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Narrative Review

Selecting Neuromodulation Devices For Chronic Pain Conditions: A Narrative Review

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Background: Neuromodulation is a rapidly advancing field in pain medicine, providing targeted, reversible interventions for patients with chronic pain unresponsive to conventional therapies. Advances in waveform technology, device design, and stimulation strategies have shifted neuromodulation from a last-resort approach to a core element of multidisciplinary pain management. Despite its growing adoption, variability in training, terminology, and clinical implementation underscores the need for consensus-driven frameworks to ensure safety, efficacy, and uniformity across practice settings.

Objectives: This review aims to define current and emerging concepts in neuromodulation, summarize the supporting evidence, and offer clinicians an evidence-informed framework for individualized application in chronic pain management.

Study Design: Narrative review.

Methods: We conducted a comprehensive synthesis of neuromodulation strategies spanning spinal cord stimulation (SCS), dorsal root ganglion stimulation (DRGS), peripheral nerve stimulation (PNS), motor cortex stimulation (MCS), deep brain stimulation (DBS), and targeted drug delivery (TDD). The review integrates data from published studies and reviews to cover emerging concepts, classifications, indications, technological advancements, device features, clinical applications, and practical guidance for patient-specific decision-making.

Results: Over the past decade, neuromodulation use has expanded significantly, driven by technological and mechanistic innovations. Peripheral nerve stimulation (PNS) has become increasingly precise for focal neuropathic pain, demonstrating efficacy in migraine, hemiplegic shoulder pain, persistent spinal pain syndrome, post-amputation neuropathic pain, trigeminal neuralgia, plexus injuries, and multifidus dysfunction. SCS remains a mainstay for widespread neuropathic pain, including CRPS, painful diabetic neuropathy, and post-surgical syndromes, with innovations such as 10-kHz high-frequency and burst stimulation offering paresthesia-free analgesia and improved patient satisfaction. DRGS provides targeted relief for localized neuropathic pain, including post-herniorrhaphy and post-thoracotomy syndromes, with more predictable outcomes. Neurophysiological refinements, including differential target multiplexed (DTM) stimulation and closed-loop systems with evoked compound action potential (ECAP) feedback, enable real-time spinal control and consistent analgesia. Multiphase and surround-inhibition paradigms further enhance segmental coverage, energy efficiency, and rapid analgesic onset. TDD has evolved into a precise adjunctive therapy, with programmable pumps delivering morphine, baclofen, and ziconotide safely, minimizing systemic exposure while allowing individualized dosing. Collectively, these innovations support precision-guided, personalized neuromodulation with durable efficacy and improved patient-centered outcomes across diverse chronic pain conditions.

Limitations: Heterogeneity in published evidence and the lack of large-scale, head-to-head randomized trials for certain waveforms and technologies limit the conclusions of this review.

Conclusions: Neuromodulation continues to advance at the intersection of neuroscience, bioengineering, and clinical practice. Harmonizing definitions, classifications, and education will guide future innovation and help ensure that neuromodulation fulfills its promise of safe, effective, and equitable patient care.

Key words: Neuromodulation, neurostimulation, closed-loop stimulation, tonic stimulation, intrathecal drug delivery, lumbar radiculopathy, multiphase stimulation, pain, motor cortex stimulation

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Pain is a complex physiological and neurological phenomenon that arises from intricate interactions between the peripheral nervous system and the central nervous system. Although acute pain serves an essential protective function, chronic pain—particularly in refractory cases—remains a major clinical challenge. The economic and societal burden of chronic pain is considerable, with healthcare costs in the United States alone estimated at $560–$635 billion in 2010 (1-3). These figures highlight the urgent need for effective and sustainable therapeutic alternatives.

Approximately 34,000 patients currently undergo spinal cord stimulation (SCS) implantation each year, reflecting the growing acceptance of neuromodulation techniques in the management of chronic pain (4). In parallel, the market for SCS devices has expanded substantially, with expenditures projected to increase from $3.14 billion in 2024 to $3.42 billion in 2025, representing a compound annual growth rate (CAGR) of 8.8% (5). By 2029, the market is expected to reach $4.78 billion, driven by increasing demand for innovative pain management solutions (5). Together, these trends emphasize the expanding role of SCS and other neuromodulation therapies in addressing chronic pain conditions.

The overarching goal of neuromodulation therapies for chronic pain that is unresponsive to conservative measures or surgical interventions is to improve function and enhance quality of life while simultaneously reducing the broader societal healthcare burden. Through electrical stimulation of the central or peripheral nervous system, neuromodulation provides targeted pain relief with minimal systemic side effects. For select conditions, it may represent one of the most effective long-term strategies for achieving meaningful and sustained pain control (6).

Despite its benefits, the success of neuromodulation is highly dependent on appropriate training and clinical experience. Careful selection of the optimal neuromodulation approach is critical not only for maximizing therapeutic outcomes but also for ensuring patient safety and minimizing complications, including device revisions or explantation. Although the use of neuromodulation continues to expand, consensus regarding standardized training pathways remains limited. This lack of unified guidance presents a particular challenge for early-career pain physicians navigating a rapidly evolving field. The development of structured educational resources and consensus-based training materials is therefore essential. Standardizing both technical skills and decision-making frameworks for therapy selection can enhance treatment efficacy and support the education of future pain specialists. By prioritizing comprehensive and consistent training, the field can progress toward safer, more effective, and more accessible chronic pain management.

Neurostimulation Classification

According to the International Neuromodulation Society, neuromodulation is defined as the alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents, to specific neurological sites within the body. In the context of pain management, neuromodulation is broadly divided into two categories: Neurostimulation and targeted drug delivery (TDD). Neurostimulation is employed across multiple medical specialties, encompasses a wide range of conditions, and can be applied to various anatomical regions. It may be invasive or non-invasive and can be further classified based on the anatomical site of application (Tables 1 and 2) (Fig. 1) (7-9). From a pain medicine perspective, SCS, peripheral nerve stimulation (PNS), and dorsal root ganglion stimulation (DRGS) have emerged as the most commonly utilized modalities. Their increasing use further underscores the importance of standardized training and evidence-based guidelines to optimize clinical outcomes and broaden access to these advanced therapies (9).

Neurostimulation Mechanism of Action

Neurostimulation delivers electrical impulses to the nervous system to produce therapeutic effects across a range of conditions, including chronic pain. The processes underlying pain perception and modulation have been studied extensively, and multiple theories have been proposed to explain these mechanisms. Among these, the Gate Control Theory remains the most influential model for understanding stimulation-based pain modulation, as it describes how activation

of inhibitory interneurons within the dorsal horn can suppress ascending nociceptive signals (10).

In 1965, Ronald Melzack and Patrick Wall introduced the Gate Control Theory of Pain, a landmark concept that integrated elements of the Specificity and Pattern Theories while addressing their limitations (11). By synthesizing experimental evidence, they proposed a unified framework that reconciled previously conflicting observations. According to this model, nociceptive and non-nociceptive afferent fibers synapse in distinct yet functionally interconnected regions of the dorsal horn, particularly within the substantia gelatinosa (Rexed lamina II) and the transmission cells. Sensory input from primary afferent neurons activated at the skin level is conveyed to three principal spinal cord regions: the substantia gelatinosa, the dorsal column, and the transmission cells.

Within this framework, the "gate" is located in the dorsal horn at the level of the substantia gelatinosa and regulates the flow of sensory information from primary afferent fibers to spinal cord transmission cells. This gating process is determined by the relative activity of large-diameter Aβ fibers and small-diameter C fibers, which exert opposing influences. Aβ fibers, which transmit non-nociceptive stimuli such as touch, inhibit transmission cells and effectively close the gate, thereby reducing the propagation of pain signals. In contrast, C fibers convey nociceptive input and facilitate transmission cell activity, opening the gate and allowing pain signals to ascend to higher centers (7,12).

