

Neuromonitoring during surgery for metastatic tumors to the spine: intraoperative interpretation and management strategies

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The main goal of surgery in patients who have metastatic spinal tumors is alleviation of the mass effect on neural structures without compromise of spinal stability. The benefit of achieving this goal must be weighed against the attendant morbidity associated with the procedure and the clinical status of the patient's primary disease. Many stabilization techniques have evolved over the past decades, allowing for aggressive resections. Intraoperative monitoring of neurophysiology has decreased the morbidity associated with these procedures by providing real-time assessment of spinal cord function. Different neuromonitoring techniques including somatosensory-evoked potentials (SSEPs) have been used to monitor surgery in the spine. Some groups have used SSEPs and motor-evoked potentials (MEPs) during resection of intramedullary tumors [1–4], and these same techniques have been applied for the treatment of metastatic spinal tumors.

This article reviews various neuromonitoring techniques available to surgeons during the

management of metastatic spinal tumors. As with any surgical adjunct, each monitoring technique is a tool that must be applied within the appropriate context. Accordingly, patient selection based on preoperative functional status and effects of neuroanesthesia on electrophysiology recordings must all be taken into consideration.

Anesthetic considerations for optimization

A variety of protocols exists for optimizing anesthesia while performing neuromonitoring. At the authors' institution, we administer low-dose halogenated anesthesia maintained at less than 0.5 MAC (Desflurane at 2.5%–3.5%) with a continuous propofol infusion (50–75 µg/kg/min). Narcotic administration includes remifentanyl or fentanyl bolus. To facilitate measurement of motor responses, paralytic agents are not used after induction and intubation of the patient. A "bite block" is used to prevent tongue lacerations or endotracheal tube damage from motor stimulation of the jaw. Before myelotomy, Desflurane levels are reduced to 2.0% or lower with a concordant increase in propofol infusion to 75–120 µg/kg/min. Narcotic administration is also increased to facilitate analgesia with careful concordant monitoring of blood pressure. As will be discussed later, a secondary decrease in blood pressure after narcotic administration can affect spinal cord perfusion and associated neurophysiologic readings.

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Neuromonitoring techniques

Somatosensory-evoked potentials

SSEPs evaluate the integrity of the spinal cord dorsal columns and can be recorded throughout surgery without motor stimulation. Accordingly, the surgeon can operate while obtaining data in real-time with minimal risk of patient movement. Intraoperative changes in SSEPs correlate with postoperative reduction in sensory modalities, particularly proprioception. Kothbauer and colleagues [2] have shown that patients sustain at least a transient loss of joint position sense when intraoperative SSEPs are normal at baseline but lost during myelotomy. This phenomenon has also been described after resection of primary intramedullary spinal cord tumors [5].

Although the predictive value and real-time data acquisition associated with SSEPs are advantageous, the application of this modality is sometimes compromised by the fragile nature of dorsal column circuitry. In particular, the myelotomy at the beginning of the case for resection of intramedullary spinal cord lesions can result in a reduction of dorsal column integrity, rendering SSEP data useless [4]. Cases have been described in which intraoperative SSEPs deteriorated as the myelotomy was retracted and then subsequently recovered during the course of the procedure, with associated recovery of proprioception following surgery [2].

Somatosensory-evoked potentials: intraoperative set-up and surgical technique

After initiating and documenting the appropriate level of general anesthesia, surface stimulating electrodes are placed over each ulnar nerve at the wrists, and over each posterior tibial nerve at the ankles. A constant current duration of 200 milliseconds at a rate of 4.1 Hz for the median nerve and 2.1 Hz for the posterior tibial nerve is applied. Sterile needle electrodes are placed over the somatosensory foot cortex at scalp sites Cz'–Fz, and also at C3'–C4', to record the primary cortical responses. Both left and right posterior tibial nerves as well as ulnar nerves are stimulated asynchronously to avoid artifacts and facilitate data interpretation. Surface-stimulating electrodes are also placed over each ulnar nerve at the wrists, and needle electrodes are placed over Erb's point bilaterally. At the authors' institution, electrophysiologic responses are recorded in patients using a 16-channel Cadwell Cascade (Cadwell Laboratories, Inc., Kennewick, WA) data acqui-

sition platform with contemporary multimodality SSEP/EEG/Triggered-EMG software. SSEPs involving bilateral ulnar and posterior tibial recordings are commonly obtained using standardized recording protocols at a bandwidth of 30 to 300 Hz [6,7].

