

# Peripheral Neuromodulation for Headache and Craniofacial Pain: Indications, Outcomes, and Complications From a Single Center

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The neurosurgical management of chronic headache and craniofacial pain syndromes has evolved over the past several decades. Early interest in neurostimulation for these conditions focused on deep brain targets. In 1973, Hosobuchi et al<sup>1</sup> described the use of thalamic stimulation to treat facial anesthesia dolorosa. Mazars and Pull<sup>2</sup> in 1976 described intermittent stimulation of the ventroposterolateral nucleus of the thalamus to treat intractable headache. Although these techniques were successful, there continued to be great interest in peripheral targets to minimize operative morbidity.

In 1997, Goadsby et al<sup>3</sup> reported that stimulation of the greater occipital nerve in cats resulted in increased metabolic activity of the trigeminal nucleus caudalis and cervical dorsal horn. These were among the first experiments to implicate the role of the greater occipital nerve in modulating the trigeminal system. This was translated clinically in 1999 when Weiner and Reed<sup>4</sup> reported that stimulation of the greater occipital nerves can alleviate pain associated with occipital neuralgia. Subsequently, the utility of occipital nerve stimulation in treating occipital neuralgia became firmly established. In 2004, Matharu et al<sup>5</sup> reported that occipital nerve stimulation was efficacious in treating chronic migraine, sparking further interest in the use of peripheral neurostimulation (PNS) in a number of headache and craniofacial pain syndromes.<sup>6-12</sup>

## PATIENTS AND METHODS

### Study Objectives

The purpose of this study was to review the indications and outcomes of PNS for headache and craniofacial pain from a single-center experience. Furthermore, we aimed to adopt a uniform classification scheme for headache and craniofacial pain that is understood by the headache community across multiple disciplines. Finally, we undertook a review of complications to promote strategies for complication avoidance.

### Study Design

After obtaining institutional review board approval, we performed a retrospective chart review of all patients who

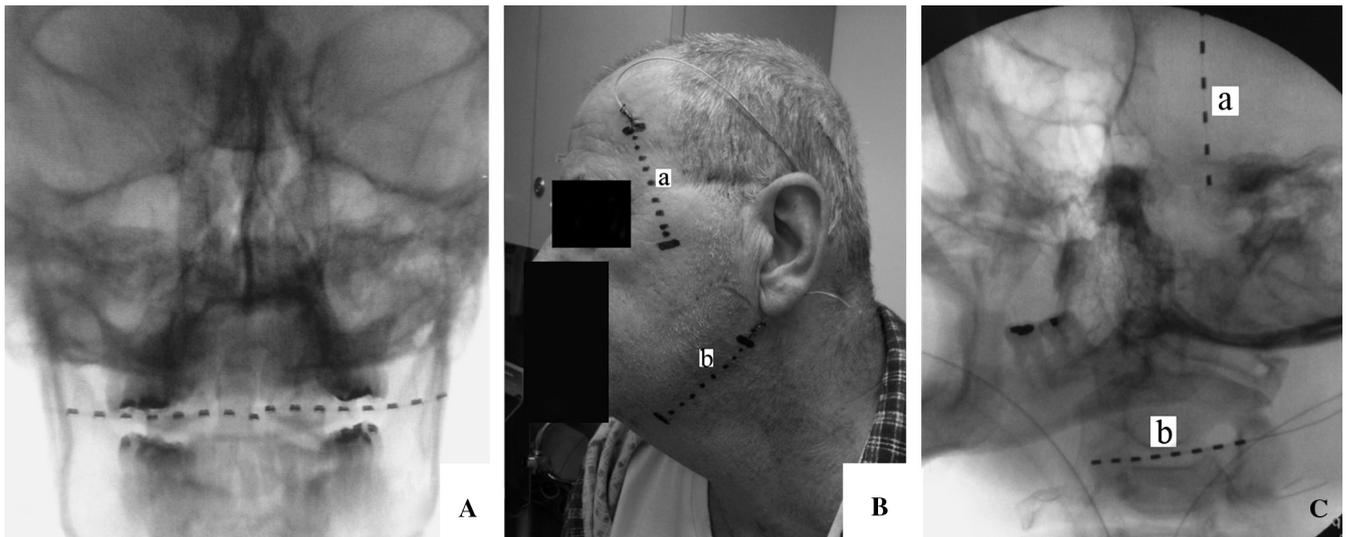
underwent PNS trials for headache or craniofacial pain from a single center between 2004 and 2011. In all, 99 patients were reviewed for this study. There were 74 female and 25 male patients with a mean age of 43 years (range, 11-68 years). Diagnoses were retrospectively classified according to the International Headache Society's International Classification of Headache Disorders II (ICHD-II) classification scheme.<sup>13</sup> Of the migraine patients, 8 were part of a multicenter randomized study (St. Jude Medical).

