

## Long-Term Peripheral Nerve Stimulation for Painful Nerve Injuries

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**Background:** Although peripheral nerve stimulation (PNS) has been used for the treatment of pain since 1985, only a few follow-up studies have been published. The aim of the present retrospective study was to describe the long-term efficacy and safety of PNS in the treatment of painful nerve injuries.

**Methods:** Patients suffering from intractable pain due to peripheral nerve injuries underwent PNS after a 2- to 4-month long-term successful treatment. Patients were evaluated based upon patients' reports of pain intensity on a visual analog scale (VAS) and their consumption of analgesics. Two categories of result were chosen: good, referring to 50% or more relief of pain with abstinence from analgesic medications; and poor, with less than 50% improvement.

**Results:** Of 151 screened patients, 75 (26 women and 49 men) were found suitable for PNS. Pain etiologies were identified; the most common being plexus lesion following an operation in the region of the hip or knee. Other etiologies included a stump neuroma, polytrauma following nerve injury, and painful neuropathy following a traumatic rupture. The follow-up period was 3 to 16 years. Of the 45 patients who underwent surgery, the results were classified as good in 15 (33%) patients and as poor in 30 (22%) patients. Ours 1-year success rate approximated a VAS of  $69 \pm 12$  versus a preoperative value of  $24 \pm 28$  postoperatively ( $P < 0.001$ ).

**Conclusions:** PNS can produce pain relief in the majority of carefully selected patients suffering from isolated painful neuropathies.

**Key Words:** neuropathic pain, traumatic neuropathy, sympathetic, peripheral nerve stimulation

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Chronic pain due to peripheral nerve injury often results in significant suffering and impaired quality of life. It appears to be less responsive to opioid drugs than nociceptive

pain and is therefore difficult to treat. Several drugs, such as antidepressants, anticonvulsants, and tramadol derivatives, are known to have clinical efficacy, but complete pain control is rarely achievable.<sup>1</sup> Therefore, the treatment of neuropathic pain still remains a major clinical challenge.

Peripheral nerve stimulation (PNS) for the treatment of chronic peripheral neuropathic pain has been used since 1985, but only a few follow-up studies have been published in the literature thus far. Sweeney<sup>2</sup> reported on "great relief and freedom" in 17 of 69 patients who underwent electrode implantation around peripheral nerves. "Successful relief of pain" or "good to excellent results" was reported by Nasrallah et al.,<sup>3</sup> Stegge et al.,<sup>4</sup> Novak and Vacklimer,<sup>5</sup> as well as by Waisbrod et al.<sup>6</sup>

The exact mechanism by which PNS produces analgesia is unclear. One of the possible mechanisms is based on the assumption that direct application of high-frequency low-intensity electrical current acts on nerve conduction velocity myelinated A $\beta$  fibers and produce analgesia by activating the "gate control" mechanism.<sup>7</sup> Thus, our working hypothesis was that implantation of PNS proximal to the site of injury is likely to produce analgesia in patients with traumatic nerve injuries, possibly by activating fast-conduction. In the present retrospective study, we attempt to examine the long-term outcome of PNS in a larger group of patients with chronic neuropathic pain of the same etiology.

### MATERIALS AND METHODS

#### Patients

Patients who were suffering from intractable pain due to peripheral nerve injuries and who were referred for advanced pain treatment during the years 1992-1995 were considered for PNS. Prior to implantation, all patients underwent careful selection in accordance with the following criteria: (1) clear identification of a lesion of a motor nerve (eg, sciatic nerve, ulnar nerve) as the principal cause of pain; (2) complete (although temporary) pain relief following a diagnostic nerve block with local anesthetics; (3) failure to respond to all other treatments, including medications, intrathecal electrical nerve stimulation (ITENS), and neurolytic procedures; (4) absence of major contraindications, such as personality disorders or drug or depression, upon psychological examination; (5) signing of a written informed consent for the surgical procedure.<sup>8</sup>

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## Procedure

Surgeries were performed at the Red Cross Pain Center in Mainz, Germany, during the years 1982 and 1988, the Institute for Back Care in Bad Kreuznach, Germany, between 1989 and 1993, and the Lina Medical Center in Hanko, Israel, between the years 1993 and 1995. A common implantation and follow-up protocol was used at all three sites. All implantations were performed under general anesthesia and under strict sterile conditions by the surgeon (J.W.). The nerves selected for surgery were exposed proximal to the site of injury. The trocars were placed along the nerves and attached from there with 3-0 absorbable sutures. Three types of electrodes were used (Cliff Electrode, Avery Laboratories, Farmingdale, NY; Resurge Electrode and Stimax Electrode, Medtronic Inc., Minneapolis, MN), with each type used in roughly one-third of the patients.

