ul style="list-style-type: none"> ▪ Using BIS™ monitoring technology to deliver light propofol sedation was associated with a 50% decrease in postoperative delirium compared to deep sedation. ▪ For every 4.7 patients receiving light sedation, 1 case of delirium is avoided. ▪ Light sedation may be a safe and cost-effective method for preventing postoperative delirium in elderly patients.



WHITLOCK 2014

Whitlock EL, et al. **Postoperative delirium in a substudy of cardiothoracic surgical patients in the BAG-RECALL clinical trial.** *Anesth Analg.* 2014;118(4):809-817.

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STUDY INFORMATION

BACKGROUND	Postoperative delirium is common in cardiothoracic surgical patients. Previous studies in noncardiothoracic surgery patients demonstrated a decrease in the incidence of delirium using BIS™ monitoring-guided anesthesia.
PURPOSE	To determine the association between BIS™ monitoring-guided anesthesia and postoperative delirium compared to end-tidal anesthetic concentration (ETAC) monitoring in cardiothoracic surgery patients at risk for intraoperative awareness
METHODS	<ul style="list-style-type: none"> ▪ Single-center, randomized controlled trial ▪ Two groups were studied: <ul style="list-style-type: none"> – BIS™ monitoring-guided anesthesia (n=149): Titration of anesthetics to achieve a BIS™ monitoring value of 40 to 60 – ETAC-guided anesthesia (n=161): BIS™ monitoring value was not made available; anesthetics were titrated to achieve an age-adjusted minimum alveolar concentration of 0.7 to 1.3 ▪ Delirium was assessed twice daily in the ICU for 10 days or until discharge. ▪ A <i>post hoc</i> meta-analysis was performed to aggregate the BAG-RECALL results with those from 3 previously published randomized controlled trials in noncardiac surgery patients with postoperative delirium as the primary endpoint.¹⁻³
RESULTS	<ul style="list-style-type: none"> ▪ BIS™ monitoring-guided anesthesia was associated with a: <ul style="list-style-type: none"> – Trend toward a lower incidence of delirium (18.8 vs. 28.0%; P=0.058) – Shorter ICU length of stay (3 vs. 4 days; P=0.006) ▪ Delirium was associated with: <ul style="list-style-type: none"> – Longer ICU length of stay (8.0 vs. 2.0 days; P<0.001) – Longer hospital length of stay (17.0 vs. 7.0 days; P<0.001) – Lower survival rate at last follow-up (84.1 vs. 94.3%; P=0.008) ▪ The meta-analysis demonstrated that BIS™ monitoring-guided anesthesia was associated with a lower odds of delirium (odds ratio = 0.56).
CONCLUSION	<ul style="list-style-type: none"> ▪ BIS™ monitoring-guided anesthesia was associated with a 9.2% relative reduction in the incidence of delirium compared to ETAC-guided anesthesia, with an odds ratio of 0.60. ▪ Although not statistically significant, this result is consistent with 3 other randomized controlled trials which, when assessed together in a meta-analysis, demonstrated an odds ratio of 0.56 in favor of BIS™ monitoring-guided anesthesia.¹⁻³ ▪ No preoperative cognitive dysfunction or delirium assessment was performed prior to enrolling patients in this trial.



NICE 2012

National Institute for Health and Care Excellence (NICE). **Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M.** <https://www.nice.org.uk/guidance/dg6>. Published November 2012.

