Spinal Cord Stimulation Seminar

EE519, 04.12.2024

Pucci Valentina
Neuro-X, EPFL
valentina.pucci@epfl.ch

Curcuruto Martina
Neuro-X, EPFL
martina.curcuruto@epfl.ch

Camba Losada Sebastian
Robotics/NX-minor, EPFL
sebastian.cambalosada@epfl.ch

***Abstract*—Over the last two decades, Spinal Cord Stimulation (SCS) has become a standard in managing chronic pain. This seminar delves into the development and applications of SCS, starting with its foundational principles and advancing through surgical implantation techniques, anatomical considerations, and device operation methods. Modern SCS systems incorporate innovations such as programmable pulse generators, minimally invasive lead placement, and diverse stimulation waveforms, customized for specific pain profiles. This seminar also examines progress in patient selection, trial protocols, and electrode designs, emphasizing their influence on therapeutic outcomes. By providing a comprehensive review, this seminar report aims to enhance understanding of SCS operating mechanisms, clinical effectiveness in treating chronic pain, and its potential for broader applications.**

I. Introduction

Chronic pain represents a significant burden, affecting individuals' quality of life and imposing substantial societal and economic costs. When conventional medical management (CMM) fails to provide relief, alternative therapies such as SCS offer a potential solution. SCS is a neuromodulation therapy utilized to manage medically refractory chronic pain conditions. The therapy involves the implantation of a pulse generator that produces electrical signals delivered to the spinal cord via electrode arrays. By modulating neural signaling at both spinal and supraspinal levels, SCS aims to alleviate pain and improve quality of life. Over the decades, SCS technology has evolved significantly. Modern systems utilize minimally invasive percutaneous lead insertion and programmable implantable pulse generators (IPGs) with multiple electrodes in the epidural space, allowing for tailored stimulation.

II. Anatomy

SCS occurs in the spinal cord, as the name suggests. The spinal cord is a cylindrical structure made of nerve tissue that extends from the base of the brain down through the vertebral column, ending around the L1-L2 vertebrae. It is protected by three layers of membranes called the meninges: the dura mater, arachnoid mater, and pia mater. The spinal cord consists of white matter (nerve fibers that transmit signals) and gray matter (nerve cell bodies).

The main functions of the spinal cord are to send motor commands from the brain to the body, transmit sensory information from the body to the brain, and coordinate reflexes. It also contains central pattern generators, which are neural networks that can produce rhythmic, patterned movements without sensory feedback. These networks are responsible for basic locomotion patterns, such as walking or swimming.

In SCS, electrodes are placed in the epidural space, which is located between the dura mater and the bony vertebrae as shown in Figure 2. The exact placement of the electrodes depends on the location of the pain being treated. For lower back and leg pain, electrodes are usually placed in the thoracic or lumbar regions (T8–T12 vertebrae). For upper back or arm pain, they are placed in the cervical region (C3–C7 vertebrae). Electrodes can also target specific areas to address nerve roots for more localized pain relief.

The main concept that allows SCS to work is based on the paper published by Melzack and Wall's Gate-Control Theory of Pain in 1965. When pain is detected, a chemical reaction generates an action potential that travels in specialized sensory neurons called a nociceptor to a section of the spinal cord. From that point on, this first-order neuron will excite the second-order neuron in the spinothalamic tract, which will send the action potential to the thalamus for further processing. However, the skin is also connected to nerves called mechanoreceptors. These work similarly, but allow the sense of touch. When touch is detected, the action potential will also flow to the spinal cord. However, spinal cord mechanoreceptors will excite interneurons in the spinal cord that, in turn, will inhibit the second-order neuron in the spinothalamic tract, effectively blocking pain. SCS achieves pain gating using electrodes that deliver electrical pulses to mechanoreceptors, effectively reducing pain perception.[4][5].

