The Zeiss-MKM system for frameless image-guided approach in epidural motor cortex stimulation for central neuropathic pain

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Object. Twelve patients (seven female, and five male, mean age 55.6 years) suffering from refractory central (ischemic/traumatic [eight cases]) and neuropathic pain (trigeminal neuropathy [four cases]) underwent surgery for the implantation of an epidural motor cortex stimulation (MCS) device in which the authors used a frameless neuronavigation system, the Zeiss-MKM microscope.

Methods. The authors assessed the spatial accuracy of the neuronavigation system and its potential contribution to improve the quality of targeting pain. In these patients, the positions of the central sulcus, defined by stereotactic magnetic resonance MR imaging, intraoperative somatosensory evoked potentials (SSEPs) and subdural visual verification, were correlated into the stereotactic neuronavigation planning procedure. The mean spatial accuracy of distance between (MR) imaging–defined and actual central sulcus was 2.4 mm (range 5–10 mm). The intraoperative SSEP–defined central sulcus was close to that defined by MR imaging (mean distance 6.4 mm). Although very precise, intraoperative SSEP recordings were impaired by artifacts and wave attenuation in six of the 12 patients. Stereotactic correlations between anatomical and functional data in the navigation system corrected final targeting in 10 of 12 cases. Pain relief was obtained in eight patients. Indeed, inappropriate targeting probably explains the reported variable success rate of MCS and certainly underestimates the actual efficacy.

Conclusions. Since intraoperative SSEP monitoring has, for many years, been considered the standard procedure to approach motor target, the development of an accurate stereotactic image guidance system could help to increase the efficacy of MCS on the alleviation of pain. The excellent spatial accuracy provided by the Zeiss-MKM navigation system allows precise data correlations that represent a remarkable means to validate functional MR imaging as an alternative to SSEP. The authors believe that developing stereotactic image guidance with such a navigation system could improve the success rate of MCS.

KEY WORDS • pain • motor cortex stimulation • stereotaxy • neuronavigation

The actual efficacy of epidural chronic MCS in the alleviation of refractory central and neuropathic pain is still being evaluated. Indeed, different success rates of long-term pain relief ranging from 45 to 75% have been reported, mainly in chronic pain syndromes related to central poststroke pain or trigeminal neuropathy.1–4,7,18,20,21,24,32–34 These variable results could be related to inaccurate positioning of the stimulation electrode, and the actual efficacy of MCS could be underestimated.3,13,14,16,18,20,32–34

Since first described, intraoperative epidural SSEP recording became the standard procedure to localize the functional central sulcus and motor target.33,34 The surgical approach consisting initially in a trephination in the "estimated motor area"7,33,34 was even reduced to a burr-hole.12,13,18 A stereotactic neuronavigator with superficial computerized tomography reconstruction was later used21–23

Because appropriate targeting seems to be a crucial step in efforts to obtain pain relief in afflicted individuals, we developed a procedure in which an MCS device is implanted using a stereotactic image guidance frameless navigation system, the Zeiss-MKM microscope (Carl Zeiss, Oberkochen, Germany). In this preliminary series of 12 patients, our aim was to assess the spatial accuracy of this technique and to emphasize its potential use to improve the efficacy of MCS.

CLINICAL MATERIAL AND METHODS

Patient Population and Pain Assessment

Twelve patients (seven women and five men, who ranged in age from 33 to 70 years [mean 55.6 years], suf-
ferring from a chronic pain syndrome secondary to central or neuropathic lesions, have been treated since 1997 by chronic stimulation of the motor cortex. The underlying lesion and somatic distribution of pain are summarized in Table 1. Pain was refractory to extensive oral or intrathecal pharmacotherapy, and some patients had undergone different neurosurgical procedures to obtain resolution of symptoms. All patients gave informed consent to the procedure and were treated according to the ethical guidelines of our institution. The pain and changes in pain level were assessed by a neurologist and a psychiatrist of the Pain Clinic. Pain level was preoperatively evaluated using a visual analog scale with scores ranging from 0 to 100. The efficacy of MCS to reduce pain was classified into four previously described categories: 1) excellent (80–100% pain reduction); 2) good (60–79% improvement); 3) satisfactory (40–59% improvement); and 4) failure (< 40% improvement). ²⁰

