

Research of Spinal Cord Stimulation and its Applications

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Abstract. Spinal cord stimulation (SCS) is a neurostimulation technique that has emerged as a promising therapeutic option for the management of chronic pain and other neurological disorders. An SCS consists of a implantable pulse generator (IPG) connected to a lead with a cathode (negative electrode) and an anode (positive electrode). The cathode and anode create an electrical field within the biological tissue that can depolarize the target nerves. In order to achieve the best results, the stimulation parameters in spinal cord stimulation (SCS) are carefully adjusted. The standard variables used in SCS include frequency, pulse width, and amplitude. In traditional SCS therapies, the primary goal has been to alleviate pain by replacing it with a tingling or paresthesia sensation. This approach involves mapping the stimulation to the specific region of pain to effectively mask the sensation of discomfort. In recent years, there have been significant advancements in the field of stimulation frequencies, particularly in the use of high-frequency SCS (at 10,000 Hz) and burst SCS. High-frequency 10 SCS (HF10) is a groundbreaking advancement in the field of spinal cord stimulation (SCS) technologies. This innovative approach involves delivering a unique waveform at 10,000 Hz, which operates below the threshold for sensory perception, thereby providing effective pain relief without causing any paresthesia or abnormal sensations. Another exciting development is burst SCS, which involves delivering bursts of closely spaced electrical pulses instead of continuous stimulation.

Keywords: Spinal cord stimulation; burst SCS; HF-SCS.

1. Introduction

Spinal cord stimulation (SCS) is a neurostimulation technique that has emerged as a promising therapeutic option for the management of chronic pain and other neurological disorders. This non-pharmacological approach involves the implantation of a device that delivers electrical impulses to the spinal cord, modulating the transmission of pain signals and providing relief to patients. Over the years, SCS has evolved significantly, with technological advancements and a growing body of evidence supporting its efficacy.

Chronic pain is a complex and debilitating condition that affects millions of people worldwide. Conventional treatment options such as medication, physical therapy, and surgery may not always provide satisfactory relief or may be associated with significant side effects. In this context, SCS has emerged as a valuable alternative for patients who have failed conservative therapies or are not suitable candidates for invasive procedures. The fundamental principle underlying SCS is the modulation of pain signals by delivering electrical impulses to the spinal cord. The electrical stimulation interferes with the transmission of pain signals to the brain, effectively reducing the perception of pain. This is achieved by activating the large-diameter A β fibers that carry non-painful sensations, thereby closing the "gate" for the transmission of pain signals carried by smaller-diameter C fibers.

Technological advancements have played a crucial role in enhancing the safety and efficacy of SCS devices. Early SCS systems utilized simple, continuous stimulation patterns. However, modern devices incorporate more sophisticated features such as burst stimulation, high-frequency stimulation, and closed-loop systems. Burst stimulation delivers a series of closely spaced pulses, mimicking the natural firing pattern of sensory neurons. On the other hand, high-frequency stimulation delivers pulses at a frequency above 10,000 Hz, which has been shown to provide superior pain relief in certain

patient populations. Closed-loop systems utilize feedback mechanisms to adjust stimulation parameters based on the patient's physiological responses or pain levels, allowing for personalized therapy.

Clinical applications of SCS extend beyond chronic pain management. Research has demonstrated its efficacy in various conditions, including failed back surgery syndrome, complex regional pain syndrome, peripheral neuropathy, and ischemic pain. Moreover, SCS has shown promise in the treatment of movement disorders such as Parkinson's disease and dystonia, as well as psychiatric disorders like depression and obsessive-compulsive disorder. These emerging applications highlight the potential of SCS as a versatile therapeutic modality. This review aims to provide an overview of the current state of SCS, including its technical aspects, clinical applications.

2. Spinal cord stimulation

A spinal cord stimulator consists of an implanted IPG that is connected to a lead containing a negative electrode and a positive electrode. By creating an electrical field within the biological tissue, the cathode and anode can activate the target nerves. Empirical evidence obtained from laboratory experiments, along with observations made in clinical settings; undeniably demonstrate that applying SCS to different locations along the neuro-axis produces distinct effects on various target organs or anatomical regions [1]. This is illustrated in Fig. 1.

