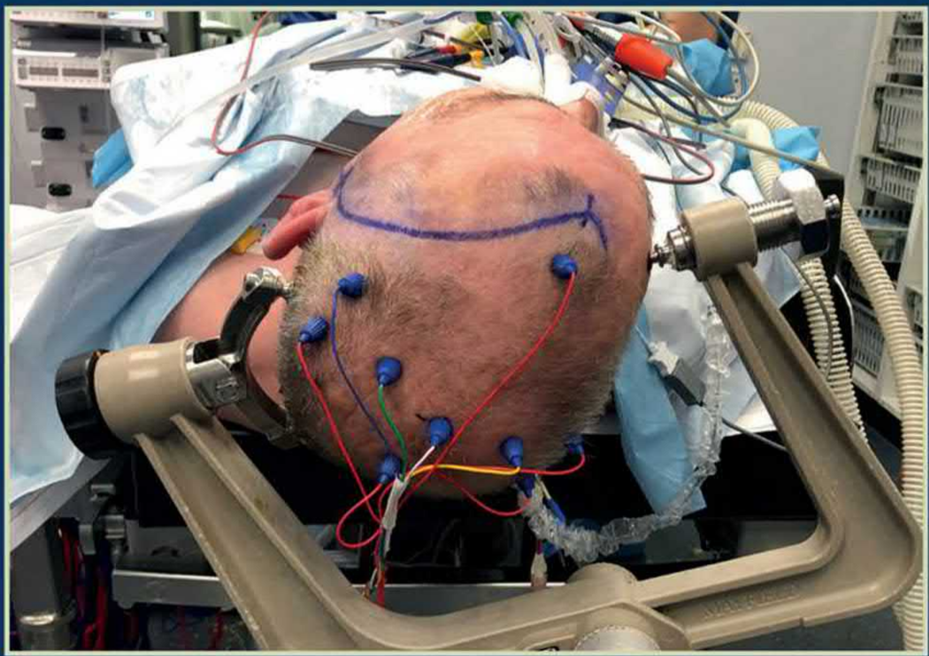
Neurophysiology *in* Neurosurgery

A Modern Approach

Second Edition



Edited by
Vedran Deletis, Jay L. Shils
Francesco Sala *and* Kathleen Seidel

NEUROPHYSIOLOGY IN NEUROSURGERY

SECOND EDITION

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Neurophysiology in Neurosurgery

Vedran Deletis, Jay L. Shils, Francesco Sala, Kathleen Seidel, Editors

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- Chapter 12 - Neurophysiological identification of long sensory and motor tracts within the spinal cord (Videos 12.1, 12.2, 12.3)
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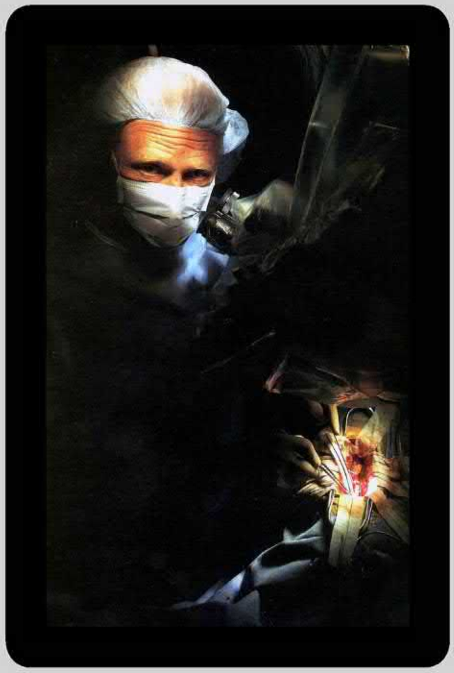

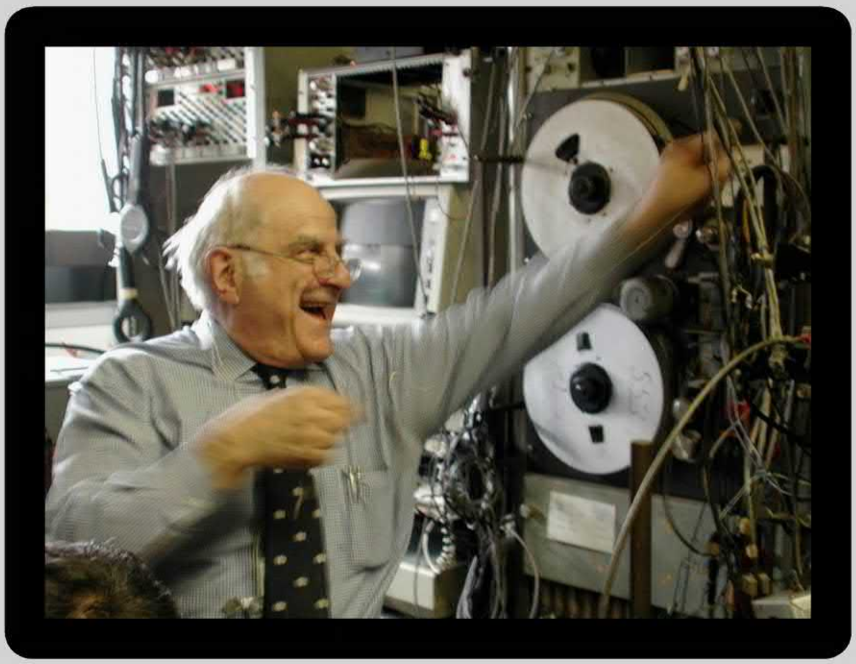

Fred J. Epstein,
(1937 -2006)

and

Vahe E. Amassian
(1924-2013)

Dedication

This book is dedicated to two extraordinary men, Vahe Amassian and Fred Epstein. Both of these extraordinary individuals changed our professional lives and made a significant impact on the fields of intraoperative neurophysiology and neurosurgery.

