



Benefits and Risks of Intraoperative Neuromonitoring for Intramedullary Spinal Cord Tumors: A Technical Report

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ABSTRACT

Intramedullary spinal cord tumors (IMSCT) are a rare condition that can have adverse effects on both the sensory and motor tracts, as well as the gray and white matter of the spinal cord. One type of IMSCT, known as ependymomas, is typically seen in adults, and is characterized by an enhancing mass with clear borders extending outward from the central canal's ependymal lining. In this study, over 800 patients have undergone intramedullary spinal cord tumor surgeries with intraoperative neurophysiological monitoring (IONM), and the majority have successfully overcome any postoperative deficits.

Multimodal IONM techniques, such as Somatosensory Evoked Potentials (SSEPs), Motor Evoked Potentials (MEPs), Epidural recordings (D-waves), Electromyography (EMG), Bulbocavernosus Reflex (BCR), and Train of Four (TOF), were used to monitor the procedures. While intramedullary spinal tumors can be challenging to treat, early surgery can lead to better outcomes. Intraoperative modalities like D-waves and MEPs have shown promise in reducing neurological outcomes, but more research is needed to understand their effectiveness fully.

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INTRODUCTION

Intramedullary spinal cord tumors (IMSCT) are a rare type of central nervous system tumor, accounting for only 2-4% of cases (Figure 1,2). These tumors pose a significant risk to neurological function, particularly affecting sensory and motor tracts. Both gray and white matter can be adversely affected, as noted by Yanni et al. [1]. in 2010. In children, astrocytoma is a type of IMSCT originating from astrocytes and can affect the brain and spinal cord. It is mostly found at the thoracic level and accounts for 40-60% of pediatric tumors,

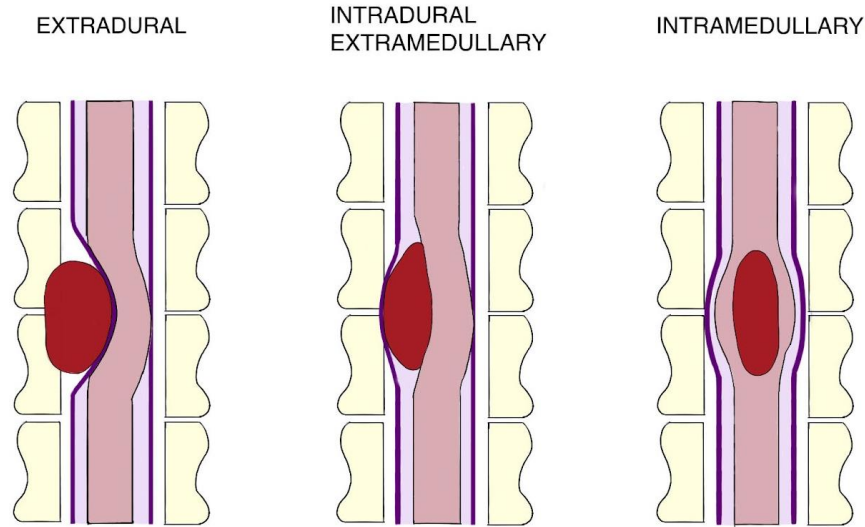


Figure 1. Spinal cord tumors are distinguished based on their location into the following categories: extradural, intradural extramedullary, and intramedullary (illustrations by Lily Nguyen).

