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Spinal Cord and Peripheral Nerve Stimulation for Painful Disorders

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Keywords

• Spinal cord stimulation • Peripheral nerve stimulation
• Dorsal root ganglion stimulation • Neuromodulation

Key points

- Spinal cord stimulation is effective therapy for many intractable chronic pain conditions, including complex regional pain syndrome, failed back surgery syndrome, and peripheral neuropathy.
- Peripheral nerve stimulation is effective therapy for more localized chronic pain conditions, targeting specific nerves and/or more discrete anatomic structures.
- Stimulation technology is evolving at a rapid pace and, associated with the improvements in technology, outcomes are improving and indications are expanding.

INTRODUCTION: NATURE OF THE PROBLEM

Chronic pain represents one of the most significant public health problems in terms of the number of patients affected and in terms of health care costs. Pain affects more Americans than diabetes, heart disease, and cancer combined. Despite advances in treatments, a significant number of patients with chronic pain fail to improve with standard conservative medical therapy.

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Medical therapy is the most common treatment of chronic pain, but a recent evidence-based review of medical therapy for chronic neuropathic pain concluded that, "Existing pharmacologic treatments for NP pain are limited, with no more than 40-60% of patients obtaining partial relief of their pain." [1] As many as half of all patients who present to their medical providers with common chronic painful conditions such as diabetic peripheral neuropathy, postherpetic neuralgia, complex regional pain syndrome (CRPS), and failed back surgery syndrome (FBSS) with a neuropathic component therefore fail to improve sufficiently with conservative pain care measures.

Neuromodulation is one of the fastest growing fields in medicine. Spinal cord stimulation (SCS) and peripheral nerve stimulation (PNS) are two common examples of neuromodulation used for the treatment of pain and have been shown to be effective treatment options for many patients with refractory neuropathic pain. However, studies indicate that most clinicians are not familiar with these treatment options [2–5]. As a result, many patients who could potentially benefit are not referred to a qualified pain specialist to determine candidacy for these therapies. Because many chronic pain conditions are lifelong problems, failure to refer patients for appropriate therapy potentially subjects them to needless long-term suffering. Another important consideration is that SCS and PNS may be viable and effective alternatives to oral opioid therapy for patients with intractable or complex pain problems. Opioid treatment of chronic pain is common and has contributed to the opioid crisis in the United States. The widespread use of opioids for chronic pain has occurred despite only limited evidence for long-term efficacy. In the past, SCS and PNS were considered by many physicians to be later-stage pain therapies, mainly because of the invasive nature of the therapy. More recently, because of the limited efficacy and the myriad problems associated with chronic opioid therapy, many pain specialists rightfully consider implementing SCS or PNS earlier in the treatment algorithm for patients with intractable pain [3,6]. The major advantage of these therapies is that medications are not involved and the side effects commonly associated with pain medications, such as drowsiness, mental clouding, and constipation, are avoided. This article discusses SCS and PNS therapies that have been shown to be effective treatments for patients with refractory chronic pain. It covers indications, contraindications, and technical details of the procedures, clinical outcomes, and adverse events.

INDICATIONS AND CONTRAINDICATIONS

Spinal cord stimulation

SCS is indicated for the treatment of chronic pain resulting from many common as well as uncommon conditions, including FBSS or postlaminectomy pain, CRPS, painful diabetic peripheral neuropathy, neuropathic pain of the trunk and/or limbs, chronic intractable back and lower limb pain, and refractory angina pectoris. Originally approved for the indication of neuropathic pain of the trunk and legs in 1989, indications for its use have grown as this therapeutic modality has become better understood and mechanisms of its delivery have evolved and improved (Table 1). Traditional or conventional (also referred

Table 1
Indications for spinal cord stimulation

Indication	Proposed neuromodulation modality
FBSS	SCS (conventional/HF)
CRPS	SCS (conventional/HF) or DRG[a]
PDN	SCS, consider DRG[a] for severe plantar foot pain
Neuropathic trunk or limb pain	SCS, consider DRG[a] for focal pain
LBP + lower limb pain	SCS (consider HF for primarily axial low back pain)
RAP	SCS (conventional/HF)

Abbreviations: DRG, dorsal root ganglion stimulation; HF, high frequency; LBP, low back pain; PDN, painful diabetic neuropathy; RAP, refractory angina pectoris.
[a] Note that DRG is approved for low thoracic and lumbar placement only.

to as tonic stimulation) SCS involves the delivery of an electric current (measured in milliamperes) to the dorsal columns in the form of perceptible paresthesia that is traditionally tailored to patient comfort by the adjustment of parameters including amplitude, pulse width, and frequency. This delivery is achieved by percutaneous or surgical placement of electrodes in the epidural space, with electrode contacts positioned either according to reported patient response (a process commonly referred to as paresthesia mapping) in the case of conventional SCS, or electrodes positioned over the T9 to T10 disc space in the case of high-frequency (HF) SCS. This process is discussed in greater detail later. Burst stimulation is another form of SCS involving alteration of the parameters listed earlier in the development of a proprietary and distinct waveform. Burst SCS has been shown in large-scale randomized controlled trials (RCTs) to be an effective therapy for back and/or limb pain. There is some preliminary evidence that the burst waveform may modulate the affective or medial pathway components of pain, including pain vigilance and awareness, possibly via activation of the dorsal anterior cingulate cortex [7].

Dorsal root ganglion (DRG) stimulation involves placement of lead contacts in the neural foramen from an epidural approach, and, because of this specific location in close proximity to the DRG, the amount of electricity that is delivered is much smaller (measured in microamperes). DRG stimulation is distinct from SCS, but both involve neuromodulation of spinal structures that can be achieved using a percutaneous approach, with some overlapping indications. Note that there are multiple emerging indications for DRG, including pelvic pain, visceral pain, postherniorrhaphy pain, and other focal pain syndromes. DRG stimulation is currently US Food and Drug Administration (FDA) approved only for lumbosacral placement (below T10).

From an anatomic standpoint, SCS may be the only viable option for advanced interventional therapies in cases in which spinal anatomy is altered to such a degree that further surgery is unlikely to improve the patient's symptoms or the patient's comorbidities are such that risks of further spine surgery outweigh potential benefits. Epidural access for lower limb or low back pain is typically at the thoracolumbar junction or L1 to L2 epidural space, often above

the area of prior lumbar surgery. Epidural access for cervical pain is typically in the upper thoracic region and may be considered for patients with prior cervical surgery that has been accessed using an anterior approach as long as posterior elements, including the ligamentum flavum, remain intact. Anatomic considerations are discussed further later in the article.

As a neuromodulation therapy, SCS is most effective in treating pain with neuropathic or ischemic components. In general, it is most strongly indicated for medically refractory neuropathic pain of the trunk or limbs in patients with appropriate spinal anatomy for safe and effective lead placement.

Failed back surgery syndrome

FBSS is perhaps the most studied indication for SCS. Multiple prospective RCTs have shown the efficacy of FBSS, including superiority compared with reoperation as well as conventional medical management [8,9]. SCS may be effective not only in reducing pain following FBSS but also in improving anxiety, depression, and pain intensity, and reducing opioid usage [10]. Conventional paresthesia-based SCS as well as some of the newer stimulation paradigms, such as HF SCS and burst SCS, have all been shown to be effective therapies for FBSS [11].

