INTERFACE

SOCIETY FOR TECHNOLOGY IN ANESTHESIA

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OCTOBER 1996 • VOLUME 7 • NO. 3

Program Finalized for 7th Annual STA Meeting

INVENTION, CREATIVITY & TECHNOLOGY

Fort Lauderdale Marina Marriott • Fort Lauderdale FL
January 16-18, 1997

This year's meeting integrates the know-how of clinical anesthesiologists and biomedical engineers with the resources of industry in workshops and panels to explore the creation of new equipment and technology.

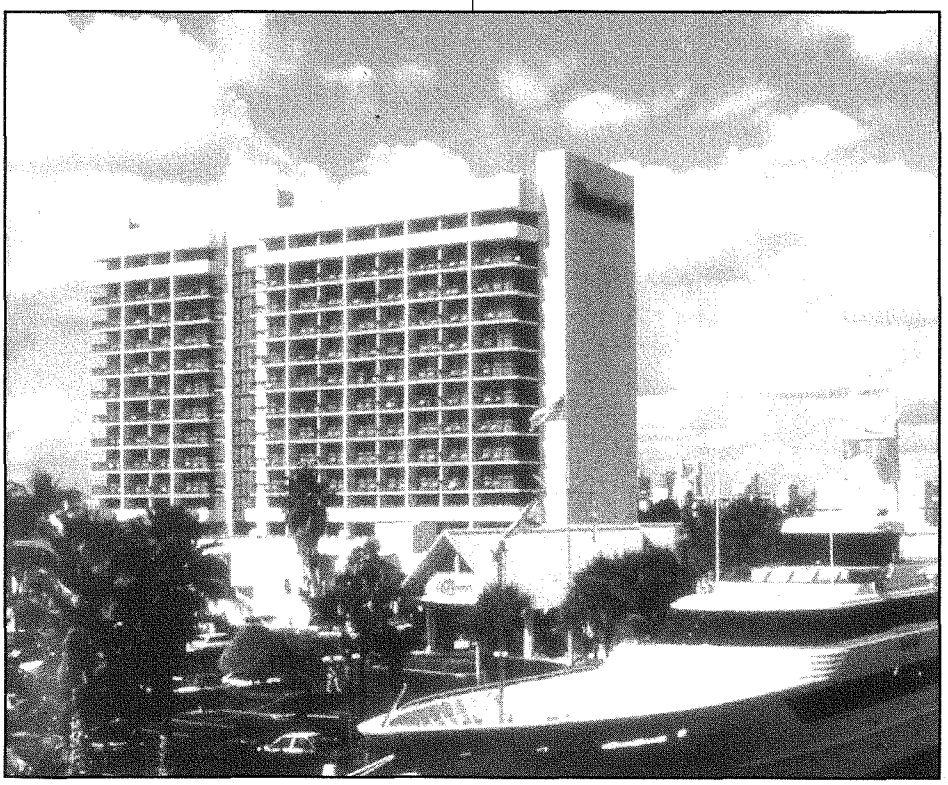
Annual Meeting program chairman, Dr. Paul Barash and the program committee have put the finishing touches on an academic and social program which will surely rival previous meetings.

Formal panels include: the evolution of new technology, from the creative concept to funded production with speakers from academia, and venture capital firms, and successful inventors; unanticipated morbidity and mortality from new products with a medical examiner's perspective on inventions gone awry; and the impact of standards and quality control on the creative process, development and safety (see page 2 for full list of featured speakers and their topics).

During the workshop series, members will generate ideas for a new product and follow growth through inception, performance to industry standards, quality control and improvement, government approval, and marketing. Prizes await the team with the most successful stock offering on the final day.

Abstract sessions and a "Create your own "CD-Rom" workshop are also part of the program. For a change of pace, field trips introduce you to the National Hurricane Center, Bertram Yacht Company, or Heico Jet Avion. A dinner cruise with an STA Talent Show rounds out the meeting program. ◆

-Jane Fitch-



Fort Lauderdale Marine Marriott Hotel.

Fort Lauderdale in January and the Marine Marriott should provide a great venue. Plan to attend.

INSIDE THIS ISSUE:

"The Technology of Forensics"

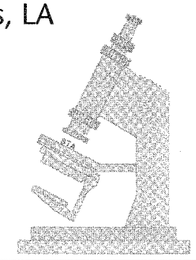
Dinner with Cyril Wecht, M.D., J.D.

