

Narrative Review

e Comparison of FDA-Approved Electrical Neuromodulation Techniques for Focal Neuropathic Pain: A Narrative Review of DRG, HF10, and Burst Neuromodulation

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Background: Evidence suggests that dorsal root ganglion stimulation (DRGS) is a more effective treatment for focal neuropathic pain (FNP) compared with tonic, paresthesia-based dorsal column spinal cord stimulation (SCS). However, new advancements in waveforms for dorsal column SCS have not been thoroughly studied or compared with DRGS for the treatment of FNP.

Objectives: The purpose of this review was to examine the evidence for these novel technologies; to highlight the lack of high-quality evidence for the use of neuromodulation to treat FNP syndromes other than complex regional pain syndrome I or II of the lower extremity; to emphasize the absence of comparison studies between DRGS, burst SCS, and high-frequency SCS; and to underscore that consideration of all neuromodulation systems is more patient-centric than a one-size-fits-all approach.

Study Design: This is a review article summarizing case reports, case series, retrospective studies, prospective studies, and review articles.

Setting: The University of Miami, Florida.

Methods: A literature search was conducted from February to March 2020 using the PubMed and EMBASE databases and keywords related to DRGS, burst SCS, HF10 (high-frequency of 10 kHz), and FNP syndromes. All English-based literature from 2010 reporting clinical data in human patients were included.

Results: Data for the treatment of FNP using burst SCS and HF10 SCS are limited ($n = 11$ for burst SCS and $n = 11$ for HF10 SCS). The majority of these studies were small, single-center, nonrandomized, noncontrolled, retrospective case series and case reports with short follow-up duration. To date, there are only 2 randomized controlled trials for burst and HF10 for the treatment of FNP.

Limitations: No studies were available comparing DRGS to HF10 or burst for the treatment of FNP. Data for the treatment of FNP using HF10 and burst stimulation were limited to a small sample size reported in mostly case reports and case series.

Conclusions: FNP is a complex disease, and familiarity with all available systems allows the greatest chance of success.

Key words: Dorsal root ganglion, high frequency, burst, spinal cord stimulation, neuromodulation, focal neuropathic pain

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Neuropathic pain is defined by the International Association for the Study of Pain (IASP) as pain arising as a direct consequence of a lesion or disease affecting the somatosensory system (1,2).

The pain can be distributed centrally involving lesions or disease of the spinal cord and/or brain, or peripherally

involving lesions or disease of the A β , A δ , and C fibers. Peripheral neuropathic pain can be further subdivided into focal and generalized distributions (3). Although the latest IASP terminology does not include a definition for focal neuropathic pain (FNP; also referred to as local or discrete neuropathic pain), the following defini-

tion was proposed by Mick et al (4) in 2012 as a type of neuropathic pain that is characterized by consistent and circumscribed area(s) of maximum pain associated with negative or positive sensory signs and/or spontaneous symptoms characteristic of neuropathic pain. To further distinguish FNP from widespread pain, the authors suggested that the area of pain should be easily identifiable by patients and that this area should remain constant over time. The prevalence of neuropathic pain in the general population ranges from 3% to 9.8%. FNP is the most common presentation of neuropathic pain, accounting for 60% (5). There are many different etiologies of FNP, including infectious (e.g., postherpetic neuralgia or HIV), metabolic (diabetic peripheral neuropathy), postsurgical, nerve entrapment, radiculopathies, mixed disorders (e.g., complex regional pain syndrome [CRPS]), and iatrogenic (e.g., chemotherapy) (5,6). The pathophysiology of neuropathic pain is not fully understood but several postulated mechanisms exist including plastic changes in the peripheral nervous system and central nervous system leading to hyperexcitability and central sensitization, impairment of descending inhibitory pathways, ectopic neural pacemakers associated with ion channel changes, alterations in chemical mediators, and transcriptional and posttranslational changes (4,5). Neuropathic pain sensations are described as positive (e.g., shooting pain, burning) or negative (e.g., loss of perception) and are frequently associated with concomitant nonpainful symptoms (e.g., paresthesias, numbness). Several screening and diagnostic tools exist for neuropathic pain (e.g., Leeds Assessment of Neuropathic Symptoms and Signs, Douleur Neuropathique 4, painDETECT, Neuropathic Pain Questionnaire) (7). However, only one screening tool for FNP exists and defines focal arbitrarily as less than the size of an A4 paper (8). Although some examples of FNP are agreed on by most clinicians (e.g., postherpetic neuralgia and postsurgical scar pain), it is less clear whether focal applies to other neuropathic pain syndromes such as CRPS or painful diabetic peripheral neuropathy (pDPN) (3,6).

Pharmacologic treatment is considered the first-line therapy for FNP. However, up to two-thirds of patients are unable to achieve effective pain relief with these therapies (9). For nonresponders and patients who experience intolerable side effects, spinal cord stimulation (SCS) has been utilized. When traditional (also known as conventional, tonic, or low-frequency) SCS (tSCS) was first employed for the treatment of FNP, the highest quality of evidence existed for CRPS (10). Although an estimated pain relief of 40% to 50% was achieved, specific challenges existed (11). Shortcomings

of tSCS in treating FNP included difficulty in targeting focal areas, unpleasant paresthesias, unwanted stimulation in nonpainful areas, quality of life impairments (e.g., inability to drive), positional variations, lead migrations, suboptimal pain relief, loss of therapeutic effect over time, high energy requirements, and shunting of energy by the cerebrospinal fluid (CSF). These limitations persisted despite attempts to improve techniques, hardware, and programming (12). Dorsal root ganglion stimulation (DRGS) was developed to improve on these limitations and to help target areas that were difficult to treat with tSCS such as FNP (6,13,14). In the initial patent proposal for DRGS, the authors argued that tSCS was nonspecific and indiscriminate and that DRGS would facilitate a more precise stimulation method (15). Supporting this claim and facilitating DRGS approval by the US Food and Drug Administration (FDA) in February 2016, the ACCURATE study demonstrated both noninferiority and superiority of DRGS to tSCS in treating CRPS. Furthermore, DRGS demonstrated improvements on tSCS limitations, including greater quality of life, less postural interference, and a reduction in unwanted paresthesias (11). DRGS was theorized to improve outcomes for FNP for several reasons, including more precise anatomic targeting of sensory afferent fibers; access to a well-organized and somatotopically arranged structure; less CSF permitting decreased impedance, more stable stimulation, and lower energy requirements; reduced paresthesia sensations; and less positional variation owing to closer proximity to the target (6,11,16-18).

