

ORIGINAL ARTICLE

# Monitoring rate and predictability of intraoperative monitoring in patients with intradural extramedullary and epidural metastatic spinal tumors

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**Study design:** Single-center retrospective study.

**Objectives:** To evaluate the monitoring rate, sensitivity and specificity of intraoperative monitoring (IOM) during removal of intradural extramedullary (IDEM) or epidural metastatic spinal tumors. Also, to assess the efficacy of monitoring somatosensory-evoked potentials (SSEP) when motor-evoked potentials (MEP) are not measurable.

**Setting:** The Neuro-Oncology Clinic, National Cancer Center, Korea.

**Methods:** Patients ( $n=101$ ) with IDEM or epidural metastatic spinal tumors at the cord level underwent surgeries monitored with SSEP and/or MEP. The monitoring rate was defined as negative when MEP or SSEP could not be measured after reversal of the neuromuscular block under general anesthesia. Positive IOM changes included more than a 50% change in the MEP or SSEP amplitude and more than a 10% delay in SSEP latency.

**Results:** MEP was measurable in 73% of patients. The MEP monitoring rate in patients with motor power grades of 3 or less was 39%, which was lower than that of SSEP (83%). The sensitivity, specificity and predictability of MEP for motor changes were 93, 90 and 91%, respectively. Conversely, the sensitivity, specificity and predictability of SSEP were 62, 97 and 89%, respectively. In patients in whom MEP was not measurable ( $n=24$ ), SSEP was monitored with a predictability of 83%.

**Conclusion:** In cases of extramedullary spinal tumors, MEP shows a higher sensitivity than SSEP does. However, the monitoring rate of MEP in non-ambulatory patients was lower than that of SSEP. In those cases, SSEP can be useful to monitor for postoperative neurological deficits.

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## INTRODUCTION

Intraoperative neurophysiological monitoring (IOM) allows surgeons to monitor the functional integrity of the spinal cord using electrophysiological recordings, such as motor-evoked potentials (MEP) and somatosensory-evoked potentials (SSEP), and it has become an essential procedure during spinal surgery.<sup>1–4</sup>

The importance of SSEP was understood fairly early with regard to spinal deformity surgeries,<sup>1,2,5</sup> whereas MEP has played a particular role in intramedullary spinal cord tumor surgeries in which the motor and sensory pathways can be separately dissected.<sup>6,7</sup> Notably, surgeries involving intradural extramedullary (IDEM) or epidural metastatic spinal tumors are ideal for monitoring the influence of surgical manipulations to the spinal cord as the anatomical integrity of spinal cord conserved during the surgery.

Some studies have reported that MEP is a more reliable method for predicting postoperative neurological deficits, with a higher sensitivity, than SSEP.<sup>7–9</sup> However, in cases where the patient had preoperative impaired motor function, it is often impossible to measure MEP due to cord dysfunction and/or intraoperative conditions.<sup>8,10</sup> In these cases, it may be preferable to rely on SSEP, which is less vulnerable to

systemic conditions, including neuromuscular junctions, although it does not reflect the state of the corticospinal tract directly.<sup>2,3,7,9,11–14</sup> At present, the reliability and accuracy of SSEP for monitoring motor function in patients with preoperative motor deficits is not clear. Reports on the use of IOM in spinal tumor surgeries are relatively rare and frequently not distinguished from other spinal procedures. Moreover, there exist only a few studies reporting specifically on the results of IOM during IDEM or epidural metastatic spinal tumor surgeries.<sup>8,15,16</sup>

Therefore, we conducted a retrospective study to analyze the following: (1) the percent of patients with measurable MEP and SSEP (monitoring rate) according to preoperative motor power grades, (2) the sensitivity, specificity and predictability of MEP and SSEP, and (3) the efficacy of using SSEP to predict postoperative motor deficit in patients with unmeasurable MEP.

## METHODS

### Eligibility

Between 2009 and 2015, 121 consecutive patients received operations with IOM for spinal tumors in the National Cancer Center, Goyang, Korea. Among them,

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nine patients with intramedullary spinal tumors and 11 patients with lesions below L1 were excluded. Data from the remaining 101 patients were analyzed retrospectively. This retrospective study was approved by the institutional review board at the National Cancer Center (NCC2015-0260).