Noted Forensic Pathologist and Author of *Causes of Death,* his memoirs and perspectives on the notable forensic cases of John F. and Robert F. Kennedy, Elvis Presley, Mary Jo Kopechne, Sunny von Bulow, the Waco Branch Davidians, and many others.

Sunday, October 20, 1996

7:30 p.m.

Westin Hotel – New Orleans, LA



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Brief Listing of Internet Mailing Lists

Listserver	Subscribe Command	Command Address	Message Address
Anesthesiology Discussion Group	subscribe anesthesiology Your Name	listproc@ gasnet.med.yale.edu	anesthesiology@ gasnet.med.yale.edu
American Society of Anesthesiologist	subscribe ASA Your Name	listproc@ gasnet.med.yale.edu	
STA Mailing List	subscribe STA Your Name	listproc@ gasnet.med.yale.edu	sta@ gasnet.med.yale.edu
STA Mailing List	subscribe ACCRI-L Your Name	listserv@ uabdpo.dpo.uba.edu	
Pediatric Pain Mailing List	subscribe pediatric-pain	mailserv@ac.dal.ca	pediatric-pain@ac.dal.ca

(Very) Brief Listing of Internet Resources

Internet Resource	UR
WWW Virtual Libra: Anesthesiology	http://gasnet.med.yale.edu/index.html
Anesthesiology and Critical Care Resources on the Internet	http://www.eur.nl/FGG/ANEST/wright
Catalog of Electronic Journals	http://www.edoc.com/ejournal
Erasmus University Department of Anaesthesia	http://www.eur.nl/FGG/ANEST
GASNet Anesthesiology	http://gasnet.med.yale.edu
World Societies for Technology in Anesthesia	http://gasnet.med.yale.edu/wsta
University of Alabama at Birmingham Anesthesiology Gopher	gopher://gopher.anes.uab.edu
University of Queensland Anesthesia Web Server	http://www.uq.oz.au/anaesth/home.html

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INTERFACE

SOCIETY FOR TECHNOLOGY IN ANESTHESIA

INTERFACE is the official newsletter of the Society for Technology in Anesthesia.
The newsletter is published quarterly and mailed directly to the membership of the society.The editors invite suggestions, contributions and commentary about published items
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Springtime in The Netherlands

Fields of blooming tulips, like carpets laid on the Dutch landscape, welcomed an international group of visitors who attended the 16th International Symposium on Monitoring and Computing in Anesthesia and Intensive Care held in Rotterdam from May 9 through 11, 1996. The meeting organizers, Drs. Jan Klein, Rene Hagenouw and Wilhelm Erdmann put on a program filled with quality presentations, time for collegial interaction and social amenities.

The meeting began with two sessions devoted to Clinical Information Systems. Speakers from Europe, Russia, the United States and Australia presented work in progress designed to improve the presentation and analysis of data in the operating room and ICU. The afternoon session was devoted to Echocardiography and technical aspects of medical technology. On the second day, there were additional presentations on clinical information systems and measuring the depth of anesthesia. Meeting participants also had the opportunity to attend a hands on workshop on educational software development presented by Drs. Tom Engel and Keith Ruskin. Workshop attendees actually built their own mini-application using tools available for the Apple Macintosh. The final day focused on the Internet and its support for practitioners in Anesthesia and Intensive Care.

As if the scientific program was not enough, the social activities were

continued on page 26

Editorial...

"Mr. Jones Open Your Eyes!"

As crude as it is, yelling commands at our patients is a common method to assess emergence. A more sophisticated monitor which reliably measures sedation and hypnosis may finally be here in the form of the Bispectral Index (BIS Index) [the BIS Index is a construct which utilizes E.E.G. feature extraction and a discriminate function to closely correlate with clinical sedation.] BIS Index does not correlate with MAC. It does not directly measure analgesia. What BIS Index may do is provide an endpoint to allow the titration of sedative/hypnotic drugs more acurately than our current methods (i.e., rather than using the ED95 of a drug--thus having few failures, but effectively overdosing 95% of our patients).

In this issue of Interface Jeff Sigl PhD., Manager of Analytical Research for Aspect Medical Systems describes the design of the BIS index. He clarifies how the BIS Index differs from the first generation of EEG monitors touted to be "depth" monitors. He also provides current data suggesting that the risk of intra-operative awareness when using BIS Index clinically to guide sedative/hypnotic titration is low.

