Tonic, Burst, High-Density, and 10-kHz High-Frequency Spinal Cord Stimulation: Efficiency and Patients' Preferences in a Failed Back Surgery Syndrome Predominant Population. Review of Literature

Jean-Baptiste Peeters and Christian Raftopoulos

■ BACKGROUND: **Spinal cord stimulation (SCS) is a neuromodulation process to treat neuropathic pain, initially developed on tonic paresthesia-based stimulation. In the last decade, 3 major paresthesia-free SCSs have emerged. Several studies show their superiority over tonic stimulation.**

■ OBJECTIVE: **We summarize the data on SCS efficacy and patients' preferences.**

■ METHODS: **We selected studies from the last decade to clarify whether the different paresthesia-free SCSs are superior to tonic or not and for which SCS the patient has a preference. Study selection was focused on a failed back surgery syndrome predominant population.**

■ RESULTS: **SCS is an effective way to treat intractable neuropathic pain of the limbs and back, compared with conventional medical management and reoperation. Paresthesia-free SCSs as burst, high-density, and 10-kHz frequency are equal to tonic SCS in some studies and superior in most. Analysis of patients' preferences shows a clear trend toward paresthesia-free SCS.**

■ CONCLUSIONS: **Recent studies show superiority of paresthesia-free SCS compared with tonic SCS and those results are corroborated by analysis of patients' preferences. Taking these data into account should motivate physicians to opt for multimodal capable devices before implanting SCS.**

INTRODUCTION

Spinal cord stimulation (SCS) is a neuromodulation process to treat chronic drug-resistant neuropathic pains, used since 1967[1] and initially based on the gate control theory presented in 1965 by Melzack and Wall.[2] It consists of depolarizing the large myelinated Aβ fibers of the dorsal columns of the spinal cord with an electric impulse, which activates the inhibitory interneuron of the substantia gelatinosa. This stimulation results in the emergence of paresthesia over the painful area and pain relief. Tonic SCS is the initial electric waveform, consisting of a constant stimulation with a typically low 40–60 Hz frequency and a high enough amplitude to produce paresthesia over the painful area.

In the last decade, 3 new major SCS waveforms have appeared, showing regularly impressive positive results in reducing intractable neuropathic pain of the back and limbs. However, the various study designs, the variable cohort, and the population heterogeneity make them difficult to compare among themselves and with tonic SCS.

Our purpose is to report our analysis of studies dealing with the main 4 SCS waveforms (tonic, burst, high-density [HD], and 10-kHz) and particularly the efficacy and patient preferences of the

Key words
- 10 kHz
- Burst
- Failed back surgery syndrome
- High density
- High frequency
- Patient preferences
- Spinal cord stimulation
- Tonic paresthesia-based stimulation

Abbreviations and Acronyms
CMM: Conventional medical management
CPT: Conventional pain therapy
FBSS: Failed back surgery syndrome
HD: High-density
NPRS: Numeric pain rating scale
SCS: Spinal cord stimulation
VAS: Visual analog scale

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Citation: World Neurosurg. (2020). https://doi.org/10.1016/j.wneu.2020.08.128

*Journal homepage: **www.journals.elsevier.com/world-neurosurgery***

*Available online: **www.sciencedirect.com***

1878-8750/$ - see front matter

different SCS waveforms to treat intractable neuropathic pain of the back and limbs.

METHODS

To assess the evidence of the efficacy of the 4 SCS modalities, we identified and reviewed 3 essential aspects of this pain therapy, to provide a comprehensive overview of the purpose and legitimacy of SCS in the care process. We focused on raw pain reduction, statistically significant results, and patients' preferences. We limited our searches to studies dealing mainly with failed back surgery syndrome (FBSS), which is considered the most recognized SCS indication.

For pain reduction, we searched the literature using the terms "tonic, burst, high density or high frequency + SCS + FBSS" in PubMed and the Cochrane Library. Then, we selected the studies published between 2008 and 2018, comparing tonic SCS with conventional medical management (CMM), and comparing subperception SCS (burst, HD, and 10-kHz) with CMM, placebo, or tonic SCS. The literature was updated in July 2019. Only studies dealing with back and/or leg pain and studies having a distinctive cohort for those pain locations and with FBSS as the major SCS indication were retained.

Of the 17 studies[3-5,6-19] gathered, we identified the assessment methods of SCS efficacy used to end up with 16 different scales, of which only 2 were recurrent in all the studies: the numeric pain rating scale (NPRS) and the visual analog scale (VAS). We decided to choose these 2 scales solely to compare SCS pain reduction among the different studies. We then reduced the strong heterogeneity within the different studies by keeping those with a follow-up $\geq$6 months. As a result, the selection was reduced to 10 studies[3-5,7,8,12,14,16-18] including 689 patients for a follow-up ranging from 6 to 24 months.

