Treatment of CRPS with Spinal Cord Stimulation of the Dorsal Root Ganglion: A Case Series

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■ Abstract: According to the International Association for the Study of Pain (IASP), complex regional pain syndrome is defined as a collection of locally appearing painful conditions following a trauma which chiefly occur distally and exceed in intensity and duration the expected clinical course of the original trauma, often resulting in considerably restricted motor function. Treatment modalities include pharmacological, non-pharmacological, and interventional management techniques such as sympathetic blocks and electrical neuromodulation. According to the evidence-based guidance document on interventional pain,[1] treatment of CRPS with current neuromodulation techniques has been given a positive recommendation (Score of 2B+), despite challenges in reaching the distal areas of the extremities and diminishing effect with time. We report the findings of a case series exploring the clinical outcomes of spinal cord stimulation of the dorsal root ganglion (DRG) treating CRPS of the foot. Subjects implanted with the Axium Neurostimulator System experienced an average pain reduction of 56.3% (median of 74.7%, n=17) overall and 60.3% (median of 88.6%, n=14) in the foot at last follow-up. From these findings we conclude that spinal cord stimulation of the DRG provides excellent pain relief and can reach distal anatomies such as the foot. Especially, the last observation seems to be promising to overcome one of the earlier described challenges in more traditional stimulation of the dorsal columns. ■

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INTRODUCTION

Complex regional pain syndrome (CRPS) is a complication after surgery or trauma, although spontaneous development is also described. The pathophysiology involves peripheral, afferent, efferent and central mechanisms.[1,2] The associated pain can be described as spontaneous regional pain disproportionate to the inciting event.[3] Associated sequelae may include allodynia, hyperalgesia, edema, vasomotor abnormalities and trophic changes.[4]

According to the International Association for the Study of Pain (IASP) CRPS can be recognized as two distinct conditions: CRPS type I (formerly called reflex sympathetic dystrophy) and CRPS type II (causalgia).[5] More recently, the clinical diagnostic criteria for CRPS have been revised (also known as the "Budapest criteria"). This criterion describes CRPS as "an array of painful conditions that are characterized by a continuing regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings. The syndrome shows variable progression over time".[6]

The incidence rate of CRPS was estimated at 26.2 per 100,000 person-year from a retrospective cohort study performed in the Netherlands. Females were affected at least 3.4-4 more often than males.[1] The mean age at diagnosis is 52 years. Fracture was the most common injury leading to CRPS, with upper extremities being affected more than lower extremities.[7]

The treatment of CRPS for both types is primarily aimed at alleviating pain and restoration of function with secondary goals of improving other signs and symptoms. Based on the predominant symptom, therapies could be focused on addressing the inflammation (free radical scavengers, bisphosphonates[8,9] and steroids), vasomotor disturbances (vasodilatory therapies including limited areas for sympathetic blocks[10]), motor (baclofen[11]) and sensory (anti-neuropathic pain medication) abnormalities.[12, 13] Spinal cord stimulation (SCS) is an important treatment option and has gained widespread popularity for the treatment of chronic pain of diverse etiology.[14] The consensus opinion considers SCS as a treatment option when less invasive therapies have failed.[6,15,16] SCS is considered to be an effective and safe treatment option for CRPS.[6,17-29] More evidence is available for CRPS type 1; CRPS type 2 has a lower level of evidence.[30] However, treatment with SCS for CRPS shows some limitations to consistently achieve adequate pain relief.[29] Limitations experienced are lead breakage and migration, loss of coverage (stimulation induced paresthesias) or partial coverage of the pain area.[14, 29] Pathophysiological changes in the dorsal root ganglion (DRG) may be a contributory factor to the development of CRPS and, therefore, stimulation of this target may have beneficial effects on the painful symptoms associated with CRPS.

We report the combined long term clinical outcomes of SCS of the DRG from two prospective, multi-center studies and data collected retrospectively at multiple centers throughout Europe. In addition, we describe two representative cases, one each from the prospective and retrospective studies, in more detail.

