2018 Thomas Boulton Anaesthesia History Essay prize winner
Published in The History of Anaesthesia Society Proceedings. Vol 51, Edinburgh 2018. Page 70-72

Monitoring depth of anaesthesia, a long-standing enterprise

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Between April 2013 and March 2014, approximately 4.7 million surgical operations were performed in the United Kingdom alone[1]. In the same period, the reported annual number of general anaesthetics given varied between 2.76[2] and 3.2 million[3]. Globally, the volume of surgical operation performed in 2012 is estimated to be between 266.2 and 359.5 million, representing a 38% increase in practice over 8 years[4]. While there is a lack of standardised surgical and anaesthetics data collection worldwide, the World Health Organisation reports that the growth in surgical volumes appears to be at a faster rate in extremely low and low expenditure United Nations member states[4].

The ageing of the population, particularly steep in the Western world, is predicted to have a significant impact on the provision of surgical and anaesthetic care in the coming years[5]. The growing population as well as the progressive growth of the elderly segment of the population has led to an increase in the number of patients requiring surgery[6,7]. Alongside this growth in case number, the elderly population has been shown to have an increased clinical recourse utilisation compared to young patients. This includes higher perioperative requirements for supportive treatments (e.g. inotropes, vasopressors, antibiotics), higher rate of further surgical interventions, and longer intensive care and hospital stays[8]. Yet despite a rising number of high-risk profiles undergoing surgery, mortality rates for all types of surgery continue to decrease. Indeed, anaesthetic-related mortality has dropped from 6.4 per 100000 anaesthetics in the period between 1948-1954[9] to 0.21 per 100000 in a 2003 Japanese study of 2,363,038 anaesthetics[10].

To achieve and maintain such safety levels in the face of increased volume and proportion of high-risk cases, anaesthetic practice has constantly evolved since its infancy. One of these advance in anaesthesia has been an attempt at improving the monitoring of anaesthetic depth, evolving from the observation of clinical signs through to the development of electronic depth of anaesthesia monitoring devices. This essay will address those developments through time.

❖ A need for depth of anaesthesia monitoring

The state of general anaesthesia is defined as a controlled and reversible loss of consciousness with loss of protective reflexes[3] and is induced by anaesthetists to allow a multitude of surgical operations. From general anaesthesia in operating theatres to allow surgical interventions to general anaesthesia in the emergency department to take over the regulation of a patient's physiology, delivering a general anaesthetic is associated with significant risks. While the maintenance of adequate respiratory and cardiovascular functions is primordial, it is of importance to assess and maintain an adequate depth of anaesthesia in each patient.

Indeed, too shallow a depth and the patient will be put at an increased risk of accidental awareness during general anaesthesia (AAGA). There has been a long standing debate in the literature regarding the incidence of AAGA, with reported values as low as 0.04%[11] when actively monitoring the depth of anaesthesia but rising to 4%[12] when anaesthetists are unaware of the steps available to reduce this undesirable event. In procedures at low risk of awareness, the incidence of intraoperative awareness has been reported over several decades to be approximately 0.1-0.2%[13–16]. This incidence is greatly increased in operations at high risk of awareness (obstetric[17,18], cardiac[12,19–22], paediatric[23–25] and trauma surgery[26]). While those numbers may appear low, the 3.2 million general anaesthetics given in the UK annually[3] put the yearly incidence of AAGA between 3200 and 6400 cases using the lower estimates. In order to obtain a better assessment of the actual incidence rates, AAGA was the focus of the fifth National Audit Project (NAP5) led by the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland. The findings, reported in 2014, showed the incidence of AAGA in the total surveyed population to be 1 in 19600 anaesthetics, with a wide variation between anaesthetic techniques and surgical specialities[27]. Indeed, the use of muscle relaxants brought the incidence rate to 1 in 8200 anaesthetics from the 1 in 135900 rate seen without the use of such agents[27]. Although intraoperative awareness remains thankfully a rare event it is often reported by patients as a primary cause of pre-operative anxiety[28] and is a cause of complaints and litigation against anaesthetists[29,30]. This contrasts with the general view held by anaesthetists about AAGA. Myles et al.[31] showed that Australian anaesthetists consider AAGA as only a minor issue, underestimating its incidence and ranking their personal incidence rate below the national average. British anaesthetists surveyed using the same questionnaire[32] exhibited similar points of view, deeming AAGA even less of a problem than their Australian colleagues. Nevertheless, a significant correlation has been established between patient dissatisfaction and AAGA, presenting awareness as the principal risk factor for patient dissatisfaction in anaesthesia ahead of post-operative pain, severe nausea and vomiting, and other complications[28]. Patients experiencing AAGA can be awake and in pain without being able to move in order to make the healthcare team aware of the situation, especially if neuromuscular blocking agents have been used. In addition to the intraoperative trauma, the experience often triggers long term complications for the patient ranging from disturbed sleep and flashbacks[33] to post-traumatic stress disorder[34–37]. Most patients who experienced AAGA will in addition fear future anaesthesia and surgery[36], something which may prevent their engagement in health care.