Possibly the most important reason this new generation of processed EEG monitoring may be successful is that one does not need to be a neurologist or neuroanesthesiologist to interpret the data.-- BIS is simple! The question during clinical trials will be to prove it is accurate and reliable. ◆

Editors Note -

This article was an invited review of BIS

BIS Monitoring In Anesthesia

Jeffrey C. Sigl, PhD[1]
Aspect Medical Systems, Natick, Massachusetts

The Bispectral Index (BIS) is a new technology for intraoperative monitoring which provides the clinician with a continuous measurement of a patient's hypnotic state. This article describes the development of BIS and summarizes results of clinical trials which examine its utility.

What is the Bispectral Index (BIS)?

The Bispectral Index describes the complex electroencephalographic (EEG) pattern as a single metric that correlates closely with the hypnotic state of the brain, quantified as the level of sedation[2,3,4,5,6] and consciousness..[7,8] This metric is computed continuously in time with both the instantaneous value and the resulting time trend displayed on a monitor (Model A1050, Aspect Medical Systems, Natick, MA).

The BIS was developed using a database of EEG recordings from over 2000 subjects, collected through close collaboration with many researchers and anesthesiologists. The database incorporates thousands of hours of EEG data with multiple endpoints, including the Observer's Assessment of Alertness/Sedation (OAASS)[9] scores, memory and awareness measures, stimulus response assessments and anesthetic agent concentrations. Anesthetic agents included propofol,

isoflurane, midazolam, thiopental, methohexital, N_2O and opioids, used in a wide variety of regimens. From this database, a set of EEG features (characteristics) derived from both bispectral and power spectral analysis were identified. While traditional techniques such as power spectral analysis are limited to frequency and amplitude information, bispectral analysis also quantifies the level of synchronization in the EEG[10].

The response of a patient's brain to anesthetics is characterized by different patterns of EEG associated with specific classes of anesthetics and specific cerebral states. For instance, delta activity (slow wave EEG) is seen at deep intraoperative anesthetic levels, beta activation is characteristic of light benzodiazepine anesthesia, and burst suppression is typical of deep isoflurane anesthesia. BIS is designed so that each of its features is optimized to quantify a specific anesthetic pattern. A low frequency bispectral feature is used to quantify "deep" anesthetic effects. A high frequency feature is used to quantify light anesthetic effects and beta activation. These features were selected from among other candidate features by splitting the database into learn, test and prospective evaluation groups, and using multivariate regression and a learn/test selection methodology (Figure 1). The broad extent of the development database allowed the identification of the optimum set of EEG features required to characterize the full spectrum of anesthetic effects.

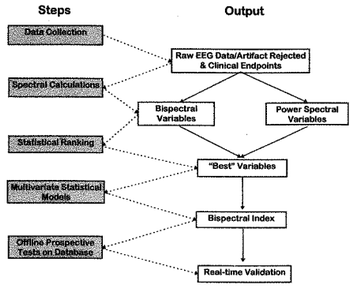

Figure 1. A graphical depiction of the BIS development process.

The bispectral and power spectral relationships in the EEG change in a nonlinear fashion with increasing hypnotic agent. The selected non-linear features were linearized in the regions where they independently provided the greatest sensitivity to changing hypnotic levels. These multiple features were then combined so as to transform simultaneous changes in the light and deep features into a single number. The degree of suppressed EEG over the prior 60 seconds is an additional third feature that is integrated into the final Bispectral Index[11].

How is BIS different from power spectral EEG?

Most other processed EEG measures (e.g., 95% Spectral Edge (SEF), Median Frequency (MF) and Relative Delta Power) are based purely on power spectral analysis. While these measures quantify the typical paradigm of an overall shift to lower frequencies with deepening anesthesia, they are not correlated with the level of sedation.[12] For example, an awake patient's EEG is typically dominated by activity in the 6-10 Hz range. Upon administration of light doses of benzodiazepines, the EEG shifts up in frequency and becomes dominated by beta activity in the 12-20 Hz range. At higher doses, this "beta activation" subsides and the EEG typically decreases in frequency. This shift upward and then downward in EEG frequency leads to a concomitant increase and then decrease in SEF, MF and Relative Delta Power (Figure 2 and Figure 3), resulting in the same parameter value at two different anesthetic states. In contrast, BIS decreases uniformly with increasing anesthetic dose.

