Spinal Cord Stimulation for Neuropathic Pain

Select Language

Powered by Google Translate

Simon Thomson, MBBS FRCA FIPP FFPMRCA
Basildon & Thurrock University Hospital
Past President of the International Neuromodulation Society

Introduction and Clinical Review

Although spinal cord stimulation (SCS) is the most-established member of the family of therapies known as neuromodulation, its uses continue to evolve. Neuromodulation is defined by the International Neuromodulation Society as therapeutic interaction with the central, peripheral or autonomic nervous system for therapeutic effect by means of targeted electrical stimulation or pharmacological delivery from implanted devices.

Spinal cord stimulation has been in therapeutic use for over 50 years. Importantly, the knowledge of how best to use it and the sophistication of the technology has advanced greatly. High quality, randomised, comparative clinical studies have demonstrated unequivocal clinical and cost effectiveness in the treatment of patients with refractory neuropathic pain.[1-6] Spinal cord stimulation is also used in ischaemic pain syndromes such as chronic critical limb ischaemia, angina pectoris and in other visceral pain syndromes including chronic pancreatitis, chronic painful bladder syndrome and chronic abdominal pain.[7] This review will be on SCS application in chronic neuropathic pain.

Neuropathic pain is pain that is generated by nervous tissue itself. It is a maladaptive response to nerve injury of either the peripheral or central nervous system. Spinal cord stimulation is used successfully in neuropathic pain of peripheral nervous system origin.[8] In a European epidemiology study, chronic pain was rated as moderate to severe in 19% of those surveyed.[9] It is estimated that neuropathic pain affects up to 8% of the population. It is responsible for 30 to 65% of activity seen at hospital pain clinics. The natural history is poorly understood, but it is a long-term condition, usually lifelong. In severe cases the health-related quality of life is rated worse than other pain conditions, heart failure and even cancer diagnoses.[4]

Typical cases include pain after nerve root injury in spinal disorders (commonly known as failed back surgery syndrome [FBSS]), post-amputation pain, other traumatic neuropathies, complex regional pain syndrome, and metabolic and viral neuropathies. With the help of expert multi-modal pain medicine, some of these patients can be adequately palliated. For others, the burden of therapy is too great or ineffective, and these patients can be offered SCS.[10]

New developments

The commonest indication for SCS is FBSS. Neuropathic back and leg pain can often be successfully treated, but the associated back pain component that may have both neuropathic and nociceptive aetiology can be more difficult to treat. A number of strategies have evolved in order to meet this need.

Design and placement of electrodes to optimise stimulation

Spinal cord stimulation involves placing a series of electrical contacts in the epidural space overlying the dorsal columns at a vertebral level that, when activated, achieve as near as possible 100% topographical coverage of the pain area of the body when a paresthesia-based program is chosen. For one stimulation approach to paresthesia-free, sub-perception, pain relief, a method using only anatomically guided placement of electrical contacts has been investigated.[25] The sensory homunculus of the dorsal columns has mostly sacral DC fibres in the midline with lumbar, thoracic and cervical layout laterally as one ascends the vertebral levels. Cerebrospinal fluid (CSF) thickness also varies, with its thickest part being in the thoracic region. Based upon the understanding generated by computer modelling of Holsheimer, it is known that successful topographic coverage is achieved with tightly placed electrodes at not too thick a CSF layer. Current flows from cathode to anode. The number of anodes determines the shape of the current field. Manipulation of these as well as pulse width, frequency and amplitude allow greater focusing and recruitment of either DC fibres, dorsal horn interneurones or dorsal root fibres as desired.[11]

Lead and anchor design, implantable pulse generator types

Leads have been developed that can be inserted through large modified epidural needles with eight or 16 contacts on each lead. Two, three or four leads can be inserted and connected to the same implantable pulse generator that can drive 16 or 32 contacts. Other leads can be surgically placed through a laminotomy or flavotomy. Strong and effective anchoring devices attached to the fascia allow non-slip lead control so reducing later lead migration. Lead design has also increased their durability. Lead migration and internal breakage was a common complication in many early SCS randomised controlled trials and case series. Surgical placement has become less necessary with the new developments in lead design, anchors and implantable pulse generators. Percutaneous placement of mini-surgical paddle leads is also possible. The trend is evermore towards minimal access day-case placement with percutaneous techniques.

