



HORIZON SCANNING

December 2016

BRIEF

Spinal cord stimulation to improve function following spinal cord injury

Background

In Australia approximately 300–400 new cases of spinal cord injury occur each year, and it has been estimated that by 2021 between 10,500 and 12,000 Australians will be living with spinal cord injury.¹

Spinal cord injury is currently incurable and treatment is limited to minimising secondary complications and maximising residual function through rehabilitation.² The severity of impairment after spinal cord injury depends on the location in the spinal cord where the injury occurred and the completeness of the injury. Severe spinal cord injury results in loss of mobility and other motor function, loss of sensation, and bowel, bladder and sexual dysfunction. As a large proportion of individuals with this type of injury

are young and live for many years after the initial injury, the medical and social consequences of the condition are considerable.³

There are no available treatments for severe spinal cord injury that have been shown to help patients with complete motor lesions regain voluntary control of movement.³ Neurostimulation is a new strategy that is currently under investigation in the management of spinal cord injury. Neurostimulation (sometimes also referred to as neuromodulation) is the process of using gentle electrical currents to stimulate the nervous system. Research has given hope that neurostimulation applied to the injured spinal cord can improve function.

It has been hypothesised that neurostimulation may lead to the development of new nerve pathways or reawaken existing pathways between the brain and limbs.⁴

Technology Overview

Spinal cord stimulation is achieved either through electrodes implanted directly into the epidural space in the spine or surface electrodes that apply current transcutaneously or through the skin. These are referred to as:

- Epidural spinal cord stimulation
- Transcutaneous spinal cord stimulation

A joint initiative of

Most spinal cord stimulation systems used in studies to control movement in individuals with spinal cord injury were originally developed for the treatment of chronic pain.⁵

NeuroRecovery Technologies, Inc. (neurorecoverytechnologies.com) has developed and plan to commercialise an implantable epidural spinal cord stimulation system and a non-invasive transcutaneous spinal cord stimulation system developed specifically to provide functional recovery for individuals with spinal cord injury.

Epidural Spinal Cord Stimulation

Epidural spinal cord stimulation systems include:

- An implantable pulse generator with a battery that creates electrical pulses
- A lead with a number of electrodes (4-16) that deliver electrical pulses to the spinal cord
- An extension wire that connects the pulse generator to the lead
- A hand-held remote control that turns the pulse generator on and off and adjusts the pulses.

The pulse generator is surgically placed under the skin to send electric currents to the spinal cord. A small wire connects the pulse generator to the electrodes which are surgically implanted in the epidural space above the spinal cord to transmit the electrical pulses to the stimulation site. The stimulation parameters can be controlled by the external programmer.^{6,7}

Transcutaneous Spinal Cord Stimulation

Transcutaneous (through the skin) electrical spinal cord stimulation is a new non-invasive spinal cord stimulation strategy that involves electrically activating the spinal cord using the NeuroRecovery Technologies, Inc. proprietary prototype device. The device delivers an electrical current to the spinal cord via hydrogel electrodes placed

on the skin of the lower back and near the tail bone. This approach uses specific stimulation parameters that do not elicit pain even when energies required to transcutaneously reach the spinal circuitry are used.⁸ The procedure eliminates the need for surgery to implant the electrodes and stimulator.

Clinical Indication

The NeuroRecovery Technologies, Inc. spinal cord stimulation systems are intended to restore function and movement in individuals with paralysis following spinal cord injury. The non-invasive transcutaneous system is for patients with partial to complete paralysis. The implantable device is intended to treat individuals with severe incomplete and complete motor paralysis.⁹

Clinical Effectiveness

Epidural Spinal Cord Stimulation

A case study of four individuals who had been paralysed for more than two years following spinal cord injury showed they were able to voluntarily flex their toes, ankles and knees during epidural stimulation of their lower or lumbosacral spine. The movements were enhanced over time when combined with physical rehabilitation. With continuous stimulation all four participants could stand independently with full weight bearing for several minutes.^{10,11}

It has also been reported that some participants regained bladder sensation and voluntary voiding, had improved bowel sensation, temperature regulation, sexual function and resolution of autonomic dysreflexia (sudden onset of high blood pressure).²

More recently, two people who had been paralysed for more than 18 months following severe spinal cord injuries demonstrated improved hand strength and voluntary hand control following epidural stimulation of

their upper or cervical spinal cords. Long-lasting improved hand and arm function was observed and resulted in an increased ability for self-care.¹²

A search of ClinicalTrials.gov (searched 8 Dec 2016) identified five ongoing trials investigating the use of epidural spinal cord stimulation to improve function following spinal cord injury. A summary of the trials is shown in Table 1. The trials will assess the effects of epidural spinal cord stimulation on ability to move, standing and stepping and cardiovascular and respiratory function.