METHODS

All study elements were ethics committee-approved and each subject gave written informed consent prior to beginning any study activities. Patients (n=20) suffering from CRPS of the lower extremity were considered candidates for SCS of the DRG. All subjects were diagnosed using the modified diagnostic criteria proposed by Harden et al (Table 1).[6] Inclusion/exclusion criteria and methods have been described in detail elsewhere.[31] Briefly, after enrollment, subjects completed baseline clinical assessments including VAS pain ratings for overall pain and specific anatomies (back, leg, foot). Subjects were then implanted with quadripolar neurostimulation leads such that the stimulating contacts were placed near relevant DRGs according to the individual's location and distribution of pain.. The neurostimulator system (Axium Neurostimulator System; Spinal Modulation, Inc.) is comprised of an external trial neurostimulator (TNS), an implantable neurostimulator (INS), quadripolar percutaneous leads, and wireless patient and clinician programming devices. Stimulation leads were connected to an external neurostimulator, and the device was programmed with combinations of pulse width, amplitude, and frequency that generated the best pain/paresthesia overlap. At the end of the trial period, stimulation was discontinued until (and if) the permanent neurostimulation system was implanted. Subjects who achieved 50% or greater pain relief in their primary pain area during the trial period completed pre-implant pain ratings as a stimulation-off internal control and then received the fully-implantable neurostimulator under standard surgical procedure. Adverse events were monitored throughout the study.

RESULTS

During the trial phase, stimulation leads were placed epidurally over the DRGs at the spinal levels appropriate to obtain sensory paresthesia or pain relief in the correct anatomical region of the patient's pain. Eighteen subjects reported >50% improvement (90% success rate), while two subjects failed the trial. One subject (with >50% improvement) did not receive the permanent implant because while 100% pain relief was achieved in one foot, no pain relief was achieved in the other. Thus the remaining seventeen subjects received the permanent implant.

Eight subjects have completed their 12-month follow-up. Average pain reduction was 61.7% (±16.4%) overall and 77.5% (±12.7%) foot (using a Visual Analog Scale) (Figure 1). Median pain relief was 76.5% (overall) and 96.0% (foot), respectively. 71.4% and 85.7% of the subjects reported >50% overall and foot pain relief, respectively.

For all seventeen subjects who received a permanent implant, average pain reduction was 56.3% (±10.0%) overall and 60.3% (±15.7%) foot (using a Visual Analog Scale) (Figure 1). Median pain relief was 74.7% (overall) and 88.6% (foot), respectively. 62.5% and 71.4% of the subjects reported >50% overall and foot pain relief, respectively.

With respect to safety and adverse effects, eleven adverse events (AEs) were reported; three were classified as mild, five as moderate and three as severe. One AE, which was discomfort associated with stimulation, was related to the device. There were two serious AEs, consisting of no paresthesia coverage in one leg and a prolonged hospital stay due to lack of care at home. Both SAEs were considered not related to the DRG stimulation and were resolved. Stimulation device was explanted in one subject after the Week Eight follow-up due to lack of benefit in pain relief. No lead revisions were required.

Table 1. Modified diagnostic criteria for CRPS[6]

1. Continuous pain, disproportionate to the inciting event.	Categories
2. Patients should have at least one symptom in each of the following categories and one sign in two or more categories:	1. Sensory (allodynia, hyperalgesia, hypoesthesia)
	2. Vasomotor (temperature or skin color abnormalities)
	3. Sudomotor (edema or sweating abnormalities)
	4. Motor/trophic (muscle weakness, tremor, hair, nail, skin abnormalities)