SCS may also influence inhibitory descending pain pathways. These pathways originate primarily in the brainstem and medulla and project downward to the dorsal columns, where they suppress activity in both Aβ and C fibers. Electrical stimulation of the lateral horns is thought to attenuate pain perception by enhancing the activity of these descending inhibitory tracts (13,14). The balance between excitatory and inhibitory inputs ultimately determines whether the gate remains open or closed, thereby modulating the neuronal signals that reach the brain. For instance, concurrent activation of Aβ and C fibers within the same region may result in gate closure and effective suppression of nociceptive transmission. In addition, descending supraspinal influences can further regulate gate activity, either amplifying or dampening pain signal transmission. When nociceptive input overwhelms inhibitory control, the gate opens, activating neural pathways that culminate in the conscious perception of pain and its associated behavioral responses (15).

Table 1. *Neurostimulation categories*.

Neurostimulation Categories
1. Invasive Neuromodulation Techniques
A. Invasive Brain Stimulators
I. Deep Brain Stimulation (DBS)
II. Motor Cortex Stimulation (MCS)
B. Invasive Spine Stimulators
I. Spinal Cord Stimulation (SCS)
II. Dorsal Root Ganglion Stimulation (DRGS)
C. Invasive Peripheral Stimulators
I. Peripheral nerve stimulation (PNS)
II. Peripheral Nerve Field Stimulation (PNFS)
III. Sphenopalatine Ganglion Stimulation (SPGS)
IV. Pulsed Radiofrequency (PRF)
2. Non-Invasive Neuromodulation Techniques
A. Non-Invasive Brain Stimulators
I. Transcranial Magnetic Stimulation (TMS)
a) Repetitive Transcranial Magnetic Stimulation (rTMS)
II. Transcranial Current Stimulation (TCS)
a) Transcranial Direct Current Stimulation (tDCS)
b) Transcranial Alternating Current Stimulation (tACS)
III. Transcranial Ultrasound Stimulation (TUS)
IV. Transcranial Random Noise Stimulation (tRNS)
V. Temporal interference (TI)
B. Non-Invasive Peripheral Stimulations
I. Transcutaneous electrical nerve stimulation (TENS)

Recent advancements in SCS technology have introduced new paradigms, including closed-loop SCS systems. These systems employ evoked compound action potentials (ECAPs) as a real-time feedback mechanism to optimize stimulation delivery by continuously monitoring neural activation. In this approach, inactive electrodes within the implanted SCS array record ECAPs generated when dorsal column nerve fibers respond to electrical stimulation (16-18). ECAPs represent the synchronized firing of populations of Aβ fibers and provide an objective, quantitative measure of neural recruitment. By continuously assessing ECAP amplitude, closed-loop systems automatically adjust stimulation intensity to maintain consistent neural engagement, thereby promoting stable pain relief while minimizing variability and unwanted sensations.

Indications For Use

Neuromodulation provides a versatile approach to the management of chronic pain by employing techniques that can be tailored to specific pain syndromes. PNS delivers low-energy electrical currents to peripheral nerve fibers, thereby disrupting the transmission of nociceptive signals. In general, PNS is particularly well suited for severe, intractable chronic pain of peripheral nerve origin. Comprehensive evidence-based guidelines for implantable PNS in the management

Table 2. *Overview of spinal cord stimulators with comparison of various waveform modalities, highlighting their features, mechanisms of action, and clinical considerations.*

Stimulation Modalities/ Waveforms	MoA/Systems	Efficacy (Indications)	Pulse Width (\ u00b5s)	Amplitude (mA or V)	Battery Consumption	Advantages	Limitations	Clinical Studies/ Key References
Tonic (LF)	Low-frequency (40–100 Hz) stimulation waveforms	PSPS Type II, CRPS, Painful Diabetic Neuropathy, ischemic limb pain, refractory angina, Peripheral neuropathies	200–450	1–10 mA	Moderate	Well-established, widely used	May cause paresthesia	Melzack and Wall, 1965 Kumar et al., 1998
10 kHz (HF)	High-frequency stimulation (200 Hz – 10 kHz)	CRPS, PSPS Type II, Pelvic pain, Abdominal pain	30	0.5–5 mA	High	Paresthesia-free	High battery usage	Kapural et al., 2015 Russo et al. 2015
Burst Stimulation	Five 1-ms spikes mimicking natural neuronal firing	PSPS Type II, CRPS, Axial back pain, Peripheral neuropathies, Facial pain.	1000	0.3–1.0 mA	High	More physiological, less habituation	Complex programming	De Ridder et al., 2010
DRGS	Stimulation of dorsal root ganglion sensory afferents	CRPS, PSPS, Post-amputation pain, Diabetic neuropathy	50–1000	0.3–1.2 V	Moderate	Targeted pain relief	Requires precise lead placement and multilevel implantation for widespread pain	Liem et al., 2015
DTM-SCS	Low- and high-frequency pulses targeting neural and glial cells rate signals	PSPS Type II	100–1000	1–5 mA	High	Targets glial and neuronal interaction		Vallejo et al.2020, Cedeno et al.2020, Deer et al., 2021
Multifidus Stimulation	Restores muscle control	Nonoperative CLBP	100–500	1–10 mA	High	Restores muscle function	Limited to CLBP	Gilligan et al., 2021, Schwab et al. 2025
Closed-loop Stimulation	Aβ-fiber guided dorsal column modulation	PSPS Type II, select cases of Pelvic pain	50–1000	0.5–4 mA	Moderate	Real-time feedback for stimulation	More complex system	Mekhail et al., 2020-24, Dietz et al, 2022
Multiphase Stimulation	Provides HF energy dispersion	PSPS Type II	100–1000	0.5–4 mA	Moderate	Improves coverage	Not widely adopted	Thomson et al., 2018 Kapural et al, 2023
Surround Inhibition	Targets afferents innervating the surround regions	PSPS Type II	50–1000	0.5–4 mA	Moderate	Fast paresthesia-free pain relief		Smith et al., 2019 Metzger et al, 2021, Gilbert et al. 2022

Abbreviations: HF, high frequency; LF, low frequency.