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STUDY INFORMATION

BACKGROUND	<ul style="list-style-type: none">▪ The BIS™ monitor, E-Entropy™* monitor (GE Healthcare), and Narcotrend™* Compact M monitor (MT MonitorTechnik) EEG monitors were evaluated.▪ Standard clinical monitoring was defined as clinical observation (of pupil size and reactivity, excessive tear formation, sweating, and patient movement) and measurement of one or more clinical markers such as pulse, blood pressure, and ETAG concentration (for inhaled anesthesia).▪ Evaluation of data from pediatric patients was included.
PURPOSE	To determine the clinical and cost-effectiveness of these monitors compared with standard clinical monitoring, in patients receiving general anesthesia
METHODS	<ul style="list-style-type: none">▪ NICE considered evidence from a number of sources, but relied primarily on the assessments performed by an external assessment group.▪ A 2007 Cochrane Review article, "Bispectral Index for improving anesthetic delivery and postoperative recovery," which included 31 randomized controlled trials of monitoring with BIS™ technology compared with standard clinical practice, provided a basis for assessing clinical effectiveness of BIS™ monitoring.⁴▪ The NICE External Assessment Group identified an additional 11 published, randomized controlled trials that were used to supplement the Cochrane Review. Of the 11 trials:<ul style="list-style-type: none">– Five involved pediatric patients, aged two to 18 years– Two studies were conducted in patients with known risk factors for awareness during surgery▪ The method for administering general anesthesia varied across the 11 trials:<ul style="list-style-type: none">– Five used inhaled anesthetic (predominantly sevoflurane) for both induction and maintenance of general anesthesia.– Three used intravenous anesthesia (propofol) for both induction and maintenance of general anesthesia (total intravenous anesthesia).– Three trials used both intravenous and inhaled anesthesia. Two used propofol for the induction of anesthesia and sevoflurane for the maintenance of anesthesia.– Muscle relaxants were used in seven of the trials.



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RESULTS	<p>Statistically significant outcomes in the BIS™ monitoring group compared to clinical monitoring:</p> <ul style="list-style-type: none"> ▪ The mean difference in total intravenous anaesthesia (TIVA) consumption was slightly reduced when combined with the Cochrane Review data. The mean difference (in MAC equivalents) in inhaled anaesthetic consumption was reduced -0.15; the mean difference in intravenous anaesthetic consumption was -1.33 mg/kg/h. Both reductions were statistically significant. ▪ Time to extubation was reduced by .5 to 5 minutes in five trials with BIS™ monitoring. ▪ Time to discharge from recovery room was reduced by 6.7 to 30 minutes in all NICE trials, including four conducted in children. (Note: One trial reported time to discharge from the end of surgery and two others reported time to discharge from the end of general anesthesia.) By comparison, the mean difference in the Cochrane Review article was -7.63 minutes in favor of BIS™ monitoring. ▪ The lower incidence of confirmed awareness in the group with BIS™ monitoring and TIVA was statistically significant in the high-risk-of-awareness group. In one trial, patients at increased risk of awareness receiving TIVA reported eight cases of confirmed or possible awareness in the group with BIS™ monitoring (n=2,919) compared with 21 cases in the standard clinical monitoring group (n=2,309). ▪ Outcomes were expressed as cost-effectiveness ratios (ICERs) per quality-adjusted life years (QALYs). For patients at high risk of adverse outcomes from TIVA, the cost-effectiveness ratio for BIS™ monitoring exceeded that of the competitors and grew increasingly more cost-effective as patient risk factors were added to the assessment model.
CONCLUSION	<ul style="list-style-type: none"> ▪ EEG-based depth of anesthesia monitors help provide the appropriate level of anesthesia to each individual patient, helping to avoid inadequate or excessively deep levels of anesthesia. ▪ Based on its research, NICE recommends EEG-based depth of anesthesia monitors, including the BIS™ monitor, as an option for all patients receiving TIVA. ▪ NICE recommends monitoring because it's cost-effective and measuring ETACs in TIVA patients isn't possible. ▪ Anesthetists using EEG-based depth of anesthesia monitors should have appropriate training and experience with these monitors, and understand the potential limitations of their use in clinical practice.



PUNJASAWADWONG 2014

Punjasawadwong Y, et al. **Bispectral index for improving anaesthetic delivery and postoperative recovery.** *Cochrane Database Syst Rev.* 2014;(6):CD003843.