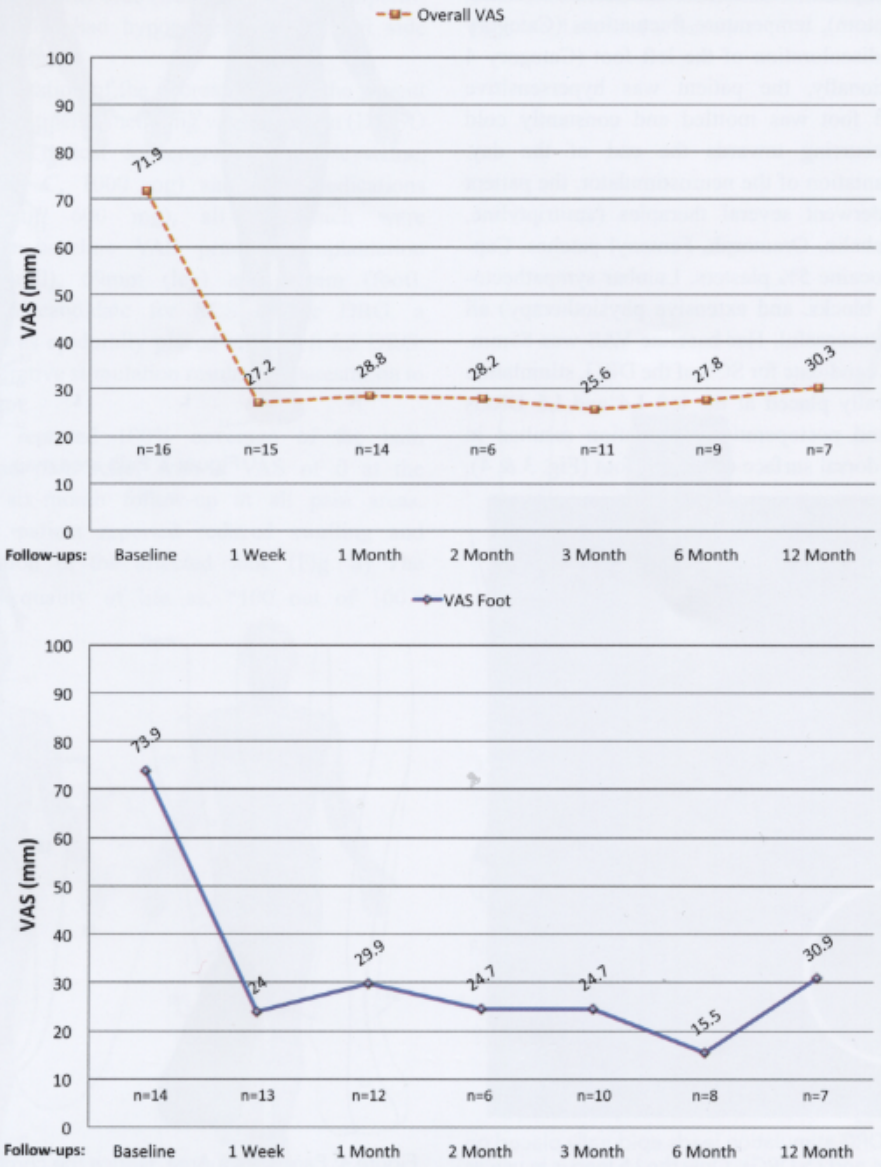

Figure 1. a. Overall VAS Score, and b. VAS Foot Score reduction in CRPS patients with SCS of the DRG included in the prospective and retrospective studies.

CASE HIGHLIGHT - PATIENT 1

We present a patient implanted with the Spinal Modulation System to treat CRPS of her foot. The patient is a 39 year-old female who has suffered fractures in her left foot (2nd, 3rd and 4th metatarsal). She reported a constant throbbing pain from her forefoot to her ankle (Diagnostic criteria 1). As a result of her condition, the patient suffered from allodynia (Category 1 symptom), localized increased sweating (Category 3 symptom), temperature fluctuations (Category 2 symptom) and discoloration of the left foot (Category 4 symptom). Additionally, the patient was hypersensitive to touch, the left foot was mottled and constantly cold with swelling occurring towards the end of the day.

Prior to implantation of the neurostimulator, the patient received and underwent several therapies (amitriptyline, Gabapentin, Pregabalin, Oramorph, Fentanyl patches, Capsaicin cream, Lidocaine 5% plasters. Lumbar sympathectomy, Guanithidine blocks, and extensive physiotherapy) all of which were unsuccessful. Her baseline VAS was 85mm.

Determined a candidate for SCS of the DRG, stimulation leads were epidurally placed at the left L4 and L5 DRGs (Fig. 2). Intra- and postoperative stimulation resulted in paresthesia to the dorsal surface of the left foot (Fig. 3 & 4).