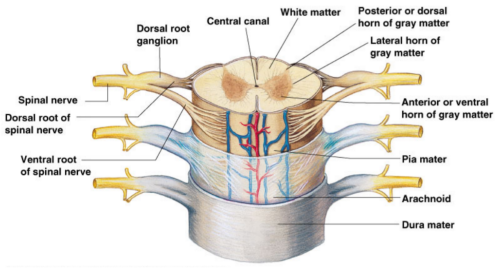

Fig. 1. Spinal cord anatomy

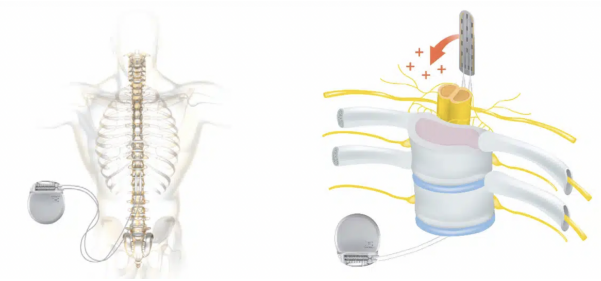

Fig. 2. Modern paddle electrode placement

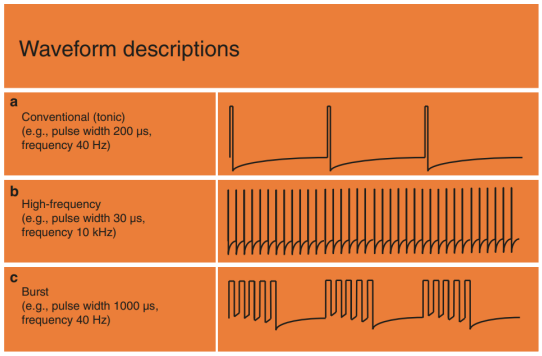

Fig. 3. Different waveforms of electrical stimulation. (a)conventional or tonic SCS, (b)KFHSCS, (c)Burst SCS. From [16]

III. Surgical Procedures and Electrical Stimulation for Pain Control

Surgical procedures for pain control are classified into three categories: anatomic, ablative, and augmentative. Anatomic procedures target physical abnormalities causing pain, such as herniated discs compressing nerve roots. Ablative procedures, such as rhizotomy and cordotomy, aim to block pain by removing or destroying neural pathways. Augmentative procedures, like SCS, modulate pain transmission by influencing the nervous system without destroying it. Introduced in 1967 by Shealy et al., SCS has become the most widely used neuromodulatory technique for managing chronic pain.

The use of electrical stimulation for pain relief has a history spanning over 5,000 years, beginning with the therapeutic application of bioelectric fish. Ancient healers used species like the Nile catfish in 3100 BC and the torpedo fish in the first century AD, which produce natural electric discharges capable of disrupting pain signals by stimulating the nervous system. These fish were applied directly to painful areas, offering temporary relief and demonstrating the potential of electrical stimulation to modulate pain long before the mechanisms were understood.

The 17th and 18th centuries marked significant progress with the advent of artificial electricity generation, leading to groundbreaking medical experiments by pioneers like Galvani, Volta, and Franklin. Despite these advancements, the electrical stimulation devices developed and marketed during the late 19th and early 20th centuries achieved limited success, primarily due to the lack of a robust scientific understanding of their mechanisms.

The modern era of electrical stimulation for pain relief began in 1965 with Melzack and Wall's Gate-Control Theory of Pain. This theory proposed that pain signals are modulated by a "gate" in the dorsal horn of the spinal cord, influenced by the balance of activity between large and small peripheral nerve fibers. Stimulation of large fibers, which are more easily activated by external electrical fields, can "close" the gate and block pain signals. This principle forms the basis of SCS, which selectively activates large fibers to provide effective pain relief. [14]

IV. Types of Spinal Cord Stimulation

Programming SCS involves adjusting parameters such as amplitude, pulse width, frequency to optimize outcomes. Pain relief through SCS may begin within seconds or take several hours, depending on the approach used. The primary variables in SCS programming include frequency, pulse width (typically 100–500 μs), and amplitude (commonly 2–8 V). These parameters can be adjusted to suit individual needs, with certain diagnostic groups, such as Failed Back Surgery Syndrome (FBSS), often requiring higher voltages (3.0–8.0 V) and broader pulse widths compared to other conditions (e.g., 2.5–4.0 V). [1], [3]

