

## 척수 종양 제거 술 중 운동유발전위의 호전과 근력 호전의 관계

표소은, 박윤길, 박진영, 고유정

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### Increased Intraoperative Motor Evoked Potentials and Motor Recovery after Spinal Cord Tumor Removal

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**Objective:** To evaluate whether the increase of the amplitude of motor evoked potentials (MEPs) during surgery can imply favorable prognosis postoperatively in spinal cord tumor surgery.

**Method:** MEPs were monitored in patients who underwent spinal cord tumor surgery between March 2016 and March 2018. Amplitude changes at the end of monitoring compared to the baselines in limb muscle were analyzed. Minimum and maximum changes were set to  $MEP_{min}$  (%) and  $MEP_{max}$  (%). Strengths of bilateral 10 key muscles which were documented a day before ( $Motor_{pre}$ ), 48 h ( $Motor_{48h}$ ) and 4 weeks ( $Motor_{4wk}$ ) after the surgery were reviewed.

**Results:** Difference of  $Motor_{48h}$  from  $Motor_{pre}$  ( $Motor_{48h-pre}$ ) and  $Motor_{4wk}$  from  $Motor_{pre}$  ( $Motor_{4wk-pre}$ ) positively correlated with  $MEP_{min}$ , suggesting that smaller the difference of MEPs amplitude, less recovery of muscle strength. There was a negative correlation between the amount of bleeding and  $MEP_{min}$ , indicating that the greater the amount of bleeding, the smaller the  $MEP_{min}$ , implying that MEPs amplitude is less likely to improve when the amount of bleeding is large. It also showed significant difference between patients with improved or no change of motor status and patients with motor deterioration after surgery according to anatomical tumor types.

**Conclusion:** Improve of muscle strength was less when the increase of MEPs amplitude was small, and improvement of MEPs amplitude was less when the amount of bleeding was large. Correlation between changes of status of muscle strength after surgery and tumor types was observed. With amplitude increase in MEPs monitoring, restoration of muscle strength can be expected.

**Key Words:** intraoperative neurophysiological monitoring, motor evoked potentials, postoperative complications, spinal cord neoplasm

## Introduction

Recently, improvements in surgical techniques have enabled more aggressive tumor resections. However, even among the most skilled surgeons, the risk of

Received September 24, 2018

Accepted October 22, 2018

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postoperative neurological deterioration is considered high in spine surgery. Intraoperative neurophysiological monitoring (IONM) is a commonly used technique for assessing the nervous system during spinal or brain surgery. It can provide real-time feedback of critical neurological pathways to the surgeon.<sup>1</sup> Somatosensory evoked potentials (SEPs) are the most widely available and commonly used monitoring modality in spine surgery.<sup>2</sup> For many years, only SEPs were monitored during spinal or brain procedures.<sup>3</sup> However, many studies have suggested that SEPs do not reflect the specificity of motor pathways, as there are several so-called false-negative results, i.e., emergence of postoperative motor deficits despite unchanged intraoperative SEPs.<sup>4,5</sup> In addition, SEP deterioration can occur in numerous situations such as dorsal column injury, stimulus failure, and distal conduction block, which may result in amplitude reduction below an arbitrary 50% and can falsely imply motor injury.<sup>6</sup>

To date, muscle motor evoked potentials (MEPs) are also monitored. Many spinal and brain surgeons now use MEP monitoring for their surgery, as it better predicts good postoperative motor outcomes than the use of SEPs alone.<sup>7-10</sup> In addition to this predictive power, MEP data recording benefits from a high temporal resolution; the data may be updated on the order of seconds, providing the surgeon with “real-time” information about possible surgical trauma.

The consensus about the alarm criteria of MEPs and SEPs has been evolving to continuously predict poor functional prognosis after surgery.<sup>8,11</sup> In recent criteria, significant changes of SEPs include amplitude decrease > 50% or increases in latency of > 10% from baseline.<sup>1,5</sup> Modest (> 50%) amplitude reduction of MEPs represents a major warning criterion for spinal cord, brain, brainstem, and facial nerve monitoring, if justified by sufficient preceding stability.<sup>8</sup> Similarly, many reports have focused on the correlation between MEP and SEP deterioration and postoperative motor deficits.

