Failed Back Surgery Syndrome And Spinal Cord Stimulation Clinical Trials – Where Are We Now?

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Citation

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Abstract

Failed back surgery syndrome (FBSS) is a term embracing a constellation of conditions describing persistent or recurring low back pain, with or without sciatica following one or more spine surgeries [1,2]. The FBSS patients with severe neuropathic pain experience greater levels of pain, greater disability, lower quality of life, and a higher rate of unemployment compared with other chronic pain models [2, 3]. Spinal cord stimulation (SCS) has been shown to be a cost effective treatment option [4]. By stimulating one or more electrodes implanted in the posterior epidural space, paresthesias are felt in the pain areas, and thus the level of pain is reduced [5].

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world [6]. At the moment, a total of 13 clinical trials are listed concerning the condition “Failed Back Surgery Syndrome” and the intervention “Spinal Cord Stimulation” (Table 1). The most common inclusion and exclusion criteria met in those trials are presented in Tables 2 and 3 respectively.

Table 1

Overview of the collected studies [6]

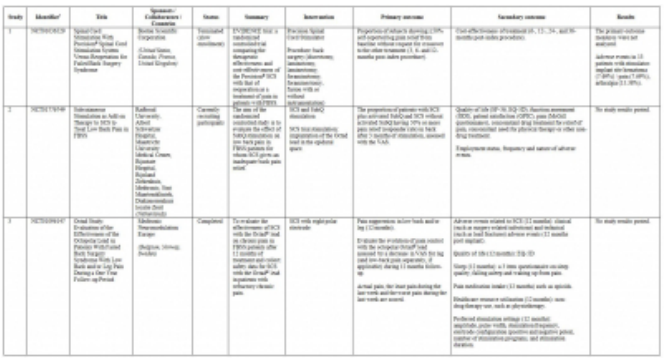
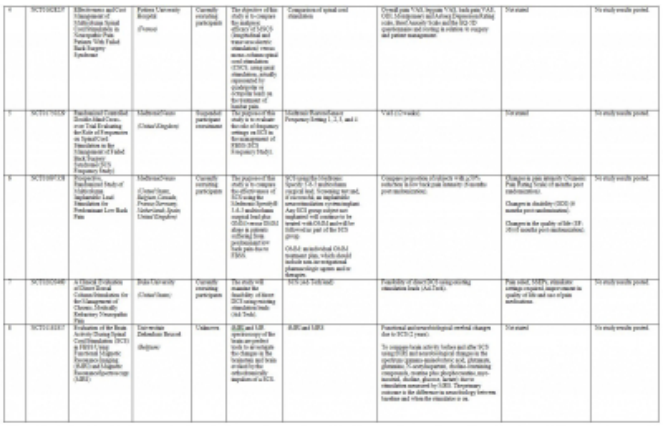


Table 1 Continued



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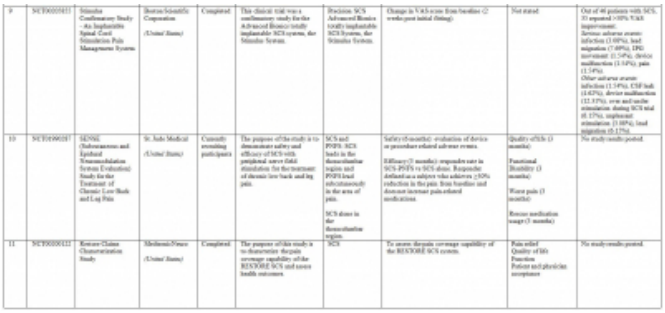

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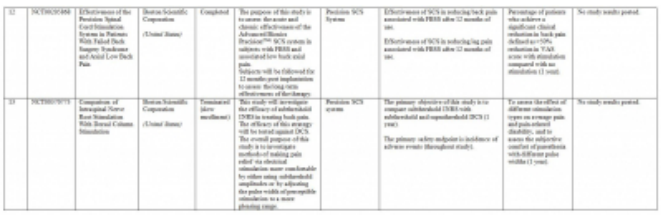

* ClinicalTrials.gov Identifier. CSF: Cerebrospinal Fluid, DCS: Dorsal Column Stimulation, FBSS: Failed Back Surgery Syndrome, fMRI: functional Magnetic Resonance Imaging, INRS: Intraspinal Nerve Root Stimulation, IPG: Implantable Pulse Generator, ODI: Oswestry disability index, OMM: Optimized Medical Management, PNS: Peripheral Nerve Stimulation, PNFS: Peripheral Nerve Field Stimulation, SCS: Spinal Cord Stimulation, SSEPs: SomatoSensory Evoked Potentials, SubQ: Subcutaneous, VAS: Visual Analogue Scale