Vahe was French-born neurophysiologist, from Armenian parents, educated in the United Kingdom, where he made part of his professional carrier as a neurophysiologist, and later on moved to the United States where he continued to work with great success and achievement. Vahe's work on the physiology of the nervous system describing D and I waves of corticospinal neurons [1] was the basis for the development of present methodologies for intraoperative monitoring of motor-evoked potentials. Vahe was actively involved throughout the development of this methodology. Vahe generously shared his enormous intellectual talent and his vast knowledge. Vahe was always an inspiration for us and our colleagues. Vahe was the quintessential great teacher and mentor you remember for life.

Fred was larger than life. Growing up he battled with circumstances that made every academic achievement a hard-earned victory. He beat that, and went on to reach further. Having become an accomplished and leading pediatric neurosurgeon, he developed pioneering surgeries in the brainstem and spinal cord. In doing this he realized the potential of intraoperative neurophysiology. Thus he was a very early advocate of the utilization of intraoperative neurophysiologic techniques to make complex operations in critical areas safer, better, and possible at all. As a world-renowned neurosurgeon he said, "Monitoring is the most interesting thing we do here!"

Fred had an amazing ability to see forest, when most of us only saw trees. And that applied to his vision of intraoperative neurophysiology. Following this vision he was instrumental in many of intraoperative neurophysiology's developments and this book is testament to the fact that he was right.

Vedran Deletis and Karl Kothbauer

Reference

[1] Patton HD, Amassian VE. Single and multiple unit analysis of the cortical state of pyramidal tract activation. J Neurophysiol 1954;17:345–63.

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Preface

It has been 18 years since the first edition of *Neurophysiology in Neurosurgery: A Modern Approach* in 2002 was published. We are happy to present an updated review of the very latest achievements in intraoperative neurophysiology (ION) from a theoretical, methodological, and clinical perspective. We have divided the book in six sections: Part I, Introduction to Intraoperative Neurophysiology; Part II, Intraoperative Neurophysiology: Neurophysiologic Perspective; Part III, Neurophysiology of Brainstem and Spinal Cord Reflexes; Part IV, Intraoperative Neurophysiology; Surgical Perspective; Part V, Functional Neurosurgery; Part VI, Other Important Aspects of Intraoperative Neurophysiology.

Due to significant changes and new developments in the field of ION, additional chapters have been added. At the time of the first edition, in 2002, some of the chapters included neurophysiologic techniques that were either in the very early stages of development or borrowed from the clinic yet not fully adapted for their intraoperative use. Since then, some of these techniques have become standard in ION; meanwhile, new methods have been developed to monitor reflex pathways within the brainstem or to perform detailed and accurate brain and spinal cord mapping. Moreover, there has been an increasing role for ION during neuromodulation procedures. Finally, technological advances have improved the quality and interpretability of existing techniques.

As the field of ION grew, so did its popularity within the neurosurgical community. The introduction of ION to this new generation of surgeons has created the need for more skilled and well-trained intraoperative neurophysiologists and technologists.

Over the past two decades, ION has played an increasingly important role in the neurosurgeon's intraoperative decision process, to the point that for certain procedures—for example, intramedullary spinal cord tumors, cerebral lower grade gliomas, or placement of permanent neuromodulation electrodes—the neurosurgeons modulates their surgical strategy based on the neurophysiological feedback from the ION team. Particularly in neuro-oncology where the goal is to maximize resection while minimizing morbidity, ION has demonstrated its essential role in achieving this. In addition, with the overall improvement in survival, preservation of the quality of life is a major issue when planning and performing surgery. Therefore the key concept of "safe surgery" can be guided by intraoperative neurophysiological monitoring and mapping methods. ION is no longer relegated to the realm of warning post an iatrogenic event but is now a critical medical discipline helping surgeons to decide on the appropriate course of the surgical intervention. Further, it is important to ensure that the ION team is included as part of the surgical team and to assure that the information obtained from ION interpretation is appropriately relayed to the surgeon and anesthesiologist, in a timely fashion, in order to have a beneficial impact on the procedure.

The material presented in this book is written for neurophysiologists as well as surgeons, anesthesiologists, biomedical engineers, and technologists. We hope our book will contribute to expanding the existing ION knowledge and to increase the awareness on the value of ION techniques for all the professionals involved in the surgical treatment of nervous system diseases. The material presented does not only give a historical perspective on the practice of ION but will hopefully induce a new way of thinking on how ION can minimize iatrogenic injury to the patient's nervous system via proper application of these techniques. We hope this book will influence the way neurosurgeons apply ION to their surgical practice, aiming for a better quality of life for their patients, compared to a time when these techniques were not applied.