However, many physicians are interested in the degree of postoperative functional improvement. In cases

of spinal cord tumors, motor impairment is frequently observed before tumor removal. An improvement in the motor status can be expected after tumor removal surgery, as it may eliminate the mass effect of the tumor that has been pressing the spinal cord.<sup>12-14</sup> In addition, if the MEP amplitude is related to motor improvement, it may be possible to deduce whether tumor removal is performing properly through intraoperative monitoring. Yet, there has been no study on predicting functional improvement by monitoring MEPs. Therefore, this study aimed to determine whether the change (including increase) in the amplitude of MEPs can imply a favorable prognosis after spinal cord tumor surgery.

## Materials and Methods

### 1) Subjects

This was a retrospective short-term study conducted between March 2016 and March 2018 at a single institution. IONM was performed in 115 patients with a spinal cord tumor, and spinal surgeons performed tumor removal surgery. Patients whose motor status cannot be evaluated because of follow-up loss were excluded. Patients with other neurological deficits and medical diseases such as stroke, radiculopathies, neuropathies, or severe cardiopulmonary disease that may affect the motor status were also excluded. After excluding 42 patients, the medical data of 73 patients were analyzed. We analyzed the patient data, including IOM records, medical records, operative narratives including bleeding amount, anesthesia records, and outpatient clinical records. We classified the patients according to the anatomical or pathologic type of the spinal cord tumor.

At 48 h after surgery, improvement in motor function was observed in 17 patients and deterioration was observed in 21 patients. There was no change in motor function in 36 patients. At 4 weeks after surgery, improvement in motor function was observed in 25 patients and deterioration was observed in 12 patients, compared with the motor function before surgery. Table 1 lists the baseline characteristics of the patients.

**Table 1.** Baseline Demographic and Clinical Characteristics of Patients

Characteristic	Total (n = 73)	Group A (n = 52)	Group B (n = 21)	p-value
Age (yr)	51.3 (12~77)	51.4 (12~77)	51.0 (24~71)	0.455
Sex				0.181
Female	26 (35.6)	21 (40.4)	5 (23.8)	
Male	47 (64.4)	31 (59.6)	16 (76.2)	
Bleeding	730.0 (50~3050)	625.8 (50~3050)	988.1 (150~3000)	0.020
Anatomical type				0.017
IM	16 (21.9)	7 (13.5)	9 (42.9)	
IDEM	42 (57.5)	32 (61.5)	10 (47.6)	
ED	15 (20.5)	13 (25.0)	2 (9.5)	
Pathologic type				
Schwannoma	32 (43.8)	25 (48.1)	7 (33.3)	
Meningioma	18 (24.7)	13 (25.0)	5 (23.8)	
Ependymoma	8 (11.0)	3 (5.8)	5 (23.8)	
Hemangioblastoma	4 (5.5)	1 (1.9)	3 (14.3)	
Other	11 (15.1)	10 (19.2)	1 (4.8)	

Values are presented as mean (range) or number (%)

IM: intramedullary, IDEM: intradural extramedullary, ED: extradural

## 2) Anesthesia

Rocuronium bromide (Esmeron 50~150 mg; Han Wha Pharma Co. Ltd., Seoul, Korea) was administered intravenously as a short-acting muscle relaxant to facilitate endotracheal intubation. No paralytic agents were subsequently administered.

General anesthesia was induced through total intravenous administration. Remifentanyl (Ultian; Han Lim Pharma Co. Ltd., Seoul, Korea), propofol (Fresofol; Fresenius Kabi, Seoul, Korea), and midazolam (Vascam; Hana Pharm, Seoul, Korea) were used in several combinations to initiate and maintain general anesthesia. During anesthesia, body temperature, direct radial artery pressure, pulse rate, oxygen saturation, and end-tidal carbon dioxide concentration were continuously monitored. All patients were kept normothermic and normotensive.

## 3) IONM techniques

Two technicians performed IONM using Cascade (Cadwell Industries Inc., Kennewick, WA, USA) and MEE-2000 (Nihon Kohden, Tokyo, Japan). Among 73 patients, upper-extremity MEPs were monitored in 38 patients and lower-extremity MEPs were monitored in 73 patients.