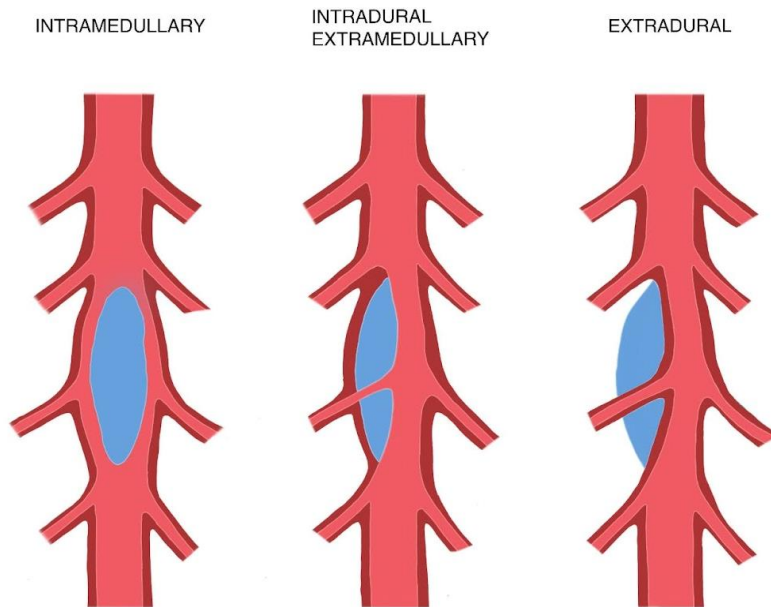


Figure 2. Spinal cord tumors are distinguished based on their location into the following categories: extradural, intradural extramedullary, and intramedullary (illustrations by Lily Nguyen).

according to Luksik et al. in 2017 [2]. Despite aggressive treatments, children with IMSCT tumors continue to have a poor prognosis. Ependymomas, another type of IMSCT, are commonly found in adults and often in the lower cord, conus, and film. Magnetic resonance imaging (MRI) can help to identify ependymoma tumors, which typically appear as an enhancing mass with well-defined margins expanding outward from the ependymal lining of the central canal (Figure 3). Pain is a common presenting symptom for both

ependymoma and astrocytoma, as IMSCT tumors expand the spinal cord parenchyma rather than displace it (Figure 4).

IONM has proven effective in the treatment and management of IMSCT. Multimodality protocols encompass a range of techniques, such as dorsal column mapping, intramedullary motor mapping, Somatosensory Evoked Potentials (SSEPs), Motor Evoked Potentials (MEPs), Epidural recordings (D-waves), Electromyography (EMG), Bulbocavernosus Reflex (BCR), and Train of Four (TOF).



Figure 3. Magnetic Resonance Imaging (MRI) of the cervical spine showing spinal cord tumor [3].

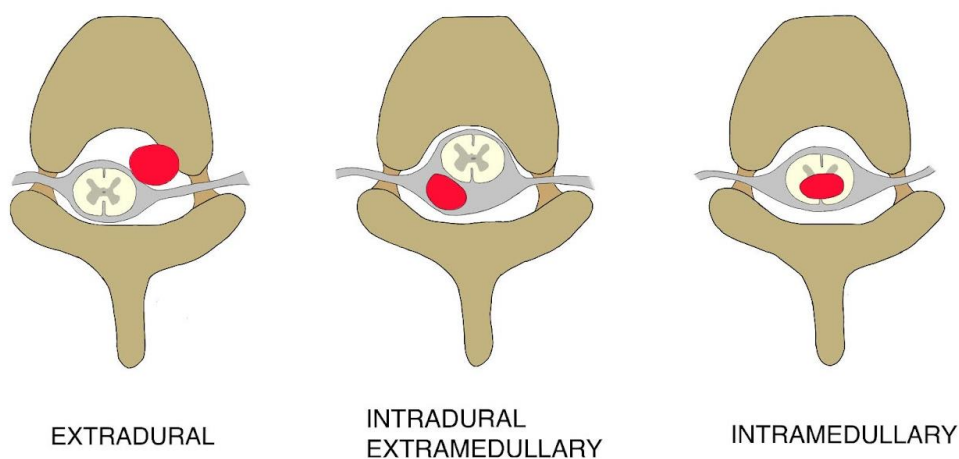


Figure 4. Cross-sectional diagram featuring anatomical locations of spinal cord tumors (illustration by Lily Nguyen).

METHODS

Search Criteria: Inclusion & Exclusion

We conducted a thorough study using PubMed and scholarly articles to investigate intramedullary spinal cord mapping and techniques. Our selection criteria for this meta-analysis encompassed all IONM modalities, including SSEP, MEP, D-waves, TOF, and others, along with their sensitivity and specificity in different neuromonitoring modalities and mapping techniques [4]. Our exclusion criteria consisted of tumor locations, resections, abnormalities in the postoperative stage, neurological injuries, and other relevant factors.

