

## Review Article

# 척수종양수술에서의 수술중 신경계 감시

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## Intraoperative neurophysiological monitoring in spinal cord tumor surgery

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### ABSTRACT

Once a spinal cord tumor (SCT) is detected, it is usually removed surgically. During this process, intraoperative neurophysiological monitoring (IONM) is widely performed to detect neural insults of the spinal cord early and prevent neurological complications after surgery. This review article introduces the basic concepts and setting of the major modalities, somatosensory evoked potentials, motor evoked potentials, and direct wave and discusses the precautions, alarm criteria, and reliability associated with IONM during SCT surgery. This review emphasizes that multimodal monitoring improves the reliability of the IONM and that it is important that an experienced professional examiner continuously monitor these surgeries.

**Keywords:** evoked potentials; intraoperative neurophysiological monitoring; spinal cord neoplasms

### Introduction

Patients with spinal cord tumors (SCTs) suffer from various neurological symptoms, such as sensory deficit, weakness, spasticity, neurogenic bladder and bowel, or neuropathic pain. Once the SCTs are diagnosed using imaging modalities, the usual treatment of choice is surgical removal. Depending on the degree of invasion of the axial anatomy, SCTs are classified as intramedullary (IM), intradural extramedullary (IDEM), or extradural (ED) tumors. Intraoperative neurophysiological monitoring (IONM) is being widely used in surgical removal of SCTs to detect the evidence of iatrogenic neural insult or ischemic injury during surgical procedures early and prevent postoperative neurological deterioration. There have been numerous IONM studies regarding IM tumors because IM tumors invade the spinal cord directly and greatly. In recent years,

IONM studies on IDEM tumors have also been conducted. This article focuses on the IONM setting and current consensus on alarm criteria, reliability, and interpretations of IONM in surgical removal of SCT.

The motor and somatosensory tracts are the main targets of IONM during surgical removal of SCT. The electrophysiological status of the ascending somatosensory pathway is examined via continuous monitoring of somatosensory evoked potentials (SEPs). The corticospinal tract is examined using transcranial electrical stimulation-motor evoked potentials (TES-MEPs) or direct waves (D-waves). The design of IONM depends on the lesion site and symptoms of the patient, and simultaneous monitoring of bilateral sides is recommended for MEPs and SEPs. This paper does not address the IONM technique in surgery for lumbosacral tumor related to spinal dysraphism caused by congenital malformations.

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## Body

### 1. Somatosensory evoked potentials

In theory, SEPs can be obtained by stimulating almost all peripheral sensory nerves. However, bilateral median or ulnar SEPs for the upper extremities and bilateral tibial or peroneal SEPs for the lower extremities are used in most cases. Bilateral median or ulnar SEPs are obtained by stimulating bilateral wrists and recorded with following hemispheric montages: C3'-Fz (right median or ulnar nerve); C4'-Fz (left median or ulnar nerve). Bilateral peroneal or tibial SEPs are obtained by stimulating bilateral ankles and recorded with a midline montage of Cz'-FPz' (Cz', right and left tibial or peroneal nerve; reference, FPz') according to the international 10-20 electroencephalography system. Stimulation intensities are usually around 10-20 mA but depend on the patient's neural condition. Unlike MEPs, SEPs do not elicit patient's truncal movement; therefore, continuous acquisition of SEP waves is possible at regular intervals. Compared to MEPs, SEPs are hardly affected by the muscle relaxant used during intubation, and a meaningful waveform can be obtained even before the muscle relaxant effect disappears. After confirming the baseline waveform, sequentially obtained waveforms are compared to that acquired at baseline in terms of amplitude, latency, and morphology. The consensus for alarm criteria has been established for decades. The most critical and definite alarm criterion is the sudden disappearance of the waveform, which could be evidence of neural transection. In addition to this criterion, the other current alarm criterion is as follows: latency prolongation > 10% or amplitude reduction > 50%, compared to the baseline values. If this alarm criterion is exceeded, the postoperative prognosis is likely to be poor; therefore, if deterioration of SEPs is observed near the alarm level during surgery, it is recommended to inform the surgeon and anesthesiologist of this situation and to look at the surgical site in advance. Moreover, IONM professionals should always be alert to confirm the cause of the electrophysiological changes and differentiate them from the possible various artifacts or technical errors.