We obtained MEPs through multipulse transcranial

electric stimulations with the Cascade electrical stimulator (Cadwell Industries Inc.) and MEE-2000 (Nihon Kohden). We recorded transcranial electric MEPs bilaterally from the deltoid and abductor pollicis brevis muscles in the upper extremities and from the tibialis anterior and abductor hallucis muscles in the lower extremities, using a pair of needle electrodes inserted 3-cm apart in each muscle. Needle electrodes delivered short trains of 6 square-wave stimuli of 0.05-ms duration, with an interstimulus interval of 3 ms. The needles delivered up to 2 Hz of repetition rate and were placed at C1 and C2, according to the 10~20 International Electroencephalography System. We gradually increased the intensity of the stimulus by 50-mV increments (from 200 mV to a maximum of 450 mV) until the MEP amplitudes were maximized above a minimum of 10 mV.

The peak-to-peak amplitude differences of the MEPs of each muscle (bilateral deltoid, abductor pollicis brevis, tibialis anterior, and abductor hallucis) were reviewed. The amplitude at the end of monitoring were analyzed and compared with the baseline values for each muscle and calculated as a percentage value. Among these changes of MEP amplitudes of each muscle, the minimum and maximum values were set to MEP<sub>min</sub> (%) and MEP<sub>max</sub> (%).

#### 4) Neurologic examination

The strengths (bilateral) of 10 key muscles of the International Standards for Neurological Classification of Spinal Cord Injury, assessed using the manual muscle test in each patient, before surgery ( $Motor_{pre}$ ), 48 h after surgery ( $Motor_{48h}$ ), and 4 weeks later ( $Motor_{4wk}$ ) were documented. We evaluated muscle strength using the Medical Research Council (MRC) scale, with a range of 0 to 5. The total score ranged from 0 to 50 points on each side. We considered any motor change of a score of 1 point or more, compared with the preoperative value, as “postoperative neurologic motor deterioration” or “postoperative neurologic motor improvement.”

#### 5) Statistical analysis

We conducted statistical analyses to reveal the correlations between intraoperative changes of MEP amplitudes and motor status (intact, motor deterioration, and motor improvement).

According to the characteristics of the variables, we used either an independent-samples t-test or chi-square test to determine significant differences between the postoperative motor intact or improved group and the motor deficit group in terms of sex, age, and bleeding amount. Pearson correlation analysis was used to determine the correlation between  $Motor_{pre}$ ,  $Motor_{48h}$ ,  $Motor_{4wk}$ ,  $MEP_{min}$ ,  $MEP_{max}$ , and bleeding amount. We analyzed the data using SPSS ver. 20.1 (IBM, Armonk, NY, USA), with p-values < 0.05 considered statistically significant.

## Results

#### 1) Baseline characteristics of the patients

We enrolled 73 patients with spinal cord tumor in this study. Of them, 21 patients showed motor deterioration, 25 showed motor improvement, and 27 showed no motor change postoperatively.

Table 1 shows the baseline demographic and clinical characteristics of the study population. There were 26

male patients (35.6%) and 47 female patients (64.4%). The mean patient age was 51.3 years.

We divided the patients into two groups, those who had neurologically improved or had no change postoperatively (group A) and those who had postoperative motor deteriorations (group B). There were no statistically significant differences in terms of age and sex. The bleeding amount was also compared between group A and group B, and a significant correlation was observed ( $p = 0.020$ ).

Table 2 shows variables related with motor outcomes of group A and B. Mean  $MEP_{min}$  was  $-9.7$  ( $-94.2 \sim 115.31$ ) in group A and  $-30.5$  ( $-99.2 \sim 41.7$ ) in group B. And  $MEP_{max}$  was  $371.6$  ( $24.6 \sim 1888.3$ ) and  $334.5$  ( $-35.9 \sim 1375.2$ ) in group A and B, respectively. The summation of MRC grade of 10 key muscles before the surgery was  $93.73$  ( $70 \sim 100$ ) in group A and  $88.90$  ( $70 \sim 100$ ) in group B, and 48 h after the surgery was  $95.94$  ( $78 \sim 100$ ) and  $79.85$  ( $60 \sim 99$ ) and 4 wk after the surgery was  $97.17$  ( $85 \sim 100$ ) and  $82.90$  ( $60 \sim 100$ ) in group A and group B, respectively.

