

# POSTOPERATIVE DELIRIUM. ADVANCED MONITORING FOR IMPROVED OUTCOMES.<sup>1,2</sup>

## BIS™ Brain Monitoring System

In 2015, a multidisciplinary group of scientists and clinicians reported that a diagnosis of postoperative delirium independently increases the likelihood of:<sup>3</sup>

- Institutionalization
- 30-day readmission
- An extended hospital stay

These outcomes may increase cost of care on average by \$8,000 to \$10,000.<sup>4,5</sup> Patients with postoperative delirium also have significantly increased odds of dying in the hospital<sup>6,7</sup> and at 3 to 6 months after surgery.<sup>6-8</sup>

The American Geriatrics Society recently elevated the issue of postoperative delirium. In 2015, they issued a best practice statement concerning risk factors, diagnosis, and perioperative mitigation strategies.<sup>9</sup> The group recommends managing intraoperative exposure to anesthetic agents by employing “processed electroencephalographic monitors of anesthetic depth during intravenous sedation or general anesthesia of older patients to reduce postoperative delirium”.<sup>9</sup> Similar recommendations were issued shortly after by a consensus group from Brazil<sup>10</sup> and the European Society of Anaesthesiology.<sup>11</sup> In 2018, The American Society of Anesthesiology Brain Health Initiative working group also recommended that anesthesia providers should “perform EEG-based anesthetic management in older adults”.<sup>12</sup>

This evidence package discusses the association between using processed EEG monitors for titrating anesthesia and a reduced risk of postoperative delirium in elderly surgical patients.

# Intraoperative EEG suppression is an independent risk factor for postoperative delirium in a general surgical population

## Intraoperative electroencephalogram suppression predicts postoperative delirium.

Fritz BA, Kalarickal PL, Maybrier HR, et al.

<b>Study design</b>	Single-center prospective observational trial (US) Sub-study of the Systematic Assessment and Targeted Improvement of Services Following Yearlong Surgical Outcomes Surveys (SATISFY-SOS)
<b>Arms</b>	All patients were monitored with BIS™ technology and divided into five groups for comparison: <ul style="list-style-type: none"> <li>▪ No time in burst suppression</li> <li>▪ First quartile of time in burst suppression (0.1 mins – 0.6 mins)</li> <li>▪ Second quartile (0.7 mins – 4.4 mins)</li> <li>▪ Third quartile (4.5 mins – 17.4 mins)</li> <li>▪ Fourth quartile (&gt; 17.4 mins)</li> </ul>
<b>Objective</b>	Examine the relationship between intraoperative EEG suppression, as reported by the BIS™ monitor, and postoperative delirium
<b>N</b>	727 (predominantly older men undergoing cardiac surgery) 619 were available for analysis
<b>Population</b>	Adult (> 18 years of age) General surgery (excluding neurosurgical procedures)
<b>Delirium assessment tool or definition</b>	Confusion Assessment Method for the ICU
<b>Timing of assessment</b>	Twice a day until ICU discharge or unless the patient was sedated to a Richmond Agitation and Sedation Score of < -3
<b>Results</b>	<ul style="list-style-type: none"> <li>▪ 89% of patients experienced EEG suppression</li> <li>▪ 42% of patients experienced BIS™ index values &lt; 20</li> <li>▪ 26% of patients were diagnosed with postoperative delirium</li> <li>▪ The median duration of: <ul style="list-style-type: none"> <li>– EEG suppression was 4.5 minutes</li> <li>– BIS™ index value &lt; 20 was 11 minutes</li> </ul> </li> <li>▪ Increased duration of EEG suppression was independently associated with 22% increased odds of postoperative delirium (p=0.0002)</li> <li>▪ Predictors of EEG suppression included: <ul style="list-style-type: none"> <li>– Less intraoperative opioid medication (OR 0.5 per 1 morphine equivalent / kg; 95% CI 0.4 to 0.6)</li> <li>– Greater end-tidal anesthetic gas concentration (OR 1.5 per 0.5 MAC unit; 95% CI 1.5 to 1.6)</li> </ul> </li> </ul>
<b>Conclusions</b>	EEG suppression is an independent risk factor for postoperative delirium in surgical patients receiving general anesthesia with volatile anesthetic agents

# Higher intraoperative burst suppression ratio, and time in burst suppression, are predictors of postoperative delirium

## Intraoperative burst suppression is associated with postoperative delirium following cardiac surgery: a prospective, observational study.

