DORSAL ROOT GANGLION STIMULATION

A Novel Stimulation Target for the Management of Chronic Intractable Pain.

The Dorsal Root Ganglion (DRG) is a subdural, intraspinal nerve structure that houses primary sensory neurons. These cells process and filter non-painful and painful information from the periphery to the central nervous system. Research has shown that during chronic pain, neurons associated with the injured anatomy exhibit measurable differences in membrane function, which allows for selective stimulation or activation without recruiting the non-painful neurons. This unique pathophysiology also makes stimulation highly selective and steerable to difficult-to-treat anatomies, such as the groin and foot. Additionally, minimal surrounding cerebrospinal fluid makes DRG amenable to neurostimulation without changes in paresthesia intensity when adjustments to body positions occur.

When used to manage chronic, intractable pain, DRG stimulation has shown significant improvements in clinical outcomes such as:

- **Precise Anatomical Targeting Ability:** By stimulating the DRG, we are able to achieve therapeutic coverage and pain relief in difficult-to-treat focal chronic intractable pain conditions.

- **Stable Long-term Pain Relief with Significant Improvements in Quality of Life:** Long-term results show stable long-term pain relief at 12 months with significant improvements in quality of life.

- **Minimal Postural Effects:** Study results show that body positions (standing versus supine) do not affect paresthesia intensity with the Axium™ Neurostimulator System.

The Axium™ Neurostimulator System is a comprehensive therapy system that targets the stimulation of the DRG for the treatment and management of chronic, intractable pain. DRG stimulation has shown to be an effective and safe therapy option for chronic pain patients. This clinical compendium summarizes key studies results demonstrating the safety and efficacy of DRG stimulation for the management of chronic pain.
Improves pain relief in focal chronic intractable pain conditions by targeting precise anatomical locations

Traditional spinal cord stimulation (SCS) has been successfully utilized since 1967 as a treatment modality for the management of chronic, intractable pain in the trunk and/or limbs. For pain locations outside the trunk and/or limbs—as seen in conditions such as complex regional pain syndrome (CRPS),* chronic intractable post-surgical knee pain and pain in the upper limbs—traditional tonic SCS has been less successful or has resulted in extraneous stimulation. The following studies support the use of DRG stimulation to provide superior pain relief in precise anatomical locations such as a single limb, the knee or the groin.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of patients</th>
<th>Pain location and/or condition</th>
<th>Key outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy and Deer, 2015</td>
<td>152</td>
<td>Lower limbs – CRPS</td>
<td>81.2% of DRG stim patients met primary endpoint (vs. 55.7% of traditional SCS patients, p &lt; 0.001)</td>
</tr>
<tr>
<td>Van Buyten, et al., 2015</td>
<td>11</td>
<td>Leg and foot – CRPS</td>
<td>61.7% VAS reduction in overall pain from baseline at 12 months</td>
</tr>
<tr>
<td>Schu, et al., 2015</td>
<td>29</td>
<td>Groin pain</td>
<td>Average 71.4% pain reduction</td>
</tr>
<tr>
<td>Eldabe, et al., 2014</td>
<td>8</td>
<td>Phantom limb pain</td>
<td>Average 52.0% pain reduction (stump and/or phantom)</td>
</tr>
<tr>
<td>Verrills, et al., 2014</td>
<td>13</td>
<td>Chronic post-surgical knee pain</td>
<td>Average 71.2% pain reduction</td>
</tr>
<tr>
<td>Huygen, et al., 2015</td>
<td>19</td>
<td>Upper limb neuropathic pain</td>
<td>Average 54.6% improvement in VAS scores at six months</td>
</tr>
<tr>
<td>Moir, et al., 2015</td>
<td>25</td>
<td>Focal neuropathic pain</td>
<td>Average 57.7% pain reduction at 12 months</td>
</tr>
<tr>
<td>Schu, et al., 2015</td>
<td>7</td>
<td>Upper and lower extremities—painful diabetic neuropathy</td>
<td>VAS scores dropped from average 94.4 mm at baseline to 47.1 mm at last follow-up (average 12.4 months)</td>
</tr>
</tbody>
</table>

*Complex Regional Pain Syndrome: According to the National Health Service (NHS), pain associated with CRPS is typically caused by an injury and is usually confined to one limb, but can spread to other parts of the body. Pain symptoms include burning, stabbing or stinging, but may also include a tingling sensation and numbness. Many CRPS patients also report symptoms of hyperalgesia (extreme sensitivity to pain) and/or allodynia (experiencing pain from a very light touch).
A Prospective, Randomized, Multi-Center, Controlled Clinical Trial to Assess the Safety and Efficacy of the Spinal Modulation Axium™ Neurostimulator System in the Treatment of Chronic Pain.