Somatosensory-evoked potentials: interpretation of data and intraoperative management

As with any monitoring technique, the acquisition of baseline measurements is critical to making informed decisions about functional status. Accordingly, the authors typically obtain three sets of measurements before beginning an operation. After the patient undergoes initiation of general anesthesia and application of monitoring equipment, a set of recordings is obtained in the supine position. Subsequently, the patient is placed in the prone or lateral position, depending on the procedure, and another set of recordings is obtained. Finally, after prepping and just before skin incision, a third set of recordings is obtained. By rigorously comparing the data from these three preoperative timepoints, we can detect problems with positioning, anesthesia, and technical issues related to equipment (eg, loss of an electrode after prepping and draping). In some cases the operative position of a patient may be modified based on changes in neuromonitoring readings. With regard to specific values, an amplitude reduction of 50% or greater from baseline or a latency delay of 10% or greater is significant and concerning for SSEP recordings of the upper extremity (N20-P25) and the lower extremity (P37-N45).

In patients undergoing surgical treatment of metastatic spinal tumors, several factors can contribute to intraoperative SSEP changes. A change in the normal curvature of the spine due to tumor compromise of elements that confer spine stability can change SSEPs. Furthermore, corrective measures to reconstitute normal curvature can iatrogenically change SSEPs. We have found that distraction, combined with hemodilution secondary to blood loss, can sometimes exacerbate the changes in the quality of the SSEP signal.

Any changes in SSEPs that occur during surgery are followed closely. Initially, every attempt is made to optimize technical, anesthetic, and hemodynamic parameters. After documenting appropriate technical and anesthetic conditions, the mean arterial blood pressure is incrementally increased by 5 to 10 torr until reaching 20 to 30 torr above the mean. Patients

with hematocrits of less than 30 are aggressively transfused. In some cases, SSEP recordings persistently suggest compromise of spinal cord function, despite optimization of technical, anesthetic, and hemodynamic parameters. In these scenarios it is important to rule out anatomic impingement of the cord secondary to hematoma or instrumentation. If changes persist, the surgical team should be aware of the potential consequences to the postoperative sensory function of the patient.

Dorsal median sulcus mapping using somatosensory-evoked potentials

The technique of dorsal column stimulation by way of recording antidromic-elicited SSEPs allows selection of a myelotomy site with the fewest conducting axons, thus minimizing damage to functional dorsal column (Fig. 1A). The monitoring is valuable for rare cases of intramedullary metastatic lesion because these tumors can distort normal spinal cord anatomy, thereby reducing the use of conventional landmarks for myelotomy [8,60].

Dorsal median sulcus mapping: intraoperative set-up and surgical technique

For dorsal median sulcus mapping using SSEPs, needle electrodes are placed over the medial malleolus to record antidromic sensory nerve action potentials. All antidromic recordings are made with a four-channel Cadwell Sierra LM signal averager system (Cadwell Laboratories, Inc.). The authors apply bandpass parameters between 30 and 300 Hz (timebase of 100 milliseconds) with a vertical display sensitivity between 1 and 5 μ V. A hand-held bipolar electrode with a spacing of 2 to 3 mm between the anodal and cathodal tips for the stimulation of the dorsal column (Fig. 1B) is used for direct cord stimulation (Kartush stimulator, Xomed-Medtronic, Rochester, MN). This stimulator is preferred because of its small size and the proximity of its stimulating points. The authors recommend using the Cadwell Sierra stimulator at a pulse rate of 4.1 to 7.1 Hz, a duration of 200 μ s, and an initial intensity of 3 mA of constant current up to but not to exceed 8 mA.

After laminectomy and durotomy, the exposed cord is irrigated with warm saline solution to maximize axonal conduction. The anatomic midline is identified based on surface venous structures or equidistance between dentate ligaments. A measuring ruler is placed dorsally on the cord, with the “5 mm” mark placed on what is thought

to be the anatomic midline. The hand-held bipolar stimulator, with the cathodal tip pointing distally, is placed on the dorsal aspect of the cord, starting 2 mm lateral to the midline reference, and the spinal cord is stimulated. Once adequate responses are obtained and amplitudes measured, the stimulator responses are measured every 1 mm from lateral to medial. The region where there is a total absence of a response, or the lowest relative amplitude, is designated the physiologic midline. Minimal damage to dorsal column function is achieved by selecting this for myelotomy (see Fig. 1A).