Since the approval of DRGS by the FDA, favorable evidence has accumulated for its use in the treatment of FNP. The most recent Neuromodulation Appropriateness Consensus Committee (NACC) guidelines for DRGS recommend level 1 grade A evidence in using DRGS for FNP secondary to identifiable pathology (consensus point 1). Other level 1 grade A evidence was given for CRPS type I or II of the lower extremity (consensus point 2), and DRGS superiority over tSCS in treating unilateral focal pain secondary to CRPS I or II of the lower extremity (consensus point 25) (6). Evidence for other FNP conditions (e.g., pDPN, postsurgical pain) was of lower quality (11,19-30). Interestingly, consensus point 4 states that there is stronger evidence for tSCS in treating pDPN in contrast to DRGS (6,31,32). Although the majority of evidence suggests that DRGS is a more effective treatment option for FNP compared with tSCS, new advancements in waveforms for SCS have not been thoroughly studied or compared with DRGS. The

purpose of this review was to examine the evidence for these novel SCS technologies, specifically burst SCS and high-frequency of 10 kHz (HF10) SCS in the treatment of FNP; to highlight the lack of high-quality evidence for the treatment of FNP pain syndromes other than CRPS I or II of the lower extremity; to emphasize the absence of comparison studies between DRGS, burst SCS, and HF10 SCS; and to underscore that a comprehensive neuromodulation approach is more patient centric than a one-size-fits-all approach.

METHODS

Literature Search Strategy

A literature search was conducted from February to March 2020 using the PubMed and EMBASE databases. The search focused on novel FDA-approved SCS technologies, predominately DRGS, burst SCS, and HF10 SCS, for the treatment of FNP syndromes. Search terms for each individual neuromodulation technology were combined with search terms for all possible iterations of FNP syndromes (Fig. 1). The 2019 NACC guidelines were used to determine which pain syndromes to include, and iterations were added when appropriate (6). A manual search of citation lists from seminal reviews was performed and appropriate literature was added.

Selection of Literature

All human, English-written literature was included from the time of FDA approval for each device: 2016 for DRGS, 2016 for burst, and 2015 for HF10. Literature included all prospective and retrospective, randomized and nonrandomized data on clinical effectiveness. The initial search yielded few studies, therefore a secondary search was conducted to include studies from 2010, correlating to the approximate pre-FDA introduction of these technologies. Literature on DRGS was also included, but focused on seminal review articles, guidelines, and randomized controlled trials. A detailed search of smaller studies was not performed, as this was not the primary focus of the review.

Exclusion of Literature

Articles were excluded based on the following criteria: indications other than FNP syndromes; indications that significantly deviated from those listed in the 2019 NACC guidelines; pain exclusively involving the head, neck, or back; literature prior to 2010; neuromodulation technologies other than DRGS, burst, or HF10 (e.g., peripheral nerve stimulation); HF10 frequencies other

than 10 kHz; animal studies; duplicate data; and studies written in a language other than English. All authors participated in the selection process.

DISCUSSION

HF10

Clinical Data

A total of 11 clinical reports and studies involving HF10 for the treatment of FNP syndromes were included (Table 1). The majority of these were case series and case reports on CRPS (n = 5), pDPN (n = 3), chronic postsurgical pain (n = 2), and chronic pelvic pain (n = 2) (9,33-41). One randomized controlled trial comparing conventional medical management to conventional medical management in combination with HF10 completed enrollment in 2019. However, these data have yet to be published in a peer-reviewed format, and only preliminary data has been presented in conference proceedings (42). No clinical evidence using HF10 was found for chemotherapy-induced peripheral neuropathy, HIV-related neuropathy, phantom limb and/or stump pain, or postherpetic neuralgia.

CRPS

Outcomes for 20 patients implanted with permanent HF10 SCS have been reported since 2010. The first report by Wohak et al (41) described 3 patients with upper limb, postsurgical-induced CRPS type II. All of the patients in this case series reported a decrease in their Visual Analog Scale (VAS) pain scores. Baseline pain scores were not reported. However, VAS pain scores for each patient ranged from 0 to 2 after an implant period ranging from 3 to 8 months. All 3 of these patients reported a complete cessation of their analgesics and near normal return of function in their affected extremity. One patient who previously trialed and failed tSCS was successfully salvaged with HF10. Of note, this patient suffered a bike accident and after repositioning the tSCS, pain relief could not be recaptured. Al-Kaisy et al (9) reported on the effectiveness of HF10 in treating neuropathic pain in a single-center retrospective chart review of 11 patients, 3 of which were diagnosed with CRPS. Outcomes were reported at an interval of 6 months and included CRPS, postsurgical, and neuropathic pain diagnoses. Numeric Rating Scale (NRS) scores were reduced by 59% (8.2–3.3, $P < 0.05$) from baseline. Reductions were also seen in brief pain inventory scores (57.6–29.4) and pain catastrophizing scales (33–7). Quality of life, assessed using the EuroQol- 5 Dimension

