Intraoperative neurophysiologic mapping of the central cortical region for epidural electrode placement in the treatment of neuropathic pain by motor cortex stimulation

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Neuropathic pain results from injury to the central or peripheral nervous system and can prove itself refractory to classical medical treatment by anticonvulsants and antidepressants. In such cases, motor cortex stimulation is among the neurostimulation techniques available for its symptomatic control. This technique is based on surgical implantation of electrodes over the motor cortical representation of the painful area. Image-guided navigation is used for precise identification of the motor cortex intraoperatively, but proper placement of the electrodes is usually ensured by electrophysiologic mapping. This article details the intraoperative electrophysiologic procedure that we currently use for refining electrode placement in the epidural space, including the recording of somatosensory and motor-evoked potentials (MEPs). Various procedures have been reported and some groups are using direct cortical mapping and subdural electrode placement rather than epidural. Our method is one of several proposed techniques and is mostly based on intraoperative MEP mapping in response to monopolar (anodal) epidural stimulation of the cortex. The limit of this approach is that MEPs cannot be recorded in patients with total or severe motor deficit. We have shown that intraoperative mapping of the cortical region corresponding to the painful area by recording MEPs could help select contacts to be activated for chronic stimulation. Therefore, the patients in whom intraoperative MEP mapping is possible could benefit from this technique, at least if we consider that it improves the accuracy of electrode placement and that motor cortex stimulation efficacy critically depends on this placement.

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Keywords cortical mapping; evoked potentials; intraoperative electrophysiologic mapping; motor cortex; neuromodulation; neuropathic pain

Chronic neuropathic pain presents challenge for treatment. Pharmacologic management is based on anticonvulsants and antidepressants. Neurostimulation techniques, which are both conservative and reversible, represent an important therapeutic option in drug-resistant cases.1 Analgesic neuromodulation can be performed at three anatomic levels: spinal cord (dorsal columns), deep brain structures (mostly sensory thalamus), or precentral cortical region (primary motor cortex). Motor cortex stimulation (MCS) can be proposed to treat refractory neuropathic pain of various origins.1 The first positive reports were made by Tsubokawa et al2-4 in patients with thalamic pain and by...
Meyerson et al in patients with trigeminal pain. These results were later confirmed in open and controlled trials.6-10

Studies have pointed out that the precision of electrode placement for chronic stimulation significantly influenced the therapeutic efficacy of MCS.11-13 Pain relief appeared to be homotopic, that is, obtained in the territory corresponding to the cortical region that is stimulated. Electrode placement is based on image-guided neuronavigation and intraoperative electrophysiologic mapping. This article details the intraoperative electrophysiologic procedure that we currently use for refining electrode placement. A more thorough review of the literature with respect to MCS efficacy and adverse events can be found elsewhere.14-21

Surgical technique

The technique originally proposed by Tsubokawa et al2-4 consisted in performing a simple burr hole while the patient is locally anesthesized. However, in our opinion, this approach should be abandoned because it increases the risk of epidural hematoma and reduces the accessibility of the cortical surface for a reliable electrophysiologic mapping. We prefer to position the cortical electrodes onto the dura mater after a small craniotomy (< 5 cm in diameter) performed under general anesthesia.6,11

The craniotomy is centered on the motor cortical area corresponding to the anatomic territory where pain is located. This target is localized by image-guided navigation according to the somatotopic representation of motor homunculus in the precentral gyrus22:

- the face is represented at the lower part of the precentral gyrus, below or at the level of the inferior frontal sulcus;
- the hand is represented at the middle part of the precentral gyrus, between the levels of the inferior and superior frontal sulci; and
- the leg is represented at the upper part of the precentral gyrus, between the level of the superior frontal sulcus and the interhemispheric longitudinal fissure.

This segmentation is debatable. First, cortical representation of the lower limb musculature is classically located on the mesial wall of the hemisphere (motor area folding into the longitudinal fissure). Therefore, cortical targets corresponding to lower limbs should be hardly accessible to epidural stimulation. However, it has been found that lower limb cortical representation could extend to the lateral surface of hemisphere.6,23 Second, most of cytoarchitectonic studies show that a large portion of Brodmann’s area 4 (BA 4, primary motor cortex) occupies the posterior wall of the precentral gyrus in the depth of the anterior bank of the central sulcus.24,25 Only a relatively small dorsomedial portion of BA 4 can be found at the exposed surface of the precentral gyrus. Therefore, epidural approach should be inadequate for the stimulation of motor cortical targets. However, it is clear that focal motor responses can be obtained by electrical stimulation of selective cortical areas on the convexity surface of the precentral gyrus.24 Such a discrepancy between electrophysiologic mapping of the motor homunculus and cytoarchitectonic data could result from the diffusion of electrical stimuli delivered at relatively high intensity to the depth of the cortical structure.

