

## Intraoperative Mapping and Monitoring of Motor Cortex—A New Paradigm

Charles D Yingling, PhD, DABNM

Director of Education, Sentient Medical Systems, President, California Neuromonitoring Services and Clinical Professor, Otolaryngology, Stanford School of Medicine

### Abstract

Surgery for tumors near the sensorimotor cortex poses risks to sensory and motor pathways. Sensory pathways are monitored successfully with somatosensory-evoked potentials (SEP), but motor pathways pose different challenges. Historically, electrical stimulation with prolonged 60 Hz trains was used to map the motor cortex, but this method has a high incidence of induced seizures. Transcranial motor-evoked potentials (tcMEP) can monitor spinal motor pathways. However, transcranial stimulation is inappropriate for intracranial tumors, since the current may activate deep corticospinal fibers, bypassing a superficial injury. In contrast, brief high-frequency trains as used for tcMEP, applied directly to the cortical surface at lower intensity, avoid this problem and do not appear to induce seizures. Once the motor cortex has been mapped, an electrode can be left in place and used for continuous monitoring of corticospinal tract function during tumor resection.

### Keywords

Somatosensory-evoked potentials, motor-evoked potentials, neurosurgery, cortical tumors, sensorimotor cortex, corticospinal tract, intraoperative monitoring, motor mapping

**Disclosure:** The author is an employee of Sentient Medical Systems.

**Received:** April 14, 2011 **Accepted:** May 16, 2011 **Citation:** *US Neurology*, 2011;7(1):64–7 DOI: 10.17925/USN.2011.07.01.64

**Correspondence:** Charles D Yingling, PhD, DABNM, 1001 Bridgeway #434, Sausalito, CA 94965. E: cyingling@sentientmedical.com

**Support:** The publication of this article was funded by Sentient Medical Systems.

Surgery for tumors near the sensorimotor cortex poses risks to both sensory and motor pathways. While the sensory pathways may be monitored successfully with somatosensory evoked potentials (SEP), the motor pathways pose different challenges. Transcranial motor evoked potentials (tcMEP) are now routinely used for monitoring motor pathways in the spinal cord.<sup>1</sup> However, tcMEP use is problematic for intracranial tumors. This is because the currents from scalp stimulation may activate corticospinal tract fibers many centimeters deep within the brain, and thus potentially bypass a more superficial site of injury. A false negative (normal tcMEP after an injury causing focal paralysis) can thus result unless steps are taken to limit the spread of current to deeper sites. This article will describe the use of mapping techniques to unequivocally locate the motor cortex itself, and then discuss recently developed techniques for monitoring the integrity of the corticospinal tract during tumor resection.

### Motor Mapping Techniques— History and Background

Motor mapping techniques have been used in surgery since the 1930s, when the American/Canadian neurosurgeon Wilder Penfield carried out an extensive series of investigations in patients undergoing surgery for epilepsy or brain tumors. The method involved stimulating the exposed cortex during craniotomies performed on patients while awake, and recording the resulting effects, which variously involved sensory, motor, language, or memory phenomena. The results were reported in a

landmark publication<sup>2</sup> that formed the basis for the modern concepts of the sensory and motor homunculi, as well as cortical organization for language and memory functions.

Penfield's method was based on prolonged (1–6 seconds) stimulation at the 60 Hz line frequency, chosen since it was the easiest to implement in the days before digital electronics. In more recent times, solid-state devices (notably, the Ojemann Cortical Stimulator, OCS-2) were developed to provide more flexibility and precise control, but the core of the technique remained the same. Patients reported sensations, movements were observed, or interference with speech or language functions was produced during stimulation. Despite producing a wealth of data about human cortical organization, the Penfield technique was not without its problems. Notably, electrocorticography (EEG) after discharges or even frank seizure activity were often observed after stimulation, and simultaneous recording of EEG became the norm in order to detect such events in a timely fashion.

A significant improvement on this technique was reported in 1999, when Yingling et al.<sup>3</sup> demonstrated that the sensitivity of motor mapping could be greatly enhanced by recording electromyogram (EMG) responses, which could be detected at much lower thresholds than overt movements (see *Figure 1*). However, this same study confirmed the tendency of prolonged 60 Hz stimulation to produce seizure activity; clinical or subclinical seizures were observed in 24 % of the patients. While most

of these were minor, and either self-limiting or easily terminated by application of cold Ringer’s solution to the cortex, the possibility remains that a significant seizure involving the upper body could pose serious risks to a patient in a head fixation system for surgery. Thus, a method for mapping that is less likely to produce such activity remains a desirable goal.