Improvements in battery technology have allowed the development of fully rechargeable implantable pulse generators (RIPGs) and extended-life primary-cell devices that are non-rechargeable. A patient may spend approximately two to five hours per week charging a device with an induction coil device without interrupting treatment. Some rechargeable IPGs have no finite limit such that one IPG may last 10 to 25 years depending upon usage.

The main bonus that rechargeability brings is the ability to run multiple programmes (anode and cathode arrays) simultaneously. Thus, for example, one array may allow buttock and leg pain relief and another low back pain relief, so running both together allows 100% target topography.

The other benefit is that the patient can use the SCS as much as he or she wants. Primary-cell IPGs were used carefully by patients in order to maximise their life span. Sometimes this need to ration had a counterproductive effect on therapy outcome. Sadly, due to poor adoption of these therapies by health funding bodies, patients may have to wait months for replacement primary-cell IPGs. On the other hand, modern primary-cell IPGs have other advantages. There is no requirement for re-charging, which for some can be a burden; and it can be placed deeper under the fat layer of the skin, thus making it more comfortable.

The IPGs are placed under the skin either in the abdominal or thoracic wall or upper outer buttock. The patient has a remote-control unit to allow adjustments to the programmes, switching between them in order to achieve desired pain relief in different postures.

One manufacturer has even incorporated accelerometers (smartphone technology) that allow the IPG to sense whether the patient is sitting or lying on the back or side and to automatically adjust programmes that have been pre-selected in each position or activity.

Another manufacturer has a sensing ability. It can monitor the activation of the nerves in the dorsal columns and through feedback can always maintain this activation whatever position the patient may be in. It can even compensate for changes in stimulation intensity seen with coughing and straining. This means that the therapeutic activation of the dorsal columns is always optimal.

Other targets and strategies for achieving better pain relief

Nerve root stimulation

Nerve root stimulation can be used in isolation or in combination with SCS. There are broadly two circumstances. When there is dense deafferentation of a nerve root it can be difficult to stimulate that dermatomal area via DC stimulation alone without intense stimulation in the other surrounding dermatomal areas. The therapy can be salvaged in a cervical or thoracic area by placing

lead and electrode contacts over the dorsal root entry zone. Alternatively, the leads can be passed retrograde from the mid-lumbar level down to the lumbo-sacral junction so picking up L5 and S1 roots directly, or anterograde via the sacral hiatus. Not all will tolerate root stimulation due to a narrow amplitude difference between threshold and toleration of sensory stimulation and motor stimulation side effects.

Peripheral field nerve stimulation

Subcutaneous stimulation of named and unnamed branches of nerves in the area of pain has been found to be therapeutic and has generated a number of interesting therapies. Occipital nerve stimulation is one such technique that may have a future in transforming management of severe headache such as migraine, cluster headache and hemicrania continua. Electrodes are threaded subcutaneously unilaterally or bilaterally at the level of the nuchal line from midline to above mastoid so stimulating the branches of occipital nerves. Other peripheral nerves such as ilioinguinal and genitofemoral can also be subcutaneously stimulated in this way and used in post-surgical traumatic neuropathies after groin or gynaecological surgery.

Placing transverse electrodes subcutaneously in the low back, presumably stimulating perforating cutaneous nerve branches, can also treat low back pain. This can even be combined with SCS to optimise back coverage in those in whom optimised coverage is difficult to achieve with SCS alone. Clinically, anecdotal work supports the notion that many localised but difficult-to-treat chronic pains may be helped by peripheral field nerve stimulation techniques. This is an area to watch if it develops.