Study Population

The study by Lakomkin et al. in 2017 involved patients aged 30 to 76, comprising both males and females. Patients under the age of 18 were also included in astrocytoma mapping. The researchers gathered various patient data points, such as demographics, tumor size, pathology, operative time, surgical procedure, immune status, and postoperative spinal nerve function [5].

Patient Selection Data

After a thorough analysis, the researchers carefully handpicked patient data using several criteria such as gender, age, operation techniques, time of surgery, and postoperative outcomes, as documented by Cheng et al. (2014), Lakomkin et al. (2017), and Sala et al. (2007). The follow-up period was 3-6 months, as indicated by the same sources [4-6].

Anesthesia

All surgeries are performed under the surgical anesthesia of intravenous infusion of propofol and fentanyl. During the surgery, all the muscles and nerve functions were monitored by an assistant surgeon [6]. No muscle relaxants were used after intubation.

Intraoperative Neurophysiological Monitoring (IONM)

Somatosensory Evoked Potentials (SSEPs)

The ulnar, posterior tibial, and pudendal nerves SSEPs were carefully observed during the monitoring process. The ulnar nerve was stimulated with an intensity of 15-25 mA, while the pudendal and posterior tibial nerves were stimulated with an intensity of 40-100 mA. The parameters used included a duration of 0.3 msec, a 30-1000 Hz filter range, and a 2.66-4.79 Hz repetition rate. Subdermal needle electrodes were used for recording, and surface adhesive electrodes were used for nerve stimulation. To ensure accuracy, warning criteria were set at a 50% drop in amplitude and a 10% prolongation in latency. The recording sites

were placed on the scalp according to the international 10-20 system, the 5th cervical spine, Erb's point, and the popliteal fossa.

Motor Evoked Potentials (MEPs)

During the stimulation process, corkscrew electrodes were utilized, while subdermal needle electrodes were used for recording. The primary motor cortex sites targeted for stimulation were the right and left sides (C1/C2, C3/C4 based on the international 10-20 system). To record the results, electrodes were placed in various muscles such as APB/ADM in the hand, adductor brevis, quadriceps, tibialis anterior, gastrocnemius, abductor hallucis muscles in the foot, and anal sphincter and urinary sphincter muscles. The parameters for the process included a width of 50 or 75 μ s, sweeps of 100-200 ms, high voltage ranging from 80-500 V, pulse train of 3-7, and filter setting at 30-30000 Hz. Notably, a 70-80% drop in amplitude, change in morphology, or an increase of threshold above 100 Volts will trigger a warning criterion.

D-Wave

This is an epidurally recorded MEP that was obtained through transcranial motor stimulation. The stimulation sites used were C3-C4/C1-C2, with a sweep of 20 (2 ms/div) and a pulse duration of 50 or 75 microseconds. The intensity ranged from 80-500 V, with 30-3000 Hz filter settings. Our alert criteria are based on a 50% amplitude drop and no latency changes. A reduction of >50% in D-wave amplitude, combined with the loss of muscle MEPs, can be associated with a permanent motor deficit.

Electromyography (EMG)

Muscles of the lower extremities were monitored using both triggered EMG (T-EMG) and Free running EMG (S-EMG). The specific muscles being monitored are abdominis rectus, adductor brevis, vastus medialis, gastrocnemius, abductor hallucis, anal sphincter, and external urinary sphincter. The stimulation intensity ranged from 0.05 to 5.0 mA, the duration was 0.2 ms, the frequency was 2.79 Hz, the filter bandpass was set to 10-5000 Hz, and the sweep was set to 200 ms/div for S-EMG and 10 ms/div for T-EMG. Any train EMG firing was immediately reported to the surgeon, and any recorded responses were communicated promptly.

Train Of Four (TOF)

For lower extremity muscles, the abductor hallucis is the recommended stimulation site. The parameters for this method include a monophasic square pulse with a duration of 0.2 msec, a stimulation rate of 2 Hz, 4 pulses, a sweep of 20 msec/div, and a sensitivity of 200 μ sec. The alert criteria for successful stimulation are the presence of all four twitches with less than a 30% fade.