The editors of this book all agree that "No monitoring is better than poor monitoring," not only does it degrade the field of neuromonitoring, but more importantly it can harm the patients that we are trying to protect.

Vedran Deletis, Jay Shils, Francesco Sala and Kathleen Seidel

Intraoperative neurophysiological monitoring—why we need it and a personal perspective of its development

Johannes Schramm[1] *and Azize Boström*[2]
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1 Introduction

Intraoperative monitoring—more precisely intraoperative neurophysiological monitoring (ION)—has found its way into the practice of many surgical specialties, mainly in neurosurgery but orthopedics as well. Why has it become such a frequently used tool? The obvious reason is that it provides previously unavailable information on the functional status of neural tissue in the anesthetized patient. This introduction to this book describes why ION is used, what advantages are associated with its use, why it has become a teaching tool improving surgical techniques and tactics, and why it is helpful even when no significant changes in the data occur. The author was involved in the early stages of ION development and was a witness to its gaining a firm place in neurosurgery. Thus this is a recollection from a neurosurgeon's perspective.

There are several positives to the use of ION:

1. detection of developing neural damage and avoidance of permanent deficits,
2. teaching the surgeon about detrimental effects of seemingly harmless surgical steps,
3. detection of adverse systemic or nonsurgical influences, and
4. reassurance to surgeon about lack of damaging effect of specific risky maneuvers.

2 Theoretical background

After the realization that evoked potential (EP) technology was available and had already been proven to be helpful in the diagnosis of spinal injury, as well as other diseases, it was shown in experimental spinal cord injury to be able to detect damage to the fiber tracts. The next step was the development of the concept of reversibility as related to the degree of injury, when a significant EP change has occurred. Thus the next logical step was the concept of ION.

To be precise, ION does not completely prevent injury, because a certain degree of impairment is necessary to induce changes in the recorded potentials. Thus the main function of ION is to indicate when damage is starting to occur, ideally before it has become irreversible or complete. Jannetta [1] coined the term—"preventive surgery"—when surgeons use ION during surgery.

In the ideal world the monitoring method would generate no false-positive or false-negative results. Motor EPs (MEPs) must be recorded with the knowledge that a potential motor deficit may affect an upper and a lower extremity and the two body halves separately or in combinations. Thus MEPs have to be interpreted precisely and carefully. If the right leg is monitored by MEP and the motor deficit occurs in the other unmonitored leg, that does not imply a false-negative monitoring event.

The concept of monitoring was not immediately welcomed by many neurosurgeons. In the early phase, I heard comments from my superiors, most likely based on the complete lack of understanding, why a neurosurgeon could possibly deal with neurophysiological recordings. "When you talk at a neurosurgical conference and mention the words 'evoked potentials' are you not aware that 90% of the audience falls asleep immediately?"

Or when presenting the first clinical series, a question came from the audience, “And what do you do with a tumor when the potential is lost, do you leave the tumor in?”, in a sardonic malicious tone, assuming that having to leave some tumor in automatically constitutes a kind of failure.

After the initial phase, where somatosensory evoked potentials (SEPs) were available for monitoring the sensory system supratentorial tracts or the spinal cord only, it was frequently argued that monitoring was not useful because it could not help to avoid motor deficits. It is, of course, true that one cannot expect to receive a warning about impending damage to motor fiber tracts when monitoring sensory fiber tracts. Such an observation does not constitute a false-negative monitoring [2]. Thus this criticism was misguided. In the meantime, after the introduction of MEP monitoring, both fiber tract systems could be interrogated and monitored separately or simultaneously, and this limitation from the initial phase of ION is no longer an issue. However, a low rate of false-negative and/or false-positive monitoring findings is unavoidable considering how many physiologic, anesthetic, and surgical factors are involved, let alone the occasional technical issue.

One basic problem persists throughout the whole period of ION use: when the observed signal has deteriorated, it is impossible to know whether the deterioration reflects a permanent damage to part of the fibers (shown as reduction in amplitude or delayed latency) or whether it is just a functional impairment of the monitored fiber tract with the potential of a full recovery. Similarly, when a monitored signal has been lost (e.g., the motor evoked potentials (MEP) during an insular glioma surgery), this is not automatically synonymous with permanent damage. There is a potential that the loss is reversible and that there will not be a permanent and/or significant motor deficit. However, at the very moment when the change occurs, it is impossible to tell. It has therefore become common practice for the surgeon to modify the surgery at this point, for example, cease manipulation, release traction, irrigate vessels with papaverine, and irrigate the cerebrospinal fluid (CSF) space around major blood vessels. Potential loss in ION does not precisely predict functional loss, but it still serves as a reliable indicator of an impending damage where corrective maneuvers such as stopping all manipulation will frequently show a recovery of the responses within a short time in a number of cases.

Recent technological advances in automatic artifact suppression, digital recording systems that include automatic peak latency and amplitude detection and vast data storage capabilities with the ability to superimpose earlier, and recent recordings have made monitoring more reliable and easier to interpret.