Image-guided navigation usually integrates morphologic magnetic resonance imaging (MRI) data in a tridimensional reconstruction that allows the identification of brain structures, such as central and frontal sulci. In selected cases, functional MRI (fMRI) can be used and coregistered with morphologic MRI scans in the navigation system to determine target location.12,26-28 Real or virtual (mental) motor activation tasks are performed in the painful region for preoperative fMRI data acquisition. This approach is particularly useful in amputees (phantom pain) or patients with total or severe motor deficit, in whom intraoperative electrophysiologic mapping cannot be applied.

Various other cortical mapping techniques could be considered preoperatively, including diffuse tensor imaging tractography, magnetoencephalography, evoked potentials, or transcranial magnetic stimulation (TMS). Application of repetitive TMS (rTMS) trains over the motor cortex can produce analgesic effects on chronic neuropathic pain.29 At present, rTMS targeting can integrate morphologic MRI or fMRI data in an image-guided procedure. Therefore, it is tempting to use navigated rTMS in a preoperative time for mapping the cortical regions over which the stimulation produces the best analgesic effects. However, the anatomical correlation between the most efficacious rTMS targets and the optimal location of MCS electrode placement for chronic pain treatment remains to be determined.

Image-guided navigation usually serves to center the craniotomy on the motor cortical region corresponding to the pain region and as a first approach for electrode placement. It provides ongoing feedback on the cortical structures encountered and the localization of the central sulcus and precentral gyrus can be obtained readily. However, inaccuracy can result from technical and biologic limits (image distortion and functional reorganization in the primary cortical areas). A functional mapping method is required because image-guided navigation may not reflect accurately the cortical target that should be stimulated. Therefore, most authors agree that intraoperative electrophysiologic mapping based on somatosensory- and motor-evoked potentials (SEPs, MEPs) is useful for refining electrode placement. Recording SEPs and MEPs does not aim at “monitoring” the functional integrity of neural pathways, but at “mapping” the functional anatomy of the central region.
Intraoperative SEPs

The goal of SEP recordings is to confirm the position of the central sulcus by showing a phase reversal on either side of the central sulcus. The use of SEP phase reversal for intraoperative localization of the sensorimotor cortex has been validated a long time ago as an important and reliable tool for neurosurgical interventions in the perirolandic region. However, this technique has several limitations. First, cortical SEPs are absent in the case of severe or complete sensory deafferentation due to the lesion causing neuropathic pain. Second, SEP phase reversal has validated anatomic-functional correlation for upper limb stimulation (median nerve stimulation at the wrist), but not for the stimulation of the face (trigeminal nerve) or the lower limb (tibial nerve). Therefore, intraoperative SEP mapping for MCS electrode placement is more accurate in upper limb pain than in other pain locations.

In practice, SEPs are elicited by the stimulation of the median nerve at the wrist of the painful side and are recorded contralateral to the stimulation, on the perirolandic cortical surface, without dura mater opening. The median nerve is stimulated bipolarly at a frequency of 2-3 Hz and an intensity of 5-20 mA until slight twitches of the thumb are obtained. A ground electrode is placed around the forearm with a loop tape strap. Recordings are performed by using a filter band pass of 20-2000 Hz, a time base of 50 milliseconds, and a grid of multiple contacts (12-24) or the epidural lead that is intended to be implanted and used for chronic MCS. This lead usually consists of a plate/strip of four electrodes of 4 mm diameter with 10 mm interelectrode spacing (quadripolar Resume, Medtronic, Minneapolis, MN). The main cortical components of the median nerve SEPs include a positive response (downward peak) over the precentral (motor) gyrus with a mean latency of 20 milliseconds (P20) and a negative response (upward peak) over the postcentral (sensory) gyrus with a mean latency of 20 milliseconds (N20) (Figure 1). There is an excellent anatomic correlation between N20-P20 phase reversal and central sulcus location. A difference in latency of up to 3 milliseconds is usually found between the precentral P20 and the postcentral N20 peaks (Figure 1). Therefore, these waves cannot be considered as mirror images of the same source. Various models have been proposed regarding the nature of the dipole generators at the origin of N20-P20 phase reversal, including two separated dipoles, both located within the postcentral gyrus.33