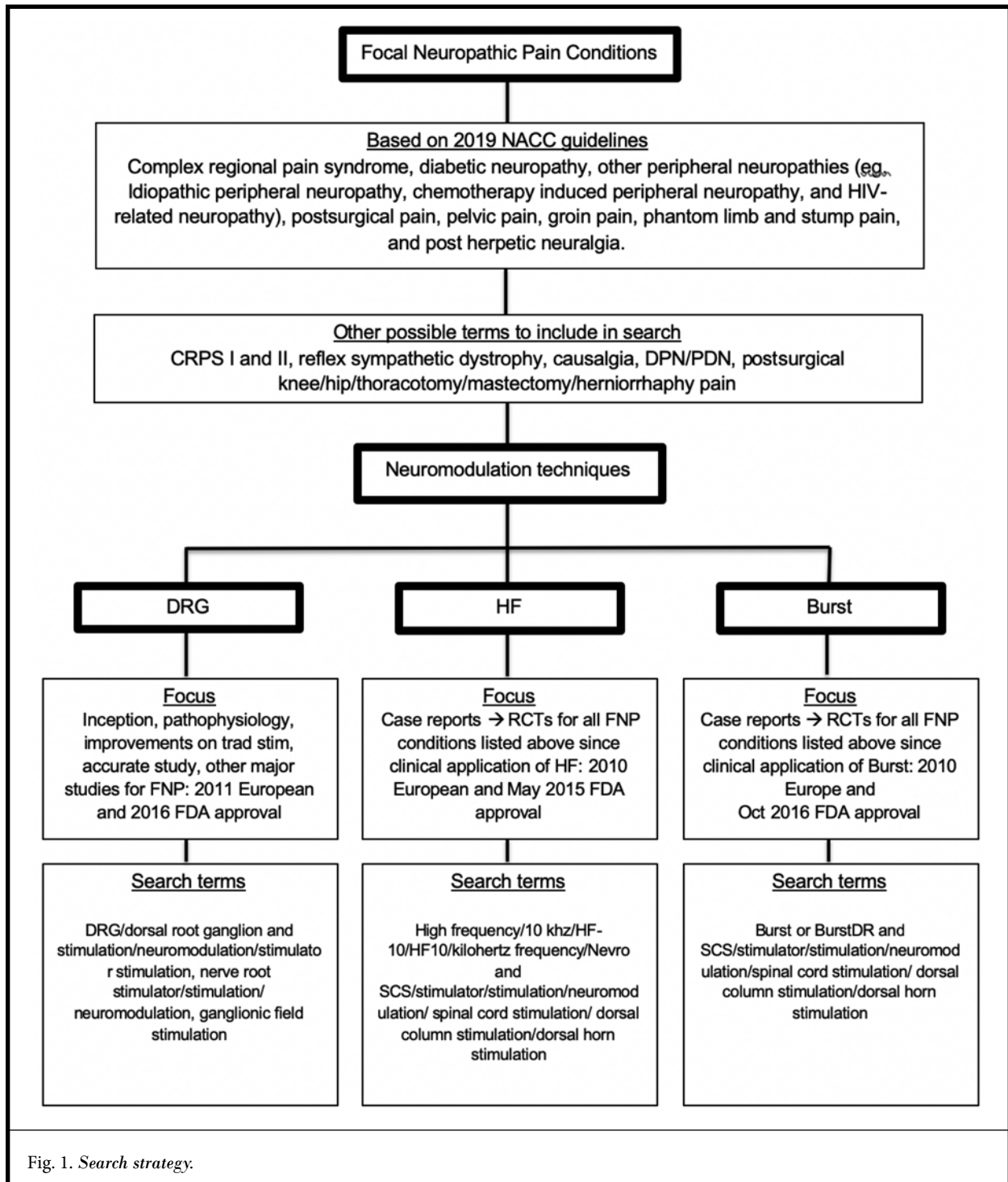


Fig. 1. Search strategy.

(EQ-5D), was increased by 101%. The majority of patients (10 out of 11) rated HF10 as excellent or good and would recommend it to other patients. Several adverse events were reported, including one surgical site infection dur-

ing the trial phase, 2 lead migrations, one of which was associated with a fall, and 3 patients with transient pain at the implantable pulse generator (IPG) site. None of these events were neurologic related. A retrospective observa-

Table 1. Summary of HF10 SCS clinical data.

Study	Study Type (n FNP permanent implant only)	Total n (permanent implant only)	Indication (latest follow-up)	Outcomes Measured	Results Summary (FNP only, if no FNP specified as overall)
Wohak 2013 (41)	Case series	3	CRPS II (3-8 months)	VAS, analgesic use, function	VAS: 1 - 0-1 2 - 1-2 3 - 1-2 Analgesic use: All stopped analgesics Function: All "near normal" return of function
Al-Kaisy et al 2015 (9)	Case series (3 CRPS, 8 CPSP)	11	CRPS and CPSP (6 months)	NRS, BPI, PCS, EQ-5D, Preference	NRS: 59% reduction (8.2-3.3, $P < 0.05$) BPI: 57.56-29.4 PCS: 33-7 EQ-5D: 101% increase Recommend: 10 out of 11
Abrecht et al 2017 (33)	Case series (1 CRPS)	4	Scoliosis, FBSS, and CRPS (4 months)	VAS, QOL, function	CRPS VAS: 50% (8-4) CRPS QOL: 62% (8-3) CRPS function: 50% (6-3)
Crapanzano et al 2017 (34)	Case report (1 CRPS)	1	CRPS	Not reported	"skin...returned to normal appearance" "more active...without pain" "discontinued all anticonvulsants and reduced opiates by 75%"
Simopoulos et al 2018 (39)	Case series (3 CPP)	3	CPP (9-12 months)	VAS, function	VAS: Pt 1 - 8.2-4.0 Pt 2 - 8.3-3.3 Pt 3 - 7.5-4.1
Gupta et al 2018 (43)	Multicenter, prospective, open-label (16 CPSP)	16	CPSP (3 months)	VAS, PDI, MPQ	VAS: 8.1-0.9 PDI: 41.2-9.8 MPQ: 5.7-0.5
Gill et al 2019 (36)	Single-center, retrospective, review (12 CRPS)	12	CRPS (mean 12.1 months)	NRS, responder rate, SF-MPQ-2	NRS: 47% reduction ($P < 0.05$) Responders: 67% SF-MPQ-2: Continuous - 45% reduction ($P < 0.05$) Intermittent - 54% reduction ($P < 0.05$) Neuropathic - 48% reduction ($P < 0.05$) Affective - 54% reduction ($P < 0.05$)
Galan et al 2019 (35)	Multicenter, prospective, open-label (8 pDPN)	18	pDPN (12 months)	VAS, PDI, MPQ	VAS pDPN only: 8.1-2.1 PDI all patients: 38.7-22.0 MPQ all patients: 4.8-2.1

Table 1 (continued). Summary of HF10 SCS clinical data.

Study	Study Type (n FNP permanent implant only)	Total n (permanent implant only)	Indication (latest follow-up)	Outcomes Measured	Results Summary (FNP only, if no FNP specified as overall)
Tate et al 2019 (40)	Multicenter, prospective, open-label (15 CPP)	15	CPP (3 months)	VAS, PDI, MPQ	<p><u>VAS:</u> 7.8–2.5</p> <p><u>PDI:</u> 43.9–20.5</p> <p><u>SF-MPQ-2:</u> Total pain – 4.2–1.69 Continuous pain – 5.75–2.28 Intermittent pain – 4.66–1.5 Neuropathic pain – 2.28–1.33 Affective descriptors – 4.08–1.63</p>
Gupta et al 2019 (37)	Case series (25 CPSP)	25	CPSP (3-6 months)	VAS, PDI, MPQ, PSQ	<p><u>VAS:</u> 7.9–1.7</p> <p><u>PDI:</u> 41.6–10.7</p> <p><u>MPQ:</u> Total pain – 5.03–1.13 Continuous pain – 1.49–0.75 Intermittent pain – 5.42–1.15 Neuropathic pain – 4.6–0.95 Affective descriptions – 3.68–0.87</p> <p><u>PSQ:</u> Trouble falling asleep due to pain – 6.95–1.99 Awakened from sleep night – 6.79–1.79 Awakened from sleep morning – 7.83–1.94</p>
Mekhail et al 2020 (42) (preliminary data)	RCT (88 pDPN)	88	pDPN (3 months)	VAS, responder rate, average pain relief	<p><u>VAS:</u> CMM – 7.0–6.5 HF10/CMM – 7.6–1.7</p> <p><u>Responders:</u> CMM – 7% (7/96) HF10/CMM – 89% (78/88)</p> <p><u>Average pain relief:</u> CMM – 5% HF10/CMM – 77%</p>
Sills 2020 (38)	Case series (3 pDPN)	6	pDPN (mean 29.8 months)	NRS, opioid medication, QOL, sensations	<p><i>pDPN Only</i></p> <p><u>NRS:</u> Pt 1 – 8–1 Pt 2 – 8–4.5 Pt 3 – 7–0.5</p> <p><u>Opioid medication:</u> Pt 1 – 100% wean Pt 2 – no change Pt 3 – 100% wean</p> <p><u>QOL:</u> Pt 1 – 99% improvement Pt 2 – walking improved by 50% Pt 3 – 100 yrd limitation to no limitation</p> <p><u>Sensations:</u> Pt 1 – improved Pt 2 – 60% improvement Pt 3 – improved</p>