Sub-perception spinal cord stimulation

Until recently it was believed that the goal of paresthesia-based SCS (PB-SCS) was to maximise the conscious sensation of pleasant paresthesia in the area of pain. Users would often have this set at a comfortable, barely perceptible level and would turn it up if more was needed.

Nowadays we have learnt that one doesn't have to have the sensation of paresthesia to achieve pain relief. This is called sub-perception SCS (sub-P). There are several ways of achieving this. Initially these required very high frequency (10kHz) or packages of high frequency (burst). These required high energy usage and were only really available to rechargeable IPGs.

As our science develops, we have started to realise that with sub-P programming we may be activating different parts of the spinal cord such as the dorsal horn inhibitory neurons or talking to the nervous system differently so achieving inhibition of different pain pathways.

High frequency 10kHz SCS required high energy consumption although nowadays we understand that it is not the frequency alone that determines the clinical outcome but rather the overall neural dose.[20] The neural dose is the product of frequency, pulse width and amplitude. Like with a drug it can be too little or too much

and has to be optimized. More energy delivery, unlike PB-SCS, does not necessarily yield better pain relief.

Targeting of the stimulation to the precise part of the spinal cord is still important for sub-P SCS as with PB-SCS, although it is still not confirmed whether the targets are different or the same. Several placement and programming strategies are used to reach the target. Careful surgical placement of the lead with or without intra-operative testing ensures correct placement. Some surgeons may rely on an anatomical placement alone but this will leave some without optimal placement. Once leads are placed, techniques of targeting can be done by the device software and can vary from a cascade of different bipoles to using a calibrated “big foot” central point of stimulation with multiple active cathodes.

Burst stimulation uses the same target as PB-SCS. One manufacturer has a fixed number of pulses per burst with a passive charge return; others have an ability to vary the burst pattern with an active charge return. As of 2019, there has not been a head-to-head comparison of clinical outcome of one burst mode against another.

The energy demand for sub-P SCS has been reduced. For burst, a duty cycle of stimulation achieves the same pain relief as constant burst.[21] In addition, it has been discovered that equivalent sub-P SCS pain relief can be achieved at normal frequencies and re-charge intervals by simply following the neural dose algorithm and carefully targeting the charge to the optimal part of the spinal cord.[22] Both these dramatically reduce the energy required so opening up the possibility to use primary-cell IPGs for such sub-P programming cost effectively or at least reduce the re-charging burden if using rechargeable IPGs.

Dorsal root ganglion stimulation

Another new technique with a different neural target is dorsal root ganglion stimulation. Specific equipment has been developed that uses fine electrodes with four contacts, which are threaded via the epidural space partway through the intervertebral foramen and allowed to lie up against the sensory dorsal root ganglia. Electrical fields are generated that can selectively stimulate different parts of the dorsal root ganglia. If needed, this allows focusing of stimulation onto specific nerve roots or parts of nerve roots. Because there is minimal CSF thickness there is very little variation in stimulation intensity on movement. Furthermore, the amplitude thresholds are so low that primary-cell IPGs will suffice with excellent device longevity.

A commercially sponsored trial compared DRG stimulation to traditional SCS in complex regional pain syndrome patients and concluded that DRG stimulation gave superior one-year outcomes.[14]

DRG stimulation has a few technique challenges such that there are increased procedural complications, but can reach those parts that some SCS can’t reach and as such is a useful addition to the armamentarium.[23, 24]

Patient-centred care

This of course should always be paramount. However there are increasing technological developments that assist in this quest. The areas of interest are in clinical outcomes, complications, tolerance and therapy burden.

Clinical outcomes
Traditionally measurement of clinical outcomes has used the change in reported pain score as a primary measure. Many other secondary measures that encapsulate the pain experience are also used. Sadly regulators tend to only look at the pain score difference. This creates what some determine as “VAS Wars” (Visual analogue score). However capturing and recording outcomes that are important to that individual are really what we are trying to achieve. More and more the technologies are including the ability for patients to manually record their satisfaction or to measure physical activity with implanted accelerometers.