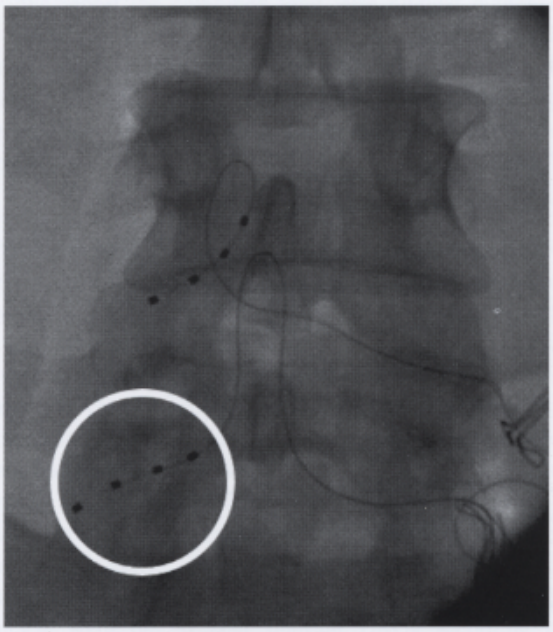

Figure 2. X-ray of DRG stimulation leads epidurally placed on the patient's left L4 and L5 DRGs. Only the L5 lead is in use as the L4 lead gives similar coverage.

The patient reported 100% coverage of the pain area and pain relief with a VAS of 8 mm at the one-week follow-up. This pain relief was obtained with stimulation only from the single L5 lead.

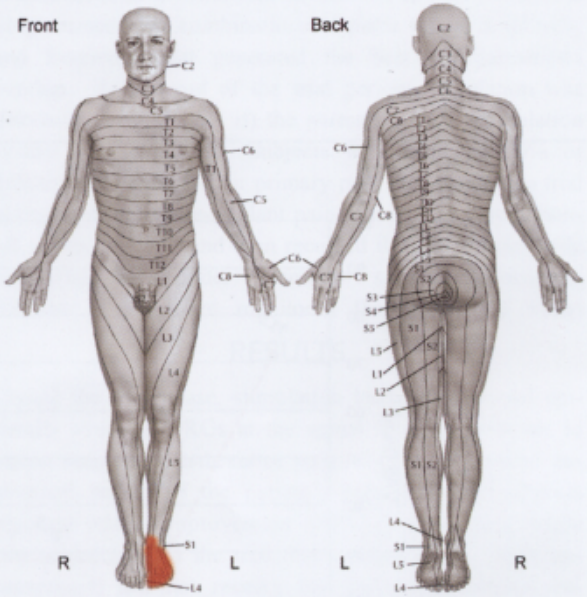

Figure 3. Pain area map

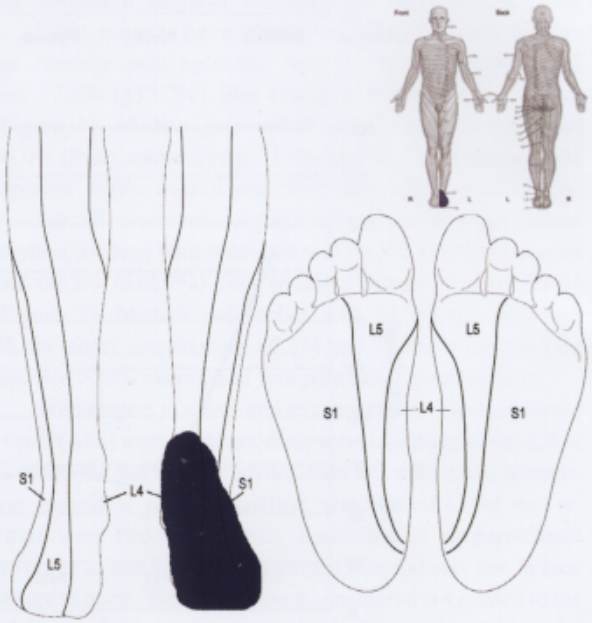

Figure 4. Paresthesia Area. Notice the complete overlap of the pain area without extraneous stimulation.