Comparing numbers and quantitative aspects of SCS efficacy in studies with different cohorts and follow-up is complex. For a less quantitative and more qualitative aspect of SCS efficacy evaluation, we then focused on studies showing a statistical difference for noninferiority or for superiority of the 3 paresthesia-free stimulation modes (burst, HD, and 10-kHz), among each other and compared with tonic stimulation, placebo, and CMM. A statistically significant difference was considered for a P value $\leq$0.05 for NPRS/VAS decrease. All studies dealt with back and/or leg pain in a predominant FBSS population. No restriction was made for follow-up time. PubMed and the Cochrane Library were searched for the terms "tonic, high density or high frequency + SCS + FBSS." This search resulted in 18 studies[6-18,20-24] totalizing 681 patients, with a follow-up ranging from 1 week to 24 months.

To explore patient preferences, we selected studies comparing patient preferences after testing tonic SCS and $\geq$1 subperception SCS waveforms. No subselection of FBSS-specific cohorts was made for this section. However, we excluded studies not focusing on low back pain or lower limb radicular pain. Studies were published between 2008 and 2018 and the search was updated in July 2019. The selection was made by searching PubMed and the Cochrane Library with the "SCS + patient + preferences + burst/HD/10 kHz" search terms and by selecting relevant references included in the selected studies, which met the inclusion criteria. We ended up with 9 studies,[10,11,20,21,23-27] including 643 patients, for a follow-up ranging from 1 week to 12 months.

RESULTS

NPRS or VAS Quantitative Reduction

We compare the 4 different SCS modalities in decreasing VAS or NPRS score with baseline (with CMM and before any SCS) (Table 1). A selection was made to minimize heterogeneity within the studies. Still, multiple diagnoses were included in the different cohort (Table 2), as well as different follow-up times (6–24 months), and some patients had a history of previous SCS therapy, whereas others did not. This selection limited the number of studies to 10[3-5,7,8,12,14,16-18] (689 patients), with the FBSS proportion extending from 36% to 100% and remaining the major SCS indication in all studies.

For leg pain, 6 studies[3,4,7,16-18] were eligible to compare SCS efficacy on decreasing the NPRS or VAS with baseline before SCS (Figure 1). Of the 6 studies, none dealt with HD efficacy. We ended up with an NPRS or VAS decrease ranging from 44% to 83%. The pain score decrease was 44%[3,4] for tonic and 50%[7] for burst and ranged from 57%[17] to 83%[16] for 10 kHz. Those 2 results from 10-kHz stimulation came from 2 different studies[16,17] sharing the same cohort, with a follow-up of 6 months[16] for 83% pain decrease and 24 months[17] for 57% pain decrease.

For back pain, 6 studies[3,5,7,16-18] were eligible (Figure 2). None of the studies gave results about HD mode efficacy. We ended up with an NPRS or VAS decrease ranging from 55%[7] to 88%,[7] with a decrease of 57%[3,5] for tonic and 88%[7] for burst and ranging from 55%[7] to 78%[16] for the 10-kHz mode. For 10 kHz, we included the same 2 studies[16,17] cited earlier, sharing the same cohort, but with a follow-up of 6 months[16] for 78% pain decrease and 24 months[17] for 61% pain decrease.

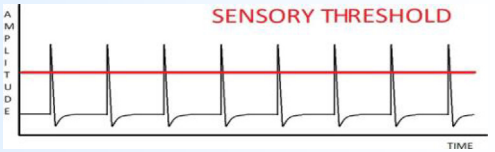
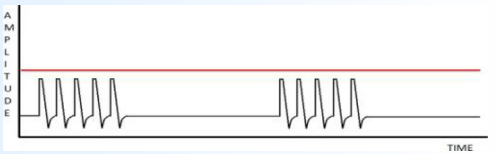
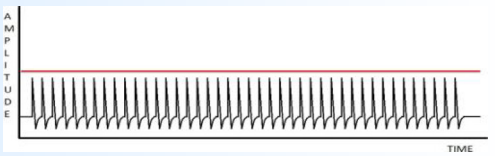
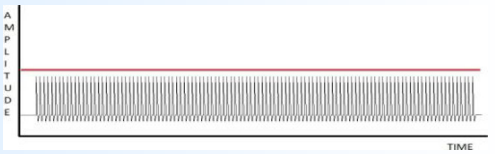
For the general pain (back + leg without distinction), 4 studies[5,8,12,14] were eligible, including data about tonic and HD SCS but none about burst or 10-kHz stimulation (Figure 3). The NPRS or VAS decrease ranged from 37%[8] to 65%.[12] Pain decrease ranged from 37%[7] to 59%[5] for tonic stimulation and from 44%[14] to 65%[12] for HD stimulation. One study[12] about HD stimulation showed a 65% NRPS decrease compared with baseline for patients without any SCS experience, and a 50% NRPS decrease for a cohort of patients previously implanted with a tonic SCS device, who desired to try paresthesia-free stimulation or wanted improvement in pain control.

Statistically Significant Results

We performed a subselection of studies showing a statistical difference for noninferiority or superiority of the 3 paresthesia-free stimulation modes among themselves and regarding CMM, placebo, and tonic stimulation. Statistical difference was assessed by a P value $\leq$0.05 for NPRS or VAS decrease. We ended up with a selection of 18 studies[6-18,20-24] including 681 patients, with a follow-up ranging from 1 week to 24 months (Table 3).

