Neuromonitoring for Intramedullary Spinal Cord Tumor Surgery

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Key words
- Intramedullary tumor
- Spinal injury
- Intraoperative monitoring
- Outcomes

Abbreviations and Acronyms

DCM: Dorsal column mapping
EMG: Electromyography
IMSCT: Intramedullary spinal cord tumors
IONM: Intraoperative neuromonitoring
MAP: Mean arterial pressure
MEP: Motor evoked potential
SSEP: Somatosensory evoked potential
TcMEP: Transcranial motor evoked potential

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BACKGROUND: **Intramedullary spinal cord tumors (IMSCT) account for about 2%—4% of tumors of the central nervous system. Surgical resection continues to be the most effective treatment modality for most intramedullary tumors, with gross total resection leading to preserved neurologic function and improved survival. However, surgical treatment is often difficult and carries significant risk of postoperative neurologic complications. Intraoperative neuromonitoring has been shown to be of clinical importance in the surgical resection of IMSCT. The main monitoring modalities include somatosensory evoked potentials, transcranial motor evoked potentials via limb muscles or spinal epidural space (D-waves), and dorsal column mapping. These monitoring modalities have been shown to inform surgeons intraoperatively and in many cases, have led to alterations in operative decision.**

METHODS: **We reviewed the literature on the usefulness of intraoperative neuromonitoring for intramedullary spinal tumor resection and its role in predicting postoperative neurologic deficits. A MEDLINE search was performed (2000—2015) and 13 studies were reviewed. Detailed information and data from the selected articles were assessed and compiled. Data were extracted showing the role of monitoring in outcomes of surgery.**

CONCLUSIONS: **By using intraoperative somatosensory evoked potentials, transcranial motor evoked potentials, D-waves, and dorsal column mapping, spinal injury could be prevented in most cases, thereby improving postoperative neurologic functioning and outcome in patients undergoing surgery for IMSCT.**

INTRODUCTION

Intramedullary spinal cord tumors (IMSCT) account for about 2%—4% of tumors of the central nervous system and about 15% of adult intradural tumors.[1-5] The most common IMSCT include ependymomas and astrocytomas. Unlike most brain tumors, these tumors are often benign and have an insidious onset, with presenting symptoms including paresthesia, weakness, spasticity, gait instability, and bowel/bladder dysfunction. Surgical resection continues to be the most effective treatment modality for most intramedullary tumors, with gross total resection leading to preserved neurologic function and improved survival.[2,6,7] However, surgical treatment is often difficult and carries significant risk of postoperative neurologic complications. Studies have reported deterioration in neurologic function in patients postoperatively,[4,8,9] with rates of dorsal column dysfunction as high as 43.6%—55.1%.[4,10,11] These deficits severely affect the postoperative functionality of patients because they are often left with significant morbidity, worse than their preoperative disease burden.[12-14] Part of the surgical difficulty stems from the inability to identify the appropriate resection plane to delineate the extent of resection. Also, the presence of tumor can distort the normal anatomic architecture of the spinal cord, making it difficult to ascertain the physiologic midline for a myelotomy. As a result of these surgical challenges, intraoperative neuromonitoring (IONM) has gained favorable grounds in facilitating maximal tumor resection and minimizing neurologic morbidity.[15-18]

IONM has been shown to be of clinical importance in the surgical resection of intramedullary spinal cord tumors.[17,19-24] The main monitoring modalities include somatosensory evoked potentials (SSEPs), transcranial motor evoked potentials (TcMEPs) via limb muscles or spinal epidural space (D-waves), and dorsal column mapping (DCM). SSEPs provide information about the functionality of sensory pathways. Despite earlier studies showing reduction of quadriplegia from 3.7% to 0%[25] and from 6.8% to 0.7%[26] using intraoperative SSEP monitoring, postoperative deficits were being reported regardless of the unchanged intraoperative SSEP.[27-30] As a result, TcMEP has been used as a direct method of monitoring motor pathways during surgery for intramedullary spinal tumor and other spinal diseases.[31-33] Consequently, the combined use of SSEP and motor evoked potential (MEP) provides increased accuracy in detecting injury to sensory and motor pathways that can be affected differently depending on the location and morphology of the tumor.[34,35] DCM using microstimulation and SSEP recording is another modality being used to determine anatomic landmarks such as the dorsal median sulcus to guide midline myelotomy. These monitoring modalities have been shown to inform surgeons intraoperatively and in many cases have led to alterations in operative decision. Herein, we reviewed the literature on the usefulness of IONM for intramedullary spinal tumor resection and its role in predicting postoperative neurologic deficits.

METHODS

The MEDLINE database was queried using the following search items: "intramedullary tumor", "spine", "spinal tumor", "monitoring", "neuromonitoring", "somatosensory evoked potential", "motor evoked potential", and "dorsal column mapping". Only articles in English published between 2000 and 2015 were considered. Publications excluded from our search were non-English articles, abstract-only publications, or articles not available via our electronic database queries. Individual case reports were also excluded. Articles were identified and reviewed. Detailed information and data from the selected articles were assessed and compiled.

RESULTS

After an extensive search for available articles, 13 studies were selected for inclusion in this review. Table 1 shows a summary of the relevant clinical studies and the intraoperative monitoring modalities and postoperative changes in neurologic status. One of the articles (study 1) was a historical control study in which patients who underwent surgery for intramedullary spinal tumor with intraoperative monitoring were matched and compared with previously operated patients without monitoring. Two of the articles (studies 5 and 6) were prospective and the remaining 10 studies were retrospective chart reviews. Full review was performed in all 13 articles. These were all clinical studies in which intraoperative neurophysiologic monitoring was used for the surgical resection of intramedullary spinal cord tumors. The number of patients ranged from a minimum of 12 (study 11) to a maximum of 203 (study 5). Among the patients in each study, intraoperative monitoring was successful in 12% of patients in study 2 and 100% of patients in studies 7, 8, and 11–13. MEP, SSEPs, and D-waves were also recorded in most of the studies. One study used DCM (study 2). In general, data collection is by an electrophysiologist under the supervision of a remote neurologist and reported to the primary surgeon responsible for making surgical decisions regarding intraoperative management. The level of experience of the individuals involved is unclear in the studies reviewed.

