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*Original Article*

# Motor cortex stimulation for phantom limb pain treatment

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## ABSTRACT

**Background:** Phantom limb pain (PLP) is a chronic neuropathic pain syndrome experienced by individuals following limb amputation. Despite the use of various pharmacological treatments, including opioids, antidepressants, and anticonvulsants, effective pain relief remains challenging for many patients. Motor cortex stimulation (MCS) has emerged as a promising alternative for managing PLP.

**Methods:** We present the management of three patients with chronic, refractory PLP who underwent epidural MCS at Lille University Hospital Center. The quadripolar electrode lead was implanted into the epidural space under local anesthesia. Stereotactic angiography was used to determine the target coordinates, and the optimal location was confirmed with the guidance of a three-dimensional brain magnetic resonance imaging reconstruction and neurophysiological testing. Pain intensity was assessed using the Visual Analog Scale (VAS) at baseline and at the end of the follow-up period, which had a mean duration of 7 ± 2.16 months.

**Results:** Two of the three patients experienced a decrease in pain by 50%, and one had a 44.4% reduction. The average preoperative VAS score significantly decreased from 7.0 ± 1.73 to 3.67 ± 1.15 at the final follow-up ($P = 0.00985$). All patients reported a reduction in analgesic medication intake, and no major complications occurred.

**Conclusion:** PLP is one of the most challenging conditions to treat. MCS is an adjustable and reversible technique that appears to be effective in treating patients with this chronic pain syndrome refractory to other treatment modalities.

**Keywords:** Motor cortex stimulation, Neuromodulation, Neuropathic pain, Peripheral pain, Phantom limb pain

## INTRODUCTION

Phantom limb pain (PLP) is a type of chronic neuropathic pain that arises as a consequence of limb amputation. This condition, primarily affecting individuals with upper or lower extremity amputations, is characterized by the sensation of pain in a limb that no longer exists.[10,22] A recent meta-analysis estimates the prevalence of PLP to be as high as 64% among limb amputees.[12]

The earliest description of PLP was described in the 16th century by Ambroise Paré who proposed two neurological models for its cause: peripheral changes in peripheral nerves and cerebral alterations.[8] In the early 1990s, motor cortex stimulation (MCS) was introduced by Tsubokawa

*et al*. as a treatment option for central pain treatments.[26] Before this, methods such as reamputation, neurectomy, and attempts at spinal cord stimulation were explored but with limited success.[23] The advancement of the MCS technique evolved in the late 2000s, with Jean-Pascal Lefaucheur establishing it as a treatment option for managing refractory peripheral neuropathic pain.[11] Today, technological advancements allow not only for better electrode placement but also functional imaging studies to offer insights into how MCS can specifically alter brain neurochemistry.[5]

MCS has demonstrated efficacy in reducing chronic neuropathic pain, as evidenced by several clinical trials.[6,11,20] However, some questions remain regarding indications, mechanisms, implantation strategies, and other technical aspects of MCS therapy.[19] In this regard, we report the management of three patients with PLP refractory to other therapeutic modalities from a larger series of twenty-seven cases treated with epidural MCS.

## MATERIALS AND METHODS

### Patient population

Three patients with chronic PLP were considered eligible for MCS treatment at Lille University Hospital Center. A summary of the patient's data is presented in Table 1. The mean follow-up was 7 ± 2.16 months (ranging from 4 to 9 months).

All patients had been treated with various combinations of medications, including antidepressants, anticonvulsants, anti-inflammatory drugs, and opioids. However, these treatments were insufficient to provide adequate pain relief. Before surgery, electrophysiological testing, imaging evaluations, and psychological assessments were conducted for all patients. Individuals displaying significant depressive or neurotic tendencies were excluded as candidates for MCS.

### Pain assessment

The pain level and characteristics of each patient were evaluated by a multidisciplinary team at the Pain Clinic associated with our service. Patients were asked to report their pain intensity using a Visual Analog Scale (VAS) at baseline and at the end of the follow-up period, which had a mean duration of 7 ± 2.16 months. Stimulation effects were categorized into four categories: excellent (80–100% pain reduction), good (60–79% reduction), fair (40–59% reduction), and poor (<40% reduction).[21]

Preoperatively, patients' VAS scores ranged from 6 to 9, with an average score of 7 ± 1.73. The mean history of pain was 21.16 years.