### MEP monitoring protocol

MEPs were monitored during the operation, upon request by the respective surgeon, using transcranial electrical stimulation. A Protektor IOM (Xltek Ltd., Ontario, Canada) monitoring system was used, along with disposable, low-profile needle electrodes, as per the manufacturer's protocol (Chalgren Enterprise Inc., CA, USA). The stimulation parameters were as follows: short trains of five rectangular stimuli, interstimulus interval of 2 ms and intensity of 300–400 V. The stimulation intensity was set to maintain adequate responses (more than 50  $\mu$ V) from all monitored muscles and then fixed throughout the procedure. Baseline recordings were attempted after the initiation of general anesthesia and before skin incision.

### SSEP monitoring protocol

SSEPs were monitored continuously during the operation in all cases. In brief, rectangular constant-current stimuli of 300  $\mu$ s duration, with intensities up to 30 mA, were applied either to the median nerve at the wrist or to the tibial nerve at the ankle at a stimulation rate of 2.31 Hz. Upper-extremity SSEPs were recorded at C2 versus Cz or C4 versus Fz, and lower-extremity SSEPs were recorded at Cz versus Fz, with a bandpass from 30 to 1000 Hz and averaging of 100 sweeps.

### Positive change of IOM

The positive parameter was the loss of MEPs or a 50% drop of the MEP amplitude. The parameter for SSEP was a 50% drop of amplitude or 10% delay of the latency. We considered these changes 'negative', if, once decreased or delayed, MEP or SSEP was recovered.

**Table 1 Clinical characteristics of the spinal tumor patients with IOM**

Characteristics	No. of patient (n = 101)
Gender (male/female)	59/42
Median age (range)	57 (13–80)
<i>Spinal location</i>	
Metastatic (epidural)	72
IDEM	29
<i>Spine level</i>	
Cervical	15
Cervicothoracic	6
Thoracic <sup>a</sup>	80
<i>Preoperative motor power</i>	
5	41
4	37
3	18
0–2	5
<i>Operation</i>	
Laminectomy and tumor removal	45
Decompression and posterior fixation	16
Decompression, anterior reconstruction and posterior fixation	39
Anterior approach to cervical spine	1

Abbreviations: IDEM, intradural extramedullary tumor; IOM, intraoperative monitoring; KPS, Karnofsky Performance Scale.

<sup>a</sup>Thoracic spine to 1st lumbar spine. Note: motor power is described by Medical Research Council motor power scale.

### Anesthesia

Anesthesia was administered to all patients with continuous infusion of propofol (80 to 150  $\mu$ g kg<sup>-1</sup> min<sup>-1</sup>). Short-acting muscle relaxants such as rocuronium were used for intubation, but not thereafter.

### Monitoring rate of IOM

If there were no measurable MEP or SSEP, even after confirmation of reversal of the neuromuscular block by a peripheral nerve stimulator, we considered the monitoring of MEP or SSEP to be impossible. The monitoring rate is defined as the number of patients for whom we could obtain a baseline recording of MEP or SSEP divided by the total number of attempted cases.

### Clinical analysis parameters

Patients' clinical information was collected from the electronic medical record archive. Motor power was graded by the Medical Research Council system<sup>7</sup> and defined as the lowest grade among the four extremities. Postoperative motor power grade was evaluated during the acute period, 2 days after the surgery, and before the rehabilitation treatment. We considered a postoperative drop in a patient's motor power by  $\geq 1$  grade as a positive event.

## RESULTS

### Clinical characteristics

Clinical characteristics of the 101 patients are summarized in Table 1. There were 59 male patients and 42 female patients at a median age of 57 years (range 13–80 years) at the time of surgery. Anatomically, 72 cases were epidural tumors and the remaining cases were IDEM tumors. Histologically, all epidural tumors were metastatic tumors and lung cancer was the most frequent primary cancer ( $n = 21$ ), whereas among IDEM tumors, schwannoma was the most common ( $n = 18$ ). The involved spinal level was mainly thoracic ( $n = 80, 79\%$ ).