3 Detection of developing neural damage and avoidance of permanent deficits

The best argument in favor of ION use is of course its proven ability to reduce the frequency of inadvertent neurological deficits in many neurosurgical procedures. ION has been shown to prevent new deficits in a number of case series, for example, in a prospective observational study with 423 undergoing ION SEP recordings performed in all patients, brainstem auditory responses [brainstem acoustic EP (BAEP)] were recorded in 33 patients. There were 84 cases of postoperative deficit of which 68 were detected with ION. The authors reported a negative predictive value of 0.95 and a positive predictive value of 0.9. A surgical intervention triggered by monitoring occurred in 42 (9.9%) of cases. The authors concluded that in 5.2% the cases ION prevented a postoperative deficit [3]. Another example of the benefit of ION is the frequency with which facial nerve weakness was reduced after the introduction of facial nerve monitoring during acoustic neuroma surgery [4]. Similarly the rates of hearing loss after the use of BAEP monitoring during microvascular decompression surgery has decreased significantly [5]. The group in Pittsburgh reported a 7% rate of hearing loss rate after MVD for hemifacial spasm prior to the introduction of ION compared with 1.4% of 140 cases with monitoring and in the Wilkins [5] study hearing loss dropped from 6.6% of 152 cases prior to ION to zero in 109 cases with monitoring of BAEP during MVD for hemifacial spasm.

In a meta-analysis, Fehlings et al. [6] found that multimodal ION in spinal surgery was useful. Sala et al. [7] demonstrated that surgery for intramedullary tumors with the use of MEP monitoring showed better outcomes when compared with historical controls that did not use monitoring.

In a series of insular glioma cases [8], MEP monitoring lead to the surgeon’s intervention in 44% of all cases, and the intervention by the surgeon restored MEPs in 83% of those cases resulting in no or only transient new paresis when stable or restored MEPs occurred (93% of cases), whereas permanent MEP loss was associated with permanent new paresis in 7% of cases. ION use in epilepsy surgery has enabled a more complete resection of the ictogenic zone with better functional preservation and led to better seizure control [9].

4 Intraoperative neurophysiological monitoring as a teaching tool

ION has demonstrated its potential as a teaching tool for improving microsurgical techniques and the handling of delicate tissue by raising an alarm that something adverse may be occurring during specific steps of an operation. Its introduction induced a change in how to approach and manipulate certain tissues. This included what not to do when handling delicate brain areas or fiber tracts, such as the pyramidal tract or working inside the medulla oblongata. A much simpler example is the influence on how long, in what direction, and with which degree of force to retract the nervous tissue, for example, the cerebellum in microvascular decompression or a cranial nerve away from a tumor surface.

The use of ION as a teaching tool was a side effect of its implementation. Some of the alarms occurred at times when iatrogenic effects were thought to be minimal: the loss of the BAEP was observed when bringing the patient into the lateral decubitus position for a posterior fossa surgery, after opening the dura and draining the CSF, using the retractor on the cerebellum, using the retractor when opening the Sylvian fissure, losing VIIIth nerve BAEP when coagulating a tumor vessel *far away* from the VIIIth nerve, loss of MEPs from perforator vasospasm in insular glioma surgery. These observations induced the development of alternating strategies and the avoidance of certain maneuvers.

Some neurosurgeons, having used BAEP monitoring for several years, learned so much about negative effects on the preservation of BAEP that they changed their surgical techniques to such a degree that they finally stopped using the monitoring but are still able to preserve hearing in a satisfying number of their cases.

ION as a teaching tool has proven helpful in increasing our knowledge of the anatomy (e.g., brain stem nuclei) and the physiology of fiber tracts. It is justified to claim that intraoperative neurophysiological recordings have made brain stem surgery an acceptably safe procedure. By carefully analyzing the observations made during surgery with ION, we learned a lot about the limitations of the surgical techniques used to manipulate these tissues. A detailed discussion of what the surgeon wins and loses with ION was provided by [10].

5 Detection of adverse systemic or nonsurgical influences

The usefulness of ION is not only related the early detection of potential new neurologic deficits to induce correctional intervention but it allows for the detection of systemic disturbances such as hypoxia, hypotension, or impairment originating from other factors outside of the surgical field. Examples include an SEP loss from damage to the brachial plexus due to an arm positioning issue or movement of a properly placed arm during the procedure or the loss of the MEP following a hyperextended cervical positioning. These events were unexpected during routine procedures when there was no suspicion that neural damage was possible. An early and famous example was Grundy et al.'s description of BAEP loss when the patient was turned into the lateral park bench position where the initial recordings performed with the patient lying on his back were normal [11].

6 Reassurance to surgeon about lack of damaging effect of specific risky maneuvers

The lack of an ION change is also useful, that is, the persistence of a robust signal during potentially dangerous surgical maneuvers can give reassurance to the surgeon that a neurological deficit is unlikely. This also exemplifies the educational aspect of ION. A typical example is the temporary clipping of a major artery during aneurysm surgery where a stable ION response allows the surgeon to keep the clip on as long as necessary. A related phenomenon occurs when an ION change occurs which is induced by a surgical maneuver returns to "normal" allowing the surgeon to with their manipulation, being reassured by the recovery of the potential. An example is the return of the response during temporary clipping of an important vessel with the elevation of systemic blood pressure. An impressive example of direct monitoring induced intervention with success.

