# Spinal Cord High-Frequency Stimulation. The Current Experience and Future Directions

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## 1 Introduction

Spinal cord stimulation (SCS) is a minimally invasive treatment option for neuropathic intractable pain [1]. Traditional SCS produces paraesthesia, which is experienced by the patient as a variable sensation overlapping the target area. A randomized control trial of traditional low-frequency SCS compared with conservative management or repeat spinal surgery showed benefits for leg pain but not for low back pain (LBP) [2, 3]. New waveforms of stimulation in SCS, including using a frequency of 10 kHz, have instead showed effectiveness against LBP [4, 5]. These paraesthesia-free stimulations produce safe and effective pain relief. Most of these observations have been collected from patients who have had unsuccessful spinal surgery and LBP for many years, as a rescue strategy in the treatment of the heterogeneous clinical conditions known as failed back surgery syndrome (FBSS) [6]. Strong efforts predominate the literature and present SCS as a potential treatment for patients with other rare conditions, such as patients experiencing chronic LBP who have not had prior spinal surgery (known as virgin-back patients) [7], patients affected by multiple sclerosis (MS) or patients with central neuropathic pain secondary to myelopathy. In particular, although SCS revealed more than 50 years ago a possible effect on motor function recovery, over the past decade, many clinical challenges have arisen in targeting motor circuits [8]. The aim of our work is to report our clinical experiences on spinal cord high-frequency (HF) stimulation. We also report two unusual clinical cases and discuss the potential future indications of this technique.

## 2 Materials and Methods

We retrospectively reviewed the clinical and outcome data of 20 patients (M/F, 4/16) who underwent an HF SCS for different clinical indications between January 2016 and December 2021. The mean age was 55.5 ± 14.9 years, and the mean follow-up (FU) was 13.6 ± 9.3 months. All patients were submitted to a trial before the definitive implantation. As outcome indicators, we evaluated their NRS (numerical rating scale) scores before the procedure, after the clinical trial and at the latest FU.

### 2.1 Statistical Analysis

The means and standard deviations (SDs) were calculated and reported when appropriate. The differences between groups were explored by using the Wilcoxon signed rank test, the Mann–Whitney U test, the $\chi 2$ test, and/or the Fisher's exact test, where appropriate. Differences were considered significant at $p < 0.05$. Statistical analyses were conducted by using StatView version 5 software (SAS Institute Inc.).

## 3 Results

Clinical and outcome data are reported in Table 1. Briefly, we observed significant improvements in NRS scores after the trial and the latest FU (9.4 ± 0.6, 3.1 ± 1.2 and 3.7 ± 1.8, respectively; $p < 0.0001$ and $p < 0.0001$) compared with the preoperative scores. The different factors studied, namely

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**Table 1** Clinical and outcome data of patients submitted to spinal cord high-frequency stimulation

| | |
|---|---|
| Patients | 20 |
| Sex (M/F) | 4/16 |
| Mean age (years) | 55.5 ± 14.9 |
| Mean follow-up (months) | 13.6 ± 9.3 |
| Trial duration (days) | 42.5 ± 18.8 |
| Diagnosis | |
| FBSS | 5 |
| Myelopathy | 7 |
| Arachnoiditis | 2 |
| SM | 3 |
| Virgin low back pain | 3 |
| Hybrid system (yes/no) | 5/15 |
| Lead level | |
| Cervical | 3 |
| Dorsal (T8-T9) | 16 |
| Double | 1 |
| NRS | |
| Preoperative | 9.4 ± 0.6 |
| After the trial | 3.1 ± 1.2 |
| At latest follow-up | 3.7 ± 1.8 |

sex, age, trial duration, diagnosis and lead level, did not significantly affect the clinical outcomes of patients.

We report on two unusual cases as follows.

### Case 1

A 53-year-old woman came with a history of surgeries for lumbosacral lipoma asportation, complicated by cerebrospinal fluid (CSF) leakage, meningitis and hydrocephalus to our attention. Owing to the development of a chronic adhesive arachnoiditis with a septate arachnoid cist at the C6-T4 level and a consequent mass effect on the cord, she underwent spinal cord decompression, arachnoid cyst fenestration and the lysis of adhesions. The magnetic resonance imaging (MRI) findings after these operations are reported in Fig. 1. Because of the persistence of severe spasticity and neuropathic pain despite maximal medical therapy (a combination of nonsteroidal anti-inflammatory drugs, tapendatol, pregabalin and baclofen) and the evidence of a neurogenic bladder and severe paraparesis, the patient was submitted to SCS with octopolar lead, with a distal extremity placed at the T8 level. During the trial period (1 month), we conducted a tonic stimulation with a comfortable paresthesia fully covering the painful area and multiple HF programs using different dipoles of stimulation. The best response was obtained from a frequency-pairing stimulation of a program combining 10 kHz therapy with the tonic spinal cord stimulation. The patient experienced a level of pain relief >60% and significant improvement in lower-limb hypertonia. Accordingly, she underwent the definitive implantation with an MRI-compatible lead system (Nevro Senza Omnia). After 8 months of follow-up, the patient reported a stable clinical improvement of pain and spasticity with no need for multiple drugs (she was taking only the pregabalin at latest FU).