CASE HIGHLIGHT - PATIENT 2

We present a patient implanted with a neurostimulation system for SCS of the DRG to treat CRPS of the foot. The patient is a 60 year-old male who is diagnosed with CRPS type-1 after a minor fracture. He was experiencing pain in the left leg and foot for over two years (Diagnostic criteria 1) (Fig.5). The leg and foot showed severe signs of erysipelas and coloration of the skin was blue (Category 2, 3, 4 symptom) (Fig. 6). Subject also had hypoesthesia on the left side (Category 1 symptom).

Prior to implantation of the neurostimulator, the patient received several treatments including vasodilatation (DMSO 50% cream), free radical scavengers (N-acetylcysteine, 1800 mg; vitamin C, 1000 mg) and pain medications (notably gabapentin 600 mg), all of which were unsuccessful. His baseline VAS prior to implantation was 66mm (overall), 69mm (leg) and 91mm (foot).

Determined a candidate for SCS of the DRG, a stimulation lead was epidurally placed at the left L5 DRG. Intra- and postoperative stimulation resulted in paresthesia to the left leg and foot.

The patient reported 100% coverage of the pain area (Fig. 7) and pain relief with a VAS of 0 at the one-month and six-month follow-up at all pain areas. Furthermore the patient reported reduced swelling and improved coloration in the affected foot. (Fig. 8) The patient rated his quality of life as, "100 out of 100."

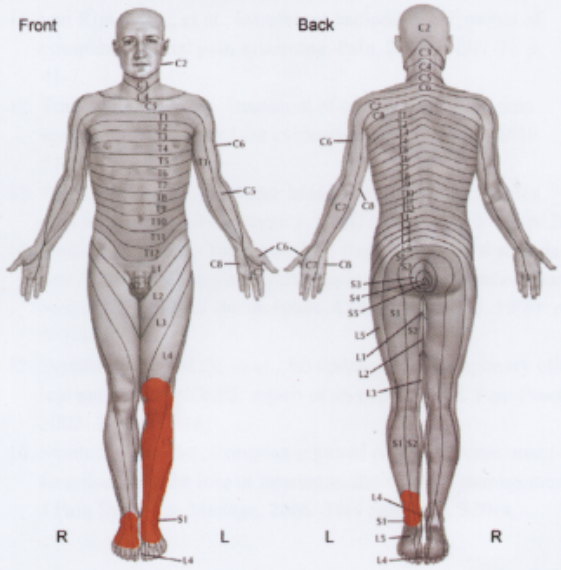

Figure 5. Pain area map at baseline.

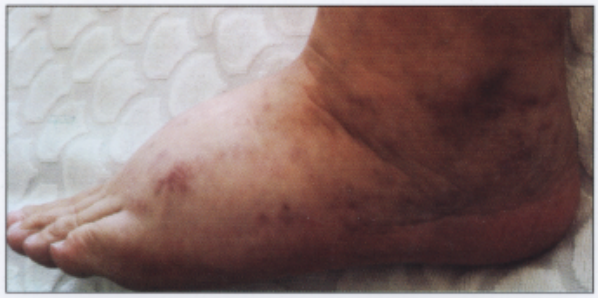

Figure 6. Left foot at baseline.

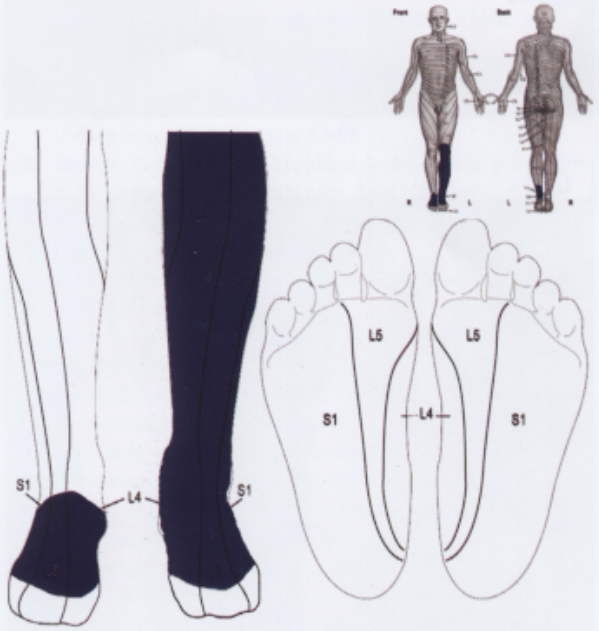

Figure 7. Paresthesia Area. Notice the complete overlap of the pain area.

