Acta Neurochir (2015) 157:2149–2155
DOI 10.1007/s00701-015-2598-y

EXPERIMENTAL RESEARCH - SPINE

Multimodal intraoperative monitoring during intramedullary spinal cord tumor surgery

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Received: 9 July 2015 / Accepted: 21 September 2015 / Published online: 7 October 2015
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Abstract
Background The aim of this work is to evaluate the utility of multimodal intraoperative monitoring (IOM) during intramedullary spinal cord tumor (IMSCT) surgery in our institution, and to investigate which IOM events are likely to be encountered during critical surgical phases.
Methods Twenty-five patients who underwent IMSCT surgery with IOM were included in this study. Our multimodal IOM assessment included SSEP, mMEP, and fEMG monitoring. Positive predictive value (PPV), negative predictive value (NPV), sensitivity, and specificity were assessed 24 h and 1 month after surgery. The IOM events during three main surgical phases were also investigated. For mMEP assessment, two warning criteria (>50 % decrease in mMEP amplitude and all-or-none mMEP amplitude presence) were employed.
Results Long-term outcome prediction was better when the all-or-none criterion was applied than when the >50 % amplitude decrease criterion was applied. Based on the all-or-none criterion, the PPV, NPV, sensitivity, and specificity were 60, 100, 100, and 91 %. Frequent IOM events were observed during the three major main surgical phases. Seven (29 %) patients showed SSEP events during opening of the spinal cord. During tumor removal, 21 of 25 patients (84 %) had IOM events, and 13 of 18 (72 %) of the fEMG events occurred prior to the mMEP events.
Conclusions Based on the association of fEMG events with upcoming mMEP events during tumor removal, we recommend inclusion of fEMG monitoring in IOM. Multimodal IOM provides useful electrophysiological information during IMSCT surgery, especially during the main surgical phases.

Keywords Intramedullary spinal cord tumor · Intraoperative monitoring · Somatosensory evoked potential · Muscle motor evoked potential · Free-running electromyography

Electronic supplementary material The online version of this article (doi:10.1007/s00701-015-2598-y) contains supplementary material, which is available to authorized users.

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Introduction

Intramedullary spinal cord tumors (IMSCT) are rare and in most cases their surgical treatment is difficult [16]. Intraoperative monitoring (IOM) has been applied during IMSCT surgery, and evidence indicating its clinical importance has been accumulated [1, 4, 7, 11, 16, 20–22]. The sensitivity and specificity of combined muscle motor evoked potential (mMEP) and somatosensory evoked potential (SSEP) data were reported to be 100 and 28.5 % [7]. When free-running electromyography (fEMG) was included, the positive predictive value (PPV), negative predictive value (NPV), sensitivity, and specificity were 0.889, 1.0, 100, and 83.33 %, respectively [22]. Monitoring of epidural (D-) waves is a well-known complementary technique in spine and spinal cord surgeries [1, 4, 11, 20, 21, 25]. However, the electrode for D-wave recording has not been approved by the Korean Food & Drug Administration (KFDA).

Here, we evaluated the use of multimodal IOM during IMSCT surgery in our institution. In addition, since we encountered IOM events during each of the main phases of the IMSCT surgical procedure, such as the SSEP events during myelotomy and fEMG or mMEP events during tumor removal, we evaluated which IOM modality can act as an indicator of presumed new corticospinal tract insult during IMSCT surgery.

Materials and methods

Patients

We retrospectively reviewed data for 30 consecutive patients who underwent IMSCT removal surgery with IOM between March 2010 and December 2013 in our institution. Five of those patients were excluded due to incomplete multimodal IOM dataset. The other 25 patients (age range, 21–74 years, nine males) were included in our study. All IMSCT surgeries were performed by two neurosurgeons (CKC and CHK). Tumor location and histopathological findings for each case are presented in Table 1. Twenty-three of the 25 patients had preoperative neurological symptoms (motor symptom, two; sensory symptom, 14; both motor and sensory symptoms, six), and three of the 25 patients reported headache (one patient) and pain (two patients). Postoperative neurological deficits were evaluated at 24 h and 1 month after surgery. Our study was approved by the Seoul National University Hospital Institutional Review Board (1306-106-500).