### Surgical procedures

Electrodes were implanted into the epidural space under local anesthesia through a burr hole, following the method originally described by Tsubokawa *et al*.,[26,27] using a Talairach stereotactic frame. Stereotactic angiography was utilized to determine the target coordinates accurately. After the induction of general anesthesia, a straight incision was made over the central sulcus under image guidance [Figure 1], followed by a rectangular craniotomy over the sensorimotor cortex, exposing the dura mater.

All patients underwent implantation of a quadripolar electrode lead, with each of the 5 mm round electrodes spaced 5 mm apart (Resume™, Medtronic, Inc., Minneapolis, Minnesota). Upon confirming the optimal location using image guidance, electrophysiological testing (including wave inversion N20-P20) [Figure 2] and motor-evoked potentials were performed. The four-electrode array was affixed to the dura overlying the motor cortex using four sutures, positioned perpendicularly according to the orientation of the central sulcus in a parietal-to-frontal alignment [Figure 3]. The free electrode was then connected to an extension lead, which was tunneled subcutaneously to a subclavicular pocket, where it was attached to a pulse generator (Itrel™, Medtronic, Inc.) in a single-stage procedure.

### Postoperative care

A postoperative skull radiograph was performed to verify the positioning of the electrode array [Figure 4].

A programmer (Medtronic, 7432) was used for the generation and adjustment of stimuli at different parameters by telemetry. Bipolar stimulation was applied using pairs of contacts, while for monopolar stimulation, one contact was designated as the anode or cathode, and the pulse generator served as the opposite pole.

**Table 1:** Demographic data of the patients.

| Patient | Sex | Age (years) | Pain origin | Pain Location | VAS | Pain duration (months) |
|---|---|---|---|---|---|---|
| 1 | M | 31 | Phantom limb | Upper limb | 6 | 162 |
| 2 | F | 60 | Phantom limb | Lower limb | 6 | 252 |
| 3 | M | 49 | Phantom limb | Upper limb | 9 | 348 |

F: Female, M: Male, VAS: Visual analog scale

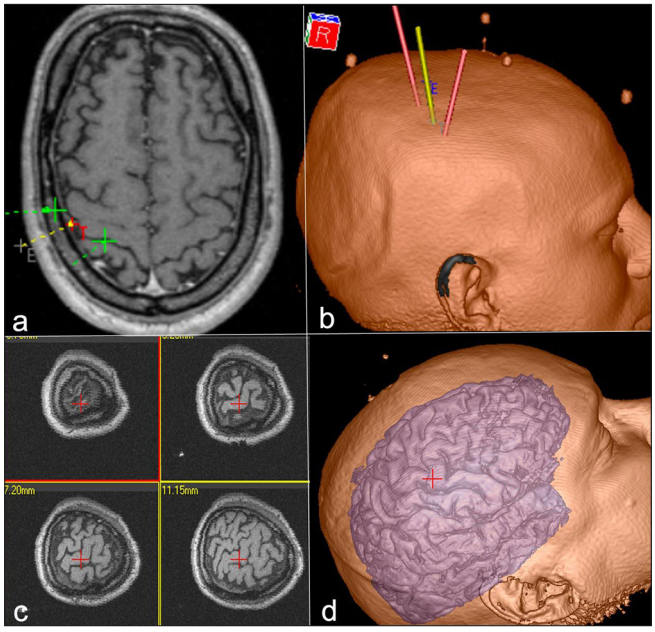


**Figure 1:** (a) Axial magnetic resonance imaging (MRI) highlighting the motor cortex (red) and the central sulcus (green) to identify the target site for motor cortex stimulation; (b) 3D reconstruction of the patient's skull showing the central sulcus projection; (c) Multiplanar views of MRI slices centered on the stimulation site; (d) 3D cortical surface reconstruction emphasizing the operative target for motor cortex stimulation in upper limb pain treatment.