Abbreviations: PCS, pain catastrophizing scale; QOL, quality of life; PDI, pain disability index; MPQ/SF-MPQ-2, McGill Pain Questionnaire/Short-Form McGill Pain Questionnaire; PSQ, pain and sleep questionnaire; CPP, chronic pelvic pain; CPSP, chronic post-surgical pain; EQ-5D, EuroQol- 5 Dimension; CMM, conventional medical management; BPI, brief pain inventory.

tional study of 4 patients, 1 of which was diagnosed with CRPS, was presented by Abrecht et al (33). Four months postpermanent implant the patient with right lower extremity CRPS experienced a 50% reduction (8–4) in their VAS, an improvement of their quality of life by 63% (8–3, 10 being described as the “worst imaginable”) and a 50% improvement (6–3, 10 being described as “completely disabled”) in their functional status. This patient had previously trialed and failed tSCS for a period of 48 months prior to HF10 implant. Crapanzano et al (34) presented a case report of a patient with postsurgical CRPS implanted with HF10. Baseline pain score was 8 out of 10 and was reduced by 75% at 1 month postimplant. This patient also reported a 75% decrease in opioid requirements, a total cessation of anticonvulsant medications, and improvement in their functional status and autonomic-associated symptoms. The largest of the case series was reported in a single-center retrospective study by Gill et al (36). Twelve patients with CRPS received a permanent implant with HF10 and were followed-up for a mean of 12.1 months. NRS scores were reduced by 47% from baseline ($P < 0.05$), and all 4 descriptors of the short-form McGill Pain Questionnaire were significantly reduced (continuous pain by 45%, intermittent pain by 54%, neuropathic pain by 48%, and affective pain by 54%, all $P < 0.05$). Clinically meaningful pain relief (decrease in pain scores by 2 or $>30\%$) was achieved in 67% (8 of 12) of patients, and 71.4% (5 of 7) patients who failed tSCS achieved $>50\%$ pain relief with HF10. The mean pain reduction using tSCS in these patients was 34% as compared with 58% when using HF10 ($P < 0.05\%$). Of note, no patients reported paresthesias or adverse events.

Painful Diabetic Peripheral Neuropathy

Three studies reporting on the treatment of pDPN with HF10 were conducted since 2010 with a total of 99 patients receiving permanent implants. A case series by Galan et al (35) observed a total of 18 implanted patients, 8 of which were diagnosed with pDPN. At 12 months all 8 patients reported a reduction in VAS scores (8.1–2.1). All patients, including patients with idiopathic polyneuropathy, experienced a reduction in pain disability index scores (38.7–22.0) and pain interference (4.8–2.1) assessed by the McGill Pain Questionnaire. The majority (80%) reported a patient global impression of change to be “better” or a “great deal better.” Of note, a total of 5 adverse events were recorded, the details of which were not reported. By far the largest of the studies to date is a multicenter, prospective, randomized controlled trial by Mekhail et al (42) comparing conventional medical management to

conventional medical management in combination with HF10. The clinical data from this study have yet to be finalized, but preliminary data at 3 months were recently reported. VAS scores experienced a greater reduction in the combination group (78% reduction, 7.6–1.7) compared with the conventional medical management alone group (7% reduction, 7–6.5). Responder rates ($>50\%$ pain relief) were also greater for the combination group, 89% (78/88) compared with 7% (7/96). This study completed its enrollment in 2019. Published outcomes are expected to include long-term pain assessment at 24 months, and assessment of functional status, emotional and affective components of pain, quality of life, health care utilization, medication usage, and disease status (e.g., wound healing, HbA1c). The most recent analysis is a case series of 6 patients by Sills (38), 3 of which were diagnosed with pDPN. At an average follow-up of 29.8 months, all 3 patients exhibited a reduction in NRS scores (8–1, 8–4.5, and 7–0.5) and improvement in the sensations they felt as a result of their neuropathy. A complete elimination of opioid medications was seen in 2 patients, with the third patient demonstrating no reduction. Each patient experienced an improvement in quality of life, with 2 patients experiencing an almost complete improvement in their ambulation, and one patient a 50% improvement.

Chronic Postsurgical Pain

A total of 2 case series with 33 patients have analyzed outcomes on the use of HF10 for chronic postsurgical pain. The first by Al-Kaisy et al (9) included a total of 11 patients, 3 with CRPS and 8 with chronic postsurgical pain of the upper ($n = 3$) and lower ($n = 5$) limbs. Outcomes were inclusive of CRPS and postsurgical pain patients and were presented in the CRPS section earlier. In summary, the majority of patients experienced a $>50\%$ reduction in their pain; NRS scores were reduced and statistically significant at 6 months; brief pain inventory, pain catastrophizing, and quality of life were all improved; and the majority of patients would recommend the therapy. Gupta et al (37,43) reported outcomes of a multicenter, prospective study on chronic postsurgical pain of the trunk, upper and lower limbs. A total of 25 patients received a permanent implant. VAS scores for all patients were decreased from 7.9 at baseline to 1.4, and a majority (87%) were responders at 12 months. These outcomes were similar for patients with lower extremity pain, 8.0 to 1.4 and 85%. Pain disability index scores were also decreased at 6 months from 41.6 to 10.7. Meaningful improvements in quality of life using the McGill Pain Questionnaire were also reported.

Chronic Pelvic Pain

HF10 for chronic pelvic pain has been described in 2 case series. Simopoulos et al (39) reported on 3 patients with chronic pelvic pain including coccydynia, perineal pain, and pudendal neuralgia. All 3 patients experienced a decrease in their VAS scores, 8.2 to 4.0 at 9 months, 8.3 to 3.3 at 12 months, and 7.5 to 4.1 at 11 months. One of the patients did increase their functional abilities, and the other achieved a 75% reduction in immediate-release opioids and complete cessation of their long-acting opioids. No other assessments were made across all patients. Tate et al (40) examined a slightly larger group of patients in a multicenter, prospective study of 15 patients who received a permanent HF10 implant. VAS scores were reduced from baseline at 3 months (7.8–2.5). Patients also experienced reductions from baseline at 3 months on pain disability index (43.9–20.5), all domains of the McGill Pain Questionnaire (total pain 4.2–1.69, continuous pain 5.75–2.28, intermittent pain 4.66–1.5, neuropathic pain 2.28–1.33, and affective descriptors 4.08–1.63), and all descriptors of the pain and sleep questionnaire (trouble falling asleep 6.86–1.44, awakened from sleep at night 7.11–2.38, and awakened from sleep in the morning 7.64–2.58).

Burst

Clinical Data

Outcomes of 11 clinical reports and studies were included for the treatment of FNP syndromes using burst stimulation (Table 2). Similar to the data on HF10, the majority of these were case series and case reports on CRPS (n = 7), pDPN (n = 1), chronic postsurgical pain (n = 1), chronic pelvic pain (n = 2), and groin pain (n = 1) (44–55). One randomized controlled trial comparing tSCS to burst stimulation was conducted. However, this study focused mostly on patients with failed back surgery syndrome (FBSS; 41.8%) and radiculopathy (36.9%) and less on FNP syndromes, CRPS (1.4%) and chronic postsurgical pain (3.5%) (47). No clinical evidence using burst was found for chemotherapy-induced peripheral neuropathy, HIV-related neuropathy, phantom limb and/or stump pain, or postherpetic neuralgia.