Dorsal sulcus mapping: interpretation of data and intraoperative management

If the posterior columns are functional, signals should decrease when stimulation proceeds from lateral to medial, identifying an area between the posterior columns that defines the physiologic midline. In patients who have a tumor that has distorted, rotated, or thinned the normal fibers of the posterior columns, the physiologic midline can be discordant from the perceived anatomic midline. Our anecdotal experience suggests that mapping the dorsal columns before doing the myelotomy can positively impact a patient's outcome by minimizing postoperative sensory deficits. In particular, patients with lesions that distort standard landmarks of the spinal cord may benefit from mapping before performing the myelotomy.

Transcranial motor-evoked potentials

Although intraoperative changes in SSEPs can be predictive of postoperative sensory deficits in patients, they provide no reliable insight into the integrity of motor function. During intramedullary spinal cord tumor surgery, function of motor and sensory pathways can be affected separately [9], and the same is true for surgery of metastatic lesions that may be compressing epidurally on the ventral aspect of the cord containing the corticospinal tracts. Several groups have reported postoperative motor deficits despite normal intraoperative SSEPs [10,11,59]. Accordingly, at the authors' institution we complement SSEPs with muscle transcranial motor-evoked potential (Tc-MEP) recordings. We have adapted a well-described technique to measure Tc-MEP recordings in patients with metastatic spinal tumors [2,12,13]. Unlike SSEPs, muscle Tc-MEPs can assess motor function from the cortex to beyond the neuromuscular junction. We prefer to monitor compound motor action potentials recorded in muscle Tc-MEPs, because these are

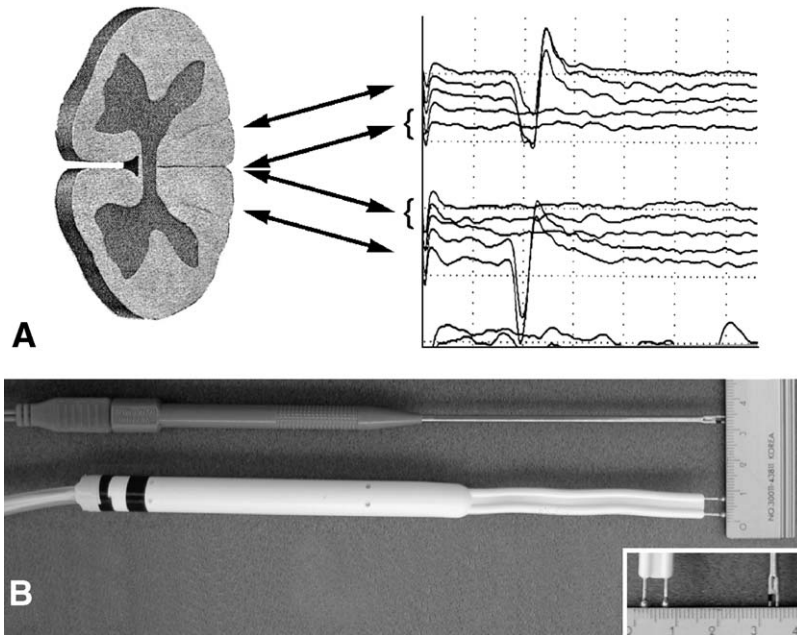


Fig. 1. (A) The technique of dorsal median sulcus mapping to help place the myelotomy is illustrated. After a durotomy, a stimulating electrode is applied to the area of the dorsal columns from left to right and recordings of elicited antidromic somatosensory evoked potentials (SSEPs) are made. Following along from left to right on a spinal cord cross section corresponds to top to bottom in this figure of SSEP mapping. At the midline, stimulation evoked no SSEPs, and the myelotomy is made at this place. (B) This photograph compares the Ojemann stimulator (Model OCS-1; Radionics, Burlington, MA) with the Kartuch stimulator (Medtronic-Xomed, Rochester, MN). The tips of the Ojemann stimulator (white) are spaced 5 mm apart, whereas the finer tips of the Kartuch stimulator (darker and smaller; see insert) are spaced less than 2 mm apart.

recorded directly in the muscles in which function is being assessed. In addition, muscle Tc-MEPs can be recorded from all four extremities, allowing evaluation of which extremity is most affected by specific surgical manipulation.