Table 1 Histopathological findings and tumor location for each case

No.	Histopathology	Tumor location
1	Cavernous angioma	T2
2	Hemangioma	C4
3	Ependymoma	C1-5
4	Astrocytoma	C1-3
5	Hemangioblastoma	C2
6	Ependymoma	C2-6
7	Hemangioblastoma	T9-10
8	Subependymoma	T10-11
9	Ependymoma	T7-8
10	Ependymoma	C4-5
11	Epidermal cyst with dystrophic calcification	L2-3
12	Ependymoma	C6-7
13	Ependymoma	C3-5
14	Hemangioma	T4-5
15	Hemangioma	C3-4
16	Astrocytoma	C4-5
17	Hemangioma	C3-4
18	Ependymoma	T3-4
19	Ependymoma	T12-L1
20	Astrocytoma	T12-L1
21	Ependymoma	C3-5
22	Ependymoma	C5
23	Subependymoma	T10-11
24	Ependymoma	C2
25	Cavernous angioma	C4

Anesthesia

General anesthesia was induced by total intravenous anesthesia (TIVA) with propofol and remifentanil. Neuromuscular blockage was induced once before intubation and was not given thereafter. Mean blood pressure was maintained at higher than 90 mmHg.

Multimodal IOM

Multimodal IOM was performed by using an Eclipse workstation (Axon Systems, Hauppauge, NY, USA). For SSEP monitoring, surface-stimulating electrodes were placed bilaterally at the median nerve at the wrist and at the posterior tibial nerve at the ankle. A 200-μs square-wave electrical pulse was presented sequentially to the bilateral median and posterior tibial nerves at a rate of 2.9 Hz with stimulus intensity ranged from 16 to 40 mA. SSEP was recorded from needle electrodes placed on the scalp at locations C3 and C4, and Cz referenced to Fpz. The upper or lower extremities were selectively monitored depending on the operation's spine level.

The mMEP recording followed application of transcranial electric stimulation. Transcranial anodal motor cortex stimulation was performed via electrical pulses through needle electrodes inserted over the C3′ and C4′ (1–2 cm anterior to C3 and C4 positions of the international 10–20 system). Trains of five biphasic pulses with an interstimuli interval of 1–2 ms at a rate of 1 Hz were delivered. Stimulation intensity ranged from 300 to 500 V. Monitored muscles generally included bilateral deltoid, biceps, thenar, tibialis anterior (TA), gastrocnemius, abductor halluces (AH), and vastus lateralis. Selection of muscles to be monitored was flexibly determined depending on the operation's spine level. Intraoperative real-time monitoring of fEMG was also performed at the same as those used in mMEP monitoring.

Baseline SSEP and mMEP were obtained after anesthetic induction but before performing the IMSCT surgical procedure. Peak-to-peak SSEP amplitude and latency were continuously monitored. Because the mMEP provokes patient movement, trials were conducted only when requested during surgery. The criteria used to indicate an abnormal SSEP were presence of a>50 % decrease in peak-to-peak amplitude or a >10 % increase in latency compared to the baseline. We evaluated mMEP by using two criteria: occurrence of a>50 % decrease in mMEP amplitude [18] and all-or-none [5, 6, 8, 14, 17] of mMEP amplitude. We defined an mMEP change as significant when the applied criterion was observed at >1 monitored muscle. Relevant fEMG activity reported to the surgeon included spikes, bursts, and trains [5]. Abnormal monitoring results were reported immediately to the surgical team in order for the surgeon to be able to modify the procedure to avoid or limit postoperative neurologic deficit, although any technical problems or other clinical factors such as anesthetic-related indices should be taken into consideration.

Statistical analysis

Sensitivity, specificity, PPV, and NPV were evaluated. Sensitivity was defined as the probability that newly developed true neurophysiological deficit would be identified by IOM. Specificity was defined as the probability that no significant neurophysiological deficit would be correctly identified by IOM. The PPV was defined as the probability that a significant IOM change reflected a true neurophysiological deficit, whereas the NPV was the probability that a finding of no IOM change truly reflected no significant neurophysiological deficit. Each value was evaluated at transient (24 h after surgery) and sustained (1 month after surgery) deficit follow-up periods.