The therapeutic concept of ION is based on the assumption of reversibility, where a return of the response is indicative of a reduction or reversal of the degree of iatrogenic injury. This assumption has been demonstrated many times in practice where ION changes were able to be fully reversed when the surgeon reacted after the alarm was raised. In our groups experience, stable MEPs indicate intact motor function in the monitored limb allowing us to proceed with surgery. An early reaction to MEP changes has usually allowed for the prevention of a permanent deficit, and an irreversible MEP loss predicted either a transient or permanent new motor deficit in all cases.

ION is not without its disadvantages: it can be expensive to do; there are, of course, problems, such as unobtainable or poorly reproducible responses. Trained manpower is needed and the individuals need to have a real interest in doing ION. When not practiced on a day-to-day basis the extra time for setting it up is often considered a nuisance. And there are, of course, low rates of false-negatives and false-positive outcomes. Despite the multiple cases with reversible EP responses, it was not easy to prove statistically significant benefits in some series. A recent review investigated the effect ION had on the outcome in 5706 pediatric scoliosis procedures monitored out of a total of 32,305 procedures using data from the US National Inpatient Sample (NIS) database. Neurological complications were noted in 0.9% of ION cases and 1.4% of cases without ION use; however, this difference was not statistically significant in a multivariate analysis [12]. It is important to note that the NIS database does not always catch the procedures where ION is used and using it for such analysis is misleading [13]. Despite its theoretical advantage, ION was not shown to be of benefit in anterior cervical discectomies in a retrospective analysis of over 140,000 cases [14]. Fehlings et al. [6] performed a meta-analysis of multimodal ION in spinal surgery and found it to be useful.

7 Value of intraoperative neurophysiological monitoring in today's world

The use of ION is now part of many surgical procedures in multiple surgical fields. It is now utilized in peripheral nervous system procedures, such as including the repair and lesion removal at the brachial plexus and peripheral nerves, the ability to monitor most of the cranial nerves in brain stem surgery and ENT procedures, the prevention of spinal cord and cortical damage during aortic surgery and carotid bifurcation surgery, ability to monitor the cranial nerves, the monitoring of the function of the cauda equina including bladder function and the monitoring for the proper placement of neuromodulation systems. It has also been used to monitor the superior laryngeal nerve in thyroid surgery as well as in the repair of neurodysplasia. In addition to SEPs, MEPs, and BAEPs, methodologies include the recording direct nerve to nerve recordings and the monitoring of nervous system reflex pathways. The combination of newer imaging tools such as functional mapping and tractography with ION has vastly improved the management of lesions located in or very close to eloquent brain areas. The imaging of fiber tracts in the white matter in combination with mapping and monitoring of motor tracts has made surgical interventions possible for many patients that would not have been touched before these modalities were available. A meta-analysis of 90 publications where a combination of stimulation driven mapping and electrophysiological monitoring was used during glioma compared with cases where they were not used in over 8000 patients demonstrated a significant reduction in severe neuro-deficits from 8.2%, with no stimulation driven mapping, down to 3.4%, with mapping, and an increase in percent of radiologically confirmed gloss total resection of up to 75% compared with only 58% in the nonmonitored group [15].

8 Conclusion on why we need intraoperative neurophysiological monitoring

ION has demonstrated its ability to reduce neurologic deficits. The combination of mapping and monitoring has not only made the surgeon feel safer, it also makes previously impossible operations possible via its ability to minimize side-effects and enable more difficult and more extensive resections. Intraoperative neurophysiology allows for maximizing of extent of resection in glioma surgeries which in turn contributes to the prolongation of survival for these patients.

9 A personal perspective on the development of intraoperative neurophysiological monitoring

This section does not aim to be a complete and comprehensive overview on the development of intraoperative monitoring covering all authors, all specialties, and all countries involved. However, it allows the development of an idea on how ION slowly developed in Japan, the United States, and Europe more or less in parallel. More comprehensive reviews of this history can be found in references [16,17].

9.1 An early period of evoked potential applications

When the concept of ION was developed in the 1970s, the recording of EPs was a relatively new method and the clinical usefulness was unclear. The first-time cerebral responses had been recorded in response to electrical stimulation of peripheral nerves occurred in 1947 [18], but at that time there was no technology that allowed multiple time locked signals to be averaged, which was eventually developed in the early 1950s. As time progressed the clinical utility of EPs started to evolve with visual EPs being used for the diagnosis of multiple sclerosis [19], BAEP for audiometry, and eventually for cerebellopontine angle (CPA) tumor. SEPs were initially used to evaluate spinal cord injury [20,21]. Early recordings of electrical activity from the *human spinal cord* were performed by anesthetists Ertekin [22] in Turkey and Shimoji et al. [23] in Japan. Looking at spinal cord physiology to detect injury was also done in man by Shimoji et al. [23], Kurokawa [24], in animals by Deecke and Tator [25] and others. We used epidural spinal and cortical EPs to monitor the extent of damage in acute, subacute, and chronic experimental spinal cord compression in the cat [26,27]. In an early publication on SEPs for diagnostic purposes in neurosurgery, Perot [20] concluded that "the technique of recording the SEP may prove valuable in monitoring the integrity of the spinal cord during operative manipulation." The concept of SEPs being used for monitoring during surgery had actually been proposed 1 year earlier.