A limitation of muscle Tc-MEP recordings is the impact of general anesthesia [14–17], and a careful review of the preoperative anesthesia plan can avoid technical compromise. Tc-MEPs evoked by multiple stimuli are much less sensitive to the effects of general anesthesia than those evoked by a single stimulus [12,13,16]. Accordingly, the authors prefer a multiple impulse technique (short train of stimuli) to elicit responses.

Transcranial motor-evoked potential: intraoperative set-up and surgical technique

At the authors' institution, we apply the Digitimer D185 constant-voltage stimulator (Digitimer LTD, Welwyn Garden City, UK) to produce multipulse transcranial electrical stimulation. Patients who have documented seizure history, implanted atrial/ventricular pacemakers,

cochlear implants, or spinal cord stimulators/pumps are excluded. The D-185 can produce one to nine pulses at a fixed duration of 50 microseconds, with an interstimulus interval (ISI) from 0.1 to 9.9 microseconds. Stimuli are delivered via two “corkscrew” stimulating electrodes (Nicolet Biomedical, Inc., Madison, WI) placed at the standardized 10–20 electrode position of C1 and C2 (overlying the motor cortex). The D-185 is interfaced to the electrophysiologic recording platform (ie, Endeavor or Cascade systems) so that upon stimulation of the D-185, a “triggered” EMG response is evoked. Subdermal (29 g, 1.5 cm length) needle electrodes (Medtronic-Xomed, Rochester, MN) are used to record evoked electromyographic and compound motor action potentials produced by transcranial stimulation. These recording needles are placed bilaterally 4 cm apart in the first dorsal intraosseous of the upper extremities as well as the tibialis anterior, the extensor hallucis longus muscle, and the foot flexors of the bilateral lower extremities.

Although there is trial-to-trial variability in MEP response amplitudes, the authors follow a criteria of maintaining a response amplitude per trial of greater than 50 μV . Provided that background noise is equivalent to 5 μV in amplitude, a good signal-to-noise ratio of the MEP response is achieved by a factor of 10. Furthermore, two to three consecutive MEP responses are elicited and averaged. Despite the effects that low-dose halogenated agents have on MEPs, we are able to obtain highly replicable and reliable MEPs at a pulse-train of five to six pulses with an ISI of 2.5 to 3.5 milliseconds. Small increments in voltage intensity (ie, increments of 25 V) or number of pulses are used during surgery to maintain MEP response amplitudes greater than 50 μV . These maneuvers can overcome the phenomenon of anesthetic settling or anesthetic fade secondary to progressive suppression of motor cortex/anterior horn cell excitability.

*Transcranial motor-evoked potential:
communication between the surgeon and the
electrophysiologist*

Clear communication between the surgeon and the electrophysiologist is mandatory for successful application of Tc-MEP monitoring. Stimulation should not be initiated unless the surgeon has verbally acknowledged clearance to do so. During tumor resection, the neurophysiologist may elicit an MEP response whenever there are periods of sustained traction with forceps, rotation of the tumor capsule to establish a plane, or more than 1 minute of cavitron ultrasonic surgical aspirator use when close to the interface between tumor and normal tissue. We have found that bilateral MEPs can be quickly assessed within 15 seconds, and that this does not interrupt the flow of the surgical procedure.

*Transcranial motor-evoked potential:
interpretation of data and intraoperative
management*

There is considerable controversy with regard to the most reliable criteria for MEPs in detecting postoperative deficits. Some neurophysiologists advocate using a drop in amplitude of more than 50% and a 10% increase in latency [18–21]. Trial-to-trial variability in MEP amplitude can reduce the predictive value of this modality [12,13,17], although the delivery of higher pulse trains can substantially reduce this variability [22]. In fact, some evidence suggests that decreases up to 80% in baseline amplitudes are not correlated with

postoperative motor deficits [23]. Other authors advocate an “all-or-none” approach (ie, MEPs are either present or not, regardless of amplitudes/voltages) [2] or MEPs are present or not under certain anesthetic regimens [21]. At the authors’ institution, the neurophysiologist alerts the surgeon whenever there is an acute increase in voltage threshold of more than 100 V during the procedure and a reduction in the duration and complexity of the MEP response (ie, polyphasic to biphasic) (Fig. 2) [24].