Conventional SCS (or tonic SCS, Fig.3A) delivers continuous electrical stimulation at moderate frequencies (e.g., 40–60 Hz) to activate large-diameter (Aβ) sensory nerve fibers in the dorsal columns, producing paresthesia, sensations like tingling or buzzing, over painful areas. Clinical experience suggested that maximizing the overlap between paresthesia and the pain region was crucial for effective relief, however new data suggested the overlap is not necessary. Despite its widespread use for decades, the success rate of conventional SCS, defined as at least 50% pain reduction, is approximately 58%.

Burst SCS, another stimulation waveform, delivers groups of electrical pulses (Fig.3C) to mimic natural thalamic bursting patterns. This approach offers two key benefits: improved pain relief and the absence of paresthesias, which can otherwise cause discomfort, disrupt sleep, or vary with body position. A 2016 clinical trial demonstrated superior effectiveness of Burst SCS, with a 60% success rate compared to 51% for conventional SCS. Unlike conventional methods, Burst SCS appears to influence both ascending pain signals and descending inhibitory pathways, suggesting a distinct mechanism of action.

Kilohertz Frequency SCS (KHFSCS) delivers high-frequency stimulation above 1 kHz (Fig.3B). In 2015, the FDA approved a KHFSCS system that applies stimulation at a rate of 10 kHz and provided dramatic pain relief ($\tilde{8}0\%$) without generating paresthesias. The pain-relief mechanisms of KHFSCS are currently unknown and it is not clear what stimulation rate in the kilohertz frequency range provides the optimal pain relief. A recent clinical study [2] demonstrated equal pain relief at several frequencies in the kilohertz range

(i.e. 1, 4, 7, and 10 kHz) and stimulation at a lower frequency (e.g. 1 kHz) may provide equivalent pain relief at lower energy demands.

Commercially available SCS systems can operate using voltage-controlled or current-controlled technologies. Voltage-controlled systems are more susceptible to impedance variability, which may require frequent parameter adjustments to maintain efficacy. In contrast, current-controlled systems provide more consistent stimulation by minimizing the impact of impedance fluctuations.

As outlined, various SCS waveforms are utilized in clinical practice (Fig.3). Modern IPGs offer extensive versatility, enabling the selection of a broad array of stimulation parameters and waveform paradigms to achieve optimal pain relief. These IPGs also support the simultaneous application of multiple paradigms, allowing for tailored treatments that address different types of pain or target specific painful areas. [1]

V. History of Devices

The evolution of spinal cord stimulation (SCS) devices has significantly advanced pain management. Early systems, developed in the 1960s, utilized solid-state electronics and radiofrequency (RF) technology to address conditions like hypertension, angina, and cardiac arrhythmias. These devices employed passive receivers powered by RF coupling, with an antenna coil placed on the skin and connected to a transistorized oscillator worn externally by the patient. However, issues such as ”hot spots”—areas of excessive electrical concentration leading to discomfort or ineffective pain relief—limited their effectiveness. These ”hot spots” arose from improper electrode positioning or configurations that caused uneven distribution of electrical stimulation. The first SCS electrodes were made of solid platinum and implanted in the subdural or subarachnoid space. While this allowed for effective stimulation, complications such as cerebrospinal fluid leaks and spinal cord compression arose, prompting the development of the ”endodural” technique by neurosurgeon Charles Burton. Early systems primarily used unipolar electrodes, but their limited paresthesia coverage led to the development of multi-electrode arrays for improved stimulation. Modern SCS systems now feature implantable pulse generators (IPGs) and advanced electrode arrays. These arrays, with 8–16 electrodes in percutaneous arrays and 16–32 in paddle arrays, allow for more precise pain targeting. Additionally, flexible lead arrays have been developed to reduce the risk of spinal cord damage and provide effective pain relief with lower stimulation amplitudes. Patients can adjust device settings using handheld telemetry programmers, enhancing both the therapeutic efficacy and patient control over pain management [14]. Figure 4

VI. Modern Device

The system comprises three primary components: an implantable pulse generator (IPG), electrode leads with multiple contact points, and extension cables. (Figure 5)
The IPG is a biocompatible battery-powered unit that is implanted in the flank, gluteal, or abdominal region and serves as the source of electrical pulses. These pulses are transmitted via the leads to the dorsal epidural space, targeting specific spinal cord regions.