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STUDY INFORMATION

BACKGROUND	<ul style="list-style-type: none">▪ Many anesthesiologists rely on somatic signs (motor responses, changes in respiratory patterns) and autonomic signs (hypertension, sweating) to guide the dosage of anesthetic agents. However, these clinical signs are not reliable measures of the conscious state of the anesthetized patient, which may lead to either overdosage or underdosage.⁵▪ The meta-analysis evaluated 36 randomized or quasi-randomized controlled trials comparing the use of BIS™ monitoring or standard care (clinical signs or ETAG monitoring) in the titration of anesthetic agents regardless of blinding or the language of the article publication.▪ All studies were screened for methodological quality and applicability.
PURPOSE	To assess whether the incorporation of BIS™ monitoring into the standard practice of management of anesthesia can reduce the risk of intraoperative recall awareness, consumption of anesthetic agents, recovery times, and total cost of anesthesia in surgical patients undergoing general anesthesia
METHODS	<ul style="list-style-type: none">▪ All relevant information from the selected studies was extracted as data, examined for methodological and clinical heterogeneity, and analyzed with Cochrane Collaboration statistical software.▪ Outcomes were summarized separately based on the type of anesthetic agent used in the procedure, i.e., propofol and volatile anesthetics (desflurane, isoflurane and sevoflurane).▪ Conversion methods and random-effects models were applied to the data so that the overall effects of monitoring with BIS™ technology could be equally compared.

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RESULTS	<ul style="list-style-type: none"> ▪ BIS™ monitoring-guided anesthesia significantly reduced the requirement for anesthetic drugs by as much as 58.9%: Propofol by 1.32 mg/kg/hr (n=672); volatile anesthetics (desflurane, sevoflurane, isoflurane) by 0.65 minimal alveolar concentration equivalents (MAC) (n=985) ▪ Irrespective of the anesthetics used, monitoring with BIS™ technology reduced recovery times. Time: <ul style="list-style-type: none"> – To eye opening reduced by 1.93 minutes (n=2557) – For response to verbal command reduced by 2.73 minutes (n=777) – To extubation reduced by 2.62 minutes (n= 1501) – To orientation reduced by 3.06 minutes (n=373) ▪ PACU stay was significantly reduced by 6.75 minutes (n=1953) ▪ BIS™ monitoring did not demonstrate a notable change in discharge time ▪ In studies using clinical signs as control, the results demonstrated a significant effect of BIS™ monitoring-guided anesthesia in reducing the risk of intraoperative recall awareness among surgical patients with high risk of awareness, with an OR of 0.24 (n=7761). This effect was not demonstrated in studies where BIS™ monitoring was compared to ETAG monitoring as standard practice.
CONCLUSION	<ul style="list-style-type: none"> ▪ Anesthesia guided by BIS™ technology could improve anesthetic delivery and postoperative recovery from relatively deep anesthesia. ▪ BIS™ monitoring-guided anesthesia could significantly reduce consumption of anesthesia. ▪ In some studies, data showed that the anesthesia providers tended to use high doses of hypnotics to manage signs of inadequate anesthesia or analgesia, which resulted in too deep anesthesia as indicated by the BIS™ monitoring values. Hence, BIS™ monitoring-guided anesthesia could be helpful in optimizing the dose of hypnotics. ▪ BIS™ monitoring-guided anesthesia did not increase intraoperative recall awareness. The combined results of four studies provided evidence that BIS™ monitoring helped reduce the incidence of intraoperative recall awareness in patients at high risk of awareness compared to monitoring depth of anesthesia using clinical signs.⁶⁻¹⁶



CHIU 2007

Chiu CL, et al. **Impact of bispectral index monitoring on propofol administration in patients undergoing cardiopulmonary bypass.** *Anaesth Intensive Care.* 2007;35(3):342-347.