Insults that produce changes in Tc-MEPs appear to be detected earlier than those detected by SSEPs (Fig. 3) [25,26]. Experimental and clinical data suggest that there is a selective vulnerability of large-diameter, highly myelinated, fast-conducting fibers to the effects of trauma [27–29]. Axonal disruption primarily of large-diameter fibers in the corticospinal tract with relative sparing of smaller-diameter fibers has been reported in postmortem histopathologic analysis of patients with compressive spinal cord insults [30]. Furthermore, it is widely believed that MEPs are mediated primarily by the large-diameter, fastest conducting corticospinal tracts [31–34], with some possible contributions by both the smaller-diameter corticospinal tract population [35] and other fiber pathways [36–38]. Hence, direct mechanical insults inflicted to the spinal cord would be first detected by the MEPs as indicated in animal studies. In the authors’ experience, distraction of the spinal cord, anemia, and hypotension have been shown to affect the complexity and duration of Tc-MEPs to a greater extent than SSEPs [21,39], a phenomenon that is likely related to global and local effects on spinal cord perfusion pressure.

For the rare intramedullary metastasis, EMG activity can be important in determining the interface between the tumor capsule and normal tissue. Sometimes traction on the tumor capsule at the margin can endanger the corticospinal tracts, and this can be seen in the acute changes in voltage threshold, as well as complexity/duration of the Tc-MEPs that are polyphasic to biphasic. Cavitation ultrasonic surgical aspiration can also affect the corticospinal tracts by either trauma, vasogenic edema, or direct transection of viable corticospinal fibers. The MEP recordings can abruptly change in voltage threshold, as well as a morphologic/duration change from a robust polyphasic to a biphasic waveform, to a complete loss of the MEP response.

When there is a significant change in the electrophysiologic recordings, the authors stop

