NEW RESEARCH SPOTLIGHT
Summary and Assessment of a Recently Published, Noteworthy Study Developed for SIS Members by the Research Division


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| SUMMARY |

**TYPE OF STUDY:** Investigator-initiated, single-center, quadruple-blinded, placebo-controlled, crossover, randomized clinical trial

**OBJECTIVE:** Investigate efficacy of spinal cord burst stimulation in patients with chronic radiculopathy after surgery for degenerative lumbar spine disorders

**TREATMENT ASSESSED:**
Two 3-month periods with spinal cord burst stimulation and two 3-month periods with placebo stimulation in a randomized order

Burst stimulation was closely spaced, high frequency electrical stimulation delivered to the spinal cord. Stimulus consisted of 40-Hz burst mode of constant-current stimuli with 4 spikes per burst and an amplitude corresponding to 50 - 70% of the paresthesia perception threshold.

Trials included mild IV sedations and local anesthetic with lead placement over dorsal columns so that paresthesia occurred in the targeted spinal dermatome (tonic conventional stimulation). A single 16-contact lead (Infinion CX, Boston Scientific) or two 8-contact leads (Linear ST, Boston Scientific) were used based on unilateral or bilateral pain, with Insertion at L1/L2 or L2/L3 and placed at T9/T10 under fluoroscopy. If successful improvement, a non-rechargeable implantable pulse generator was placed (Precision Novi, Boston Scientific).

A nurse was the only one who knew which treatment (placebo vs burst stim) was used by opening each patient’s randomly numbered envelope that stated which arm they were assigned to for the next period. Before every new period but after collection of self-reported data, the nurse would check impedance of SCS, used tonic stimulation to make sure it can still be provided in the correct dermatome, and used burst stimulation to ascertain perception threshold measurements. Of note, patients were only given the handheld SCS programmers after completing the last randomization period and collecting outcome measures.

Outcome measures were collected prior to the testing period and at the end of each of the 4 treatment allocation periods. Questionnaires were completed by patients without assistance from trial personnel.
INCLUSION CRITERIA:
• 18 years or older
• Undergone at least 1 decompressive or fusion procedure for degenerative lumbar spine disease
• Experienced postoperative chronic radicular pain (defined as pain arising from 1 or more spinal nerve roots, with diagnosis being based on pain characteristics, clinical exam, sensorimotor testing, and review of diagnostic imaging) refractory to non-surgical treatment for a minimum of 6 months
• Reported average pain intensity with a minimum of 5 on a scale of 1-10 for leg pain using Numeric Rating Scale (NRS); 0 = No pain; 10 = Worst pain imaginable
• No additional spine surgery or pharmacological treatment was assumed to be beneficial
• If all of the above criteria are met, the patient underwent a 2-week SCS testing period with an external neurostimulator and epidural leads, with inclusion requiring a minimum reduction of 2 points on NRS for leg pain

EXCLUSION CRITERIA:
• Previously treated with SCS or subcutaneous nerve stimulation
• Abnormal pain behavior
• Unresolved psychiatric illness
• Unresolved issues of possible secondary gain
• Inappropriate medication use (misuse of sedatives or substance use disorders)

KEY FINDINGS:
• No statistically significant difference in ODI scores (Primary Analysis)
• No statistically significant difference in NRS scores, EuroQol Index, steps/day, or time spent walking/standing

CRITIQUE
• Subjects were trialed with tonic waveform stimulation, but the experimental (permanent implant) arm was treated with burst waveform stimulation.
• The outcome measures for subjects being trialed (NRS) and the experimental group (permanent implant) (ODI) were different. In a real-world setting, the same outcome measures are used for trial and permanent implant (experimental group).
• A positive trial was defined as 30% pain relief – a threshold that is not clinically acceptable and introduces significant placebo effect.
• Manufacturer guidelines on therapy delivery were not followed. Simple burst waveform at a 50-70% of paresthesia threshold was deployed, not the manufacturer’s algorithm.
• Subjects could not adjust/optimize their therapy or turn off the device. Optimization of treatment using patient feedback is a critical element of effective SCS.
ASSESSMENT

Do you agree with the authors’ conclusions? Why or why not?
• No. The study has significant methodological flaws. Most importantly, the study is not appropriately designed to investigate the real-world application of SCS. The treatment algorithm was not optimized and not individually titrated to each subject. Different outcome measures were used to assess trialed and permanently implanted subjects. The time-point of assessment was more prone to placebo effect; patients are followed longer than 90 days in a real-world setting.

What recommendations would you make to these and other investigators for future studies on this topic?
• Design the study to mimic the real-world application of the treatment.

Why is this study important for members of the SIS community?
• The study has been published in a reputable journal, with a designation of a randomized blinded placebo-controlled study. If the methodological flaws and erroneous conclusion of this study are not pointed out to the scientific and medical community, it may jeopardize patient access to a procedure that is effective in the treatment of chronic pain.