Complex regional pain syndrome

Medically intractable CRPS is often debilitating and can create a challenging management problem. Presenting as a constellation of sudomotor, sensory, vasomotor, and trophic signs and symptoms caused by an inciting event (CRPS type II or causalgia) or without identifiable cause (CRPS type I), the mainstay of treatment includes physical therapy and activity modification, with refractory cases often requiring trials of various medications and injection therapies, including sympathetic nerve blocks that may achieve therapeutic efficacy. SCS is considered in refractory cases [12]. SCS has been shown to be effective in treating CRPS, including improvements in pain, quality of life, and satisfaction with SCS therapy [13]. DRG stimulation has also been shown to be effective in select patients with lower limb CRPS and superior to conventional SCS, provided pain symptoms follow an identifiable dermatomal pattern [14].

Diabetic peripheral neuropathy

SCS is also indicated for management of intractable painful diabetic neuropathy (PDN), improving pain as well as overall health and quality of life compared with conventional medical therapy [15]. SCS has been shown to be effective up to 5 years following implantation, particularly in cases in which the severity of PDN is not advanced [16]. Trials to date have investigated the use of conventional SCS for this indication, and inquiry into efficacy of HF versus conventional SCS is ongoing. Plantar foot pain may be difficult to capture with dorsal column SCS, and in such cases DRG stimulation may be considered for treatment of focal pain in PDN.

Low back pain

Although tonic stimulation historically has worked well for neuropathic limb pain, axial low back pain is often difficult to treat with conventional/tonic SCS. HF SCS has been shown to be effective for treatment of low back pain and superior in efficacy to tonic SCS for this indication [17]. The use of HF stimulation has introduced a highly effective therapy for many patients with axial low back pain with or without lower limb pain, and should be considered for patients with primarily low back pain who are otherwise appropriate candidates for neuromodulation provided there is not an anticipated need for repeated MRI.

Refractory angina pectoris

An FDA-approved indication for SCS, refractory angina pectoris (RAP) can be highly responsive to dorsal column SCS. Lead placement classically ranges from the lower cervical to upper thoracic region, and paresthesia mapping in tonic stimulation can be very helpful in confirming appropriate placement. SCS has been shown to be effective in improving angina symptoms, exercise duration, and nitrate consumption in patients with RAP [18–20]. As with all SCS indications, appropriate patient selection is critical. Implanting physicians considering SCS for treatment of RAP may find it beneficial to coordinate care with the patient's cardiologist in order to ensure appropriateness of therapy and that all diagnostic evaluation and medical treatment from a cardiovascular standpoint has been completed before consideration of trial and implantation. However, patients who have SCS placed for treatment of RAP should continue regular and appropriate cardiovascular follow-up. There is no evidence to suggest that SCS masks symptoms that are important in monitoring patients with angina symptoms.

Spinal cord stimulation: contraindications

A thorough evaluation including comprehensive history and physical examination is critical when considering patient candidacy for dorsal column SCS or DRG stimulation. From a diagnosis standpoint, neuromodulation is most effective for treatment of neuropathic or ischemic pain states, and patients with inflammatory disease or widespread myofascial pain are not as likely to experience a positive response to this therapy. MRI review should prioritize consideration of safety, and ensuring that the epidural space is adequate for safe lead placement may necessitate obtaining additional MRI of the thoracic spine in the case of treatment of lower limb or truncal pain. Intact posterior elements, including ligamentum flavum at the levels of access and final lead positioning, are necessary, and posterior spine surgery at these sites precludes percutaneous lead placement.

Beyond diagnostic and anatomic considerations, a psychological evaluation is recommended as a routine component of the comprehensive patient evaluation once a patient has been determined to be a potential candidate. Psychosocial factors such as untreated psychiatric disorders that may present barriers to successful treatment may be addressed through participation in psychotherapy,

cognitive behavior therapy, or a comprehensive pain rehabilitation program. Conditions discovered during the course of psychological evaluation, such as severe psychiatric disorders or active addiction, should be addressed in the best interests of the patient, and appropriate referrals placed.

Medical comorbidities such as poorly controlled diabetes mellitus, an immunosuppressed state, poor cardiorespiratory health, or other health conditions that would pose a danger to the patient in terms of tolerance to anesthesia, positioning during trial and/or implantation, and healing during the postoperative period should be considered and appropriately managed. Trial should only proceed if any medical comorbidities can be adequately and safely addressed. Patients who are on anticoagulant or antiplatelet therapy or who otherwise have a bleeding diathesis must be able to have their anticoagulant or antiplatelet therapy held for the appropriate time period before and after trial and implant if it is safe to do so. Joint decision making with the patient's provider prescribing such medication is critical in considering this decision and whether it is safe from a medical standpoint to hold administration of this medication in the perioperative period.

When selecting SCS or DRG therapy, MRI compatibility is another important consideration. SCS devices are compatible to varying degrees, with some devices completely incompatible with MRI, such that the need for this imaging may necessitate explant of the entire device. The need for future MRI should be considered and discussed with the patient and may factor in to specific device selection. If a patient with an SCS system does need MRI, the patient needs to confirm with the implanting SCS physician that the SCS system has MRI compatibility. This confirmation involves knowing the SCS brand and model number as well as where the SCS leads and generators are implanted. All SCS devices have an MRI safety checklist from the manufacturer and, for those devices that have MRI compatibility, the devices have an MRI safe mode that in some cases involves having the device turned off. Again, this can be confirmed by discussing with the implanting SCS physician and/or the SCS company representatives.

Peripheral nerve stimulation

Indications

PNS involves percutaneous lead placement proximal to an identified peripheral nerve lesion. This therapy may be appropriate to consider in patients with pain of the trunk or limbs with an identified peripheral nerve target accessible percutaneously. Historically, standard SCS leads were placed peripherally to achieve PNS, but there are now devices available exclusively for PNS that are more securely anchored and specific to the indication of PNS. As such, PNS is again becoming more widely considered for the indication of intractable neuropathic pain involving peripheral nerves, cranial neuralgias, and CRPS [21]. Small-scale studies have suggested that some cases of axial pain with neuropathic features refractory to SCS may respond to subcutaneous PNS, but this has not been replicated in larger RCTs [22]. More recently, implantation of PNS

devices targeting the medial branches of lumbar dorsal rami were reported in 9 patients who reported pain relief up to 4 months following implantation [23]. Poststroke hemiplegic shoulder pain is perhaps the most well-studied and classic indication for PNS, with patients showing improvement in pain and range of motion up to 2 years following implantation along the axillary nerve of the affected shoulder [24]. A variety of small-scale studies and reports have identified multiple potential targets for PNS, including postherniorrhaphy pain (including ilioinguinal and genitofemoral neuralgia) upper and lower limb peripheral nerve pain including CRPS, SI joint pain, as well as postoperative knee pain [25–30].

Contraindications

Considerations described earlier in terms of psychological factors, anticoagulation status, immunosuppressed state, and other medical comorbidities, including diabetes mellitus, must be considered as part of determining patient candidacy. PNS placement often does not require significant anesthesia beyond local infiltration, and patient positioning for implantation is highly variable depending on the target. As such, PNS is generally a safer procedure but medical contraindications must still be considered based on the target for device placement.