Finding N20-P20 phase reversal between two adjacent contacts allows investigators to determine the location of the central sulcus. Then, in our practice, the quadripolar lead is placed perpendicular to the central sulcus with two or three contacts on the precentral gyrus (anterior to the central sulcus) and one or two contacts above the central sulcus or on the postcentral gyrus (Figure 1). Other teams prefer to place the lead parallel to the central sulcus, all contacts being located on the precentral gyrus or over the central sulcus. In any case, the cortical representation of the hand corresponds to the sites where the median nerve SEPs of the greatest amplitude are obtained. Although intraoperative SEPs are valuable, the most crucial step for optimizing MCS electrode placement is to perform MEP mapping.

Intraoperative MEPs

Direct cortical stimulation (after dura mater opening) is performed for a long time in various neurosurgical procedures, for example, epilepsy or brain tumor surgery. In this application, the parameters of stimulation usually
consist of a train of biphasic stimuli (1 millisecond pulse duration) lasting from 2-5 seconds, delivered bipolarly (4-5 mm interelectrode spacing) at a frequency of 50-60 Hz and at an intensity ranging from 1.5-6 mA under local anesthesia (from 6-20 mA under general anesthesia). Later described, another validated protocol consists of a train of 5-10 monophasic rectangular stimuli (0.1-0.7 millisecond pulse duration), delivered monopolarly (anodally) at a frequency of 400-500 Hz and at a similar intensity to that used for bipolar stimulation. These methods of repetitive electrical stimulation were found to be equally sensitive for mapping the motor cortex. Maertens de Noorhout et al showed that intraoperative motor cortical mapping could also be performed by delivering single pulses. The parameters of stimulation consisted of single square waves of 1 millisecond duration, delivered anodally at an intensity ranging from 10-40 mA under general anesthesia.

For MCS electrode placement, intraoperative MEP mapping is faced with a constraint related to the epidural location of the stimulating electrodes. The dura mater considerably increases the threshold for corticospinal tract excitation. The usual parameters of direct (subdural) cortical stimulation should be inaccurate for epidural cortical mapping. Our initial procedure of epidural cortical mapping for MCS electrode placement consisted of a train of 3-5 monophasic rectangular stimuli (1 millisecond pulse duration, 20 microsecond interpulse interval), delivered bipolarly at a frequency of 16 Hz and an intensity ranging from 5-15 mA. However, these parameters of stimulation could generate seizures because the motor threshold was too close to the epileptic threshold in some patients. Therefore, we assessed the value of a single-pulse procedure for epidural motor cortical mapping similar to what was reported by Maertens de Noorhout et al for direct (subdural) cortical mapping. Single pulses were found to be able to evoke MEPs in virtually all patients, exceptions made for those with complete or severe motor deficit in the tested territory. Such parameters avoid (or at least greatly minimize) the risk of seizure during the procedure of cortical mapping.

In practice, we perform monopolar anodal stimulation, each contact of the epidural grid or quadripolar lead being successively activated as the anode. The cathode (reference electrode) is a subcutaneous needle or a steel plate electrode placed in the occipital region, to avoid direct activation of face muscles by the stimulation. The place of the reference electrode is important because facial responses caused by direct muscle activation could largely interfere with the recording of facial responses caused by the stimulation of the motor cortex. The parameters of stimulation consist of single square waves of 1-millisecond duration, delivered at an intensity ranging from 10-50 mA. The ground electrode is placed around the forearm with a loop tape strap. Electromyographic recordings should be preferred to visual inspection of movements, because it makes it possible to detect motor responses at lower intensity thresholds and provides objective, quantitative measurement (that is peak-to-peak MEP amplitude). The MEPs are recorded using a filter band pass of 20-2000 Hz, a time base of 50-100 milliseconds, and surface or subcutaneous needle electrodes placed over the target muscles. To compensate for the increase in cortical excitability threshold caused by epidural approach, MEP recordings need to be performed under a slight alleviation of the general anesthesia. Therefore, the infusion of anesthetic agents (propofol and remifentanil) is carefully monitored to maintain the bispectral index (BIS) around a value of 60 during MEP recordings. The rigorous control of the anesthetic procedure also permits the reliability and reproducibility of these recordings to increase. In rare cases, when a single pulse is not sufficient to evoke a motor response, we deliver a single train of two or three stimuli (20 microseconds interpulse interval). Of course, motor responses cannot be evoked in the case of total or severe motor deficit.