Study overview:

- The objective of the study was to evaluate the safety and effectiveness of DRG stimulation compared to a commercially available SCS device.

- 152 subjects were randomized to a DRG stimulation group or a control group (commercially available SCS device) across 22 investigational sites.

- A composite of safety and efficacy was used to define primary endpoint success, provided the subjects met the following three criteria:
  1. ≥ 50% pain relief in their primary area of pain at the end of the trial phase, and
  2. ≥ 50% pain relief in their primary area of pain at three months post implant, and
  3. Freedom from stimulation-induced neurological deficit through three months.

- Secondary and tertiary endpoints included positional effects on paresthesia, stimulation specificity, quality-of-life (SF-36), psychological disposition, functional status and patient satisfaction.

Results:

- The ACCURATE study met its primary endpoint at 3 months, demonstrating non-inferiority and superiority in its composite safety and efficacy endpoint.

- Specifically, at 3 months, 81.2% of subjects receiving DRG stimulation achieved the primary endpoint success as compared to 55.7% of subjects receiving traditional tonic stimulation (non-inferiority p<0.0001; superiority p=0.0004).

- At twelve months, in the MITT population, 74.2% of the patients receiving DRG stimulation achieved the primary endpoint vs. 53.0% of patients receiving traditional SCS stimulation (Non-inferiority p < 0.0001; Superiority p = 0.0047). See Figure 1.

- At twelve months, in the IO population, 86.0% of patients receiving DRG stimulation achieved the primary endpoint vs. 70.0% of patients receiving traditional SCS (Non-inferiority p < 0.0005; Superiority p = 0.0223). See Figure 1.

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Figure 1. Percent of patients in the MITT population (left) and the IO population (right) who met the primary endpoint success following DRG stimulation or traditional tonic stimulation at 12 months.1
Secondary and tertiary endpoints results:

- After 12 months, more than a third of patients who received DRG stimulation were experiencing greater than 80 percent pain relief with no paresthesia.

<table>
<thead>
<tr>
<th>DRG stimulation group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with paresthesia</td>
<td>35</td>
</tr>
<tr>
<td>Patients without paresthesia</td>
<td>43</td>
</tr>
<tr>
<td>% Mean VAS Decrease (SD)</td>
<td>81.4 (22.8)</td>
</tr>
</tbody>
</table>

- Using a 11-point scale to assess paresthesia intensity, 12 month results confirmed that DRG stimulation produced less change in intensity between upright and supine positions when compared to the control group. See Figure 2.

- At twelve months, subjects in the DRG group experienced greater stimulation specificity (94.5%) compared to subjects in the control group (61.2%), (p < 0.0001). In other words, patients receiving DRG stimulation had a significant decrease in extraneous paresthesia outside the area of their pain.

- At twelve months, DRG stimulation provided significant improvements in total mood disturbance (p = 0.004 vs. control) and three out of the four components of the brief pain inventory (interference, activity and affective components).

Key Takeaways:

- The ACCURATE study is the largest randomized, controlled neuromodulation trial conducted in CRPS patients to provide evidence of safety and efficacy for market approval in the United States.

- The study met both the non-inferiority and superiority primary composite endpoint of safety and efficacy.

- DRG stimulation provided consistent stimulation with minimal postural effects and resulted in significant improvements across multiple secondary outcome domains including quality of life, psychological disposition and function.

- The data from the ACCURATE study suggests that DRG stimulation may offer a meaningful option for patients suffering from chronic pain conditions that are currently underserved by traditional tonic SCS.
Stimulation of Dorsal Root Ganglion for the Management of Complex Regional Pain Syndrome: A Prospective Case Series.

- The purpose of this prospective case-series study was to evaluate the effects of DRG stimulation in CRPS patients (*n* = 11).

- Following baseline assessments, subjects were implanted with the Axium™ Neurostimulator System using quadripolar percutaneous leads placed near the DRG.

- Follow-ups occurred at one-week, one-month, five weeks (stimulation off), two months, three months, six months and 12 months post-implant.

- Overall pain, leg pain and foot pain were assessed via VAS.

- Other evaluations included Brief Pain Inventory (Short form, BPISF), Profile of Mood States (Short Form, POMS) and EuroQOL five dimensions questionnaire.