We classified the types of tumors according to anatomy; there were 42 intradural extramedullary (IDEM) tumors, 16 intramedullary (IM) tumors, and 15 extradural (ED) tumors. There was a significant difference in the distribution according to tumor type between group A and B when analyzed by chi square test. Group A had 32 IDEM tumors (61.5%), 7 IM tumors (13.5%), 13 ED tumors (25.0%) and group B had 10 IDEM tumors (47.6%), 9 IM tumors (42.9%), 2 ED tumors (9.5%). We

**Table 2.** Values Related with Changes of Motor Evoked Potentials Amplitude and Motor Grades Improvement

	Group A (n = 52)	Group B (n = 21)
$MEP_{min}$	$-9.7$ ( $-94.2 \sim 115.31$ )	$-30.5$ ( $-99.2 \sim 41.7$ )
$MEP_{max}$	$371.6$ ( $24.6 \sim 1888.3$ )	$334.5$ ( $-35.9 \sim 1375.2$ )
MRC score		
Baseline	$93.7$ ( $70 \sim 100$ )	$88.9$ ( $70 \sim 100$ )
48 h	$95.9$ ( $78 \sim 100$ )	$79.9$ ( $60 \sim 99$ )
4 wk	$97.1$ ( $85 \sim 100$ )	$82.9$ ( $60 \sim 100$ )

Values are presented as mean (range)

$MEP_{min}$ : minimum change in the amplitude of motor evoked potentials,  $MEP_{max}$ : maximum change in the amplitude of motor evoked potentials, MRC score: Medical Research Council scale score

also categorized the patients according to pathology: there were 32 schwannomas, 18 meningiomas, 8 ependymomas, 4 hemangiomas, and 11 “others” (Table 1).

### 2) Postoperative motor improvements

The difference of Motor<sub>48h</sub> from Motor<sub>pre</sub> (Motor<sub>48h-pre</sub>) positively correlated with MEP<sub>min</sub> (r = 0.338 and p = 0.003) (Fig. 1, Table 3). Furthermore, the difference of Motor<sub>4wk</sub> from Motor<sub>pre</sub> (Motor<sub>4wk-pre</sub>) showed a positive correlation with MEP<sub>min</sub> (r = 0.247 and p = 0.035) (Fig. 2, Table 3). There was no significant correlation between

the difference in Motor<sub>48h-pre</sub> and MEP<sub>max</sub> (p = 0.679) or Motor<sub>4wk-pre</sub> and MEP<sub>max</sub> (p = 0.904) (Table 3).

### 3) Amount of bleeding

Among 73 patients, 52 had postoperative motor improvement or no motor change and 21 had motor deterioration. The amount of bleeding in each group was analyzed using an independent t-test, which showed a significant difference (p = 0.020). In addition, there was a negative correlation between the amount of bleeding and MEP<sub>min</sub> (r = -0.260 and p = 0.026) (Fig. 3, Table 3).

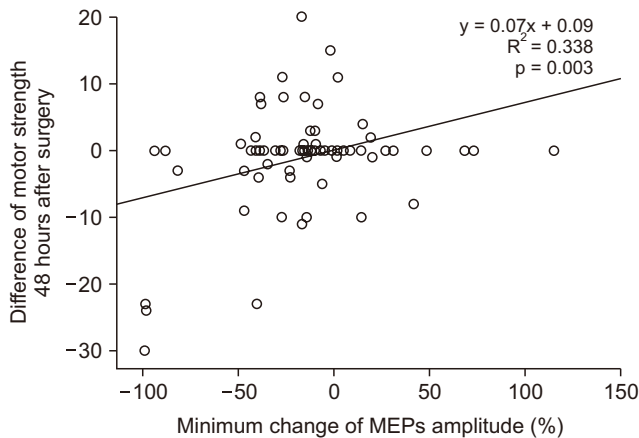


Fig. 1. Correlation between the minimum change in amplitude of motor evoked potentials and improvement in motor strength 48 h after surgery.