For burst stimulation (Figure 4) regarding limb pain, 3 studies[6,7,9] showed superiority of burst compared with CMM (without SCS). One study[6] showed superiority to placebo and 3 studies[8,20,21] showed superiority to tonic stimulation. For back

Table 1. Summary of the Spinal Cord Stimulation Modalities

Spinal cord Stimulation Modality	Paresthesia	Implanted Pulse Generator Recharge*	Pulse Frequency (Hz)	Pulse Amplitude, mA (V)	Pulse Width (microseconds)	Waveform — Sensory Threshold
Tonic	+	−	40–60	4–9 (0.5–5)	300–500	
Burst	−	++	40 Hz trains of five 1000 Hz spikes	0.05–3.5 (NR)	1000	
High density	−	++	130–1200	1–4 (0.5–4.5)	200–500	
High frequency	−	+++	10,000	1–5 (NR)	>30	

NR, not reported.
*−, recharge free; ++, weekly recharge; +++, daily recharge.

Table 2. Pain Cause in Studies Assessing Spinal Cord Stimulation Waveform Efficacy for Decreasing Leg, Back, and General Pain in Patients with Neuropathic Pain

Team	FBSS (%)	Complex Regional Pain Syndrome (%)	Other Diagnoses (%)
Kumar et al., 2008[4]	100	0	0
Van Buyten et al., 2013[16,*†]	79	No data	Chronic pain without previous surgery: 21
Al Kaisy et al., 2014[17,*†]	79	No data	Chronic pain without previous surgery: 21
De Ridder et al., 2015[8]	No data	No data	Back or limb pain mostly related to FBSS or diabetic neuropathy: 100
Kapural et al., 2016[18]	79	No data	Other: 21
Wille et al., 2016[14]	100	0	0
Provenzano et al., 2017[12]	67	33	0
Provenzano et al., 2017[12,*] (not naive to spinal cord stimulation cohort)	46	46	Neuropathic pain syndrome: 9
Remacle et al., 2017[3]	100	0	0
Muhammad et al., 2017[7] (burst cohort)	100	0	0
Muhammad et al., 2017[7] (high-frequency cohort)	100	0	0
Veizi et al., 2017[5] (classic tonic cohort)	38	6	Chronic spinal pain, 31; radiculopathies, 13; degenerative disc disease, 9; other, 4
Veizi et al., 2017[5] (neural targeting cohort)‡	36	5	Chronic spinal pain,: 34; radiculopathies, 11; degenerative disc disease, 7; other, 8

Pain causes not differentiated between back, leg, or general pain categories in the different studies. Patients' pain diagnosis as referred to the studies shown in **Figures 1–3**.
FBSS, failed back surgery syndrome.
*Some patients in these studies had already experienced spinal cord stimulation (Van Buyten et al.,[16] and Al Kaisy et al.,[17] 15%; Provenzano et al.,[12] 100% in a distinct cohort).
†Some patients in these studies were refractive to Tonic Spinal cord stimulation (Van Buyten et al.,[16] and Al Kaisy et al.,[17] 15%).
‡Tonic stimulation parameters assessed by an anatomically guided neural targeting algorithm.[3]

pain, 2 studies[6,7] showed superiority of burst compared with CMM, 1 study[6] showed superiority of burst compared with placebo, and 3 studies[8,20,21] assessed superiority of burst compared with tonic stimulation, and 2 studies[6,23] showed that burst stimulation is equal to tonic stimulation. One study[22] showed that burst is equal to 10 kHz regarding back pain. For general pain, 3 studies[6,9,20] assessed superiority of burst over CMM, 1 study[10] showed superiority compared with placebo, and 2 studies[8,11] showed superiority of burst over tonic SCS, whereas 1 study[24] showed equality of burst compared with tonic. Although superiority of burst over CMM and placebo is explicit, superiority over tonic is more ambiguous, with 4 studies[8,11,20,21] including 248 patients showing statistical superiority of burst over tonic and 3 studies[6,23,24] including 75 patients showing no statistical difference.

For HD stimulation (**Figure 5**), there were no available data with statistically significant results to assess any statement about limb and back pain NPRS or VAS decrease. Regarding general pain, 1 study[12] showed superiority of HD over CMM. One study[13] showed superiority of HD over tonic stimulation, but in a cohort in whom only 27% of preselected patients were included because they were responders to HD stimulation, with a VAS decrease $\geq$50%. Two studies[14,15] claimed superiority of HD over failed tonic stimulation (defined as a population previously treated with tonic SCS, who initially responded to it, but with recurrent pain or unwanted stimulation that required medical support). The superiority over tonic stimulation is here more doubtful, because 2 studies[24,25] including 98 patients showed no statistical superiority of HD over tonic SCS.