The mapping procedure consists of recording MEPs in a target muscle (that is located within the painful zone) in response to epidural cortical stimulation. It can be interesting to record MEPs also in territories that are situated outside or adjacent to the painful zone, to determine the anatomic precision of cortical motor mapping. In our experience of MCS electrode implantation, we had the opportunity to record intraoperative MEPs in any part of the body without any difficulty (eg, upper/lower face muscles, various segments of upper or lower limbs, trunk or perineal muscles) (Figure 2).

The first step is to determine the motor threshold that is the minimal intensity of stimulation required to evoke a reproducible MEP of more than 100 μV in amplitude in the target territory. For this purpose, the contact of the epidural grid or quadripolar lead that theoretically corresponds to the optimal motor cortical representation of the painful region (according to image-guided navigation and intraoperative SEP mapping) is selected as the anode. With the use of this montage, stimulation intensity is gradually increased by increments of 2 mA to a maximum of 50 mA for motor threshold determination. Cortical mapping is then performed at a fixed intensity set at 20-30% above the motor threshold. The complete procedure includes MEP recordings to monopolar cortical stimulation by using successively each contact of the epidural grid or quadripolar lead as an anode. From these recordings, the “best anode” is determined, that is the contact providing MEPs of maximal amplitude in the target territory when selected as an anode. The MEP measurements can also be performed by using each contact as a cathode, with the occipital reference as the anode. In our experience, we did not find the value of such recordings. In contrast, an additional interesting step is to record MEPs in the target territory in response to bipolar cortical stimulation, using the “best anode” as the anode and successively each adjacent contact of the grid or quadripolar lead as the cathode. The amplitude of
the MEPs evoked by the various bipolar combinations can be compared with that produced by the optimal anodal stimulation to estimate how much the contacts adjacent to the "best anode" interfere with this electrode.

End of the procedure

According to intraoperative mapping data and to the extent of the painful zone, one or two quadrupolar leads are positioned and sutured on the dura mater. As mentioned previously, the leads can be fixed parallel or perpendicular to the central sulcus. One important point is that at least two contacts need to be accurately placed in the precentral cortical representation of the target (painful zone). The extension wires are then tunneled underneath the skin and connected to a pulse generator, subcutaneously implanted in the subclavicular (pectoral) or abdominal region. This step is usually performed in the same operative time as epidural electrode implantation. In contrast to spinal cord stimulation, a trial period is not recommended to see whether MCS provides satisfactory pain relief without side effects before the system is permanently implanted. Actually, it can take a couple of weeks to determine whether MCS is efficacious, because analgesic after effects of the surgical procedure of MCS electrode implantation can be prolonged (more than a week). In our opinion, a trial period before permanent implantation would dramatically increase the risk of device infection at cortical level. Actually, MCS system implantation is performed right away as it is the case for deep brain stimulation.

After implantation, the patient stays in hospital for 1 week to ensure proper healing of the incision. During this time, several stimulation parameters are screened. At discharge, the stimulator can be switched "on." The parameters of stimulation required for optimal pain control are still not perfectly characterized. However, intraoperative data should help in the programming algorithm of chronic stimulation as discussed later in the article.

Correlation between intraoperative MEP and chronic epidural stimulation

Chronic stimulation parameters (pulse width: 60-180 microsecond; frequency: 20-60 Hz; voltage: 1-4 V) largely differ from those applied for intraoperative mapping. In particular, intensities used for chronic stimulation are far below motor threshold, whereas intraoperative motor mapping obviously requires suprathreshold intensities. Nevertheless, we have recently shown that the contact providing MEPs of maximal amplitude in pain territory when selected as an anode during intraoperative mapping ("best anode") corresponded to the contact providing optimal analgesic effects when selected as a cathode for chronic stimulation ("best cathode").