Soehle M, Dittmann A, Ellerkmann RK, et al.

<b>Study design</b>	Single-center prospective observational trial (Germany)
<b>Arms</b>	All patients were monitored with BIS™ technology preoperatively through discharge using the BIS™ bilateral sensor and divided into two groups for comparison: <ul style="list-style-type: none"> <li>▪ No postoperative delirium</li> <li>▪ Postoperative delirium</li> </ul>
<b>Objective</b>	Examine the relationship between BIS™ index values, time in burst suppression, burst suppression ratio (BSR), asymmetry, and postoperative delirium, Activity of Daily Living, and mortality
<b>N</b>	87 (81 remained available for analysis)
<b>Population</b>	Elderly patients (>60 years) undergoing on-pump cardiac surgery
<b>Delirium assessment tool or definition</b>	Confusion Assessment Method for the ICU
<b>Timing of assessment</b>	Once daily
<b>Results</b>	<ul style="list-style-type: none"> <li>▪ 32% were diagnosed with postoperative delirium</li> <li>▪ Patients with postoperative delirium: <ul style="list-style-type: none"> <li>– Spent twice as long in the ICU (81 hours vs. 42 hours; p=0.033)</li> <li>– Had a higher 6-month mortality rate (11.5% vs. 0%; p=0.03)</li> </ul> </li> <li>▪ Postoperative delirium was associated with: <ul style="list-style-type: none"> <li>– Higher intraoperative BSR (1.24% vs 0.44%; p=0.028)</li> <li>– More time in burst suppression (107 minutes vs 44 minutes; p=0.018)</li> </ul> </li> <li>▪ Authors questioned whether deep anesthesia was the cause for BSR values: <ul style="list-style-type: none"> <li>– There were no differences in amount of anesthetic used</li> <li>– BIS™ index values were similar between groups and were within the recommended range (45 – 46)</li> </ul> </li> </ul>
<b>Conclusions</b>	Intraoperative BSR may help identify cardiac surgery patients that are at higher risk of postoperative delirium

# Heightened sensitivity to volatile anesthetics is associated with higher odds of postoperative delirium

## Intraoperative electroencephalogram suppression at lower volatile anaesthetic concentrations predicts postoperative delirium occurring in the intensive care unit.

Fritz BA, Maybrier HR, and Avidan MS

<b>Study design</b>	Single-center prospective observational trial (US) Post hoc retrospective analysis of the Systematic Assessment and Targeted Improvement of Services Following Yearlong Surgical Outcomes Surveys (SATISFY-SOS)
<b>Arms</b>	All patients were monitored with BIS™ technology
<b>Objective</b>	Examine whether patients with EEG suppression at lower end-tidal anesthetic gas concentrations (i.e., heightened sensitivity to volatile anesthetics) are more likely to develop postoperative delirium
<b>N</b>	727 (predominantly older men undergoing cardiac surgery) 619 were available for analysis
<b>Population</b>	Adult (> 18 years of age) General surgery (excluding neurosurgical procedures)
<b>Delirium assessment tool or definition</b>	Confusion Assessment Method for the ICU
<b>Timing of assessment</b>	Twice a day until ICU discharge or unless the patient was sedated to a Richmond Agitation and Sedation Score of -4 or -5
<b>Results</b>	<ul style="list-style-type: none"><li>▪ 50% of patients had heightened sensitivity to volatile anesthetics</li><li>▪ 26% of patients were diagnosed with postoperative delirium</li><li>▪ <b>Patients with heightened sensitivity to volatile anesthetics had over twice the odds of a postoperative delirium diagnosis (OR 2.18; 95% CI 1.35 to 3.51)</b></li><li>▪ Duration of EEG suppression alone was not a predictor of postoperative delirium in this analysis</li></ul>
<b>Conclusions</b>	Patients with a heightened sensitivity to volatile anesthetics (EEG suppression at lower end-tidal anesthetic gas concentrations) had higher odds of postoperative delirium

## Using BIS™ monitoring technology to provide light sedation can help reduce the relative risk of postoperative delirium by more than 50%.

### Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair.

Sieber FE, Zakriya KJ, Gottschalk A, et al.