Results

Illustrative case

In case 12 (Fig. 1), a SSEP event at the right lower extremity was observed during spinal cord opening. Continuous neurotonic discharges in the right thenar muscle fEMG were observed during tumor removal. At the end of surgery, the SSEP at the right lower extremity did not recover. A sudden decrease of mMEP amplitude after arachnoid membrane closure was sustained when the patient left the operation room. The patient woke up with right hand weakness, but this motor symptom was not sustained deficit. This patient had hypoesthesia in the right lower extremity after surgery and at the 1-month follow-up; however, this symptom was preexisting. This case was assessed as a TP (true positive) with application of the >50 % mMEP amplitude decrease criterion, and as a FN (false negative) with the all-or-none criterion at 24 h after surgery. However, this case was assessed as a FP (false positive) with the >50 % mMEP amplitude decrease criterion, and as a TN (true negative) with application of the all-or-none criterion at the 1-month follow-up. It was noted that the fEMG events during tumor removal preceded an mMEP event that was associated with the postoperative motor deficit (Fig. 1).

Multimodal IOM

None of 25 patients had new sensory function deterioration after surgery, whereas five patients (20 %) had new motor deficits after surgery. Four of those five patients had mild motor weakness at 24 h after surgery. One patient had ambulation difficulty at the 1-month follow-up, but the symptom has gradually improved through rehabilitation. We considered a case as an FN if the patient had a new or worsened motor deficit despite the absence of significant mMEP or fEMG events. In this study, and based on the>50 % decrease in mMEP amplitude criterion, two FN were detected at 24 h after surgery. These patients (cases 2 and 12) presented with new arm weakness, but those symptoms were absent at the 1-month follow-up.

Table 2 presents a summary of the statistical category results at 24 h and 1 month after surgery. Regarding transient motor deficit, a PPV, NPV, sensitivity, and specificity of multimodal IOM were 31, 100, 100, and 57 %, respectively, with the >50 % decrease in mMEP amplitude criterion. However, with the all-or-none criterion, the PPV, NPV, sensitivity, and specificity for transient motor deficit were 40, 86, 50, and 86 %, respectively. Regarding sustained motor deficit, multimodal IOM produced a PPV of 23 %, NPV of 100 %, sensitivity of 100 %, and specificity of 55 % with the >50 % decrease in mMEP amplitude criterion. However, with the all-or-none criterion, the PPV, NPV, sensitivity, and specificity for sustained motor deficit were 60, 100, 100, and 91 %, respectively. Thus, multimodal IOM with application of the all-or-none mMEP criterion is superior to application of the 50 % decrease in mMEP amplitude criterion in terms of long-term outcome.

Regarding later-stage follow-up ranging from 1 month to 4 years depending on the subject, there were no noticeable neurologic status changes except for one case (case #15). For this particular case, a re-operation is now considered due to the progressive motor weakness with a recurrence of the tumor at the same level. Interestingly, this patient showed motor weakness after both 24 h and 1-month follow-up with IOM events, which led this case classified as a TP. Other than this case, the rest of the 24 patients have not shown any newly developed neurologic symptoms after surgery. Thus, even if we consider the clinical evaluation in later stages regardless of the different follow-up period, it is unlikely to change the predictive value.

IOM events during the main surgical phases

Individual IOM results during IMSCT surgery and a summary of the results during three of the IMSCT surgical phases are described in Tables 1 and 3.

Spinal cord opening to tumor removal phase

Of the 25 patients, 15 patients (60 %) had no IOM events in the period between opening of the spinal cord and tumor removal. The SSEP of six patients (24 %) were partly (five of

