Long-term data on the effectiveness of spinal cord stimulation (SCS) for CRPS has recently been published. While the authors conclude that SCS has no durable statistically significant effect on pain relief for chronic CRPS Type I patients, there are limitations with regard to the analysis and a more comprehensive evaluation and interpretation of the data is warranted.

**What is Complex Regional Pain Syndrome (CRPS)?**

CRPS is a neuropathic pain syndrome precipitated most commonly by minor limb trauma. Continuous, severe pain, disproportionate to the inciting event, occurs in the limb and may be accompanied by allodynia, hyperalgesia, skin color changes, edema, joint stiffness, and bone demineralization. The second most common use of spinal cord stimulation (SCS) in the United States is for the symptomatic management of CRPS.

Clinical evidence supports the use of spinal cord stimulation (SCS) using current technology as safe, effective, and cost-effective for the treatment of complex regional pain syndrome/reflex sympathetic dystrophy (CRPS/RSD).

Studies have shown that SCS provides significant pain relief and has been associated with substantial long-term success as measured by global perceived effect. One study demonstrated that SCS led to a reduction in medication use. Two studies have shown improvements in function and daily living and enabled patients to return to work. SCS can significantly enhance CRPS treatment by providing sufficient pain relief such that patients can engage in physical therapy as part of their rehabilitation process. Cost studies show that the mean first-year cost of SCS becomes substantially less in the second year.

**Background on the Kemler study for CRPS: previously reported six- and 24-month results**

Patients selected for the Kemler study were enrolled between March of 1997 and July of 1998 and were randomized 2:1 to either SCS plus physical therapy (SCS+PT) (n = 36) or PT alone (n = 18). Of the 36 patients randomized to SCS+PT, 24 (67%) were implanted.

At six months, in an intention-to-treat (ITT) analysis, the mean VAS score for SCS+PT patients decreased by 2.4 cm, while it increased by 0.2 cm for PT-only patients (p < 0.001). In the as-treated analysis, global perceived effect (GPE) was much improved in 14 (58%) of the 24 SCS+PT implanted patients, as compared to one of the 18 (6%) PT-only patients (p < 0.001). SCS+PT also resulted in significant improvements in health-related quality of life (HRQoL) both for patients with an affected hand (p = 0.02) or foot (p = 0.008).

At the two-year follow-up, in an ITT analysis, mean pain intensity (VAS) decreased by 2.1 cm for SCS+PT patients compared to 0 cm for PT-only patients (p < 0.001). In the as-treated analysis, mean VAS score decreased by 3.0 cm for SCS+PT implanted patients compared to 0 cm for PT-only patients (p < 0.001). In the as-treated analysis, GPE was much improved in 15 of the 24 (63%) SCS+PT implanted patients, as compared to 1 of 11 (9%) PT-only patients (p < 0.001) (Figure 2). HRQoL benefits remained the same.

**Figure 1.** Change in VAS (cm) at six months: SCS+PT implanted versus PT-only

**Figure 2.** Change in GPE at 24 months: SCS+PT implanted versus PT-only
**Kemler study for CRPS: five-year results**

After five years, in the main analysis the mean pain intensity for the patients randomized to SCS+PT (n = 31) was reduced by 1.7 cm versus 1.0 cm for the patient randomized to PT only (n = 13) (p = 0.25). Twenty-three percent (23%) of the SCS+PT patients reported much improvement on the GPE scale, while 15% of PT-only patients reported much improvement (p = 0.24). HRQoL changes were not statistically different between groups.\(^{18}\)

In the subgroup analysis of permanently implanted patients (n = 20) versus PT-only patients (n = 13), the average pain relief (VAS) was 2.5 cm compared to 1.0 cm (p = 0.06). Thirty-five percent (35%) of the SCS+PT implanted patients reported much improvement on the GPE scale, while 15% of PT-only patients reported much improvement (p = 0.02). HRQoL measures were not significantly different between groups. Patient satisfaction in SCS implanted patients was also very high. After five years, 90% of SCS implanted patients indicated that they had positively responded to SCS, and 95% reported that they would undergo treatment again for the same result.\(^{18}\)

**Pain scores at five years likely moderate for SCS-implanted patients and severe for PT-only patients**

In the as-treated analysis of SCS+PT implanted patients versus PT-only patients, the difference in VAS pain score change approached statistical significance (p = 0.06) in favor of SCS and that difference was likely clinically meaningful to patients. As Figure 3 demonstrates, the mean VAS score for SCS implanted patients was relatively steady over years 3-5 and was still nearly two points lower than PT-only patients at year five.\(^{18}\) Further, the average VAS score for SCS implanted patients was in the range of scores considered to equate to moderate pain, while the average score for PT-only patients was in the range of scores considered to equate to severe pain.\(^{19}\)

**The nature of the analysis was unconventional**

Kemler’s main analysis should have employed ITT analysis whereby comparisons would be made between the patients randomized to SCS+PT versus the patients randomized to PT only, regardless of what actually happened with their treatment. In fact, Kemler excludes one SCS+PT randomized patient who received a special implant, four PT-only randomized patients who received an SCS implant, and nine SCS+PT randomized patients who received PT only due to a failed SCS trial.\(^{18}\) As-treated analysis allows you to analyze the patients based upon the treatment they actually received. In the case of this study, as-treated analysis offers value because several patients randomized to SCS never received the therapy and several patients randomized to PT-only received stimulation.