- 72% (8/11) of patients had successful trials, with an average 81.9% reduction in VAS pain scores compared to baseline.

- Following permanent implantation, average decreases in VAS scores for overall pain were reported (see Table 1).

- At 12 months, 71.4% (5/7) of patients had ≥ 50% pain relief.

- Similar results were reported for foot pain and leg pain at all time points. At 12 months, 85.7% (6/7) of patients with foot pain and 80.0% (4/5) of patients with leg pain had ≥ 50% pain relief.

- Statistically significant improvements from baseline were observed in all secondary endpoints at 12 months (pain severity and pain interference, quality of life and mood disturbance).

- Pain relief remained stable over time and across all body positions.

- Eleven adverse events were reported in four patients, with no lead revisions required.

**Key takeaways:**

- This study supports the use of DRG stimulation as a viable and effective intervention in patients with CRPS, a difficult to treat pain condition.

- DRG stimulation remained stable over time and across different body positions.

<table>
<thead>
<tr>
<th></th>
<th>1 Week</th>
<th>1 Month</th>
<th>Stim off for 1 Week</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% VAS decrease from baseline</strong></td>
<td>65.2%</td>
<td>62.1%</td>
<td>28.6%</td>
<td>68.4%</td>
<td>63.1%</td>
<td>61.7%</td>
</tr>
<tr>
<td><strong>p-value vs. baseline</strong></td>
<td><em>p &lt; 0.001</em></td>
<td><em>p &lt; 0.005</em></td>
<td><em>p &gt; 0.05</em></td>
<td><em>p &lt; 0.001</em></td>
<td><em>p &lt; 0.005</em></td>
<td><em>p &lt; 0.05</em></td>
</tr>
</tbody>
</table>

Table 1. Average VAS decreases over time for overall pain. 

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6 | DRG Clinical Compendium


- In this multicenter (11 sites across Europe), retrospective study, 29 patients with neuropathic groin pain were treated with DRG stimulation.

- 86.2% (25/29) of the patients trialed had positive results and received the fully implantable neurostimulator.

  - Twelve of the patients were diagnosed with post-herniorrhaphy pain and 83.3% (10/12) of these patients received a permanent implant.

- Follow-up data of 27.8 ± 4.3 weeks was available for 23 patients:

  - 82.6% (19/23) of the patients had a pain score improvement of > 50%.
  - 47.8% (11/23) of the patients had over 80% of pain score improvement.

- Follow-up data of six months or more was available for 13 patients (mean follow-up of 42.5 ± 3.7 weeks):

  - Patients in this cohort had a mean VAS improvement of 67.5%.
  - 76.9% (10/13) of these patients had > 50% pain relief.
  - 53.8% (7/13) of these patients had > 80% pain relief.

- Average follow-up for the post-herniorrhaphy patient cohort (n = 10) was 17.4 ± 5.7 weeks:

  - Average VAS reduction for this cohort was 76.8 ± 8.2%.
  - 80% (8/10) had > 50% improvement in VAS scores at last follow-up.
  - 50% (5/10) had > 80% improvement in VAS scores at last follow-up.

- Maps of paresthesia coverage confirmed the precise coverage of painful areas with overlapping paresthesias, demonstrating the stimulation specificity of DRG stimulation and avoidance of extraneous coverage, and minimal changes in stimulation with position.

**Key takeaways:**

- Data from this retrospective review suggests that DRG stimulation may provide sustained pain relief in patients with groin pain.

- This study demonstrated the stimulation specificity of DRG stimulation, the avoidance of extraneous coverage, and minimal changes in stimulation with position.
Dorsal Root Ganglion (DRG) Stimulation in the Treatment of Phantom Limb Pain (PLP).


- The purpose of this case series study was to evaluate the use of DRG stimulation in patients suffering from phantom limb pain (PLP), defined by the International Association for the Study of Pain (IASP) as “pain referred to a surgically removed limb or portion thereof.”

- A retrospective chart review of patients suffering from PLP was performed in patients in which pain rates on a visual analogue scale (VAS) and patient-reported outcomes were assessed (n = 8).

- At baseline, average pain rating was 85.5 ± 10.5 mm. After a mean follow-up of 14.4 months, the average VAS decreased to 38.9 ± 27.1.

- Pain reduction dropped an average of 52.0%.