Complications
These can be biological, or related to the patient or the equipment. We are asking our devices to have long-term safety over years or decades. Premature corruption of the firmware, battery and leads are the areas to consider.

Tolerance
The extent of true tolerance to SCS is not well understood. There are many reasons why SCS therapy may in some patients later fail to give pain relief. Reasons can range from: poor patient selection, physical or mental health disease progression, device complications and therapy burden, to true tolerance. True tolerance is where perfectly targeted SCS no longer gives pain relief, perhaps due to adaptation of the nervous system to repetitive activation. There are several technological attempts to reduce and treat tolerance; these include being able to swap from one mode of SCS to another and changing the waveform and shape.

Therapy burden
For some, managing a SCS device is burdensome. This can relate to the re-charging process or the need to change amplitude based on posture and activity. Now that we have learnt more about sub-P SCS programming the re-charge interval is increasing from what used to be daily to weekly or monthly. Automatic feedback technologies can also automate the change in SCS delivery dependent upon posture and body habitus.

Multiple SCS options
There is a trend towards offering multiple SCS modes from the same device. No longer does one proprietary waveform or frequency necessarily dominate over another. Technological development is still ongoing but having multiple SCS modes, waveforms and wave shapes is a useful addition.

MRI conditional
MRI scans are useful, safe and effective investigations, but only rarely essential. However, we live in a world where such convenience is increasingly seen as essential in the

eyes of some. MRI scanners themselves are evolving such that they create ever-increasing demands on protecting functional electrical implants from causing harm to the patient or harm to the devices. Steadily more and more manufacturers are meeting the challenges of providing variable degrees of head/periphery-only or whole- body MRI conditional labeling of their devices.

Clinical guidelines and health technology assessments

Medicine and healthcare continue to evolve. It is only in recent times that mainstream medicine and the healthcare systems around the world are taking note of the societal burden of neuropathic pain. Pharmaceutical companies have developed products and sponsor and work with university departments to help bring products and therapy guidelines into mainstream medicine. Clinical trials with pharmaceutical products typically involve thousands of patient recruits, and placebo treatments are easier to devise. Complications tend to increase proportionally with the number of active recruits. Treatment success is not dependent upon the prescriber. Statistical analysis on large study populations with a relatively small treatment effect can become statistically significant.[16,17]

Recent re-analysis of some of these large pharmaceutical trials has questioned the extent of the beneficial treatment effect. Thus non-pharmacological management options for neuropathic pain continue to be needed.

Device manufacturers offer devices that need surgical implantation and require acquired skill. Spinal cord stimulation therapy in most circumstances has required the patient to have stimulation perception, which made blinding for clinical studies difficult. As result it was not possible to prove SCS efficacy against sham SCS. Nowadays with the advent of sub-P SCS, randomised clinical trials are being designed to try to gather this evidence of SCS superiority over sham SCS. Furthermore better clinical trial design will result in better sham SCS, even using PB-SCS techniques.

Complications reduce with implanter experience. Most trials, relative to pharmaceutical trials, consist of a small number of participants. However, the treatment effect is an order of magnitude greater than seen with most pharmaceutical trials. It is for this reason that many of the SCS studies can demonstrate clinical significance despite the restrictions of running trials with fewer subjects.

The consequences have been that the methodologies of clinical guidelines groups and health technology assessments are more suited to larger trials with small treatment effects, and as such the role of SCS does not neatly fit into this paradigm. There are still eminent guideline groups and policymaking groups that choose to ignore the contribution that SCS can make in refractory cases.