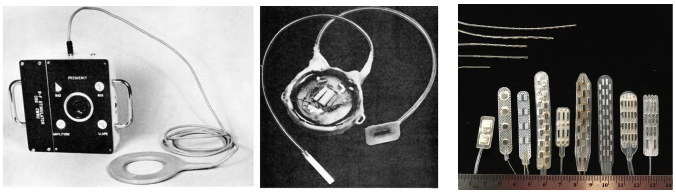

Fig. 4. On the left and in the center: The first radiofrequency SCS system implanted in 1967. Plainly visible are antenna coils in the external transmitter and implanted receiver which couple through the patient's skin to power the implant. On the right modern multicontact electrodes of percutaneous (on top left) and paddle (on bottom) design

Fig. 5. Commercially available Spinal cord stimulation system

A. Electrode Leads

Electrode leads are classified into two main types: percutaneous cylindrical leads and surgical paddle leads, both of which are strategically positioned in the epidural space. Cylindrical leads, introduced via minimally invasive procedures, offer flexibility in placement but may lack the stability of paddle leads. Surgical paddle leads, requiring a laminotomy for implantation, provide broader and more stable contact with neural tissue, making them suitable for complex or refractory cases. Modern leads incorporate arrays with 8–32 electrode contacts, enabling high spatial resolution for precise targeting of neural structures. These arrays allow for anode-cathode polarity adjustments, optimizing current flow to engage targeted spinal cord regions while minimizing unwanted stimulation [1]. Figure 4 (right).

B. Bioelectronics Functionality

The IPG operates as a programmable pulse generator, delivering electrical stimulation at adjustable parameters such as amplitude, frequency (up to 1200 Hz), and pulse width. The bioelectronics advancements include independent current control at each electrode contact, enabling customized electric field shaping and ”neural dosing”. These capabilities are further enhanced by a three-dimensional finite element model that calculates the optimal current distribution across

the dorsal column, accounting for individual anatomical and neural variability. [15]

C. Mechanisms of Action

The electrical stimulation primarily targets the dorsal column and dorsal horn, regions rich in inhibitory interneurons. The system leverages the low electrical resistance of cerebrospinal fluid (CSF) to efficiently direct current flow while high-resistance tissues, such as vertebral bone, shield adjacent organs from unintended stimulation. Activation of inhibitory interneurons helps block pain signals, leading to pain relief (analgesia). The elongated bipole configuration creates a wider electrical field along the spinal cord, making it more likely to stimulate nerve connections that run along the length of the spinal cord.

D. Trial and Optimization

Before permanent implantation, a trial phase evaluates the therapy's efficacy using temporary leads connected to an external pulse generator. This phase, lasting 3–10 days, enables patients to experience the stimulation effects and allows clinicians to adjust parameters for optimal pain relief. If patients achieve significant pain relief (typically defined as $> 50\%$), they move to the second stage, where the electrode arrays are permanently implanted and connected to an IPG.[1]

E. Advanced Features

Modern SCS systems include automation algorithms that dynamically adjust stimulation settings based on patient feedback and clinical programming goals. The patient-controller interface allows for real-time adjustments and assessment of therapy efficacy, reducing the manual programming burden.[7]

VII. Selection of patients

The selection criteria for SCS have evolved with advances in technology and diagnostics. Initially, noninvasive methods like transcutaneous electrical nerve stimulation (TENS) were used to identify candidates, but its predictive value was limited due to differences in mechanisms between TENS and SCS. TENS remained a useful negative screening tool for patients uncomfortable with electrical sensations.

