

# Depth-of-anaesthesia monitoring

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## Abstract

All anaesthetists would like to be confident that their patients are asleep throughout surgery. Depth-of-anaesthesia monitors may contribute to reducing the incidence of perioperative awareness, but they are expensive, and typically require that consumables are purchased for every case.

Recently, excessive depth of anaesthesia has been feebly associated with increased mortality, but this has not yet been proven, and may reflect patient co-morbidity, rather than clinician error.

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## Introduction

In clinical practice, progressive administration of hypnotics, typically in combination with analgesics, leads to sedation, deep sedation, and finally, anaesthesia, which is defined as loss of consciousness, with lack of response to painful stimulus.

The electroencephalogram (EEG) is the surface representation of the summed electrical activity of billions of cortical neurons. Typically, when a hypnotic, such as propofol, is applied, the EEG shows a biphasic response with initial bifrontal activation (BETA activation), followed by progressive synchronisation and slowing, producing EEG patterns with higher amplitudes and lower frequencies.<sup>1,2</sup> With high doses of anaesthetic, the electrical activity of the cortex deteriorates with periods of near silence, interspersed with bursts of activity, or burst suppression. Eventually, the bursts cease, resulting in electrical silence, also known as an isoelectric EEG.

## Making sense of the EEG

Raw EEG can be interpreted without modification, and with training, this can be achieved by ordinary anaesthetists.<sup>3</sup> In practice, most clinicians consider the EEG to be too complex, and the application of standard EEG electrodes, too difficult to be useful on a day-to-day basis.

## Recording the EEG

Whereas the electrocardiogram (ECG) is measured in millivolts, the EEG is measured in microvolts. Accordingly, issues of skin preparation, electrode resistance, electrical interference, and other artefacts from blinks and movement, provide material impediment to efficient recordings without specialist assistance, or simplified equipment. Some commercial depth-of-anaesthesia (DoA) monitors improve access to the EEG signal by using special skin electrodes which optimise signal transfer across the skin. Equally, adequate recordings can be achieved with standard ECG electrodes, provided that skin preparation is meticulous.<sup>4</sup>

Numerous approaches to extracting DoA information from EEG have been described, and in some cases, commercialised. Two main classes of monitor may be considered. One group of monitors applies a stimulus to the patients, typically to elicit auditory evoked potentials (AEP), where clicks are played to the patients' ears through a pair of headphones, and the evoked cortical activity averaged and presented as a wave form, or a numeric derivative.<sup>5</sup> Importantly, the AEP recorded during anaesthesia is reversibly perturbed by surgical stimulation, demonstrating that the AEP is truly an index of anaesthetic depth, rather than a simple bioassay of anaesthetic drug concentrations.<sup>6</sup> Alternatively, direct mathematical transformation of the EEG yields indices based on diverse mathematical principles, including polyspectral analysis,<sup>7</sup> entropy,<sup>8</sup> wavelets,<sup>9</sup> and

Fourier transformation.<sup>10</sup> Although multiple methodologies have been developed, only two have had a significant commercial impact.

### The Bispectral Index® monitor

Originally developed by Aspect Medical Systems, and subsequently, Covidien, Bispectral Index® (BIS®) monitoring<sup>7</sup> uses a secret proprietary algorithm to convert raw EEG into a single number between 100 (fully awake) and 0 (isoelectric EEG). Although the algorithm is secret, it is widely believed to contain elements based on electromyogram and polyspectral analysis, with various adjustments and filtering applied for linearisation.<sup>11</sup> BIS® monitoring has been through many subsequent variants, each reverse-validated against the original library of EEG recordings. Advances in signal processing, artefact rejection, and improvements in electrode technology, are applied in a system that is generally considered to be easy to use. However, the expense of single-use disposable electrodes, required for each patient, remains an issue for many anaesthesia providers.