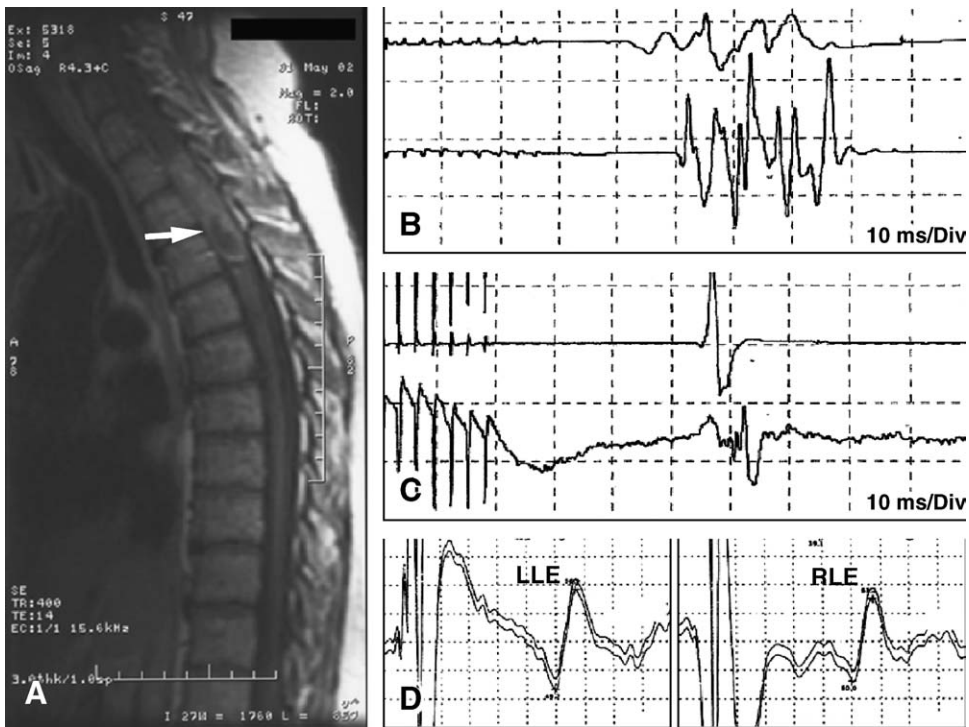


Fig. 2. A 49-year-old woman presented with back pain and a history of melanoma; she had 5/5 motor strength in the upper and lower extremities. (A) Preoperative T1-weighted MRI scan with contrast shows a lesion (*arrow*) that was found during surgery to be a metastatic malignant melanoma lesion. During surgery, transcranial motor evoked potential (Tc-MEP) recordings exhibited polyphasic (B) to biphasic (C) waveform morphology transformation in the LLE immediately after an episode of traction on the tumor capsule with forceps. Simulation voltage was also increased from a baseline of 325 V to 500 V (54% increase) in the LLE, with no recovery of polyphasic waveform morphology, and the waveform duration decreased by 67% in the same extremity. A different plane of dissection was chosen in which to continue, and the mean arterial blood pressure increased immediately. (D) The somatosensory evoked potentials remained unchanged during these Tc-MEP changes in both extremities throughout the procedure, as is shown by the two superimposed traces for each extremity, which represent the baseline and the final trace. The postoperative motor grade was 4 in the LLE, consistent with the change in duration and complexity of the signal. Strength in the upper extremities remained 5/5. LLE, left lower extremity; RLE, right lower extremity.

surgical manipulation, analyze the anatomy of the tumor and its relationship to the cord, and then reexamine the surgical goal as well as the degree of manipulation necessary to accomplish the goal (ie, gross total resection) [40,41]. In some cases, the mean arterial blood pressure can be incrementally increased by 5 to 10 torr up to 20 to 30 torr in an attempt to find a “target pressure” that improves spinal cord perfusion pressure [42]. It has been our experience that even if the MEPs are completely abolished during surgical manipulations of the tumor–spinal cord interface, the patient will make some recovery of function provided that anatomic continuity of the corticospinal tracts is intact. A significant recovery of function has been observed by other groups that monitor Tc-MEPs

if the signal is decreased or altered and/or the voltage threshold is elevated by the end of the surgery [43–45]. This sequence of events may be due to intraoperative spinal cord edema that gradually resolves, resulting in delayed functional recovery. Associating acute changes in Tc-MEPs during periods of mechanical manipulation (ie, segmental distraction or excessive traction on the tumor-normal tissue interface) could be interpreted easily. However, the neurosurgeon can be perplexed when acute changes occur in the Tc-MEPs where no mechanical forces have been applied to the tumor or the tumor has already been removed. Barring technical/anesthetic considerations, these acute losses of the Tc-MEPs may represent unpredictable vascular mechanisms