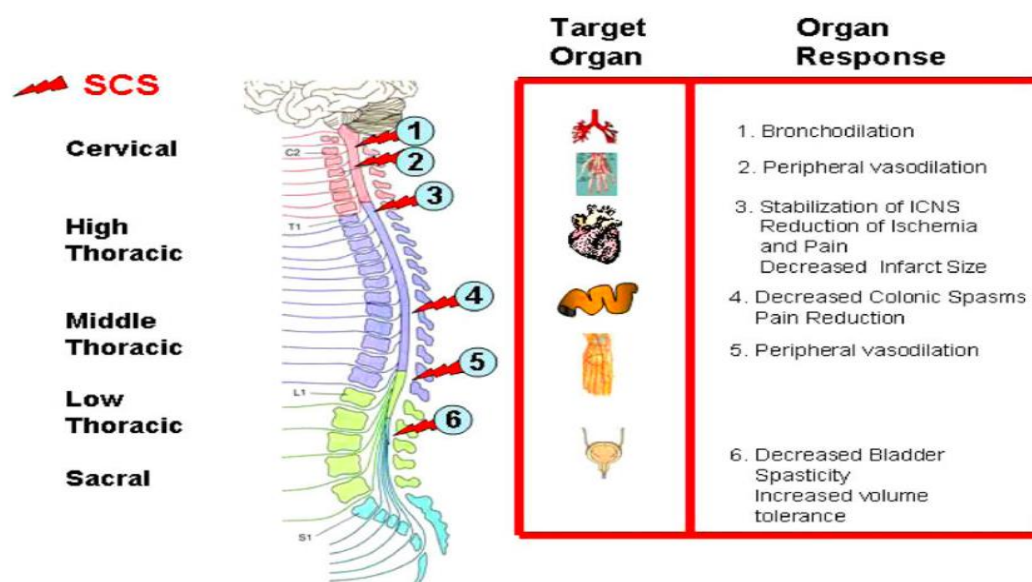


Fig. 1 The significance of accurately targeting the electrode site is highlighted by the diverse impacts observed on target organs and body regions as the stimulating SCS electrode is repositioned along the neuro-axis [1]

In order to achieve the best results, the stimulation parameters in spinal cord stimulation (SCS) are carefully adjusted. The standard variables used in SCS include frequency, pulse width, and amplitude. The pulse width refers to the duration of each electrical pulse delivered by the IPG, while frequency represents how often these pulses are delivered per second. Clinicians can modify the stimulation effect on targeted tissues or nerves by adjusting the pulse width. For example, a longer pulse width may provide more sustained activation of nerve fibers, whereas a shorter pulse width may result in more selective activation of specific nerve populations. Frequency plays a crucial role in determining the overall pattern and intensity of stimulation. Higher frequencies generally produce rapid and continuous firing of neurons, which is suitable for treating certain conditions like chronic pain. On the other hand, lower frequencies are typically used for deep brain stimulation or movement disorders where precise control over neural activity is required. It's worth noting that both constant current (CC) and constant voltage (CV) modes have their advantages depending on specific clinical needs. CC mode ensures that regardless of changes in tissue impedance or resistance during therapy sessions, a

consistent amount of current will be delivered to maintain therapeutic efficacy. In contrast, CV mode maintains a stable voltage output while allowing current variations based on impedance changes. The amplitude measurement unit also varies between these two modes: volts (V) for CC mode and milliamps (mA) for CV mode. This distinction reflects how different types of neurostimulation therapies require varying levels of electrical energy delivery to achieve optimal results. Dorsal roots are more likely to be activated with shorter pulse widths, which can target specific dermatomes. With an increase in pulse width, the medial DC fibers become preferentially recruited and a larger area of the DC is stimulated^{002E}