9.2 From diagnostics to intraoperative neurophysiological monitoring

Progressing from the using SEPs as a diagnostic tool in spinal injury, both experimentally and for human trauma, it was not a giant leap to propose the use of SEPs to monitor spinal cord function during surgery. This significant innovation was proposed independently by American neurosurgeons Croft, Brodkey, and Nulsen [28] and Japanese orthopedic surgeons, Tamaki et al. in 1972 [29]. A few years later Tamaki's group published on the use of evoked spinal cord action potentials during surgery of spinal lesions [30].

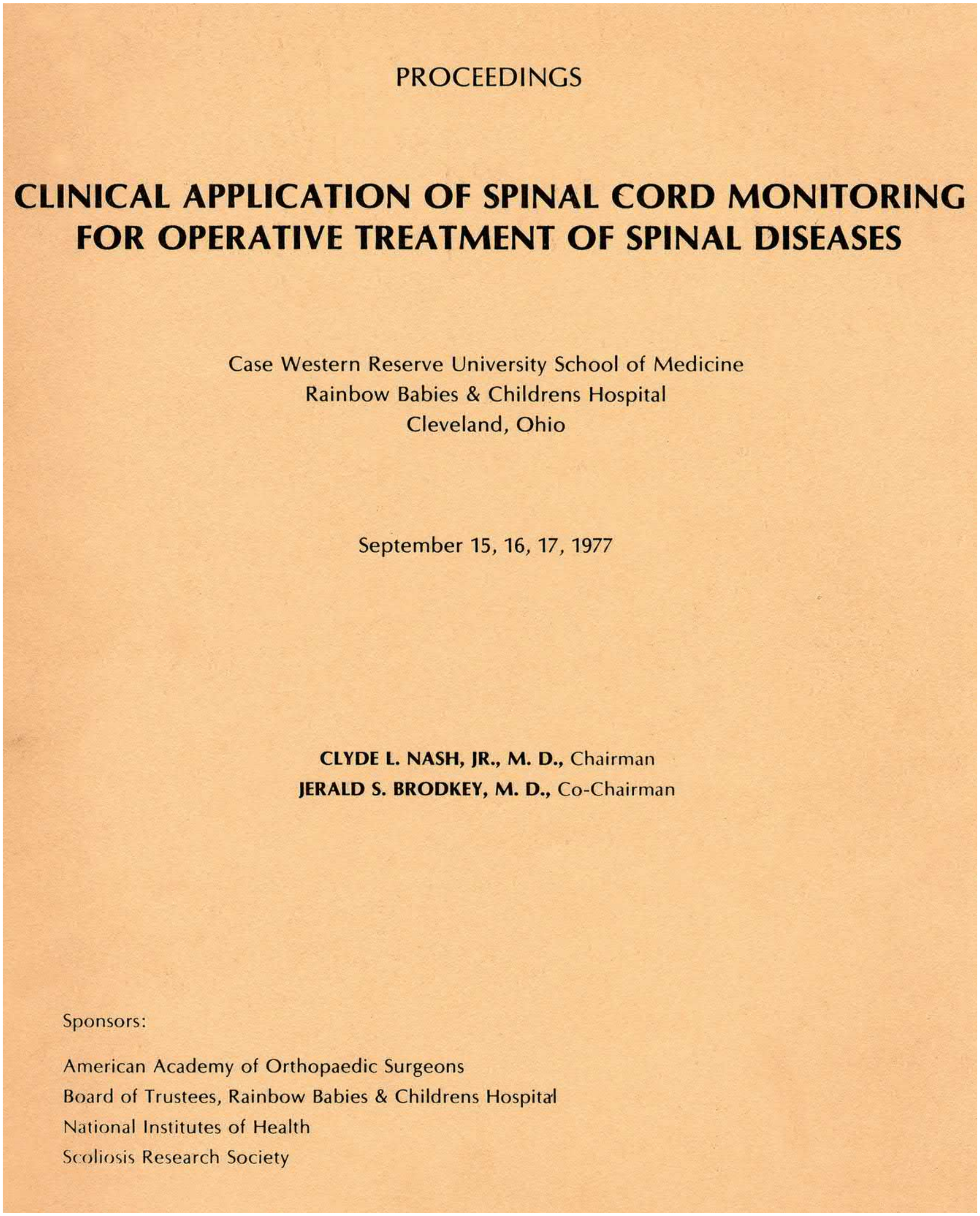
The first publication on intracranial monitoring was the use of BAEPs for the detection of hearing loss during acoustic neuroma surgery [31]. One year later, Delgado et al. published a technique that used direct VIIth stimulation and recording responses from the innervated facial muscles to "improve the identification and facilitate the dissection of the facial nerve" [32].

It is remarkable that the early work leading to ION was independently developed in several countries and by very different specialties including anesthetists, orthopedic surgeons, neurosurgeons, otologic surgeons, and neurophysiologists.