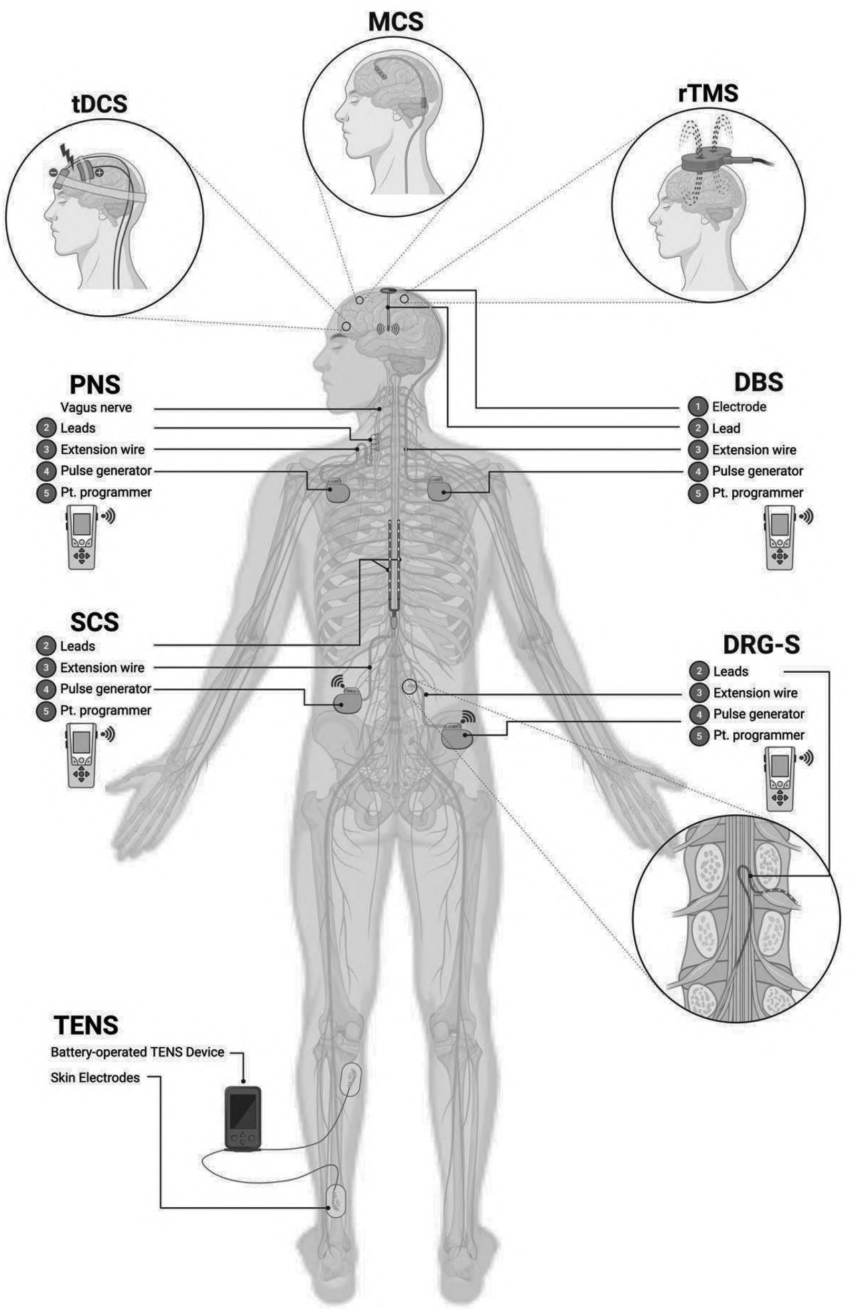

Fig. 1. *Human body map of neurostimulation techniques. A schematic illustration depicting various forms of neuromodulation and the conditions most responsive to treatment, highlighting how similar mechanisms are applied across different areas of the body. The numbered components correspond to key elements of neuromodulation systems depicted in the illustration:*
1. Electrode: Intracranial electrodes implanted in specific brain regions (e.g., subthalamic nucleus)
2. Leads: Insulated wires placed near neural structures such as the spinal cord, dorsal root ganglia, or peripheral nerves to deliver electrical stimulation.
** DBS: Lead placement requires stereotactic neurosurgical techniques for accurate brain targeting.*
3. Extension Wire: Connects the implanted pulse generator to the stimulation leads or electrodes.
**PNS: Lead wires attached to the stimulator are wrapped around the right vagus nerve*
4. Pulse Generator: A device implanted beneath the skin that produces electrical pulses for neuromodulation.
5. Patient Programmer: An external remote used by the patient to control or adjust the implanted pulse generator.
Abbreviations: SCS: Spinal Cord Stimulation, PNS: Peripheric Nerve Stimulation, DRG-S: Dorsal Root Ganglion Stimulation MCS: Motor Cortex Stimulation DBS: Deep brain stimulation TENS: Transcutaneous Electrical Nerve Stimulation, tDCS: Transcranial direct current stimulation, rTMS: Rhythmic transcranial magnetic stimulation, Pt. Programmer: Patient programmer. Created in BioRender. Yener, U. 2026, https://doi.org/10.5281/zenodo.18089918

of chronic pain from the American Society of Interventional Pain Physicians (ASIPP) provided evidence-based recommendations for the utilization of PNS. In preparation of these guidelines, evidence synthesis included 7 systematic reviews, 8 RCTs, and 9 observational studies covering all PNS treatments. The evidence was developed using GRADE criteria or certainty of evidence, and qualitative synthesis based on the best available evidence. The evidence level and recommendations are as follows:

- For implantable PNS systems following a trial or selective lumbar medial branch stimulation without a trial, the evidence is Level III or fair with moderate certainty.

Evidence Level: Fair; Strength of Recommendation: Moderate

- For temporary PNS for 60 days, the evidence is Level III or fair, with moderate certainty.
  Evidence Level: Fair; Strength of Recommendation: Moderate

Based on the available evidence, they recommended to expand the existing PNS related local coverage determination (LCD) to include craniofacial pain, phantom limb pain, and nociceptive pain in the lower back as present evidence shows Level III or IV with moderate certainty. Finally, they concluded that the evidence-based guidelines support the use of implantable PNS leads and neurostimulators in patients with moderate to severe chronic pain refractory to two or more conservative treatments. These guidelines aim to optimize patient outcomes and promote health equity through the integration of PNS technology in clinical practice.

SCS is one of the most widely utilized neuromodulation modalities and functions by targeting the dorsal columns to modulate the transmission of pain signals. SCS is effective for treating pain that involves broader anatomical regions and is Food and Drug Administration (FDA) approved for the management of complex regional pain syndrome (CRPS), Persistent Spinal Pain Syndrome (PSPS) Type 2, and painful diabetic neuropathy (19,20). It is also commonly used in the treatment of post-herniorrhaphy pain as well as pelvic and abdominal pain. Although SCS has demonstrated established efficacy across numerous chronic pain conditions, some patients may experience limited benefit, with inadequate initial response or loss of sustained pain relief over time (21).

DRGS offers a more focal approach by directly modulating sensory input at the level of the dorsal root ganglia. This technique has shown particular effectiveness in the treatment of CRPS, isolated peripheral nerve pain, post-herniorrhaphy neuralgia, post-amputation and phantom limb pain, post-surgical chest wall pain including post-mastectomy and post-thoracotomy pain, chronic pelvic pain, knee pain following total joint arthroplasty, post-herpetic neuralgia, and diabetic peripheral neuropathy (22).

Motor cortex stimulation (MCS) involves the application of electrical stimulation to the motor cortex and is primarily used for neuropathic and central pain conditions. Deep brain stimulation (DBS) targets specific brain regions involved in pain perception and processing and is generally reserved for highly refractory pain states. DBS is used off label for recalcitrant chronic pain due to poor outcomes reported in most clinical trials; however, modest improvement has been observed in select cases of atypical facial pain (23-25).

Taken together, the distinct mechanisms of action and clinical indications associated with each neuromodulation modality support the development of personalized treatment strategies that align with the patient's specific pain condition and therapeutic needs.

Timeline Of Neuromodulation

Advancements in Targeted Drug Delivery

Targeted Drug Delivery (TDD) has evolved substantially over time, providing increasingly precise and localized therapeutic options for the management of chronic pain and other medical conditions. A major milestone was achieved in 1981 with the implantation of the first implantable drug delivery device, which enabled direct administration of medications to the spinal cord or other targeted anatomical sites rather than relying on systemic delivery. This innovation marked the beginning of a new era in localized pain management strategies (26-28).

In 1982, the first implantable intrathecal drug delivery system (IDDS) received FDA approval. Although initially designed for the administration of chemotherapeutic agents, the technology was rapidly adapted for cancer-related pain management through intrathecal morphine, which itself gained FDA approval for this route of administration in 1984 (29).

The approval of second-generation IDDS in 1991 represented a significant advancement, introducing programmable delivery systems that improved safety, flexibility, and dosing precision. Shortly thereafter, the FDA approval of intrathecal baclofen in 1992 for the treatment of severe spasticity expanded the clinical utility of these systems beyond pain management, further establishing the role of implantable TDD platforms in neurological care (30,31).