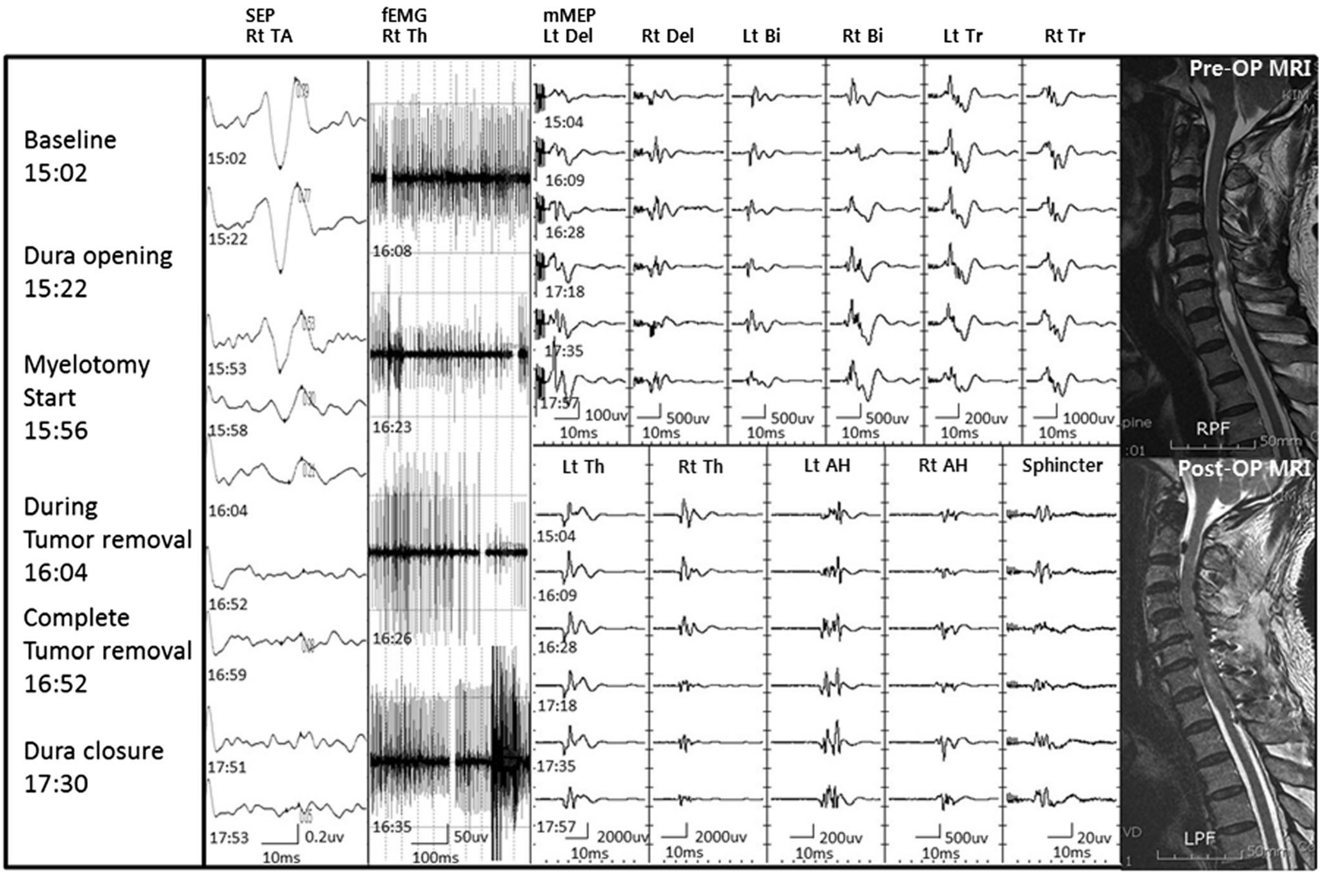

Fig. 1 Example of data from study case 12. Baseline traces show normal SSEP (15:02) elicited by stimulating the right tibialis anterior (TA), normal mMEP (15:04), and quiet fEMG. The SSEP trace started to decrease during myelotomy (15:58), was absent during tumor removal (16:52), and did not recover at the end of surgery. No significant events were detected in the left TA and upper SSEP when the right TA SSEP event happened. Continuous neurotonic discharges in the right thenar muscle fEMG were observed during tumor removal. A sudden decrease of mMEP amplitude (17:35) occurred after dura closure and was sustained when the patient left the operation room (17:57). (*AH* abductor hallucis, *Bi* biceps, *Del* deltoid, *fEMG* free-running electromyography, *Lt* left, *mMEP* muscle motor evoked potential, *Rt* right, *SSEP* somatosensory evoked potential, *TA* tibialis anterior, *Th* thenar, *Tr* triceps)

six) or totally (one of six) unmonitorable at baseline. Excluding the totally unmonitorable patient, seven of 24 patients (29 %) had SSEP events. Five of the 24 patients had fEMG events (20 %) and one of the 24 cases had an mMEP event. Two of the 24 patients had IOM events in more than two modalities.