The use of a post-randomization baseline pain measure raises concern. As the study was not blinded, the patients’ perceived baseline pain intensity may have been influenced by knowing which treatment they were about to receive.

Analyzing five-year outcomes versus baseline values may no longer be a valid comparison for two reasons. First, patients may reframe their pain, meaning that the patient considers his or her pain experience from a new reference point. Treatment may allow them to increase their level of functioning. This enhanced level of activity might then become their new normal. As they push their bodies to do more, they may perceive their pain as being worse, when in fact they are performing an activity that previously was difficult or impossible due to pain. Second, their disease may have progressed or changed over time to involve additional painful regions or different painful regions.

**CRPS responds to treatment best when it is diagnosed and treated early**

A clinical treatment pathway for patients who have not responded to conservative therapy (Figure 4), developed under the auspices of the International Association for the Study of Pain (IASP), recommends SCS at 12-16 weeks. This guideline was developed by a panel of internationally recognized experts in the care of CRPS.
patients. Patients in the Kemler study at enrollment had CRPS on average for more than three years.7

Figure 4. Treatment Pathway for CRPS16

CRPS symptoms are heterogeneous and dynamic17

The character of CRPS pain evolves over time, and in 10% of patients spreads to a new region or limb.16 As Kemler notes, the pain may, on occasion, even resolve.18 Whether programming was adjusted to treat the changing nature of the patients’ pain in Kemler’s study is unknown. Further, the ability to adjust programming was limited for patients with the Itrel 3 and quadripolar leads compared to the systems and software available today. Significant differences in pain relief and the ability to recapture pain relief without reintervention have been reported in retrospective analysis for patients with dual lead octapolar systems versus single lead quadripolar systems.9

SCS technology in the Kemler study now outdated

Patients were implanted with the Itrel® 3 Model 7425 neurostimulator and Model 3487A leads, which are quadripolar with four electrodes.7 This is a single lead system providing unilateral stimulation designed for simple neuropathic pain, the only therapy available at the time. Today’s therapy provides bilateral stimulation using up to 16 electrodes and powers multiple lead arrays with rechargeable neurostimulators and advanced programming features to handle the complex and high-power needs of CRPS patients. Neurostimulation can be adjusted to address the changing nature of CRPS pain over time. A physician can give patients the ability to adjust their therapy to accommodate fluctuations in day-to-day pain.

Complications should be interpreted with caution

Over five years of treatment, 10 (42%) of 24 SCS+PT implanted patients underwent reoperation as a result of complications.17 The most common complication was lead migration. Today’s 16-electrode systems may reduce the number of interventions required to correct lead migration as reprogramming may recapture the loss of or shift in paresthesia coverage or the change in pain patterns. Finally, the stimulator replacements were listed in the complications table of the article, which is misleading. Appropriately, they were not counted as complications in the Kemler study. The typical high-power needs of CRPS patients routinely exhausted the natural battery life sooner in older generation technology. Today’s rechargeable neurostimulators can minimize the number of stimulator replacements for CRPS patients with high-power needs.

SCS for CRPS is a cost-effective therapy

CRPS is a serious, debilitating medical condition and patients are often refractory to more conservative treatments.20-21 Spinal cord stimulation offers these patients a chance to achieve significant pain relief. While the pain relief may diminish over time, as the authors note, two to three years of significant pain reduction must be considered an important achievement.18 Finally, spinal cord stimulation remains a cost-effective therapy. Despite a higher cost in the first year, due largely to trial and implant costs, economic analysis has demonstrated that the mean first-year cost becomes substantially less in the second year14,15 and lifetime costs for SCS+PT patients are lower compared to costs for PT-only patients (Figure 5).14 Regardless of the figure selected, discount rate, implantation rate, and complication rate, the costs of conventional treatment exceed those of spinal cord stimulation.14 Similarly, SCS for failed back surgery syndrome (FBSS) patients has been shown to be cost-effective versus conventional treatment22-25 and this has been reported to occur approximately two years following implant.24,25

Figure 5. Mean cost from first year to death14

References

References (continued)


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