Transcutaneous Spinal Cord Stimulation

A study published in 2015, showed that five men, each paralysed for more than two years, were able to voluntarily generate step-like movements following treatment with transcutaneous electrical spinal cord stimulation. The men participated in a series of 45-minute sessions, once per week for 18 weeks. In addition to the stimulation the men also received several minutes of conditioning each session, during which their legs were moved manually. For the final four weeks the men received the drug buspirone, which has been shown to induce locomotion in animals with spinal cord injury. Because the men responded so quickly to the therapy, it is believed the stimulation may have awakened dormant connections between the brain and the limbs.¹³

A search of ClinicalTrials.gov (searched 8 Dec 2016) identified four ongoing trials investigating the use of transcutaneous spinal cord stimulation to improve function following spinal cord injury. A summary of the trials is shown in Table 2. The trials will assess the effects of transcutaneous spinal cord stimulation on sensory and motor function in the upper and lower extremities as well as effects on spasticity, respiratory and cardiovascular function, independence and quality of life.

The University of Technology Sydney, Professor Reggie Edgerton,

Table 1: Ongoing trials-epidural spinal cord stimulation

Identifier	Title	Sponsor	Expected completion
NCT02037620	Recovery of Cardiovascular Function With Epidural Stimulation After Human SCI	University of Louisville*	Dec 2016
NCT02313194	Spinal Cord Neuromodulation for SCI	University of California, Los Angeles	Dec 2017
NCT02936453	STIMO: Epidural Electrical Stimulation (EES) With Robot-Assisted Rehabilitation in Patients With Spinal Cord Injury	Centre Hospitalier Universitaire Vaudois	Jun 2018
NCT02592668	Spinal Cord Injury Epidural Stimulation	Mayo Clinic	Jul 2018
NCT02339233	Epi Stim to Facilitate Standing and Stepping	University of Louisville	Jan 2020

Table 2: Ongoing trials-transcutaneous spinal cord stimulation

Identifier	Title	Sponsor	Expected completion
NCT01906424	Restoring Arm and Hand Function With Non-invasive Spinal Stimulation	NeuroEnabling Technologies, Inc.	Aug 2016
NCT01949285	Transcutaneous Electrical Spinal Cord Stimulation for Lower Limbs	NeuroEnabling Technologies, Inc.	Aug 2016
NCT02469675	Brain and Nerve Stimulation for Hand Muscles in Spinal Cord Injury and ALS	Bronx VA Medical Center	Oct 2017
NCT02331979	Improving Bladder Function in SCI by Neuromodulation	University of California, Los Angeles	Oct 2018

SpinalCure Australia and Spinal Cord Injuries Australia have collaborated on Project Edge to establish the first clinical neurostimulation research program outside the USA. Subject to securing funding, Project Edge will be involved in Australian trials to further investigate the use of transcutaneous stimulation in spinal cord injury. Trials are expected to commence in 2017 and will be initially focused on using transcutaneous stimulation to restore upper limb function in patients with quadriplegia.¹⁴

Safety

The safety of epidural and transcutaneous stimulation for

recovery in spinal cord injury has not been reported. Adverse events are likely to be similar to those seen with neurostimulation for other indications such as chronic pain.

Potential adverse events associated with the use of implanted epidural stimulation systems include surgical complications such as infection, bleeding and damage to nervous tissue. Device-related complications may also occur including movement of the implanted electrodes, lead breakage or disconnection and device failure or malfunction.¹⁵

Potential adverse events associated with transcutaneous spinal cord stimulation include skin burns or irritation at the electrode site.¹⁶

It is not yet clear if all individuals with spinal cord injury will respond to treatment, or if there are any situations in which the procedure should not be used because it may be harmful to the patient.

Setting for Technology Use

It is anticipated that epidural and transcutaneous spinal cord stimulation to improve function following spinal cord injury has the potential to be used in the outpatient rehabilitation and home settings. Epidural spinal cord stimulation would require experienced surgeons in appropriate sterile surgical suites for the implantation of the device.

Potential for Impact

If shown to be safe and effective epidural and transcutaneous spinal cord stimulation in spinal cord injury has the potential to improve health, quality of life and independence of individuals with spinal cord injury.

Cost

No information is available about the likely cost of the NeuroRecovery Technologies spinal cord stimulation systems.

Costs associated with the use of these devices will include the extensive training and rehabilitation that is part of the treatment protocols, ongoing maintenance of the devices, replacement of batteries as well as surgical implantation if an epidural stimulation device is used.

It is estimated that an intervention that uses transcutaneous spinal cord stimulation could be one-tenth the cost of an implanted epidural stimulator.¹⁷

Regulatory Approval

The use of spinal cord stimulation systems including the NeuroRecovery Technologies systems to restore function and movement following spinal cord injury are still at an experimental stage of development and should only be used within a clinical trial setting.