CRPS

Permanent burst stimulation for CRPS has been described in a total of 7 studies since 2010, including a total of 13 patients. One of the 7 studies reported on a heterogeneous patient population including failed back

surgery, bladder disorder, and plexus neuropathy and did not report on individual outcomes for CRPS (44). In 2013, Kriek et al (51) presented a case report on one patient who trialed and failed tSCS. Assessment at 3 weeks revealed a decrease in NRS scores from 8 to 2. A follow-up case report on the same patient was presented 2 years later by Kriek et al (50) to highlight the long-term effects of burst stimulation. Pain relief persisted at 2 years with the patient reporting a sustained 75% decrease (8 to 2). The patient also reported a decrease in medication requirements (diclofenac from 225–50 mg, amitriptyline from 75–40 mg and a complete cessation of pregabalin) and that nonpain-related CRPS symptoms remained stable. Courtney et al (45) reported outcomes in a multisite, open-label cohort of 22 patients. Pain diagnoses were heterogeneous including FBSS (n = 7), radiculopathies (n = 8), CRPS (n = 1), and other (n = 6). The data reported were not individualized to any one condition, hence no conclusions could be made about the benefits of burst for CRPS in this study. Of note, this cohort compared burst in patients who had previously trialed and failed tSCS >90 days. Satisfaction scores for all pain conditions were in favor of burst by a sizeable margin (91%). The number one cited reason was better pain relief. Given that tSCS has been shown to be effective in patients with CRPS, an improvement in effectiveness is clinically important (10). A third case report was presented by Kriek et al (52) in 2016 that described using burst for a patient with CRPS of the lower extremity. Burst was implanted after a trial and failure of tSCS secondary to tolerance. NRS scores initially declined from 8 to 9 but increased again after the conversion of the patient's cold CRPS to warm CRPS causing edema and pain. After the burst amplitude was adjusted from 1.2 to 0.9 mA and a topical anti-inflammatory was added the inflammation was improved and the amplitude of 1.2 mA was restored. No follow-up data were provided. The largest case series to date was reported by Love-Jones et al (53) on 5 patients, 3 with lower limb CRPS and 2 with upper limb CRPS. Follow-up assessment period was short, occurring at the end of the 7-day trial. VAS scores were reduced from 8.0 to 2.1 ($P < 0.05$), and quality of life assessed by the EQ-5D was improved but not statistically different (0.23–0.5, $P = 0.064$). Two of the largest studies to assess burst for CRPS patients (44,47) did not report individual outcomes for CRPS patients. The report by Babbolin and Villa (44) included multiple pain etiologies (e.g., FBSS, bladder disorder, and plexus neuropathy) and did not report outcomes specific to CRPS. Overall NRS scores were significantly reduced at 6 months ($P < 0.05$), pain catastrophizing scores and mental component sum-

Table 2. Summary of burst SCS clinical data.

Study	Study Type (n FNP permanent implant only)	Total n (permanent implant only)	Indication (latest follow-up)	Outcomes Measured	Results Summary (FNP only, if no FNP specified “all subjects”)
Kriek et al 2013 (51)	Case report (1 CRPS)	1	CRPS (3 weeks)	NRS	NRS: 75% (8–2)
Wahlstedt et al 2013 (54)	Feasibility (1 groin)	15	Abdominal, groin, arm and/or hand, back and/or leg (2 weeks)	VAS	Not reported
De Vos et al 2014 (46)	Prospective, single-center, open-label (12 pDPN)	48	FBSS responders, FBSS PR, pDPN (2 weeks)	VAS and preference	VAS pDPN only: tSCS – 60% (70–28) burst – 77% (70–16, P < 0.05)
Kriek et al 2015 (50)	Case report (1 CRPS)	1	CRPS (2 years)	NRS	NRS 75% (8–2)
Courtney et al 2015 (45)	Prospective, multicenter, open-label (1 CRPS)	22	FBSS, radiculopathies, CRPS, other (2 weeks)	VAS, PCS, paresthesia mapping, preference	FNP not reported VAS all patients: tSCS – 54 mm burst @ 14d – 28.3 (P < 0.05) PCS all patients: tSCS – 17.9 burst @14d – 10.3 (P < 0.05) Preference all patients: 91% for burst
Kriek et al 2016 (52)	Case report (1 CRPS)	1	CRPS (not reported)	NRS	NRS: 8–9 to not reported Other: “conversion cold to warm CRPS”
Love-Jones et al 2017 (53)	Case series (5)	5	CRPS (7 days)	VAS and QOL	VAS: Pretrial – 8.0 Posttrial – 2.1 (P < 0.05) QOL (EQ-5D): Pretrial – 0.23 Posttrial – 0.5 (P = 0.064)
Babbolin and Villa 2018 (44)	Cohort (not reported)	39	CRPS, FBSS, bladder disorder, and plexus neuropathy (6 months)	NRS, PCS, MCS, and preference	FNP not reported NRS all patients: Burst > tSCS @ 3,6 mo (P < 0.05) PCS all patients: “significant improvement” MCS all patients: “significant improvement” Preference all patients: 100% for burst
Deer et al 2018 (47)	RCT (2 CRPS, 5 postoperative)	100	FBSS, radiculopathy, CRPS, postoperative chronic pain (1 year)	Noninferiority, superiority, responder rates, preference, MPQ, BDI, PCA, PGI	FNP not reported Effectiveness all patients: Noninferior (P < 0.05) Superior (P < 0.05) Responder rates all patients: tSCS – 51% Burst – 60% Paresthesia-free all patients: tSCS – 2.7% Burst – 61.6% Preference @ 1 yr all patients: tSCS – 23.9% Burst – 68.2% MPQ, BDI, PCS, PGI all patients: No significant difference
Hassanain et al 2018 (49)	Case report (1 postsurgical)	1	Postsurgical (not reported)	Not reported	“considerable improvement”

Table 2. Summary of burst SCS clinical data (continued).

Study	Study Type (n FNP permanent implant only)	Total n (permanent implant only)	Indication (latest follow-up)	Outcomes Measured	Results Summary (FNP only, if no FNP specified “all subjects”)
Yousef and Monroe 2019 (55)	Case report (1 postsurgical)	1	Postsurgical (5 months)	VAS and satisfaction	VAS: 100% (6–8 to 0) Satisfaction: High satisfaction
Faridi et al 2019 (48)	Case report (1 postsurgical)	1	Postsurgical (not reported)	–	“only 1 episode of less severe pain”

Abbreviations: PCS, pain catastrophizing scale; QOL, quality of life; MCS, mental component summary; MPQ, McGill Pain Questionnaire; EQ-5D, EuroQol- 5 Dimension; PR, poor responders; BDI, beck depression inventory; PCA, patient catastrophizing scale; PGI, patient global impression.

maries were improved, and 100% of patients preferred burst attributed to a more comfortable perception. Deer et al (47) did record the number of CRPS patients ($n = 2$). However, this represented a very small proportion (1.4%) of the total study population ($n = 141$). This randomized controlled, crossover trial found noninferiority and superiority of burst compared with tSCS. Treatments utilizing burst resulted in clinically significant responder rates (60% with $> 30\%$ decrease in VAS scores), less paresthesias, and a greater and sustained preference for burst (70.8%–18.8% at 24 weeks and 68.7%–23.9% at 1 year) secondary to lack of paresthesias and better pain relief. No significant difference was found in psychological and physical function measures. Of note, adverse event rates were similar to other SCS studies. Despite the large amount of data collected in these 2 studies, individual outcomes for CRPS cannot be assessed.