Stereotactic Image Guidance and Surgical Procedure

We applied a technique combining the intraoperative epidural SSEP recordings with stereotactic image guidance. ²⁰ We used a frameless neuronavigation system, the Zeiss-MKM microscope, and acquired MR imaging data in frameless stereotactic conditions with the skin-based markers. Axial 3D T₁-weighted MR images (130 slices) of the brain were transferred into a stereotaxis planning workstation (STP4.0; Leibinger/Fischer, Freiburg, Germany), allowing multiplanar visualization of the brain structures, especially the cortical sulci. The central sulcus was localized³⁶ and its precise shape registered in the 3D coordinates of the central sulcus were then visually verified using the Zeiss-MKM microscope. A 5 × 5-cm-square craniectomy was performed after induction of general anesthesia with propofol and sufentanil. The patient’s head was fixed in a Mayfield clamp to allow for stereotactic navigation.

A quadripolar electrode (Resume II; Medtronic Inc., Minneapolis, MN) was placed at different locations on the dural surface to cover the central sulcus region. The location of the central sulcus was defined by means of the phase reversal of the N₂₀P₃₀ wave on the intraoperative SSEP after stimulation of the contralateral median nerve, as has been previously described. ³⁷ Stimulation of some areas of the contralateral side of the face was performed in patients with facial pain, according to a previously described technique. ¹⁷ The location of the motor cortex was again confirmed by ES of the cortex through the Resume II electrode (pulse duration 1 msec, 5-Hz trains) in the last five patients to undergo the procedure. We used a Pathfinder Viking IV stimulator (Nicolet Biomedical Inc., Madison, WI). With this method, an epidural map of the functional central sulcus was designed by intraoperative SSEP as previously described. ²⁰ ²¹ ³⁷

After definition of the functional central sulcus by intraoperative SSEP, spatial coordinates of the intraoperative SSEP-defined central sulcus and motor target were projected on the stereotactic navigation planning station. Before fixating the stimulation electrode epidurally, the dura mater was opened and immediately sutured (without perforation of the arachnoid layer) to abolish local stimulation pain. ²⁰ ²¹ ³² The actual coordinates of the central sulcus were then visually verified and registered using the Zeiss-MKM microscope.

In all patients, fMR imaging was also performed. Our intention was only to assess its feasibility and to compare its results with data obtained by the standard localizing technique.

Stereotactic Correlations

At this stage of the procedure, we registered and correlated in the stereotactic navigation planning system all the targets obtained by anatomical imaging and observation

### TABLE 1

Summary of neurological data in 12 patients with refractory chronic pain syndromes*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Pain Territory</th>
<th>Underlying Lesion</th>
<th>Unsuccessful Therapies</th>
<th>Sensitivity</th>
<th>Allosthesia</th>
<th>Voluntary Movements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40, F</td>
<td>face (V₂–₃)</td>
<td>trigeminal neuralgia</td>
<td>TC, BMC, MVD</td>
<td>+</td>
<td>+</td>
<td>normal</td>
</tr>
<tr>
<td>2</td>
<td>62, M</td>
<td>upper limb</td>
<td>capsular stroke</td>
<td>NSAID, TR, BZD</td>
<td>++</td>
<td>+</td>
<td>paralysis</td>
</tr>
<tr>
<td>3</td>
<td>65, F</td>
<td>lower limbs</td>
<td>spinal cord ependymoma</td>
<td>ITB, ITM, SCS</td>
<td>+</td>
<td>++</td>
<td>paresis</td>
</tr>
<tr>
<td>4</td>
<td>33, F</td>
<td>upper limb</td>
<td>brainstem stroke</td>
<td>NSAID, TR, BZD</td>
<td>+</td>
<td>+</td>
<td>normal</td>
</tr>
<tr>
<td>5</td>
<td>66, F</td>
<td>upper limb</td>
<td>subcortical Stroke</td>
<td>NSAID, TR, BZD</td>
<td>+</td>
<td>+</td>
<td>paresis</td>
</tr>
<tr>
<td>6</td>
<td>34, M</td>
<td>upper limb</td>
<td>plexus avulsion</td>
<td>NSAID, TR, BZD, TENS</td>
<td>+</td>
<td>++</td>
<td>paralysis</td>
</tr>
<tr>
<td>7</td>
<td>38, F</td>
<td>face (V₂)</td>
<td>dental avulsion</td>
<td>TC, CBZ</td>
<td>+</td>
<td>+++</td>
<td>normal</td>
</tr>
<tr>
<td>8</td>
<td>70, M</td>
<td>upper limb</td>
<td>cervical syrinx</td>
<td>syrinx drainage</td>
<td>+</td>
<td>+</td>
<td>paresis</td>
</tr>
<tr>
<td>9</td>
<td>65, F</td>
<td>upper limb</td>
<td>postradic plexopathy</td>
<td>NSAID, TR, BZD, TENS</td>
<td>+++</td>
<td>+++</td>
<td>paralysis</td>
</tr>
<tr>
<td>10</td>
<td>50, F</td>
<td>face (V₂–₃)</td>
<td>multiple sclerosis</td>
<td>NSAID, TR, BZD, CBZ</td>
<td>+</td>
<td>+</td>
<td>normal</td>
</tr>
<tr>
<td>11</td>
<td>73, M</td>
<td>upper limb</td>
<td>arm avulsion/amputation</td>
<td>NSAID, TR, BZD</td>
<td>++</td>
<td>+</td>
<td>none</td>
</tr>
<tr>
<td>12</td>
<td>70, M</td>
<td>face (V₂)</td>
<td>tumor</td>
<td>RT, TR, CBZ, BZD</td>
<td>+</td>
<td>+</td>
<td>normal</td>
</tr>
</tbody>
</table>