Table 2 Summary of statistical results for multimodal intraoperative monitoring of 25 patients with intramedullary spinal cord tumors

Statistic	24 h after surgery		1 month after surgery	
	SEP-mMEP (>50 %)-fEMG	SEP-mMEP (all-or-none)-fEMG	SEP-mMEP (>50 %)-fEMG	SEP-mMEP (all-or-none)-fEMG
TP (n)	4	2	3	3
TN (n)	12	18	12	20
FP (n)	9	3	10	2
FN (n)	0	2	0	0
PPV (%)	31	40	23	60
NPV (%)	100	86	100	100
Sensitivity (%)	100	50	100	100
Specificity (%)	57	86	55	91

TP true positive, *TN* true negative, *FP* false positive, *FN* false negative, *PPV* positive predictive value, *NPV* negative predictive value

Table 3 Intraoperative electrophysiological events during three main surgical phases

	Opening of spinal cord to before tumor removal	During tumor removal	After tumor removal to dura closure
None (*n*)	15	4	24
SEP (*n*)	7 (6 unmonitorable)	11	0
mMEP (*n*)	1	18	1
fEMG (*n*)	5	18 (13 indicator of upcoming MEP event)	0
More than two modalities	2	18	0

Tumor removal phase

Only 16 % (4/25) patients had no IOM events during tumor removal. There were 11 SSEP events (52 %), 18 mMEP events (86 %), and 18 fEMG events (86 %) during tumor removal. Eighteen of the 25 patients had IOM events in more than two modalities. Noticeably, in 13 (72 %) of those 18 patients fEMG events were observed prior to the mMEP events. In case 19, a fEMG event occurred in the absence of either a SSEP or mMEP event; that case had no postoperative motor deficit.

After tumor removal to closure phase

There was only 1 mMEP event that occurred in this phase. Interestingly, an fEMG event was observed prior to this mMEP event in case 12, presenting a transient motor deficit.

Discussion

In our study, we evaluated the utility of multimodal IOM during IMSCT surgery at our institution and investigated which IOM events are likely to be encountered during critical phases of the IMSCT surgical procedure.

In this retrospective review for 25 IMSCT patients, multimodal IOM results after application of the all-or-none mMEP criterion provided the best indication of a successful long-term outcome. At 24 h after surgery, the number of false-positive (FP) cases reduced from 9 to 3, while two false-negative (FN) cases were detected after application of the all-or-none criterion. At the 1-month follow-up, the initial ten FP cases were reduced to two FP with application of the all-or-none criterion. Compared to the all-or-none criterion results, applying the >50 % decrease in mMEP amplitude criterion increased PPV and specificity. It should be noted that even if a stricter warning criterion is applied, FP cases are still detected. Thus, multimodal IOM with the >50 % decrease in mMEP amplitude criterion is favored for indicating short-term outcome, whereas multimodal IOM with the all-or-none criterion on mMEP applied is favored for indicating long-term outcome.

Previous studies have indicated that the absence of mMEP is not necessarily associated with postoperative motor deficit. In IMSCT surgery, an absence of mMEP with transient paralysis has been repeatedly observed [2, 10, 21], suggesting that intramedullary dissection can temporarily reduce intact lower motor neuron excitability to intact corticospinal tract input by disrupting background facilitation systems [2, 15]. In historical case–control studies, a combination of mMEP and D-wave monitoring was recommended because it improved long-term outcome without limiting tumor removal [2, 10, 21]. No similar efficacy data exist for other monitoring techniques. However, it was noted that in about one-third of the cases, the D-wave is not recordable because of a desynchronization phenomenon [2]. When D-waves are unavailable, one must rely on mMEP data while realizing that even their absence is compatible with good long-term function [3]. Skinner et al. [22] reviewed 14 patients who underwent IMSCT surgery with the combined monitoring of SSEP, mMEP with >90 % loss of amplitude, and fEMG, and were no FN and one FP. In our study, the best performance produced PPV of 60 %, NPV of 100 %, sensitivity of 100 %, and specificity of 91 %. Even with application of the all-or-none criterion, we had two FP cases (cases 9 and 21). Interestingly, both cases showed mMEP absence in one muscle, but mMEP presence in other muscles. This suggests that monitoring multiple muscles is advantageous and the loss of mMEPs in one monitored muscle is compatible with good long-term function.