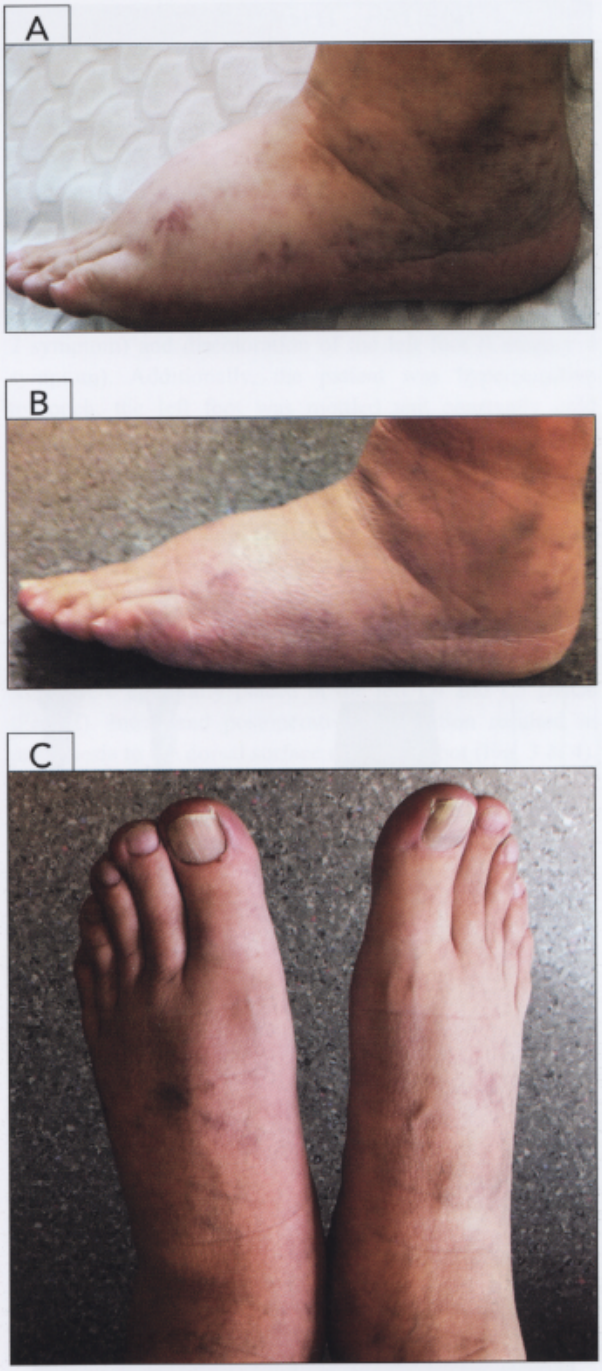

Figure 8
a. Left foot at baseline.
b. Left foot after four weeks of stimulation.
c. Left foot after six months of stimultion.

DISCUSSION

Complex regional pain syndrome continues to be a difficult condition to treat.[1-5,7-11] Depending upon the pain location, traditional SCS technologies may not provide adequate therapeutic effect.[26] This case series suggests that SCS of the DRG can provide excellent pain relief long term in patients suffering from this condition in the lower extremities. Additionally, secondary effects were observed in a cohort of these patients in which allodynia was reduced and swelling mitigated. In addition, the patients did not report deleterious effects of postural changes on the quality of the stimulation or pain relief from the therapy.

Furthermore, the ability to create targeted paresthesias in the foot and lower limbs may be an advantage over traditional SCS in patients presenting with lower limb pain. SCS of the DRG is a promising treatment option for patients presenting with CRPS.

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