The first intraoperative use of spinal cord monitoring was published by Nash et al. in Cleveland [33] and Tamaki et al. in Japan [30,34] who were very much concerned about the incidence of paraplegia occurring during the correction of scoliosis deformities in young children. The first workshop on the "Clinical Application of Spinal Cord Monitoring for Operative Treatment of Spinal Diseases" was organized at Case Western Reserve University. That workshop took place in September 1977 and was cochaired by an orthopedic surgeon, Clyde Nash, and a neurosurgeon, Jerald S. Brodkey [35]. The proceedings from that meeting are depicted in Fig. 1. Institutional sponsors included the American Academy of Orthopedic Surgeons, the National Institutes of Health, and the Scoliosis Research Society. A second meeting organized by Richard Brown (a neurophysiologist who built one of the first dedicated ION systems) and Clyde Nash (an orthopedic surgeon) followed 1979 in St. Louis (Fig. 2).

Soon after a number of ION series followed: Engler et al. on the use of ION during Harrington instrumentation for the treatment of scoliosis [36]; Macon et al. on EP use during spinal surgery [37]; Allen et al. on the use of ION under anesthesia [38]; and Raudzens on ION [39]. The epidural recording technique pioneered by Shimoji et al. [23] was used by British orthopedic surgeons for spinal cord monitoring during scoliosis as early as 1983 [40]. The first book devoted to spinal cord monitoring came from Japan and was based the lectures given during the proceedings of the first International Spinal Cord Monitoring Symposium (Fig. 3). The editors were the physiologist from S. Homma from Chiba, Japan, and the orthopedic surgeon T. Tamaki from Toyama, Japan. Coeditors included K. Shimoji, an anesthesiologist, and T. Kurokawa, an orthopedic surgeon. That book was published in 1984 [41].

At that time monitoring equipment was not commercially available; many of the initial recording apparatus were large and not easy to move and frequently designed with valve (vacuum tube) operated amplifiers. The ability to store the data was poor and even worse was the artifact rejection capabilities. These pioneers deserve a lot of credit for their perseverance.



PROCEEDINGS

CLINICAL APPLICATION OF SPINAL CORD MONITORING FOR OPERATIVE TREATMENT OF SPINAL DISEASES

Case Western Reserve University School of Medicine
Rainbow Babies & Childrens Hospital
Cleveland, Ohio

September 15, 16, 17, 1977

CLYDE L. NASH, JR., M. D., Chairman
JERALD S. BRODKEY, M. D., Co-Chairman

Sponsors:

American Academy of Orthopaedic Surgeons
Board of Trustees, Rainbow Babies & Childrens Hospital
National Institutes of Health
Scoliosis Research Society

FIGURE 1 Title page of the proceedings of the first ever meeting devoted to the clinical application of spinal cord monitoring in 1977 in Cleveland, OH, United States. *(Used with permission from Case Western Reserve University School of Medicine).*

FIGURE 2 Participants of the second Spinal Cord Monitoring Workshop, 1979, St. Louis, MO, United States. First row from left: Brown, Nash. Second row from left: Young, third Schramm. Third row from right: Tamaki, Cracco.

