International Neuromodulation Society

Spinal Cord Stimulation for Neuropathic Pain

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 nearly 50 years. Importantly, the knowledge of how best to use it and the sophistication of the technology have 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 which may have both neuropathic and nociceptive aetiology can be difficult to treat. A number of strategies have evolved in order to meet this need.

Electrode design and arrays

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 to 100% topographical coverage of the pain area of the body. The sensory homunculus of the dorsal columns has mostly sacral DC fibres in the midline with lumbar, thoracic and cervical being laid on 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 topography is achieved with tightly placed electrodes at not too thick a CSF layer. Current flows from cathode to anode. The shape of the current field is determined by the number of anodes. Manipulation of these as well as pulse width, frequency and amplitude allow greater focussing and recruitment of DC fibres so achieving 100% target topography.[11]

Lead and anchor design

Leads have been developed that can be inserted through large modified epidural needles with 8 and even 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 now 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.

Rechargeable implantable pulse generator

Improvements in battery technology have allowed the development of fully rechargeable implantable pulse generators (RIPGs). A patient may spend approximately 2 hours per week charging their device with an induction coil device without interrupting their treatment. Some IPGs have no life 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 coverage and another low back coverage; running both together allows 100% target topography.

The other benefit is that the patient can use their SCS as much as they want. Non- rechargeable IPGs (non-RIPGs) 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, because of poor adoption of these therapies by health funding bodies patients may have to wait months for replacement non-RIPGs.

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 their programmes, switching between them in order to achieve desired coverage in different postures.

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

Other targets and strategies for achieving better coverage

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 severe headache management 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 picking up 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.

Low back pain can also be treated by placing transverse electrodes in the low back, presumably stimulating perforating cutaneous nerve branches. This can even be combined with SCS to optimise back coverage in those 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 as it develops.

High frequency spinal cord stimulation

A recent new development has been the discovery that high frequency (HF) stimulation between bipoles placed between T9 and T10 can achieve pain relief of the back and leg. A recent commercially sponsored clinical trial compared 10KHz stimulation to traditional SCS in FBSS patients with dominant back pain over leg pain and concluded that in these circumstances HF 10KHz stimulation gave superior 2-year outcomes.[12] The mechanism of action of HF SCS is speculated upon but remains to be demonstrated. Until HF10 KHz technology, the belief was that one needs nerve action potentials to achieve pain reduction. Action potentials in sensory nerves that reach sensory perception are felt by the patient. At these high frequency levels the patient is unaware of the stimulation. Typically these therapeutic frequencies are at 1K to 10KHz. Conventional SCS operates at frequencies from 40 to 80Hz. Perception of stimulation is lost at about 300Hz.

The challenges faced by many of the concepts that were used to explain SCS effects will help to further refine our understanding. Further work will need to be done to understand the mechanism of action of HFSCS and its clinical effectiveness.

The frequently asked question is, “Why 10KHz? Can the same effect be achieved at lower KHz frequencies?” The answer is yes it can. However the precision by which this is achieved may be different. Equipoised randomised clinical studies are evaluating this.

Dorsal root ganglion stimulation

Another new technique with a different neural target is dorsal root ganglion stimulation. Fine electrodes with 4 contacts are threaded via the epidural space part way 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 focussing 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 non-RIPG will suffice with excellent device longevity.

A recent commercially sponsored trial compared DRG stimulation to traditional SCS in complex regional pain syndrome patients and concluded that DRG stimulation gave superior 1 year outcomes.[14]

DRG stimulation has a few technique challenges, but can reach those parts that traditional SCS can't and as such is a useful addition to the armamentarium.

New stimulation waveforms

As well as HF 10KHz stimulation there are newer developments in programming of the devices. Burst stimulation was developed following the observations that the natural nervous system communicates with itself not just in tonic regular signals but also in packages (or bursts) of neural activity. The hypothesis arose whereby mimicking this natural phenomenon may be applied to neurostimulation for pain. Some encouraging anecdotal and then systematic data have confirmed the pain-relieving effect of burst stimulation. Furthermore burst stimulation can salvage the pain relief from traditional SCS patients who have developed tolerance. Burst stimulation is another high-energy-consumption programme and can only be used with rechargeable devices. Usually burst stimulation is sub-perception so that the patient is also parasthesiae free. Crucially the stimulation must be delivered via the same array of contacts that at low-rate traditional stimulation is felt in the area of pain to be treated.[15]

High frequency stimulation at 1200Hz using electrode arrays that at traditional rates would cover the whole pain area is also feasible providing that the technology has multiple independent current control (MICC). This sub-perception stimulation may also achieve pain relief at reasonable energy consumption but without the patient being aware of stimulation.

Many of these high-energy sub-perception programmes are notable for their delayed onset of pain reduction (up to 48 hours) compared to traditional SCS where pain relief is induced within 10 to 20 minutes.

Clinical guidelines and health technology assessments

Medicine and healthcare continues 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 by sponsoring and working with university departments have helped bring products and therapy guidelines into mainstream medicine. Clinical trials with pharmaceutical products typically involve thousands of patient recruits, and placebo treatments are easy to devise. Complications tend to increase proportionally with the amount 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]

Device manufacturers offer devices that need surgical implantation and require acquired skill. Spinal cord stimulation is a therapy that in most circumstance requires the patient to have stimulation perception, which makes patient blinding for clinical studies difficult. 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 has been bypassed. This has got to stop. 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. Put more bluntly, failure to commission SCS wastes the 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 there are countries that perform better and others worse. 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. For example, in Belgium those who receive SCS compared to those who need it is still only at about 10%. In the UK, with only 1,000 implants per year, a similar estimate is only 3%.

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 more reliable SCS treatments
- Neurostimulation implantation technology will in the future be as frequent a modality as cardiac brady- and tachy-arrhythmia technology in modern medicine today.

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