THERAPEUTIC OPTIONS AND SURGICAL TECHNIQUES

Spinal cord stimulation

SCS modalities can be differentiated based on the type of electrical charge delivered to surrounding tissues, the frequency (in Hertz) at which this charge is delivered, the presence or perception of paresthesia, and stimulation target of the implanted device. The 3 major types of SCS are:

- Conventional paresthesia-based SCS
- High-frequency 10 (HF10) SCS
- DRG stimulation

The hardware components of all SCS systems include an electrode array or lead, an implantable pulse generator (IPG), and a portable wireless programmer (Fig. 1). Most pulse generators are implanted generators similar to a pacemaker battery, but some SCS systems use an external generator that communicates with the stimulator leads via radiofrequency (RF) energy or Bluetooth. Before implantation, the ideal candidate undergoes a trial period usually between 5 and 7 days. For the trial, temporary percutaneous SCS leads are inserted into the epidural space with the IPG remaining external to the skin with sterile dressing, and during the trial period the patient is instructed to perform usual/typical daily activities to determine the pain-relieving impact of the temporary stimulation. The purpose of this trial is to determine whether the patient obtains sufficient clinical improvement to justify a surgical implantation. At the completion of the trial, the temporary leads are removed and a decision is made about whether or not the pain improvement was sufficient

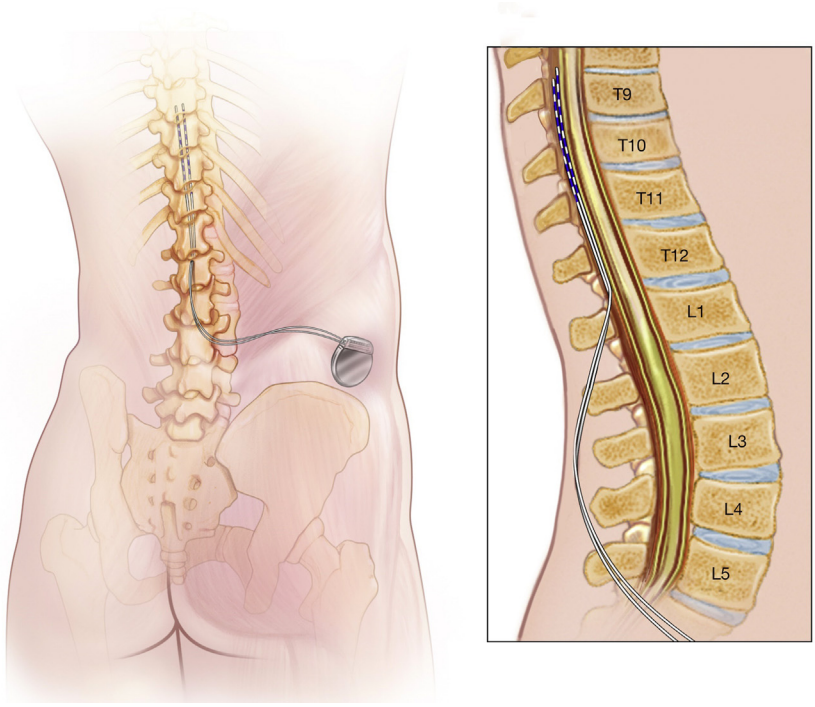

Fig. 1. Components of a typical spinal cord stimulator system. There are 2 spinal cord stimulator leads in the epidural space and an implanted pulse generator in the right lower flank/upper buttock area. (Used with permission of Mayo Foundation for Medical Education and Research. All rights reserved.)

to move forward with the surgically inserted permanent system. The period between the trial phase and implantation phase is typically 3 to 4 weeks.

Conventional spinal cord stimulation

Conventional SCS, often referred to as tonic SCS, is a modality that uses stimulation frequencies between 40 and 200 Hz. This modality is most commonly thought to function through the gate control mechanism [31]. It involves stimulation of large dorsal column sensory fibers, specifically A-beta fibers, which in turn suppresses both central hyperexcitability and the activation of pain signaling from A-delta and C fibers. There is also evidence that SCS increases the levels of several dorsal horn neurotransmitters that are known to be pain modulating, including serotonin, norepinephrine, GABA (gamma-aminobutyric acid), and acetylcholine. SCS has been shown to modulate sensitized dorsal horn wide-dynamic-range neurons, which are implicated in many neuropathic pain states. SCS may also antidromically stimulate the peripheral release of vasodilatory neurotransmitters, including CGRP (calcitonin gene-related peptide) and nitric oxide [32]. Action potentials generated by stimulation subsequently lead to the generation of paresthesia over the area of pain.

Conventional SCS percutaneous technique usually involves placement of 2 SCS leads into the dorsal epidural space following epidural access using a Touhy needle under fluoroscopy guidance (Fig. 2A). The patency of the epidural space is verified via advanced imaging, such as a computed tomography or MRI scan obtained preprocedurally. The target level and laterality bias of the placed leads depend on the location of the patient's symptoms. The leads are advanced under fluoroscopy guidance via anteroposterior view to the target level. To ensure the leads are maintained in the dorsal epidural space, lateral and contralateral oblique views are used. The appropriate physiologic location of the epidural leads is verified by ensuring the presence of paresthesia over the area of pain, a process known as paresthesia mapping [33]. In addition to the percutaneous SCS lead placement technique described earlier, an alternative is an open surgical technique to place leads directly into the epidural space via a laminotomy/laminectomy. There are pros and cons to each technique. The percutaneous technique is less invasive, whereas the open surgical approaches can be useful for patients with challenging spine anatomy.

High-frequency spinal cord stimulation

HF10 SCS is another modality of SCS that involves the use of a proprietary waveform with frequency at 10,000 Hz [34]. Stimulation at this higher frequency does not generate the perception of paresthesia. The exact mechanism of action of this stimulation mode remains to be elucidated. Possible targets in the pain perception pathway include modulation of wide-dynamic-range neurons, regulation of inhibitory and excitatory neurotransmitter release from the dorsal horn, and activation of the inhibitory descending pathway [32,35].

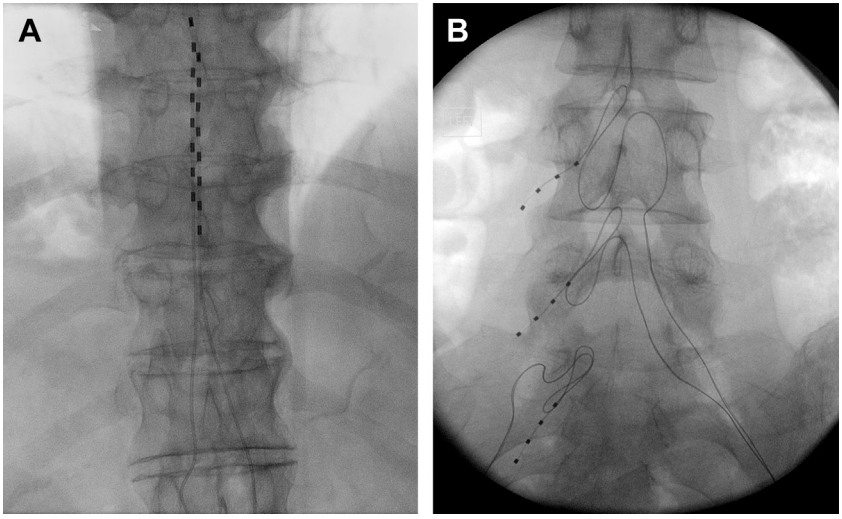

Fig. 2. (*A*) Radiograph of 2 epidural spinal cord stimulator leads. (*B*) Radiograph of 3 DRG stimulator leads placed at L4 (forth lumbar level), L5, and S1 on the left side.