On the other hand, anaesthesia is oriented towards patient safety thus, so as to minimize the risk of awareness, practitioners tend to over-titrate hypnotic drugs beyond what is necessary to achieve surgical depth of anaesthesia[3,38]. While this generous approach may limit the incidence of AAGA, an excessively deep anaesthesia will produce an unnecessary suppression of cardiovascular functions (with its associated requirement for supportive drugs such as vasopressors or inotropes), delayed recovery time and other cognitive complications[39,40]. Through a series of case reports in 1955, Bedford[41] showed that anaesthesia seems to have adverse cerebral effects on elderly patients. Post-operative cognitive impairments have since been recognised as complications of surgery and divided in two categories: post-operative delirium[42] and post-operative cognitive dysfunction (POCD)[43,44]. Post-operative delirium is characterized by sudden reversible impaired cognition, oscillating consciousness levels, impaired memory and sensory perception as well as fluctuating symptoms of anger, fear and anxiety [42]. The similar condition of POCD is defined by Bekker and Weeks as "a condition characterized by impairment of memory, concentration, language comprehension, and social integration. This syndrome may be detected days to weeks after surgery and may remain as a permanent disorder. Socioeconomic implications of POCD are profound; they include loss of independence, extra nursing care and a high rate of discharge to long-term care."[42]

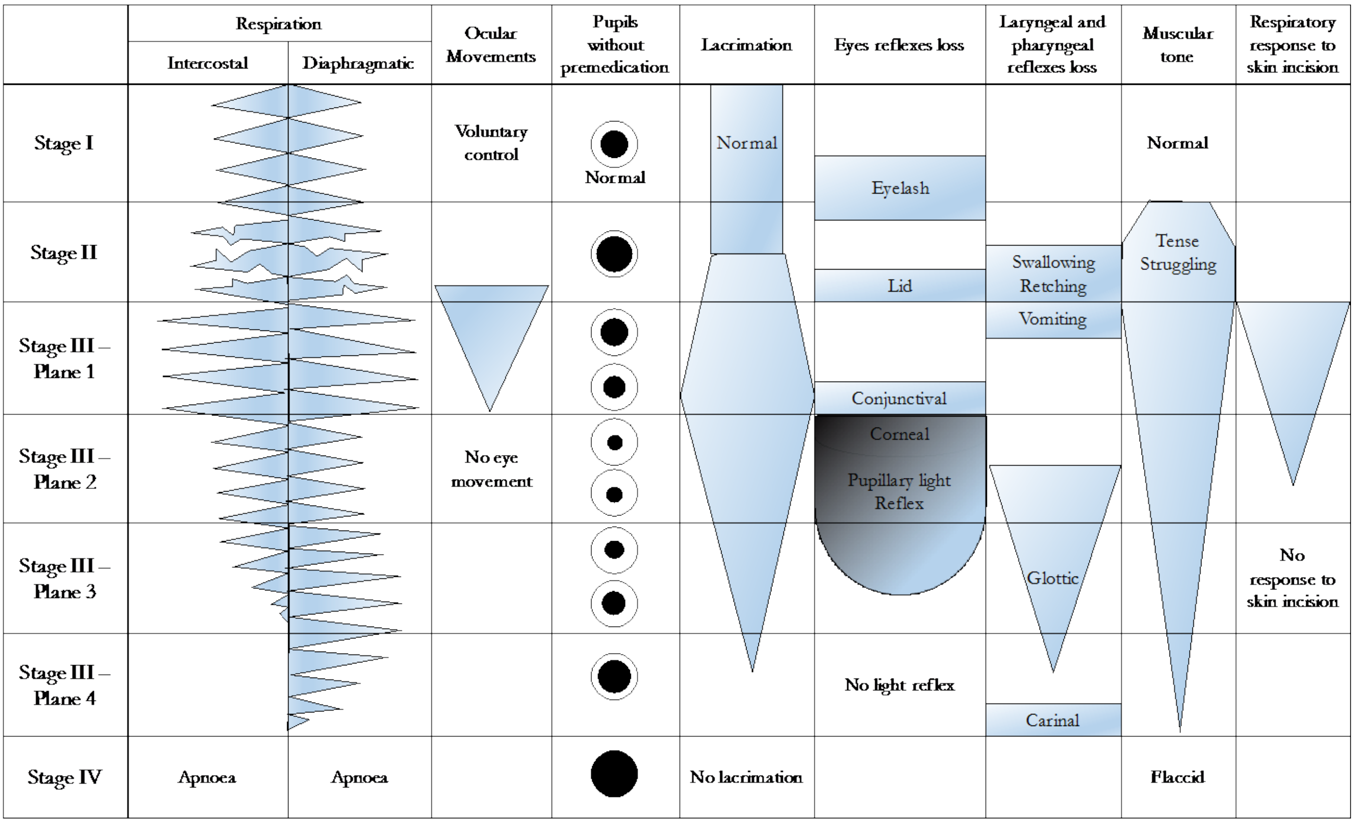
Those alterations in cognitive function following surgery have been shown to lead to a reduced quality of life at one[45] and five years[46] post-surgery, decreased functional capacity[47], increased mortality[48,49] and increased burden on health care systems through a lengthened hospital stay and increased long-term nursing costs[42,50]. As an effective therapy for POCD has yet to be found[51,52], prevention of its occurrence remains the main objective. Prevention of POCD currently includes optimisation of haemodynamic stability, therapeutic hypothermia, minimising surgical invasiveness and reduction of preoperative anxiety[51,53].