3. Sub-threshold Spinal Cord Stimulation

3.1. New Stimulation Mode

In traditional SCS treatments, the primary objective has been to alleviate pain by substituting it with a tingling or paresthesia sensation. This approach involves accurately targeting the stimulation to the specific area of pain in order to effectively mask any discomfort. The underlying assumption is that electrical currents can modify pain processing and provide relief by replacing it with a more tolerable sensation. Although many patients are able to adapt and manage well with paresthesia, a significant portion still find this feeling unpleasant, particularly when they change positions. These positional adjustments may result in variations in the intensity or distribution of paresthesia, causing some individuals discomfort or dissatisfaction with their treatment experience. It is important for healthcare professionals and researchers in this field to acknowledge these patient reports regarding the sensations associated with SCS therapy being unpleasant. By understanding these concerns, further progress can be made in developing techniques that effectively alleviate pain and enhance patient comfort during various activities and movements. Efforts should be focused on enhancing personalized programming options for SCS devices so that patients have greater autonomy over their therapy settings.

Additionally, exploring alternative methods such as closed-loop systems that dynamically adjust stimulation parameters based on real-time feedback could potentially address issues related to positional changes and improve overall satisfaction among those undergoing SCS treatments. Overall, while traditional SCS therapies have shown promise in managing chronic pain conditions through sensory substitution, it is crucial to continue refining these approaches based on patient experiences and preferences. By doing so, people can strive towards optimizing outcomes and ensuring better quality of life for individuals seeking relief from persistent pain. In recent years, there have been significant advancements in the field of stimulation frequencies, particularly in the use of high-frequency SCS (at 10,000 Hz) and burst SCS. As shown in Fig.2, they have different hypothetical mechanisms.

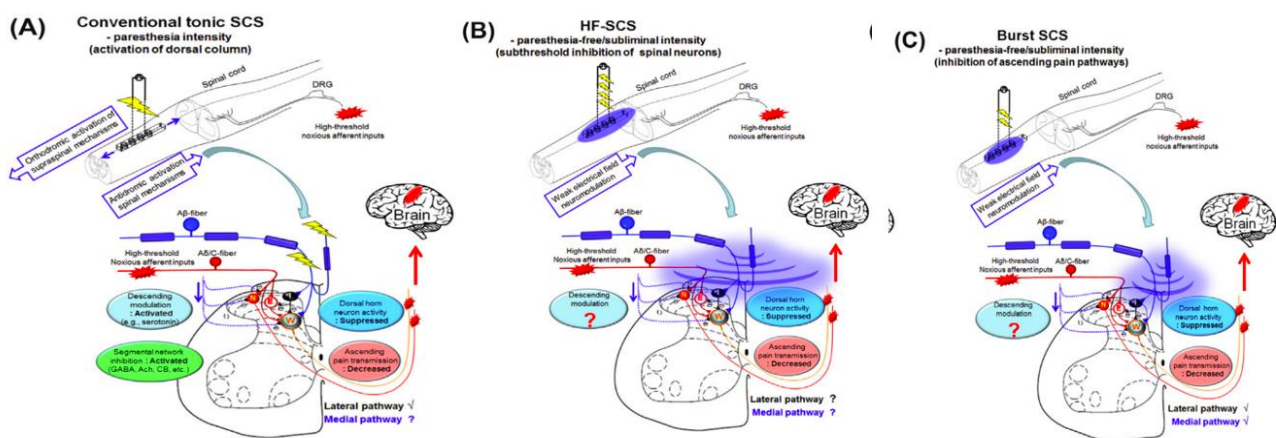


Fig. 2 Schematic diagram illustrating hypothetical mechanisms underlying pain inhibition by different paradigms of spinal cord stimulation (SCS).[2]

These novel approaches have revolutionized the efficacy and applicability of SCS, offering new possibilities for patients suffering from chronic pain.