Two studies reported the sensitivity and specificity in predicting postoperative sensory deficits using SSEP only. In study 7, sensitivity and specificity were 75% and 50%, respectively, for SSEP, whereas in study 12, sensitivity and specificity were 80% and 100%, respectively, for SSEP only. TcMEP was more commonly reported. When the all-or-none criterion was used, the sensitivity/specificity of muscle or myogenic TcMEP only was reported as 95%/98.1% in study 5 and 53%/93% in study 13. When the criterion for a significant TcMEP was defined as greater than 70% deterioration in signal amplitude, the sensitivity increased from 53% (all-or-none criterion) to 79% and the specificity decreased from 93% (all-or-none criterion) to 49% in study 13. In using the combined approach of motor and sensory monitoring, study 7 showed an increase in sensitivity from 100% in MEP only and 75% in SSEP only to 100% in the combined approach. However, in the same study, there was a difference in specificity from 25% in MEP only and 50% in SSEP only to 28.5% in the combined approach. Similarly, in study 13, there was an increase in sensitivity from 80% in SEP and 75% in MEP to 100% in the combined approach, whereas the specificity decreased from 100% in both SEP and MEP to 83.3% when both approaches were combined. Thus, combining SSEP and MEP resulted in increased sensitivity with an overall decrease in specificity.

IONM accurately predicted postoperative outcome in all of the studies included. Sala et al.[17] (study 1) showed the importance of applied MEPs on postoperative neurologic outcomes using a historical control study. The study evaluated 100 patients who underwent surgery for intramedullary spinal tumor and compared the outcomes of patients who had intraoperative monitoring with D-waves or muscle MEP with those without monitoring. These investigators observed a significantly greater improvement in functional outcomes using the McCormick grade 3 months postoperatively in the patients who had intraoperative monitoring (mean, +0.28) compared with the historical cohort without monitoring (mean, −0.54; $P = 0.0016$). Another study (study 6) of 110 patients with spinal tumors (44, intramedullary; 66, extramedullary)[40] showed significantly better motor outcomes in patients with successful intraoperative monitoring during discharge from the hospital. In the same study, postoperative worsening of motor deficits was present in 8% of patients with TcMEP recording compared with 17.1% in patients without monitoring ($P = 0.052$). In addition, Mehta et al.[36] showed a 41% relative decrease in the rate of dorsal column dysfunction. Furthermore, Quinones et al.[37] showed that loss of MEP was associated with worst motor deficits postoperatively. In most of the studies, patients with significant changes in intraoperative monitoring had worse neurologic outcomes postoperatively. Therefore, use of IONM adequately predicted outcomes in patients undergoing surgery for IMSCT.

The extent of resection was also influenced by intraoperative neuromonitoring. Choi et al.[42] (study 9) showed that gross total resection was attainable in 76% of patients with IONM compared with 58% in patients without monitoring ($P = 0.049$). Skinner et al.[20] also indicated that that gross total resection without new postoperative deficits was successful only in patients with no significant change in intraoperative signals. For patients with notable change in signal who still received gross total resection, there were postoperative deficits, including hemiparesis, loss of proprioception, and worsening quadriparesis. This finding implies that the safety of tumor resection can be guided by neuromonitoring.

DISCUSSION

Surgical resection for intramedullary spinal tumors remains a challenging

Table 1. Summary of Clinical Studies Using Intraoperative Neurophysiologic Monitoring During Surgical Resection of Spinal Intramedullary Tumors

Study	Type	Total Number of Patients	Number of Patients with IONM	IMST/EMST	Modality of Interest	Surgical Intervention	Study Conclusions/Postoperative Outcome
1. Sala et al. (2006)[17]	H/C	100	50	100 IMST	mMEP and D-waves	Surgical field adjustment; warm irrigation, correct hypotension; abort surgery if loss of D-waves	Better improvement in McCormick grade at 3 months in the IONM group (mean, +0.28) vs. historical control group (mean, −0.54), $P = 0.0016$
2. Mehta et al. (2012)[36]	R	91	11	91 IMST	DCM and SSEP	—	Dorsal column dysfunction = 9% in patients with DCM and 50% in patients without DCM ($P = 0.01$)
3. Quinones-Hinojosa et al. (2005)[37]	R	28	27	28 IMST	MEP and SSEP	—	Loss of TcMEP waveform in 12 patients correlated with worse motor deficits compared with patients without loss of waveform ($P < 0.0001$)
4. Jin et al. (2015)[38]	R	30	25	30 IMST	mMEP and SSEP	—	1month postoperatively, all/none SEP-mMEP with fEMG Sensitivity/specificity = 100%/91% PPV/NPV = 60%/100% fEMG accurately predicted upcoming MEP events
5. Forster et al. (2012)[39]	P	203	47	50 IMST	MEP and SSEP	Resection halted; blood pressure increased; operative modifications	MEP (all or none): sensitivity = 95.0%; specificity = 98.1% in detecting motor deficits SSEP: sensitivity = 94.4%; specificity = 96.8% in detecting sensory deficits
6. Rajshekhar et al. (2011)[40]	P	110	75	44 IMST	mMEP	—	Postoperative worsening in 8% of patients with MEP recording vs. 17.1% in patients without MEP ($P = 0.052$)
7. Hyun et al. (2009)[34]	R	19	19	19 IMST	mMEP and SSEP	Temporarily halt; correct hypotension; change strategy to piecemeal resection; warm irrigation; steroids	MEP: sensitivity = 100%; specificity = 25% SSEP: sensitivity = 75%; specificity = 50% Combined MEP/SSEP: sensitivity = 100%; specificity = 28.5%
8. Ando et al. (2015)[41]	R	13	13	13 IMST	Sp-SCEP and Br-SCEP	Temporarily halt	Combined Br/Sp-SCEP Sensitivity and PPV = 66.7%; specificity and NPV = 90%
9. Choi et al. (2014)[42]	R	76	50	76 IMST	mMEP and SSEP	—	GTR rate was 76% in IONM group vs. 58% in non-IONM group ($P = 0.049$)
10. Costa et al. (2013)[23]	R	101	97	23 IMST	mMEP, D-waves, and SSEP	—	Presence of persistent stable D-waves (n = 13) predicted good motor outcome despite deterioration/loss in mMEPs
11. Cheng et al. (2014)[43]	R	12	12	12 IMST	mMEP and SSEP	Temporary halt; release traction	TcMEP Sensitivity = 80%; specificity = 71.4%; PPV = 66.7%; NPV = 83.3%