Table 2

Most common inclusion criteria

- Age >18 years.
- One or more prior lumbosacral surgical procedures.
- Subject has been diagnosed with FBSS.
- At least 3-6 months duration of persistent or recurrent radicular leg pain, with or without low back pain.
- Pain intensity in leg(s) and low back of 5 or higher for leg and back measured separately on a weighted visual analogue scale (VAS).
- MRI or CT myelogram of the lumbar and thoracic spine (within 12 months prior to screening) that rules out pathology that might compromise SCS electrode placement or pathology, in addition to neural compression, that might contribute to the subject's pain.
- Failure of a well conducted conservative treatment (insufficient pain relief and / or unacceptable side-effects).
- No further therapeutic surgical options available as assessed by appropriate investigation.
- Subject is willing and able to sign informed consent.
- Subject is willing and available to attend visits as scheduled and to comply with the study protocol.
- Subject is willing and able to undergo assessments as part of the evaluation for eligibility and endpoints.
- Subject is willing and able to use the external neurostimulator, recharging equipment (if applicable), and patient programmer per the schedule required by the protocol.
- Understanding and accepting the constraints of the study.
- Absence of psychosis or progressive malignancy.

Table 3

Exclusion criteria

- Age <18 and >80 years.
- Mechanical low back pain (e.g. pain that a recumbent position relieves completely).
- Pain intensity of always 10 on a 0-10 Numerical Rating Scale over the past 6 months based on subject recall.
- A predominance of non-organic signs on physical exam.
- A concurrent clinically significant or disabling chronic pain problem or condition that is likely to confound evaluation of study endpoints (chronic migraine, significant arthrosis of the hip associated with groin pain as primary complaint).
- A disabling or potentially disabling neurologic deficit (foot drop, neurogenic bladder) in the distribution of a nerve root/s caused by surgically remediable compression.
- Significant substance abuse issues.
- Major untreated psychiatric comorbidity.
- History of coagulation disorders, lupus erythematosus, diabetes mellitus, rheumatoid arthritis or Morbus Bechterew.
- Immune deficiency (HIV-positive, corticosteroids with a dose equivalent to prednisolone 10 mg, immunosuppressives).
- Active local or systemic infection.
- Medical or cardiac condition(s) or therapies, or foreseeable need for therapies or diagnostic tests (e.g., MRI), that preclude SCS and/or reoperation.
- Pregnancy (existing or planned).
- Life expectancy less than 1-3 years due to other serious medical condition(s).
- Radiographic evidence of instability (spondylolisthesis or subluxation) requiring fusion.
- Radiographically demonstrated critical cauda equina compression.
- Expected inability to report treatment outcome adequately.
- Expected inability of the patient to properly operate the neurostimulation system.
- Prior SCS procedure.
- Presence of intrathecal drug pump or pacemaker.
- Participation in another clinical study that would confound data of this study.
- Allergy or known hypersensitivity to any materials of the device system which come in contact with the body.
- Subject is involved in current litigation regarding back pain.
- Absence of informed consent signature.

In the majority of the trials (10/13), three large medical technology companies (Medtronic, Boston Scientific, St. Jude Medical) were involved. Universities participated in three trials and various hospitals in two. The countries where the studies were conducted were: United States of America (8/13), United Kingdom (3/13), France (3/13), Belgium (3/13), Netherlands (3/13), Canada (2/13), Germany (1/13), Spain (1/13), Norway (1/13), and Sweden (1/13). As long as the status of the trials is concerned, four studies have been already completed, five of them are still recruiting patients, one has suspended recruitment (enrollment was temporarily suspended to align study materials with field safety notice) and two were terminated due to slow enrollment. The status of one trial is unknown.

The investigated primary outcome was a self-reported pain improvement of ≥50% (VAS). Quality of life, extent of disability, pain medication intake, sleep, and patients' satisfaction were defined as secondary outcomes. Results were listed only for two trials.

The first one (NCT01036529) was early terminated due to the small number of participants. The primary outcome measures were not analyzed. However, adverse events were noted in 13 patients with a stimulator: implant site hematoma, pain, and arthralgia. The second (NCT00205855) evaluated 46 patients with SCS. Thirty-five of them reported >50% VAS improvement. Infection, lead migration, IPG movement, device malfunction, and pain were considered as serious adverse events. Some other adverse events were also encountered: CSF leak, over and under stimulation during the SCS trial, and unpleasant stimulation.

For those patients with FBSS, an interdisciplinary care model for pain control and function improvement is of utmost importance. Attention to social as well as psychological factors is crucial too [2]. Spinal cord stimulation (SCS) provides relief to patients with a variety of painful disorders including FBSS [2, 5]. Moreover, SCS has been shown to be safe and effective, and the technique is also cost-effective as compared with medical management alone [5]. Yet, it seems that the number of ongoing clinical trials is limited. It is certain that a more extended conduction of such trials (with more patients, from more countries, and over a longer time-frame) would be of benefit to both patients and health care providers.

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