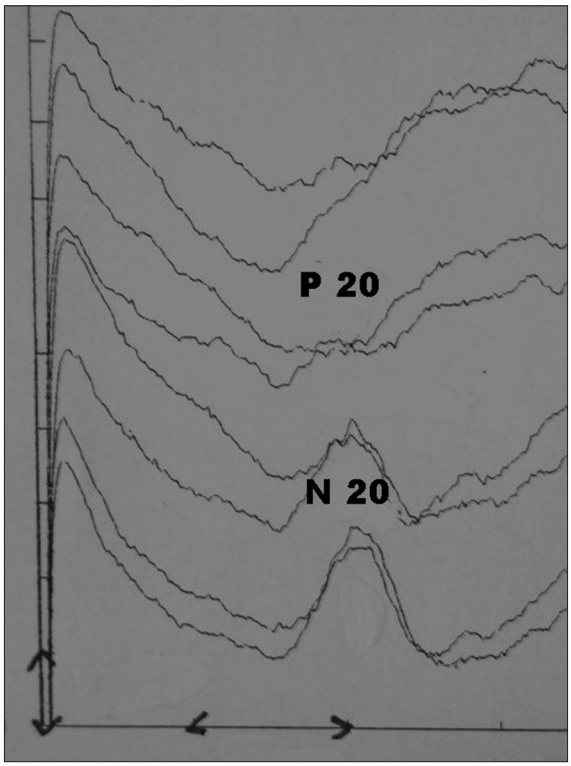


**Figure 2:** Perioperative somatosensory evoked potential showing a N20-P20 inversion corresponding to the central sulcus (median nerve stimulation: 3.7 Hz; 19 mA; active electrodes poles [0, 1, 2, 3]).

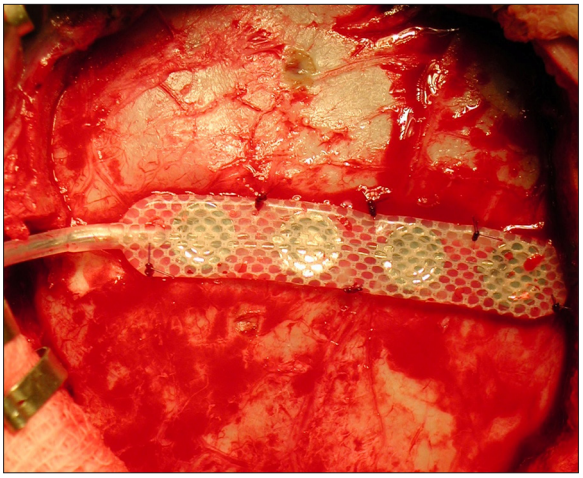

**Figure 3:** Perioperative image demonstrating the quadripolar electrode array fixed to the dura mater.

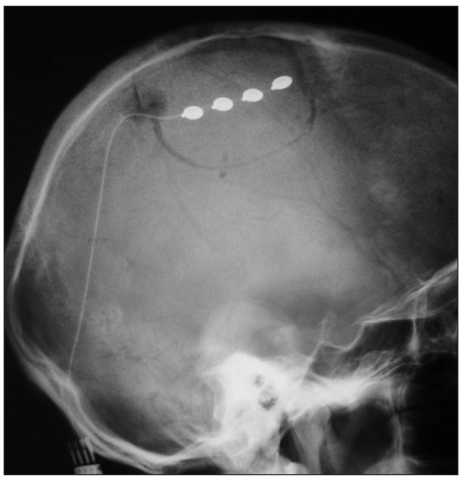

**Figure 4:** Postoperative cranial plain radiograph illustrating the epidural four-electrode array position over the motor cortex.

### Statistical analysis

Pearson's Chi-square ($\chi^2$) test was applied to analyze parametric data, and Student's *t*-test was used for nonparametric variables. All statistical analyses were conducted using Epi-Info 2000™ software (version 6.0, Centers for Disease Control, Atlanta, USA).

## RESULTS

### Pain relief

Among the three patients with PLP refractory to different therapeutic modalities that epidural MCS treated, two patients experienced a 50% reduction in pain, and one patient experienced a 44.4% reduction. The difference between the mean VAS scores before MCS and at the end of the follow-up period was statistically significant ($P = 0.00985$) [Table 2].