SEF, MF and Relative Delta Power were developed to describe changes in the power spectrum. In contrast, BIS was developed to quantify the effects of anesthetics on the patient's

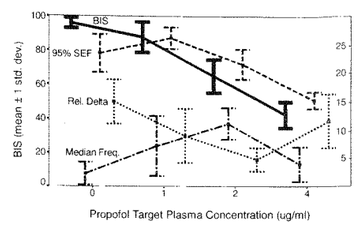

Figure 2. Response of BIS, Spectral Edge, Relative Delta Power and Median Frequency to increasing steady-state infusions of propofol.

hypnotic state. The use of bispectral analysis, coupled with the development of an index composed of many features, enables BIS to track a patient's hypnotic response to anesthetics.

Clinical use of the Bispectral Index

Balanced anesthesia provides, in part, both adequate hypnosis (i.e., that component of anesthesia associated with sedation and responsiveness) and analgesia (insensitivity or indifference to painful stimuli). Different anesthetic agents provide differing proportions of hypnosis and analgesia, with agents such as midazolam and propofol providing primarily hypnosis, and opioids such as alfentanil providing primarily analgesia. The BIS is designed to correlate closely to the hypnotic state of the patient, that is, with sedation and responsiveness.

As a measure of hypnotic state, BIS monitoring may be used to guide titra-

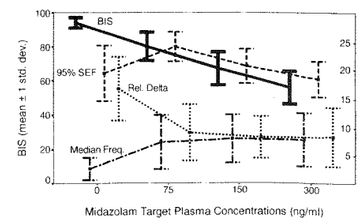

Figure 3. Response of BIS, Spectral Edge, Realtive Delta Power and Median Frequency to increasing steady-state infusions of midazolam.

tion of anesthetic agents that provide hypnosis. This technique allows the anesthesia provider to adjust a patient's anesthetic state by measuring the effect of the administered agent on that individual, rather than dosing based on population norms. A multicenter study of four commonly used anesthetics, propofol, midazolam, alfentanil and isoflurane,[5,7,11] resulted in the set of clinical ranges in Figure 4.

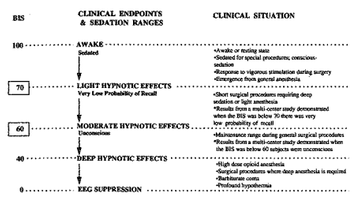

Figure 4. The relationship between various BIS ranges and clinical endpoints.

While BIS does not directly quantify analgesia, it is important to recognize that a patient's analgesic adequacy can directly impact their hypnotic state.[14] Intense nociceptive stimuli in a patient who has an inadequate level of analgesia can "break through" the analgesia and arouse the subject hypnotically. Therefore, it is important that when using BIS monitoring to titrate hypnotic agents, the clinician provide sufficient analgesia to protect the subject from hypnotic arousal by sudden increases in intraoperative stimulation. For this reason, selection of a BIS level at which to maintain a patient is a decision that must be made by the individual clinician with full knowledge of the patient's analgesic adequacy.

Clinical trials using BIS Monitoring

Recently, a multisite clinical trial was conducted to assess the clinical utility of BIS monitoring. A population of surgical patients received propofol/alfentanil anesthesia. Half of those enrolled received typical doses of propofol titrated according to standard clinical practice. In the other half of those enrolled, propofol was titrated to maintain the patients' BIS levels between 45 and 60 intraoperatively, increasing to between 60 and 75 fifteen minutes before the end of the case. A set of clinical endpoints in this BIS-monitored (BIS) group were compared with those of the non-monitored standard practice (SP) group. The BIS-monitored patients emerged from anesthesia faster than the SP patients, responding to verbal command 42% sooner (7±6 min. (BIS) vs. 12±11 min. (SP); $p < 0.05$).[17] The BIS-monitored patients were eligible for PACU discharge 21% sooner than the SP patients (33±17 min. (BIS) vs. 42±26 min. (SP); $p < 0.05$) and 43% of the BIS-monitored patients were fully oriented on arrival in the PACU, vs. 23% of the SP patients ($p < 0.001$).[18] Finally, the BIS-monitored group received 19F% less propofol than the SP group (95±25 ug/kg/min (BIS) vs. 116±41 ug/kg/min (SP); $p < 0.05$)[19]. These advantages were achieved with no significant difference in intraoperative hemodynamic or somatic events.