In terms of technique, the placement of HF10 SCS leads into the dorsal epidural space is similar to that of conventional SCS described earlier. However, unlike conventional SCS, physiologic or paresthesia mapping over the area of pain is not needed or required following lead placement with the HF10 system. The leads are usually placed in the anatomic midline with electrodes staggered to facilitate optimal coverage. Impedance level, which is a surrogate of resistance and energy requirement in the system, is usually confirmed along with radiographic evidence.

When percutaneous devices are placed, minimal procedural analgesia is usually needed during placement of conventional and HF10 leads for both trials and implantation. Subcutaneous infiltration of the epidural needle access area with local anesthetic only usually suffices for SCS trials and can be supplemented with other intravenous agents (conscious sedation vs monitored anesthesia care) as deemed appropriate by the anesthetic provider. Regardless of the anesthetic modality used, the patient needs to be awake and interactive during SCS lead maneuvering in the epidural space to ensure that the patient is able to communicate any signs of neural integrity violation to the proceduralist. If a laminotomy/laminectomy procedure is performed for lead placement, then general anesthesia is most commonly used, and intraoperative neurophysiologic monitoring is used.

Dorsal root ganglion stimulation

Despite the well-established benefits of conventional and HF10 SCS in the treatment of neuropathic pain associated with FBSS and CRPS, adequate coverage of focal and localized areas of pain, such as in the feet, inguinal area, and groin, can be challenging [36]. Targeting the DRG that supplies these specific locations has been proposed as an effective alternative [37]. The DRG is usually located in or close to the neural foramen. It contains cell bodies of primary sensory neurons and regulates the transmission of sensory signals from the periphery via primary afferent nerves to the dorsal spinal cord column, acting essentially as a gatekeeper [38]. DRG stimulation has been shown to decrease neuronal hyperexcitability and chronic neuropathic pain signaling [39].

Similar to dorsal column SCS, the ideal patient for DRG stimulation undergoes a trial period before implantation of the IPG. However, major differences exist between DRG stimulation and dorsal column SCS. DRG leads have 4 electrode contacts, unlike those used in dorsal column systems, which vary in the number of electrode contacts (8–16 electrodes). Because of the close lead proximity to the DRG needed for stimulation, as well as small foraminal opening, DRG lead placement can be stimulating and uncomfortable in awake patients. As such, the procedure can be safely performed under general anesthesia with the use of neurophysiologic monitoring in the form of evoked potentials such as electromyography, motor evoked potentials, and somatosensory evoked potentials [40].

For DRG lead placement, the target DRG is identified based on the patient's pain location [41]. For example, foot pain is typically treated with L5 and

S1 DRG lead placement, and inguinal pain is treated with T12 and/or L1 lead placement. Skin entry with the epidural needle is performed on the contralateral side of the target DRG, usually about 2 vertebral levels caudal in the upper lumbar area (L1–L4). For the L5 DRG, skin entry is performed 1 vertebral level down on the contralateral side. Entry into the sacral DRG is performed ipsilateral at the same level [34]. Once the lead is in its final position in the dorsal neural foramen, strain relief loops (S loops) are made in a cephalocaudal fashion to anchor the leads and prevent migration (Fig. 2B). As with dorsal column SCS, optimal placement of DRG leads is confirmed via stimulation, level of impedance, and radiographic imaging. Similar to HF10 SCS, DRG stimulation is usually paresthesia free.

Peripheral nerve stimulation

Neuromodulation targeting peripheral nerves has been used to treat painful conditions for decades [42]. Although SCS and DRG target regional pain conditions, PNS allows the targeting of specific nerves and thus more discrete anatomic structures and painful conditions.

Historically, PNS required an open surgical procedure with direct visualization of the nerve to place a flat plate electrode either next to or around the nerve [43]. It then required the lead be tunneled to a location where the IPG could be connected and surgically implanted under the skin. In 1999, Weiner and Reed [44] published a case series showing that cylindrical SCS leads placed percutaneously could successfully treat occipital neuralgia. Ultrasonography-guided placement of a cylindrical lead PNS system was first reported by Huntoon and Burgher [45] in 2009, thus visualizing the nerve and lead juxtaposed without an open procedure. However, specific systems designed specifically for PNS did not exist. Instead, SCS systems were used, which still required a lead tunneled to distant location, typically the abdomen, trunk, buttock, or thigh, where a surgical pocket housed a large IPG. These systems were prone to lead migration, skin erosion, and surgical revision or explant [46].

Only recently have specifically designed systems for percutaneous PNS become widely available. Design-specific PNS systems are less invasive, easier to place, and may be less intrusive for patients. As interest in innovative PNS systems grows, so has the interest in applying it to patients with postamputation pain, shoulder pain, knee pain, postherniorrhaphy pain, and low back pain [23,24,29,47–51].

Although these systems are uniquely different from one another, they have at least 2 common components: a lead and an external energy source. The leads are typically placed with ultrasonography guidance next to the nerve of interest. The leads vary in their diameter, number of contacts, three-dimensional structure, and whether they activate via monopolar or bipolar stimulation. They all have a unique, nonsurgically deployable anchoring system not found in the SCS systems historically used. This feature reduces the risk of lead migration but still keeps the procedure minimally invasive. They

have also eliminated the IPG and replaced it with an external pulse transmitter (EPT) or external stimulator. Amplitude, pulse width, and frequency can all be adjusted to varying degrees but with much fewer waveform choices compared with SCS. Each of these devices has a patient-controlled handheld remote that can adjust the amplitude, power the device on/off, and in some cases cycle preset programs.

StimRouter (Bioness, Inc., Valencia, CA) and StimQ PNS (Stimwave, Inc., Pompano Beach, FL) are two design-specific PNS systems that use a fully implanted lead and an EPT system. The distal end of the lead with the electrodes is placed percutaneously via ultrasonography guidance near the nerve. The proximal end of the lead is then brought near the skin surface while remaining fully implanted under the skin. This proximal end acts as a receiver for the EPT, which uses wireless power transfer and RF signals to power and communicate with the implanted lead.

The StimRouter implant procedure requires only a 1.0-cm incision placed approximately 7 to 10 cm from the nerve of interest. The 15-cm lead containing 3 electrodes is introduced through this incision and often by ultrasonography guidance to the proper location near the identified nerve. Proximity to the nerve is confirmed with electrical stimulation. Once confirmed, the proximal end of the lead is tunneled subcutaneously from the incision site approximately 5 cm away. The EPT can then be placed on the skin over the proximal end of the tunneled lead, which contains the receiver. This EPT is secured by means of a disposable electrode pad with a skin adhesive.

The StimQ PNS lead has the potential advantage of 4 electrodes and uses a wearable antenna assembly that is approximated over the implanted lead receiver by means of an adjustable belt, band, or fabric.

SPRINT PNS System (SPR Therapeutics, Inc., Cleveland, OH) is a temporary PNS system with an externalized lead and pulse generator. It is intended for 60 days of use, at which point the entire lead is removed and therapy ceases. The lead is a 0.- mm diameter, open-coiled design with a single monopolar contact. The coiled structure is designed to encourage fibrotic ingrowth, minimizing migration. No incision is required. Instead an introducer and stimulating probe are inserted simultaneously through the skin to the target nerve. Once nerve proximity is confirmed with electrical stimulation, the stimulating probe is removed and replaced with the lead. In addition, the introducer is removed over the externalized lead. The lead is then trimmed to a manageable length, connected to the external pulse generator, and secured with an occlusive bandage. The bandage is changed every 2 to 3 days until the lead is removed.