- Three of the eight patients had poor outcomes. In two of those cases pain gradually increased over time and it was determined that leads were placed sub-optimally. The authors believe that therapy could be recaptured through lead revision or reprogramming. In the third case, the reason for decreased pain relief after one month was not determined though the investigators suspect that placebo effect, delayed dislike of paresthesia or inappropriate patient selection may have played a role.

- All patients reported that DRG stimulation resulted in appropriately localized paresthesia at the stump sites. Five of the patients reported that the paresthesia was perceived in their phantom limb or interacted with the perception of their phantom.

- No complications were reported for any of the patients.

**Key takeaways:**

- This pilot study suggests that DRG stimulation may provide pain relief to PLP patients.

- The outcomes in this study suggest that the DRG may be the site of PLP generation and/or maintenance. Further studies are warranted to confirm this.


- The purpose of this retrospective case-series review was to evaluate the effectiveness of DRG stimulation in patients with chronic post-surgical knee pain (n = 13).

- L3 and/or L4 of the DRG were targeted for stimulation following epidural access.

- Twelve out of 13 patients (92%) proceeded to permanent implant.

- Numerical rating scale (NRS) scores, pain/paresthesia map drawings, and ratings of satisfaction and function were collected at baseline and post-implant follow-ups.

- Average follow-up was 6.0 ± 5.2 months (n = 8).

- 92% (12/13) of patients proceeded to permanent implant.

- Pain reduction reported during trial was reduced by an average 71.8% and sustained through the last follow-up with an average pain reduction of 71.2%.

- Self-reported improvements in function ranged from 60-95%.

**Key takeaways:**

- These preliminary results suggested that DRG stimulation may be used to treat challenging pain conditions such as post-surgical knee pain.

- In this study, there was an average pain reduction of 71.2% which was sustained through the follow-up time of six months.

- Two patients in this study reported a complete resolution of baseline allodynia symptoms.
This study reports on four ongoing prospective European studies in which patients with chronic neuropathic pain of the upper extremities were treated with DRG stimulation (n = 19).

- Ten patients were diagnosed with CRPS.
- Four patients had post-amputation pain.
- Four patients were diagnosed with peripheral nerve injury.
- One patient had post-surgical radicular pain.

Patients with successful trials (> 50% pain relief) were implanted with the Axium™ Neurostimulation System. Pain was assessed using the visual analog scale (VAS) while quality of life was evaluated using the EuroQoL (EQ-5D-3L) questionnaire.

This study had an 84.2% trial-to-permanent success rate.

Patients had an average 57.3% (± 8.8%) improvement in VAS scores at three months follow-up, and 54.6% (± 10.2%) improvement in VAS scores at six months follow-up (see Table 2).

- No lead revisions or migrations, and no changes in paresthesia with body position were reported in this study.

### Key takeaways:

- This study provides clinical support that DRG stimulation may be an effective treatment option for chronic neuropathic pain of the upper limbs.
- Patients in this study had an average 54.6% improvement in VAS scores at six months follow-up.
- No changes in paresthesia with body position were reported.

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### Treating Focal Neuropathic Pain with Dorsal Root Ganglion (DRG) Stimulation: Single Centre Prospective Case Series.


- A total of 25 patients with neuropathic pain were treated with DRG stimulation. Pain etiologies included complex regional syndrome (n = 11), phantom limb pain (n = 1), failed back surgery syndrome/radicular pain (n = 2), failed neck surgery syndrome (n = 1) and brachial plexus avulsion (n = 1).

- Following a successful trial, all patients were implanted with a permanent device.

- Significant improvements in VAS, pain relief and quality of life (EQ-5D) scores were seen at six and 12 months. See Table 3.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Baseline (n = 25)</th>
<th>6 Months (n = 14)</th>
<th>12 Months (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS (mm)</td>
<td>78.4 ± 11.3</td>
<td>39.6 ± 31.4*</td>
<td>36.4 ± 37.7**</td>
</tr>
<tr>
<td>Pain relief (%)</td>
<td>-</td>
<td>49.2 ± 40.6</td>
<td>57.7 ± 42.0</td>
</tr>
<tr>
<td>EQ-5D Index Score</td>
<td>0.332 ± 0.183</td>
<td>0.623 ± 0.290*</td>
<td>0.586 ± 0.298**</td>
</tr>
</tbody>
</table>

Table 3. Improvements in VAS (mm), pain relief (%), and quality of life at baseline, six months and 12 months (*p < 0.005 vs. baseline, **p < 0.05 vs. baseline).¹²

- The majority of patients (14/25) reported feeling better or much better at last follow-up while 18/25 rated their satisfaction as eight on a scale of 0-10.