Painful Diabetic Peripheral Neuropathy

Study of burst stimulation for the treatment of pDPN is limited to one study by De Vos et al (46). This single-center study assessed 3 separate groups, one of which included patients ($n = 12$) with pDPN that had previously received tSCS for at least 6 months (average 2.5 years). All assessments were made at 2 weeks. Overall the reduction in VAS scores was greater for burst (52%) compared with tSCS (37%). However, pain reduction was strongly correlated with pain etiology with pDPN achieving the best reduction (77%) compared with patients with FBSS who were previously responders to tSCS (57%) and who were previously poor responders (23%). Specific to the diabetic group baseline, general pain scores were significantly decreased from 70 to 16, a 44% greater reduction than tSCS (70–28, $P < 0.05$). When compared with tSCS, burst was shown to be more effective in treating pain in the feet (70–14 for burst compared with 70–28 for tSCS, $P < 0.05$) than pain

in the legs (70–4 for burst and 70–7 for tSCS, $P = 0.5$). Eight of the 12 diabetic patients preferred burst over tSCS mostly citing absence of paresthesias. The 4 that preferred tSCS disliked the inability to adjust the amplitude of burst. It is important to note that this study was published in 2014 when the technology was in its infancy. Patient ability to adjust certain burst parameters has advanced since the time of this study. Supporting previous safety studies, the authors reported minimal side effects.

Chronic Postsurgical Pain

Hassanain et al (49) described a case of a single patient who developed intractable left shoulder pain following a radical neck dissection. A single Octrode was placed at the C2/3 level, and a burst waveform was used. All outcomes were patient-reported and no validated scoring system was utilized. The patient reported considerable improvement in pain. No time frame was given.

Chronic Pelvic Pain

Two recent case reports have presented outcomes on burst stimulation for the treatment of chronic pelvic pain. Yousef and Monroe (55) described a case of chronic pelvic pain secondary to endometriosis. At baseline, the patient reported a VAS pain score of 6 to 8 and functional impairment. Five months postimplant with burst stimulation the patient reported a 100% reduction in pain, complete cessation of oral analgesics, increased activities of daily living, and improved quality of life. Specific to pelvic pain, the authors note that despite some evidence for the use of tSCS, paresthesias are undesirable in this region and result in limitations to stimulation intensity and effectiveness. A second case report by Faridi et al (48) reported on a patient with pain secondary to fibroids and surgical interven-

tion. After receiving a permanent burst stimulation implant the patient reported cessation of their typical pain and only one episode of less severe pain. The time frame and numerical assessment of this improvement were not reported.

Groin Pain

Groin pain and the use of burst was reported in one case series by Wahlstedt et al (54). A total of 15 patients were implanted with burst stimulation, including abdominal (n = 1), groin (n = 1), occipital neuralgia (n = 1), arm and or hand (n = 5), and back and or leg pain (n = 7). Outcomes for the entire group were positive with a significantly different decrease in pain between tSCS and burst (9.13–6.4 and 9.13–5.4, *P* < 0.05) and a larger responder rate to burst (66.7%). Time frame and study design were not mentioned in the report. Despite these findings, no individual analysis was performed for the single groin pain patient. Furthermore, the authors reported that 2 patients had similar responses for burst and tSCS, and 3 patients had increased pain with burst. It is unclear if the patient suffering from groin pain was one of these cases.

Comparison of tSCS, Burst, and HF10

To date the only known comparison of tSCS, burst, and high-frequency was conducted on CRPS patients by Kriek et al (56) (Table 3). A recent review by Kirketeig et al (57) from 2019 mentions 2 other trials, however, the study population in these trials focused on FBSS (58,59). This multicenter, double-blind, randomized and placebo-controlled crossover trial was performed on patients with CRPS. Patients underwent a 2-week trial with tSCS stimulation at 40 Hz and, if successful, were implanted

with an EON IPG (St. Jude Medical, Saint Paul, MN) and continued 40 Hz therapy for a total of 3 months before entering the crossover period. This was followed by randomization of 5 different settings (40 Hz, 500 Hz, 1200 Hz, burst, and placebo). Each frequency was tested for 2 weeks with a 2-day washout period in-between, followed by 3 months of each patient’s preferred program. All methods were significantly better than placebo at achieving pain relief. However, no clear preference was demonstrated for burst or high-frequency in this study, and equal pain relief was obtained with both tSCS and nonstandard stimulation methods. These results should be interpreted with caution due to several limitations. First, the frequency used to represent high-frequency stimulation was paresthesia-based 1 kHz, not the FDA-approved high-frequency of 10 kHz used in the HF10 system (Nevro Corp, Redwood City, CA). The IPG used in this study was not capable of higher frequencies nor was it originally designed for burst stimulation. Another downside of the IPG was that it required more frequent charging when using burst and 1 kHz waveforms. The authors acknowledge that these limitations could negatively influence a patient’s decision for tSCS despite better pain relief with another system. The washout period in-between each waveform was short lasting for 2 days. No optimal washout time has been recommended in the literature, but the concern about such a short period is carryover from a previous stimulation method. The authors did report a significant increase in pain scores during the washout period suggesting that it was appropriate. Furthermore, all patients received tSCS for the first 3 months of the study. It is possible that patients were conditioned to associate paresthesias with pain relief and that this

Table 3. Summary of HF10 and burst SCS comparison clinical data.

Kriek et al 2017 (56)	RCT (29 CRPS)	29	CRPS	VAS, NRS, MPQ, GPE, preference	<p>VAS: Significant difference all frequencies vs. placebo No difference between individual frequencies</p> <p>MPQ: Average/minimal pain – significant difference all frequencies vs. placebo Maximal pain/pain during exertion – significant difference all frequencies</p> <p>GPE: Satisfaction – significant difference all frequencies vs. placebo</p> <p>Improved scores – significant for 40 and 500 Hz only Standard vs. preferred stimulation: VAS – 39.83–34.86 (<i>P</i> < 0.05) NRS – 4.69–4.00 (<i>P</i> < 0.05) GPE – satisfaction 5.28–5.69, improvement 4.93–5.28</p>
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Abbreviations: GPE, global perceived effect; MPQ, McGill Pain Questionnaire; RCT, randomized controlled trial.

conditioning negatively impacted outcomes measured for other waveforms. Other limitations include more CRPS I than II patients, no evaluation of CRPS symptoms other than pain, and a small sample size.