In 2012, an additional delivery system with enhanced mechanical precision and improved flow control received FDA approval. This system enabled more accurate and reliable intrathecal administration of approved agents, including morphine and baclofen, particularly benefiting patients requiring consistent and stable long-term therapy (32).

Another pivotal development occurred in 2004 with the FDA approval of ziconotide, a synthetic peptide derived from cone snail venom. As a non-opioid

does not mandate trialing due to limited evidence of definitive benefit. Trialing is optional and should be determined jointly by the treating physician and patient (76).
2. Trialing may be performed using single or intermittent boluses or continuous infusion via epidural or intrathecal routes, with no method clearly superior.
3. Morphine and ziconotide are the only FDA-approved agents for intrathecal analgesia. PACC recommends morphine, hydromorphone, or fentanyl, with or without bupivacaine, as first-line therapy for patients with limited life expectancy. For patients with a favorable prognosis (six months to years), morphine, hydromorphone, fentanyl, or ziconotide alone, or bupivacaine combined with morphine, hydromorphone, or fentanyl, is recommended. This recommendation accounts for the slow titration required for ziconotide, which may delay achieving adequate analgesia in patients with short life expectancy (35).
4. Patients experiencing a pain reduction greater than 50% during the IDD trial are considered responders, indicating a high likelihood of benefit from permanent implantation (76).

Intrathecal Drug Delivery Implantation

1. Preoperative spine imaging, including lumbar and/or thoracic levels, should be reviewed to identify an appropriate and safe pump placement site.
2. Catheter placement should consider the patient's pain distribution, tumor location or progression, and spinal anatomy.
3. Postoperative monitoring is critical. The recommended starting daily intrathecal dose is less than 50% of the trial dose if a trial was performed, with demand doses ranging from 5% to 20% of the total daily dose. More aggressive titration may be necessary in cases of rapidly progressive disease (76).

In summary, IDD is a powerful modality for managing cancer-mediated pain. Clinical success depends on appropriate patient selection and education, accurate device implantation, and careful postoperative monitoring and titration to achieve effective analgesia tailored to each patient.

Approach to Abdominal Pain

Chronic abdominal pain encompasses a spectrum of debilitating conditions that affect many patients, often resulting in limited relief from conventional medical, pharmacologic, and interventional treatments. Causes include structural abnormalities, functional gastrointestinal disorders, and inflammatory processes.

SCS is currently considered an off-label treatment for select types of chronic abdominal pain. Conventional SCS has been investigated in literature; however, the abdominal paresthesias it produces are often uncomfortable or intolerable for patients. The paresthesia-free nature of 10 kHz SCS makes it particularly suitable for managing many forms of abdominal pain. This modality is believed to reduce pain signals by activating inhibitory interneurons to suppress superficial dorsal horn circuits while modulating WDR neurons (78). Because chronic abdominal pain frequently involves central sensitization, emerging evidence suggests that 10 kHz SCS may provide meaningful therapeutic benefits.

Patients have reported not only improvements in pain scores but also reduced opioid use, enhanced sleep quality, and decreases in associated symptoms such as nausea and vomiting (79,80). Additionally, 10 kHz therapy minimizes challenges commonly associated with paresthesia-based SCS, such as variability with postural changes and the need for paresthesia mapping during lead placement.

Ideal candidates for 10 kHz SCS include patients with abdominal pain of visceral origin, post-surgical pain, or functional gastrointestinal disorders such as dysmotility who have failed conventional medical therapies and are not candidates for definitive surgical treatment. Epidural lead placement for 10 kHz therapy should span T4–T8 vertebral levels. A thoracic spine MRI is essential prior to lead placement to exclude significant space-occupying lesions that could compromise procedural safety. Trial and implantation procedures should follow the protocols outlined previously.

Following implantation, multidisciplinary care is critical. This includes routine follow-ups to monitor progress, programming adjustments, behavioral health support, physical rehabilitation, and medication management. Durable success depends on both pain relief and improvement in patient function.

Approach to Multifidus Dysfunction

Diagnosing and managing multifidus dysfunction in patients with axial low back pain requires a structured approach. MRI remains the gold standard for assessing multifidus atrophy and fatty infiltration, with grading systems classifying atrophy from mild to severe.

analgesic that selectively blocks N-type calcium channels, ziconotide provided a powerful alternative for patients with severe chronic pain, especially those for whom opioid-related adverse effects or limitations were a concern (33).

The most recent advancement in intrathecal therapy occurred in 2023 with the FDA approval of a third-generation programmable delivery system. This platform incorporates enhanced safety features, expanded drug compatibility, improved battery longevity, and refined programmability, including updated firmware and cybersecurity enhancements. By supporting all three FDA-approved intrathecal agents—morphine, baclofen, and ziconotide—these systems reflect a continued shift toward more personalized, durable, and effective approaches to chronic pain and spasticity management (34). Collectively, the evolution of TDD has had a substantial impact on patient care by enabling medication delivery directly at the site of action, reducing systemic exposure, and optimizing therapeutic efficacy.

Advancements in Waveforms & Stimulation Modalities

Paresthesia-Based Tonic, Low-Frequency Stimulation

SCS therapy was first clinically applied in the 1960s by Norman Shealy and was developed based on the "Gate Control Theory of Pain" proposed by Melzack and Wall in 1965. The traditional paresthesia-based Tonic Waveform (low-frequency) used in SCS delivers stimulation at low frequencies (40–100 Hz) with high amplitudes (3.6–8.5 mA) and pulse widths ranging from 300 to 600 μs. This combination results in a high charge per pulse that produces paresthesia and modulates neuronal activity to mask pain perception (35). SCS therapy has demonstrated particular efficacy in conditions such as PSPS type II, CRPS, painful diabetic neuropathy, and neuropathic limb pain (Table 2) (21).

10-kHz High-Frequency

The introduction of 10-kHz SCS in 2015 represented a major advancement in SCS technology (36). This modality delivers stimulation at frequencies up to 10 kHz, with a pulse width of 30 μs and amplitudes ranging from 1 to 5 mA. In contrast to traditional systems that operate at approximately 50 Hz, 10-kHz SCS does not require or generate paresthesia to achieve clinical benefit (37). The SENZA randomized controlled trial demonstrated that 10-kHz stimulation provided superior relief of both low back and leg pain compared with paresthesia-based tonic stimulation, establishing its enhanced efficacy for chronic pain management (36).

Burst Waveform

Burst SCS, introduced in 2016 and pioneered by Dr. Dirk De Ridder, was designed to replicate natural neuronal firing patterns (38). This approach consists of a sequence of five 1000 μs pulses delivered at 500 Hz, with each burst repeated at 40 Hz. By closely approximating endogenous neuronal firing, burst stimulation aims to improve analgesia while reducing or eliminating paresthesia. The SUNBURST study demonstrated that burst stimulation provided greater pain relief than paresthesia-based stimulation, thereby expanding the therapeutic options available for SCS (38,39).

Dorsal Root Ganglion Stimulation

In 2016, DRGS emerged as a promising alternative to address several limitations associated with traditional SCS. Although traditional SCS is well established in the literature, it is associated with drawbacks such as unwanted paresthesia, waning efficacy over time, position-dependent variability in stimulation intensity, and limited ability to target focal regions including the foot or pelvic area (40-42). A major challenge of traditional SCS is its limited effectiveness in providing sustained relief for chronic, focal neuropathic pain. The DRG was historically viewed as a passive relay structure between the peripheral and central nervous systems; however, contemporary research has demonstrated its active role in the development and maintenance of chronic neuropathic pain through mechanisms such as neuronal hyperexcitability and spontaneous ectopic firing (43-45). Its involvement in sensory processing and nociceptive modulation, along with its consistent anatomical location and minimal cerebrospinal fluid interference, makes the DRG an optimal target for neurostimulation (46).