12. Skinner et al. (2005)[20]	R	13	13	13 IMST	mMEP and SSEP	Wake-up test; temporary halt; increase SBP; abort surgery	fEMG abnormality leads to anticipation of MEP loss and predicts postoperative motor deficits SEP: sensitivity = 80%; specificity = 100% TcMEP: sensitivity = 75%; specificity = 100% Combined SEP/MEP: sensitivity = 100%; specificity = 83.3% fEMG: sensitivity = 87.5%; specificity = 83.33%
13. Muramoto et al. (2014)[44]	R	13	13	13 IMST	mMEP	Temporary halt; warm irrigation; increase SBP; abort surgery with steroid administration	MEP (all-or-none criterion): sensitivity = 53%; specificity = 93% MEP (<70% criterion): sensitivity = 79%, specificity = 49%

IONM, intraoperative neuromonitoring; IMST, intramedullary spinal tumor; EMST, extramedullary spinal tumor; H/C, historical control; mMEP, muscle motor evoked potential; R, retrospective; DCM, dorsal column mapping; SSEP: somatosensory evoked potential; MEP: motor evoked potential; TcMEP: transcranial motor evoked potential; fEMG, free-running electromyography; P, prospective; PPV, positive predictive value; NPV, negative predictive value. Sp-SCEP, spinal cord evoked potentials; Br-SCEP, brain evoked potentials; GTR, gross total resection; SBP, systolic blood pressure.

operative dilemma and the extent of resection is often sacrificed for impending neurologic damage. Studies have reported transient and permanent neurologic impairment after resection of these tumors.[6,30] With the steady increase in microsurgical techniques, diagnostic imaging, and intraoperative monitoring modalities, there has been a decline in postoperative neurologic morbidities in patients undergoing surgery for intramedullary spinal tumors.[16,17,19-24] This situation has allowed for a more aggressive approach toward resection, aiming at maximizing resection and minimizing neurologic deficits.[2,45-47] Neurophysiologic monitoring not only guides the extent of resection but serves as a predictor of neurologic outcomes and, in many cases, provides critical information to the surgeon intraoperatively to alter the surgical approach and avoid spinal injury. We reviewed 13 studies and overall, changes in SSEP, TcMEP, and D-waves correlated with postoperative neurologic outcomes.

SSEP

SSEP monitors sensory pathways in the posterior column of the spinal cord. For SSEP monitoring, surface stimulating electrodes are mostly placed in bilateral extremities, usually the median nerve at the wrist and posterior tibial nerve at the ankle. The posterior tibial nerve, at the medial malleolus, is easily accessible for intraoperative stimulation and provides reliable data.[48] Monitoring of nerves in the upper and lower extremities allows for comparison and changes may indicate anesthesia-related effects or preoperative positioning effects as seen in brachial plexus injury.[49] Electric stimulation of varying frequency, amplitude, and duration is applied to the surface electrodes on the nerves. These signals are then acquired using continuous averaging of hundreds of consecutive sweeps of electric stimulation over several minutes and are repeatedly compared with initial baseline recordings normally made after incision. SSEP is then recorded from scalp electrodes, which provides cortical and subcortical data regarding the sensory pathways.[50] Because of the averaging of this SSEP signal, the amplitude and latency recordings from the scalp electrodes always lag behind real-time physiologic constraints by approximately 5–20 minutes.[51] Intraoperative changes in the amplitude of SSEP of greater than 50% and increase in latency of 10% compared with baseline values are typically considered abnormal.[52] Despite these studies showing the crucial role of IONM, false-negative results have been reported, especially when using SSEPs only, because some patients present with postoperative motor deficits. These isolated motor pathway–related injuries are not merely flaws of the SSEP monitoring modality but rather represent injuries outside the monitoring capability of SSEP. Combined modalities are increasingly being used to provide a broader coverage in avoiding neurologic injury.

TcMEP

TcMEP provides data on the descending corticospinal tracks by stimulation at the level of the cerebral cortex. Transcranial stimulation of the motor cortex is achieved via scalp electrodes. Stimulation can be magnetic through coils placed over the cortex[53] or electric stimulus via subdermal electrodes.[54] Peripheral data for TcMEP recordings can be obtained either from the end muscle via electromyography (EMG) or from the spinal cord via D-waves. Common muscles monitored include the tibialis anterior and abductor hallucis in the lower extremities and the abductor pollicis and extensor digitorum in the upper extremities.[19,24,42,55]

D-waves indicate corticospinal action potentials initiated by activation of fast axonal fibers with a velocity of approximately 50 m/second.[56,57] This conduction speed of the fast fibers makes it possible to monitor motor pathways in real time without any delays as seen in SSEP. Monitoring of D-waves is achieved by electrodes placed in the spinal epidural or subdural space, rostral and caudal to the tumor being resected.[8,58,59] This technique involves direct visualization of the dorsal epidural or subdural space during surgical exposure. A study of 16 patients undergoing cervical spinal fusion[60] showed that transcutaneous placement of the caudal epidural electrodes in the midthoracic level was also a safe and reliable approach to record MEP. The rostral electrode serves as the control because it detects signals from the cortex before being transmitted through the distorted tumor environment. Recordings from the caudal electrode are then compared with the rostral, and changes in peak-to-peak amplitude of D-waves by 50% or increase in latency by 10% were considered abnormal by most studies.[19,39,44] Some advantages of D-waves include less sensitivity to halogenated anesthetics, which could interfere with signal recordings in SSEP and muscle TcMEP.[61] In addition, neuromuscular blocking agents commonly used during surgical procedures do not affect D-wave recordings.[62] Also, because D-waves monitor the fast motor fibers, they are more sensitive in detecting early injury to the spine.