- The evolution of depth of anaesthesia monitoring:

Monitoring the effects of anaesthetic agents has been a concern for medical practitioners since the first use of primitive anaesthetic methods in surgery. In 1847, John Snow wrote a treatise on how to optimize the inhalation of ether vapours during surgery. He emphasized in the opening sentence the importance of discerning when the patient has received enough ether "The point requiring most skill and care in the administration of the vapour of ether is, undoubtedly, to determine when it has been carried far enough"[54]. In his treatise on the inhalation of the vapour of ether in surgical operations, Snow divides the effects of ether into five degrees, although he admits that the transition between degrees is gradual and not always clearly distinguishable.

The first degree of etherisation (sic) is characterized by a change in the sensations experienced by the subject while they retain consciousness and voluntary movement. When the application of ether is continued, the subject transitions to the second degree in which mental functions are still present but the ability to execute voluntary movement is markedly impaired. Following on comes the third degree of etherisation during which all mental functions are stopped, leading to complete inhibition of voluntary movement. It is noted though that ether administration and external stimulation of the patient can produce muscular contraction. Snow describes the fourth degree as a state where only respiratory movements are seen, with no muscular contraction even during external stimulation. The fifth and last degree, which Snow states is not seen in humans, consists of a quasi-paralysis of the respiratory muscles with only few, irregular and weak movements.

The five degrees described by Snow in 1847 became the mainstay for depth of anaesthesia monitoring for almost a century until the publication of Arthur E. Guedel's four stages of anaesthesia in 1937[55,56] (Figure 1). Guedel refined Snow's work on diethyl ether and published a classification of anaesthetic depth in four stages according to the clinical signs observed. The third stage of anaesthesia, corresponding to an appropriate depth for surgical operation, is further divided into four planes according to changes in breathing patterns and the disappearance of reflexes (Figure 1). The first plane corresponds to the disappearance of eyeball movement and the onset of automatic respiration, followed by loss of laryngeal and corneal reflexes and reduction of physiological reaction to skin incision (plane one). With further administration of an anaesthetic agent, intercostal breathing cessation occurs with loss of pupillary light reflexes (plane three) evolving to complete apnoea with loss of muscle tone and gag reflex (plane four).