The electrodes were tunneled under the skin and connected to a pacemaker that was implanted subcutaneously in the abdominal wall for pain in the lower extremities and in the chest wall for pain in the upper extremities, the chest wall, or in the head. An external generator was used for stimulation via an antenna, which was taped to the skin against the implanted receiver. Thirty stimulators were implanted onto nerves in the lower extremities, 12 in the upper extremities, and 6 in the head (greater occipital nerves). The nerves selected for surgery are summarized in Table 1. In 3 patients, who suffered from intercostal neuralgia, the implantation technique was different. In these patients, a subcutaneous spinal electrode (Stimovox, Medtronic Inc., Minneapolis, MN) was inserted into the intercostal space under fluoroscopy and was directed at the origin of the involved nerve, because it is possible to stimulate an isolated intercostal nerve.

The pulse rate, width, and voltage that produced the best response were selected. Patients were instructed to activate the stimulator for 1 hour, every other hour, for the first several days and to gradually reduce the stimulation time to the minimum necessary for pain relief thereafter.

## Pain Measurements

Patients were requested to evaluate their pain intensity with the use of a 0–100 visual analog scale (VAS), where "0" means "no pain" and "100" means "the worst imaginable pain". Additionally, they were asked to describe their pain with the use of the Mainz Pain Center Questionnaire,<sup>8</sup> which is a modification of the McGill Pain Questionnaire,<sup>9</sup> and to keep a record of their consumption of analgesics. On the basis of these measurements, two categories of results were chosen: (1) good—50% or more relief of pain (per VAS) with abstinence from analgesic medications; and (2) poor—less than 50% improvement with or without the use of analgesics.

Patients were seen at follow-up appointments for efficacy evaluations on a monthly basis for the first 6 months following surgery, and every 6 months thereafter for the next 2

TABLE 1. Nerves Selected for Implantation (n = 46)

| Lower Extremity |          | Upper Extremity/Head/Trunk |          |
|-----------------|----------|----------------------------|----------|
| Nerve           | Patients | Nerve                      | Patients |
| Sciatic         | 29       | Medial                     | 6        |
| Tibial          | 15       | Ulnar                      | 4        |
| Peroneal        | 4        | Radial                     | 2        |
| Proximal        | 4        | Intercostal                | 3        |
| LUMB            | 2        | Greater occipital          | 1        |

LUMB, lumbosacral truncal nerve.

years. However, patients who lived for many or who had difficulties attending the clinic for extended periods of time were followed up by telephone calls. An attempt was made to contact all patients either by mail or by phone during the year 1997 to obtain information regarding their long-term pain intensity and consumption of analgesics. Whenever personal contact could not be made, the results used were those recorded at the last follow-up visit. A 2-tailed *t* test was used to compare VAS values and analgesic consumption prior to surgery with those obtained in 1997. Results at the  $P < 0.05$  level were regarded as statistically significant.

## RESULTS

### Patients

Of 137 referred patients, 46 (26 women and 20 men) were found suitable for PNS. Their age ranged from 24 to 75 years, with a median age of 49. Pain duration prior to PNS was at least 2 years in all patients. The mean baseline VAS was 69 ± 13, indicating moderate to severe chronic pain intensity before surgery. The words most commonly chosen by patients from the Mainz Pain Questionnaire to describe their pain before surgery were "dragging," "grinding," "pulling," and "burning." All patients had previously received conservative treatment, consisting of medications (analgesics, antidepressants, anticonvulsants, etc), transcutaneous electrical nerve stimulation (TENS), and repeated nerve blocks. Additionally, 42 of the 46 patients had undergone neurolysis.