One explanation was found to explain this paradox. According to differential membrane properties, axons are more prone than cell bodies to be activated by neurostimulation techniques. The contact providing MEPs of maximal amplitude in the painful territory when selected as an anode ("best anode") should be located right above the origin of the corticospinal tract corresponding to this territory. However, when selected as a cathode, a contact preferentially activates the fibers that run parallel to it. The analgesic effects of MCS are essentially produced by cathodal activation of horizontal fibers located in the superficial layers of the cortex and in the vicinity of the origin of the pyramidal tract corresponding to the painful region, but not by direct activation of the pyramidal tract.

Beyond pathophysiologic hypotheses, the correlation between intraoperative "best anode" and chronic "best cathode" provides valuable information in practice, for optimizing MCS settings: the contact that is the intraoperative "best anode" should be selected as the negative electrode (cathode) for chronic stimulation. However, bipolar stimulation is generally performed. The selection
### Table 1  
Review of the literature about the intraoperative methods used for cortical electrode placement in the treatment of pain by motor cortex stimulation

<table>
<thead>
<tr>
<th>Ref no.</th>
<th>Team (city, country)</th>
<th>Authors</th>
<th>Journal</th>
<th>Patients (n)</th>
<th>Motor cortex localization</th>
<th>Intraoperative SEPs (stimulated nerves)</th>
<th>Intraoperative MCS (stimulation parameters)</th>
<th>Intraoperative MCS (type of assessment)</th>
</tr>
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<tbody>
<tr>
<td>53</td>
<td>Brussels - AZ-VUB, Belgium</td>
<td>Herregodts et al</td>
<td>Acta Neurochir Suppl</td>
<td>7</td>
<td>Landmarks using preoperative 3D-MRI mapping</td>
<td>NO</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td>54</td>
<td>Brussels-Erasme, Belgium</td>
<td>Pirotte et al</td>
<td>Neurosurg Focus</td>
<td>12</td>
<td>Navigation using 3D-MRI</td>
<td>YES</td>
<td>YES (median and trigeminal nerves)</td>
<td>Not detailed</td>
</tr>
<tr>
<td>13</td>
<td>Brussels-Erasme, Belgium</td>
<td>Pirotte et al</td>
<td>Neurosurgery</td>
<td>18</td>
<td>Navigation using 3D-MRI and fMRI</td>
<td>YES (median nerve)</td>
<td>YES (bipolar, 1 ms-pulse delivered at 60Hz)</td>
<td>MEP recordings</td>
</tr>
<tr>
<td>52</td>
<td>Brussels - Saint-Luc, Belgium</td>
<td>Delavallée et al</td>
<td>Neurosurgery</td>
<td>8</td>
<td>Anatomic landmarks and navigation using ?</td>
<td>YES (median nerve)</td>
<td>YES (bipolar, 0.2 ms-pulse delivered at 50 Hz)</td>
<td>Visual inspection and MEP recordings</td>
</tr>
<tr>
<td>55</td>
<td>Burlington, NH</td>
<td>Arle and Shils</td>
<td>Neurotherapeutics</td>
<td>8</td>
<td>Anatomic landmarks</td>
<td>YES (median and ulnar nerves)</td>
<td>YES (monopolar, 5-pulse train [0.5 ms pulse duration, 4 ms interpulse interval] delivered at 5 Hz)</td>
<td>MEP recordings</td>
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<tr>
<td>35</td>
<td>Cleveland, OH</td>
<td>Henderson et al</td>
<td>Stereotact Funct Neurosurg</td>
<td>6</td>
<td>Navigation using 3D-MRI</td>
<td>YES (median nerve)</td>
<td>YES (bipolar, 0.05-0.45 ms-pulse delivered at 30-150 Hz)</td>
<td>Visual inspection</td>
</tr>
<tr>
<td>56</td>
<td>Créteil, France</td>
<td>Nguyen et al</td>
<td>Acta Neurochir Suppl</td>
<td>20</td>
<td>Landmarks using preoperative MRI</td>
<td>YES (median nerve)</td>
<td>YES (bipolar, 0.1 ms-pulse delivered at 30-40 Hz)</td>
<td>Visual inspection</td>
</tr>
<tr>
<td>6</td>
<td>Créteil, France</td>
<td>Nguyen et al</td>
<td>Pain</td>
<td>32</td>
<td>Navigation using 3D-MRI and CT scan reconstructions</td>
<td>YES (median nerve)</td>
<td>YES (bipolar, 3-pulse train [1 ms pulse duration, 0.02 ms interpulse interval] delivered at 16-20 Hz)</td>