When transcranial motor-evoked potentials (tcMEP) were first introduced, there were similar concerns about the possibility of eliciting seizure activity; transcranial electrical stimulation had been used for years to intentionally induce seizures in the context of electroconvulsive therapy for treatment of severe depression. However, these fears turned out to be largely baseless. In a review of the safety of tcMEP monitoring, MacDonald<sup>4</sup> identified only five events of intraoperative seizures in over 15,000 cases monitored with tcMEP. Many of these were suspected to be spontaneous or possibly related to specific anesthetic agents. In any event, this incidence of 0.03 % is clearly far superior to the 24 % observed in the Yingling et al. study.<sup>3</sup> As a consequence, many investigators are now adapting the tcMEP technique to direct mapping of the exposed cortex, a technique we will term dcMEP (direct cortical motor-evoked potentials).

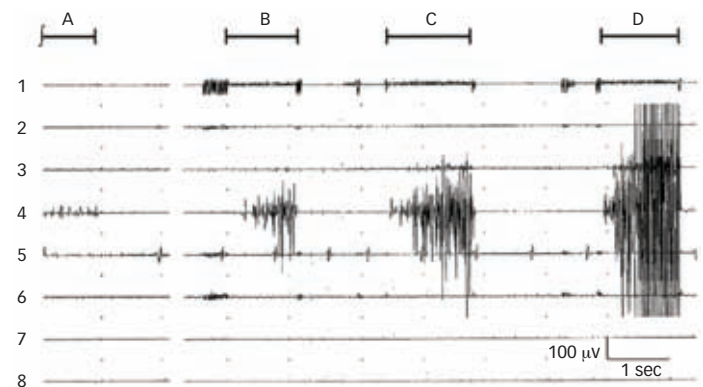
Taniguchi et al.<sup>5</sup> first described the principle of multi-pulse direct cortical stimulation with brief high-frequency trains. They calculated that the total charge per train was <8  $\mu\text{C}$ , compared with 600–5,000  $\mu\text{C}$ /train for the traditional Penfield 60 Hz technique. Subsequent clinical studies<sup>6,7</sup> reported a zero incidence of seizures using the dcMEP technique, with an overall success rate of 97 % in obtaining dcMEP responses. Subsequently, Szelényi et al.<sup>8</sup> compiled the data reported in several published series using each of the two techniques. The overall incidence of seizures using the dcMEP method was 5 of 421 patients (1.2 %), compared with 26 of 272 (9.5 %) for the 60 Hz method, which was a highly significant reduction. This technique is now beginning to supplant the Penfield method in most European centers,<sup>9</sup> but despite its advantages it has been slower to be adopted in the US, mainly owing to the lack of appropriate Food and Drug Administration (FDA) approved cortical stimulators.

A further advantage of the dcMEP technique is that, unlike prolonged 60 Hz stimulation, it does not produce any visible movements. Thus, after mapping of the cortical motor cortex, a strip electrode can be left in place and used for continuous monitoring of corticospinal tract function during tumor resection (the surgeon will of course avoid resecting primary motor cortex, so the electrode will not interfere with the surgical procedure). Unlike transcranial stimulation, which may activate corticospinal axons deep within the internal capsule and produce responses in multiple muscles in different limbs, direct cortical stimulation is much more focal and only activates a limited cortical area under the anodal contact. This is clearly illustrated in *Figure 2*, which shows responses elicited in the same patient by direct cortical versus transcranial stimulation.