Having said that, the UK Health policymaking advisory

group, the National Institute of Clinical Excellence, did publish Technology Assessment guidance on SCS in Neuropathic and Ischaemic Pain (TAG 159).[18] This was published in October 2008 and mandated that across the UK, SCS should be commissioned for the treatment of refractory neuropathic pain. This was because the clinical evidence demonstrated both clinical and cost effectiveness in refractory neuropathic pain. Thus failure to fund SCS in selected cases wastes UK healthcare resources in these patient groups. It remains a problem that there is still a 20-fold difference in therapy access across a nationalized healthcare system that is designed to prevent such inequity.

Across Europe, and even within countries, patient access to SCS varies significantly. Much of it depends upon the relative difference in health funding streams rather than clinical need. Spinal cord stimulation market penetration is not present in many countries and is universally under-achieving in all countries across the European Union and USA.

Efforts by clinicians are being translated into ever-increasing numbers of patients treated with SCS. However, there are those patients that do not benefit and have complications.

Successful SCS outcomes depend upon the four pillars of success –

1. Good patient selection
2. Good surgical technique
3. Good follow up arrangements
4. Good SCS technology.

Conclusions

- Neuropathic pain is a common healthcare problem with some patients who are refractory to standard treatment guidelines or burdened with the effects of such treatment
- Spinal cord stimulation offers a clinical and cost-effective treatment at lower lifetime healthcare cost with better long-term outcomes in such patients[19]
- Technological advances and increased understanding of the therapy area have resulted in better and more reliable SCS treatments.
- A prediction is that neurostimulation implantation technology will in the future be as frequent a modality as cardiac brady- and tachy-arrhythmia technology is in modern medicine today.

References

1. North RB et al. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomised, controlled trial. *Neurosurgery* 2005;56:98–106.

2. Kemler MA et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Eng J Med* 2000;343:618–624.

3. Kemler MA et al. Spinal cord stimulation for chronic reflex sympathetic dystrophy--five-year follow-up. *N Eng J Med* 2006;354:2394–2396.

4. North RB et al. Spinal cord stimulation versus re-operation in patients with failed back surgery syndrome: an international multicenter randomised controlled trial (EVIDENCE Study). *Neuromodulation* 2011;14:330–6.

5. Kumar K et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain* 2007;132:179–188.

6. Kumar K et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomised controlled multicenter trial of the effectiveness of spinal cord stimulation. *Neurosurgery* 2008;63(4):762–770.

7. Ekre O et al. Long-term effects of spinal cord stimulation and coronary artery bypass grafting on quality of life and survival in the ESBY study. *Eur Heart J* 2002;23:1938–1945.

8. Cruccu G et al. EFNS guidelines on neurostimulation therapy for neuropathic pain. *Eur J Neurol* 2007;14:952–970.

9. Breivik H et al. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain* 2006;287–33.

10. Thomson S, Jacques L. Demographic characteristics of patients with severe neuropathic pain secondary to failed back surgery syndrome. *Pain Pract* 2009;9:206–214.

11. Holsheimer J, Struijk. How do geometric factors influence epidural spinal cord stimulation? A quantitative analysis by computer modelling. *Stereotact Funct Neurosurg* 1991;234–249.

12. Novel 10-kHz high-frequency therapy (HF10 therapy) Is superior to traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain: the SENZA-RCT randomized controlled trial. Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, Amirdelfan K, Morgan DM, Brown LL, Yearwood TL, Bundschu R, Burton AW, Yang T, Benyamin R, Burgher AH. Anesthesiology 123(4):851-860, 2015.

13. Liem, L., Russo, M., Huygen, F. J. P. M., Van Buyten, J.-P., Smet, I., Verrills, P., Cousins, M., Brooker, C., Levy, R., Deer, T. and Kramer, J. (2013), A Multicenter, Prospective Trial to Assess the Safety and Performance of the Spinal Modulation Dorsal Root Ganglion Neurostimulator System in the Treatment of Chronic Pain. Neuromodulation: Technology at the Neural Interface, 16: 471–482.

doi: 10.1111/ner.12072.