**Table 2:** Long-term results among patients treated with motor cortex stimulation, comparing the preoperative VAS score and the postoperative VAS score at the last follow-up assessment.

| | Mean VAS score | SD | t | *P*-value |
|---|---|---|---|---|
| Preoperative | 7.00 | 1.73 | 10.00 | 0.00985 |
| Postoperative | 3.67 | 1.15 | | |

VAS: Visual analog scale, SD: Standard deviation

In all patients, a reduction in the amount of analgesic medication intake was possible.

### Stimulation parameters

Stimulation was initially delivered at a pulse width of 45–60 μs, which increased to 60–210 μs by the final follow-up. The frequency began at 45–60 Hz and was adjusted to 45–130 Hz by the end of treatment. The amplitude initially ranged between 2 and 4 V (mean 2.9 ± 0.57), increasing to 2–5.3 V (mean 4 ± 0.8) over time. The active electrodes were determined through perioperative neurophysiological assessments and adjusted postoperatively based on the patient's response. Bipolar stimulation was used, with the negative pole positioned over the motor cortex and the positive over the sensory cortex.[15] The stimulation mode varied according to patient response and was adjusted multiple times, even for the same patient.

### Morbidity

No major complications were observed.

## DISCUSSION

PLP is the most prevalent form of postamputation pain syndrome, although its management remains a significant challenge. The pathophysiology underlying PLP involves both peripheral and central nervous system processes. The peripheral mechanisms, in particular, are linked to nerve damage, sensitization from ischemia, and reduced nociceptive thresholds.[13] The central processes, on the other hand, involve maladaptive plasticity within the somatosensory cortex, where compensatory reorganization occurs, as well as defects in the spinal cord's ability to differentiate nonpainful stimuli.[3]

The treatment guidelines generally follow a multidisciplinary approach to the management of pain, with nonsteroidal anti-inflammatory drugs being the most common pharmacological treatment for PLP. Other therapies include opioids, antidepressants, and anticonvulsants. Nonpharmacological therapies, such as transcutaneous electrical nerve stimulation, mirror therapy, and behavioral therapy, are also employed.[9,25] Among surgical options, spinal cord stimulation, deep brain stimulation, and MCS, the focus of this paper, are notable.[25]

MCS is a nondestructive, adjustable, and reversible technique, making it a preferable option over central neuroablative procedures for managing chronic neuropathic pain [17,18] despite being a relatively costly therapeutic approach.

Positron emission tomography studies have shown that cortical stimulation enhances cerebral blood flow to regions such as the cingulate gyrus, ipsilateral thalamus, orbitofrontal cortex, and brainstem.[14] In addition, activation of the brainstem's periaqueductal gray area is a potential effect of this treatment.[1]

Brodmann area 4 has established connections with the primary and secondary sensory cortices, Brodmann area 5, sensory and motor thalamic nuclei (ventral anterior, ventral lateral, ventral posterolateral, and posterior medial), hypothalamus, periventricular gray matter, and locus coeruleus.[4] Reciprocal pathways between the motor and sensory cortices mainly convey nonnoxious information related to targeted muscle movements. Stimulation of the precentral gyrus likely activates nonnociceptive neurons in the sensory cortex, potentially restoring its pain-inhibitory function.[27] The role of Brodmann area 4 in pain modulation is further supported by a clinical trial conducted by Saitoh *et al.*,[20], which identified the optimal point of stimulation for alleviating PLP and other neurogenic pain as being within this area through the central sulcus.

The rate of patients achieving approximately 50% pain relief in this study aligns with findings from other research, which reported that around half of MCS-treated patients experienced more than 50% reduction in pain.[7,16] Carroll *et al.*[2] have highlighted that this success rate is promising for a patient population that typically does not respond to other treatment options. Furthermore, a review by Smith *et al.*[24] demonstrated that the positive response rates to MCS range between 44% and 100%.

It is important to note that even achieving a 40% reduction in pain, while not ideal, represents a meaningful improvement for patients with severe, treatment-resistant pain. Considering the efficacy of other therapeutic approaches, converting intolerable pain into a manageable condition can substantially enhance a patient's quality of life.

## CONCLUSION

PLP is common and one of the most challenging conditions to treat. MCS is an adjustable and reversible technique that appears to be effective in treating patients with this chronic pain syndrome refractory to other treatment modalities.

**Ethical approval:** The Ethics Committee in Research at the Federal University of São Paulo approved this study on September 9, 2005, under registration number CEP 0969/05.
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