D-wave recording can also be achieved from ventral placement of the epidural or subdural electrodes during anterior cervical spine surgery.[63] A case report by Eicker et al.[63] showed successful ventral subdural electrode placement and recording of MEP in a 20 year-old patient with intramedullary cavernous malformation who underwent partial C2-corpectomy. Thus, ventral D-wave electrode placement can be safely accomplished with reliable MEP recordings in select cases of anterior cervical spine surgery.

Myogenic TcMEP recordings from extremity electrodes are derived from the same transcranial electric stimulation as D-waves. They indicate compound muscle action potentials and like D-waves are real time and do not require averaging. There are certain advantages of the muscle MEP over the D-waves. When measuring signals from the muscles, not only does this reflect functionality of the entire motor system, it helps delineate laterality. Given that D-waves monitor only corticospinal tract axons, recordings are not reliable below the level of T12 and conus tumors cannot be monitored with D-waves. Recordings from muscle electrodes make it possible to monitor lower sacral roots, including sphincter muscles. To determine which change in recorded signal from muscles is considered significant, some studies have used the all-or-nothing approach as a criterion for significant signal change intraoperatively.[29,64] Other studies have used a decrease in signal amplitude by more than 50% or 70% to indicate significant change from baseline.[17,34,38,44]

DCM

DCM is mainly performed to identify anatomic landmarks such as the dorsal median sulcus to guide a safe midline myelotomy. This procedure is useful in cases in which the tumor has distorted the normal spinal anatomy. Here, needle electrodes are placed in the lower extremities to capture data from peripheral nerves (eg, posterior tibial nerve at the medial malleolus). Microstimulation is applied around the margins of the tumor using a handheld bipolar electrode. The bipolar tip is placed on the dorsal aspect of the cord and stimulation is applied form lateral to medial. The physiologic midline is the region where there is complete absence of a response or the point of lowest relative amplitude in the sweep from lateral to medial. SSEP recordings acquired during the stimulation help determine the myelotomy site, identify the resection plane, and guide extent of resection.[36,43] DCM serves only as a guide to facilitate maximum resection with distorted tumor architecture and does not serve as a substitute for insufficient surgical experience.

Role of Neuromonitoring in Spinal Tumor Resection

This review highlights the critical role of intraoperative neurophysiologic monitoring during resection of intramedullary spinal tumors and how recorded data can affect management and predict neurologic outcomes. Overall, neuromonitoring was associated with prediction of postoperative functional outcomes, reduction in neurologic deficits, and guiding the extent of resection. We did not observe any differences in outcomes based on anatomic location of the spinal tumor.

Several studies have shown that no single modality sufficiently monitors all pathways in the spinal cord[24,65] with the goal of avoiding injury to both sensory and motor pathways.[48] By directly manipulating the spinal tracts during resection of infiltrating intramedullary tumors, there is a high risk of injury to both motor and sensory tracts. However, to circumvent the delayed acquisition in SSEP recordings caused by signal averaging, the use of TcMEP allows for real-time monitoring and feedback, thereby enabling surgeons to engage in immediate corrective actions before an injury to the spine becomes irreversible.

Studies[16,17,66] have reported that with less than 50% change in D-wave amplitude even with complete loss of TcMEP from muscle electrodes, there is only transient paraplegia, with most patients achieving full recovery within hours to weeks postoperative. Intraoperative loss of D-waves results in permanent paraplegia postoperatively.[16,17] Thus D-wave is a highly specific predictor of postoperative motor deficits. Changes in D-wave amplitude/latency directly signify change in signal transduction of the fast action fibers in the corticospinal tract rather than in the muscle. Therefore when available, D-wave recording should be used, because it provides a better predictive value of postoperative outcome.

The all-or-nothing approach to TcMEP monitoring presents inherent dangers to the spinal cord during tumor resection. Despite studies advocating for the all-or-nothing rule because of the difficulties in establishing threshold amplitude,[16,39] there is potential increased risk of injury to the spine with this modality. Decreasing the threshold to 75% or 50% increases the sensitivity and decreases the specificity but allows for early detection of injury before complete loss of signal. Skinner et al.[20] showed that abnormality in free-running EMG leads to anticipation of TcMEP deterioration and predicted postoperative motor deficits with a sensitivity of 87.5% and specificity of 83.3%. Therefore, in the absence of the more predictive D-waves, free-running EMG can be an adjunct to MEP in detecting early and continuous signal change. Awaiting a complete loss of TcMEP to alter surgical decision (as in the all-or-none rule) can be detrimental to the patient.

DCM can also provide additional surgical benefit. The study by Mehta et al.[36] of 91 patients undergoing surgery for intramedullary tumor showed a significant decrease in rate of postoperative dorsal column dysfunction, from 50% in patients without mapping to 9% in patients with intraoperative DCM. Mapping facilitates localization of the anatomic midline in diffusely infiltrative tumors with distortion of spinal architecture. DCM helps in identification of the operative tumor/spinal cord plane and guides the extent of resection with the goal of maximum tumor resection with minimal neurologic morbidity.

Combination of Neuromonitoring Methodologies

The combined monitoring approach allows the surgeons to sample a broader range of the spinal tracts to detect injury. However, there are variations in the sensitivity and specificity when SSEP and MEP are combined, with a trend toward increased sensitivity and decreased specificity. This is partly because of differences in tumor anatomy, location and architecture, the extent of infiltration, and the threshold for signal change. Because more IMSCTs are approached dorsally, there is a higher risk of damage to sensory fibers, resulting in changes in SSEP signals. Regardless, the combination of SSEP and MEP should be carefully interpreted to avoid high false-positive and false-negative results. With increased sensitivity, there are more intraoperative signal changes with no corresponding postoperative neurologic deficits. This situation results in premature termination of the surgical procedure, thus precluding complete tumor resection. Likewise, with decreased specificity, there is the imminent risk of damage to the spinal cord before signal change is noted. The potential for erroneous information should be evaluated by the surgeon preoperatively, in deciding the optimum threshold for signal deterioration to maximize specificity. Also, based on the tumor location, more emphasis could be placed on one modality over another. Modalities that have increased the accuracy in depicting signal change include the use of free-running EMG and the addition of D-waves to motor mapping. Free-running EMG is crucial in detecting early abnormalities before detection by MEP threshold. Regarding D-waves, studies have shown that when combined with MEP recording, D-waves are more accurate in predicting postoperative outcomes. Despite studies showing the importance of muscle MEP in predicting postoperative deficits,[17,37,59] there are several false-positive results, which may be minimized only by using the D-wave monitoring. A study by Kothbauer et al.[16] showed that for patients with a complete loss of MEP, postoperative neurologic deficit corresponded only to changes in D-waves. In the event of a <50% loss in D-wave amplitude, there was no postoperative deficit. However, if D-wave amplitude declined by >50% from the baseline, patients were permanently paraplegic. Thus, when available, affordable, and appropriate, D-wave monitoring should be encouraged in monitoring motor pathways to decrease false-positive results and maximize resection. However, without D-waves, muscle MEP has been shown to be better than preoperative motor status in predicting postoperative functional outcomes.[59]