<b>Study design</b>	Single-center randomized controlled trial (US)
<b>Arms</b>	Deep sedation: BIS™ monitoring-guided anesthesia titrated to a BIS™ value of approximately 50 Light sedation: BIS™ monitoring-guided anesthesia titrated to a BIS™ value of $\geq 80$
<b>Objective</b>	Compare the risk of postoperative delirium between patients receiving deep and light sedation
<b>N</b>	114
<b>Population</b>	Elderly patients ( $\geq 65$ years) undergoing hip fracture repair with spinal anesthesia
<b>Delirium assessment tool or definition</b>	Confusion Assessment Method
<b>Timing of assessment</b>	Daily in the morning, starting on the second postoperative day until hospital discharge
<b>Results</b>	<ul style="list-style-type: none"> <li>▪ 39% of patients developed postoperative delirium</li> <li>▪ Deep sedation was associated with: <ul style="list-style-type: none"> <li>– More propofol (10.2 mg/kg vs. 2.5 mg/kg, <math>p &lt; 0.001</math>)</li> <li>– Less midazolam (1.26 mg/kg vs. 5.53 mg/kg, <math>p = 0.04</math>)</li> <li>– Lower mean BIS™ value (49.9 vs. 85.7, <math>p &lt; 0.001</math>)</li> <li>– Longer duration with a BIS™ value <math>&lt; 50</math> (48 minutes vs. 4 minutes, <math>p &lt; 0.001</math>)</li> <li>– More than twice the odds of developing postoperative delirium (OR 2.69; 95% CI 1.04 to 6.93)</li> </ul> </li> <li>▪ Light sedation was associated with a 52% relative reduction in the risk of postoperative delirium (19% vs 40%, <math>p = 0.02</math>)</li> <li>▪ The number needed to treat with light sedation to prevent one case of postoperative delirium was 4.7 patients</li> </ul>
<b>Conclusions</b>	In elderly patients undergoing hip fracture repair under spinal anesthesia, using BIS™ monitoring technology to titrate anesthesia to lighter levels can help reduce the risk of postoperative delirium by more than 50%

The combination of light general anesthesia and peripheral nerve block is associated with lower incidence of postoperative delirium.

### Peripheral nerve block as a supplement to light or deep general anesthesia in elderly patients receiving total hip arthroplasty: a prospective randomized study.

Mei B, Zha H, Lu X, et al.

<b>Study design</b>	Single-center randomized controlled trial (China)
<b>Arms</b>	General anesthesia (GA) alone GA (light sedation) plus lumbosacral plexus block GA (deep sedation) plus lumbosacral plexus block
<b>Objective</b>	Evaluate combination of general anesthesia and peripheral nerve blockage in elderly patients undergoing hip arthroplasty.
<b>N</b>	203
<b>Population</b>	Patients aged $\geq 65$ years undergoing total hip arthroplasty
<b>Delirium assessment tool or definition</b>	Confusion Assessment Method
<b>Timing of assessment</b>	First through third postoperative days
<b>Results</b>	<ul style="list-style-type: none"><li>▪ The following comparisons in the incidence of postoperative delirium were made:<ul style="list-style-type: none"><li>– Deep GA plus lumbosacral plexus vs. GA alone (38% vs 40%, <math>p&gt;0.99</math>)</li><li>– Light GA plus lumbosacral plexus vs. GA alone (17% vs. 40%, <math>p=0.007</math>)</li><li>– <b>Light GA plus lumbosacral plexus vs. deep GA plus lumbosacral plexus (17% vs. 38%, <math>p=0.007</math>)</b></li></ul></li><li>▪ There was no difference in complications between groups <math>\leq 30</math> days post-surgery</li></ul>
<b>Conclusions</b>	In elderly patients undergoing total hip arthroplasty, the combination of light general anesthesia and lumbosacral plexus block was associated with significant reduction in incidence of postoperative delirium compared to nerve block with deep sedation, and general anesthesia alone.

# BIS™-guided anesthetic delivery is associated with 42% lower odds of postoperative delirium.

## BIS™-guided anesthesia decreases postoperative delirium and cognitive decline.

Chan MT, Cheng BC, Lee TM, et al.