* BMC = balloon microcompression; BZD = benzodiazepines; CBZ = carbamazepine; ITB = intrathecal baclofen; ITM = intrathecal morphine; MVD = microvascular decompression; NSAID = nonsteroidal antiinflammatory drugs; RT = radiation therapy; SCS = spinal cord stimulation; TENS = transcutaneous electrical nerve stimulation; TC = thermocoagulation; TR = tricyclic antidepressants; V₂, V₃ = second and third branches of the trigeminal nerve; + = moderate; ++ = severe; +++ = maximum.
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Results

Analgesic Efficacy

Motor cortex stimulation induced significant, reproducible, and long-lasting pain relief in eight patients (excellent reduction in six [Cases 2, 4, 5, and 10–12] and good relief in two [Cases 1 and 8]; Table 2). The alleviation of pain occurred from 10 to 15 minutes after the start of stimulation and lasted from 15 to 120 minutes after the 1-hour duration of ES was switched off. Two patients reported that pain relief remained stable for more than 24 hours if the stimulation period was longer than 4 hours. Moreover, the first three patients in whom the MCS system was implanted described that severe pain recurred when they switched the ES off for more than 2 days. In four patients (Cases 3, 6, 7, and 9) no response to MCS was elicited. In one patient (Case 12), a 10-minute ES period at low amplitude (<1 V), induced focal seizures, although it was associated with excellent pain relief. In four patients (Case 3, 6, 7, and 9), no analgesic effect was observed. The patients in Cases 6 and 9 were those in whom the most significant wave attenuation was observed on intraoperative SSEP recordings. In these cases, repeated intraoperative SSEP recordings provided inconsistent reproducibility and difficult definition of the final motor target. After the failure was observed, we proposed reoperation to both patients (with intraoperative SSEP recordings) for repositioning the electrode. The patient in Case 6 agreed to undergo the procedure, but repositioning did not yield clinical effect. The patient with refractory lower-extremity pain (Case 3) experienced no clinical effect. Finally, although MCS failed to alleviate pain, no additional surgery was performed in the patient in Case 7 because operative...
Clinical Efficacy