Seventy-eight patients (77%) maintained ambulatory function preoperatively with a motor grade of  $\geq 4$ . Laminectomy and tumor removal, without any other surgical procedures, was the most frequently performed type of surgery ( $n = 45$ ). Another 39 patients received surgical decompression of the involved vertebral body with anterior reconstruction, in addition to laminectomy and posterior fixation.

A postoperative decrease in the motor power grade occurred in 23 patients (23%).

### Monitoring rate of IOM according to preoperative motor power grade

The monitoring rate of MEP and SSEP, according to the preoperative motor grade, is summarized in Table 2. The monitoring rate of SSEP (93%) was higher than that of MEP (73%;  $P < 0.01$ ).

MEP was measurable for 38 out of 41 patients (93%) who had a motor grade of 5 and for 27 of the 37 patients with a motor power grade of 4 (73%). However, the monitoring rate of MEP in patients, with a motor grade of 3 or less, was only 39% (9 out of 23), which was significantly lower than that for ambulatory patients ( $P < 0.001$ ).

SSEP was obtainable for all 41 (100%) patients with a motor grade of 5, for 34 out of 37 patients (92%) with a grade of 4, for 16 out of 18 patients (89%) with a grade of 3 and for 3 out of 5 patients (60%) with a motor grade of 0–2. For patients with a motor grade of 3 or less, the monitoring rate of SSEP was significantly higher than that of MEP (82 vs 39%, respectively,  $P < 0.01$ ).

### Sensitivity, specificity and predictability of MEP and SSEP

Among the 74 patients with measurable MEP, 19 patients showed a positive MEP change during the operation. Of those patients, thirteen exhibited postoperative worsening of motor power (true positive). Of the six patients without postoperative motor deficits (false

**Table 2 Feasibility of lower-extremity MEP and SSEP according to preoperative motor grade in only metastatic tumors**

Preoperative status	Feasible/total	
	MEP (%)	SSEP (%)
Total	74/101 (73)	94/101 (93)
<i>Motor grade</i>		
5	38/41 (93)	41/41 (100)
4	27/37 (73)	34/37 (92)
3	7/18 (39)	16/18 (89)
0–2	2/5 (40)	3/5 (60)

Abbreviations: IOM, intraoperative monitoring; MEP, motor-evoked potential; SSEP, somatosensory-evoked potentials. Note: the numbers in parenthesis are percentage of IOM feasible cases out of total trial.

**Table 3 Predictability of MEP and SSEP for spinal tumors**

IOM modality	Postoperative motor grade	
	Decreased	Not decreased
<i>MEP (n = 74)</i>		
Changed	13	6
Not changed	1	54
<i>SSEP (n = 94)</i>		
Changed	13	2
Not changed	8	71

Abbreviations: IOM, intraoperative monitoring; MEP, motor-evoked potential; SSEP, somatosensory-evoked potentials. Note: the sensitivity, specificity and predictability of MEP were 93% (95% confidence interval, 0.56–0.97), 90% (0.79–0.96) and 91% (0.81–0.96), respectively. The sensitivity, the specificity and the predictability of SSEP for postoperative motor decrease was 62% (0.37–0.81), 97% (0.90–1.00) and 89% (0.81–0.95), respectively.

positives), four experienced intraoperative hypothermia (<35 °C), which could be a possible cause of the false positives. Another false-positive patient showed decreased MEP in only the lower right extremity, but not in the other three extremities. At the time of the MEP drop, intraoperative hypotension occurred due to massive blood loss of over 3 l. Finally, the 6th patient showed an MEP drop during the fixation procedure. Accordingly, MEP had a sensitivity of 93% (95% confidence interval, 0.56–0.97), specificity of 90% (0.79–0.96), positive predictive value of 68% (0.43–0.86) and negative predictive value of 98% (0.89–1.00; Table 3).