Differential Target Multiplex (DTM) SCS

Differential target multiplexed (DTM) SCS was introduced in 2020 as a notable innovation in neuromodulation for pain management. This modality is distinguished by its dual targeting of neurons and glial cells, which outnumber neurons in the spinal cord by approximately 12:1. Given the critical role of glial cells in chronic pain processing, the proprietary DTM waveform is designed to modulate both neuronal and

glial activity to enhance therapeutic outcomes. Clinical evidence suggests that DTM-SCS provides superior relief of back and leg pain compared with traditional paresthesia-based stimulation, offering a more effective approach for the treatment of chronic pain (47-49).

Multifidus Stimulation

In 2021, research into multifidus stimulation emerged as a promising strategy for managing chronic mechanical low back pain. This therapy targets the multifidus muscle, a critical stabilizer of the spine. Chronic low back pain is often associated with multifidus dysfunction or atrophy, leading to spinal instability and compensatory strain on surrounding structures. Traditional physical therapy may be insufficient for some patients, but ReActiv8 (Mainstay Medical, Dublin, Ireland), a rehabilitative neurostimulation system, has demonstrated potential in reactivating the multifidus by electrically stimulating its controlling nerves. By restoring proprioceptive signaling through targeted multifidus activation, this approach re-establishes segmental spinal stability and interrupts maladaptive neuromuscular patterns contributing to persistent pain. Unlike therapies aimed at neuropathic pain, this method addresses mechanical pain linked to musculoskeletal dysfunction, offering an alternative for patients unresponsive to conventional treatments (50).

Closed-Loop Stimulation

The introduction of closed-loop SCS technologies in 2022 marked a significant advancement in neuromodulation. Unlike traditional open-loop systems that deliver constant stimulation, closed-loop devices continuously monitor spinal cord electrical activity and adjust therapy in real time. This adaptive approach reduces overstimulation and helps maintain therapy within the optimal therapeutic range (51). Closed-loop systems use ECAP recordings to sustain consistent dorsal column fiber activation, resulting in more stable and effective pain control (18). Clinical studies have shown that closed-loop systems provide superior long-term pain relief, with benefits maintained for up to 12 months compared with open-loop systems. A pivotal study with two-year follow-up reported that 79% of patients achieved at least a 50% reduction in pain, along with improvements in quality of life, physical and emotional functioning, sleep, and reduced opioid use (52,53). The ability of closed-loop systems to maintain optimal spinal cord activation without frequent manual adjustments highlights their potential as a transformative advancement in pain management. Data from the ECHO-MAC trial further confirmed these benefits, showing that ECAP-controlled closed-loop stimulation significantly reduced overstimulation during daily activities. In this prospective randomized study, 97.6% of patients reported less stimulation-related discomfort with closed-loop therapy compared with open-loop, and 88.1% preferred the closed-loop experience, underscoring its tolerability and effectiveness in real-world settings (54).

Multiphase Stimulation

Following 2022, multiphase stimulation has been evaluated in clinical trials as a novel SCS strategy that distributes electrical charges across multiple stimulation phases to enhance analgesia, particularly for chronic back and leg pain, while minimizing device-related complications (55). This approach employs a proprietary charge-neutral design, delivering current simultaneously through multiple electrodes to create a spatial-temporal stimulation pattern that engages broader regions of the dorsal horn across several spinal segments. Mechanistically, multiphase stimulation functions as a low-energy, subthreshold therapy. Although its precise neuromodulatory mechanisms remain under investigation, it is hypothesized to modulate dorsal horn signaling similarly to high-frequency stimulation, potentially recruiting a wider range of spinal segments (12). Clinically, the BENEFIT-02 randomized trial evaluated 122 patients with chronic lumbar or leg pain who were randomized to receive either higher-frequency (600–1500 Hz) or lower-frequency (300–600 Hz) multiphase therapy following successful nonmultiphase SCS trials. Both groups achieved comparable outcomes, with approximately 64% of participants reporting improved pain relief compared with prior nonmultiphase therapy. Multiphase stimulation achieved these effects with reduced energy requirements, suggesting potential advantages for device longevity and patient comfort (55).

Surround Inhibition

The concept of using surround inhibition in SCS was introduced in 2023. This approach employs low-frequency stimulation patterns below the sensory threshold to activate the dorsal columns (56). By stimulating fibers surrounding the site of injury, it enhances inhibition of adjacent pain pathways, providing rapid and sustained analgesia with minimal side effects (57). Surround inhibition leverages the anatomical organiza-

tion of the dorsal columns, where inhibitory Aβ fibers surround central wide-dynamic range neurons responsible for nociceptive signaling. Subperception low-frequency pulses, typically under 150 Hz, activate spinal inhibitory interneurons and suppress pain transmission through wide dynamic range (WDR) neurons (10,57). Building on this concept, Metzger et al conducted a clinical trial using the FAST protocol (90 Hz, 210 μs) to reprogram patients with chronic pain (56). Pain scores decreased from an average of 7.1 pre-implantation and 5.2 pre-reprogramming to 1.3 within approximately 11 minutes of FAST activation. These improvements were immediate and sustained for up to six months, including in patients with leg and lower back pain. The evidence positions surround inhibition as an efficient and precise SCS strategy that combines rapid onset, anatomical targeting, and low energy consumption.

Advancements in Neuromodulation Devices

Since their inception, neuromodulation devices have evolved significantly, with successive innovations enhancing both therapeutic effectiveness and patient experience.

In 2011, positional and motion sensing stimulation was introduced, representing a major advancement in SCS technology. This feature allows devices to adjust stimulation automatically based on the patient's body position or movements, improving comfort and analgesic efficacy for individuals whose pain varies with posture or activity. By reducing the need for frequent manual adjustments, this innovation benefited patients while decreasing the burden on healthcare providers.

By 2013, full-body MRI compatibility became available, marking a critical breakthrough in neuromodulation. Patients with implanted stimulators could safely undergo MRI scans without device removal or risk of complications. This advancement enhanced diagnostic capabilities and expanded treatment options, enabling more comprehensive care for patients requiring imaging for other health conditions (58-60).

In 2020, remote programming of SCS was introduced, allowing healthcare providers to adjust device settings without in-person visits. This development reduced travel time and costs for patients while enabling rapid, personalized therapy adjustments. Yang Lu et al further advanced this approach by implementing a remote, wireless system that allows real-time video-based programming of SCS implants. Their study demonstrated that this system can safely and effectively facilitate device programming, providing a valuable option for palliative care, particularly during situations limiting in-person visits such as a pandemic (61).

The miniaturization of implantable pulse generators (IPG) has also been a significant milestone. Over the past decade, spinal SCS systems have shifted toward smaller, more intelligent, and patient-specific designs. In 2015, the first fully wireless, injectable eight-electrode, multi-programmable miniature stimulator was introduced, with a volume of approximately 0.4 cm^3. This system eliminated the need for a traditional implanted pulse generator by relying on external power delivery (62). In 2019, a micro-implant system with a volume of approximately 1.5 cm^3 was developed, powered by an external wearable unit, allowing battery-free operation and minimally invasive placement (63).

By 2020, larger platforms with 16-electrode configurations and Bluetooth connectivity became available, offering multiple waveform options and full-body MRI compatibility to expand therapeutic flexibility. In 2022, a next-generation rechargeable IPG was introduced as the smallest implantable device of its type, with a volume of 13.6 cm^3 and dimensions of 3.87 × 4.80 × 0.89 cm. This system emphasized ergonomic design, patient comfort, and extended battery life while maintaining advanced stimulation capabilities (64).