For 10-kHz stimulation (**Figure 6**), regarding limb pain, 3 studies[16-18] showed superiority over CMM and 1 study[18] attested superiority over tonic SCS. Regarding back pain, 4 studies[7,16-18] showed superiority of 10 kHz over CMM and 1 study[18] showed superiority over tonic SCS. There were no statistically significant results about efficacy of 10-kHz stimulation on general pain compared with other SCS waveforms.

Patient Preferences

We selected 9 studies[10,11,20,22-27] dealing with patients' preferences, in which patients were given the opportunity to easily shift from one waveform to another (**Figure 7**) or were assessed to various waveforms then crossed over, with or without a washout period. In 4 of these studies,[11,20,21,23] patients had the opportunity to test tonic and burst stimulation. In 1 study,[25] patients were assessed for tonic and HD stimulation, and in 3 studies,[10,24,26] they were assessed for tonic, burst, and HD stimulation. No study offered the opportunity for patients to switch to 10-kHz stimulation. One reason might be that 10-kHz

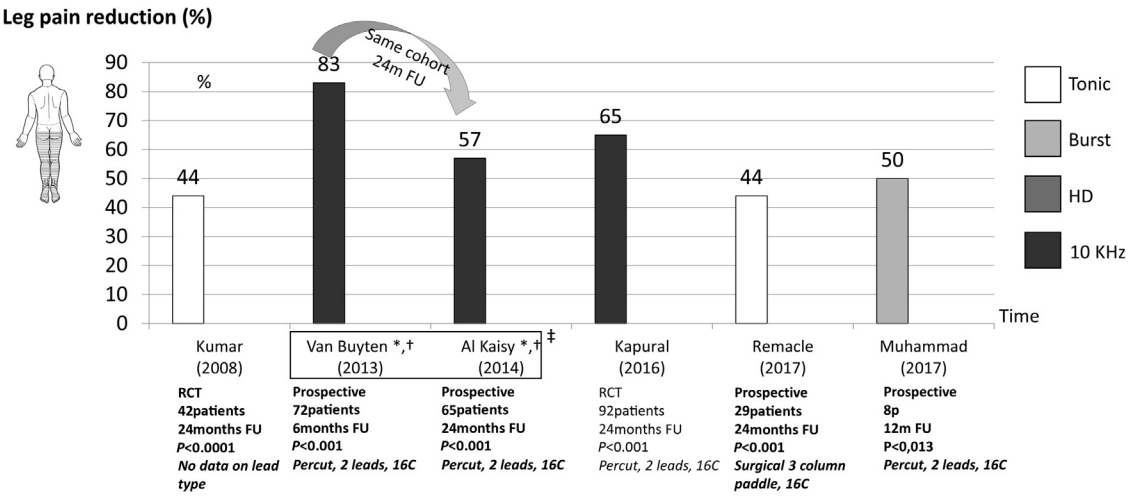


Figure 1. Spinal cord stimulation (SCS) waveform efficacy to decrease limb pain (% numeric pain rating scale or visual analog scale decrease) in patients with neuropathic leg and/or back pain, as a result of multiple diagnosis (see **Table 3**). Exposed studies include a follow-up (FU) time ≥6 months and a *P* value <0.05 for statistical pain decrease compared with no SCS. *Some patients are not naive to SCS (Van Buyten and Al Kaisy, 15%). †Some patients are refractive to tonic SCS (Van Buyten et al.,[16] and Al Kaisy et al.,[17] 15%). ‡Two different studies with the same cohort at different follow-up times. C, electrode contact; HD, high-density; Percut, percutaneous; RCT, randomized controlled trial.

stimulation differs from other modalities because stimulation leads are invariably placed at the T8-T11 level and stimulation parameters are not based on paresthesia mapping. It is therefore more complex for 10-kHz stimulation to be switched to another stimulation waveform with an optimized result.

Analysis of the 4 studies including tonic and burst stimulation[11,20,21,23] showed a vivid preference for burst stimulation. Burst was preferred by 50%–91% of patients, whereas tonic was preferred by 5%–46% patients and 5%–8% had no preference or failed stimulation satisfaction with either of the 2 waveforms.