### Surgical Technique

The procedures performed included occipital nerve stimulation and/or trigeminal branch stimulation (Figure 1). All procedures were performed by the senior author (A.Y.M.). All surgeries were performed with C-arm fluoroscopic guidance, and every permanent stimulator implantation was preceded by a successful trial.

Percutaneous stimulator trials were performed with standard surgical technique. Trials were performed using local anesthesia with intravenous sedation. The patient was positioned prone or supine with the head turned, depending on where the leads were being placed. After infiltration with local anesthetic, a curved Tuohy needle was advanced subcutaneously under radiographic guidance to its desired position. A 4- or 8-pole spinal cord-stimulating electrode was advanced through the needle. After removal of the stylette and needle under fluoroscopic guidance, the lead was sutured to the skin with 2-0 silk ties. Intraoperative testing was not performed in most cases. Testing typically began in the recovery room and continued for 4 to 7 days on an outpatient basis. All patients were encouraged to maintain a headache/pain diary during the trial period, documenting headache/pain duration, frequency, and severity on the Visual Analog Scale.

Patients who reported a significant reduction in the frequency and severity of the headaches or facial pain during the trial period proceeded to permanent implantation, with the majority of the procedures performed under general anesthesia. Since early 2010, all patients have undergone a screening for methicillin-resistant *Staphylococcus aureus* colonization before permanent implantation. Patients who screened positive underwent a course of oral trimethoprim/sulfamethoxazole, intranasal mupirocin, and topical chlorhexidine soap.



**FIGURE 1.** Intraoperative anteroposterior radiograph demonstrating bilateral placement of octrode neurostimulator arrays (A). This 58-year-old man developed left V<sub>1</sub> and V<sub>3</sub> distribution pain after a brainstem infarct. Trigeminal branch stimulation trial leads were placed in the V<sub>1</sub> (a) and V<sub>3</sub> (b) regions, corresponding to the painful areas (B). Intraoperative lateral radiograph of the same patient demonstrating the final position of the implanted V<sub>1</sub> (a) and V<sub>3</sub> (b) region leads (C). Of the patients in this study, 71% underwent occipital neurostimulation only, 15% underwent trigeminal branch stimulation only, and 14% underwent both occipital and trigeminal branch stimulation.

Decolonization would be confirmed by nasal swab before implantation. Lead introduction proceeded in a fashion similar to that in the trial procedures. All leads were anchored to fascia with a plastic anchor or with multiple 2-0 silk ties in a purse-string fashion. The pulse generator was placed in a subcutaneous pocket, which was in an infraclavicular position, in most cases. All patients were discharged home on the day of surgery and received postoperative follow-up.

## RESULTS

### ICHD-II Classification

Ninety-five patients underwent percutaneous stimulator trials. Patient charts were critically reviewed and diagnoses were retrospectively made on the basis of the ICHD-II classification system. The most common diagnoses included Chiari I malformation (29%), migraine headache with or without aura (25%), posttraumatic headache (12%), postcraniotomy pain (7%), and occipital neuralgia (7%). Of note, all patients with Chiari I malformation who were considered for stimulation had already undergone suboccipital craniectomy and remained refractory. Furthermore, the group classified as having postcraniotomy pain included all patients whose headache syndrome developed after craniotomy and does not include any of the Chiari I patients who had undergone suboccipital craniectomy. The diagnoses are summarized in the Table.

### Patient Outcomes

Of 95 patients, 76 (81%) reported significant improvement during the trial, as defined by > 50% improvement in pain on the Visual Analog Scale, and proceeded to permanent implantation surgery. Lead distribution was 79% with occipital

only (59 patients), 11% with trigeminal branch only (9 patients), and 11% (8 patients) with both occipital and trigeminal branch leads. Follow-up ranged from 3 to 65 months. At the last follow-up, 82% (62 of 75) of those implanted reported continued significant benefit from stimulator use.