Four etiologic factors were identified (Fig. 1), the most common being nerve lesion following an operation in the region of the hip or knee. Table 2 summarizes the specific operative procedures. The second most common etiology was entrapment neuropathy. Other etiologies included neuropathic pain following a traumatic injection and pain following nerve graft surgery (for repair of nerve loss following previous nerve injury). None of the patients met the research diagnostic criteria for complex regional pain syndrome (CRPS) suggested by Brühl et al.<sup>10</sup>

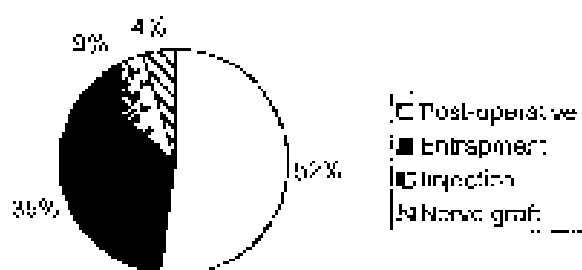


FIGURE 1. Four identified etiologies for nerve injuries.

**Pain measurement**

The follow-up period was 3–16 years, with a median of 10.8 years. Of the 46 patients who underwent surgery, 33 were reached by mail or by phone in 1997. The results were classified as good in 20 (60%) patients and as poor in 10 (30%) patients. Overall, pain intensity dropped from a VAS of 85 ± 12 before surgery to 24 ± 28 at follow-up ( $P < 0.001$ ). When examined according to etiologic factors, good results were achieved in 82% of patients who had post-surgical nerve injuries, in 80% of patients with carpal tunnel neuropathy, and in 50% of patients with neuropathic pain following a traumatic injection. The 2 patients with pain following nerve graft failed to respond to PNS. Table 3 summarizes the results according to etiologic factors. The results of the 30 patients who underwent explantation in the lower extremity were classified as good in 22 (73%) patients, whereas in the upper extremity 10 (83%) of the 12 patients had good results. All three surgeries involving intercostal nerves and the greater occipital nerve had good results. Figure 2 shows the results according to the stimulated nerves. No differences in outcome was found between the 2 types of electrodes implanted.

**Complications**

Complications occurred in five patients, including 2 with a wound infection at the receiver implantation site, 1 with skin necrosis over the receiver implantation site, and 2 with

TABLE 3. Results According to Etiologic Factors

| Etiology         | n  | Results |      |
|------------------|----|---------|------|
|                  |    | Good    | Poor |
| Operative trauma | 24 | 20      | 4    |
| Entrapment       | 16 | 14      | 2    |
| Post-injection   | 4  | 2       | 2    |
| Post-nerve graft | 2  | 0       | 2    |

electrode migrations. The electrodes were repositioned in the last 2 patients, and the receivers were reimplanted at different sites in one patient with infection and necrosis, thus allowing the stimulation to be continued in all of these patients.

**DISCUSSION**

Peripheral nerve stimulation (PNS) for the treatment of chronic pain has been used since 1965, but only a few follow-up studies have been published in the literature (Larsen, Sweet<sup>2</sup> reported on "pain relief until death" in 17 of 69 patients who underwent electrode implantation around peripheral nerves, and Nashold et al<sup>3</sup> referred to "successful relief of pain" in more than 50% of their patients. "Good to excellent" results were reported by Strigo et al<sup>4</sup> in 18 of 21 patients with chronic peripheral nerve injury, as well as by Neeze and Mackinnon<sup>5</sup> in 21 of the 27 patients with peripheral nerve injury. In the initial study, which had a mean follow-up period of 22 (± 13) months, neither gender differences, worker's compensation litigation, nor if a extremity involved (upper versus lower) were found to have an effect on outcome. Waihsund et al<sup>6</sup> reported their preliminary results in a group of 19 patients with chronic pain caused by traumatic peripheral nerve injury treated with PNS. In line with these reports, the results presented in this paper demonstrate that PNS can result in long-term pain relief in patients with postoperative as well as with painful carpal tunnel neuropathy.