<u>Figure 1. Diagram of Guedel's four stages of ether anaesthesia.</u>

Stage I: From the induction of general anaesthesia to patient's loss of consciousness. This stage is characterized by analgesia and disorientation.

Stage II: From loss of consciousness to the beginning of automatic breathing. Irregular breathing with breath-holding can be observed. This stage shows the disappearance of corneal reflexes while other reflexes are unaffected. Coughing, vomiting and struggling have been shown to happen during stage two. This stage is characterized by a state of excitement or delirium.

Stage III: This is the stage of surgical anaesthesia, from the onset of automatic breathing to paralysis of respiration. Stage three is divided into four planes; the **first plane** starts with onset of automatic respiration and lasts until the eyeball movements cease. Conjunctival, swallowing and eyelid reflexes are completely lost in this plane. **Plane two** immediately follows. It is characterised by an increasing paralysis of the intercostal muscles, loss of laryngeal and corneal reflexes, and increased lacrimation. Muscular and respiratory reactions

to skin incision are dampened. **Plane three** consists of the period during which intercostal breathing decreases and ceases. It is accompanied by the abolition of the light reflex with dilated pupils. The following **plane four** lasts until complete cessation of breathing and disappearance of lacrimation, glottis reflex and muscular tone occur.
Stage IV: The last of Guedel's stages is reached during anaesthetic overdose. It exhibits medullary paralysis with arrest of respiration and collapse of the cardiovascular system. Adapted from Gillepsie[56].

In 1953, Joseph F Artusio further refined the classification described by Snow and Guedel by dividing the first stage into three planes (Figure 2)[57]. Through the use of incremental doses of di-ethyl ether in 115 patients undergoing cardiac surgery, Artusio assessed the patients' higher neurological function during increasingly deep anaesthesia.
Plane 1 is present from the onset of anaesthesia to the beginning of impaired nociception, it characterised by normal cognitive functions with the patients responding to voice and obeying commands. Following on, plane 2 begins with onset of partial analgesia and terminates at the onset of complete analgesia. The last plane of stage one follows, ending with loss of consciousness. Throughout plane 2 and 3, the patients still exhibit unimpaired cognition and retrograde memory but demonstrate complete amnesia for concurrent events when questioned subsequently.

STAGES OF ANESTHESIA

STAGE I	PLANE 1. PRE-ANALGESIA – PRE-AMNESIA
STAGE I	PLANE 2. PARTIAL ANALGESIA – TOTAL AMNESIA
STAGE I	PLANE 3. TOTAL ANALGESIA – TOTAL AMNESIA
	LOSS OF CONSCIOUSNESS
STAGE II	DELIRIUM (ONLY SEEN UPON INDUCTION)
STAGE III	SURGICAL ANESTHESIA
STAGE IV	RESPIRATORY PARALYSIS

Figure 2. Stages of anaesthesia with subdivision of stage 1.
From [57]

The introduction of alternative anaesthetic gases, the cessation of ether anaesthesia in developed countries, and the development of intravenous induction of general anaesthesia has rendered Guedel's classification slightly obsolete[58,59]. Moreover, the classification relies on muscular signs that will be abolished by the muscle relaxants used in certain types of surgery[60]. Yet, this classification -- in addition to drug concentration, heart rate, blood pressure and response to verbal commands -- provides the basic clinical standards for monitoring depth of anaesthesia: assessments of ventilation, pupil diameter, lacrimation, autonomic ocular and pharyngolaryngeal reflexes and muscular tone[61].

An innovative method allowing an assessment of depth of anaesthesia when neuromuscular blocking agents are used operatively was described in obstetric anaesthesia in 1977 by M E Tunstall[62]. Tunstall's isolated forearm method came about from the observation that obstetric anaesthesia is particularly prone to AAGA. This is mostly due to the tendency of anaesthetists to maintain a shallow depth of anaesthesia until delivery so as to prevent depression of the baby's physiology. In this method the patient's forearm is isolated from the systemic circulation following induction of anaesthesia, and before administration of muscle relaxants, by inflating a cuff on the upper arm above systolic blood pressure. In the event of intraoperative awareness, the patient is able to spontaneously manifest themselves by movement of the isolated, non-paralysed, forearm. The patient can additionally be asked at regular intervals to move their hand, so as to assess for awareness[63]. One major limitation is that the method is only applicable for a short period of time before nerve tissue ischaemia prevents muscle contractions. Thus the tourniquet is deflated after fifteen to twenty minutes and may be re-inflated at a later point if neuromuscular blockade is to be reinstated[62]. Even though one would think that response to command during an anaesthetic is a sign of awareness and thus a late marker of too light anaesthesia, multiple studies have shown that while awareness may happen during anaesthesia, recall does not always ensue[64,65]. The isolated forearm method is still used both in research and clinical setting to this day[63].