For example, if the latency of SEPs is continuously delayed from the beginning of the surgery and exceeds 10% of the baseline value, it may be because the surgical site has been exposed to cold conditions for a long time or because the blood pressure is constantly decreasing for certain reasons. In this case, IONM professionals should communicate with the anesthesiologist to check the patient's body temperature or blood pressure. If hypothermia or hypotension is confirmed, correction of the condition can result in return of the SEP parameters to their baseline values in some cases. Multimodal monitoring with combination of MEPs and D waves has been recommended in SCT surgery for favorable long-term outcomes [1-3]. The sensitivity and specificity of the test used to predict postoperative motor deterioration in SCT surgery are known to be lower in SEPs than in MEPs [4-6]. According to a meta-analysis of eight studies on intramedullary SCT (IMSCT) surgery, the pooled sensitivity of SEPs was 85% (range, 70-95; 95% CI, 75-91) and specificity was 72% (range, 61-96; 95% CI, 57-83) [7]. Although SEPs do not directly reflect the neurophysiological function of the corticospinal tract, SEPs are monitored to enhance the specificity of IONM in combination with MEPs [4]. Moreover, there have been reports of cases in which postoperative motor deterioration was observed, even though only SEP was significantly changed without MEP change [4,8,9].

SEP mapping is sometimes used to find midline of the spinal cord to reduce the possible neural insult during myelotomy in IMSCT surgery [10].

### 2. Motor evoked potentials

MEPs can be obtained in several ways, such as through transcranial electrical stimulation (TES), epidural stimulation, and subcortical stimulation. However, TES-MEPs are usually used in SCT removal surgeries where craniotomy is not required.

#### 1) Transcranial electrical stimulation-Motor evoked potentials

TES-MEPs can be obtained from any muscle in the extremities. It is recommended that TES-MEPs be recorded in at least two muscles within one extremity

for precise monitoring. Identifying differences in MEP responses of different muscles within one extremity helps to discriminate artifacts during monitoring. In the case of a patient suspected of postoperative motor deterioration of the right lower limb after surgery, it is recommended to monitor MEPs of two or more muscles of the right lower limb and compare them with those of the left side. Train stimuli consisting of 5-7 square-wave stimuli with a 1-4 ms interstimulus interval are used rather than a single stimulus because of the muscle MEP's build-up effect [2,11]. For stimulation, the interhemispheric montage of C1/C2 or C3/C4 is commonly used so that simultaneous bilateral stimulation is possible. Unlike SEPs, MEP waves are not obtained by averaging, so that the responses may appear slightly different for each stimulus. Particularly, in patients whose baseline MEP amplitude is not large, even a small change can affect the reliability of the examination; therefore, these characteristics should be carefully considered and tested with a real-time interpretation by a skilled IONM professional. The absolute alarm criterion for persistent PMD in IMSCT surgery is still the presence/absence criterion [1,12]. The loss of muscle MEPs indicates postoperative motor impairment with a specificity of approximately 90% during IMSCT [13]. The current consensus for MEP alarm criterion in SCT surgery is  $> 80\%$  amplitude reduction compared to the baseline value. A less conservative standard is used in brain surgery, where 50% reduction is considered the alarm level, but some institutions set it to 50%-70% or more than 80% in spinal surgery [14]. Unlike that of SEP, latency is not included in the alarm criterion for MEP. During MEP monitoring, examiners should be aware of the effects of muscle relaxants. Even in the case of total intravenous anesthesia, the baseline wave must be acquired by considering the half-life and dose of the muscle relaxant used for safe and easy intubation. For example, if the baseline values are smaller than the original value taken while the muscle relaxant effect remains, it can be interpreted as a false negative even if a serious neural insult occurs during surgery. The pooled sensitivity of MEPs was 90% (range, 75-99; 95% CI, 84-94) and specificity was 82% (range,

27-97; 95% CI, 70-90) according to a meta-analysis of 13 previous studies on IMSCT [7]. Other than amplitude reduction, threshold elevation is considered as another sensitive early warning sign. Empirical alarm consensus has been set at  $\geq 100$ -V threshold elevation for spinal cord monitoring [15]. This means that the need to increase the stimulation intensity to obtain a amplitude similar to that of the previous waveform suggests neural insult. If the waveform is not obtained even with an elevated simulation intensity of  $\geq 100$  V, postoperative motor weakness is expected. The increase in stimulation intensity can only be noticed by an examiner who continuously monitors the surgery. Depending on the examiner, if the amplitude of an MEP is reduced or the threshold intensity increases, not only the simulation intensity but also the duration of stimulus or the number of trains can be modulated to obtain the waveform appropriately.

In addition to unexpected outcomes such as false negative/positive outcomes, adverse effects have been reported for TES-MEPs, and there have been safety concerns regarding the risk of inducing seizures by TES. However, the occurrence rate is very low (5 out of 15,000 cases) and the reported duration of seizure is very brief, within few seconds [16]. There are also the non-neurological adverse effects, such as bite injury resulting in tongue/lip laceration or tooth breakage, which can be prevented by using soft bite blocks [16,17]. Hair loss or minor scalp burns around the stimulation site have been also rarely reported [17].