<b>Study design</b>	Multicenter randomized controlled trial (China) Cognitive Dysfunction After Anesthesia (CODA) Trial
<b>Arms</b>	Control: Blinded monitoring; routine care to manage anesthetic delivery Intervention: BIS™ monitoring-guided anesthesia titrated to a BIS™ value of 40 – 60
<b>Objective</b>	Determine the association between BIS™ monitoring-guided anesthesia and the risk of postoperative cognitive dysfunction (POCD) and delirium
<b>N</b>	921
<b>Population</b>	Elderly patients (≥ 60 years) undergoing elective major surgery ≥ 2 hours and expected to stay in the hospital ≥ 4 days
<b>Delirium assessment tool or definition</b>	Acute fluctuating course of inattention AND disorganized thinking OR altered level of consciousness
<b>Timing of assessment</b>	Daily in the morning, starting on the second postoperative day until hospital discharge
<b>Results</b>	<ul style="list-style-type: none"> <li>▪ 20% of patients developed postoperative delirium</li> <li>▪ BIS™ monitoring-guided anesthesia was associated with: <ul style="list-style-type: none"> <li>– Less propofol and volatile anesthetic gas use</li> <li>– Higher mean BIS™ values (53.2 vs 38.6, p&lt;0.001)</li> <li>– Shorter duration with a BIS™ value &lt; 40 (7.2 mins vs 22.8 mins, p&lt;0.001)</li> </ul> </li> <li>▪ Fewer patients experienced postoperative cognitive issues in the BIS™ monitoring group: <ul style="list-style-type: none"> <li>– 38% lower odds of developing POCD at 3 months (p=0.02)</li> <li>– <b>35% relative reduction in the risk of postoperative delirium (15.6% vs 24.1%, p=0.01)</b></li> <li>– <b>42% lower odds of developing postoperative delirium (p=0.01)</b></li> </ul> </li> <li>▪ In 1,000 elderly patients undergoing major surgery, use of BIS™ monitoring-guided anesthesia is expected to prevent 23 cases of POCD and 83 cases of postoperative delirium</li> </ul>
<b>Conclusions</b>	Use of BIS™ monitoring-guided anesthesia reduced duration of time with BIS™ values < 40, subsequently reducing the risk of postoperative cognitive issues

# Use of BIS™ monitoring technology is associated with a reduced incidence of deep anesthesia and 22% lower relative risk of postoperative delirium.

## Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction.

Radtke FM, Franck M, Lendner J, et al.

<b>Study design</b>	Single-center randomized controlled trial (Germany)
<b>Arms</b>	Control: Blinded monitoring; routine care to manage anesthetic delivery Intervention: BIS™ monitoring-guided anesthesia
<b>Objective</b>	Determine the association between BIS™ monitoring-guided anesthesia and the risk of postoperative delirium
<b>N</b>	1,155
<b>Population</b>	Elderly patients (≥ 60 years) undergoing elective major surgery ≥ 1 hour
<b>Delirium assessment tool or definition</b>	Diagnostic and Statistical Manual of Mental Disorders (DSM IV)
<b>Timing of assessment</b>	Twice daily starting on the first postoperative day through the seventh day
<b>Results</b>	<ul style="list-style-type: none"><li>▪ 18.8% of patients developed postoperative delirium</li><li>▪ BIS™ monitoring-guided anesthesia was associated with a<ul style="list-style-type: none"><li>– Lower number of average BIS™ values &lt; 20 (p=0.04)</li><li>– <b>22% relative reduction in postoperative delirium (16.7% vs 24.1%, p=0.036)</b></li><li>– Trend towards lower risk of postoperative cognitive dysfunction at 7 days (18.1% vs 23.9%, p=0.062)</li></ul></li><li>▪ The percentage of BIS™ values &lt; 20 was independently associated with higher odds of postoperative delirium (OR 1.027, p=0.006)</li></ul>
<b>Conclusions</b>	BIS™ monitoring technology was associated with a reduced incidence of low BIS™ values and a reduced risk of postoperative delirium

## BIS™ monitoring-guided anesthesia results in less anesthetic use, faster cognitive recovery, and less postoperative delirium.

### Bispectral index monitoring during anesthesia promotes early postoperative recovery of cognitive function and reduces acute delirium in elderly patients with colon carcinoma: a prospective controlled study using the Attention Network Test.

Zhou Y, Li Y, Wang K.