Another more invasive technique used to assess depth of anaesthesia has been the measurement of lower oesophageal sphincter contractility. First described by Evans and colleagues in 1984, the technique relies on the fact that the non-striated muscles of the lower oesophageal sphincter retain their contractility event after the use of muscular blocking agents[66]. The two types of smooth muscle contractions in the sphincter, spontaneous and provoked by the inflation of a balloon on a catheter, can be measured by an endoscopic pressure transducer[67]. While the frequency, latency and amplitude of spontaneous and evoked muscular contractions significantly reduced with induction of unconsciousness and increased with regaining of consciousness[67], an exact threshold indicating presence or high risk of consciousness has not been described thus the use of this method in clinical practice is seriously limited.

A further proposed depth of monitoring technique has been the assessment of heart rate variability on the electrocardiogram (ECG), first suggested by C J Pomfrett and colleagues in the early 1990s. In the conscious subject, heart rate variation is seen during the respiratory cycle (sinus rhythm arrhythmia), mediated predominantly by a parasympathetic reflex linking stretch receptors in the lungs and aorta to cardiac vagal motor neurons[68]. This is a non-pathological variation, usually accepted to be defined by a greater than 10% variation in the ECG R-R interval over 5 minutes. It has been shown in multiple small studies that heart rate variation with respiration reduces during deep anaesthesia and increases during light anaesthesia emergence of anaesthesia[68–70], in correlation with variation in EEG[69,71]. Yet, studies have found inconsistent regarding the accuracy of this method in discerning awareness from anaesthesia. While some have shown it to be highly successful and a potential foundation for the development of new depth of anaesthesia monitors[72,73], some others have reported it to be greatly inferior to EEG-based assessments of anaesthetic depth[74]. Additionally, limited data is available regarding the usefulness heart rate variation measurement in assessing depth of anaesthesia and awareness in clinical, non-research based practice.

- Modern depth of anaesthesia monitoring systems:

Technological advances have led to the introduction of computerised devices designed to assist depth of anaesthesia monitoring. The rationale behind those monitors is to provide, in conjunction with clinical signs, a more sensitive and specific assessment of anaesthetic depth than clinical signs alone[58]. The commonest depth of anaesthesia monitors currently used in clinical practice are divided into those using evoked potentials and those deriving information from the spontaneous electroencephalogram (EEG).

Evoked potential monitoring systems assess the electrical activity elicited in certain part of the central nervous system in response to stimulation of selected sensory nervous pathways, i.e. the EEG response to a set stimulus. Attempts at assessing depth of anaesthesia by analysing evoked potential were first reported in the 1960s[75]. Since then, the technology has evolved to monitoring systems relying on auditory, visual or somatosensory evoked potentials analysis.

Auditory evoked potentials (AEP) are a waveform of electrical activity from the cochlea to the cerebral cortex elicited by auditory stimuli such as clicks delivered via headphones[76,77]. The AEP waveform is composed of three individual components (brainstem AEP, Middle latency AEP and Long latency AEP) that are thought to arise from different anatomical regions of the brain. AEPs, being much smaller than EEG waves, are not visible on raw EEG traces and the signal recorded from forehead electrodes requires averaging over several minutes before information can be extracted[76,77]. Studies have shown that the level of Middle Latency AEP activity correlates with depth of anaesthesia when using most general anaesthetic agents[76,78,79] but not when administrating ketamine[80] or nitrous oxide[81].