The extent of resection remains a crucial component of spine tumor surgeries. Kothbauer et al.[16] reported that gross total resection was aborted when MEP deteriorated and reattempted during a second surgery. Choi et al.[42] showed the benefits of neuromonitoring in gross total resection. Skinner et al.[20] reported that significant changes in intraoperative signal predict outcomes after gross total resection. Surgeons should include in the goals of surgery discussion about the risks and benefits of gross total resection and what the threshold for signal change should be to terminate the procedure.

Not all methods should be used for each case of IMSCT surgery. This review shows the variability in sensitivity and specificity and it is at the discretion of the surgeon to use different modalities based on the tumor anatomy, preoperative functional status, overall goals of surgery, and technological availability at practicing centers. If the goal of surgery is to prevent motor deficits, then, the single use of MEP would adequately predict outcome. Likewise, if the tumor mostly involves the dorsal aspect of the cord and the goal is to preserve sensory function, then, SSEP alone could be used. These decisions should be carefully evaluated preoperatively, including discussion with the patient regarding the overall goals of care. These modalities are not meant to replace the surgeon's intraoperative tumor resection skills but to enhance maximum possible resection with minimum neurologic deficits. In addition, determination of the threshold for signal change is surgeon dependent and plays a role in false-positive and false-negative results. Therefore, surgeons should select monitoring modalities appropriately based on their experience to maximize tumor resection and minimize postoperative deficits.

Intraoperative Intervention When Signal Deteriorates

One critical role of intraoperative monitoring is the effect on operative decisions. Once changes in recorded amplitude of SSEP, muscle MEP, or D-waves are deemed significantly worse, a decision has to be made by the surgeon whether to abort the procedure, change surgical approach, or execute other intraoperative measures and later resume tumor resection. In the immediate period after a loss in MEP or deteriorating SSEP during resection of intramedullary tumors of the spine, 3 key factors have been identified to promote signal recovery and improve outcome: time, irrigation, and blood pressure.[24,34,67-69] By temporarily halting the surgical resection with continuous monitoring of neurophysiologic parameters, surgeons can obtain real-time data as to the degree of injury to the spinal cord and if further manipulations are possible.[24] Despite the paucity of data on the exact wait time, the general trend was to immediately suspend the surgical resection and release retractors and continue SSEP and TcMEP monitoring until signals return to below critical levels. Sala et al.[19] reported transiently stopping surgery for about 30 minutes or more to allow signals from TcMEP and D-waves to return to less than critical levels before further manipulating the cord. Recovery of signal often leads to continuation of the tumor resection. Thirty minutes of wait time is a considerably long duration in spinal procedures that last approximately 2–4 hours and thus leads to increased operating room time and associated cost. However, we believe that the benefits of increased duration of surgery, as a result of awaiting return of signal, outweighs the postoperative management of permanent neurologic deficits caused by spinal cord injury. Nonetheless, it remains unclear what the optimum wait time should be in the event of a loss in signal recording. Continuous deterioration of signal or complete loss for an extended period may lead to aborting the procedure entirely. Therefore, a transient halt in tumor resection and releasing retraction from the surgical bed could be the most critical variable in affecting recovery and postoperative outcome. The second factor is irrigation of the surgical field with warm saline solution, which dilutes accumulated potassium in the extracellular matrix, thereby preventing blockage of nerve impulse transmission. Furthermore, irrigation clears out residual blood products and cellular metabolites.[67,68] The third factor is increasing mean arterial blood pressure to enhance local perfusion of the spinal cord and prevent ischemia. Several studies[20,34,48,70] have reported favorable neurologic outcomes when mean arterial blood pressure was increased in the event of decreasing intraoperative monitoring signals. Hyun et al.[34] increased mean arterial pressure (MAP) to 91 mm Hg to facilitate increased blood flow to the spinal cord. Another study by Choi et al.[42] reported that increasing the MAP to at least 60 mm Hg facilitated recovery. Despite the absence of a consensus in the reviewed literature on optimum parameters for MAP, the trend continues to be toward MAP increase from intraoperative baseline during signal loss. Overall, these 3 intraoperative measures are often used in combination and are targeted toward recovery of spinal cord signal, minimizing neurologic injury to resume maximum possible resection of the intramedullary tumor.

Another measure to decrease spinal cord injury is the administration of steroids preoperatively. All the patients in the study by Mehta et al.[36] were administered steroids before surgical resection. High-dose intravenous corticosteroids may improve transient neurologic function by reducing inflammation and vasogenic edema around the tumor, thereby relieving the spinal cord from the compressive effects of the tumor. Experimental studies on laboratory animals have shown that early delivery of methylprednisolone after acute traumatic spinal cord injury can be beneficial, with larger animals having more favorable outcomes.[71-74] However, the role of steroids after spinal cord injury in humans is still highly controversial. Although not reported by most studies, preoperative steroid administration is a common therapeutic adjunct in patients undergoing surgery for intramedullary spinal tumor to avoid intraoperative swelling. Only 2 studies (studies 3 and 7) reported corticosteroid administration intraoperatively once surgery was stopped because of loss of TcMEP from multiple muscles. Without standard treatment protocols, it remains at the discretion of the surgeon whether to administer intraoperative corticosteroids when injury to the spinal cord is suspected.