BCR (Bulbocavernosus Reflexes)

The researchers in Overzet et al. 2020 utilized two surface needle electrodes to stimulate the pudendal nerve at the dorsal penile surface in males and labia majora in females. Recording subdermal electrodes were

placed bilaterally in the external anal sphincter muscles. The cathode, located proximally, and the anode, located medially, were used to administer a pulse count of 5 with an intensity of 20-30 mA and a pulse width of 500 us. The interstimulus interval was also set to 3.1 ms, the filter bandpass was 5-1500 Hz, and the sweep was 10 ms/div. The alert criteria implemented was a reduction of >50% [7].

RESULTS

Study Characteristics

As stated, inclusion criteria include IONM modalities like SSEP, MEP, D-waves, BCR, and TOF; exclusion criteria include tumor locations other than IMSCT and resections, abnormalities in the postoperative stage, and neurological injuries (Table 1). The total cohort consisted of 804 patients, with 512 divided into patients who received IONM (Table 2). The postoperative deficit rate among the overall group was 51.4% (263/512)

| Inclusion Criteria | Exclusion Criteria |
|--------------------|--|
| SSEP | Tumor Locations |
| MEP | Resections |
| D-waves | Abnormalities in the postoperative stage |
| TOF | Neurological injuries |

Table 1. Both the inclusion and exclusion criteria of the selected reports (created by Prasanth Chalamalasetty).

for the studies in which proper data was given (Table 3). The postoperative surgical recovery rate among the overall group was 22.7% (116/512) for the studies in which proper data was given (Table 3). As mentioned by a specific report, “The decrease in the duration of the response correlated with motor grade loss immediately after surgery ($P < 0.001$), at discharge ($P < 0.0001$), and at follow-up ($P < 0.005$)” [8]. This statement is supported by “Muscle MEP loss predicted short-term postoperative worsening ($p < 0.0001$) only, while the strongest predictors of a good functional long-term outcome were lower preoperative MMS grades ($p < 0.0001$) and D-wave preservation” [9].

Among the reports, it is commonly noted that between the two groups (monitored vs. unmonitored), the group monitored had fewer postoperative deficits overall [9]. Furthermore, a set of researchers found that “SSEPs predicted deficits in the resection of intramedullary tumors ($P = 0.015$) (area under cover, $AUC = 0.83$)” (Lakomkin et al., 2018) [5].

| Study | Overall Sample Size (n) | IONM | |
|--------------------------------|-------------------------|-----------------|----------------------|
| | | Sample Size (n) | Techniques Utilized |
| Costa et al., 2013 | 23 | 23 | SEP, mMEP, D-waves |
| Fujiwara et al., 2021 | 60 | 60 | TsMsEP |
| Jin et al., 2015 | 25 | 25 | SEP, MEP |
| Kimchi et al., 2021 | 28 | 28 | SSEP, tcMEP, D-waves |
| Kothbauer et al., 1998 | 100 | 59 | mMEP, D-waves |
| Kurokawa et al., 2018 | 58 | 58 | MEP |
| Lakomkin et al., 2017 | 52 | 52 | SEP, MEP |
| Li et al., 2014 | 210 | 8 | SEP, MEP |
| Muramoto et al., 2014 | 37 | 37 | mMEP |
| Quiñones-Hinojosa et al., 2005 | 28 | 13 | SEP, MEP |
| Rajshekhhar et al., 2011 | 44 | 44 | mMEP |
| Skrap et al., 2021 | 89 | 67 | SSEP, mMEP, D-waves |
| Zielinski et al., 2013 | 74 | 38 | SEP, MEP |
| Total | 804 | 512 | N/A |

Table 2. Shows the overall and IONM sample sizes for the selected reports with the addition of IONM techniques utilized during surgery [5,8-19] (created by Prasanth Chalamalasetty).