**Key takeaways:**

Preliminary results from this single-center prospective study suggest that focused therapy using DRG stimulation may provide significant long-term pain relief in patients suffering neuropathic pain.

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### An Upper Limb Neuropathic Pain Cohort Treated with Stimulation of Dorsal Root Ganglia (DRG): Pooled Data from Four Prospective European Studies.


- This study reports on four ongoing prospective European studies in which patients with chronic neuropathic pain of the upper extremities were treated with DRG stimulation (n = 19).

- Ten patients were diagnosed with CRPS.
- Four patients had post-amputation pain.
- Four patients were diagnosed with peripheral nerve injury.
- One patient had post-surgical radicular pain.

Patients with successful trials (> 50% pain relief) were implanted with the Axium™ Neurostimulation System. Pain was assessed using the visual analog scale (VAS) while quality of life was evaluated using the EuroQoL (EQ-5D-3L) questionnaire.

This study had an 84.2% trial-to-permanent success rate.

Patients had an average 57.3% (± 8.8%) improvement in VAS scores at three months follow-up, and 54.6% (± 10.2%) improvement in VAS scores at six months follow-up (see Table 2).

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Baseline (n = 19)</th>
<th>3 Months (n = 14)</th>
<th>6 Months (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS (mm)</td>
<td>82.0 ± 2.7</td>
<td>37.0 ± 7.6</td>
<td>30.0 ± 7.9</td>
</tr>
<tr>
<td>EQ-5D index score</td>
<td>0.252 ± 0.052 (n = 16)</td>
<td>0.605 ± 0.104 (n = 14)</td>
<td>0.757 ± 0.072 (n = 10)</td>
</tr>
</tbody>
</table>

Table 2: VAS and EQ-5D index scores at baseline, three months follow-up and six months follow-up. Scores are presented as mean ± SE of the mean.¹

- No lead revisions or migrations, and no changes in paresthesia with body position were reported in this study.
Sustained Pain Relief in Painful Diabetic Neuropathy (PDN) Achieved through Targeted Spinal Cord Stimulation (SCS): A Retrospective Case Series.


- Seven patients diagnosed with PDN were implanted with a permanent DRG stimulation device following successful trials.

- Average follow-up time was 12.4 ± 8.2 months.

- VAS scores dropped from 94.4 ± 7.6 mm at baseline to 47.1 ± 9.5 mm at last follow-up.

- Long-term follow-up data was collected for four patients (12, 14, 16 and 25 months):
  - All four patients were satisfied with the therapy, continued to report good pain relief, and had reduced medication intake.

**Key takeaway:**

DRG stimulation may provide therapeutic benefit to patients suffering from PDN, an often difficult-to-treat pain condition with conventional SCS therapy.
**CONSISTENT, LONG-TERM SUPERIOR PAIN RELIEF**

The studies outlined in this section provide support the use of DRG stimulation as a long-term solution for the treatment of chronic neuropathic pain.

**One-year Outcomes of Spinal Cord Stimulation of the Dorsal Root Ganglion in the Treatment of Chronic Neuropathic Pain.**


- The purpose of this multicenter, prospective, open-label, single arm, internally controlled study was to evaluate the clinical safety and effectiveness of targeted SCS of the DRG.
  - Following a trial period lasting no more than 30 days, 32 patients in total were implanted with the Axium™ Neurostimulator System.
  - VAS scores (0-100 mm) were collected at baseline prior to the trial.
  - Internal controls were assessed at pre-implantation (after trial) and five weeks post-implant when stimulation was turned off.
  - Clinical endpoints were assessed at one-week, four weeks, two months, three months, six months, and one-year post-implant.
  - At all time-points, more than half of the patients reported pain relief of at least 50%. VAS and percentage pain reduction at various follow-up time points are summarized in Table 4:

    - Stimulation was selective and highly steerable, resulting in distinct paresthesia coverage at specific locations of pain.
    - Stimulation-induced paresthesia intensity was stable across body positions. Paresthesia intensity ratings were $4.0 \pm 0.5$ and $3.8 \pm 0.5$ for supine and upright positions, respectively ($p > 0.05$).
    - As a measurement for quality of life, a single composite score (EQ-5D index value) derived from the combined individual dimension scores of the EQ-5D-3L VAS was used in this study. EQ-5D index score improved from $0.298 \pm 0.238$ (n = 22) at baseline to $0.698 \pm 0.267$ (n = 18; $p < 0.001$) at 12 months.$^5$ As a reference, the average quality of life in the United Kingdom is 0.83.$^8$
    - Brief Pain Inventory (BPI) assessments demonstrated significant and sustained reductions in pain severity and interference of pain through 12 months of targeted SCS compared to baseline ($p < 0.001$ for all).
      - Pain severity at 12 months: $3.2 \pm 0.6$ (baseline: $6.9 \pm 0.2$).
      - Interference of pain with activities at 12 months: $3.3 \pm 0.5$ (baseline: $6.5 \pm 0.4$).