<td>Visual inspection</td>
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<td>44</td>
<td>Créteil, France</td>
<td>Holsheimer et al</td>
<td>Clin Neurophysiol</td>
<td>8</td>
<td>Navigation using 3D-MRI and CT scan reconstructions</td>
<td>YES (median nerve)</td>
<td>YES (monopolar, single anodal 1 ms-pulse)</td>
<td>MEP recordings</td>
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<th>Intraoperative MCS (stimulation parameters)</th>
<th>Intraoperative MCS (type of assessment)</th>
</tr>
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<tr>
<td>9</td>
<td>Créteil, France and Mexico City, Mexico</td>
<td>Nguyen et al</td>
<td>Brain Stim</td>
<td>10</td>
<td>Navigation using 3D-MRI and CT scan reconstructions</td>
<td>YES (median nerve)</td>
<td>YES (monopolar, single anodal 1 ms-pulse)</td>
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<td>Detroit, MI</td>
<td>Brown and Pilitsis</td>
<td>Neurosurgery</td>
<td>10</td>
<td>Navigation using MRI</td>
<td>YES (median nerve)</td>
<td>YES (bipolar, single 5-pulse trains?)</td>
<td>MEP recordings</td>
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<td>57</td>
<td>Halle, Germany</td>
<td>Rainov et al</td>
<td>Clin Neurol Neurosurg</td>
<td>2</td>
<td>Not detailed</td>
<td>YES (median nerve)</td>
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<tr>
<td>58</td>
<td>Halle, Germany and Liverpool, UK</td>
<td>Rainov and Heidecke</td>
<td>Neurol Res</td>
<td>2</td>
<td>Navigation using MRI</td>
<td>YES (median nerve)</td>
<td>NO</td>
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<tr>
<td>59</td>
<td>Heidelberg and Giessen, Germany</td>
<td>Ebel et al</td>
<td>Acta Neurochir (Wien)</td>
<td>7</td>
<td>Anatomic landmarks</td>
<td>YES (median nerve)</td>
<td>YES (not detailed)</td>
<td>Visual inspection</td>
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<td>8</td>
<td>Heidelberg, Germany</td>
<td>Rasche et al</td>
<td>Pain</td>
<td>17</td>
<td>Anatomic landmarks and navigation using 3D-MRI or fMRI</td>
<td>YES (median and tibial nerves)</td>
<td>YES (bipolar?, 0.21 ms-pulse delivered at 5-100 Hz)</td>
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<td>7</td>
<td>Lyon, France</td>
<td>Mertens et al</td>
<td>Stereotact Funct Neurosurg</td>
<td>16</td>
<td>Navigation using MRI</td>
<td>YES (not detailed)</td>
<td>YES (not detailed)</td>
<td>Not detailed</td>
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<td>37</td>
<td>Lyon, France</td>
<td>Nuti et al</td>
<td>Pain</td>
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<td>Navigation using MRI</td>
<td>YES (not detailed)</td>
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<td>Marburg, Germany</td>
<td>Tirakotai et al</td>
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<td>10</td>
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<td>Velasco et al</td>
<td>J Neurosurg</td>
<td>11</td>
<td>Landmarks using anatomy and preoperative MRI</td>
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<td>34</td>
<td>New York, NY</td>
<td>Mogilner and Rezai</td>
<td>Neurosurg Focus</td>
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<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
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<td>61</td>
<td>Osaka, Japan</td>
<td>Saitoh et al</td>
<td>J Neurosurg</td>
<td>8</td>
<td>Landmarks using preoperative MRI mapping</td>
<td>YES (median and tibial nerves)</td>
<td>NO</td>
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<td>62</td>
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<td>15</td>
<td>Landmarks using preoperative MRI mapping</td>
<td>YES (median and tibial nerves)</td>
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<td>63</td>
<td>Osaka, Japan</td>
<td>Saitoh et al</td>
<td>Acta Neurochir Suppl</td>
<td>19</td>
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<td>Hosomi et al</td>