**Cortical Motor Mapping—Technique and Interpretation**

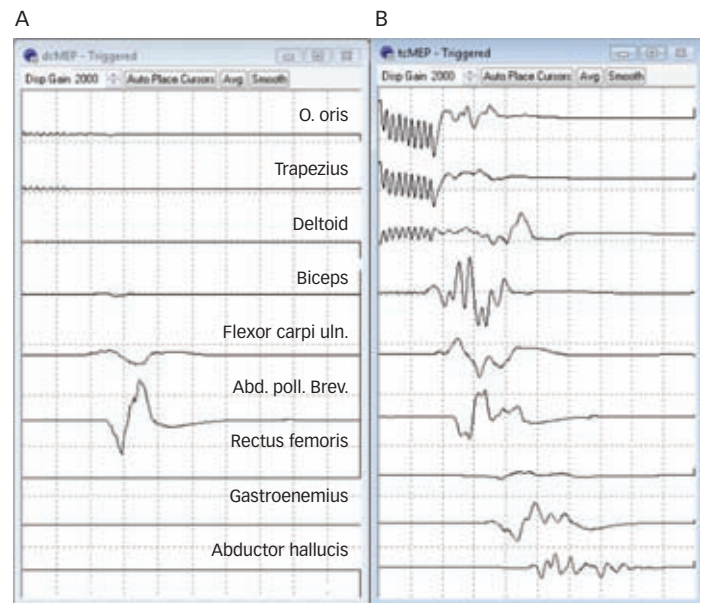
The first step in mapping the sensorimotor cortex is often locating the central sulcus by the polarity reversal of the median nerve SEP. Pyramidal cells located in the postcentral sulcus, which are oriented

**Figure 1: Electromyogram Responses to Prolonged Stimulation of Motor Cortex**



Stimulation (60 Hz, 1 ms pulse duration) was applied at 3.6 mA (A and B), 5 mA (C), and 6.2 mA (D). Only at the highest stimulation, when the electromyogram (EMG) response was off-scale, was any overt movement noted by the anesthesiologist. Traces from top to bottom represent shoulder, upper arm, forearm, hand, trunk, upper leg, lower leg, and foot. Source: Reprinted with permission from Yingling et al., 1999.<sup>3</sup>

**Figure 2: Responses Elicited by Direct Cortical Stimulation (A) Versus Transcranial Stimulation (B) in the Same Patient**



Identical time base (10 ms/div) and vertical calibration (2,000  $\mu\text{V}/\text{div}$ ) for each set of traces. Transcranial stimulation (75  $\mu\text{s}$  pw, nine pulses at 2 ms interstimulus interval (ISI) (B) at 330 V (~600 mA) produces responses in all contralateral muscles, owing to subcortical activation of corticospinal tract. In contrast, direct cortical stimulation (75  $\mu\text{s}$  pw, seven pulses at 2 ms ISI (A) at 40 V, (~28 mA) produces focal responses primarily seen in hand and forearm muscles.

so that the response is negative posteriorly, and positive anteriorly, generate the initial cortical response, N20.

A strip electrode with 4–8 contacts spaced 1 cm apart is placed perpendicular to the presumed central sulcus and used to record SEP from median nerve stimulation. The electrode position is adjusted until a clear polarity reversal of N20 is observed; the central sulcus lies between the contacts showing the reversal.<sup>10</sup>

The motor cortex is then identified with electrical stimulation. There are two options for cortical stimulation: a handheld electrode or the same strip electrode previously used for locating the SEP polarity reversal. The handheld electrode may be either bipolar (such as the electrode supplied with the Ojemann stimulator, which has two ball tips separated by 5–10 mm) or monopolar (a 3 mm ball tip probe such as those commonly used for pedicle screw stimulation is satisfactory). The bipolar electrode has the advantage that a separate return electrode is not necessary; however, bipolar stimulation is inherently ambiguous, since it is difficult to determine which of the two contacts was the effective stimulation site. This limits the spatial resolution that can be obtained. In contrast, a monopolar electrode requires a separate cathodal return (typically a scalp electrode at some distance from the stimulation site) but the location of the single stimulating anode is unambiguous. For this reason, monopolar anodal stimulation is preferred for mapping, if precise delineation of the motor homunculus is desired.

On the other hand, if the tumor is not in close proximity to the presumed precentral motor cortex (based on SEP reversal), then stimulation through the same strip electrode used for SEP recording is quite satisfactory. Recall that to record the polarity reversal of the SEP, the electrode contacts should be oriented perpendicular to the central sulcus, so that some contacts are over precentral and others over postcentral regions. Once the site of reversal has been determined, the electrode should be rotated 90° so that it lies parallel to the central sulcus, with all contacts over the presumed precentral motor cortex. Once again, either bipolar or monopolar stimulation may be employed; in either case, it will be necessary to survey the effect of various combinations of electrodes (a second pair of hands in the operating room is very helpful during this phase of the procedure). Monopolar stimulation is easier, since the number of trials necessary is simply the number of electrode contacts, each being connected to the anode in turn, with all referred to the same distant cathodal return. For bipolar stimulation, the number of possible permutations is much greater, as each contact may be used as either anode or cathode in combination with any of the other contacts. For a four-contact strip, this results in 12 possible combinations; 30 combinations for a six-contact strip; and 56 for eight contacts.