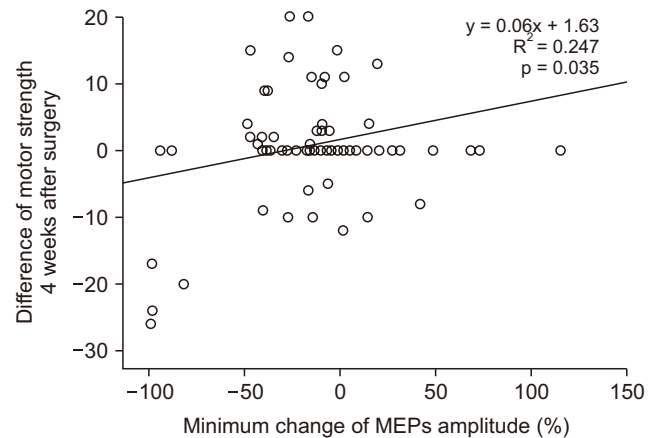


Fig. 2. Correlation between the minimum change in amplitude of motor evoked potentials and improvement in motor strength 4 weeks after surgery.

Table 3. Correlations between Changes of Motor Evoked Potentials Amplitude and Motor Grades Improvement

	Amount of bleeding	Motor <sub>48hrs-pre</sub>	Motor <sub>4wks-pre</sub>	MEP <sub>min</sub>	MEP <sub>max</sub>
Amount of bleeding					
Pearson correlation coefficient	1.000	-0.150	-0.120	-0.260	-0.091
p-value		0.205	0.313	0.026	0.442
Motor <sub>48hrs-pre</sub>					
Pearson correlation coefficient	-0.150	1.000	0.773	0.338	0.049
p-value	0.205		0	0.003	0.679
Motor <sub>4wks-pre</sub>					
Pearson correlation coefficient	-0.120	0.773	1.000	0.247	-0.014
p-value	0.313	0		0.035	0.904
MEP <sub>min</sub>					
Pearson correlation coefficient	-0.260	0.338	0.247	1.000	0.358
p-value	0.026	0.003	0.035		0.002
MEP <sub>max</sub>					
Pearson correlation coefficient	-0.091	0.049	-0.014	0.358	1.000
p-value	0.442	0.679	0.904	0.002	

Motor<sub>48h-pre</sub>: difference in muscle strength at 48 h after surgery from that before surgery, Motor<sub>4wks-pre</sub>: difference in muscle strength at 4 weeks after surgery from that before surgery, MEP<sub>min</sub>: minimum change in the amplitude of motor evoked potentials, MEP<sub>max</sub>: maximum change in the amplitude of motor evoked potentials

However, no significant correlation was found between the amount of bleeding and Motor<sub>48h-pre</sub> ( $p = 0.205$ ) or Motor<sub>4wk-pre</sub> ( $p = 0.313$ ).

## Discussion

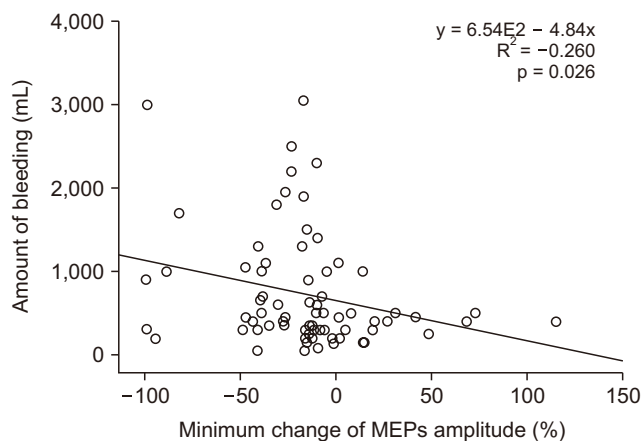
In surgeries for the removal of spinal cord tumors, a decrease in amplitude during SEP and MEP monitoring serves as an alarm criterion, and such an amplitude reduction has been found to be important in predicting postoperative motor deterioration.<sup>1,4,7</sup> This study aimed to determine the effect on motor status when the MEP amplitudes increased. In this study, we studied 115 patients who underwent spinal cord tumor removal and evaluated 73 patients who underwent follow-up monitoring. Baseline characteristics were analyzed by categorizing the patients into 2 groups, and there was no significant difference in sex or age between the 2 groups.