Patient outcomes were also substratified by preoperative diagnosis and analyzed. The data are summarized in the Table. When diagnoses with < 4 patients were excluded, trial success rates ranged from 64% (Chiari malformation headache patients) to 100% (postcraniotomy pain). Long-term success rates of those implanted ranged from 25% (trigeminal/terminal branch neuralgia) to 100% in chronic cluster and occipital neuralgia. On an intent-to-treat basis, success rates ranged from 20% (poststroke pain) to 88% (occipital neuralgia). One patient with hemicrania continua underwent a successful trial and reports long-term successful pain relief. The 1 patient with headache from a pituitary tumor and acromegaly reported a successful stimulator trial and underwent permanent implantation (100%). She did not report continued successful use of the stimulator at the last follow-up. Results are summarized in the Table.

### Complications

Complications, albeit minor, were not infrequent, similar to what has been reported in the literature. Lead migration necessitating revision occurred in 5 patients (7%; Figure 2). Infection necessitating explantation and replacement occurred in 6 patients (8% of all patients), of which 3 of 6 (50%) were on initial implantation and 3 of 6 (50%) followed surgical revision. Furthermore, in 3 of 6 patients (50%), there was erosion of the wound with exposed hardware, whereas in 3 of 6 (50%), there was clear surgical-site

**TABLE.** Neurostimulator Outcomes by Headache Diagnosis

Diagnosis	Patients, n	Successful Trials, n	Trial Success Rate, %	Permanent Systems Still Used at Last Follow-up, n	Long-term Implantation Success Rate, %
7.7: Headache attributed to Chiari malformation type I	28	18	64	15	83
1.1 or 1.2: Migraine headache with or without aura	24	21	88	19	90
5.2.2: Chronic posttraumatic headache attributed to mild head injury	11	10	91	8	80
13.8: Occipital neuralgia	8	7	88	7	100
5.7.2: Postcraniotomy headache	7	7	100	6	86
3.1.2: Chronic cluster headache	5	4	80	4	100
6.1.1: Headache attributed to ischemic stroke	5	3	60	1	33
13.7: Other trigeminal or terminal branch neuralgias	5	4	80	1	25
11.2.1: Cervicogenic headache	4	3	75	3	100
4.7: Hemicrania continua	1	1	100	1	100
7.4.4: Headache attributed to hypothalamic or pituitary hypersecretion or hyposecretion	1	1	100	0	0

infection without wound erosion. All impending wound erosions were revised preemptively to prevent infection. None of the patients who were preemptively revised developed a wound erosion or infection. The overall rate of complications was 15%. Revision surgery for a variety of other indications was performed in 17 of 79 of the implanted patients (22%). Most of these cases were done on an elective basis for cosmetic reasons. Whenever possible, the distal-to-proximal lead revision technique was used. This technique has previously been described and allows quick corrections of lead position without exposing the pulse generator site.<sup>14</sup>

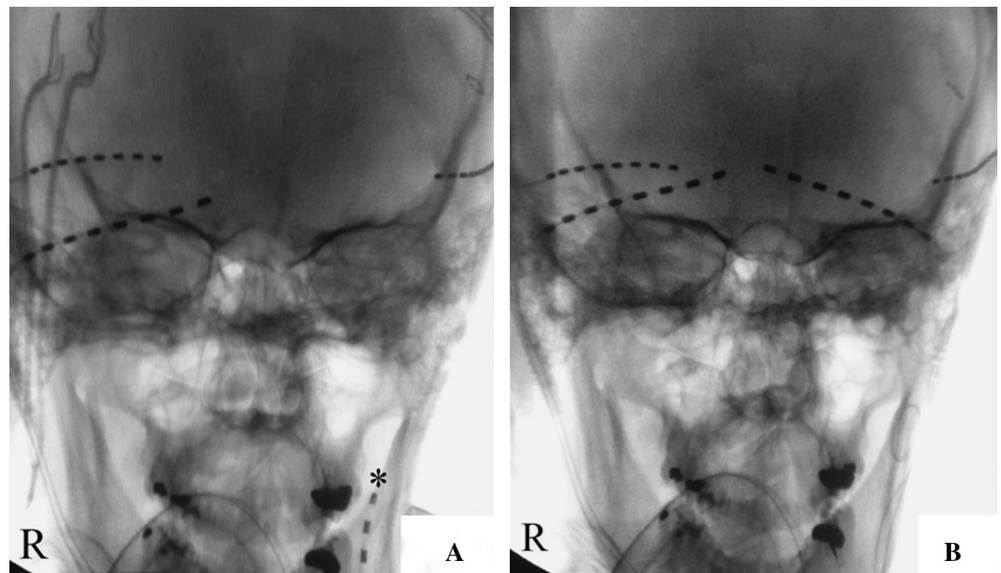
## DISCUSSION

The literature demonstrating good clinical outcomes with peripheral nerve stimulators for the treatment of medical refractory headache disorders continues to grow.<sup>5-12,15</sup>