In this trial, the individual propofol infusion rates required to maintain an adequate intraoperative hypnotic state varied by more than fourfold[20], yet there were substantial savings in overall propofol usage. This indicates that titration of anesthetic agents using BIS can reduce agent usage for the patient population by reducing the overall level of relative overdosing. However, because BIS monitors the *effect* of the anesthetic, BIS may allow the anesthetist to identify those patients at risk for awareness due to a higher than normal anesthetic tolerance and *increase* their dosage to achieve sufficient hypnosis.

Data on Intra-operative Awareness

In the several thousand surgical cases in which BIS monitoring has been used, there has been only one reported case of recall of intraoperative events, which in retrospect was correctly identified by high intraoperative BIS values.[21] There have been numerous cases in which an increase in the BIS trend warned the clinician of a impending problem, such as the infusion pump failure documented in Figure 5.

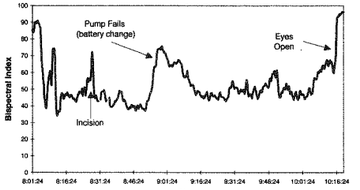

Figure 5. Example of a intraoperative BIS trend. The rise of BIS mid-case reflects the unexpected failure of the propofol infusion pump battery.

A recent clinical study[22] used the isolated forearm technique to examine responsiveness during recovery from standard induction boluses of thiopental (4 mg/kg). The BIS values for each patient from the time of induction to the time of response to verbal command (indicated by squeezing the investigator's fingers) are depicted in Figure 6. The BIS starts at a high level when the patient is awake and decreases with induction. As the induction bolus wears off, BIS again increases. Despite the variability in the duration of response to a fixed induction dose, no patient responded below a BIS of 60. There were no incidents of postoperative recall of the response to command.

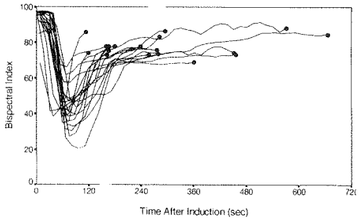

Figure 6. Response to command following bolus induction. Each line is an individual patients BIS trend; the dot at the end of the trend indicates the time of response.

Summary

The BIS is a new technology which can be used to monitor the effect of anesthetic agents on a patient's hypnotic state. The correlation between BIS and a patient's hypnotic state has been validated by a number of clinical studies.[1,3,4,5,6,7] The results of clinical utility studies have shown that intraoperative BIS monitoring allows a clinician to titrate the dosage of anesthetic agents to individual requirements, resulting in faster emergence from anesthesia[16], better patient orientation on PACU arrival, quicker eligibility for PACU discharge[17] and decreased usage of anesthetic agents.[18]

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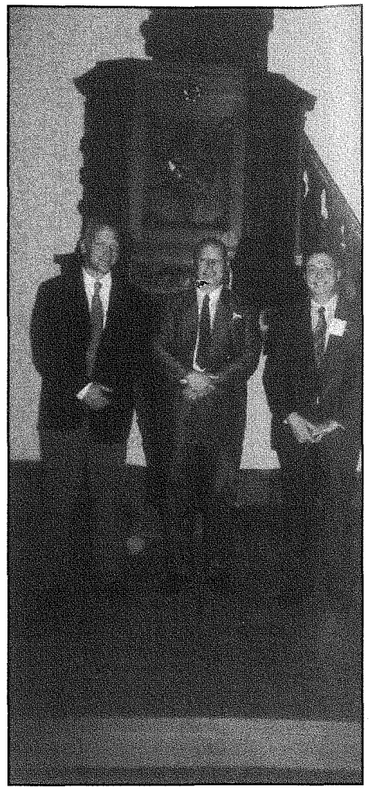
SPRINGTIME IN THE NETHERLANDS

continued from page 23

a true delight. On the evening of the second day, a dinner was held at the Municipal Museum in the town of Schiedan just outside of Rotterdam. This "museum" is in fact a centuries old church which has been renovated and now serves as an art museum. The



From left to right, Drs. Jan Klein, Wilhelm Erdmann and Rene Hagenouw of Erasmus University. Photo taken in the historic Municipal Museum of Schiedam, The Netherlands.

main room was filled with tables where guests were treated to fine music, fine food and fine friends. Jan Klein entertained everyone with a very warm and personal accounting of the history of the town and the museum building. Everyone would have been delighted to have gone home at the end of the meeting Saturday but the meeting organizers were intent on providing at least one additional memory of the trip. Dr. Erdmann hosted all who could come at his farm in the country on the evening of the final day. Again, fine food, camaraderie and excellent time was the order of the day. ◆

-Jeff Feldman-