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<td>Visual inspection</td>
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<td>Smith et al</td>
<td>Neurosurg Focus</td>
<td>12</td>
<td>Anatomic landmarks</td>
<td>NO</td>
<td>YES (bipolar?, 5-10 Hz)</td>
<td>Visual inspection</td>
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<td>67</td>
<td>Oxford, UK</td>
<td>Nandi et al</td>
<td>J Clin Neurosci</td>
<td>6</td>
<td>Anatomic landmarks</td>
<td>NO</td>
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<td>Visual inspection</td>
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<tr>
<td>18</td>
<td>Roma, Italy</td>
<td>Cioni and Meglio</td>
<td>Acta Neurochir Suppl</td>
<td>14</td>
<td>Not detailed</td>
<td>YES (median nerve)</td>
<td>YES (bipolar, 5-pulse train (0.5 ms pulse duration, 4 ms interpulse interval) delivered at 2 Hz)</td>
<td>MEP recordings</td>
</tr>
<tr>
<td>68</td>
<td>San Francisco, CA</td>
<td>Hosobuchi et al</td>
<td>Adv Neurol</td>
<td>6</td>
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<td>YES (median nerve)</td>
<td>YES (not detailed)</td>
<td>Visual inspection</td>
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<tr>
<td>69</td>
<td>Seoul, Korea</td>
<td>Son et al</td>
<td>J Neurosurg</td>
<td>1</td>
<td>Navigation using 3D-MRI</td>
<td>NO</td>
<td>YES (bipolar, 1-2 Hz)</td>
<td>Visual inspection</td>
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<tr>
<td>2</td>
<td>Tokyo, Japan</td>
<td>Tsubokawa et al</td>
<td>PACE</td>
<td>7</td>
<td>Anatomic landmarks</td>
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<td>NO</td>
<td>MEP recordings</td>
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<td>3</td>
<td>Tokyo, Japan</td>
<td>Tsubokawa et al</td>
<td>Acta Neurochir Suppl</td>
<td>12</td>
<td>Anatomic landmarks</td>
<td>YES (not detailed)</td>
<td>NO</td>
<td>MEP recordings</td>
</tr>
<tr>
<td>4</td>
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<td>Tsubokawa et al</td>
<td>J Neurosurg</td>
<td>11</td>
<td>Anatomic landmarks</td>
<td>YES (not detailed)</td>
<td>NO</td>
<td>Visual inspection</td>
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<tr>
<td>70</td>
<td>Tokyo, Japan</td>
<td>Yamamoto et al</td>
<td>Pain</td>
<td>28</td>
<td>Anatomic landmarks</td>
<td>YES (not detailed)</td>
<td>NO</td>
<td>Visual inspection</td>
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<td>71</td>
<td>Tokyo, Japan</td>
<td>Katayama et al</td>
<td>J Neurosurg</td>
<td>31</td>
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<td>Not detailed</td>
<td>YES (bipolar, 1-2 Hz)</td>
<td>Visual inspection</td>
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<td>72</td>
<td>Tokyo, Japan</td>
<td>Fukaya et al</td>
<td>Neurol Res</td>
<td>31</td>
<td>Anatomic landmarks</td>
<td>Not detailed</td>
<td>YES (bipolar, 1-2 Hz)</td>
<td>Visual inspection</td>
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</tbody>
</table>
of a contact as the positive electrode (anode) is more arbitrary. The contact that is just posterior to the cathode is usually selected as the anode. Optimal location for the anode may be over the central sulcus or the anterior wall of the postcentral gyrus. It should be underlined that according to interelectrode spacing, MCS is rather a “bifocal monopolar” than a true bipolar stimulation: different circuits can be concomitantly activated by the anode and the cathode. Therefore, selecting more distant contacts for chronic stimulation does not increase the volume of cortical activation as previously suggested, but results in a more bifocal stimulation, activating more distinct neural pathways. Similarly, increasing stimulation intensity does not improve MCS efficacy that probably relates to fiber activation in superficial cortical layers, but recruits additional neural circuits that originate in deeper cortical layers.