3.2. Burst SCS

An exciting advancement is burst SCS, which involves the delivery of bursts of closely spaced electrical pulses rather than continuous stimulation. Burst SCS has shown superior results compared to traditional tonic stimulation methods by closely mimicking natural patterns of neuronal activity. This approach enhances pain relief and reduces energy consumption and battery usage in implanted devices. A 74-year-old individual was diagnosed with Parkinson's disease at the age of 71. The initial observed symptoms were an abnormal shuffling gait and a stooped posture. Initially, paresthesia in the specific pain region was confirmed through tonic stimulation, where the optimal pulse amplitude ranged from 2.5 to 2.8 mA. Subsequently, the stimulation mode was switched to Burst stimulation with an amplitude ranging from 0.6 to 0.8 mA. Burst stimulation consists of bursts occurring at a frequency of 40 Hz and containing five spikes at a rate of 500 Hz. With the implementation of burst stimulation, improvements were observed in postural stability and a decrease in Hoehn and Yahr scale score from 3 to 2. Also, Burst stimulation had effect on the “mental health score” as measured with the SF36, as shown in Fig.3.

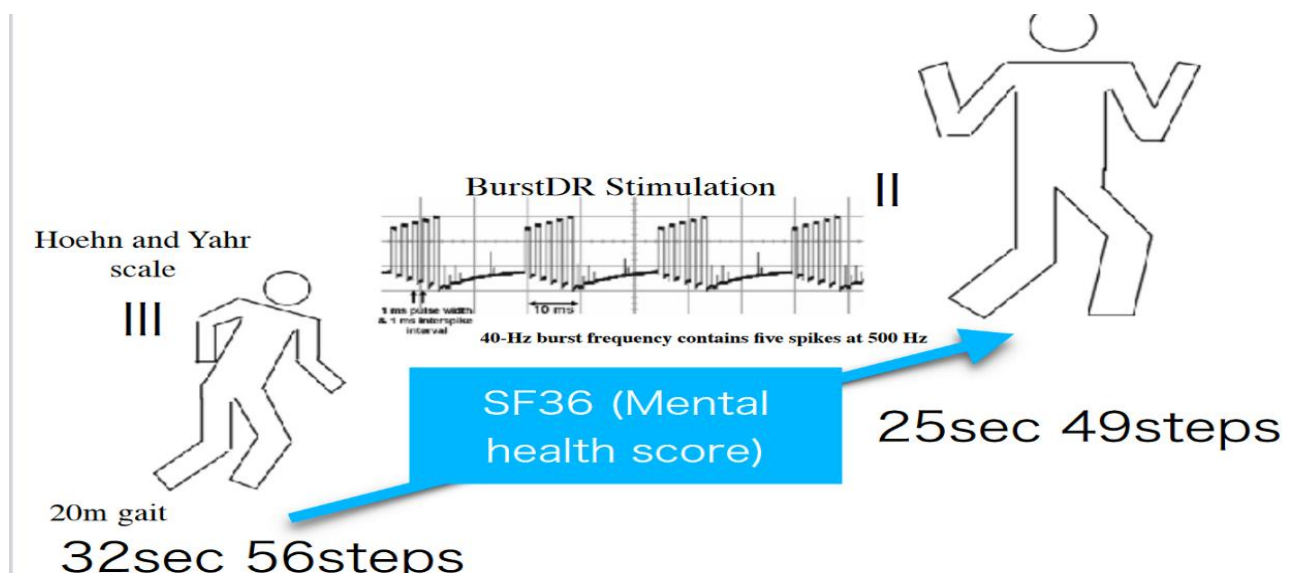


Fig. 3 burst SCS [3]

They discovered two notable clinical observations. Firstly, Burst stimulation exhibited improvements in low back pain (LBP), gait, and stooping posture when compared to tonic stimulation, while inducing a lower amplitude that did not lead to paresthesias. Additionally, postural stability was enhanced and the Hoehn and Yahr scale decreased from 3 to 2. Previous studies have indicated that SCS might suppress abnormal beta-frequency synchronous corticostriatal oscillations, thereby restoring neural activity in the primary cortex and dorsolateral striatum to a state observed prior to spontaneous locomotion onset. The required amplitude for Burst stimulation was significantly below the threshold for inducing paresthesia. This suggests that Burst stimulation delivered a considerably higher charge per second than tonic stimulation at equivalent amplitudes. Another plausible explanation is that burst activation necessitates less temporal integration in order to reach the neuron's threshold, potentially activating neurons unresponsive to tonic stimulation.