Somatosensory evoked potentials (SEP) involve the delivery of a supramaximal stimulus to specific peripheral nerves whilst the subsequent evoked potential is recorded with an electrode placed over the corresponding sensory area. Studies have shown that most anaesthetic agents decrease the amplitude and increase the latency of SEP in a dose-dependent manner[77,82]. Interestingly, etomidate seems to consistently increase the amplitude of SEP in contrary to other agents[83].

Visual evoked potentials (VEP) form a third modality of evoked potential recordings used to assess anaesthetic depth. It was found in 1934 by Adrian and Matthew that the EEG recorded over the visual cortex is affected by light stimulation[84]. The current monitoring system consists most commonly in light-emitting diodes inserted into goggles that can stimulate the optic nerve at a frequency of 2 Hz. Electrodes placed over the occiput then record an EEG trace of the activity in the visual cortex. Analyses of VEP during anaesthesia with various agents has shown that most anaesthetic agents increase the latency and decrease the amplitude VEP in a dose-dependent manner[77,85]. Although VEP have been shown to be less accurate than AEP in the assessment of anaesthetic depth, the technology has been used to monitor the function of and potential injuries to the visual pathway during surgery for lesions involving the pituitary gland, optic nerve and chiasma, and optic radiations[77,86,87].

The use of evoked potentials as a mean to assess depth of anaesthesia developed mainly in the late 1970s and throughout the 1980s, but it has since been superseded by the introduction of spontaneous EEG-based monitoring devices.

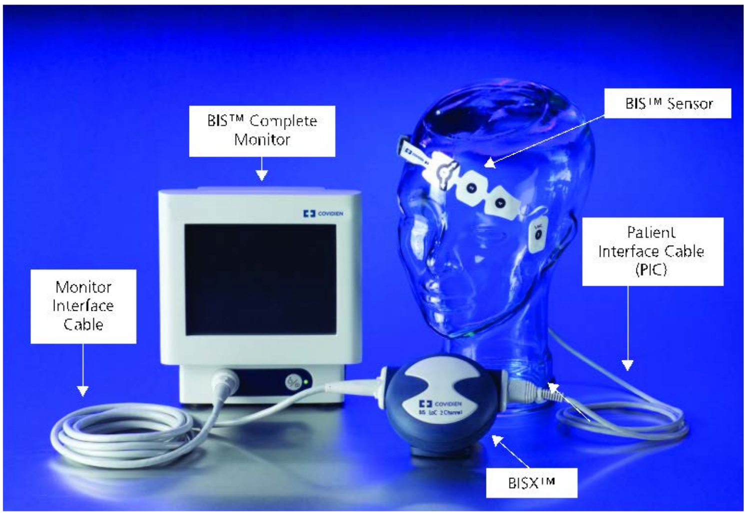


Figure 3. The BIS monitoring system.
From BIS monitor operator's manual[93]

General anaesthetics, both intravenous agents and inhaled volatile gases, cross the blood brain barrier to exert their effects on synaptic transmission in the central nervous system[59]. The exact mechanisms by which those effects are elicited still remain to be demonstrated but the altered EEG activity following administration of general anaesthetic agents is generally accepted[58,59,77,88,89]. Monitors deriving parameters from spontaneous EEG first digitise the signal and secondly analyse it using proprietary algorithms to extract specific indices.

The Bispectral (BIS) Index monitor (Covidien, Mansfield, MA, USA) was introduced in 1992 by Aspect Medical Systems. Four EEG electrodes designed for the BIS monitor to reduce skin impedance are linked together on one sensor (BIS Quatro Sensor, Covidien, Mansfield, MA, USA) placed on the patient's forehead so as to record the spontaneous EEG signals (Figure 3).

The EEG signal is then analysed through a proprietary algorithm by the BISx component of the monitoring system to produce the BIS Index and the EMG interference level displayed on the monitor[39,90] (Figure 3). The BIS index is a dimensionless number between 0 (isoelectric EEG trace) and 100 (awake EEG trace), with adequate surgical anaesthesia depth considered to be between 40 and 60[59]. The BIS depth of anaesthesia monitoring device has been used in most studies investigating accidental awareness during general anaesthesia and has been the benchmark for most similar EEG-based devices developed subsequently. It is the device recommended in most national and international guidelines regarding depth of anaesthesia monitoring. More detailed analyses of the BIS monitor and its uses are provided by Hajat et al.[91] and Musizza et al[92].