Without an automated switching matrix, this rapidly becomes unfeasible unless the surgeon is willing to take an extended break while stimulation mapping is performed, which is unlikely to happen in practice. Thus, monopolar stimulation is preferred for initial mapping. However, for extended monitoring during tumor resection, bipolar stimulation may be preferable. This is owing to the greater spatial selectivity of direct cortical as compared with transcranial stimulation (see *Figure 2*). Since any one contact will typically produce dcMEP responses in a very limited set of muscles, monitoring by repetitive stimulation of a single contact could miss an injury affecting a different part of the corticospinal tract.

Again, without an automated switching matrix, repeated surveying of all possible combinations is not practical. The best compromise may be to choose two contacts, which individually produce responses in different anatomical regions (i.e., upper and lower extremities), and connect these together as a bipolar pair. With this technique, simply switching the anode and cathode in software can produce dcMEP responses in

one or the other extremity at will, without the necessity for replugging at the stimulator output.

The final consideration concerns the parameters for electrical stimulation. At the time of writing (April 2011), there are only three stimulators on the market that are FDA approved for direct cortical stimulation: the Ojemann OCS-2 (now manufactured by Integra LifeSciences), the Grass S12X, and the Nicolet Cortical Stimulator. Unfortunately, these are all implementations of the traditional Penfield 60 Hz technique. The Grass and Nicolet devices incorporate switching matrices so that electrocorticograms can be recorded from an array of electrodes, and any pair of electrodes can be selected to connect to the stimulator while the others remain connected to the EEG inputs. All of these devices have a limited range of stimulation parameters that can be selected (typically 60–100 Hz maximum), and none can be triggered by an external device, which would allow brief high frequency trains to be elicited. Grass Instruments also markets constant current stimulus isolation units, which can be coupled to research stimulators to provide safely isolated outputs; however, these are all marketed for research purposes only, and none have FDA clearance for clinical use in humans.

As this article goes to press, Digitimer, the manufacturer of the D-185 transcranial stimulator, is developing a new cortical stimulator. This device, the DCS2, will emulate the historic Ojemann protocol, but will also be capable of delivering triggered high frequency trains for dcMEP stimulation as described above. Prototypes of this device will be evaluated in late 2011, and FDA approval will be sought as soon as testing is complete. The availability of the DCS2 should facilitate the transition to the preferred dcMEP technique in the US.

Currently, all of the following potential methodologies are predicated on off-label use of FDA approved devices. While there is no reason to suppose that cortical stimulation with these devices, if performed correctly within the parameters given, poses any significant additional risks to patients, appropriate patient notification and informed consent should be obtained by the surgeon, who holds the ultimate responsibility for such off-label uses.

There are two possible categories of currently available stimulators that may be employed: the electrical stimulators originally designed for stimulation of peripheral nerves, and devices such as the Digitimer D-185 or its equivalents, that are FDA approved for transcranial, but not direct cortical stimulation. The choice of which to use may be determined by the limitations of software in specific intraoperative monitoring systems. For example, the peripheral stimulators supplied with Cadwell Cascade systems cannot be programmed to deliver trains at a frequency higher than 60 Hz, corresponding to an interpulse interval of 16.67 ms, too slow by almost an order of magnitude. Thus with this commonly deployed system, the only practical way to deliver dcMEP stimulus trains without an add-on device is to use the transcranial TCS-1 or TCS-1000 units and limit the output voltage delivered.

For mapping with a handheld probe, the optimum stimulus is a train of 4–5 pulses at ~2 ms interstimulus interval (ISI), with the train itself repeating at a rate of approximately 3 Hz. Similar to common techniques for stimulating pedicle screws or cranial nerves, the probe is placed at

a candidate location, and stimulus intensity increased until a response is obtained or a predetermined maximum level is reached. The monitoring neurophysiologist reports the muscles responding and the threshold. Once a threshold has been established, the probe can be left active at a value a little above threshold, and simply moved around to define the limits and topography of motor cortex.

Thresholds using this method are not yet well established. Using the TCS-1 stimulator with a 50  $\mu$ s pulse width and train of 4–5 pulses at 2 ms ISI, we have typically obtained thresholds of 20–60 V and rarely had to exceed 100 V. Given the impedance of the strip electrodes used, this translates to roughly 20–100 mA. While this sounds like a relatively high current, a simple calculation can show that the effective threshold is in fact comparable to that obtained with the Ojemann OCS-2.