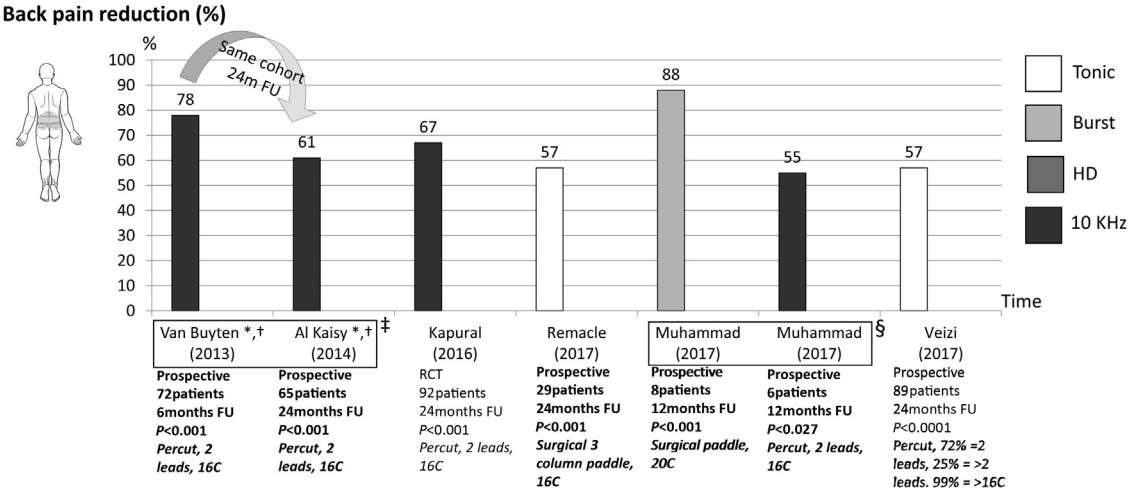


Figure 2. Spinal cord stimulation (SCS) waveform efficacy to decrease back pain (% numeric pain rating scale or visual analog scale decrease) in patients with neuropathic leg and/or back pain, as a result of multiple diagnosis (see **Table 2**). Exposed studies include a follow-up (FU) time ≥6 months and a *P* value <0.05 for statistical pain decrease compared with no SCS. *Some patients are not naive to SCS (Van Buyten and Al Kaisy, 15%). †Some patients are refractive to tonic SCS (Van Buyten et al .,[16] and Al Kaisy et al.,[17] 15%). ‡Two different studies with the same cohort at different follow-up times. §Same study including 2 cohorts: 1 with burst stimulation and 1 with 10-kHz stimulation. C, electrode contact; HD, high-density; Percut, percutaneous; RCT, randomized controlled trial.

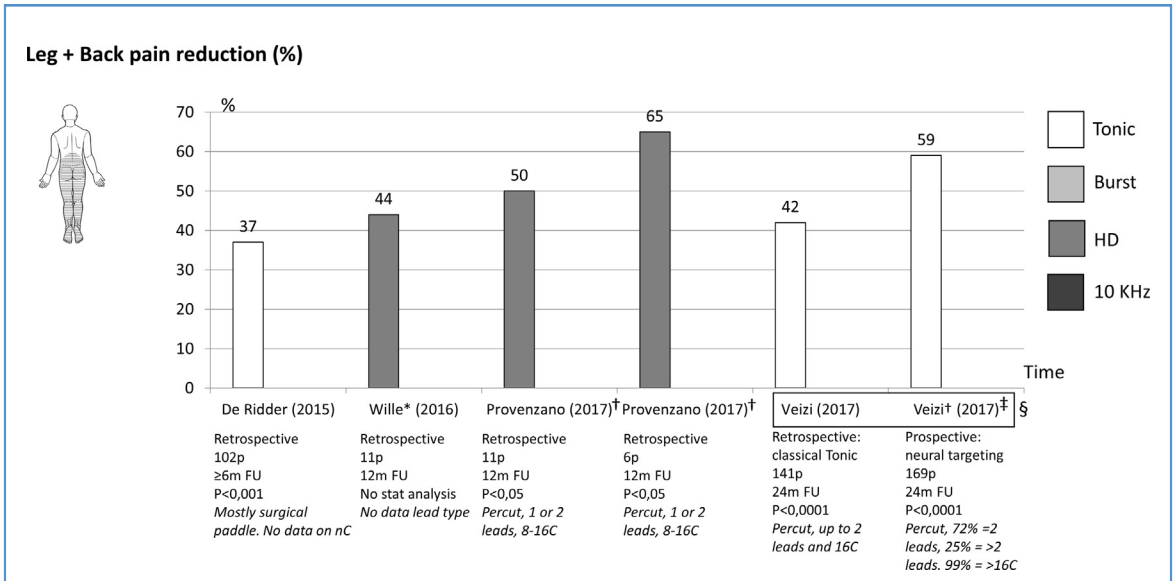


Figure 3. Spinal cord stimulation (SCS) waveform efficacy to decrease general pain (% numeric pain rating scale or visual analog scale decrease) in patients with neuropathic leg and/or back pain, as a result of multiple diagnosis (see Table 3). Exposed studies include a follow-up (FU) time ≥6 months. *100% are refractive to tonic SCS. †100% were previously implanted with a tonic SCS device and wanted an improvement or to experience paresthesia-free SCS. ‡100% were implanted with a tonic SCS device in which programming was performed using a three-dimensional neural targeting algorithm. §Same study with 2 distinct cohorts: 1 retrospective with traditional tonic SCS and 1 prospective with a three-dimensional neural targeting algorithm. C, electrode contact; HD, high-density; Percut, percutaneous; RCT, randomized controlled trial.

One study[25] allocated 70 patients to receive tonic stimulation and 70 patients to receive a ≤1.2-kHz subperception waveform (HD) for 3 months. Patients were then switched to the alternative waveform. When asked, 66% of the patients indicated the subperception waveform as their favorite, but still, if they were given the choice, 62% preferred to keep the 2 options available, to easily switch from one to another to manage their pain. A post hoc analysis showed that offering multiple waveform options provided superior outcomes than did supraperception settings alone (overall responder rate increased by 74%, compared with for supraperception alone).