Each of these specifically designed PNS systems is potentially less invasive, requires less energy, and is more cost-effective than central nervous system stimulation or using an SCS-adapted system for PNS. However, there still may be a role for an SCS-adapted system when multiple leads are desired or an external power source is not tolerated.

CLINICAL OUTCOMES

Spinal cord stimulation outcomes

Several RCTs and systematic reviews have shown the effectiveness of SCS in chronic pain states (Table 2). In a prospective RCT with 2-year follow-up, SCS combined with physical therapy provided superior pain improvement compared with physical therapy alone in patients with refractory CRPS [52]. SCS was superior to repeat lumbar spine surgery in patients who had recurrent or persistent pain after previous lumbar spine surgery [8]. Forty-seven percent of patients randomized to SCS versus 12% randomized to repeat surgery achieved greater than 50% pain improvement. In an RCT of 100 patients with intractable neuropathic pain in the setting of failed lumbar spine surgery, Kumar and colleagues [9] showed that SCS plus medical therapy was superior to medical therapy alone. In this trial, 45% of patients with SCS compared with only 5% of medical management patients achieved greater than 50% relief of pain at 1-year follow-up. The patients with SCS also experienced significant improvements in function and quality of life compared with the medical therapy group. A recently completed RCT comparing 2 different types of SCS for patients with chronic back and leg pain showed that both types of SCS offered significant improvement in pain and function. HF SCS (using a stimulation frequency of 10,000 Hz) was superior to conventional, low-frequency stimulation, with 65% of patients in the HF group experiencing significant pain relief at 18-month follow-up, a result that was statistically superior to conventional low-frequency SCS [17]. Several recent trials, including 2 RCTs, have shown SCS to be effective for the treatment of intractable pain related to PDN [15,53]. Each of the chronic pain conditions discussed earlier is notoriously difficult and stubborn to manage effectively with medical therapy. Patients that do not respond to reasonable attempts at conservative medical therapy should be referred sooner rather than later for consideration of neuromodulation approaches. As further evidence of efficacy, recent systematic review and meta-analysis of RCTs showed that SCS was significantly more likely than medical therapy to relieve pain in a variety of chronic painful conditions, including PDN, CRPS, and intractable spine and limb pain.

In addition to the common chronic neuropathic pain problems described earlier, SCS has been shown to provide significant pain reduction in patients with other challenging painful medical conditions; for example, painful vasospastic diseases [54,55]. Patients with refractory chest pain from coronary vasospasm or small vessel disease that is not amenable to definitive coronary stenting or bypass procedures can have significant improvement in pain and quality of life, and reduced physician and emergency room visits following treatment with SCS [18–20]. SCS has shown promise in several other difficult-to-treat chronic neuropathic pain states, including postherpetic neuralgia, postamputation pain, and limb pain secondary to peripheral vascular disease.

A recently published prospective randomized multicenter trial comparing traditional SCS with DRG spinal stimulation in patients with CRPS showed

Table 2
Randomized controlled trials of spinal cord stimulation for spine and/or limb pain

Study	Intervention	Control/Comparison	Results	Pain condition
Kemler et al [52]	SCS plus PT	PT	SCS + PT superior pain improvement vs PT	CRPS
North et al [8]	SCS	Repeat spine surgery	SCS superior pain improvement vs surgery	FBSS
Kumar et al [9]	SCS plus medical management	Medical management	SCS + medical management superior pain	FBSS
	—	—	Improvement vs medical management	—
Kapural et al [17]	Conventional SCS	HF SCS	Both treatments were effective: HF SCS superior	Chronic back and/or leg pain
	—	—	Pain improvement vs conventional SCS	—
de Vos et al [15]	SCS	Medical therapy	SCS superior pain improvement vs medical therapy	Painful diabetic neuropathy
Deer et al [14]	DRG stimulation	Conventional SCS	Both treatments were effective: DRG stimulation superior pain improvement vs conventional SCS	CRPS/causalgia
	—	—		—
Deer et al [75]	Burst SCS	Conventional SCS	Both treatments were effective: 69% of all patients	Chronic pain of the trunk and/or limbs
	—	—	Achieved clinically significant pain improvement	—
Slangen et al [53]	Conventional SCS	Medical management	SCS superior pain improvement vs medical therapy	PDN

Abbreviation: PT, physical therapy.

that both types of stimulation were effective in relieving pain and improving function [14]. Seventy-five percent of patients in the DRG stimulation group versus 53% in the conventional stimulation group achieved 50% or greater pain relief at 12-month follow-up. Safety data were similar in each group.

Because SCS is a surgical procedure with its associated costs and potential risks, it has been argued that this therapy should only be used as a last resort. In addition to the significantly superior outcomes compared with medical or surgical treatments for many of the commonly associated pain syndromes, as discussed earlier, recent studies have shown not only that SCS may be less costly but also that SCS is cost-effective and represents value-based therapy for many patients with intractable pain [5,56]. The costs of lifelong medical therapy with multiple rounds of medications, physician and emergency room visits, and other therapies such as injections and nerve blocks that patients with chronic pain are often subjected to over a period of years can quickly escalate into the tens of thousands of dollars or more. Two recent studies have shown the cost-effectiveness of SCS plus medical management compared with medical management alone for several chronic neuropathic pain conditions, including FBSS and CRPS. The study by Kumar and Rizvi [5] showed an incremental cost-effectiveness ratio (ICER) well below most commonly accepted willingness-to-pay per quality-adjusted life year thresholds. The ICER for FBSS was $9293 Canadian (~US$7000) and the ICER for CRPS was $11216 [5,32].

In light of several RCTs that have shown the effectiveness of SCS compared with medical therapy as well as the cost-effectiveness data, many pain specialists no longer consider SCS to be a therapy of last resort. Knowing that chronic neuropathic pain is notoriously resistant to medical therapy and knowing that SCS therapy provides cost-effective pain relief and improved quality of life compared with conventional medical management has led many pain specialists to move the consideration of SCS therapy much earlier in the chronic pain treatment algorithm. Several recent studies have shown that earlier intervention with SCS leads to better outcomes and that the longer therapy is withheld, the less likely it is to be successful [3,57,58].

Peripheral nerve stimulation outcomes

Most of the percutaneous PNS literature is observational studies, retrospective reviews, and case series. Varied indications for PNS, rapidly advancing SCS technology, and late-emerging design-specific PNS technology have limited the number of high-quality PNS clinical studies. In spite of few long-term outcome data, new design-specific PNS systems seem to improve pain and function in patients with chronic neuropathic injuries.

In a rare prospective, multicenter, randomized, double-blinded, partial crossover study, Deer and colleagues [59] documented that patients with chronic, severe peripheral nerve pain treated with a design-specific PNS system had significant pain relief compared with the control. Ninety-four patients with arm, leg, or trunk peripheral nerve pain were implanted with the StimRouter system

and randomized to either the treatment group (N = 45) with stimulation on or the control group (N = 49) with stimulation off. At 3 months, 38% of the treatment group and 10% of the control group achieved greater than 30% pain relief ($P<.0048$). At crossover the treatment group again showed significant pain relief. The treatment group also experienced significant improvement in quality of life and satisfaction at 3 months.