Currently, however, Class I evidence on this topic is absent. The data, albeit favorable, are predominantly from small clinical trials and case series with few randomized controlled trials. Moreover, the largest randomized controlled trial for occipital nerve stimulators for chronic migraine treatment did not achieve its primary outcome.<sup>16</sup> The relatively short follow-up periods reported in the available literature also limit the interpretation of good clinical results. Our series is among the largest to be published to date and demonstrates successful outcomes with peripheral neurostimulators given proper patient selection.

Our experience suggests that although PNS is clearly beneficial in a wide variety of headache syndromes of diverse origins, the degree of efficacy varies with headache type/classification. The exact mechanisms of action of PNS remain unclear. The response of headaches of such disparate origins to peripheral nerve stimulation supports multiple mechanisms of action. Proposed mechanisms include both central and

**FIGURE 2.** Intraoperative anteroposterior radiograph demonstrating migration of the left occipital lead (asterisk) in a patient with migraine headaches (A). The left occipital lead was then replaced during revision surgery (B). Of the patients in this study, 5% had lead migrations requiring revision surgery.



peripheral sites of action such as the gate control theory and slow neuromodulatory activation of descending pain control pathways with stimulation of the perigenual anterior cingulate cortex and posterior hypothalamus.<sup>15,17</sup> In the gate control theory, activation of large-fiber afferent fibers, involved in vibratory or proprioceptive modalities, leads to simultaneous inhibition of small-fiber afferents, which transmit pain via inhibitory interneurons. This mechanism is likely harnessed in cases of peripheral field stimulation in which regions of localized neuropathic pain are modulated with stimulation. Although the favorable clinical response of occipital neuralgia to PNS, for instance, could be explained by the gate control theory, the favorable response seen in chronic cluster headache suggests a central site of action.

The trigeminocervical complex has been proposed as a mechanism to explain the interaction between peripheral afferent fibers and central pain generation mechanisms.<sup>18,19</sup> The greater occipital nerve is derived from the sensory medial branch of the C2 dorsal ramus; the lesser occipital nerve is derived from the C2 ventral ramus. Meanwhile, afferents from pain-producing intracranial structures such as the dura and blood vessels are the likely source of primary headache syndromes. Pain generated during primary headache syndromes is oftentimes not constrained within trigeminal innervation territories. There is frequently involvement of greater occipital nerve territories. This suggests an anatomic overlap between occipital nerve innervation and trigeminal innervation. This convergence is likely occurring at the level of C2. Afferents from the meninges terminate in the caudal trigeminal nucleus in the medullary dorsal horn, which extends down to C2. Similarly, afferent transmission from the occipital nerves is also to C2. Peripheral stimulation along the occipital nerves may modulate trigeminocervical complex-mediated pain at the C2 trigeminocervical convergence. The importance of the convergence of peripheral neuromodulation with central pain generation is supported by recent data from Magis et al<sup>20</sup> demonstrating benefit in patients with compared with those without perigenual anterior cingulate cortex hyperactivity. A more comprehensive understanding of the mechanism(s) responsible for headache modulation and knowledge of the pathophysiology of the different headache disorders will help guide future treatments.

Our data and data published in the literature illustrate the importance of an accurate and reproducible classification of headache disorders. The use of the ICHD-II classification scheme will provide standardization for criteria used for the diagnoses, subsequent treatments, and interpretation of data across disciplines.

The use of PNS for medically refractory headaches continues to grow. However, large blinded, randomized controlled trials remain absent. Optimization of treatment will require standardization of headache classification schemes, proper patient selection, complication avoidance, and further clinical and basic science investigation.

## CONCLUSION

Peripheral neuromodulation is efficacious in a number of headache and craniofacial pain disorders. The classification

of diagnoses with the International Headache Society ICHD-II system allows an efficient and standardized means of communication across multiple disciplines within the headache community. In this study, 82% of patients who underwent permanent neurostimulator implantation continued to report benefit at last follow-up. The rates of revision surgery are high, although most are elective cosmetic adjustments. Wound and device complications can be minimized by anchoring leads and preemptively revising impending wound erosions. Continued refinement of the technique with improvements in patient selection criteria, implant hardware, and surgical technique will likely improve outcome and decrease the rate of surgical complications.

## Disclosure

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