Percutaneous methods later became the preferred screening approach, involving temporary electrode placement in the epidural space to replicate SCS effects. This minimally invasive technique offered better prognostic value than other diagnostic procedures and had a comparable safety profile.

Modern selection incorporates MRI to identify structural or nerve injuries and refined psychological screening to ensure suitability. Patients with demonstrable nerve injuries, like failed back syndrome (chronic pain following back surgeries), are strong candidates. In some cases, bypassing trials for direct implantation, as with angina (chest pain that does not respond to conventional treatments), has proven cost-effective, with ongoing studies exploring broader applications.

VIII. Current developments

From a regulatory point of view, in recent years, FDA approved the introduction to the market of devices using a closed-loop approach allowing the continuous monitoring and adjusting of the electrical stimulation in real-time based on feedback from the patient's body. Other approvals include the use of SCS devices in cases of non-surgical back pain and the use of telehealth with artificial intelligence to improve patient individualization.[6].

From a technological point of view, new, improved computational models are being developed. These models could potentially lead to better design and implementation of the devices, and therefore allowing even more personalization of treatment for patients.

SCS has also show promising results in other domain, most notably the stimulation of central pattern generators, motor and autonomic function in the spinal cord.

IX. Other usages

Epidural electrical stimulation (EES) of the spinal cord has been used for 40 years to alleviate chronic pain syndromes [8]. However, the therapeutic potential of EES may not be limited to pain treatment. There is growing evidence that EES may also contribute to improving motor execution and recovery after spinal cord injury [9], Parkinson's disease[10], multiple sclerosis [11], and possibly other neurological disorders affecting descending control systems [12] [13]).

X. Conclusion

Spinal Cord Stimulation (SCS) has evolved into a powerful and versatile treatment for chronic pain, offering significant improvements in patient outcomes through advanced bioelectronics, precise electrode design, and tailored stimulation protocols. Modern SCS systems leverage adaptive algorithms, real-time feedback, and individualized settings to optimize pain management, while minimizing side effects and enhancing overall therapeutic efficacy. The expansion of SCS beyond pain relief, including applications for motor function recovery, autonomic regulation, and treatment of neurological disorders, underscores its potential as a broad-spectrum neuromodulation therapy. As research continues to explore new avenues for SCS, including its role in spinal cord injury rehabilitation and neurodegenerative diseases like Parkinson's and multiple sclerosis, the future of this technology holds promise for revolutionizing the way we treat a variety of neurological conditions. With ongoing advancements in computational modeling, device personalization, and closed-loop systems, SCS is poised to become an even more dynamic and essential tool in modern medicine. The growing understanding of SCS's mechanisms of action and its expanding clinical applications highlight its transformative potential, offering hope for patients seeking relief from chronic pain and other debilitating conditions.

REFERENCES

[1] S.F. Lempka, P. G. Patil, Innovations in spinal cord stimulation for pain, Current Opin- ion in Biomedical Engineering, Vol. 8, 2018, pp. 51-60, DOI: https://doi.org/10.1016/ j.cobme.2018.10.005.

[2] Thomson SJ, Tavakkolizadeh M, Love-Jones S, Patel NK, Gu JW, Bains A, Doan Q, Moffitt M: Effects of Rate on Analgesia in Kilohertz Frequency Spinal Cord Stimulation: Results of the PROCO Randomized Controlled Trial. Neuromodulation 2018, 21:67–76. [PubMed: 29220121]

[3] D M Moore, C McCrory, Spinal cord stimulation, BJA Education, Vol. 16, No 8, August 2016, pp. 258–263, DOI: https://doi.org/10.1093/bjaed/mkv072

[4] Focus Physiotherapy, "Who Needs Electrical Stimulation Therapy? Benefits for Injury Recovery & Chronic Pain," available at: https://www.focusphysiotherapy.com/who-needs-electrical-stimulation-therapy-benefits-for-injury-recovery-chronic-pain, accessed on the 26.11.2024.