CONCLUSIONS

IONM using modalities including DCM, SSEP, muscle TcMEP, and D-waves (or a combination thereof) provides surgeons with anatomic landmarks for midline myelotomy, indications of the resection plane, and guidance to the extent of maximum tumor resection with minimal neurologic morbidity. Studies continue to show favorable postoperative outcomes when these monitoring modalities are used in combination. However, combining modalities leads to variability in false-positive and false-negative results and should be evaluated with care. Reports of intraoperative factors such as time, irrigation, and blood pressure optimization to facilitate recovery from a lost intraoperative signal remain promising as means of mitigating neurologic injury. Cost, access, and availability of the technology, resources, and personnel for IONM present a challenge for some medical centers. Not all intramedullary tumor cases are performed with IONM. It is not standard of care to use IONM for IMSCT surgery. Nonetheless, the data suggest that patients with IONM have better postoperative outcomes. Therefore, larger multicenter randomized controlled studies are needed to determine standardized treatment protocols in the event of a loss in intraoperative SSEP or TcMEP during surgery for spinal intramedullary tumor.

REFERENCES

1. Brotchi J. Intrinsic spinal cord tumor resection. *Neurosurgery*. 2002;50:1059-1063.

2. Constantini S, Miller DC, Allen JC, Rorke LB, Freed D, Epstein FJ. Radical excision of intramedullary spinal cord tumors: surgical morbidity and long-term follow-up evaluation in 164 children and young adults. *J Neurosurg*. 2000;93: 183-193.

3. Hanbali F, Fourney DR, Marmor E, Suki D, Rhines LD, Weinberg JS, et al. Spinal cord ependymoma: radical surgical resection and outcome. *Neurosurgery*. 2002;51:1162-1172 [discussion: 72-74].

4. Cristante L, Herrmann HD. Surgical management of intramedullary spinal cord tumors: functional outcome and sources of morbidity. *Neurosurgery*. 1994;35:69-74 [discussion: 74-76].

5. McCormick PC, Torres R, Post KD, Stein BM. Intramedullary ependymoma of the spinal cord. *J Neurosurg*. 1990;72:523-532.

6. Epstein FJ, Farmer JP, Freed D. Adult intramedullary spinal cord ependymomas: the result of surgery in 38 patients. *J Neurosurg*. 1993;79: 204-209.

7. Guidetti B, Mercuri S, Vagnozzi R. Long-term results of the surgical treatment of 129 intramedullary spinal gliomas. *J Neurosurg*. 1981;54: 323-330.

8. Jallo GI, Kothbauer KF, Epstein FJ. Intrinsic spinal cord tumor resection. *Neurosurgery*. 2001;49: 1124-1128.

9. Schwartz TH, McCormick PC. Intramedullary ependymomas: clinical presentation, surgical treatment strategies and prognosis. *J Neurooncol*. 2000;47:211-218.

10. Manzano G, Green BA, Vanni S, Levi AD. Contemporary management of adult intramedullary spinal tumors-pathology and neurological outcomes related to surgical resection. *Spinal Cord*. 2008;46:540-546.

11. Sandalcioglu IE, Gasser T, Asgari S, Lazorisak A, Engelhorn T, Egelhof T, et al. Functional outcome after surgical treatment of intramedullary spinal cord tumors: experience with 78 patients. *Spinal Cord*. 2005;43:34-41.

12. Yang S, Yang X, Hong G. Surgical treatment of one hundred seventy-four intramedullary spinal cord tumors. *Spine*. 2009;34:2705-2710.

13. Yanni DS, Ulkatan S, Deletis V, Barrenechea IJ, Sen C, Perin NI. Utility of neurophysiological monitoring using dorsal column mapping in intramedullary spinal cord surgery. *J Neurosurg Spine*. 2010;12:623-628.

14. Quinones-Hinojosa A, Gulati M, Lyon R, Gupta N, Yingling C. Spinal cord mapping as an adjunct for resection of intramedullary tumors: surgical technique with case illustrations. *Neurosurgery*. 2002;51:1199-1206 [discussion: 1206-1207].

15. Ney JP, van der Goes DN. Evidence-based guideline update: intraoperative spinal monitoring with somatosensory and transcranial electrical motor evoked potentials. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the American Clinical Neurophysiology Society. *Neurology*. 2012;79:292 [author replies 292-294].

16. Kothbauer KF, Deletis V, Epstein FJ. Motor-evoked potential monitoring for intramedullary spinal cord tumor surgery: correlation of clinical and neurophysiological data in a series of 100 consecutive procedures. *Neurosurg Focus*. 1998;4:e1.

17. Sala F, Palandri G, Basso E, Lanteri P, Deletis V, Faccioli F, et al. Motor evoked potential monitoring improves outcome after surgery for intramedullary spinal cord tumors: a historical control study. *Neurosurgery*. 2006;58:1129-1143 [discussion: 1129-1143].

18. Nuwer MR, Emerson RG, Galloway G, Legatt AD, Lopez J, Minahan R, et al. Evidence-based guideline update: intraoperative spinal monitoring with somatosensory and transcranial electrical motor evoked potentials: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the American Clinical Neurophysiology Society. *Neurology*. 2012;78:585-589.

19. Sala F, Bricolo A, Faccioli F, Lanteri P, Gerosa M. Surgery for intramedullary spinal cord tumors: the role of intraoperative (neurophysiological) monitoring. *Eur Spine J*. 2007;(16 Suppl 2):S130-S139.

20. Skinner SA, Nagib M, Bergman TA, Maxwell RE, Msangi G. The initial use of free-running electromyography to detect early motor tract injury during resection of intramedullary spinal cord lesions. *Neurosurgery*. 2005;56:299-314 [discussion: 299-314].

21. Kothbauer KF. Intraoperative neurophysiologic monitoring for intramedullary spinal-cord tumor surgery. *Neurophysiol Clin*. 2007;37:407-414.

22. Matsuyama Y, Sakai Y, Katayama Y, Imagama S, Ito Z, Wakao N, et al. Indirect posterior decompression with corrective fusion for ossification of the posterior longitudinal ligament of the thoracic spine: is it possible to predict the surgical results? *Eur Spine J*. 2009;18:943-948.