<table>
<thead>
<tr>
<th>Subjects with &gt; 50% pain relief (%)</th>
<th>Baseline</th>
<th>End of Trial</th>
<th>1 Week</th>
<th>4 Weeks</th>
<th>5 Weeks$^*$</th>
<th>2 Months</th>
<th>3 Months</th>
<th>6 Months</th>
<th>1 Year$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with &gt; 50% pain relief (%)</td>
<td>-</td>
<td>100</td>
<td>53.1</td>
<td>62.5</td>
<td>-</td>
<td>59.1</td>
<td>60.0</td>
<td>52.0</td>
<td>60.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Leg pain reduction (%)</th>
<th>Baseline</th>
<th>End of Trial</th>
<th>1 Week</th>
<th>4 Weeks</th>
<th>5 Weeks$^*$</th>
<th>2 Months</th>
<th>3 Months</th>
<th>6 Months</th>
<th>1 Year$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg pain reduction (%)</td>
<td>-</td>
<td>69.5</td>
<td>68.6</td>
<td>-</td>
<td>-</td>
<td>72.4</td>
<td>69.3</td>
<td>62.4</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Foot pain reduction (%)</th>
<th>Baseline</th>
<th>End of Trial</th>
<th>1 Week</th>
<th>4 Weeks</th>
<th>5 Weeks$^*$</th>
<th>2 Months</th>
<th>3 Months</th>
<th>6 Months</th>
<th>1 Year$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot pain reduction (%)</td>
<td>-</td>
<td>78.5</td>
<td>58.6</td>
<td>-</td>
<td>-</td>
<td>67.8</td>
<td>84.5</td>
<td>79.5</td>
<td></td>
</tr>
</tbody>
</table>

*Table 4. Summary of pain score and pain reduction (*p < 0.001 vs. baseline, *p < 0.05 vs. baseline, 'stimulation off').$^{14}$*
Results from 78-item McGill Pain Questionnaire (MPQ) shows that weighted pain rating index (PRI), calculated based on choice of descriptor words and their weighted rank, and number of words chosen (NWC) decrease significantly at 12 months (n = 21, p < 0.0001). See Figure 4.

Key takeaways:

- These data support the long-term stability of pain relief with DRG stimulation to effectively manage chronic pain.
  - DRG stimulation results in sustained pain relief over 12 months with concomitant improvement in quality of life.
  - Paresthesia intensity was not affected by body position while remaining stable with time.
- DRG stimulation is selective and highly steerable, resulting in distinct paresthesia coverage at specific locations in pain.
- The effectiveness of DRG stimulation may be further supported by the internal controls in this study (i.e. turning stimulation “off” after trial and again after five weeks of permanent implant) since VAS scores rebounded to near baseline levels when stimulation was turned off.
Stimulation of Dorsal Root Ganglion for the Management of Complex Regional Pain Syndrome: A Prospective Case Series.*


- The purpose of this prospective case-series study was to evaluate the effects of DRG stimulation in CRPS patients (n = 11).
- Following baseline assessments, subjects were implanted with the Axium™ Neurostimulator System using quadripolar percutaneous leads placed near the DRG.
- Follow-ups occurred at one-week, one-month, five weeks (stimulation off), two months, three months, six months, and 12 months post-implant.
  - Overall pain, leg pain, and foot pain were assessed via VAS.
  - Other evaluations included Brief Pain Inventory (Short form, BPISF), Profile of Mood States (Short Form, POMS), and EuroQOL five dimensions questionnaire.
- 72% (8/11) of patients had successful trials, with an average 81.9% reduction in VAS pain scores compared to baseline.
- Following permanent implantation, average decreases in VAS scores for overall pain were reported (see Table 1).
- At 12 months, 71.4% (5/7) of patients had ≥ 50% pain relief.
- Similar results were reported for foot pain and leg pain at all time points. At 12 months, 85.7% (6/7) of patients with foot pain and 80.0% (4/5) of patients with leg pain had ≥ 50% pain relief.
- Statistically significant improvements from baseline were observed in all secondary endpoints at 12 months (pain severity and pain interference, quality of life and mood disturbance).
- Pain relief remained stable over time and across all body positions. The authors suggest that the smaller electrode spacing in DRG stimulation allows for more focused neurostimulation, making it less likely to shift due to movement or postures.
- Eleven adverse events were reported in four patients, with no lead revisions required.