Most recently, in 2024, a closed-loop system incorporating real-time feedback based on Aβ-fiber activation was released. With a volume of 13.9 cm^3 and a weight of 29 grams, this device features ECAP-driven adaptive stimulation, 3T MRI full-body compatibility, and smartphone-enabled management tools (54). Collectively, these innovations demonstrate a clear trend toward miniaturized, personalized, and biologically responsive systems that enhance the overall patient experience.

Remote patient monitoring also became commercially available in 2023, enabling continuous tracking of device performance and patient condition. This functionality allows real-time data collection, supports timely therapy adjustments, and reduces the need for frequent office visits. By facilitating proactive interventions, this technology improves clinical outcomes and reduces healthcare utilization, enhancing efficiency for both patients and healthcare systems (12).

Each of these technological advancements has progressively improved patient experience by making treatment more personalized, effective, and less disruptive to daily life while simultaneously advancing healthcare delivery.

Tailoring Device Features And Waveforms To Patient Needs

Neurostimulation therapy is increasingly customized to meet individual patient needs, with specific device features and waveforms designed to optimize outcomes for various conditions. For patients with a history of cancer, MRI compatibility is essential. These individuals often require regular imaging for disease monitoring, and MRI-safe devices allow necessary scans without risking device damage or malfunction. This ensures that pain management through neurostimulation can continue without interfering with critical cancer-related diagnostics.

For elderly patients, features such as primary cell technology and remote programming offer significant advantages. Older patients may face mobility challenges and difficulty attending frequent clinic visits. Primary cell devices reduce the need for regular charging, which can be challenging for patients with limited technical experience, while remote programming enables healthcare providers to adjust therapy settings without requiring in-person visits, reducing the burden on elderly patients.

Patients who have difficulty adhering to treatment plans, including non-compliant individuals, benefit from primary cell technology, remote monitoring, and remote programming. Remote monitoring allows continuous tracking of device performance and patient condition, facilitating timely adjustments without a clinic visit. Remote programming enables real-time modifications to therapy, ensuring optimal stimulation even if the patient does not attend regular appointments.

For patients living in remote areas or far from healthcare providers, remote programming and remote monitoring are particularly valuable. These features allow continuous therapy adjustments and consistent monitoring regardless of patient location, reducing the need for travel and ensuring uninterrupted care.

Patients concerned about the cosmetic appearance of their devices can benefit from miniaturized IPGs, integrated systems, and hybrid power sources. Miniaturized IPGs are compact and discreet, providing a less noticeable and more comfortable implant. Integrated systems further reduce external components, enhancing the device's aesthetic appeal. Hybrid power sources combine rechargeable and primary batteries, prolonging device longevity while maintaining a sleek and user-friendly profile.

For patients at increased risk of complications from anesthesia, integrated systems and hybrid power devices are particularly suitable. These technologies minimize the need for frequent surgical interventions, reducing exposure to anesthesia and lowering procedural risk. This is especially beneficial for patients with comorbidities or those at higher surgical risk.

By incorporating these targeted features and waveforms, neurostimulation therapies can deliver more personalized care while enhancing safety, comfort, and therapeutic effectiveness, ultimately optimizing outcomes across a wide range of patient populations.

Decision-Making In Choosing The Right Neuromodulation Therapy For The Right Patient And Condition

Approach to Failed Surgery Syndrome or Persistent Spinal Pain Syndrome

Selecting the optimal neuromodulation therapy for patients with failed surgery syndrome, lumbar radiculopathy, or PSPS involves a structured, stepwise decision-making process tailored to individual clinical needs and patient preferences. Among the most effective therapies for PSPS are advanced SCS systems, including multiphase, closed-loop, DTM, 10-kHz, burst, and paresthesia waveforms. DRGS and PNS are generally not recommended for these conditions (Fig. 2).

The process begins with assessing the patient's willingness to undergo implantation of a power source. Patients who decline implantation are limited to waveforms compatible with external systems, such as hybrid or integrated paresthesia-based waveforms. For patients who consent to implantation, the next step is determining their acceptance of a rechargeable IPG. Rechargeable IPGs offer extended device lifespan and fewer replacement surgeries but require routine charging and are more expensive than non-rechargeable systems, with coverage dependent on insurer policies.

- Non-rechargeable IPG preference: Burst, glial cell, and surround inhibition waveforms are suitable due to efficient energy usage and compatibility with non-rechargeable devices.
- Rechargeable IPG acceptance: A broader range of waveforms becomes available, including multiphase, closed-loop, glial cell, HF10, burst, and paresthesia. Selection depends on patient compliance and medical history, for example, cancer patients may benefit from closed-loop or glial cell systems.