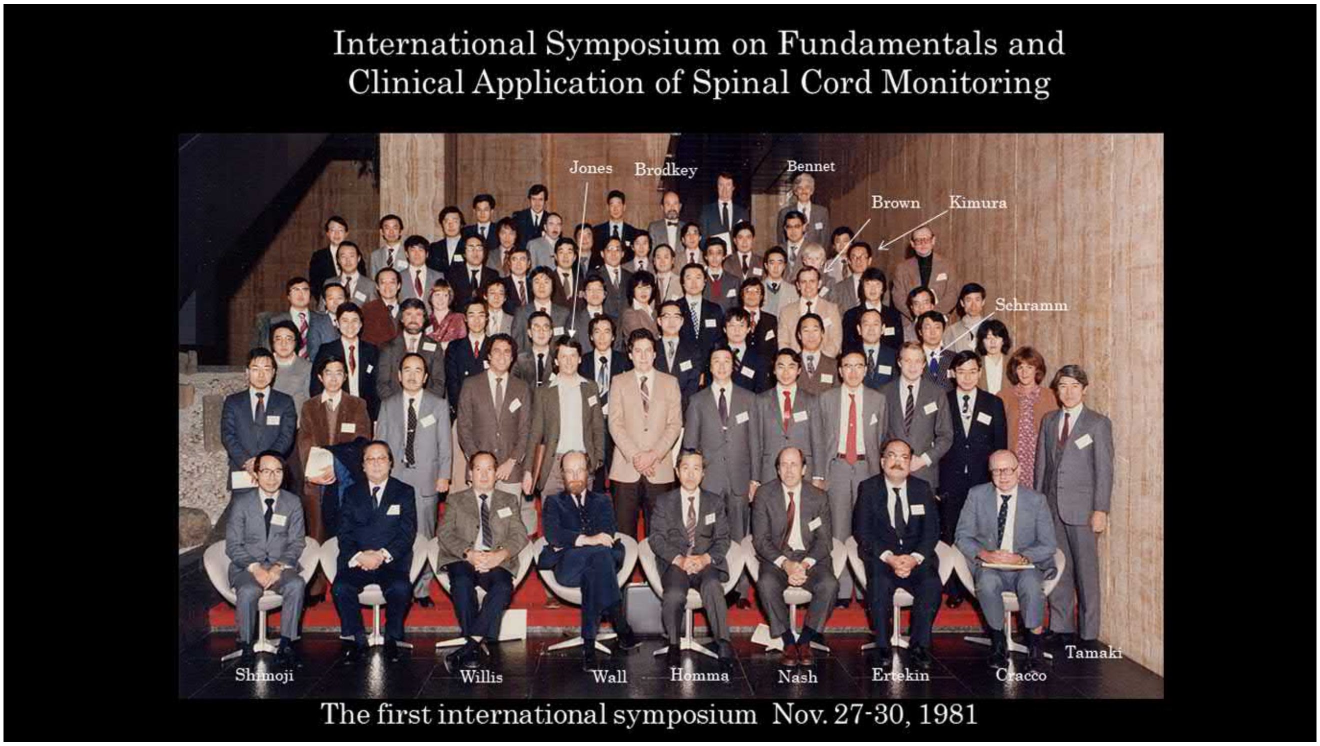


FIGURE 3 Participants of the first International Symposium on Spinal Cord Monitoring 1981, in Tokyo, Japan.

The practitioners involved in the early days of ION came from a diverse set of specialties including neurophysiologists, anesthetists, orthopedic surgeons, neurosurgeons, and to a lesser extent neurologist. Frequently the driving force was a combination of a neurophysiologist (MD or PhD) with a clinician. Over time as more reliable and sophisticated monitoring equipment became commercially available the majority of ION is performed by technicians who are now supervised by physicians, which is the standard practice in many countries. In the United States, commercial ION companies were created to offer ION to hospitals and surgeons who may not have the resources or number of procedures justifying an in-house program.

9.3 *Further clinical development*

Once ION established a presence in the operating room, and the first publications demonstrated its benefit, the next step was to establish technical standards of for the practice of ION. In addition, a standard criterion for determining abnormality and rules for intervention based on these criteria were necessary. This included a combination of imaging, data storage, definitions of waveform abnormalities, understanding the normal variability of EPs, and at what point is intervention necessary as well as defining best practices for the practice of ION.

Equipment standards were also needed. These included the best electrode for a particular modality or stimulation versus recording, what are the best electrode position to optimize the recordings, where to stimulate and what are the best stimulation parameters, how best to set-up the amplifier and filters to get the best recordings in the fastest time, whether to use bipolar or referential recording montages, and the effects of anesthetic agents and other physiologic parameters. It was soon discovered, for example, that the stimulation rate should not be a multiple of the line frequency (50 or 60 Hz). There was no formalized decision-making process, but over time studies were published and discussions at meetings started to formalize the practice of ION, although it is important to note that it took a lot of time for societal formal publications to define standards [42−44].

Parallel to that a number of new phenomena were observed. It was discovered that the position of the body, loss of CSF, level of blood pressure, and other technical factors could influence the recordings. One way to define a "significant" change was, for example, recording a BAEP in anesthetized patients who did not have a cranial pathology or were not being operated on for a cranial intervention, and compare these recordings to those from patients who did have an auditory pathway pathology such as during a CPA tumor. Another method was to compare the response between the side ipsilateral to the tumor and the side contralateral to the tumor. One example of how comparing the normal and abnormal side was beneficial for patient's being operated on for procedures that were nonbrain stem related it was discovered latencies changes of waves I and V were more likely. Particularly was the fact that the wave V latency increased more on the ipsilateral side to the tumor.

Of particular interest was the definition of so-called warning criteria, which are based on decrements of amplitude loss and/or increases in latency. Several proposals were made regarding amplitude, for example, a loss of 40% [45], of more than 50%, or of over 60%, sometimes including the number of repeatable responses and the time course of the change (summarized in Ref. [16]). It also became clear that all responses needed to referenced to one that was obtained after induction of anesthesia but before the beginning of "manipulation." In this way the influence of the anesthetic drugs on the interpretation of the defined "alarm" criteria was reduced. It is also evident that warning criteria vary for different monitoring modalities.

Other waveform parameters and stimulation paradigms such as interpeak latencies, effects of paired pulse or train stimuli, area under the curve, conduction velocity, and spectral analysis were investigated in relation to their ability to predict injury.

Most of these methods were too cumbersome and unprecise and were given up. It all came down to a very simple rule. The potential was unchanged, a persistent deficit was unlikely, or the potential was lost permanently, a deficit was likely or pretty sure. An amplitude reduction of over 50% for SEPs remains a concern.

On the technical side a number of improvements happened. Commercial equipment was now available, dedicated for the purpose of intraoperative monitoring, including automatic artifact suppression. The ideal filter settings were determined and the ideal electrode positions on the head were defined. Recorded EPs could now easily be stored digitally and automated peak detection and amplitude measurements could be defined. Digitalization of the recording and amplifier design led to more user-friendly monitoring equipment. It was now easy to obtain recordings from multiple channels simultaneously and store hundreds of responses for later analysis.

9.4 *The problem of motor-evoked potentials monitoring*

For many years MEPs were not available for recording under general anesthesia. It became clear that SEP monitoring could not reliably predict whether motor deficits were likely to occur or not. The classification of *motor* deficits as false-negative in cases where only *somatosensory* EPs were monitored is a misnomer. In fact, a false-negative should only be defined in relation to the modality monitored, for example, if motor tract