Among the 94 patients with measurable SSEP, 15 patients showed a positive SSEP change, of which 13 patients presented with a postoperative decrease in motor power. The other 79 patients did not show significant changes in SSEP, and 71 of these patients were free from motor power decreases. Thus, SSEP had a sensitivity of 62% (0.37–0.81), specificity of 97% (0.90–1.00), positive predictive value of 87% (0.58–0.98) and negative predictive value of 90% (0.81–0.95) (Table 3).

**Usefulness of SSEP in patients for whom MEP was not measurable**

We identified 24 patients for whom SSEP, but not MEP, was measurable. Of those, 7 patients presented with a postoperative decrease in motor power, and 4 of these 7 patients showed a positive SSEP change. Conversely, of the 17 patients in whom a postoperative decrease in motor power did not occur, one patient showed a positive SSEP change (false positive). Hence, in patients without measurable

**Table 4 Predictability of SSEP for motor change in patients whose MEP was not measurable**

SSEP change (n = 24)	Postoperative motor grade	
	Decreased	Not decreased
(+)	4	1
(–)	3	16

Abbreviations: MEP, motor-evoked potential; SSEP, somatosensory-evoked potentials. Note: the sensitivity, the specificity and the predictability of SSEP for motor change was 57% (95% confidence interval, 0.18–0.90), 94% (0.69–1.00) and 83% (0.62–0.95), respectively

MEP, the sensitivity, specificity and positive and negative predictive values of SSEP were 57% (0.18–0.90), 94% (0.69–1.00), 80% (0.28–0.99) and 84% (0.60–0.96), respectively (Table 4). Based on this, we believe that in cases in which MEP is ‘not measurable’, SSEP has a predictability for postoperative motor power of 83% (0.62–0.95).

**DISCUSSION**

**Monitoring rate of IOM in patients with preoperative neurological deficits**

Several studies have shown that the monitoring rates of SSEP and/or MEP are decreased in patients with preoperative neurological deficits.<sup>6,8,10</sup> In one, Chen *et al.* reported that the monitoring rate of MEP in patients with a preoperative ‘motor deficit’ was significantly lower than that of patients without motor weakness (39.1 vs 78.9%, respectively,  $P < 0.001$ ).<sup>8</sup> In our study, we investigated the monitoring rate of IOM according to preoperative motor grade, which is a more detailed analysis than that of previous studies. We observed a significant difference in the monitoring rate of MEP between patients with a preoperative motor power grade of more than 3 and those with a lower preoperative motor grade (83 vs 39%). Similar results were found in a study of MEP during surgery for intramedullary spinal cord tumors by Morota *et al.* (76 vs 27%).<sup>6</sup>

In general, MEP is affected more frequently by several conditions, such as anesthesia, hypotension, hypothermia, lesion location and preoperative motor deficit, than is SSEP.<sup>8,17</sup> Hence, the reported monitoring rates of MEP are lower than those of SSEP in the same patient settings. For example, Quraishi *et al.*<sup>4</sup> reported monitoring rates of SSEP and MEP, in surgeries of adult spinal deformity, as 99 and 75%, respectively. Similarly, Pelosi *et al.* reported monitoring rates of SSEP and MEP as 97 and 84%, respectively, in patients with heterogeneous diseases ranging from spinal deformity to trauma. The relatively low monitoring rate of MEP could be attributed to several causes, including a vulnerable neuromuscular junction, few functional axons, sensitive anterior spinal cord function to ischemia and myelopathy from previous radiation.<sup>6,17,18</sup>

**Sensitivity, specificity and predictive values of MEP and SSEP for postoperative motor deficits**

Differences in the IOM-related values can be found when comparing spinal surgeries for deformity versus spinal tumors. Specifically, IOM in spinal deformity surgeries has been reported to have a much higher specificity (~99%) than in intramedullary tumor surgeries because postoperative neurological deterioration happens in less than 1% of cases, unlike for intramedullary tumor cases.<sup>2,6,7,19</sup>

Our study is unique in that it deals with spinal tumors while preserving the anatomical integrity of the spinal cord throughout all surgeries by strong protection of dura. In our study, MEP had a sensitivity of 93%, but a positive predictive value of 68%. When we observed an MEP drop, we routinely checked the integrity of the