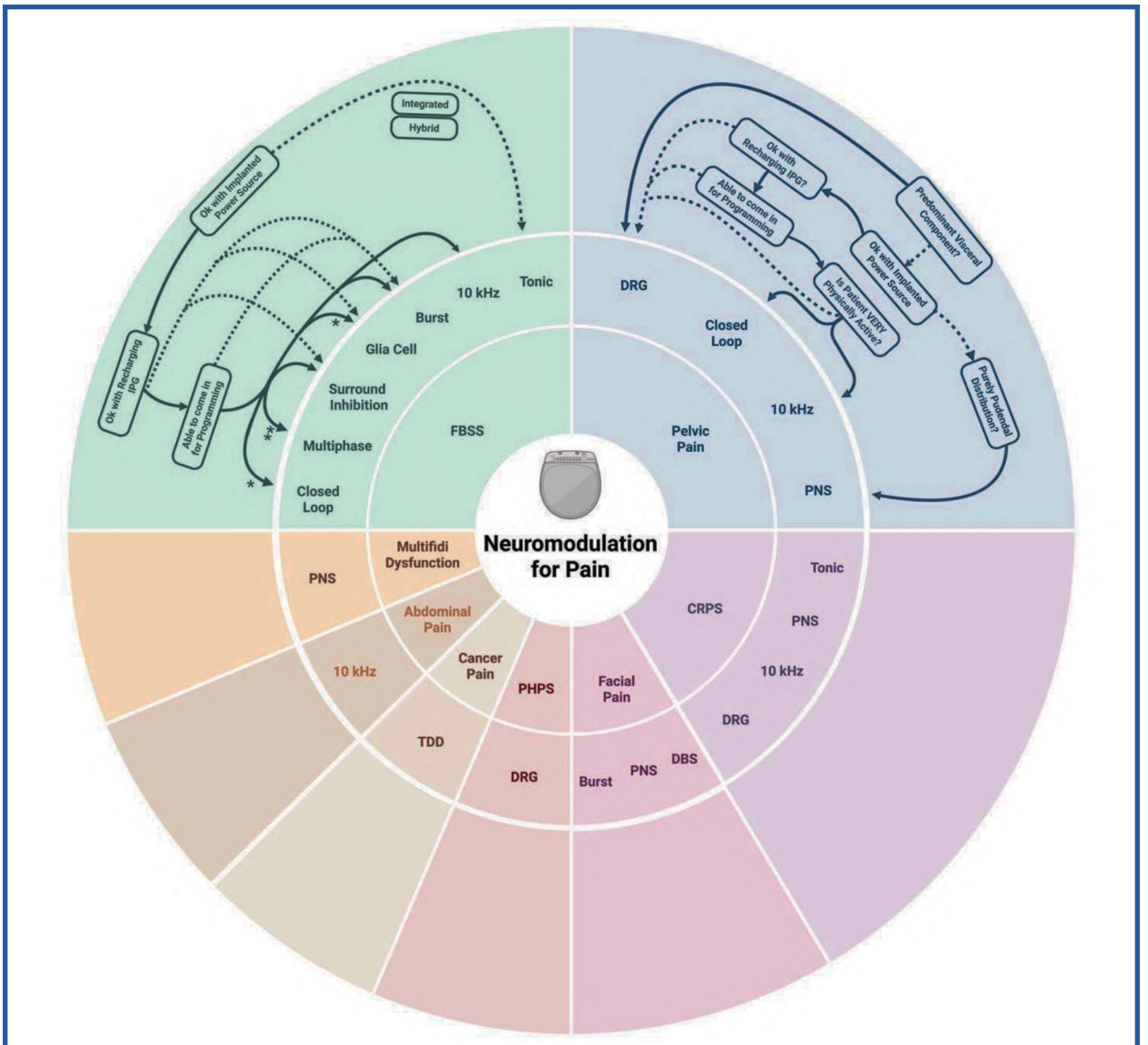

Fig 2. *Neuromodulation circle.*
*: If the patient has a history of cancer, closed loop or glial cell therapies are preferred.
**: If the patient has compliance issues, Multiphase therapy is preferred.
The dashed line indicates the pathway to follow if the answer to the respective question is "no."
The solid line indicates the pathway to follow if the answer to the respective question is "yes."
Created in BioRender. Yener, U. 2026, https://BioRender.com/3a0jboy

Patients unable to attend programming sessions are limited to low-maintenance waveforms, such as Burst, Glial Cell, and Surround Inhibition. This stepwise approach supports patient-centered therapy selection, optimizing both therapeutic outcomes and satisfaction.

Approach to Pelvic Pain

Management of pelvic pain requires a systematic, patient-centered approach. The initial step is determining whether the pain has a predominant visceral component. If visceral pain is present, DRGS is the preferred therapy due to its ability to target localized visceral pain.

If there is no visceral component, the next consideration is whether the patient is willing to undergo implantation of a power source. Patients who decline implantation are evaluated for pudendal-specific pain, in which case PNS provides targeted relief.

For patients who accept implantation, the next factor is acceptance of a rechargeable IPG. Non-rechargeable devices limit therapy to DRGS, which provides stable and consistent analgesia. For patients who accept a rechargeable IPG and have insurer approval, the next step is evaluating the ability to attend programming sessions.

Patients able to attend programming appointments are further stratified by physical activity level. Highly active individuals benefit most from ultra-high frequency or closed-loop waveforms, as these modalities adapt effectively to movement. Closed-loop SCS provides real-time modulation in response to activity. Less active patients are better suited to DRGS, which delivers stable, tailored pain control.

- Non-rechargeable preference: DRGS is favored.
- Rechargeable acceptance: Therapy depends on physical activity:
- Highly active: Ultra-high frequency or closed-loop waveforms, with closed-loop SCS providing superior adaptability.
- Less active: DRGS remains the preferred option.

Patients unable to attend programming sessions are limited to DRGS due to minimal ongoing adjustment requirements. This framework ensures therapy aligns with each patient's condition and lifestyle.

Approach to Chronic Regional Pain Syndrome and Focal Neuropathic Pain

CRPS can be effectively treated with all commercial waveforms; however, therapy selection for focal neuropathic pain requires structured evaluation. The first step is assessing willingness to undergo implantation. Patients who decline implantation are limited to non-implantable therapies, such as PNS or paresthesia waveforms, which are effective alternatives.

For patients accepting implantation, the next consideration is comfort with a rechargeable IPG. Non-rechargeable devices favor DRGS or paresthesia waveforms due to compatibility and established efficacy.

For patients amenable to rechargeable IPGs, therapy selection is guided by pain characteristics. DRGS is highly effective for focal neuropathic pain, offering precise targeting and significant relief. Ultra-high frequency waveforms are better suited for broader pain syndromes or cases requiring intensive modulation.

Programming session feasibility is also critical. Patients unable to attend follow-ups are best treated with DRGS, which requires minimal adjustment and maintains long-term efficacy. Patients able to attend programming may benefit from ultra-high frequency waveforms, which require periodic fine-tuning for optimal outcomes.

By integrating factors such as implantation willingness, IPG preference, pain characteristics, and programming feasibility, therapy can be tailored to the patient's specific needs, ensuring optimal pain control and improved quality of life.

Approach to Facial Pain

For refractory facial pain, neuromodulation may be considered. Techniques are divided into central and peripheral approaches. Central targets include the deep brain, motor cortex, high cervical spinal cord (C1–3), and the Gasserian ganglion. Among these, high cervical SCS and Gasserian ganglion stimulation are most commonly used by pain practitioners, as DBS has limited efficacy data.

High cervical SCS can be performed via a percutaneous antegrade approach with a low cervical–high thoracic entry point or a retrograde approach using a paddle lead placed over the C1 arch, which requires neurosurgical assistance. The target is the lower portion of the trigeminal spinal nucleus (nucleus caudalis) spanning C1–2. Level 4 evidence supports its use for trigeminal neuropathy and occipital neuralgia, while level 5 evidence exists for trigeminal neuralgia and Eagle's Syndrome (glossopharyngeal neuralgia caused by an elongated styloid process) (65-67). Most outcome studies employed traditional paresthesia stimulation with low amplitudes.

Gasserian ganglion stimulation was first described by Taub in 1997 and demonstrated success in a small cohort of patients with peripheral facial pain. Mansano and colleagues reported a first-of-its-kind case using a DRGS electrode to treat trigeminal neuralgia (68).

Peripheral approaches involve subcutaneous lead placement targeting peripheral branches of the trigeminal nerve, constituting peripheral field stimulation rather than PNS, as the electrode is not placed directly on the nerve, which could induce painful muscle contractions. Depending on the pain distribution, one to three electrodes are positioned using combined ultrasound and fluoroscopic guidance to ensure subcutaneous placement above the fascial plane of the muscle.

Level 4 evidence supports this approach for trigeminal neuralgia and neuropathy (65).

Approach to Postherpetic Neuralgia

DRGS has clinical application for postherpetic neuralgia (PHN) patients who do not respond to standard treatments and conservative interventions. PHN is characterized by severe, persistent neuropathic pain in specific dermatomes following herpes zoster due to peripheral nerve injury and DRG afferent cell apoptosis. The effectiveness of DRGS may be limited by the reduced number of viable DRG neurons available for stimulation (22).

The current literature on DRGS for PHN is limited. Chapman et al reported eight publications describing 20 trialed patients, with 10 proceeding to implant. Several patients achieved pain relief greater than 50% over 12–18 months, although some experienced minimal improvement or required device removal due to treatment failure.

DRGS provides better dermatomal specificity compared with conventional SCS, which may benefit segmental PHN pain patterns. However, apoptosis in DRG somata caused by viral infection reduces viable targets and may decrease treatment effectiveness (22). Stimulation of adjacent undamaged DRG segments via collateral pathways could activate Aβ fibers, although this mechanism requires further clarification (22). Comparative studies of SCS and pulsed radiofrequency (PRF), including short-term SCS, demonstrate superior pain relief, higher success rates, and improved quality of life with SCS for PHN during both intermediate and long-term periods (69-72).

Most dorsal column SCS studies do not include DRGS. Available literature reports 13 PHN patients treated with DRGS, showing significant VAS improvements exceeding 50% and reduced medication use, although the small sample size limits the strength of conclusions (73). DRGS provides technical advantages, including targeted stimulation, lower power requirements, and meaningful analgesia for patients experiencing allodynia (73,74). Complications primarily relate to implant procedures and device maintenance, similar to other neuromodulation interventions (74). Key challenges for DRGS implementation include higher cost and the requirement for specialized technical expertise (72). Modality selection should be individualized based on pain distribution, technical feasibility, and available expertise (22,73).