23. Costa P, Peretta P, Faccani G. Relevance of intraoperative D wave in spine and spinal cord surgeries. *Eur Spine J*. 2013;22:840-848.

24. Deletis V, Sala F. Intraoperative neurophysiological monitoring of the spinal cord during spinal cord and spine surgery: a review focus on the corticospinal tracts. *Clin Neurophysiol*. 2008;119: 248-264.

25. Epstein NE, Danto J, Nardi D. Evaluation of intraoperative somatosensory-evoked potential monitoring during 100 cervical operations. *Spine*. 1993;18:737-747.

26. Meyer PR Jr, Cotler HB, Gireesan GT. Operative neurological complications resulting from thoracic and lumbar spine internal fixation. *Clin Orthop Relat Res*. 1988;237:125-131.

27. Jones SJ, Buonamassa S, Crockard HA. Two cases of quadriparesis following anterior cervical discectomy, with normal perioperative somatosensory evoked potentials. *J Neurol Neurosurg Psychiatry*. 2003;74:273-276.

28. Lesser RP, Raudzens P, Luders H, Nuwer MR, Goldie WD, Morris HH 3rd, et al. Postoperative neurological deficits may occur despite unchanged intraoperative somatosensory evoked potentials. *Ann Neurol*. 1986;19:22-25.

29. Lang EW, Chesnut RM, Beutler AS, Kennelly NA, Renaudin JW. The utility of motor-evoked potential monitoring during intramedullary surgery. *Anesth Analg*. 1996;83:1337-1341.

30. Zileli M, Coskun E, Ozdamar N, Ovul I, Tuncbay E, Oner K, et al. Surgery of intramedullary spinal cord tumors. *Eur Spine J*. 1996;5: 243-250.

31. MacDonald DB, Al Zayed Z, Khoudeir I, Stigsby B. Monitoring scoliosis surgery with combined multiple pulse transcranial electric motor and cortical somatosensory-evoked potentials from the lower and upper extremities. *Spine*. 2003;28:194-203.

32. DiCindio S, Theroux M, Shah S, Miller F, Dabney K, Brislin RP, et al. Multimodality monitoring of transcranial electric motor and somatosensory-evoked potentials during surgical correction of spinal deformity in patients with cerebral palsy and other neuromuscular disorders. *Spine*. 2003;28:1851-1855 [discussion: 1855-1856].

33. Hilibrand AS, Schwartz DM, Sethuraman V, Vaccaro AR, Albert TJ. Comparison of transcranial electric motor and somatosensory evoked potential monitoring during cervical spine surgery. *J Bone Joint Surg Am*. 2004;86-A:1248-1253.

34. Hyun SJ, Rhim SC. Combined motor and somatosensory evoked potential monitoring for intramedullary spinal cord tumor surgery: correlation of clinical and neurophysiological data in 17 consecutive procedures. *Br J Neurosurg*. 2009;23: 393-400.

35. Pelosi L, Lamb J, Grevitt M, Mehdian SM, Webb JK, Blumhardt LD. Combined monitoring of motor and somatosensory evoked potentials in orthopaedic spinal surgery. *Clin Neurophysiol*. 2002; 113:1082-1091.

36. Mehta AI, Mohrhaus CA, Husain AM, Karikari IO, Hughes B, Hodges T, et al. Dorsal column mapping for intramedullary spinal cord tumor resection decreases dorsal column dysfunction. *J Spinal Disord Tech*. 2012;25:205-209.

37. Quinones-Hinojosa A, Lyon R, Zada G, Lamborn KR, Gupta N, Parsa AT, et al. Changes in transcranial motor evoked potentials during intramedullary spinal cord tumor resection correlate with postoperative motor function. *Neurosurgery*. 2005;56:982-993 [discussion: 982-993].

38. Jin SH, Chung CK, Kim CH, Choi YD, Kwak G, Kim BE. Multimodal intraoperative monitoring during intramedullary spinal cord tumor surgery. *Acta Neurochir (Wien)*. 2015;157:2149-2155.

39. Forster MT, Marquardt G, Seifert V, Szelenyi A. Spinal cord tumor surgery—importance of continuous intraoperative neurophysiological monitoring after tumor resection. *Spine*. 2012;37: E1001-E1008.

40. Rajshekhar V, Velayutham P, Joseph M, Babu KS. Factors predicting the feasibility of monitoring lower-limb muscle motor evoked potentials in patients undergoing excision of spinal cord tumors. *J Neurosurg Spine*. 2011;14:748-753.

41. Ando M, Tamaki T, Yoshida M, Kawakami M, Kubota S, Nakagawa Y, et al. Intraoperative spinal cord monitoring using combined motor and sensory evoked potentials recorded from the spinal cord during surgery for intramedullary spinal cord tumor. *Clin Neurol Neurosurg*. 2015;133:18-23.

42. Choi I, Hyun SJ, Kang JK, Rhim SC. Combined muscle motor and somatosensory evoked potentials for intramedullary spinal cord tumour surgery. *Yonsei Med J*. 2014;55:1063-1071.

43. Cheng JS, Ivan ME, Stapleton CJ, A Quinones-Hinojosa, Gupta N, Auguste KI. Intraoperative changes in transcranial motor evoked potentials and somatosensory evoked potentials predicting outcome in children with intramedullary spinal cord tumors. *J Neurosurg Pediatr*. 2014;13:591-599.

44. Muramoto A, Imagama S, Ito Z, Ando K, Tauchi R, Matsumoto T, et al. The cutoff amplitude of transcranial motor evoked potentials for transient postoperative motor deficits in intramedullary spinal cord tumor surgery. *Spine*. 2014; 39:E1086-E1094.

45. Iwasaki Y, Hida K, Sawamura Y, Abe H. Spinal intramedullary ependymomas: surgical results and immunohistochemical analysis of tumour proliferation activity. *Br J Neurosurg*. 2000;14: 331-336.

46. Xu QW, Bao WM, Mao RL, Yang GY. Aggressive surgery for intramedullary tumor of cervical spinal cord. *Surg Neurol*. 1996;46:322-328.

47. Shrivastava RK, Epstein FJ, Perin NI, Post KD, Jallo GI. Intramedullary spinal cord tumors in patients older than 50 years of age: management and outcome analysis. *J Neurosurg Spine*. 2005;2: 249-255.