Three studies[10,24,26] proposed using tonic, burst, or HD stimulation. This situation led to some contradictory results among studies. Schu et al.[10] performed a prospective randomized double-blind placebo-controlled study, with an extremely short follow-up of 1 week, of 20 patients with an FBSS diagnosis. These investigators ended up with an 80% patient preference for burst stimulation, whereas 10% preferred HD and 10% chose tonic stimulation. Berg et al.[26] performed a prospective analysis of 250 patients with various diagnoses, with a follow-up ranging from 1 to 12 months. These investigators reported that 68% of patients preferred tonic or tonic-like (anode intensification) stimulation, whereas 8% preferred HD stimulation, 2% preferred burst stimulation, and 3% had no preference or failed satisfactory pain reduction with any of the SCS waveforms. Of patients, 18% used alternately tonic stimulation with a paresthesia-free waveform pattern, and 1% preferred to use the 2 paresthesia-free waveforms (Burst and HD) alternately, without using tonic stimulation. Duse et al.[24] performed a prospective randomized crossover single-blind study, with 1 week follow-up, of 28 patients with an FBSS diagnosis. These investigators reported that 50% of patients preferred tonic stimulation, whereas 21% preferred burst stimulation, 14% preferred HD stimulation, and 7% had no preference or failed satisfactory pain reduction with any of the SCS waveforms. Of patients, 4% used a mix of tonic and paresthesia-free waveform, and 4% used burst and HD alternately without tonic stimulation.

To assess patients' preferences, in every study but one,[4] patients were asked their preferred stimulation type at the end of the trial. In 1 study,[26] implanted pulse generator use data were collected and analyzed at the end of the trial.

Four studies[11,21,25,26] were industry sponsored. Of these 4 studies, 3 were favorable to the paresthesia-free waveforms provided by the sponsoring industry and 1 showed preference for tonic stimulation. Regarding all 9 studies, 1 of 4 sponsored studies (25%) showed patients' preference for tonic stimulation whereas 2 of 5 independent studies (40%) showed patients' preference for tonic stimulation.

DISCUSSION

Comparison of NPRS or VAS reduction obtained with subperception SCS with tonic stimulation and with CMM alone shows that SCS is superior to CMM alone and that subperception SCS is at least as effective as tonic stimulation. However, those numbers cannot be properly compared to show superiority of one SCS waveform to another, because of cohort and study design heterogeneity. A proper comparison of similar studies and a meta-analysis are not possible, because of the lack of available data.

Table 3. Pain Cause in Spinal Cord Stimulation Studies Reporting Statistically Significant Results for Decrease in Neuropathic Leg and/or Back Pain

Team	FBSS (%)	Complex Regional Pain Syndrome (%)	Other Diagnoses (%)
De Ridder et al., 2013[6]	80	0	Failed neck surgery syndrome, 10; myelomalacia, 10
Van Buyten et al., 2013[16,*†]	79	No data	Chronic pain without previous surgery, 21
De Vos et al., 2013[20]	100	0	0
Al Kaisy et al., 2014[17,*†]	79	No data	Chronic pain without previous surgery, 21
Schu et al., 2014[10]	100	0	0
De Ridder et al., 2015[8]	No data	No data	Back or limb pain mostly related to FBSS or diabetic neuropathy, 100
Kinfe et al., 2015[22]	100	0	0
Sweet et al., 2015[13]	100	0	0
Courtney et al., 2015[21]	32	1	Radiculopathies, 8; others, 26
Wille et al., 2016[14]	55	45	
North et al., 2007[15,†]	45	No data	Degenerative disc disease, 23; other, 32
Kapural et al., 2016[18]	79	No data	Other, 21
Tjepkema-Cloostermans et al., 2016[23,*]	100	0	0
Provenzano et al., 2017[12,*]	53	41	Neuropathic pain syndrome, 6
Deer et al., 2017[11]	42	No data	Radiculopathies, 38; chronic pain nonpostoperative, 9; other, 11
Muhammad et al., 2017[7]	100	0	0
Demartini et al., 2018[9]	57	0	Radiculopathies, 43
Duse et al., 2019[24,*]	100	0	0
North et al., 2020[25,*]	46	17	Radiculopathies, 46; other, 45

Patients' pain diagnosis as referred to the studies shown in **Figures 4–6**.

Pain causes are not differentiated between the back, leg, or general pain categories in the different studies.

FBSS, failed back surgery syndrome.

*Some patients in these studies have already experienced spinal cord stimulation (Van Buyten et al.,[16] and Al Kaisy et al.,[17] 15%; Tjepkema-Cloostermans et al.,[23] 100%; Provenzano et al.,[12] 65%; Duse et al.,[24] 100%; North et al.,[25] 100%).

†Some patients in these studies are refractive to tonic spinal cord stimulation (Van Buyten et al.,[16] and Al Kaisy et al.,[17] 15%; North et al.,[15] 100%).