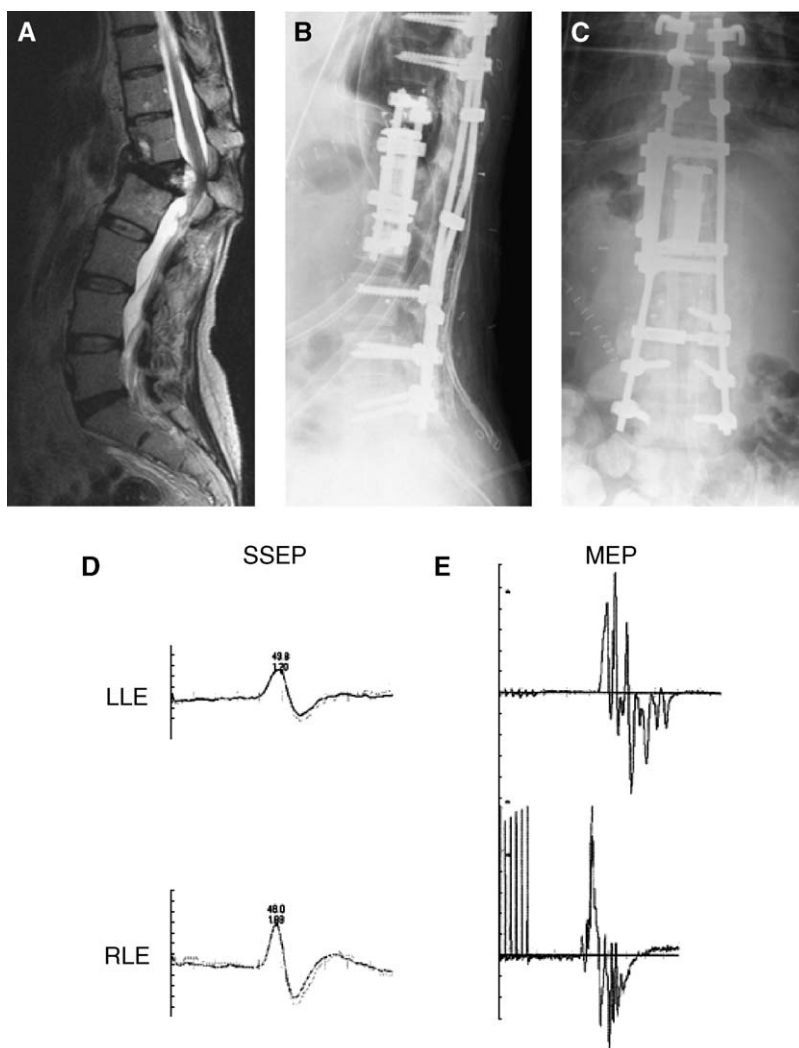


Fig. 3. A 50-year-old woman with a history of breast cancer and known spinal metastasis and status after radiation therapy to the spine 1 year before her presentation presented with exquisite back pain but within the normal neurologic range. She underwent an anterior two-level corpectomy and fusion as well as a posterior decompression and fusion. During surgery, somatosensory evoked potentials and motor evoked potentials were recorded and showed minimal variations throughout the procedure but nothing that would be considered dangerous to the spinal cord. One year later, she is neurologically intact and has no evidence of spinal disease.

usually associated with chronic compression of the spinal cord [46], venous congestion [47], hyperemia [48], or loss in autoregulation. Acute losses of the Tc-MEPs, under these circumstances, may represent a significant decline in spinal cord perfusion and generous increases in MAP are warranted. In summary, MEPs should be considered a semiquantifiable measure of intraoperative motor grade function that can be effected by both primary mechanical as well

as secondary mechanisms of spinal cord injury (Fig. 4).

Intraoperative spinal cord mapping by way of direct stimulation

Direct stimulation of the spinal cord with EMG recording, or intramedullary spinal cord mapping, can be used to identify the extent of the