Approach to Cancer Mediated Pain

Patients with cancer-mediated pain often require multi-pharmacological regimens, including both opioid and non-opioid medications. Systemic oral opioids are frequently associated with significant side effects, and up to 20% of patients continue to experience uncontrolled pain despite high doses of available medications. Intrathecal drug delivery (IDD) provides potent analgesia with substantially reduced opioid doses, potentially minimizing systemic side effects. IDD should be considered for cancer patients with uncontrolled pain despite high-dose opioid therapy or for those experiencing intolerable systemic side effects (75).

To address issues related to IDD, the PolyAnalgesic Consensus Conference (PACC) panel was established in 2000. The PACC guidelines have been published and updated multiple times to review emerging evidence, provide clinical practice strategies, and identify best practices for optimizing patient outcomes. The most recent update (2024) identifies Level I evidence supporting the use of IDD for cancer pain. The following approaches are recommended when IDD is considered (76).

Patient Consideration

1. Treating physicians and patients should discuss the benefits and risks of IDD thoroughly.
2. Patients should be assessed for major psychological, emotional, cognitive, personality disorders, pain-related coping and behaviors, expectations, insight, social support, and secondary gains (77). IDD should not be delayed in patients with such psychological conditions, as it can provide substantial pain relief.
3. Ongoing antineoplastic treatments and comorbidities, including bloodstream infections, coagulopathy, cardiovascular disorders, and central nervous system disorders, should be evaluated prior to IDD.
4. Historically, IDD was less commonly offered to patients with a projected life expectancy of less than three months. Recent consensus guidelines recommend considering IDD for all cancer patients with inadequate pain control, regardless of expected survival, acknowledging the right of all patients to effective pain management.

Intrathecal Drug Delivery Trialing

1. IDD trialing in cancer patients remains controversial. While trialing can establish analgesic response and support patient selection, the PACC guideline

Moderate to severe atrophy is often associated with impaired segmental stability and chronic axial low back pain (81-83). Complementary physical examination tools, such as the Prone Instability Test (PIT) and Multifidus Lift Test (MLT), help identify functional deficits. A positive PIT, indicated by pain reduction with active lumbar stabilization, and a positive MLT, demonstrated by absent or diminished multifidus contraction during an upper extremity lift, confirm dynamic instability and motor inhibition contributing to symptoms (84,85).

For patients meeting these clinical and imaging criteria, neuromodulation targeting the multifidus may be a compelling option. Restorative neurostimulation offers a safe, effective, and durable treatment for chronic low back pain associated with multifidus dysfunction, addressing a significant unmet need in non-operative spine care (50). ReActiv8 delivers restorative neurostimulation directly to the medial branch nerves supplying the multifidus, aiming to reverse arthrogenic inhibition and restore segmental control. Therapy consists of ongoing 30-minute sessions twice daily, requiring patient adherence. The system uses a primary cell IPG, which, while larger than rechargeable alternatives, eliminates routine charging. In 2024, ReActiv8 received FDA approval for full-body 1.5T MRI conditional labeling in the U.S., ensuring imaging access for patients with implanted leads.

Discussion

Current State of Spinal Cord Stimulation

Over the past decade, SCS has advanced significantly. Hardware improvements include smaller IPGs, MRI-compatible devices, more efficient charging, and remote monitoring. However, these technological gains are secondary to the primary goal of broadly improving stimulation therapy outcomes.

New waveforms and stimulation approaches have expanded beyond traditional paresthesia models. SCS has demonstrated superiority over conservative management and repeat spinal surgery (86,87). Despite positive outcomes, the literature reports that up to 20% of explants occur annually due to loss of efficacy (88,89). Limited long-term efficacy poses challenges for reimbursement, as some payors have indicated potential non-coverage. Long-term outcome data are needed to secure sustained payor support. An algorithmic approach to selecting waveform therapy for each patient may improve outcomes, while flexible systems capable of delivering multiple waveforms on demand may enhance durability by adapting to evolving pain states over time (12,90).

Different Therapies with Varying Mechanisms of Action

The gate control theory of pain provides a foundational framework for SCS, remaining the predominant theory for managing pain resistant to interventional and surgical therapies. Its principle involves activating A-beta fibers to enhance inhibitory nociceptive tone within the spinal cord, producing analgesia. As neuromodulation has matured, multiple new waveforms and stimulation modalities have emerged, each with described mechanisms of action and clinical benefits (12,36,91).

Neurostimulation is not the only form of neuromodulation. Intrathecal therapy operates through multiple mechanisms depending on the agents delivered near the spinal cord. Its versatility makes it valuable for generalized chronic pain, particularly in patients with cancer pain, those unable to receive SCS, or those who have failed other neuromodulation therapies. In contrast, PNS is supported by literature for treating facial, pelvic, and multifidus dysfunction. However, waveform science for PNS is less developed than SCS, and the impact of novel waveforms on clinical outcomes remains under investigation.

Artificial Intelligence for Spinal Cord Stimulation Advancements

Pain is dynamic and exhibits day-to-day variability, challenging the effectiveness of single treatments. Chronic pain patients often present with multiple pain pathologies, requiring a combination of waveforms, including SCS-specific waveforms described in this article. Advances in AI may facilitate identification of the optimal waveform or combination of waveforms for a given pain state. Data repositories could collect pain and functional information, using algorithms to inform decisions or predict responses, potentially enabling real-time automatic SCS waveform adjustment.

Currently, neuromodulation lacks open-access data banks like those in oncology or cardiology, limiting the development of robust AI models for precision-guided therapy (92). Previously, discrete and wide interval data measurements can be accelerated to measure multiple intervals even within a single day (93). Data collection at frequent intervals could reveal optimal stimulator settings, allowing automatic adjustments based on pattern recognition. Comprehensive stimulators could vary

frequency, pulse width, and amplitude in real time to meet symptomatic needs (94).

Neuropathic pain intensity and frequency fluctuate, such as night-time pain disrupting sleep (95) or waxing and waning diabetic neuropathy (96). Stimulators capable of adjusting to pain signals, sleep disturbances, or activity could provide superior outcomes. For example, a patient with radiculopathy and diabetic neuropathy could alternate between paresthesia-based stimulation for radiculopathy and high-frequency, paresthesia-free stimulation for neuropathic pain. ECAP-based stimulators could automatically adjust dose for patients with high-intensity or variable spinal cord movements. Dormant or washout periods could prevent overstimulation or understimulation, reducing therapy loss and device failure (97).

Proprietary Languages

Variations in stimulation amplitude, frequency, and pulse width influence nerve physiology differently (98). High-frequency and burst stimulation have demonstrated advantages over traditional tonic paresthesia stimulation (36,39). However, their superiority is relative to older paradigms, which may be insufficient to establish definitive clinical benefit. Head-to-head studies comparing high-frequency, burst, multiphase, surround inhibition, and closed-loop stimulation are necessary to determine superiority or non-inferiority.

Currently, multiphase, closed-loop, glial cell, HF10, burst, and paresthesia waveforms have proposed mechanistic actions but lack a unified consensus for clinical application. Proprietary waveform settings pose a barrier to comparative studies. Collaboration from industry to allow interchangeable use of waveform parameters would facilitate research, improve clinical guidance, and advance the field (12,99).

Conclusion

Interventional pain physicians now have a wide range of neuromodulatory options for managing chronic pain. This article presents an evidence-based, algorithmic approach to guide decision-making for SCS waveforms and device selection across chronic pain conditions. We propose that future systems capable of delivering multiple SCS waveforms may enhance patient outcomes. Furthermore, the integration of AI software to autonomously adjust waveforms in response to dynamic patient pain patterns and conditions could further optimize therapeutic effectiveness.

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