The charge delivered to the brain during each stimulus pulse is the product of intensity and duration. Since the OCS-2 pulses are 500  $\mu$ s long (for each phase of the biphasic waveform), they are 10 times the duration of a 50  $\mu$ s pulse. Dividing the current for the brief pulses by 10, we obtain an equivalent value of 2–10 mA per pulse, comparable to thresholds obtained with the OCS-2. Since the trains are only five pulses long (compared to 60 for a 1 s train at 60 Hz), each train using the brief high frequency technique delivers roughly an order of magnitude less charge to the brain than a single train from the OCS-2. This is presumably the reason for the much lower incidence of induced seizures.

Once mapping of the motor cortex is complete, the strip electrode is left in place to permit continuous monitoring of corticospinal tract function. Since stimulation at near-threshold values produces no overt movements, the stimulator can be set to present repeated trains at any desired rate. Since no signal averaging is required, stimulation at a rate of one train per 10 seconds allows virtually real-time monitoring of corticospinal tract function during tumor resection. This method has two significant advantages compared with tcMEP monitoring; no movements are produced so surgery does not have to be interrupted to elicit responses, and the superficial currents from direct cortical stimulation eliminate the possibility of false negatives from activating motor tracts deeper than the site of resection and possible injury.

An exciting recent development is the use of subcortical stimulation with brief high-frequency trains to judge the distance to the corticospinal tract from the margins of the resection cavity. Several recent studies,<sup>11–13</sup> combining electrical stimulation with diffusion-tensor imaging, have suggested that the distance to the corticospinal tract is proportional to the threshold current required to elicit EMG responses. The data suggests that the calibration is approximately 1 mA/mm, an easily remembered figure for surgeons. In conclusion, the dcMEP technique offers a safe method for mapping the motor cortex that can also be used for continuous monitoring of corticospinal tract function during tumor resection. Routine use of these techniques should improve surgeons' ability to maximize tumor resection while avoiding new post-operative motor deficits. ■

1. MacDonald DB, Intraoperative motor evoked potential monitoring: Overview and Update, *J Clin Monit Comp*, 2006;20:347–77.
2. Penfield W, Boldrey E, Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation, *Brain*, 1937;60:389–43.
3. Yingling CD, Ojemann S, Dodson B, et al., Identification of motor pathways during tumor surgery facilitated by multichannel electromyographic recording, *J Neurosurg*, 1999;91:922–7.
4. MacDonald DB, Safety of intraoperative transcranial electrical stimulation motor evoked potential monitoring, *J Clin Neurophysiol*, 2002;19:416–29.
5. Taniguchi M, Cedzich C, Schramm J, Modification of cortical stimulation for motor evoked potentials under general anesthesia: Technical description, *Neurosurgery*, 1993;32:219–26.
6. Cedzich C, Taniguchi M, Schäfer S, et al., Somatosensory evoked potential phase reversal and direct motor cortex stimulation during surgery in and around the central region, *Neurosurgery*, 1996;38:962–70.
7. Kombos T, Suess O, Funk T, et al., Intra-operative mapping of the motor cortex during surgery in and around the motor cortex, *Acta Neurochir*, 2000;142:263–8.
8. Szelényi A, Joksimovic B, Seifert V, Intraoperative risk of seizures associated with transient direct cortical stimulation in patients with symptomatic epilepsy, *J Clin Neurophysiol*, 2007;24:39–43.
9. Szelényi A, Bello L, Duffau H, et al., Intraoperative electrical stimulation in awake craniotomy: methodological aspects of current practice, *Neurosurg Focus*, 2010;28:E7.
10. Wood CC, Spencer DD, Alison T, et al., Localization of human sensorimotor cortex during surgery by cortical surface recording of somatosensory evoked potentials, *J Neurosurg*, 1988;68:99–111.
11. Kamada K, Todo T, Ota T, et al., The motor-evoked potential threshold evaluated by tractography and electrical stimulation, *J Neurosurg*, 2009;111:785–95.
12. Nossek E, Korn A, Shahar T, et al., Intraoperative mapping and monitoring of the corticospinal tracts with neurophysiological assessment and 3-dimensional ultrasonography-based navigation, *J Neurosurg*, 2011;114:738–46.
13. Prabhu SS, Gasco J, Tummala S, et al., Intraoperative magnetic resonance imaging-guided tractography with integrated monopolar subcortical functional mapping for resection of brain tumors, *J Neurosurg*, 2011;114:719–26.