In a feasibility case series, Rauck and colleagues [60] treated chronic postamputation pain, both phantom and residual limb pain, with an externalized PNS system. Nine patients completed a 2-week stimulation trial with a 4-week follow-up. Greater than 30% pain relief was achieved for 8 of the 9 patients at 2 weeks and 7 patients at 4 weeks. The mean worst daily postamputation pain was reduced 56% at 2 weeks ($P>.005$) and at 4 weeks ($P>.005$). Prospective postamputation studies are forthcoming.

The first report to use ultrasonography-guided PNS for acute postoperative pain has recently been described. Five patients with refractory post–total knee arthroplasty (TKA) pain (≤60 days postoperative) were treated with the SPRINT PNS system for less than 1 hour. Four of the 5 patients had immediate and complete pain relief. One patient had immediate 67% pain reduction. No further follow-up was reported [49]. This study was followed by a second case series of 5 patients with similar inclusion criteria and treatment parameters. Immediate and significant pain relief (≥50%) at rest was reported in 4 of the 5 patients [48]. A third case series describes placing SPRINT PNS leads in 7 patients before undergoing a TKA. Continuous stimulation was initiated within 20 hours of surgery for up to 6 weeks postsurgery. During the first postoperative week the average daily pain overall, at rest, and with ambulation was reported as mild (less than or equal to 4 out of 10) in 6 of 7 patients. Pain remained mild at weeks 2, 3, and 4 in 6 of 7 patients. Four of the 7 patients discontinued opioids within the first week compared with recent studies reporting that more than 80% of patients continue to take opioids 2 weeks after a TKA. Functional recovery was assessed using the 6-minute walk test (6MWT). Within 2 weeks from surgery, 6 of 7 subjects were able to perform the 6MWT at a level equal (≥95% baseline performance) to their preoperative performance, and by 12 weeks all subjects were at baseline [50].

Recent studies report PNS stimulation for varied causes of chronic shoulder pain. In a case series for hemiplegic shoulder pain, 28 patients were trialed for 3 weeks with an externalized PNS system placed to stimulate the axillary nerve motor points. Sixteen patients had a successful trial (≥2-point pain reduction). Ten of these had no return of baseline pain within 6 months. Five eventually advanced to have an IPG placed for long-term PNS stimulation. At 6 and 12 months, all 5 participants experienced at least 50% pain reduction and, at 24 months, 4 experienced at least 50% pain reduction. The implant group also experienced significant improvement in pain interference at 6, 12, and 24 months [24]. Another cohort of patients with subacromial impingement syndrome was trialed for 3 weeks with an externalized PNS system. Pain,

disability, shoulder range of motion, and pain interference improved significantly through the 16-week follow-up [47].

A recent case series reported that 6 of 9 patients with chronic low back pain achieved clinically significant reduction (≥50%) in average pain intensity at 4 weeks while using the SPRINT PNS system. Four months after the start of treatment, 4 of 5 experienced clinically significant reduction in average and worst pain intensity. The Oswestry Disability Index was significantly reduced (≥10 points) in 67% patients at 4 weeks, and 60% of patients at 4 months [23].

COMPLICATIONS AND ADVERSE EVENTS

Although generally considered safe procedures that are typically performed in an outpatient setting, placement of implantable SCS and PNS devices is associated with multiple potential complications, as described in Table 3. Complications may be biological or mechanical [46]. In addition, they may be shared by both types of devices or be specific to SCS or PNS. Major biological complications, similar to many invasive pain procedures, include infection, bleeding, and nerve injury, with the most common biological complication being infection, estimated to occur in approximately 2.5% to 10% of SCS placements and up to 6% of PNS placements [15,53,61–63]. Lead complications are the most common mechanical complications, and include lead migration, fracture, and failure. Lead migrations, likely the most common lead complication, may require reprograming or surgical revision. Distinct from lead complications, there are also complications related to the device itself, including malfunction or early battery failure. Moreover, complications may occur at the time of device placement, including injury to vasculature, nerves, or other nearby structures, or months to even years later. Additional concerns include device intolerability, new or worsening pain after device placement (including over the generator site), lack of improvement in physical function despite appropriate device placement, and issues related to insurance coverage. Although characterization of these potential complications (eg, incidence, typical severity) remains largely incomplete, patients must be counseled on these before implantation and consent must be explicitly documented.

SUMMARY AND FUTURE CONSIDERATIONS

The future of spinal cord and peripheral nerve stimulation therapies

The past 25 years have seen remarkable advancements in advanced interventional pain-relieving devices such as PNS and SCS. Outcomes are improving because of improvements in equipment, generator software, and surgical techniques. For example, approximately 50% of patients improved with SCS in the early RCTs for SCS (older hardware and software platforms), whereas more recent trials with improved technology such as HF10 SCS, burst SCS, and DRG stimulation, have shown success in 75% to 80% of patients [14,17,75]. There has been a rapid expansion of therapies, with many new devices approved in the last few years, including HF SCS, DRG stimulation, and minimally invasive PNS devices. There are several promising therapies

Table 3
Potential complications and adverse events from spinal cord stimulation and peripheral nerve stimulation

Category	Shared complications	SCS-specific complications	PNS-specific complications
Biological	Infection	Infection (2.5%–10%) [15,53,61,62]	Infection (1%–6%)
	Superficial surgical site	Meningitis	[63–66]
	Deep surgical site		
	Bleeding	Bleeding	Bleeding
	Major (eg, neurologic deficit, requires surgery)	Neuraxial hematoma (≤0.3%) [67,68]	
	Minor (eg, superficial hematoma)		
	Nerve injury	Nerve injury	Nerve injury
	Transient neuropraxia	Spinal cord injury	Peripheral
	Permanent injury	Paralysis (0.03%) [67]	nerve injury
	Miscellaneous	Miscellaneous	Miscellaneous
	Seroma	Erosion (0.2%) [67]	
	Allergic reactions		
	Fistula formation		
	Erosion		
Mechanical	Lead complications	Lead complications	Lead complications
	Migration	Migration (13%–23%) [62,67,69–71]	Migration
	Fracture	Fracture (6%–9%) [62,72,74]	Fracture (2% for
	Failure		ONS) [66]
	Device complications	Device complications	Device complications
	Malfunction		
	Early battery failure (≤1.7%) [67]		
	Overstimulation		

Other	New pain Implant, lead anchor sites Neuropathic Placement complications Injury to surrounding structures Vascular injury Additional concerns Device Intolerability Worsened pain after placement Lack of improvement in function Early removal (secondary to above) Lack of insurance coverage	New pain Implant, lead anchor sites (1%–12%) [15,54,62,67,72,73] Placement complications Dural puncture (0%–0.3%) [62,67] Nerve root or cord injury —	New pain Implant, lead sites (6% ONS) [66] Placement complications Peripheral nerve injury —

Abbreviation: ONS, Occipital Nerve Stimulation.

in development [76]. One promising new technology currently in clinical trials in the United States and Australia involves an evoked compound action potential controlled closed-loop SCS system. This system uses real-time measurement of spinal cord neuronal stimulation to control the amount of SCS energy being delivered [76]. This technique allows more precise control of the dose or amount of electrical energy being delivered and has the potential for improved pain control and reduced generator/battery use (prolonged generator life).