The second finding suggested that Burst stimulation had a notable positive effect on the evaluation of "emotional description" and "psychological well-being" using SF-MPQ-2 and SF36, respectively. It is hypothesized that Burst stimulation regulates the lateral pain discrimination system while also influencing the medial emotional/attentional pain system. De Ridder et al. observed a decrease in SF-MPQ scores related to the emotional aspect of pain perception following laminectomy. This

observation suggests that Burst stimulation holds promise for improving psychological welfare among individuals with PD.

3.3. High-frequency SCS

The introduction of High-frequency 10 SCS (HF10) has revolutionized the field of SCS technologies. This innovative technique offers a promising solution for individuals suffering from various conditions such as failed back surgery syndrome, complex regional pain syndrome, and neuropathic pain by delivering electrical pulses at a significantly higher frequency than traditional SCS methods. By specifically targeting nerve fibers responsible for transmitting pain signals, high-frequency SCS effectively disrupts these signals and provides relief from discomfort. The unique waveform employed in this approach operates below the sensory perception threshold at 10,000 Hz, ensuring effective pain relief without causing any abnormal sensations or paresthesia. Unlike tonic stimulation which utilizes frequencies between 40-100 Hz to describe the characteristics of energy application regardless of power source type (constant current or voltage), high-frequency stimulation surpasses 500 Hz in energy delivery.. Most of the studies demonstrating positive benefit were 10,000 Hz, as shown in Fig.4.

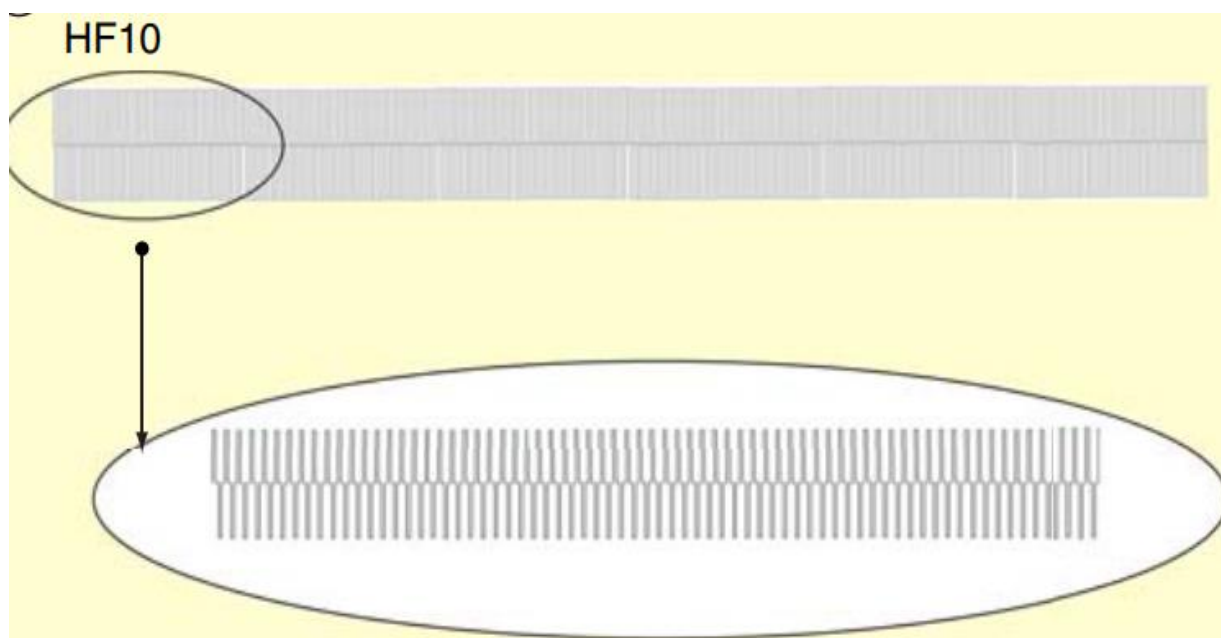


Fig. 4 High frequency at 10,000 Hz [4]