[5] Ali, Rushna MD*; Schwalb, Jason M. MD‡. "History and Future of Spinal Cord Stimulation." *Neurosurgery*, vol. 94, no. 1, pp. 20-28, January 2024. DOI: 10.1227/neu.0000000000002654.

[6] Ho, Johnson S., Poon, Cynthia, North, Richard, Grubb, William, Lempka, Scott, Bikson, Marom. "A Visual and Narrative Timeline Review of Spinal Cord Stimulation Technology and US Food and Drug Administration Milestones." *Neuromodulation: Technology at the Neural Interface*, vol. 27, no. 6, 2024, pp. 1020-1025. ISSN 1094-7159. DOI: https://doi.org/10.1016/j.neurom.2024.05.006. Available at: https://www.sciencedirect.com/science/article/pii/S1094715924001120.

[7] Khanna, Vinod Kumar. "Epidural Spinal Cord Stimulation." Implantable Medical Electronics, 2015, pp. 331–40, https://doi.org/10.1007/978-3-319-25448-7_17.

[8] A. Mailis-Gagnon, MD Furlan, AD Sandoval, and RS Taylor, "Spinal cord stimulation for chronic pain," *Cochrane Database of Systematic Reviews*, no. 3, 2004, John Wiley & Sons, Ltd. DOI: 10.1002/14651858.CD003783.pub2.

[9] Harkema, S., Gerasimenko, Y., Hodes, J., Burdick, J., Angeli, C., Chen, Y., Ferreira, C., Willhite, A., Rejc, E., Grossman, R.G., and Edgerton, V.R., "Effect of epidural stimulation of the lumbosacral spinal cord on voluntary movement, standing, and assisted stepping after motor complete paraplegia: a case study," *The Lancet*, vol. 377, no. 9781, pp. 1938-1947, Jun. 2011. DOI: 10.1016/S0140-6736(11)60547-3.

[10] Santana, M.B., Halje, P., Simplício, H., Richter, U., Freire, M.A.M., Petersson, P., Fuentes, R., and Nicolelis, M.A.L., "Spinal cord stimulation alleviates motor deficits in a primate model of Parkinson disease," *Neuron*, vol. 84, no. 4, pp. 716-722, Nov. 2014. DOI: 10.1016/j.neuron.2014.08.061.

[11] Illis, L.S., Sedgwick, E.M., and Tallis, R.C., "Spinal cord stimulation in multiple sclerosis: clinical results," *Journal of Neurology, Neurosurgery, and Psychiatry*, vol. 43, no. 1, pp. 1-14, Jan. 1980. DOI: 10.1136/jnnp.43.1.1.

[12] Danner, S.M., Hofstoetter, U.S., Freundl, B., Binder, H., Mayr, W., Rattay, F., and Minassian, K., "Human spinal locomotor control is based on flexibly organized burst generators," *Brain*, vol. 138, pt. 3, pp. 577-588, Mar. 2015. DOI: 10.1093/brain/awu372.

[13] Musienko, P., Heutschi, J., Friedli, L., van den Brand, R., and Courtine, G., "Multi-system neurorehabilitative strategies to restore motor functions following severe spinal cord injury," *Experimental Neurology*, vol. 235, no. 1, pp. 100-109, May 2012. DOI: 10.1016/j.expneurol.2011.08.025.

[14] R. B. North, J. P. Prager, "History of Spinal Cord Stimulation", Chapter 45 in Neuromodulation (Second Edition), Academic Press, pp. 587-596 2018. DOI: https://doi.org/10.1016/B978-0-12-805353-9.00045-0

[15] Clark S. Metzger, M. Blake Hammond, Stephen T. Pyles, Edward P. Washabaugh III, Romanth Waghmarae, Anthony P. Berg, James M. North, Yu Pei & Roshini Jain, "Pain relief outcomes using an SCS device capable of delivering combination therapy with advanced waveforms and field shapes"

[16] Adler, Alexandra R., et al. "Neuromodulation for Spine Pain Care." Spine Pain Care, edited by Jianren Mao, 2019, pp. 311–20, https://doi.org/10.1007/978-3-030-27447-4_24.