TABLE 2. Specific Operative Procedures That Led to Painful Nerve Injuries (n = 24 Patients)

| Type of Surgery        | Patients |
|------------------------|----------|
| Total hip replacement  | 6        |
| Total knee replacement | 4        |
| Thoracotomy            | 3        |
| Bone graft removal     | 3        |
| High tibial osteotomy  | 2        |
| Knee arthroscopy       | 2        |
| Hemiarthroplasty       | 2        |
| Nerve tumor resection  | 1        |

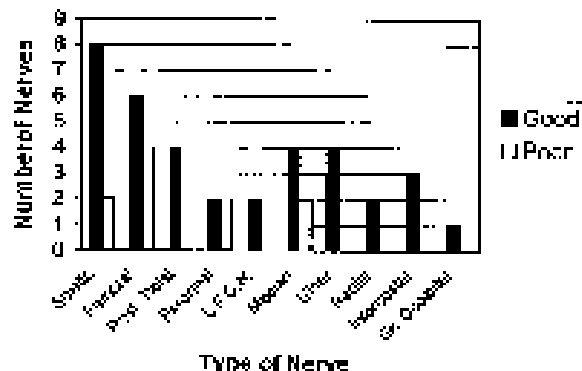


FIGURE 2. Results according to the stimulated nerves.

It is time that more of the studies on PNS have been carried out in a randomized, controlled fashion. However, a study of lidocaine row catheters, which consistently supports the notion that PNS is indeed efficacious. One study, though, found that neuropathic pain is extremely difficult to treat, and that even the most efficacious anticonvulsants, anticonvulsants and opioids used in the treatment of neuropathic pain rarely produce more than 70–80% of reduction in pain.<sup>11</sup> Furthermore, the long-term efficacy of these drugs is unknown. Thus, regardless of the use of controlled trials, PNS seems like a reasonable alternative if it can be offered to patients with intractable nerve injury pain after all other modalities fail.

Not unexpectedly, some patients failed to respond to PNS. In the present report, 8 lower extremity and 2 upper extremity systems did not provide adequate analgesia. Unfortunately, it is difficult to predict which patient, which nerve, or which etiology is at high risk for non-response rates. Nasirid et al<sup>9</sup> reported that the posterior tibial nerve was the primary site for failure in their patients and suggested that the areas of weight bearing and the anatomic position of the nerve may account for it. We, however, could not demonstrate a similar tendency in our patients. Recently, Schen et al<sup>12</sup> presented a new algorithm for the treatment of chronic lower extremity neuropathic pain.<sup>12</sup> They found that electrophysiological studies of the nerve predictive value regarding presence or absence of intervention (eg, TNS, neurectomy, vein wrapping). Alternatively, they suggested neurectomy according to which the mechanism of injury (stretch, trauma, entrapment, or mass effect) together with the findings at the time of surgery (at the affected nerve) can help to determine which procedure (nerve ablation, neurectomy, etc) should be recommended. However, careful observation of their suggested treatment algorithm shows that the use of TNS is recommended somewhere along each of them. The use of a prognostic nerve block prior to PNS has become a common practice, and it is well accepted that failure to respond to a nerve block is a bad prognostic factor for PNS.<sup>13</sup> In our study, complete (although temporary) pain relief following a diagnostic nerve block with local anesthetics was acquired prior to PNS in the present study. However, 10 of the 46 subjects (nearly 22%) who met this selection criteria eventually failed to respond to PNS. Thus, a lack of clear and well-established factors for predicting

failure, even among carefully selected patients, remains the most significant disadvantage of using PNS, especially as the cost of the system is still rather high.

The use of a percutaneous PNS, used in the 3 patients with intercostal neuralgia, has also been found to be effective in the treatment of occipital neuralgia.<sup>14</sup> Based on these reports, it seems that stimulation of occipital or intercostal nerves can be continued for extended periods of time. However, the applicability of this method in the treatment of other forms of neuralgia should be confirmed through further trials.

In conclusion, PNS can represent a long-term pain relief in the majority of carefully selected patients and has a relatively low complication rate. It should therefore be considered as a reasonable treatment of patients suffering from otherwise intractable and isolated painful neuropathies.

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