| Study | Postoperative Deficits | | Postoperative Surgical Recovery | |
|--------------------------------|------------------------|------------|---------------------------------|------------|
| | RECOVERED | PERMANENT | RECOVERED | PERMANENT |
| Costa et al., 2013 | 14 | 7 | 16 | 7 |
| Fujiwara et al., 2021 | 5 | 4 | 55 | 4 |
| Jin et al., 2015 | N/A | N/A | N/A | N/A |
| Kimchi et al., 2021 | N/A | N/A | N/A | N/A |
| Kothbauer et al., 1998 | 35 | 8 | 51 | 8 |
| Kurokawa et al., 2018 | N/A | N/A | N/A | N/A |
| Lakomkin et al., 2017 | 11 | 14 | 38 | 14 |
| Li et al., 2014 | N/A | 47 | 163 | 47 |
| Muramoto et al., 2014 | N/A | 13 | 24 | 13 |
| Quiñones-Hinojosa et al., 2005 | N/A | 12 | 16 | 12 |
| Rajshekhhar et al., 2011 | N/A | N/A | N/A | N/A |
| Skrap et al., 2021 | 82 | 11 | 89 | 11 |
| Zielinski et al., 2013 | N/A | N/A | N/A | N/A |
| Total | 147 | 116 | 452 | 116 |

Table 3. Postoperatively, the postoperative and surgical recovery populations are subdivided into fully recovered or permanent deficits [5,8-19] (created by Prasanth Chalamalasetty).

Statistical Analysis

Most studies used statistical software, including, but not limited to, Microsoft Excel-2013, SPSS 21, Kruskal-Wallis U-test, and Man-Whitney U-test. Studies that were included without statistical analysis were case reports.

Assessment of Bias

Researchers mention various ways there could have been bias in their studies post-hoc. However, no studies mention an assessment of bias via a tool used for risk of bias.

DISCUSSION

Intramedullary spinal cord tumors in individuals typically result in symptoms such as back pain, temperature or sensation sensitivity, issues with motor control, and loss of internal organ function. With a meager diagnostic rate of less than 1%, IMSCTs are seen by imaging techniques such as MRI and CT scans and tissue samples in a biopsy to determine the potentiation of malignancy. Treatment for such an ailment has been focused on resection, radiation, and chemotherapies, as well as pain management and rehabilitation through physical exercise. The ideal surgical patient for resection can be challenging to identify due to the narrow nature of the spinal canal and the combination of tracts located within each other, making tumor resection a very delicate and calculating affair. Intraoperative monitoring techniques, such as direct waves (D-waves) and motor evoked potentials (MEPs), are used to preserve as much spinal cord integrity and function as possible.

Affecting 2% of adults and 10% of pediatric neoplasms, primary intramedullary spinal cord tumors (IMSCTs) are one of the most challenging tumors for resection. The white matter fibers are located within the spinal cord parenchyma and are extremely susceptible to manipulation. Approximately 40-50% of patients face postoperative neurological deficits from an IMSCT procedure, and the use of D-waves can partially limit this high rate of deficit [20]. This modality of neuromonitoring preserves the lateral corticospinal tract specifically and is useful in adjunct with spinal cord stimulation mapping and diffusion tensor imaging. Although neuromonitoring can mitigate the possibility of post-operative deficits, the reliability of the recordings depends on pre-existing conditions and comorbidities. The recordability status of D-waves has been seen to correlate with a patient's neurological status. In the study by Costa et al., in three patients, the D-waves were absent from recordings, and MEP signals were lost and concluded to be absent due to the patients' poorly compromised neurological status [11]. In one of those three, the D-wave baseline recording was absent, the patient had transient paraparesis, and the remaining two patients suffered motor deficits (Costa et al., 2013). The singular patient experienced a phenomenon noted as "surgically induced transient paraplegia," which does show promising recovery in patients who lost D-wave

recordings. However, the patients who underwent motor deficits were not able to regain control so quickly afterward, indicating that the D-waves and MEPs are two components that are critical checkpoints of spinal cord functionality [10].