For this reason, we performed a subselection of studies with a statistical analysis of the results of the 3 paresthesia-free SCS modes among themselves and with tonic stimulation or placebo. This analysis showed that paresthesia-free SCS is superior to CMM and placebo. Paresthesia-free SCS is superior to tonic stimulation in most studies. However, there are not enough data to show statistical superiority of one subperception SCS over another.

An analysis of patient's preference was carried out, with mixed results, with a trend toward subperception SCS, with 6[10,11,20,21,23,25] of 9 studies in favor of subperception SCS whereas 3[24,26,27] of 9 showed patient preference for tonic. This analysis also showed the requirement among patients to use >1 SCS waveform, with a better responder rate among patients able to combine tonic and subperception SCS. One possible bias of this analysis is the high number of sponsored studies in the literature (4 of 9 studies).

CONCLUSIONS

In a selection of studies in which FBSS is the major SCS indication and in which the 4 SCS waveforms are compared with CMM, placebo, and among themselves, SCS is an effective way to decrease neuropathic pain of the limbs and back, with a follow-up ≥12 months. NPRS or VAS percentage reduction stands between 44%[4] and 88%,[7] all pain location and all waveforms included. Leg pain is relieved more by 10-kHz stimulation, with 65%[12] VAS reduction (50%[7] for burst and 44%[4] for tonic; no data for HD). Back pain is helped most by burst, with 88%[7] VAS reduction (67%[18] for 10-kHz and 57%[5] for tonic; no data for HD). General pain is well relieved by HD, with 65%[12] VAS reduction (59%[5] for tonic; no data for burst and high frequency).

In another study selection with FBSS as major SCS indication but without follow-up limitation, the 3 paresthesia-free SCS

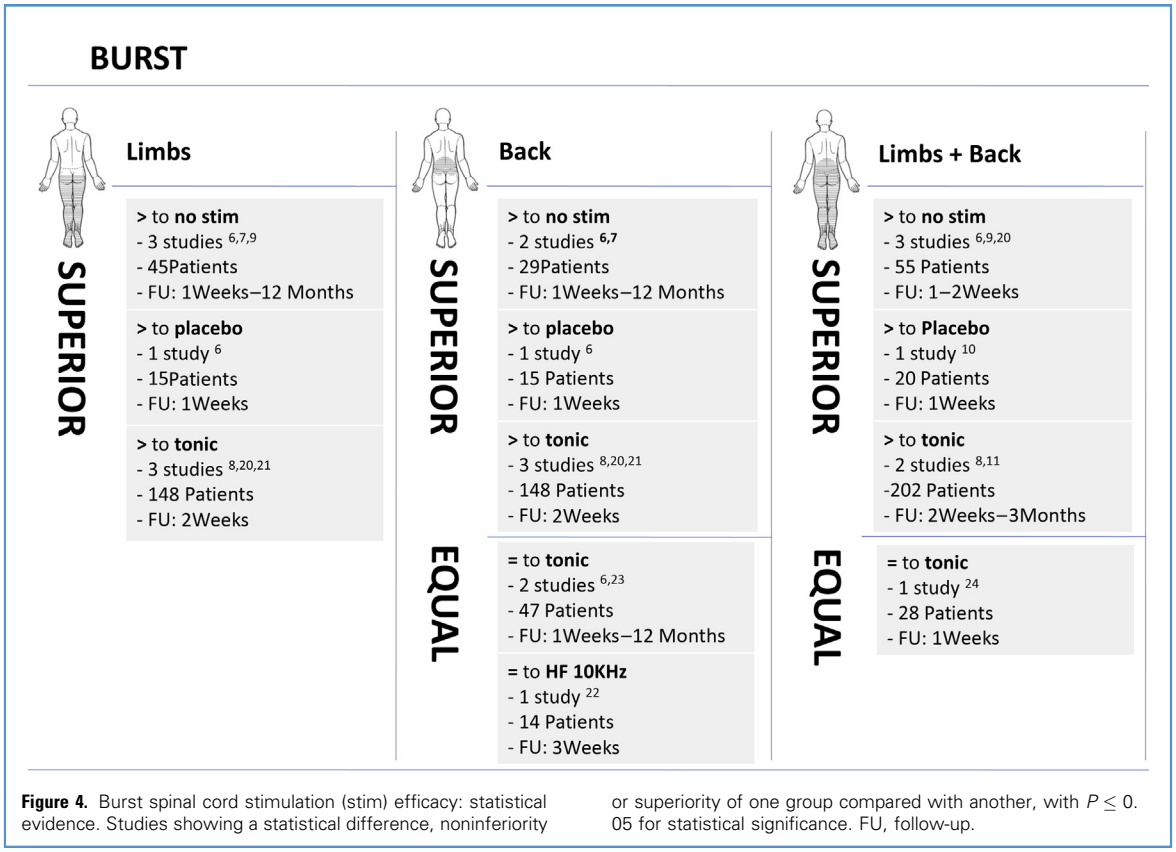


Figure 4. Burst spinal cord stimulation (stim) efficacy: statistical evidence. Studies showing a statistical difference, noninferiority or superiority of one group compared with another, with $P \leq 0.05$ for statistical significance. FU, follow-up.