References

1. Norton L. Spinal cord injury, Australia, 2007-08. Injury research and statistics series no. 52. Cat. No. INJCAT 128. Canberra: Australian Institute of Health and Welfare, 2010. Available from: www.aihw.gov.au/publication-detail/?id=6442468335
2. Ramer LM et al. Restoring function after spinal cord injury: towards clinical translation of experimental strategies. *Lancet Neurol* 2014; 13: 1241 – 1256.
3. Vasudeva VS et al. Lumbosacral spinal cord epidural stimulation enables recovery of voluntary movement after complete motor spinal cord injury. *Neurosurgery* 2014; 75: N14 – N15.
4. Mayr W et al. Epidural and transcutaneous spinal electrical stimulation for restoration of movement after incomplete and complete spinal cord injury. *Curr Opin Neurol*. 2016; 29: 721-726.
5. Minassian K and Hofstoetter US. Spinal cord stimulation and augmentative control strategies for leg movement after spinal paralysis in humans. *CNS Neurosci Ther*. 2016; 22: 262-270.
6. Rejc E et al. Effects of lumbosacral spinal cord epidural stimulation for standing after chronic complete paralysis in humans. *PLoS One* 2015; 10: e0133998.
7. Mayfield Brain & Spine [Internet]. Ohio: The Mayfield Clinic of Cincinnati 2016. Health Topics, Spinal cord stimulation. [cited 2016 December 9]. Available from: www.mayfieldclinic.com/PE-Stim.htm
8. Gerasimenko Y et al. Transcutaneous electrical spinal-cord stimulation in humans. *Ann Phys Rehabil Med* 2015; 58: 225 – 231.
9. NeuroRecovery Technologies, Inc. Improving the quality of life through neuromodulation [Internet]. California: NeuroRecovery Technologies Inc. Research and Development, Products [cited 2016 December 8]. Available from: neurorecoverytechnologies.com
10. Harkema S et al. Effect of epidural stimulation of the lumbosacral spinal cord on voluntary movement, standing, and assisted stepping after motor complete paraplegia: a cast study. *Lancet* 2011; 377: 1938 – 1947.
11. Agnelli CA et al. Altering spinal cord excitability enables voluntary movements after chronic complete paralysis in humans. *Brain* 2014; 137: 1394 – 1409.
12. Lu DC et al. Engaging cervical spinal cord networks to reenable volitional control of hand function in tetraplegic patients. *Neurorehabil Neural Repair* 2016; 30: 951-962.
13. Gerasimenko YP et al. Noninvasive reactivation of motor descending control after paralysis. *J Neurotrauma* 2015; 32: 1968 – 1980.
14. Project Edge, Leading the world to a new reality for spinal cord injury recovery [Internet]. Australia: ProjectEdge, 2016. About, FAQ's, What is the Project Edge? [cited 2016 December 8]. www.projectedge.org.au/about/faqs/
15. Bendersky D & Yampolsky C. Is spinal cord stimulation safe? A review of its complications. *World Neurosurg* 2014; 82: 1359 – 1368.
16. Moreno-Duarte I et al. Targeted therapies using electrical and magnetic neural stimulation for the treatment of chronic pain in spinal cord injury. *Neuroimage* 2014; 85: 1003 – 1013.
17. Electrical stimulation helps spinal cord injury patients move their legs [internet] 2015]. Available from: www.techtimes.com/articles/73660/20150801/electrical-stimulation-helps-spinal-cord-injury-patients-move-their-legs.htm

Learn more about ISCRR: iscrr.com.au

Follow us on Twitter: [@iscrr](https://twitter.com/iscrr)

Subscribe to our eNews: iscrr.com.au/subscribe

Contact us: info@iscrr.com.au

(03) 9903 8610

Have you heard about a new health technology you think will have an impact on people injured on the roads or at work? Please let us know by contacting us at:

iscrr.horizon.scanning@monash.edu

Disclaimer

ISCRR is a joint initiative of WorkSafe Victoria, the Transport Accident Commission and Monash University. The accuracy of the content of this publication is the responsibility of the authors. Opinions, conclusions and recommendations expressed in this publication are those of the authors and not necessarily those of the sponsor organisations of ISCRR. All information in this publication is designed to help health care decision makers, patients and clinicians, health system leaders and policymakers make well-informed decision to improve the quality of health care services. The contents of this publication should be considered in conjunction with all other relevant information including the context of available resources, current evidence of effectiveness and individual patient circumstances. This publication is not intended to be a substitute for the application of clinical judgement.

Copyright © ISCRR 2017.