Motor cortex stimulation induced complete pain relief in six (50%) of the 12 patients and significant but incomplete pain relief in two others. This effect was reproducible and persistent on long-term follow up. We observed that the analgesic effect occurred a few minutes after stimulation. It also remained stable for several minutes after the ES was discontinued. This small series does not allow us to discuss the results according to the type and location of the underlying lesion. Our results can be compared with those reported in other series in the literature.3,7,9,11,13,15,17,18,20,25,28,30–34 Various success rates of long-term pain relief, however, ranging from 45 to 75%, have been reported.3,7,18,20,21,24,32–34 The best results were obtained in patients with chronic painful syndromes due to central post-stroke pain and trigeminal neuropathy.7,18,21,32 The variability of these results could be related to multiple factors including the quality of patient selection. Different techniques have been proposed to improve the quality of patient selection, including barbiturates and an morphine test and the observation that transcranial magnetic coil stimulation of the motor cortex could predict the response to epidural MCS in patients with deafferentation pain.5,6,19 This suggests that a better patient selection process could improve the MCS success rate.10,11,15,25,35

In the assessment period of the four patients in whom no response to MCS was demonstrated, we also wondered about the inaccuracy of targeting. The variability of the reported results could also be related to inaccurate positioning of the stimulation electrode.18,33 Because appropriate targeting is a crucial step in the effort to induce pain relief, the actual efficacy of MCS could be underestimated. This possibility led us to the conviction that the optimization of MCS efficacy will require the development of an accurate stereotactic image guidance system.22,23,29

**TABLE 2**

Effect of MCS on alleviation of pain*  

<table>
<thead>
<tr>
<th>Case No.</th>
<th>VAS</th>
<th>Result</th>
<th>Duration (hrs)</th>
<th>Delay Before Effect (mins)</th>
<th>Duration of Effect (mins)</th>
<th>Intake of Analgesic Drugs or Movements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 &gt; 2</td>
<td>good</td>
<td>1/4</td>
<td>10</td>
<td>15–20</td>
<td>not reduced</td>
</tr>
<tr>
<td>2</td>
<td>6 &gt; 1</td>
<td>excellent</td>
<td>2/3</td>
<td>15</td>
<td>30</td>
<td>reduced by 50%</td>
</tr>
<tr>
<td>3</td>
<td>7 &gt; 6</td>
<td>failure</td>
<td>2/4</td>
<td>15</td>
<td>45</td>
<td>reduced by 75%</td>
</tr>
<tr>
<td>4</td>
<td>8 &gt; 1</td>
<td>excellent</td>
<td>1/3</td>
<td>10</td>
<td>60</td>
<td>reduced by 50%</td>
</tr>
<tr>
<td>5</td>
<td>7 &gt; 0</td>
<td>excellent</td>
<td>1/4</td>
<td>10</td>
<td>60</td>
<td>reduced by 50%</td>
</tr>
<tr>
<td>6</td>
<td>8 &gt; 8</td>
<td>failure</td>
<td>1/6</td>
<td>10</td>
<td>120</td>
<td>reduced by 75%</td>
</tr>
<tr>
<td>7</td>
<td>8 &gt; 7</td>
<td>failure</td>
<td>2/3</td>
<td>15</td>
<td>30</td>
<td>reduced by 50%</td>
</tr>
<tr>
<td>8</td>
<td>7 &gt; 2</td>
<td>good</td>
<td>1/4</td>
<td>10</td>
<td>60</td>
<td>reduced by 50%</td>
</tr>
<tr>
<td>9</td>
<td>7 &gt; 7</td>
<td>failure</td>
<td>1/4</td>
<td>15</td>
<td>45</td>
<td>not reduced</td>
</tr>
<tr>
<td>10</td>
<td>8 &gt; 0</td>
<td>excellent</td>
<td>1/6</td>
<td>10</td>
<td>120</td>
<td>reduced by 75%</td>
</tr>
<tr>
<td>11</td>
<td>8 &gt; 1</td>
<td>excellent</td>
<td>2/3</td>
<td>15</td>
<td>30</td>
<td>reduced by 50%</td>
</tr>
<tr>
<td>12</td>
<td>7 &gt; 1</td>
<td>excellent</td>
<td>1/4</td>
<td>15</td>
<td>45</td>
<td>reduced by 50%</td>
</tr>
</tbody>
</table>

* The VAS graduated from 0 to 100. The analgesic efficacy of MCS was classified into 4 categories: 1) excellent (80 to 100% pain reduction); 2) good (60 to 79% improvement); 3) satisfactory (40 to 59% improvement); 4) failure (<40% improvement). The duration of stimulation is given as the lowest ratio between the length of stimulation period and duration separating the start of the two stimulation cycles.