It has been observed that a majority of patients who undergo SCS treatment express a preference for stimulation without experiencing paresthesia. HF-SCS, which encompasses frequencies of both 1kHz and 10kHz, has demonstrated promising outcomes in inhibiting mechanical hypersensitivity associated with neuropathic pain in animal models. Interestingly, specific types of HF-SCS may exhibit an even more pronounced impact or necessitate lower intensity levels compared to conventional SCS techniques when it comes to effectively alleviating pain.

Moreover, a clinical trial that was both randomized and controlled has presented evidence indicating that HF-SCS without subliminal or paresthesia sensations may yield more favorable long-term treatment outcomes for individuals experiencing back and leg pain in comparison to conventional SCS methods. This discovery emphasizes the potential advantages of employing HF10 technology as an alternative approach for managing chronic pain conditions. The advancement and implementation of HF-SCS signify significant progress in enhancing patient experiences during spinal cord stimulation therapy. By providing effective relief from pain without causing undesired sensations such as paresthesia, this advanced technique addresses one of the primary concerns associated with traditional SCS approaches. The positive findings observed in preclinical investigations and clinical trials further validate its potential as a valuable tool for managing chronic pain.

A senior gentleman, 85 years old, with a medical background of hypertension, prediabetes, and a previous cerebrovascular accident approached our clinic seeking further medical attention for pain in his lower right limb (LRL). Roughly one year ago, the patient sought care at another emergency department due to sudden left-sided weakness. At that time, an MRI scan revealed recent occlusion of blood supply in the lateral medulla on the left side and minor tissue damage in both basal ganglia regions as well as the right cerebellum. Following an intensive rehabilitation program post-stroke, the patient achieved near-complete recovery from left-sided weakness. However, approximately six months ago he began experiencing novel abnormal sensations and intense discomfort in his LRL. A comprehensive examination conducted at that time did not yield any positive results in the search for another stroke. The pain persisted and was described as sharp, accompanied by a burning sensation. On average, its intensity was rated at 8 out of 10 on a numerical rating scale (NRS). Furthermore, it was accompanied by abnormalities in the perception of somatosensory stimuli such as sensitivity to non-painful stimuli (allodynia), heightened sensitivity to painful stimuli (hyperalgesia), and reduced ability to perceive pinprick or touch sensations.[4] Due to the persistent nature of these symptoms, it was recommended that the patient undergo a trial of HF-SCS at a frequency of 10 kHz. Following a successful percutaneous trial lasting seven days, permanent implantation took place under local anesthesia and fluoroscopic guidance. Two electrode leads with eight contacts each were implanted in the epidural space between T8 and T11 vertebral bodies(Fig. 5a,b). At the six-month follow-up assessment, he experienced sustained relief exceeding 80% in symptoms related to his right lower extremity (RLE), with an average Numeric Rating Scale (NRS) score of 2/10. Additionally, significant progress was observed in his level of physical activity participation and ability to walk without relying on his cane. Moreover, notable improvements were noted in sleep quality, reduction of abnormal sensations, and overall life satisfaction.