In the analysis with Pearson coefficient configuration, there was a positive correlation between Motor<sub>48h-pre</sub> and MEP<sub>min</sub> (Fig. 1), suggesting that the smaller the difference in MEP amplitude, the less the recovery of muscle strength ( $p = 0.003$ ). Moreover, when Motor<sub>4wk-pre</sub> and MEP<sub>min</sub> were analyzed, a positive correlation was observed ( $p = 0.035$ ) (Fig. 2), implying a similar conclusion as seen in the analysis of Motor<sub>48h-pre</sub> and MEP<sub>min</sub>. Elec-

tromyographic recording of muscle MEPs allows for the assessment of the entire motor axis, including the motor cortex, corticospinal tract, nerve root, and peripheral nerve.<sup>1</sup> Spinal cord tumors may be directly or indirectly holding the motor pathway depending on their location and degree of invasion to the spinal cord. So it is understandable that in the case of tumor removal, cord compression by the tumor can be eliminated<sup>15</sup> and the affected spinal cord is released, therefore mechanical or vascular burden can be elicited and may affect motor recovery after surgery.

The bleeding amount during surgery was 625.8 (50~3050) mL in group A (patients with motor improvement or no motor change) and 988.1 (150~3000) mL in group B (patients with motor deteriorations after surgery), respectively. The bleeding amount of group A was significantly lower than that of group B in the t-test ( $p = 0.020$ ), which means that the less the amount of bleeding, the less the possibility of motor deterioration. Furthermore, there was also a negative correlation between the amount of bleeding and MEP<sub>min</sub> (Fig. 3), indicating that the greater the amount of bleeding, the smaller the MEP<sub>min</sub>, which then implies that the MEP amplitude is less likely to improve when the amount of bleeding is large.

Previous study has reported that the amount of bleeding is significantly correlated with motor deterioration.<sup>16</sup> Moreover, it is believed that in the presence of a large amount of bleeding, neurological damage derived from cord ischemia, intraoperative or postoperative hypotension, or metabolic imbalances may occur. If the amount of bleeding is large, the possibility of hypoperfusion of the neural tissue is high and subsequently there may be some tissue damage, which can affect the motor status after surgery.<sup>16</sup> Because a large amount of bleeding can be corrected through early fluid supply or transfusion,<sup>17</sup> when MEP amplitude decrement is observed during surgery, surgeons can call attention to the bleeding amount or total fluid loss amount.<sup>16</sup> Therefore, the use of IONM allows for the identification of any change at a still-reversible stage,



**Fig. 3.** Correlation between the amount of bleeding and the minimum change in amplitude of motor evoked potentials.

permitting a prompt correction of the cause and avoiding permanent neurological impairment.

In the analysis of tumor type, there was significant difference between group A and B ( $p = 0.017$ ). Compared to group B, group A showed higher proportion of IDEM and ED tumors and in group B, proportion of ED tumors were higher than group A. Thus, in patients with motor improvement or no motor change there were larger number of IDEM or ED tumors and a fewer IM tumors compared to the patients with motor deterioration. In spinal cord tumors IDEM or ED tumor may press the spinal cord, therefore removing the IDEM or ED tumors may result in improvement of motor function. Likewise, IM tumors is positioned within the spinal cord so that removal of IM tumors can impair motor track directly, causing motor deterioration.

This study has a few limitations, which include the small number of patients enrolled and the lack of long-term follow-up to assess neurological deteriorations or improvements. Moreover, in this study, we strictly defined “motor improvement” or “motor deterioration” as even a single-point improvement or deterioration in the MRC scale score. Therefore, even the mildest improvements or deteriorations were included, which presumably affected the sensitivity and specificity of the study. In addition, we took into account only MEP amplitudes, without considering the changes in SEP parameters such as latencies or amplitudes. And there were no specific analysis with spinal cord tumor type, which can affect motor outcome after surgery. Furthermore, there was no direct correlation between the amount of bleeding and improvement in muscle strength, which may be due to the small sample size and the small correlation coefficients.

## Conclusion

This is the first study to investigate the correlation between amplitude changes (including increase) in MEPs and the amount of motor recovery in patients undergoing surgery for a spinal cord tumor. This study

showed that the recovery of muscle strength was less when the increase of MEP amplitude was small, and that the improvement of MEP amplitude was less when the amount of bleeding was large. A previous study suggested that preservation (no appreciable deterioration) of MEPs generally makes new weakness unlikely;<sup>18</sup> however, no study has ever documented predicting favorable prognosis with MEP monitoring.

For delicate analysis, further studies including various parameters of IONM such as SEPs and D-waves and large number of patients is needed to better predict postoperative prognosis.

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