Various factors make MCS programming a very complex task. First, there are a lot of possible parameter combinations. Second, no sensory or motor signs are produced during the stimulation. Third, clinical effects usually become noticeable several days beyond the time of stimulation parameter changes: analgesia is delayed when the stimulator is switched “on” and after effects are prolonged when the stimulator is switched “off.” This is the reason why it is useless to assess the possible anagelsic effects that could be produced by the stimulation of the cortex intraoperatively. Conversely, in other neurostimulation techniques, programming can be guided by the clinical effects that are produced as soon as the stimulator is switched “on,” like paresthesias in the painful limb after spinal cord stimulation or tremor arrest after thalamic or subthalamic nucleus stimulation.

**Conclusion**

Chronic MCS is a therapeutic option in refractory neuropathic pain syndromes of various origins. The results published in the literature cover more than 300 patients with a large majority of responders. The current article did not address MCS efficacy, but the neurophysiologic methods of electrode placement. Various approaches have been reported (Table) and the method described here is not the only acceptable option available to neurosurgeons. In addition, we perform epidural cortical stimulation, whereas some groups prefer direct cortical stimulation with subdural electrode placement rather than epidural. Our approach is mostly based on MEP recordings in response to monopolar (anodal) stimulation of the cortical region corresponding to the painful area. We cannot prove that our procedure is the best one, but we have shown that there was a correlation between intraoperative MEP results and outcome. We also do not know if there could be a subpopulation that would benefit most from MEP mapping. In contrast, it is clear that MEP mapping cannot be used in patients with total or severe motor deficit. In

**Table 1 (continued)**

<table>
<thead>
<tr>
<th>Ref no.</th>
<th>Team (city, country)</th>
<th>Authors</th>
<th>Journal</th>
<th>Patients (n)</th>
<th>Motor cortex localization</th>
<th>Intraoperative SEPs (stimulated nerves)</th>
<th>Intraoperative MCS (stimulation parameters)</th>
<th>Intraoperative MCS (type of assessment)</th>
<th>Intraoperative MCS (stimulation parameters)</th>
<th>Intraoperative MCS (type of assessment)</th>
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<tr>
<td>26</td>
<td>Toulouse, France</td>
<td>Roux et al</td>
<td>Neurosurgery</td>
<td>1</td>
<td>Navigation using 3D-MRI and fMRI</td>
<td>YES (not detailed)</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
</tr>
<tr>
<td>27</td>
<td>Toulouse, France</td>
<td>Roux et al</td>
<td>Neurosurgery</td>
<td>6</td>
<td>Navigation using 3D-MRI and fMRI</td>
<td>YES (not detailed)</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
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<td>12</td>
<td>Toulouse, France</td>
<td>Sol et al</td>
<td>Stereotact Funct Neurosurg</td>
<td>3</td>
<td>Navigation using 3D-MRI and fMRI</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
<td>Visual inspection or MEP recordings</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
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<td>16</td>
<td>Turin Italy</td>
<td>Canavero and Bombari</td>
<td>Acta Neurochir Suppl</td>
<td>11</td>
<td>Landmarks using preoperative CT</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
<td>Visual inspection or MEP recordings</td>
<td>YES (not detailed)</td>
<td>Visual inspection or MEP recordings</td>
</tr>
</tbody>
</table>

SEP = somatosensory-evoked potential; MCS = motor cortex stimulation; 3D = three-dimensional; MRI = magnetic resonance imaging; ms = millisecond; CT = computed tomography; MEP = motor-evoked potential; fMRI = functional MRI; MEG = magnetoencephalography.
this case, the most reliable method of electrode placement may be fMRI-guided navigation. Actually, concordance between contours of fMRI activation area and intraoperative electrophysiologic mapping with SEPs and MEPs was found in a large majority of patients.28

Finally, we hypothesize that intraoperative electrophysiologic mapping adds something in terms of electrode placement and therefore of better outcome, because we assume that MCS efficacy critically depends on the accuracy of electrode placement. The therapeutic efficacy of MCS also depends on the quality of postoperative management, and particularly on the adaptation of optimal parameters for chronic stimulation.

Acknowledgments

Prof. Jean-Pascal Lefaucheur gratefully thanks Prof. Jean-Paul Nguyen for their fruitful collaboration for 10 years in the development of MCS treatment for chronic pain and Prof. Jan Holsheimer for his major work on MCS modeling that allowed to gain a better understanding of the mechanism of action of epidural cortical stimulation in pain.

References