Key takeaways:
- This study supports the use of DRG stimulation as a viable and effective intervention in patients with CRPS, a difficult to treat pain condition.
- DRG stimulation remained stable over time and across different body positions.

Long-term Follow-up of Treatment of Groin Pain with Dorsal Root Ganglion Stimulation.


- This case study reports on the 19 month follow-up data of patients who failed conservative management but were successfully treated with DRG stimulation for groin pain (n = 2).
- The first patient in this report was a 47 year old female who has suffered from groin pain since 1999. The second patient was a 66-year-old man who has suffered from testicular pain since 2003.
- These two patients reported 65% overall pain relief with average VAS reduction from 66.5 mm pre-operatively to 6 mm post-operatively. Details from each case are reported in Table 5.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up period</td>
<td>19 months</td>
<td>19 months</td>
</tr>
<tr>
<td>Painful area coverage</td>
<td>80-90%</td>
<td>80%</td>
</tr>
<tr>
<td>VAS (Pre-operatively)</td>
<td>72 mm</td>
<td>61 mm</td>
</tr>
<tr>
<td>VAS (Post-operatively)</td>
<td>12 mm</td>
<td>0 mm</td>
</tr>
<tr>
<td>EQ-5D (pre-operatively)</td>
<td>0.362</td>
<td>-0.484</td>
</tr>
<tr>
<td>EQ-5D (post-operatively)</td>
<td>0.796</td>
<td>0.189</td>
</tr>
<tr>
<td>Usage</td>
<td>9-11 hours/day</td>
<td>24 hours/day</td>
</tr>
</tbody>
</table>

Table 5. Results from two case studies treated with DRG stimulation for groin pain.

Key takeaway:

This small study reporting on two patients suggests that DRG stimulation may be an effective long-term treatment option for patients suffering from chronic groin pain.

* This article also supports the use of DRG stimulation to treat chronic focal conditions.
Lack of Body Positional Effects on Paresthesias when Stimulating the Dorsal Root Ganglion (DRG) in the Treatment of Chronic Pain.


- This study aimed to 1) validate a new tool for quantifying paresthesia intensity and 2) compare the paresthesia intensities and distributions generated by DRG stimulation between two body positions (supine and standing) over time (n = 10).
  - An 11-point numerical rating scale (0 = no paresthesia and 10 = very intense paresthesia) was developed for this study. Subjects were blinded and were asked to rate the perceived paresthesia intensity at different stimulation intensities.
  - Paresthesia distributions (patients were asked to draw the location of their paresthesia intensity) were tested at upright and supine postures at nine different time points: at trial programming, end of trial, post-implant programming, one-week post implant, one-month, two months, three months, six months and 12 months post-implant.
  - Results showed a strong relationship between perception and maximum tolerable paresthesia thresholds across subjects ($R^2 = 0.92$).
  - The average threshold for perception of paresthesia was 1159 µA ($\pm 907$, range 350-2900).
  - The average threshold for maximum tolerable paresthesia sensation was 1521 µA ($\pm 939$, range 475-3200).
  - Across all 10 subjects, there was a strong positive association between stimulation amplitude and perceived paresthesia intensity (grand mean $R^2 = 0.83$).
  - Overall, paresthesia intensity ratings did not differ significantly between body positions or across time (ps > 0.05). See Figure 3.

**Key takeaways:**
- The results from this study show that with DRG stimulation, paresthesia intensities and coverage locations remain consistent when standing or sitting through 12 months post-implant.
- Anatomically, the DRG may be less susceptible to biomechanical perturbations than the dorsal column of the spinal cord, which may help to minimize any changes in paresthesia intensities or location due to changes in position.

### Figure 3

Paresthesia intensity at different follow-up time points did not vary significantly with body position or with time (ps > 0.05).[^19]

### Key Takeaways

- The results from this study show that with DRG stimulation, paresthesia intensities and coverage locations remain consistent when standing or sitting through 12 months post-implant.