The Narcotrend monitor (Monitor Technik, Bad Bramstedt, Germany) was released in 2001. Alike the BIS, it records EEG and EMG signals from electrodes placed on the patient's forehead (Figure 4a). The Narcotrend monitor can be used with dedicated Narcotrend electrodes[94] or with standard pre-gelled electrocardiogram electrodes[39]. The recorded EEG signal is subjected to an artefact-removal algorithm and then computerized by another proprietary algorithm to determine the Narcotrend Stage and Index[95].

a) b)

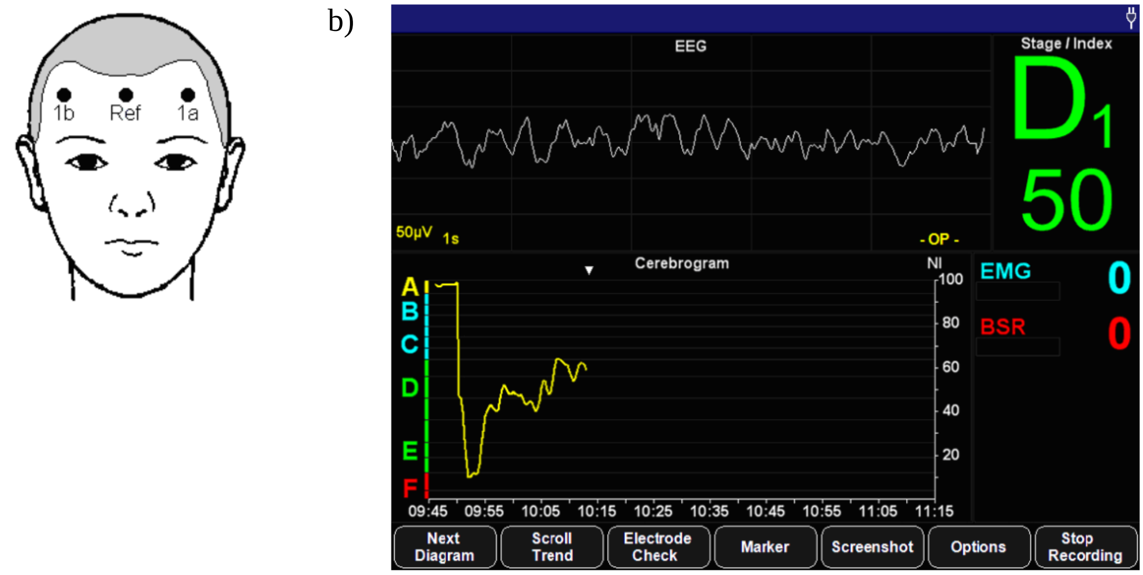


Figure 4. The Narcotrend electrodes placement pattern suggested by the manufacturer (a) and the recording screen of the Narcotrend monitor (b). The recording screen presents the Narcotrend stage (here D1) as well as the Narcotrend Index (here 50). From the Narcotrend Compact M Operating Instructions[96].

The older versions of the Narcotrend monitor displayed EMG interference and a letter classification referred to as Narcotrend Stage to represent depth of anaesthesia, with sub-categories adding in precision (A, B0-2, C0-2, D0-2, E0,1, F0,1). The more modern Narcotrend monitors are displaying the EMG interference value as well as both the Narcotrend Stage and a dimensionless 0-100 numerical index called the Narcotrend Index (Figure 4b).

The corresponding Narcotrend Index values for each Narcotrend Stage are presented in Table 1. There are two modes of recording on the Narcotrend; the most common one is the one-channel mode which is the standard for assessment of depth of anaesthesia during surgery. The two-channel mode is used when comparison of the signals from both hemisphere of the brain is required, such as during carotid artery operations[59,96].

Table 1. Narcotrend stages with their respective equivalent Narcotrend Index values. Adapted from Kreuer et al.[110].