14. Liem, L., Russo, M., Huygen, F. J.P.M., Van Buyten, J.-P., Smet, I., Verrills, P., Cousins, M., Brooker, C., Levy, R., Deer, T. and Kramer, J. (2015), One-Year Outcomes of Spinal Cord Stimulation of the Dorsal Root Ganglion in the Treatment of Chronic Neuropathic Pain. Neuromodulation: Technology at the Neural Interface, 18: 41–49. doi: 10.1111/ner.12228.

15. Kinfe TM, Pintea B, Link C, Roeske S, Güresir E, Güresir Á, Vatter H. High Frequency (10 kHz) or Burst Spinal Cord Stimulation in Failed Back Surgery Syndrome Patients With Predominant Back Pain: Preliminary Data From a Prospective Observational Study. Neuromodulation. 2016 Apr;19(3):268-75. doi: 10.1111/ner.12379. Epub 2016 Jan 13. PubMed PMID: 26762585.

16. NICE. (2010) Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings. Available at: www.nice.org.uk/CG96 (Accessed: 13 March, 2012).

17. Attal N et al. EFNS guidelines on pharmacological treatment of neuropathic pain. Eur J Neurol 2006;13:1153–1169.

18. NICE. (2008) Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. Available at: www.nice.org.uk/TA159 (Accessed: 13 March, 2012).

19. Krames E et al. Using the SAFE principles when evaluating electrical stimulation therapies for the pain of failed back surgery syndrome. Neuromodulation 2011;14:299–311.

20. Thomson S., Tavakkolizadeh M., Love-Jones S.,Patel N, Gu W., Bains, A., DoanQ., Moffitt, M. Effects of Rate on Analgesia in Kilohertz Frequency Spinal Cord Stimulation: Results of the PROCO Randomized Controlled Trial – Neuromodulation 2018; 21.1: 67 – 76.

21. Deer T, Patterson D, Baksh J, Pope J, Mehta P, Raza A, Agnesi F, Chakravarty K. Novel microdosing paradigm using non-linear burst spinal cord stimulation – submitted to Neuromodulation 2019.

22. Paz J, Thomson S, Jain R, Chen L, Huertas I, Doan Q.The HALO Study: Exploration of high andlow frequency outcomes insub-perception SCS International Neuromodulation Society's 14th World Congress: Leading a Global Medical Revolution, Sydney, Australia May 25–30, 2019. Neuromodulation: Technology at the Neural Interface, 2019;22: doi:10.1111/ner.12958.

23. PMA P150004: FDA Summary of Safety and Effectiveness Data. FDA.gov website. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150004b.pdf.

(Accessed 23 September 2019).

24. Thomson, S. A Prospective Global Registry of Real-World Outcomes Using Spinal Cord Stimulation Systems for Chronic Pain. International Neuromodulation Society's 14th World Congress: Leading a Global Medical Revolution, Sydney, Australia May 25–30, 2019. Neuromodulation: Technology at the Neural Interface, 2019;22: doi:10.1111/ner.12958.

25. Pope, J. E., Schu, S. , Sayed, D. , Raslan, A. M., Baranidharan, G. , Heros, R. D., Blomme, B. , Capobianco, R. A. and Deer, T. R. (2019), Anatomic Lead Placement Without Paresthesia Mapping Provides Effective and Predictable Therapy During the Trial Evaluation Period: Results From the Prospective, Multicenter, Randomized, DELIVERY Study. Neuromodulation: Technology at the Neural Interface. doi:10.1111/ner.13019

Date: 10 October, 2019

More information

Handouts:

- **Neuropathy**
- **Painful Peripheral Neuropathy**
- **Neuropathic Pain**
- **Spinal Cord Stimulation Treatment**

Articles:

- **Pain Patient Aided by Spinal Cord Stimulation (Profile, September 2013)**
- **Offering Spinal Cord Stimulation Earlier Could be Better in Complex Regional Pain Syndrome (News Release, July 2013)**

Last Updated on Monday, October 14, 2019 07:33 AM