### Entropy

In contrast to BIS®, the entropy monitor comprises two numeric descriptors [spectral entropy (SE) and response entropy (RE)] of EEG complexity, using clearly described and public, if complex, mathematics.<sup>8</sup> Like the BIS® monitor, the entropy monitor yields a monotonic numeric summary of depth of anaesthesia.

What might a DoA monitor do to improve the quality of anaesthesia for patients? Typically, individual clinicians use DoA monitors to reassure themselves that the patient is adequately anaesthetised during surgery. Research investigations of DoA monitoring have attempted to prove reduced anaesthetic drug use,<sup>12</sup> improved wake up, and recovery.<sup>13</sup> A 2007 Cochrane report concluded: "Anaesthesia guided by BIS®...could improve anaesthetic delivery and postoperative recovery from relatively deep anaesthesia".<sup>14</sup> Being aware while under anaesthesia is terrifying<sup>15</sup> and infrequent, but not rare. Many research publications indicate an incidence of approximately 1:600 cases in adult practice,<sup>16,17</sup> with more frequent occurrence during high-risk (obstetric, cardiac and airway surgery), as well as during anaesthesia in children.<sup>18</sup> Even with an incidence of 1:600, the size of a prospective randomised control trial to demonstrate a statistically significant reduction in perioperative awareness is daunting.<sup>19</sup> Instead, trialists have focused on high-risk cases, where the baseline incidence is believed to be around one per cent. The B-Aware study showed a reduction of anaesthetic awareness among high-

risk patients to whom BIS® monitoring had been applied.<sup>20</sup> In contrast, the B-Unaware study<sup>21</sup> reported no difference in awareness between patients to whom a BIS® monitor had been applied, and others who were anaesthetised without one. Instead, it used a rigorous protocol of inhalational anaesthesia with target end-tidal anaesthetic gas concentrations and an active alarm system. These large randomised studies, in combination with mixed literature before-and-after reports from institutions where DoA monitoring was introduced, present a mixed picture. DoA monitoring may be useful in high-risk patients, but equally, satisfactory anaesthesia can be achieved using large quantities of an inhalational anaesthetic agent, with the end-tidal anaesthetic gas concentration alarms turned on.

What about patient outcomes, and DoA monitoring? In 2005, Monk reported that death during the 12 months after elective major non-cardiac surgery was primarily related to co-morbidities, but even after these had been accounted for, intraoperative hypotension and inappropriately deep anaesthesia were independent predictors of mortality.<sup>22</sup>

Subsequently, several other reports have addressed this question, with inconclusive results. Analysis of outcomes data from the B-Unaware study showed that co-morbidities, especially cancer, are powerful predictors of mortality, but after correction for covariates, excessive DoA was not associated with excess mortality.<sup>23</sup>

Recently, a combination of depressed EEG (low BIS®) with hypotension, despite low concentrations of an anaesthetic agent (a so-called "triple low"), has been associated with greatly increased adverse outcomes following anaesthesia and surgery.<sup>24</sup> Whether the adverse outcomes associated with excessive DoA (if indeed they actually exist), were precipitated by an excess of anaesthesia, or simply reflect underlying co-morbidities, especially malignant disease, remains unclear.<sup>25</sup> Certainly, this is an area for further research and vigilance. If existing anaesthesia is indeed harmful to patients, particularly those who are already at high risk, then DoA monitoring may be easier to justify in terms of improved patient survival.

Should anaesthetists use a DoA monitor? At present, the evidence can only be described as equivocal. Those who do so, speak positively of it, and would not wish to be deprived of it. Equally, in terms of resources, the cost may be difficult to justify in a cash-limited healthcare environment. In the UK, the National Institute for Clinical Excellence is currently investigating DoA monitoring, and its recommendations are likely to determine whether or not the technology will be extensively adopted for elective anaesthesia and surgery. In the meantime, knowing that the evidence is equivocal, the

choice will be that of clinicians. If they choose not to use a DoA monitor, then an additional personal responsibility of anaesthetists must be to have confidence that appropriate quantities of an anaesthetic agent, either inhalational or intravenous, are being effectively delivered to the patient.

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