DISCUSSION

This preliminary series represents the first step of a prospective study of MCS in patients with refractory central and neuropathic pain. The following results were obtained: 1) confirmation of the clinical efficacy of MCS; 2) emphasis of the usefulness of a stereotactic image guidance in MCS; 3) confirmation of the excellent spatial accuracy of the Zeiss-MKM microscope; and 4) presentation of the interest of stereotactic data correlations.

Stereotactic Correlations

The mean distance between the MR imaging–defined and actual central sulcus was 2.4 mm, and between the MR imaging–defined and intraoperative SSEP-defined central sulcus it was 6.4 mm (Table 3). These correlations are detailed in the Discussion.
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**Stereotactic Image Guidance**

This preliminary experience confirms the potential role of stereotactic image guidance in MCS. Although intraoperative SSEP recordings had early become the standard procedure to localize the functional central sulcus and motor cortex,7,18,28,33 the surgical approach was initially limited to a trephination or a burr hole in the “estimated motor area”7,12,13,18,33,34 to reduce the invasiveness of the technique. A simple procedure involving a 3D MR image with an external reference grid was proposed to define the central area grossly.12 Nguyen and coworkers20–24 were the first to use a stereotactic neuronavigator with superficial computerized tomography reconstruction to develop the technique further.

The Zeiss-MKM microscope is a commercially available frameless navigation system. From a surgical point of view, a large bone opening, skin incision, and shaving of the scalp appeared less important to these disabled patients than the actual therapeutic challenge of pain. Technically, the method is minimally invasive as long as the procedure remains epidural. In our experience, there is no need to implicate the epidural site of the stimulation electrode as a cause of the clinical failure; when no analgesic effect is obtained by stimulation of more than 6 V, there is no benefit to increasing the amplitude or placing the electrode subdurally.

**Spatial Accuracy of the Navigation System and Interest of Stereotactic Data Correlations**

These preliminary results show the excellent spatial accuracy obtainable when using the Zeiss-MKM microscope, which was compatible with the degree of precision required for MCS. This led us to consider the navigation planning system as a remarkable tool that allows spatial correlation between targets from different anatomical and functional methods.

First, the correlation between the MR imaging– and intraoperative SSEP-defined central sulcus data confirmed the high precision of latter to localize the central sulcus.26,27,36 Unfortunately, the correlation of data obtained using these modalities revealed the practical limitations of intraoperative SSEP recordings, thus indicating the potential superiority of fMR imaging as a localizing technique in this indication. Indeed, in all patients fMR imaging was also performed. Our goal was only to assess its feasibility. In this preliminary study, the fMR imaging–defined motor target was not considered for guiding MCS placement. We introduced the fMR imaging sequences in the stereotactic navigation planning,29 however, and compared the results with data obtained using intraoperative SSEP (Fig. 1).

During the navigation planning, we measured vertically and horizontally, in the sagittal plane, the distance between the intraoperative SSEP-defined motor target and the center of the fMR imaging–defined target of the hand. The mean distance between intraoperative SSEP- and fMR imaging–defined precentral activation signal was always vertically inferior to 9 mm and anteroposteriorly inferior to 5 mm. These correlations illustrated the precision of localizing the functional central sulcus in all cases. Functional MR imaging always provided a highly reproducible focal target diameter ranging from 5 to 10 mm whereas the quality of intraoperative SSEP recordings presented some limitations in 50% of patients. Additionally, in 10 of 12 patients (Cases 1, 2, 4–6, and 8–12), the correlations between the intraoperative SSEP- and fMR imaging–defined motor targets could correct the targeting, either confirming the intraoperative SSEP-defined targeting or helping to localize the target precisely obtained by artifacted/attenuated intraoperative SSEP recordings. These last two points will be developed in another work in which the feasibility of using fMR imaging as an alternative to intraoperative SSEP monitoring is assessed.

**CONCLUSIONS**

We believe that the use of a stereotactic image guidance could improve the success rate of MCS in the alleviation of central neuropathic pain. The navigation system of the Zeiss-MKM microscope provided excellent spatial accu-
racy that allowed precise correlations of data obtained using different techniques. These correlations helped to correct the final targeting and allowed prospective validation of new techniques such as fMRI imaging.

References


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