STUDY INFORMATION

BACKGROUND	<ul style="list-style-type: none"> ▪ TIVA is a preferred method for helping reduce the need for vasoconstrictors to maintain blood pressure during hypothermic cardiopulmonary bypass (CPB). ▪ ETAC cannot be monitored with TIVA, so BIS™ monitoring is used to control the infusion rate needed to induce and maintain the appropriate depth of anesthesia during hypothermic CPB. ▪ The dose of propofol needed during hypothermic CPB is lower than the amount needed during other surgeries. As the patient's metabolic rate decreases during hypothermia, the anesthetic effect of propofol significantly increases.
PURPOSE	To evaluate the impact of monitoring with the BIS™ system on propofol use and hemodynamic stability during hypothermic CPB
METHODS	<ul style="list-style-type: none"> ▪ Randomized controlled trial ▪ Two groups were studied: <ul style="list-style-type: none"> – Group B (n=10): The BIS™ technology-controlled adjustment of propofol infusion was used to achieve a BIS™ monitoring value of 40 to 50. – Group C (n=10): The BIS™ monitoring value was not made available; propofol administration was only titrated due to fluctuations in perfusion pressure (PP). ▪ Target propofol concentration of 2.0 µg/mL was started in both groups once ventilation was stopped (i.e., commencement of CPB), increased to 2.5µg/mL if PP was persistently >90 mmHg, and was decreased to 1.5 µg/mL if the PP was consistently <70 mmHg. ▪ The amount of phenylephrine and sodium nitroprusside used to maintain targeted PP was recorded. ▪ Anesthesia was maintained with sevoflurane both prior to and after CPB. ▪ The total amount of propofol used was measured after procedures.

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RESULTS	<ul style="list-style-type: none">▪ Propofol administration during CPB was 50% lower in the BIS™ monitoring group versus the control group, with a median propofol dose of 2.9 mg/kg/hr and 6.0 mg/kg/hr, respectively.▪ Cumulative doses of nitroprusside and phenylephrine, inotropic support after weaning from CPB, and mean arterial pressure values did not differ between groups.▪ BIS™ monitoring values were significantly and consistently higher at each time interval during CPB in the group whose propofol dosing was adjusted based upon the BIS™ monitoring system.
CONCLUSION	<ul style="list-style-type: none">▪ The 50% reduction in propofol administration in the group monitored with the BIS™ monitoring system was achievable only because hypnosis was titrated on the BIS™ monitoring values.▪ The low propofol doses achieved in the study are not recommended in the absence of monitoring with the BIS™ monitoring system.▪ Despite the higher propofol administration and lower BIS™ monitoring values in the control group, there was not an associated increase in the use of inotropes and phenylephrine. This is most likely because propofol does not affect hemodynamics during CPB, which are primarily under the control of a CPB pump.▪ The results support the notion that titration of propofol based on pharmacodynamic effects, such as BIS™ values derived from the EEG, is superior to administration based on pharmacokinetic modeling alone.

ZHANG 2011

Zhang C, et al. **Bispectral index monitoring prevents awareness during total intravenous anesthesia: a prospective, randomized, double-blinded, multi-center controlled trial.** *Chin Med J.* 2011;124(22):3664-3669.

STUDY INFORMATION

BACKGROUND	<ul style="list-style-type: none"> ▪ Avoidance of intraoperative awareness is one goal of general anesthesia all over the world. ▪ In China, the incidence of intraoperative awareness during surgical cases managed with TIVA is approximately 1%. ▪ The BIS™ monitoring device has proven to be effective at preventing awareness in several significant clinical trials, including Ekman et al, which showed BIS™ monitoring reduced the incidence of awareness from 0.18 to 0.04% (a reduction of 77%) when compared with a historical control group.¹⁰ ▪ Myles et al used BIS™ monitoring in a randomized controlled trial to guide anesthesia in patients at risk of awareness and found the incidence of awareness reduced by 82%.⁶
PURPOSE	<p>To conduct a larger scale, randomized, double-blinded, controlled trial evaluation of the efficacy of BIS™ monitoring-guided anesthesia for preventing awareness during TIVA</p>
METHODS	<ul style="list-style-type: none"> ▪ Patients who were ≥18 years of age and without any apparent mental defect were eligible if they were scheduled for TIVA and gave informed consent. ▪ A total of 13 domestic (Chinese) academic general hospitals used computer-generated randomization to divide participants into two groups. Interviewers and patients were blinded to group allocation. ▪ Patients were not premedicated with sedatives or hypnotic drugs. Anesthesia induction was initiated with midazolam and propofol. Propofol was infused for maintenance. Administration of analgesics and muscle relaxants were left to the discretion of the anesthetist. ▪ In the BIS™ monitoring-guided anesthesia group, anesthesia was adjusted and recommended to maintain BIS™ monitoring values between 40 and 60 (n=2919). ▪ In the control group, anesthesia was adjusted according to clinical signs. The screen of the BIS™ monitor was covered and could not be observed by the anesthetists (n=2309). ▪ Patient interviews for awareness occurred at the first and fourth day of surgery with a structured questionnaire, and were assessed to identify confirmed or possible awareness occurrence.