HF10 and Burst Study Limitations

Data available for the treatment of FNP using HF10 and burst stimulation are limited to a handful of studies with a small number of patients. Of the HF10 and burst studies that identified the number of FNP patients a total of 82 and 27 patients were included. On completion of the study by Mekhail et al (42), the number of patients for HF10 studies will more than double to 170. The large majority of data comes from case reports and case series. These reports are small, single-center, nonrandomized, noncontrolled, retrospective analyses with short follow-up duration. The majority reported outcomes less than 12 months, with several studies recording outcomes as short as days to weeks. To date there are only 2 randomized controlled trials for HF10 and burst. However, the randomized controlled trial for HF10 has yet to publish finalized data in a peer-reviewed journal, and the randomized controlled trial for burst is limited to a total of 2 patients with FNP. Additional limitations include heterogeneous study populations (e.g., FBSS and CRPS); reporting of statistical and not clinical significance; industry sponsorship; outcomes assessments not made by validated tools; lack of head-to-head comparisons; and use of IPGs not optimized for each specific technology.

Shortcomings of DRGS

DRGS was designed to target areas of pain that could not be captured or maintained by tSCS, specifically FNP (6,18). Although DRGS has emerged as a convincing treatment option for FNP, it is not without its limitations. Currently there are 2 level I, grade A recommendations for the use of DRGS (6). The first is for patients who have FNP with a documented nerve pathology. The second is for the treatment of CRPS types I and II of the lower extremity. All other FNP syndromes (e.g., diabetic neuropathy, postsurgical) have a lower level and grade of recommendation. For example, DRGS for pDPN is a level III, grade C recommendation, and the NACC guidelines suggest that, although initial studies show promise, the data are limited. Until more robust studies are conducted, DRGS, like HF10 and burst, lacks high-quality evidence for the treatment of most FNP syndromes. Placement of DRGS leads may be more difficult or not recommended in patients with certain anatomic abnormalities. Consensus

point 13 and 15 in the 2019 NACC guidelines states that DRGS lead placement requires suitable anatomy and should not occur in a location associated with moderate or severe central or lateral spinal stenosis. For example, the use of DRGS may not be possible in a patient with spinal fusion. Furthermore, previous surgery at the target site is a relative contraindication for placement of DRGS leads and can lead to increased risk of dural puncture or lead placement failure. Scar tissue can also increase impedance and lower DRGS efficacy (60). FNP can be associated with more than one dermatome and require leads to be placed at multiple spinal levels. Although data suggest that additional DRGS leads are more efficacious than fewer leads and current guidelines recommend targeting multiple levels for most FNP conditions (e.g., T12-L2 groin pain, L3-L4 knee pain) (6,61), more interventions have the potential to lengthen surgical times and increase adverse events. The ACCURATE (11) study found that the time it takes to place a DRGS system is on average longer than tSCS (107 vs. 76 mins) (11), and that DRGS was associated with more nonserious procedure-related adverse events (46% vs. 26%, $P < 0.05$). However, there was no statistical difference in serious adverse events (10.5% vs. 14.5%, $P = 0.62$), device-related adverse events (36.9% vs. 26.3%, $P = 0.22$), or simulation-related events ($P = 0.8025$). The clinical significance of these findings across all forms of SCS and all providers continues to be debated in the literature (13,62,63). Overall, safety data appear promising and should improve as providers increase their experience with DRGS (6,13). FDA approval for DRGS is limited to T10 and below, whereas SCS is FDA-approved for pain of the trunk and limbs (i.e., both upper and lower extremities). Despite expert opinion that DRGS is safe up to the C5 level and that the level of implantation is unrestricted in Europe and Australia, there is limited published efficacy and safety data at levels higher than T10 (6). The small number of devices and manufacturers is another limitation for DRGS. At the time of the 2019 NACC guidelines there was one device approved in the United States, the Proclaim DRG (Abbott Neurological, St. Jude Medical, Minneapolis, MN). This device is capable of supporting a maximum number of 4 leads (NACC consensus point 16) (6). Two new leads, a wireless device and paddle lead, are either not approved or under development. Two IPGs are currently available with 3 IPGs in clinical study (6). Targeting the correct DRG can be complicated as FNP syndromes become more advanced and centralized. For example, in situations in which severe deafferentation or central sensitization occurs (e.g., postamputation pain) the level associated with pain generation might not correspond

to the expected level (64). Methods for predicting DRGS placement (64,65) have been proposed but are currently untested. Chronic pain is a continuum, and it is possible that DRGS might not be as adaptable to changes in pain pathology over time. Revision of DRGS leads would be required, whereas SCS could be adapted simply by adjusting current from one contact to another or alternating waveforms. A final limitation of DRGS is its lack of salvageability. As mentioned previously, there is only one IPG and lead package available on the market. The IPG is limited to tonic stimulation and is not interchangeable with other IPGs. In the 2019 NACC guidelines, additional waveforms, frequencies, or pulse trains have been recommended as future improvements for DRGS (6). Novel waveforms have improved the overall effectiveness and long-term capabilities of tSCS. It is feasible that more versatility will have the same effect on DRGS.

Novel SCS Advantages and Improvements

Traditional SCS was first introduced in 1967 by Shealy et al (66) and has experienced minimal technological advancements over the first 50 years since its inception (67,68). Most of the initial developments were related to hardware; batteries were made more compact, electrode steering was improved, wireless connectivity was added, and systems were made magnetic resonance imaging compatible. In comparison, the past 1 to 2 decades has seen a rapid increase in development, including novel waveforms such as HF10 and burst (69). These innovations have improved on the limitations of tSCS and helped SCS become a more viable option in treating FNP syndromes, especially in circumstances where DRGS implantation is difficult or not recommended. The overall effectiveness of tSCS has been reported to range between 40% and 50%, and long-term sustainability has been challenging (68,70). In comparison to tSCS, evidence for newer technologies has shown improvements in treating FNP, mostly for CRPS with DRGS (6,11). Similarly, high-quality data have shown improvements from tSCS with HF10 and burst, but these data have focused mostly on FBSS (68,71,72). On average, tSCS improves preoperative pain from 8/10 to 5/10, burst from 8/10 to 3/10, and HF10 from 8/10 to 3/10 (73). Although the clinical significance and superiority of HF10 and burst in treating FNP syndromes has not been directly compared with tSCS in randomized controlled trials, a few smaller studies have shown promise (44,46,72,74). Long-term data also show favorable sustained results for HF10 and burst, again mostly in FBSS (68,75). Several smaller studies have demonstrated sustained pain relief greater than