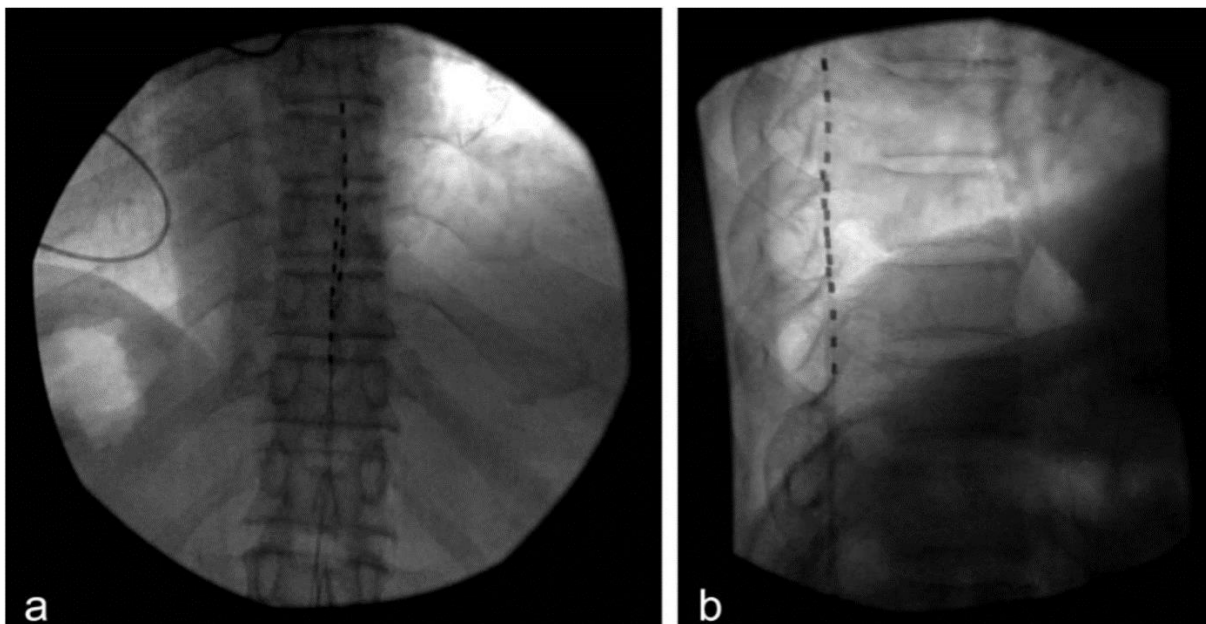


Fig. 5 (a) AP view of eight-contact SCS leads with distal tips at superior edges of T8 and T9 vertebral bodies. (b) Lateral view of SCS leads in the dorsal epidural space.[5]

4. Conclusion

SCS has emerged as a valuable therapeutic option for the management of chronic pain and other neurological disorders. The advancements in technology and the growing body of evidence supporting its efficacy have significantly improved the outcomes for patients.

One of the recent developments in SCS is burst stimulation, which delivers a series of closely spaced electrical pulses to the spinal cord. Burst stimulation has shown promising results in providing superior pain relief compared to traditional tonic stimulation. It mimics the natural firing pattern of

sensory neurons, potentially leading to better pain modulation and improved patient satisfaction. Further research is needed to elucidate the mechanisms underlying burst stimulation and optimize its parameters for different patient populations.

Another significant advancement in SCS is HFS, which delivers electrical pulses at frequencies above 10,000 Hz. HFS has been found to provide effective pain relief with reduced paresthesia compared to conventional SCS. It modulates neural activity in a manner that inhibits pain transmission while minimizing unwanted sensory side effects. The use of HFS has expanded the indications for SCS, including painful diabetic neuropathy and peripheral vascular disease. Ongoing studies are exploring the long-term efficacy and safety of HFS and its potential applications in other neurological disorders.

Despite these advancements, there are still challenges and areas for further improvement in SCS. Patient selection criteria, optimization of stimulation parameters, and understanding the mechanisms of action remain areas of active research. The integration of SCS with other neurostimulation techniques, such as dorsal root ganglion stimulation and motor cortex stimulation, may provide additional therapeutic options for patients.

In conclusion, SCS has revolutionized the field of chronic pain management and holds promise for the treatment of various neurological disorders. The continued advancements in technology and our understanding of neural mechanisms will further enhance the efficacy and customization of SCS therapy, improving the quality of life for patients suffering from chronic pain.

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