<b>Study design</b>	Single-center randomized controlled trial (China)
<b>Arms</b>	Control: Blinded monitoring; routine care to manage delivery of total intravenous anesthesia (TIVA) Intervention: BIS™ monitoring-guided TIVA to BIS™ index value of 40 – 60
<b>Objective</b>	Examine the effect of BIS™ monitoring-guided TIVA on anesthetic use and postoperative neurocognitive decline
<b>N</b>	81
<b>Population</b>	Elderly colon carcinoma patients: <ul style="list-style-type: none"> <li>▪ 65 – 75 years of age</li> <li>▪ Expected duration of surgery &gt; 2 hours</li> <li>▪ Expected hospital length of stay &gt; 7 days</li> </ul>
<b>Delirium assessment tool or definition</b>	Confusion Assessment Method
<b>Timing of assessment</b>	Daily in the morning, starting on the first postoperative day until day 5
<b>Results</b>	Compared to the control group, the BIS™ monitoring group: <ul style="list-style-type: none"> <li>▪ Had higher BIS™ index values (51 vs. 41; <math>p &lt; 0.001</math>)</li> <li>▪ Received less propofol and remifentanyl (<math>p &lt; 0.001</math>)</li> <li>▪ Showed recovery in alerting and orienting functions to preoperative values by day 5 (which continued to be impaired in the control group)</li> <li>▪ Had fewer patients with postoperative delirium (17% vs. 27.5%; <math>p &lt; 0.001</math>)</li> </ul>
<b>Conclusions</b>	Using BIS™ monitoring technology to help guide TIVA in an elderly colorectal surgical population was associated with less anesthetic use, quicker recovery of alerting and orienting functions, and a reduced risk of postoperative delirium.

# Processed EEG monitoring-guided anesthesia is associated with a 29% reduction in the risk of postoperative delirium and cognitive dysfunction.

## Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and non-neurosurgical procedures in adults.

Punjasawadwong Y, Chau-in W, Laopaiboon M, et al.

<b>Study design</b>	Systematic review and meta-analysis of randomized controlled trials studying the effect of depth of anesthesia monitoring on postoperative delirium and postoperative cognitive dysfunction
<b>Arms</b>	Control: routine care to manage anesthetic delivery Intervention: monitoring-guided anesthesia (all studies included in the meta-analysis were performed with the BIS™ monitor)
<b>Objective</b>	Evaluate the effectiveness of guiding anesthesia with depth of anesthesia monitoring (processed EEG or auditory evoked potentials) to reduce the risk of postoperative delirium and postoperative cognitive dysfunction
<b>N</b>	Three studies reporting postoperative delirium: 2,197 patients Three studies reporting postoperative cognitive dysfunction: 2,270 patients
<b>Population</b>	Adult non-cardiac and non-neurosurgical patients undergoing general anesthesia (patients in the included studies were all > 60 years of age)
<b>Delirium assessment tool or definition</b>	Postoperative delirium: Confusion Assessment Method, Diagnostic and Statistical Manual (DSM-IV) Postoperative cognitive dysfunction: Mini-Mental State Exam
<b>Results</b>	<ul style="list-style-type: none"> <li>▪ <b>BIS™-monitoring guided anesthesia was associated with:</b> <ul style="list-style-type: none"> <li>– 29% reduction in the risk of postoperative delirium (RR 0.71; 95% CI 0.59 to 0.85)</li> <li>– 29% reduction in the risk of postoperative cognitive dysfunction at 12 weeks after surgery (RR 0.71; 95% CI 0.53 to 0.96)</li> </ul> </li> <li>▪ The authors did not find a significant reduction in postoperative cognitive dysfunction at 1 week after surgery</li> <li>▪ The number needed to treat (NNT) to prevent one case of the outcomes of interest were as follows: <ul style="list-style-type: none"> <li>– Postoperative delirium NNT = 17</li> <li>– Postoperative cognitive dysfunction NNT = 38</li> </ul> </li> <li>▪ The evidence quality was rated as moderate due to lack of blinding of the anesthesia providers and some incomplete outcome data</li> </ul>
<b>Conclusions</b>	In non-cardiac and non-neurological surgical patients > 60 years of age, processed EEG monitoring was associated with a reduced risk of postoperative delirium and postoperative cognitive dysfunction.

# A selection of clinical studies about BIS™ monitoring technology and postoperative delirium

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# Medtronic

IMPORTANT: Please refer to the package insert for complete instructions, contraindications, warnings and precautions.

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