	Narcotrend Stage	**Narcotrend Index**
Awake	A	95-100
Sedated	B0	90-94
	B1	85-89
	B2	80-84
Light Anaesthesia	C0	75-79
	C1	70-74
	C2	65-69
General anaesthesia	D0	57-64
	D1	57-56

	D2	37-46
General anaesthesia with deep hypnosis	E0	27-36
	E1	20-26
	E2	13-19
General anaesthesia with increasing burst suppression	F0	5-12
	F1	1-4

Multiple other depth of anaesthesia monitoring devices relying on analyses of the patient's spontaneous EEG have been developed in the last decade. For example, the Cerebral State Monitor (Danmeter A/S, Odense, Denmark) processes the patient's spontaneous EEG to determine the Cerebral State Index ranging from 0 (flat EEG) to 100 (EEG activity of an awake subject) [97]. As for the BIS monitor, the adequate range for surgical anaesthesia is believed to be between 40 and 60[77].

Similarly, the M-Entropy monitor (GE Healthcare, Chalfont St Giles, UK) relies on the principle that increasing anaesthetic depth leads to an increase in the EEG signal regularity and a simultaneous decrease in its entropy[59,77]. The monitor divides the signal into State Entropy (EEG alone) and Response Entropy (EEG and frontal electromyogram (EMG) signals)[98]. State Entropy and Response Entropy are given indices of anaesthetic depth between 0-91 and 0-100 respectively, ranging from no cerebral electrical activity to EEG of an awake subject[77]. While published data demonstrates that Entropy indices relate to clinical signs of anaesthetic depth, no clinical trials however are available that conclusively show that entropy monitoring reduces the incidence of intraoperative awareness.

❖ The future of depth of anaesthesia monitoring:

Through the use of the depth of anaesthesia monitoring techniques described above, it was identified in the last two decades that some patient groups are at an elevated risk of AAGA[37,92,98]. These include patients who cannot tolerate adequate anaesthetic drug dosing due to their condition and the ones in which inadequate anaesthesia levels may be masked (e.g., when paralysed by muscle relaxants)[99]. On the contrary, some patients are at risk of excessive anaesthetic depth such as for example patients with advanced age, liver disease, high body mass index, or poor cardiovascular function[99]. To address these issues, the National Institute for Health and Care Excellence now recommends the use of spontaneous EEG-based depth of anaesthesia monitors as an option in patients at risk of under or over-dosing of anaesthetic drugs as well as in patients receiving total intravenous anaesthesia[99]. The Association of Anaesthetists of Great Britain and Ireland have published similar recommendations[100].

Nevertheless, reports are starting to appear in the literature regarding the limitations of EEG-based depth of anaesthesia monitors, and doubts regarding the accuracy and safety of those modern devices have recently emerged. The BIS monitor has been available clinically for over 20 years and it has been used as the standard to which other less extensively validated

depth of anaesthesia monitors have been compared[101]. This EEG processing depth of anaesthesia monitor is commonly used in Europe, as well as other similar devices such as the Narcotrend monitor. Yet, the evidence base for the hypothesis that the use of these depth of anaesthesia monitors reduces the incidence of intraoperative awareness is conflicted. Large clinical trials, such as the B-AWARE[102] and Zhang et al.[103] trials, have shown that the BIS monitor reduces the incidence of AAGA, while some others (Michigan Awareness Control Study[104], B-UNAWARE[15], BAG-RECALL[105]) have pointed out the lack of effect of the monitor on awareness incidence. In regard to the Narcotrend monitor, some published trials report a reduction in the incidence of intraoperative awareness when using the monitor to guide anaesthetic agents administration[106,107], while others did not[108,109].
Indeed, awareness during general anaesthesia still occurs when depth of anaesthesia monitors are employed to prevent it. Multiple randomized controlled trials have reported a decreased incidence of intraoperative awareness when using the BIS monitor compared to traditional clinical signs, yet most trials still reported intraoperative awareness[11,14,15,102] or even an increased incidence of awareness in the BIS-monitored group[105].

It emerges from the literature that after almost 175 years of anaesthesia, we are still looking for a safe, reliable, and accurate methods to assess depth of anaesthesia to a high level of certainty. In the future, a safe and reliable way of assessing anaesthetic depth would be to use a device accurately measuring the real-time electrical activity in specific areas of the cerebrum and brain stem known to be involved in consciousness. This monitoring device would have to be non-invasive, readily usable in the operating theatre, financially affordable and accurate regardless of the surgical stimulus or anaesthetic agent used. While research is currently being undertaken in assessing current technology and developing new equipment, the future of depth of anaesthesia monitoring is still very much a work in progress.

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