The incidence of FN mMEP results was previously reported to be 0 % [12, 22], but in the present study, two FN (cases 2 and 12) were observed at 24 h after surgery with application of the >50 % decrease in mMEP amplitude.

Since transient weakness was absent at the 1-month follow-up, all cases were TN at the 1-month follow-up with application of the all-or-none mMEP criterion. Our results support the suggestions in previous studies that it is favorable to adopt the all-or-none mMEP criterion [9, 13, 21, 24].

During opening of the spinal cord, seven patients showed SSEP events in the present study. Although SSEP events were not necessarily associated with postoperative neurological deficit [20, 25], changes in or even absence of SSEP was reported during incision of the dorsal median raphe [20], which might be due to midline distortion by aspects of the IMSCT procedure [20, 25].

During tumor removal, 21 of the 25 patients (84 %) had IOM events with fEMG events occurring as often as mMEP events in those 21 patients. In a previous review of the utility of fEMG, five of 14 patients (36 %) had no fEMG events during surgery [22]. Six of 14 patients (43 %) showed significant fEMG events, and three of 14 patients (21 %) showed mMEP events [22]. In our study, only 16 % (four of 25) of the patients did not exhibit IOM events. The remaining 21 showed IOM events during tumor removal. Interestingly, 18 of the 21 fEMG events (86 %) were observed and 72 % of those 18 fEMG events were observed prior to an mMEP event. This suggests that fEMG activities may act as a precursor or, a predictor of an upcoming mMEP event. The usefulness of fEMG monitoring was suggested in a report by Hyun et al. [7], who observed that fEMG changes can occur without EP changes and that fEMG changes can precede EP changes during spinal cord surgery, although no neurological outcomes related to these changes were presented. Monitoring fEMG during IOM is useful because its high-frequency discharges are likely to be associated with true injury [19]. Compression or stretch of a nerve as well as hypothermia and ischemia can produce depolarization of the axons resulting in the appearance of spontaneous action potentials. These action potentials subsequently produce contractions of muscle fibers that can be recorded by electrodes placed in the muscle [23]. Potential irritation to and/or compression of nerve roots can be monitored by using fEMG [18]. We presume that fEMG events can result from transient traction on the corticospinal and other descending motor tracts or from vascular compromise to the cord during tumor removal. Considering the instantaneous characteristic of fEMG activity [23], fEMG monitoring has advantages over D-wave monitoring. Moreover, since patient movement is not induced, fEMG is favored when proceeding to IMSCT surgery.

The present study has several limitations, i.e., retrospective study, no D-wave recordings, limited follow-up, and small number of patients. Although we could not include D-wave recording due to unavailability of the electrode for D-wave recording in our country, it would be interesting to review the multimodal IOM including D-wave recording during IMSCT surgery. Even though we included a relatively larger number of patients than previous IOM studies in IMSCT [7, 22], it is still true that the number of patients is small. Longer follow-up than our limited follow-up and a larger number of patients would be required to confirm the importance of multimodal IOM and its clinical values during IMSCT surgery.

Despite these limitations, from our results we conclude that multimodal IOM via SSEP, mMEP, and fEMG is helpful during IMSCT surgery. Based on the association of fEMG events with upcoming mMEP events during tumor removal, we recommend inclusion of fEMG monitoring in IOM. Multimodal IOM provides useful electrophysiological information during IMSCT surgery, especially during the main surgical phases.

Acknowledgments This research was supported by a grant of the Seoul Business Agency (Grant no. PA140020) and Ministry of Knowledge and Economy (MKE) through Standard Reference Data Program (Grant no. 10044282), Republic of Korea.

Compliance with Ethical Standards

Conflict of interest The author(s) declare that they have no competing interests.

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