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RESULTS	<ul style="list-style-type: none"> ▪ 15 confirmed awareness patients in the control group and four in the BIS™ monitoring-guided group. BIS™ monitoring-guided TIVA reduced the incidence of confirmed awareness by 78% (from 0.65 to 0.14%). ▪ Eight cases of confirmed or possible awareness in the BIS™ monitoring-guided group, and 21 cases in the control group. ▪ The incidence of possible awareness and dreaming was comparable between the BIS™ monitoring-guided group and the control group.
CONCLUSION	<ul style="list-style-type: none"> ▪ The use of BIS™ monitoring and BIS™ monitoring-guided anesthesia significantly reduced the incidence of awareness. The results support previous findings by Ekman and Myles. ▪ The incidence of awareness in the control group was 0.65%, lower than the incidence of 1% in the previous Chinese large-scale survey, perhaps due to the anesthetists' increased alertness of awareness and the difference in patient American Society of Anesthesiologists (ASA) status values. ▪ The patients had significant variances in their surgery history, ASA status, and the types of surgery they received. These were not confounding factors of the results when analyzed using univariate analyses. ▪ This study drew similar conclusions with other studies showing that light anesthesia was the main reason for confirmed awareness.^{11,12} ▪ Intraoperative BIS™ monitoring data was available in six cases of confirmed awareness. In five cases, BIS™ monitoring values > 60 occurred for 19–106 minutes. In one case, BIS™ monitoring values were below 60. ▪ BIS™ monitoring-guided TIVA (between 40 and 60) reduces the risk of awareness compared with routine TIVA.

GAN 1997

Gan TJ, et al. **Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia.** *Anesthesiology*. 1997;87(4):808-815.

STUDY INFORMATION

BACKGROUND	<ul style="list-style-type: none">▪ The BIS™ algorithm is a variable derived from the EEG that has the ability to measure the hypnotic component of the anesthetic state. It is represented as a number from zero to 100, with decreasing values indicating more sedation and hypnosis.▪ Past studies demonstrate that BIS™ monitoring may be used to measure the effect of anesthetic agents on the level of consciousness.¹³⁻¹⁸▪ The anesthetic state is achieved with a hypnotic or sedative and an analgesic to provide absence of consciousness, amnesia, and analgesia.
PURPOSE	<ul style="list-style-type: none">▪ Primary objective: Demonstrate the efficacy of BIS™ monitoring as a pharmacodynamic measure of patient response to propofol during general anesthesia.▪ Secondary objective: Determine whether the addition of BIS™ monitoring to standard anesthetic practice improved patient outcomes.
METHODS	<ul style="list-style-type: none">▪ This multicenter, prospective, randomized clinical utility study compared “standard practice (SP)” with “standard practice plus BIS™ monitoring” treatment groups.▪ Four participating sites established a baseline of relevant outcome results from a series of patients receiving propofol-alfentanil-N₂O anesthesia to establish preexisting clinical practice. These 34 patients became the historical control group.▪ Subsequent surgical patients were selected based on set criteria and randomized to the SP (n=125) or BIS™ monitoring (n=115) groups. Demographics were similar between groups.▪ In all patients, the anesthesiologist attempted to provide a stable anesthetic with the fastest possible recovery.▪ In the BIS™ monitoring group, propofol infusions were adjusted to achieve a target BIS™ monitoring value between 45 and 60, increasing to 60 to 75 during the final 15 minutes of the case.▪ In the SP group, propofol dose adjustments were made based only on standard clinical signs. Drug use, intraoperative responses, and patient recovery parameters were recorded. The BIS™ monitor recorded data, but the screen was covered.