## 2) Direct wave

D-waves are generated by direct activation of the corticospinal tract from the primary motor cortex. Unlike muscle MEPs, D-waves are recorded at the spinal cord by placing a recording electrode in the epidural or subdural space. The response of the TES is recorded in the muscle through synapses of the vertically oriented excitatory interneurons in muscle MEPs, whereas the D-wave directly reflects the activation of the motor neuron axon, so it is relatively less affected by anesthetics with muscle relaxation effect. Thus, unlike muscle MEPs, it is useful to obtain semi-quantitative data on the functional integrity of the

corticospinal tract [3]. A wire-type recording electrode with two metal wrappings 1.5–2 cm apart from each other at the end is used for recording. In general, the recording electrode is placed at the planned spinal level, usually 2–4 levels below the lowest level of SCT, in an aseptic manner by a surgeon. The recording electrode itself cannot specify the left-right direction of the recording, and as the interhemispheric montage (C1–C2 or C3–C4) is used to obtain muscle MEPs, differential recording from the left or right corticospinal tract is not possible. Below the T10 bony level, the corticospinal fiber is not sufficient; therefore, it is not a recommended location for obtaining sufficient waveforms of D-waves. D-waves are elicited by a single pulse stimulus, whereas muscle MEPs are obtained by train stimuli. Unlike muscle MEPs, D-waves have the advantage of relatively continuous monitoring without eliciting the patient's movement, because it can obtain a stable waveform with a single pulse stimulus of small intensity. In IMSCT surgery, > 50% reduction in the amplitude of a D-wave is considered a significant change. D-waves are helpful in predicting the postoperative prognosis accurately, especially when muscle MEPs have deteriorated. When there is amplitude reduction or threshold increment of muscle MEPs with D-wave amplitude reduction less than 50%, it is suggested to transiently move surgical manipulation to a different area, make warm irrigation or correct hypotension, and the postoperative motor deficit is not predicted. When the muscle MEPs are lost with D-wave amplitude reduction less than 50%, transient motor deficit is predicted, so that it is recommended to stop surgery transiently and/or improve spinal cord blood flow through the local irrigation with papaverine. Nevertheless, if the muscle MEPs do not reappear, it is recommended to abandon surgery in selective cases. When muscle MEPs were lost with significant D-wave changes, it is recommended to stop surgery immediately since the permanent motor deficit is predicted. If the D-wave does not recover, abandonment of surgery is recommended [3].

The preserved D-wave is predictive of a favorable motor outcome even when MEPs or SEPs are lost during IDEM tumor resection. D-waves demonstrated

a higher sensitivity (100%) than muscle MEPs (62.5%) or SEPs (37.5%) in IDEM tumors [1].

Although D-wave monitoring is limited because of lack of approval regarding use of epidural recording electrodes and lack of approved cost codes in Korea, it is a necessary modality for precise neurophysiological monitoring.

### 3. Free running electromyography

The usefulness of free running electromyography (fEMG) is mostly studied in brain surgery that can invade the facial nerves, but there are few studies in spinal cord or spinal surgery than expected. Spikes, bursts, neurotonics, or trains are regarded as relevant fEMG activities reflecting the neural injury. Skinner et al. has suggested fEMG as a useful modality to detect early motor tract invasion in IMSCT surgery [18]. A recent study supported that fEMG precedes the MEP deterioration during SCT surgery [19]. They also reported on the reliability of fEMG (sensitivity, 87.5%; specificity 83.3%) and suggested the warning criteria as follows: 1) Irregular aperiodic electromyographic bursts were repeatedly elicited by similar surgical maneuvers within the tumor bed; 2) Prolonged (> 3 s), focal, semirhythmic tonic discharges occurred with or without an obvious surgical event; 3) An active electromyographic signal in one or more limbs became acutely silent. However, these are based on only 14 cases, so that it is difficult to say that the academic consensus has been reached on the warning criteria [18].

## Conclusion

During spinal cord removal surgery, multimodal IONM is recommended to prevent postoperative neurological complications. SEPs basically represent the electrophysiological state of the somatosensory tract, but when monitored with MEPs, the specificity of IONM in predicting the postoperative motor outcome is increased. Since intraoperative MEPs are obtained through TES, possible adverse effects should be considered. Concurrent monitoring of D-waves while monitoring muscle MEPs increases the specificity of the

electrophysiological test of the motor tract. Thus, approval of the D-wave recording electrode is required in Korea, and the National Health Insurance system should cover D-wave monitoring as soon as possible. Above all, for accurate interpretation of the results, continuous monitoring by an experienced IONM professional is needed, and active communications with surgeons and anesthesiologists should follow.

## Ethical approval

This article does not require IRB/IACUC approval because there are no human animal participants.

## Conflicts of interests

No potential conflict of interest relevant to this article was reported.

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