Summary

Approximately 40 million people in the United States have chronic pain. Of these, approximately 10 million have what has been termed high-impact chronic pain, meaning pain that has lasted 3 months or longer and is accompanied by at least 1 major activity restriction, such as being unable to work outside the home, go to school, or do household chores [77]. Most of these patients are treated with medications as the mainstay of therapy, but most medically treated patients continue to report ongoing pain. In addition to suboptimal pain relief, many patients experience significant adverse events from medications, including drowsiness, cognitive decline, and constipation. SCS and PNS therapy are well-established techniques that have been used for more than 25 years, and many RCTs and systematic reviews have shown superiority of these techniques compared with medical therapy for many common chronic pain conditions. Patients with intractable pain that have failed reasonable attempts at conservative pain care measures should be referred to a qualified interventional pain specialist to determine candidacy for the procedures discussed in this article.

References

[1] Dworkin RH, O'Connor AB, Backonja M, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. Pain 2007;132:237–51.
[2] Compton AK, Shah B, Hayek SM. Spinal cord stimulation: a review. Curr Pain Headache Rep 2012;16:35–42.
[3] Deer TR. Spinal cord and peripheral nerve stimulation should be used earlier in the treatment algorithm for neuropathic pain. Pain Manag 2011;1:7–10.
[4] Kumar K, Abbas M, Rizvi S. The use of spinal cord stimulation in pain management. Pain Manag 2012;2:125–34.
[5] Kumar K, Rizvi S. Cost-effectiveness of spinal cord stimulation therapy in management of chronic pain. Pain Med 2013;14:1631–49.
[6] Deer TR. Neurostimulation should be used as a method of reducing or eliminating opioids in the treatment of chronic pain: the digital drug revolution. Expert Rev Med Devices 2013;10:697–9.
[7] De Ridder D, Plazier M, Kamerling N, et al. Burst spinal cord stimulation for limb and back pain. World Neurosurg 2013;80(5):642–9.
[8] North RB, Kidd DH, Farrokhi F, et al. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. Neurosurgery 2005;56(1):98–106.
[9] Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. Pain 2007;132(1–2):179–88.

[10] Robb LP, Cooney JM, McCrory CR. Evaluation of spinal cord stimulation on the symptoms of anxiety and depression and pain intensity in patients with failed back surgery syndrome. Ir J Med Sci 2017;186(3):767–71.
[11] De Andres J, Monsalve-Dolz V, Fabregat-Cid G, et al. Prospective, randomized blind effect-on-outcome study of conventional vs high-frequency spinal cord stimulation in patients with pain and disability due to failed back surgery syndrome. Pain Med 2017;18(12): 2401–21.
[12] Poree L, Krames E, Pope J, et al. Spinal cord stimulation as treatment for complex regional pain syndrome should be considered earlier than last resort therapy. Neuromodulation 2013;16(2):125–41.
[13] Visnjevac O, Costandi S, Patel BA, et al. A comprehensive outcome-specific review of the use of spinal cord stimulation for complex regional pain syndrome. Pain Pract 2017;17(4):533–45.
[14] Deer TR, Levy RM, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain 2017;158(4):669–81.
[15] de Vos CC, Meier K, Zaalberg PB, et al. Spinal cord stimulation in patients with painful diabetic neuropathy: a multicentre randomized clinical trial. Pain 2014;155(11):2426–31.
[16] van Beek M, Geurts JW, Slangen R, et al. Severity of neuropathy is associated with long-term spinal cord stimulation outcome in painful diabetic peripheral neuropathy: five-year follow-up of a prospective two-center clinical trial. Diabetes Care 2018;41(1):32–8.
[17] Kapural L, Yu C, Doust MW, et al. Novel 10-kHz high-frequency therapy (HF10 Therapy) is superior to traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain: the SENZA-RCT randomized controlled trial. Anesthesiology 2015;123(4): 851–60.
[18] Imran TF, Malapero R, Qavi AH, et al. Efficacy of spinal cord stimulation as an adjunct therapy for chronic refractory angina pectoris. Int J Cardiol 2017;227:535–42.
[19] Pan X, Bao H, Si Y, et al. Spinal cord stimulation for refractory angina pectoris: a systematic review and meta-analysis. Clin J Pain 2017;33(6):543–51.
[20] Eldabe S, Thomson S, Duarte R, et al. The effectiveness and cost-effectiveness of spinal cord stimulation for refractory Angina (RASCAL Study): a pilot randomized controlled trial. Neuromodulation 2016;19(1):60–70.
[21] Nayak R, Banik RK. Current innovations in peripheral nerve stimulation. Pain Res Treat 2018;2018:9091216.
[22] Burgher AH, Huntoon MA, Turley TW, et al. Subcutaneous peripheral nerve stimulation with inter-lead stimulation for axial neck and low back pain: case series and review of the literature. Neuromodulation 2012;15(2):100–6 [discussion 6-7].
[23] Gilmore CA, Kapural L, McGee MJ, et al. Percutaneous Peripheral Nerve Stimulation (PNS) for the treatment of chronic low back pain provides sustained relief. Neuromodulation 2019;22(5):615–20.
[24] Wilson RD, Bennett ME, Nguyen VQC, et al. Fully implantable peripheral nerve stimulation for hemiplegic shoulder pain: a multi-site case series with two-year follow-up. Neuromodulation 2018;21(3):290–5.
[25] Shaw A, Sharma M, Zibly Z, et al. Sandwich technique, peripheral nerve stimulation, peripheral field stimulation and hybrid stimulation for inguinal region and genital pain. Br J Neurosurg 2016;30(6):631–6.
[26] Bouche B, Manfiotto M, Rigoard P, et al. Peripheral nerve stimulation of brachial plexus nerve roots and supra-scapular nerve for chronic refractory neuropathic pain of the upper limb. Neuromodulation 2017;20(7):684–9.
[27] Dewandre Q, Dubuisson A, Kaschten B, et al. Refractory neuropathic pain from a median nerve injury: spinal cord or peripheral nerve stimulation? A case report. Acta Neurol Belg 2019. [Epub ahead of print].