### Case 2

A 37-year-old man with a 5-year history of MS and experiencing LBP and lower extremity pain with relevant spasticity came to our attention. These symptoms affected his deambulation, with gait disturbances and the progressive reduction of walking speed and walking distance despite the best medical therapy. The MRI showed multiple cerebral and spinal cord lesions without significant neural foraminal stenosis or spinal canal narrowing. A SCS was carried out with the octopolar lead placed at the top of T8. During the trial (1 month), the patient did not tolerate the paresthesia associated with tonic stimulation, so an HF stimulation was attempted, which led to significant improvements in LBP and leg pain, a decrease in spasticity and a correspondingly improvement in walking. Thus, the patient underwent a definitive implantation of an MRI-compatible lead system (Nevro Senza Omnia). At a 3-month FU, the patient reported stable improvements in his clinical conditions.

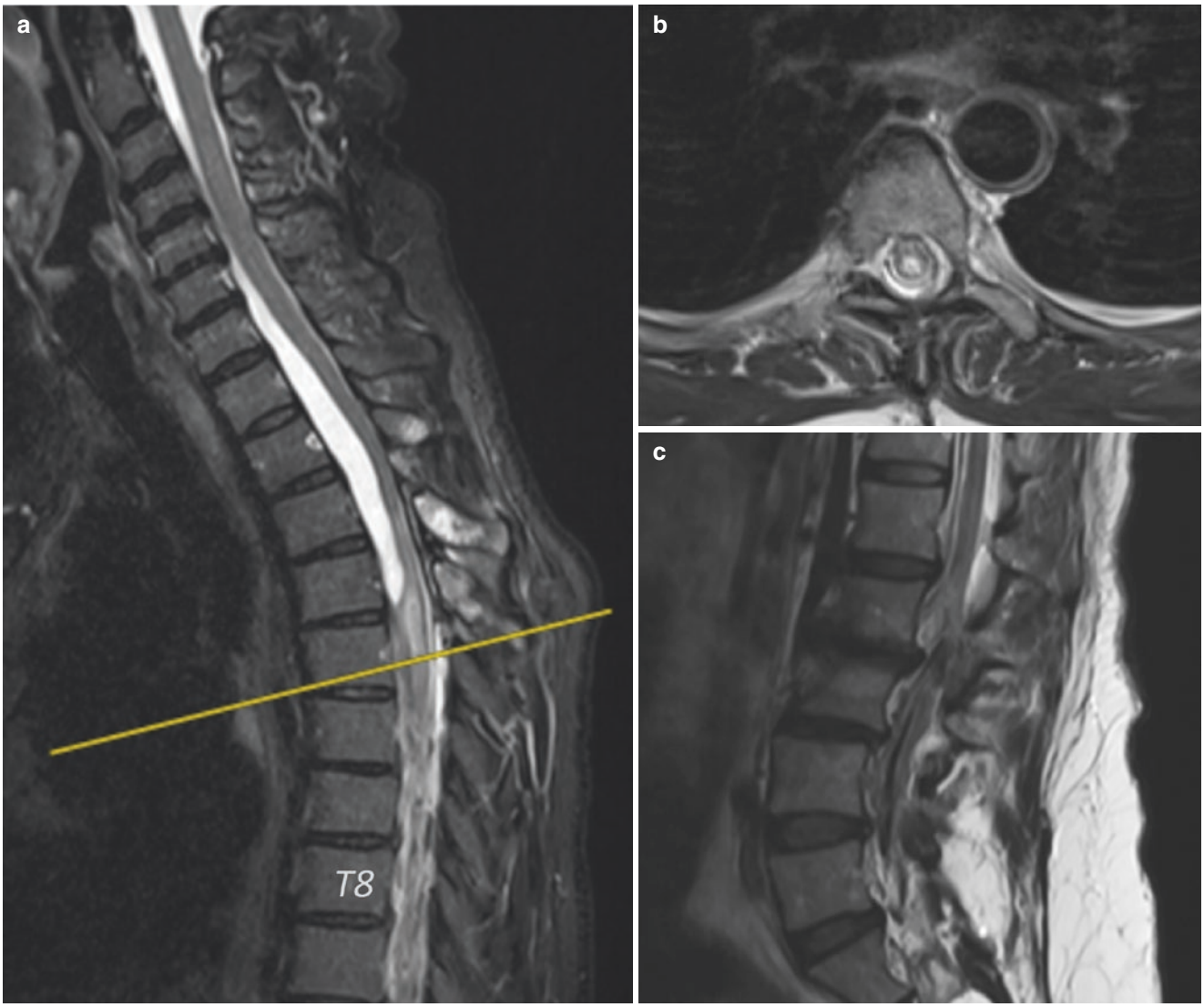


**Fig. 1** Radiological finding of the last MRI before SCS trial. (**a**) sagittal images and (**b**) axial images showing a cervicothoracic septated arachnoid cyst and a caudal area of myelopathy. (**c**) Lumbosacral findings are the results of lipoma asportation and CSF leakage repair

## 4 Discussion

SCS is strongly recommended in FBSS and complex regional pain syndrome [9]. HF SCS using 10 kHz frequencies might expand the utility of SCS, particularly for mixed nociceptive-neuropathic or axial pain components [10]. HF SCS has been proved efficient in reducing LBP and leg pain, improving quality of life and reducing medication use, and it may also result in cost savings for public health systems [11]. As reported in our study, after a standardized trial period, HF SCS results in significant stable pain relief with well-preserved improvements in both radicular and central axial back pain during the FUs in all subjects. Prospective studies and a randomized control trial provided evidence to support the use of HF SCS in subjects with predominant chronic back pain [5]. SCS is now being applied as a potential therapy for a wide range of indications, including neurological, cardiac, and gastrointestinal disorders [11]. Potential effects on the outcomes of ischemic and traumatic brain injuries have also been reported. SCS has been able to to increase cerebral blood flow and induce modification in cerebral microcirculation [12, 13].

Regarding motor disorders, early studies exploring the use of SCS on spasticity were carried out in 1980 [14], but they were obscured by the extensive use of botulinum toxin and intrathecal baclofen therapy with a programmable pump.

Over the past decade, the widespread application of SCS brought a renewed interest in spasticity treatment and further insights into the mechanisms of action for SCS. Epidural