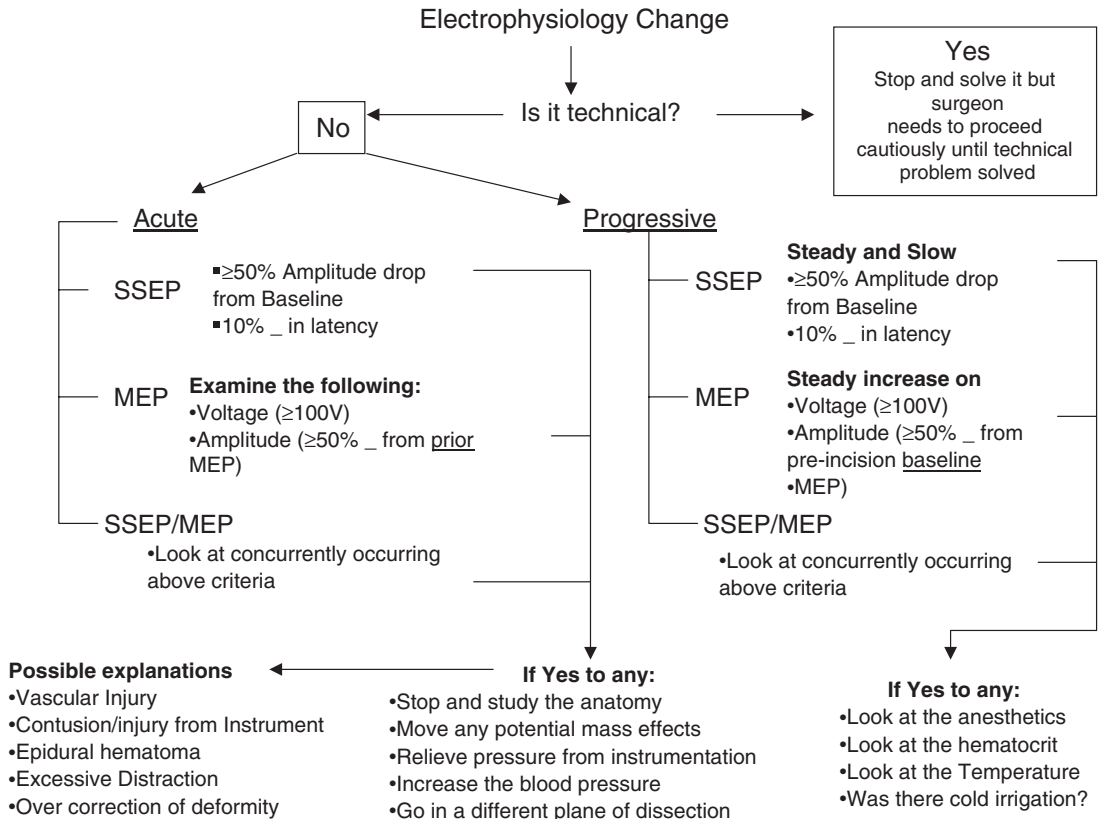


Fig. 4. Diagram depicting the intraoperative protocol recommended for the interpretation of somatosensory evoked potential and motor evoked potential electrophysiology data and subsequent recommendations and maneuvers to follow in the event of a change.

tumor margin at the interface with functional tracts. In the authors' experience, this has been particularly important in the ventral aspect of tumors. Intraoperative mapping by way of direct spinal cord stimulation is different from any of the techniques described thus far. It relies on monopolar stimulation of a tumor field. This technique has been used by skull base surgeons at our institution to identify the margin of the tumor capsule in relation to cranial nerve VII [49]. In recent years, this technique has been applied during resection of supratentorial tumors and other lesions within the sensorimotor cortex and adjacent to the internal capsule [50].

For the intramedullary spinal cord mapping, we rely on the principles of conventional mapping during resection of supratentorial tumors. Direct cortical stimulation with monopolar or bipolar electrodes is followed by observation of the contralateral body part for any associated move-

ment [51–57] either clinically or with EMG recordings in the extremities. As expected, EMGs are more sensitive than clinical observation [50].

Intraoperative spinal cord mapping: intraoperative set-up and surgical technique

Intramedullary spinal cord mapping can be performed using direct stimulation of the spinal cord with an Ojemann cortical stimulator (Model OCS-1, Radionics, Burlington, MA) or with the Kartuch (Medtronic-Xomed). Subdermal needle electrodes are inserted into the abductor pollicis brevis-flexor digiti minimi brevis manus, tibialis anterior-gastrocnemius, and abductor hallucis-abductor digiti minimi pedis [50]. Four channels of EMG responses are recorded using a Nicolet Viking IV P system (Nicolet Biomedical, Madison, WI) with a bandpass of 30 to 1000 Hz and a display gain of 200 $\mu\text{V}/\text{division}$. The traces are displayed in a free-run EMG protocol at a

timebase of 1 second. After myelotomy, both tumor and surrounding functional tracts are localized and stimulated. The stimulator is set to deliver 60 Hz pulses, with a 1-millisecond pulse width, beginning at 1 mA. Intramedullary stimulation is applied for approximately 1 second, with the surgeon announcing when it was applied. During tumor debulking, the tumor plane is periodically stimulated beginning at 1 mA and then restimulated at lower current levels with 0.25-mA increments to help define the extent of the tumor margin in relation to functional tracts.

Intraoperative spinal cord mapping: interpretation of data and intraoperative management

The combination of heightened voltages/reductions in the complexity/duration of Tc-MEPs, coupled with EMG responses upon direct stimulation of the tumor capsule, can influence the surgeon to pursue a less aggressive resection of a metastatic intramedullary tumor to avoid compromising functional tracts. Pronounced EMG activity in one side of the body can suggest close proximity of the corticospinal tracts and prompt modification of the resection. Clinical evidence suggests that most motor deficits, whether transient or permanent, occur during removal of the last tumor adhering at its margins in the spinal cord during aggressive attempts at a total gross resection of the lesion [15,58].

Summary

Resection of metastatic tumors of the spine poses great technical challenges, with the potential of creating severe neurologic deficits. Several modalities of electrophysiologic monitoring, including SSEPs and MEPs, have evolved to aid in resection of these tumors. This review has presented additional techniques—such as mapping of the dorsal columns with antidromic-elicited SSEPs to plan the myelotomy and direct intramedullary stimulation—that help to identify the extent of the tumor margin at its interface with functional tracts. Neuromonitoring can potentially minimize the sensory and motor damage that can occur during resection of metastatic tumors of the spine. Further experience with these techniques should allow improved results following surgical procedures in functionally eloquent areas of the spinal cord during the surgical management of metastatic tumors.

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