Along with D-waves, TcMEP recordings are used as a reliable form of recording in IMSCT resections. Quinones-Hinojosa et al. reported that nearly 50% of patients undergoing the procedure experienced changes in the TcMEP waveforms. True-positives were seen in 12 patients, all with a morphological change in waveform and significant motor grade loss for an extensive period with checkpoints post-operatively, at discharge, and the follow-up appointment [8]. This alarmingly high rate of true-positives supports intraoperative monitoring in IMSCT procedures because the alerts allow for surgical correction techniques and minimize permanent postoperative deficits. Along with intraoperative neuromonitoring, these data relay a more significant problem for surgeons. Changes in TcMEPs and SSEP waveforms may indicate that it is essential for surgeons to navigate the resection with a conservative amount of physical force and modify the current techniques used.

Muscle motor-evoked potentials (MMEPs) are valuable in IMSCT resections to reduce the risk of postoperative motor system deficits. However, the reliability of modality recordings depends on the patient's pre-existing condition. For instance, pre-operative muscle power ratings significantly predict the success of MMEP recordings during resection. Lower limb MMEPs were successfully obtained in about 70% of patients with a muscle power of 3/5 or higher. The study also revealed that preoperative muscle power is a definitive predictor of post-operative motor condition, as preoperative deficits can leave the spinal cord's motor system more vulnerable to permanent deficits. Although motor weaknesses can recover after a lengthy resection, false alerts can occur due to the variability in sensitivity and specificity of the signals in each patient. Kurokawa et al. (2018) reported a false-positive rate of 59% and a false-negative rate of 7% in the patient population. This indicates the need to reconsider how MEP recordings are collected and interpreted to minimize false alarms. Navigate the alerts without performing corrective techniques for false-positives [15].

The use of IONM modalities in IMSCT resections is not yet standardized globally to the extent it should be. While each patient's demographics and physical status present unique limitations that must be considered, most intramedullary tumor resections carry minimal risk thanks to IONM. Specifically, patients who undergo IONM-enhanced resections of these lesions experience significantly fewer postoperative deficits than those who do not. Due to their location within the spinal cord, intramedullary tumors leave the cord more vulnerable to incidents [10].

While common non-invasive techniques for IMSCTs are chemotherapy, radiotherapy, and monitoring, a few select patients can qualify for a spinal cord stimulator (SCS). These stimulators have been studied in patients with intradural tumors, and there are little to no studies published regarding a patient population with intramedullary tumors. However, the success in preventing neuropathic pain in intradural tumor patients shows a promising future for individuals with intramedullary tumors. As with the presence of a

spinal cord tumor, the pain that results in post-resection can negatively impact a patient's recovery, like that of an acute spinal injury. When pain is this intense and persistent, clinicians may recommend the implantation of an SCS to reduce the post-operative recovery time [20]. The chronic pain post-resection was observed to go down to a minimal level six months after implantation, and the patient successfully terminated the use of analgesics [21-22]. While this case may not reflect the same outcome in a patient with an intramedullary tumor, more insight and research should be dedicated to reducing pain in cases where resection does occur, especially in situations where resection is far riskier to the prognosis.

CONCLUSION

The approach to treating intramedullary spinal tumors varies considerably based on the patient population. A common method involves surgically removing the tumor, which presents its own set of difficulties. Intraoperative neuromonitoring has been utilized to minimize the occurrence of postoperative deficits in highly sensitive procedures, such as tumor excisions. MEP, SSEP, and D-wave recordings have considerably reduced the risk of spinal cord paralysis, paresthesia, or other permanent complications. In cases where surgery does not provide a positive prognosis, spinal cord stimulator implantation has been found to reduce neuropathic pain and expedite recovery for those who have undergone resection. However, the limitations of each study examined were that some were retrospective rather than prospective. Retrospective studies can devalue the effectiveness of treatments due to the possibility of data gaps. In contrast, prospective studies can provide a more accurate account of procedures and outcomes. Furthermore, many journal articles did not include the demographics of the patient population, which is a vital factor in the outcomes of these resections. It is difficult to identify the cause of each patient's outcome with certainty since it is possible that demographic or other intentionally and unintentionally omitted details could have played a role. The study's authors considered these constraints when evaluating the impact of each intervention and result. Including prospective studies, sensitivity and specificity data, and patient population demographics could help enhance the confidence and dependability of the results and conclusions drawn by clinicians and researchers.

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