SCS seems to modify lower-limb electromyography (EMG) activity in patients with a spinal cord injury and spasticity. As proved in other pathologic models, variation in stimulation protocols could modify clinical and electrophysiological outcomes [15, 16]. In detail, stimulation frequency, amplitude and electrode configuration could induce different patterns of EMG activity (rhythmic, tonic, or continuous), potentially achieving different motor outputs during standing and stepping [17]. Davis et al. described the effects of SCS on 101 patients, most of whom had MS, and Koulousakis et al. reported epidural stimulation in paraplegic patients [18, 19]. Most of the major effects have been reported in spinal spasticity because the benefits in cerebral spasticity have been less impressive. However, some results have been collected on supraspinal spasticity. Cioni et al. reported on 13 patients affected by spastic hemiparesis following a stroke [20]. As reported by Dekapov et al., chronic SCS may be a potential treatment for patients with moderate spinal and cerebral spasticity with predominant spastic lower paraparesis. In patients with spastic tetraparesis, SCS therapy has not proved to be effective [21].

A recent meta-analysis showed considerable variability in using SCS on motor disfunction in MS patients, stressing the needing for a better selection of cases and the implementation of stimulation protocols [22]. In this paper, we presented two unusual clinical cases of neuropathic pain associated with the spasticity of lower limbs caused by different aetiologies. In both cases, HF SCS has resulted in stable and significant pain control, according to the reported NRS scores. The patients showed reductions in medication use and higher levels of quality of life. The consequences of SCS on their spasticity levels offer interesting points of view on the potential different effects gained by varying frequency stimulation. In fact, the patient with the MS diagnosis (Case 2) reported a considerable improvement in motor function using HF stimulation, and in Case 1, a pairing stimulation was required. Even in the presence of a similar clinical pattern, the etiopathogenesis and the pathophysiology sustaining the motor disfunctions are profoundly different. Different hypotheses have been reported in the literature to explain the potential mechanisms of action for SCS in muscle hypertonia. SCS seems to facilitate the processing of sensory information, restore some supraspinal control in order to produce movement and stimulate medullary neuroplasticity [23]. Our paper has several limitations, including its retrospective design and small sample analysed. During the follow-up, no quality-of-life scores were collected, and we did not perform a walking and gait computerized analysis for patients with spasticity or motor disorders. Nonetheless, our results confirm the efficacy of HF SCS in controlling LBP and leg pain and highlight the potential role of HF SCS in patients with different motor conditions.

**Conflicts of Interest** The authors declare no conflicts of interest.

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