48. Owen JH. The application of intraoperative monitoring during surgery for spinal deformity. *Spine*. 1999;24:2649-2662.

49. Labrom RD, Hoskins M, Reilly CW, Tredwell SJ, Wong PK. Clinical usefulness of somatosensory evoked potentials for detection of brachial plexopathy secondary to malpositioning in scoliosis surgery. *Spine*. 2005;30:2089-2093.

50. Mendiratta A, Emerson RG. Neurophysiologic intraoperative monitoring of scoliosis surgery. *J Clin Neurophysiol*. 2009;26:62-69.

51. Schwartz DM, Auerbach JD, Dormans JP, Flynn J, Drummond DS, Bowe JA, et al. Neurophysiological detection of impending spinal cord injury during scoliosis surgery. *J Bone Joint Surg Am*. 2007; 89:2440-2449.

52. Dawson EG, Sherman JE, Kanim LE, Nuwer MR. Spinal cord monitoring. Results of the Scoliosis Research Society and the European Spinal Deformity Society survey. *Spine*. 1991;16:S361-S364.

53. Gugino LD, Romero JR, Aglio L, Titone D, Ramirez M, Pascual-Leone A, et al. Transcranial magnetic stimulation coregistered with MRI: a comparison of a guided versus blind stimulation technique and its effect on evoked compound muscle action potentials. *Clin Neurophysiol*. 2001; 112:1781-1792.

54. Calancie B, Harris W, Broton JG, Alexeeva N, Green BA. "Threshold-level" multipulse transcranial electrical stimulation of motor cortex for intraoperative monitoring of spinal motor tracts: description of method and comparison to somatosensory evoked potential monitoring. *J Neurosurg*. 1998;88:457-470.

55. Taniguchi M, Cedzich C, Schramm J. Modification of cortical stimulation for motor evoked potentials under general anesthesia: technical description. *Neurosurgery*. 1993;32:219-226.

56. Macdonald DB, Skinner S, Shils J, Yingling C, American M. society of Neurophysiological. Intraoperative motor evoked potential monitoring—a position statement by the American Society of Neurophysiological Monitoring. *Clin Neurophysiol*. 2013;124:2291-2316.

57. Park JH, Hyun SJ. Intraoperative neurophysiological monitoring in spinal surgery. *World J Clin Cases*. 2015;3:765-773.

58. Kothbauer K, Deletis V, Epstein FJ. Intraoperative spinal cord monitoring for intramedullary surgery: an essential adjunct. *Pediatr Neurosurg*. 1997;26: 247-254.

59. Morota N, Deletis V, Constantini S, Kofler M, Cohen H, Epstein FJ. The role of motor evoked potentials during surgery for intramedullary spinal cord tumors. *Neurosurgery*. 1997;41:1327-1336.

60. Gokaslan ZL, Samudrala S, Deletis V, Wildrick DM, Cooper PR. Intraoperative monitoring of spinal cord function using motor evoked potentials via transcutaneous epidural electrode during anterior cervical spinal surgery. *J Spinal Disord*. 1997;10:299-303.

61. Sloan TB, Heyer EJ. Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord. *J Clin Neurophysiol*. 2002;19:430-443.

62. Malhotra NR, Shaffrey CI. Intraoperative electrophysiological monitoring in spine surgery. *Spine*. 2010;35:2167-2179.

63. Eicker SO, Szelenyi A, Mathys C, Steiger HJ, Hanggi D. Custom-tailored minimally invasive partial C2-corpectomy for ventrally located intramedullary cavernous malformation. *Neurosurg Rev*. 2013;36:487-491.

64. Dong CC, MacDonald DB, Janusz MT. Intraoperative spinal cord monitoring during descending thoracic and thoracoabdominal aneurysm surgery. *Ann Thorac Surg*. 2002;74: S1873-S1876 [discussion S92-S98].

65. Eggspuehler A, Sutter MA, Grob D, Jeszenszky D, Dvorak J. Multimodal intraoperative monitoring during surgery of spinal deformities in 217 patients. *Eur Spine J*. 2007;16(suppl 2):S188-S196.

66. Kearse LA Jr, Lopez-Bresnahan M, McPeck K, Tambe V. Loss of somatosensory evoked potentials during intramedullary spinal cord surgery predicts postoperative neurologic deficits in motor function [corrected]. *J Clin Anesth*. 1993;5: 392-398.

67. Young W, Rosenbluth J, Wojak JC, Sakatani K, Kim H. Extracellular potassium activity and axonal conduction in spinal cord of the myelin-deficient mutant rat. *Exp Neurol*. 1989;106:41-51.

68. Young W, Koreh I. Potassium and calcium changes in injured spinal cords. *Brain Res*. 1986; 365:42-53.

69. Sala F, Lanteri P, Bricolo A. Motor evoked potential monitoring for spinal cord and brain stem surgery. *Adv Tech Stand Neurosurg*. 2004;29:133-169.

70. Polo A, Tercedor A, Paniagua-Soto J, Acosta F, Canadas A. [Neurophysiological monitoring during scoliosis surgery using controlled hypotension]. *Rev Esp Anestesiol Reanim*. 2000;47:367-370 [in Spanish].

71. Akhtar AZ, Pippin JJ, Sandusky CB. Animal studies in spinal cord injury: a systematic review of methylprednisolone. *Altern Lab Anim*. 2009;37: 43-62.

72. Taoka Y, Okajima K, Uchiba M, Johno M. Methylprednisolone reduces spinal cord injury in rats without affecting tumor necrosis factor-alpha production. *J Neurotrauma*. 2001;18:533-543.

73. Chikawa T, Ikata T, Katoh S, Hamada Y, Kogure K, Fukuzawa K. Preventive effects of lecithinized superoxide dismutase and methylprednisolone on spinal cord injury in rats: transcriptional regulation of inflammatory and neurotrophic genes. *J Neurotrauma*. 2001;18:93-103.

74. Harrop JS. Spinal cord injury: debating the efficacy of methylprednisolone. *Neurosurgery*. 2014; 61(suppl 1):30-31.

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