- Anatomically, the DRG may be less susceptible to biomechanical perturbations than the dorsal column of the spinal cord, which may help to minimize any changes in paresthesia intensities or location due to changes in position.

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[^19]: The results from this study show that with DRG stimulation, paresthesia intensities and coverage locations remain consistent when standing or sitting through 12 months post-implant.
Stimulation of Dorsal Root Ganglion for the Management of Complex Regional Pain Syndrome: A Prospective Case Series.*


- The purpose of this prospective case-series study was to evaluate the effects of DRG stimulation in CRPS patients (n = 11).
- Following baseline assessments, subjects were implanted with the Axium™ Neurostimulator System using quadripolar percutaneous leads placed near the DRG.
- Follow-ups occurred at one-week, one-month, five weeks (stimulation off), two months, three months, six months, and 12 months post-implant.
  - Overall pain, leg pain and foot pain were assessed via VAS.
  - Other evaluations included Brief Pain Inventory (Short form, BPISF), Profile of Mood States (Short Form, POMS), and EuroQOL five dimensions questionnaire.
- 72% (8/11) of patients had successful trials, with an average 81.9% reduction in VAS pain scores compared to baseline.
- Following permanent implantation, average decreases in VAS scores for overall pain were reported (see Table 1).
- At 12 months, 71.4% (5/7) of patients had ≥ 50% pain relief.
- Similar results were reported for foot pain and leg pain at all time points. At 12 months, 85.7% (6/7) of patients with foot pain and 80.0% (4/5) of patients with leg pain had ≥ 50% pain relief.
- Statistically significant improvements from baseline were observed in all secondary endpoints at 12 months (pain severity and pain interference, quality of life and mood disturbance).
- Pain relief remained stable over time and across all body positions. The authors suggest that the smaller electrode spacing in DRG stimulation allows for more focused neurostimulation, making it less likely to shift due to movement or postures.
- Eleven adverse events were reported in four patients, with no lead revisions required.

Key takeaways:
- This study supports the use of DRG stimulation as a viable and effective intervention in patients with CRPS, a difficult to treat pain condition.
- DRG stimulation remained stable over time and across different body positions.

An Upper Limb Neuropathic Pain Cohort Treated with Stimulation of Dorsal Root Ganglia (DRG): Pooled Data from Four Prospective European Studies.*


- This study reports on four ongoing prospective European studies in which patients with chronic neuropathic pain of the upper extremities were treated with targeted SCS therapy (n = 19).
- Ten patients were diagnosed with CRPS.
- Four patients had post-amputation pain.
- Four patients were diagnosed with peripheral nerve injury.
- One patient had post-surgical radicular pain.
- Patients with successful trials (> 50% pain relief) were implanted with the Axium™ Neurostimulation System. Pain was assessed using the visual analog scale (VAS) while quality of life was evaluated using the EuroQoL (EQ-5D-3L) questionnaire.
- This study had an 84.2% trial-to-permanent success rate.
- Patients had an average 57.3% (± 8.8%) improvement in VAS scores at three months follow-up, and 54.6% (± 10.2%) improvement in VAS scores at six months follow-up (see Table 2).
- No lead revisions or migrations, and no changes in paresthesia with body position were reported in this study.

Key takeaways:
- This study provides clinical support that targeted SCS may be an effective treatment option for chronic neuropathic pain of the upper limbs.
- Patients in this study had an average 54.6% improvement in VAS scores at six months follow-up.
- No changes in paresthesia with body position were reported.

*This article also supports the use of DRG stimulation to treat chronic focal conditions.*
References


Indications and Usage:

CE Mark: The Spinal Modulation Neurostimulator System is indicated for the management of chronic intractable pain. Australia: The Spinal Modulation implantable neurostimulation system is indicated for spinal cord stimulation (SCS) for the management of chronic, intractable pain of the trunk and/or limbs.

Contraindications:

CE MARK and Australia: Patients contraindicated for the Axium Neurostimulator System are those who: have an active implantable medical device including but not limited to cardiac pacemakers and cardiac defibrillators, are unable to operate the system, and are poor surgical risks.

Potential Adverse Events:

The implantation of a neurostimulation system involves risk. Implant Manual must be reviewed for detailed disclosure.

Refer to the User’s Manual for detailed indications, contraindications, warnings, precautions and potential adverse events.

Rx Only

Brief Summary: Prior to using these devices, please review the User's Manual for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

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