IOM device, and an anesthesiologist made every attempt to correct hypothermia or hypotension if they occurred. If, at that point, MEP had not recovered, we stopped the procedure for several minutes as MEP recordings have the potential to spontaneously recover after suspending surgical manipulations of the cord. Also, we carefully irrigated the surgical field with warm saline to keep the surgical field warm.<sup>20</sup>

In general, SSEP is less affected by systemic conditions and is rather specific than sensitive for postoperative motor deficits.<sup>18</sup> SSEP relays information regarding dorsal column integrity, which is less sensitive to postoperative motor deficits. Hence, cases, in which serious postoperative deficits have occurred despite intact SSEP measurements, have been reported in previous studies.<sup>21–26</sup> In our study, SSEP had an overall sensitivity of 62% and a specificity of 97%, in agreement with other reports. In addition, very few previous studies have investigated SSEP changes with regard to postoperative sensory deficits in terms of either quantitative analyses or objective descriptions of sensory change.<sup>15,27</sup> Unfortunately, we were unable to measure postoperative sensory changes as the only retrievable data obtainable by us were subjective descriptions of sensory change and vague dermatomal distributions documented in the patients' medical records.

#### Effectiveness of SSEP in patients without measurable MEP

SSEP was the standard method for IOM in spinal deformity surgeries before MEP became available, and it indirectly represents the functional integrity of the corticospinal tract.<sup>2,9</sup> We assume that, if cord integrity is preserved, ischemia from cord compression or stretching affects both the motor and sensory pathways.

It is important to note that monitoring only SSEP could have detrimental effects in selective cases.<sup>21,22</sup> A report by Deletis *et al.* advised against monitoring only SSEP in intramedullary spinal cord tumor surgeries where surgical manipulations can selectively damage either the motor or sensory pathways.<sup>9</sup> However, the authors also suggested that SSEP can be used as an alternative to MEP, when MEP cannot be measured, if the integrity of spinal cord is ensured. Moreover, Nuwer *et al.* reported results of a multicenter, retrospective survey showing that the false-negative rate of SSEP was only 0.063% (34 out of 50 207 surveyed cases) after scoliosis surgery.<sup>2</sup> Furthermore, Khan *et al.* reported that SSEP monitoring, without MEP or EMG, can reduce neurological injury even during anterior cervical surgeries.<sup>28</sup> In our study, 24 patients had only their SSEP measurements taken for monitoring during spinal surgery and SSEP showed predictability of 83% for postoperative motor deficits. Although there were three false-negative cases, resulting in a sensitivity of 57%, the 94% specificity of SSEP is encouraging for its use in IDEM and epidural metastatic spinal tumor surgeries for patients without measurable MEP.

#### Effect of intraoperative hypotension and hypothermia on IOM

In our study, five of six false-positive MEP cases involved intraoperative hypotension and/or hypothermia. Intraoperative hypothermia may result in false-positive readings for IOM changes, but does not result in harmful effects on postoperative motor function. However, intraoperative hypotension has been implicated in unexpected postoperative neurological deficits in some studies.<sup>9,29,30</sup>

#### CONCLUSION

We evaluated the respective feasibilities and efficacies of using MEP and/or SSEP to monitor 101 surgeries of IDEM and epidural metastatic spinal tumors. The monitoring rate of SSEP in

non-ambulatory patients was better than that of MEP (83 vs 39%). MEP and SSEP showed sensitivities of 93 and 62%, respectively, for postoperative motor deficits. Also, we investigated whether SSEP could be substituted for MEP to predict postoperative neurologic deficits when MEP was unavailable, and we found a predictability of 83%. In summary, IOM can reduce postoperative neurologic deficits after spinal tumor surgery, and monitoring both MEP and SSEP is better than monitoring SSEP alone. However, for non-ambulatory patients for whom MEP is unmeasurable, monitoring SSEP is helpful.

#### DATA ARCHIVING

There were no data to deposit.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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