12 months, with one study reporting data up to an average of 29.8 months, when using HF10 or burst to treat FNP syndromes (35,36,38,50). Salvageability is another key improvement of novel SCS systems over tSCS. For the 50% to 60% of patients who do not achieve adequate pain relief or maintain sustained pain relief, HF10 and burst have shown the capability to salvage tSCS. Gill et al (36) reported that 71.4% (5 of 7) of patients who failed tSCS for CRPS were salvageable with HF10. Salvage capability has also been documented with burst in CRPS and pDPN patients (45,46,68). Critical to the success of novel SCS in salvaging tSCS is the interchangeability of these devices, their unique mechanisms of action, and their lack of paresthesias. The Spectra WaveWriter (Boston Scientific, Marlborough, MA) IPG provides interchangeability between waveforms within a single IPG. This stimulator has the capability of providing all 3 major waveforms, tonic, high frequency (up to 1.2 kHz), and burst, and thus permits internal salvageability. Another option to salvage is to exchange one IPG for another during the trial period. Termed salvage during trial, most leads can be connected to another manufacturer's IPG via a converter kit, which helps optimize resources and increase the chances for a successful trial (76). For example, if BurstDR (Abbott, Chicago, IL) stimulation fails to provide >50% pain relief for a patient during the trial period, their leads can be left in place and the BurstDR IPG can be exchanged with an HF10 IPG (Nevro, Redwood City, CA). This technique is also possible in the reverse order (i.e., from HF10 IPG to BurstDR IPG) and for other SCS waveforms and devices. This partial exchange is less invasive than a full system exchange (i.e., leads and IPG) required for DRGS systems. This practice is supported by the 2014 NACC guidelines that suggest failure with one system does not correlate to potential future success with another system, and that physicians should consider using novel SCS when other waveforms and frequencies have failed (10). The second factor essential to salvageability is the unique mechanism of action of HF10 and burst. There are many proposed mechanisms of action for novel SCS, but no definitive explanation exists (73). However, a key difference is burst stimulation's activation of the medial pathway. Pain is processed by 2 pathways, a medial pathway (affective/attentional) and a lateral pathway (discriminatory/perceptive) (77). Traditional SCS activates the lateral pathway, whereas burst activates both the medial and lateral pathways. This difference has been suggested to contribute to improved and sustainable pain relief in patients using burst, and the loss of pain relief and patient satisfaction over time

in patients using tSCS (71). HF10 has also been shown to modulate the medial pathway, although to what extent compared with burst is not known (78). Other unique mechanisms of action exist and may contribute to the improved outcomes seen with novel SCS. Paresthesia-free is another potential contributor to salvageability. The effectiveness of tSCS relies on its ability to cover the precise area of pain with paresthesias, and simultaneously it must be tolerable to the patient (79). Complicating this delicate balance, tSCS is very susceptible to postural changes. A report by Russo et al (80) suggested that up to 71% of patients with tSCS experience uncomfortable paresthesias when changing position. As a consequence of the anatomic relationship between the device and the spinal cord, patients sense unwanted paresthesias and overstimulation leading to a lack of use, decreased amplitude causing loss of effectiveness, and eventually explantation (69,71,81). HF10 and burst have significantly improved on this limitation, with HF10 being the only FDA-approved SCS labeled as paresthesia-free. In comparison to tSCS, these paresthesia-free systems have resulted in better pain relief, increased patient preference, improved functionality, and enhanced quality of life (57,75). Other novel SCS improvements include the ability to target more spinal levels. DRGS can support a maximum of 4 leads. In contrast, novel SCS can span 5 levels when using standard Octrode leads in a staggered technique (e.g., HF10), and even more levels with the introduction of the Precision Spectra 16-lead system (Boston Scientific, Marlborough, MA). Furthermore, each DRG contains fibers that belong to a specific dermatome, whereas each level of the dorsal column contains fibers ascending and descending from multiple levels (16). Although this may be a disadvantage for treating fixed FNP, it may provide adaptability as the FNP pathology progresses and/or becomes more centralized. Novel SCS systems can also be placed, with caution (level III, grade C recommendation), in patients with structural abnormalities (e.g., spinal stenosis, surgical instrumentation) by inserting the device above the level of deformity (6,10). Anatomic placement has also eliminated the need for paresthesia mapping and simplified the implantation process. For example, HF10 is placed in the anatomic midline at prespecified levels, T8 to T11 for trunk and lower extremity pain, and C2-C7 for upper extremity pain (80).

Future Direction

A common theme in this review is that there is low-quality evidence for novel SCS in treating most

FNP syndromes. Currently there are no randomized controlled trials evaluating HF10 and burst in the treatment of FNP syndromes. Most of the data for HF10 and burst have focused on FBSS (68,74) and this has led to a gap in evidence-based knowledge for other pain conditions. Despite many limitations, the data that are available show promise and help to inform the implementation and design of more robust studies. Furthermore, many advances and new mechanisms of action have been discovered (6), and comparison of DRGS to SCS warrants revisiting. Neuromodulation technology is evolving faster than outcomes can be assessed. As such, it is imperative that more high-quality comparison studies be completed to understand the advantages and disadvantages of using DRGS, HF10, and burst. This will provide better guidance for applying the appropriate technology to the appropriate pain condition and set of patient circumstances. Moving forward, randomized, controlled, double-blinded, multicenter trials simultaneously comparing DRGS, HF10, and burst for the treatment of FNP syndromes are needed. Because novel SCS systems are paresthesia-free, the implementation of a sham control will help facilitate blinding. Furthermore, paresthesia conditioning should no longer plague study outcomes (46,82). Longer duration follow-up is also important. Tolerance is a significant disadvantage of tSCS systems, and data for many SCS technologies have cited 2 years as evidence for sustained long-term effects (47,80,83). At a minimum, future studies should report outcomes of at least 2 years to evaluate the long-term effectiveness of HF10 and burst in the treatment of FNP syndromes. The ongoing randomized controlled trial evaluating novel SCS for the treatment of pDPN is an example of the quality of study needed (42). Although this review focused on FDA-approved devices, it is also important to acknowledge new advances that have the potential to improve FNP outcomes, and that deserve equal evaluation when performing future head-to-head studies. These include peripheral nerve stimulation devices, closed-loop SCS (i.e., the first available dynamic waveform), hybrid systems (e.g., Waverider), algorithm-based platforms (e.g., Workflow, Medtronic Dublin, Ireland), high-pulse width systems, high-density SCS and wireless systems (e.g., Stimwave, Pompano Beach, FL) (69). Two additional areas of particular interest are systems that allow connection of SCS and DRGS systems to one IPG, and functional imaging studies that help further elucidate the mechanism of action of individual stimulation techniques (6,10).

CONCLUSIONS

FNP is a complex disease and there is no best system or target. There is limited comparative data between novel SCS, DRGS, and other suitable systems (e.g., peripheral nerve stimulation) to provide high-quality evidence-based guidance for one technology over another. DRGS has demonstrated promise. However, HF10 and burst have advanced the capabilities of tSCS and warrant consideration. Familiarity with all the available systems allows the greatest chance of success.

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Authorship Statement

Drs. Edward Podgorski III, Pedro Mascaró, and Dennis Patin designed the study. Dr. Edward Podgorski III conducted the literature search and review. Drs. Edward Podgorski III and Pedro Mascaró prepared the manuscript draft with important intellectual input from Dr. Dennis Patin. All authors approved the final manuscript.

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