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RESULTS	<ul style="list-style-type: none"> ▪ The BIS™ monitoring group: <ul style="list-style-type: none"> – Required lower normalized propofol infusion rates compared with the SP group (134 vs. 116 microg x kg^[-1] x min^[-1]; P < 0.001) – Was extubated sooner (11.22 vs. 7.25 minutes; P < 0.003) – Had a higher percentage oriented on arrival to PACU (43 vs. 23%; P < 0.02) – Had better PACU nursing assessments (P < 0.001), and became eligible for discharge sooner (37.77 vs. 31.70 minutes; P < 0.04) ▪ No significant difference in the incidence of intraoperative responses between the groups
CONCLUSION	<ul style="list-style-type: none"> ▪ The study demonstrated the safety and efficacy of BIS™ monitoring as a pharmacodynamic measure of patient response to propofol during propofol-alfentanil-N₂O anesthesia. ▪ Titrating propofol with BIS™ monitoring during balanced anesthesia decreased propofol use and significantly improved recovery. ▪ Patients in the BIS™ monitoring group emerged from anesthesia faster than the SP or control patients. When comparing mean values, BIS™ monitoring patients opened their eyes, responded to verbal command, and were extubated 34 to 38% faster than SP subjects. ▪ If potential indirect cost savings associated with faster OR and PACU turnover are considered, BIS™ monitoring may facilitate cost-effective anesthetic delivery.



KLOPMAN 2011

Klopman MA, et al. **Cost-effectiveness of bispectral index monitoring.** *Curr Opin Anesthesiol.* 2011;24(2):177-181.

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STUDY INFORMATION

BACKGROUND	<ul style="list-style-type: none"> ▪ Cost-effectiveness studies in medicine are difficult to conduct. Devices and technology are used because they improve care and outcomes, even though their cost-effectiveness cannot always be quantified. ▪ BIS™ monitoring has been shown in multiple prospective randomized studies to positively affect several important aspects of an anesthetic, including less use of hypnotic anesthetic drugs,¹⁹⁻²² decreased time to extubation,^{21,22,24} earlier orientation,^{21,22} decreased times to PACU discharge,²³ and decreased intraoperative awareness.^{6,10}
PURPOSE	To draw a conclusion regarding the cost-effectiveness of using BIS™ monitoring with general anesthesia
METHODS	<ul style="list-style-type: none"> ▪ 30 randomized trials ▪ Analyzing the cost-effectiveness of BIS™ monitoring involved considering which negative outcomes would be reduced or which positive outcomes would be promoted by using BIS™ monitoring.
RESULTS	<ul style="list-style-type: none"> ▪ The benefits associated with use of the BIS™ monitoring are achieved for an additional cost of approximately \$5 per anesthetic. ▪ BIS™ monitoring has been shown in randomized controlled trials to make a difference in many anesthetic outcomes and should be used routinely irrespective of cost.
CONCLUSION	<ul style="list-style-type: none"> ▪ Two modeling studies previously estimated the cost-effectiveness of the BIS™ monitoring for preventing intraoperative awareness. Taking into account various assumptions, the cost of preventing a single case of awareness ranged \$4,410–11,111.^{24,25} ▪ In a clinical study, the cost of preventing a single case of awareness in high-risk patients was determined to be \$2,200.⁶ ▪ Taking into account the decreased use of anesthetic and decrease in PACU stays, one study found that BIS™ monitoring use resulted in a net cost of only \$5.55 per use.¹⁹ ▪ A diagnostic guidance assessment review by NICE determined that BIS™ monitoring technology is cost-effective during TIVA anesthetics because it provides an alternative to ETAC monitoring.²⁶



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