[28] Guentchev M, Preuss C, Rink R, et al. Long-term reduction of sacroiliac joint pain with peripheral nerve stimulation. Oper Neurosurg (Hagerstown) 2017;13(5):634–9.
[29] Ilfeld BM, Gilmore CA, Grant SA, et al. Ultrasound-guided percutaneous peripheral nerve stimulation for analgesia following total knee arthroplasty: a prospective feasibility study. J Orthop Surg Res 2017;12(1):4.
[30] Ilfeld BM, Said ET, Finneran JJT, et al. Ultrasound-guided percutaneous peripheral nerve stimulation: neuromodulation of the femoral nerve for postoperative analgesia following ambulatory anterior cruciate ligament reconstruction: a proof of concept study. Neuromodulation 2019;22(5):621–9.
[31] Melzack R, Wall PD. Pain mechanisms: a new theory. Science 1965;150:971–9.
[32] Lamer TJ, Deer TR, Hayek SM. Advanced Innovations for Pain. Mayo Clin Proc 2016;91:246–58.
[33] Verrills P, Sinclair C, Barnard A, et al. A review of spinal cord stimulation systems for chronic pain. J Pain Res 2016;9:481–92.
[34] Russo M, Van Buyten JP. 10-kHz high-frequency SCS therapy: a clinical summary. Pain Med 2015;16(5):934–42.
[35] Linderoth B. Spinal cord stimulation: a brief update on mechanisms of action. Eur J Pain Suppl 2009;3(2):89–93.
[36] Abejon D, Feler C. Is impedance a parameter to be taken into account in spinal cord stimulation? Pain Physician 2007;10:533–40.
[37] Morgalla M, Fortunato M, Lepski G, et al. Dorsal Root Ganglion Stimulation (DRGS) for the treatment of chronic neuropathic pain: a single-center study with long-term prospective results in 62 cases. Pain Physician 2018;21(4):E377–87.
[38] Pope JE, Deer TR, Kramer J. A systematic review: current and future directions of dorsal root ganglion therapeutics to treat chronic pain. Pain Med 2013;14:1477–96.
[39] Krames ES. The dorsal root ganglion in chronic pain and as a target for neuromodulation: a review. Neuromodulation 2015;18:24–32.
[40] Falowski S, Dianna A. Neuromonitoring protocol for spinal cord stimulator cases with case descriptions. Int J Acad Med 2016;2:132–44.
[41] Vancamp T, Levy RM, Pena I, et al. Relevant anatomy, morphology, and implantation techniques of the dorsal root ganglia at the lumbar levels. Neuromodulation 2017;20:690–702.
[42] Wall PD, Swert WH. Temporary abolition of pain in man. Science 1967;155(3758):108–9.
[43] Nashold B, Goldner J, Mullen J, et al. Long-term pain control by direct peripheral nerve stimulation. J Bone Joint Surg Am 1982;64:1–10.
[44] Weiner R, Reed K. Peripheral neurostimulation for control of intractable occipital neuralgia. Neuromodulation 1999;2:217–21.
[45] Huntoon M, Burgher A. Ultrasound-guided permanent implantation of peripheral nerve stimulation (PNS) system for neuropathic pain of the extremities: original cases and outcomes. Pain Med 2009;10:1369–77.
[46] Eldabe S, Buchser E, Duarte R. Complications of spinal cord stimulation and peripheral nerve stimulation techniques: a review of the literature. Pain Med 2016;17(2):325–36.
[47] Wilson R, Harris M, Gunzler D, et al. Percutaneous peripheral nerve stimulation for chronic pain in subacromial impingement syndrome: a case series. Neuromodulation 2014;17:771–6.
[48] Ilfeld B, Grant S, Gilmore C, et al. Neurostimulation for postsurgical analgesia: a novel system enabling ultrasound-guided percutaneous peripheral nerve stimulation. Pain Pract 2017;17(7):892–901.
[49] Ilfeld B, Ball S, Gabriel R, et al. A feasibility study of percutaneous peripheral nerve stimulation for the treatment of postoperative pain following total knee arthroplasty. Neuromodulation 2019;22(5):653–60.

[50] Ilfeld B, Ball S, Cohen S, et al. Percutaneous peripheral nerve stimulation to control postoperative pain, decrease opioid use, and accelerate functional recovery following orthopedic trauma. Mil Med 2019;184:157–64.
[51] Elahi F, Reddy C, Ho D. Ultrasound guided peripheral nerve stimulation implant for management of intractable pain after inguinal herniorrhaphy. Pain Physician 2015;18:E31–8.
[52] Kemler MA, De Vet HC, Barendse GA, et al. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. Ann Neurol 2004;55:13–8.
[53] Slangen R, Schaper NC, Faber CG, et al. Spinal cord stimulation and pain relief in painful diabetic peripheral neuropathy: a prospective two-center randomized controlled trial. Diabetes Care 2014;37:3016–24.
[54] Ubbink DT, Vermeulen H. Spinal cord stimulation for non-reconstructable chronic critical leg ischaemia. Cochrane Database Syst Rev 2013;(2):CD004001.
[55] Deogaonkar M, Zibly Z, Slavin KV. Spinal cord stimulation for the treatment of vascular pathology. Neurosurg Clin N Am 2014;25:25–31.
[56] Kemler MA, Raphael JH, Bentley A, et al. The cost-effectiveness of spinal cord stimulation for complex regional pain syndrome. Value Health 2010;13:735–42.
[57] Kumar K, Rizvi S, Nguyen R, et al. Impact of wait times on spinal cord stimulation therapy outcomes. Pain Pract 2014;14:709–20.
[58] Rizvi S, Kumar K. Spinal cord stimulation for chronic pain: the importance of early referral. Pain Manag 2014;4:329–31.
[59] Deer T, Pope J, Benyamin R, et al. Prospective, multicenter, randomized, double-blinded, partial crossover study to assess the safety and efficacy of the novel neuromodulation system in the treatment of patients with chronic pain of peripheral nerve origin. Neuromodulation 2016;19:91–100.
[60] Rauck R, Cohen S, Gilmore C, et al. Treatment of post-amputation pain with peripheral nerve stimulation. Neuromodulation 2014;17:188–97.
[61] Hoelzer BC, Bendel MA, Deer TR, et al. Spinal cord stimulator implant infection rates and risk factors: a multicenter retrospective study. Neuromodulation 2017;20:558–62.
[62] Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: challenges in treatment planning and present status, a 22-year experience. Neurosurgery 2006;58:481–96 [discussion: 96].
[63] Paemeleire K, Van Buyten JP, Van Buynder M, et al. Phenotype of patients responsive to occipital nerve stimulation for refractory head pain. Cephalalgia 2010;30:662–73.
[64] Sator-Katzenschlager S, Fiala K, Kress HG, et al. Subcutaneous target stimulation (STS) in chronic noncancer pain: a nationwide retrospective study. Pain Pract 2010;10:279–86.
[65] Verrills P, Vivian D, Mitchell B, et al. Peripheral nerve field stimulation for chronic pain: 100 cases and review of the literature. Pain Med 2011;12:1395–405.
[66] Saper JR, Dodick DW, Silberstein SD, et al. Occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. Cephalalgia 2011;31:271–85.
[67] Cameron T. Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review. J Neurosurg 2004;100:254–67.
[68] Moeschler SM, Warner NS, Lamer TJ, et al. Bleeding complications in patients undergoing percutaneous spinal cord stimulator trials and implantations. Pain Med 2016;17:2076–81.
[69] North RB, Recinos VR, Attenello FJ, et al. Prevention of percutaneous spinal cord stimulation electrode migration: a 15-year experience. Neuromodulation 2014;17:670–6 [discussion: 6–7].
[70] Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. Spine (Phila Pa 1976) 2005;30:152–60.

[71] Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for complex regional pain syndrome: a systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. Eur J Pain 2006;10:91–101.
[72] Mekhail NA, Mathews M, Nageeb F, et al. Retrospective review of 707 cases of spinal cord stimulation: indications and complications. Pain Pract 2011;11:148–53.
[73] Turner JA, Loeser JD, Deyo RA, et al. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications. Pain 2004;108:137–47.
[74] Kumar K, Taylor RS, Jacques L, et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. Neurosurgery 2008;63:762–70 [discussion: 770].
[75] Deer T, Slavin KV, Amirdelfan K, et al. Success using neuromodulation with BURST (SUNBURST) study: results from a prospective, randomized controlled trial using a novel burst waveform. Neuromodulation 2018;21:56–66.
[76] Maheshwari A, Pope JE, Deer TR, et al. Advanced methods of spinal stimulation in the treatment of chronic pain: pulse trains, waveforms, frequencies, targets, and feedback loops. Expert Rev Med Devices 2019;16:95–106.
[77] Pitcher MH, Von Korff M, Bushnell MC, et al. Prevalence and profile of high-impact chronic pain in the United States. J Pain 2018;20:146–60.