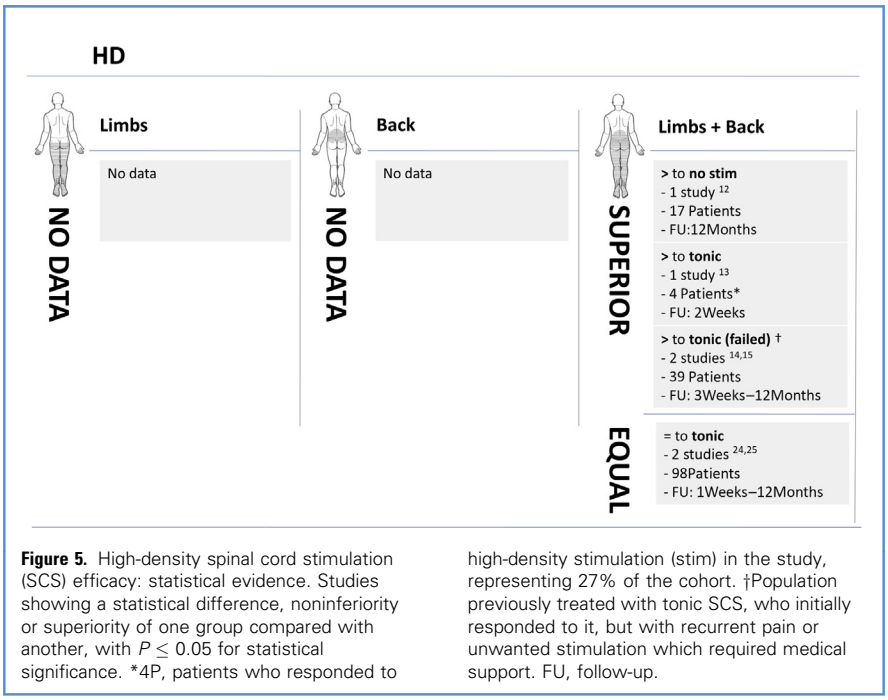


Figure 5. High-density spinal cord stimulation (SCS) efficacy: statistical evidence. Studies showing a statistical difference, noninferiority or superiority of one group compared with another, with $P \leq 0.05$ for statistical significance. *4P, patients who responded to high-density stimulation (stim) in the study, representing 27% of the cohort. †Population previously treated with tonic SCS, who initially responded to it, but with recurrent pain or unwanted stimulation which required medical support. FU, follow-up.

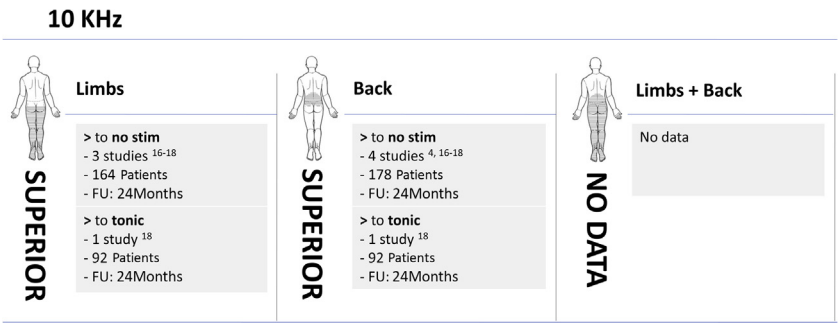


Figure 6. High-frequency spinal cord stimulation (stim) efficacy: statistical evidence. Studies showing a statistical difference, noninferiority or superiority of one group compared with another, with $P \leq 0.05$ for statistical significance. FU, follow-up.

waveforms are univocally statistically superior to CMM and placebo. Nevertheless, even if paresthesia-free SCS is superior to tonic SCS in most cases, some studies[6,23-25] show contradictory results, with no statistical superiority of burst and HD compared with tonic to lower neuropathic pain.

Patients' preferences studies show a clear trend toward paresthesia-free waveforms. When patients are given the opportunity to easily switch from one waveform to another, 8%[24] to 26%[27] of them use >1 waveform during the day. Some patients refractive to tonic SCS can be improved by another SCS waveform and multimodal capable devices should improve the responder rate.

SCS is an efficient tool to decrease limb, back, and general neuropathic pain after FBSS. Most studies show that paresthesia-free SCS is statistically better than tonic SCS in decreasing NPRS or VAS scores and this statement is confirmed by real-life use patterns of SCS waveforms. However, even if 10-kHz SCS superiority over tonic is best assessed by good-quality studies compared with burst and HD, there are not enough data to show a clear trend toward one paresthesia-free waveform over another. More level 1 studies and randomized placebo-controlled trials with standardized inclusion criteria, assessing tools and follow-up, are needed to assess such superiority. Regarding available data, a multimodal capable implanted pulse generator should be proposed to all future

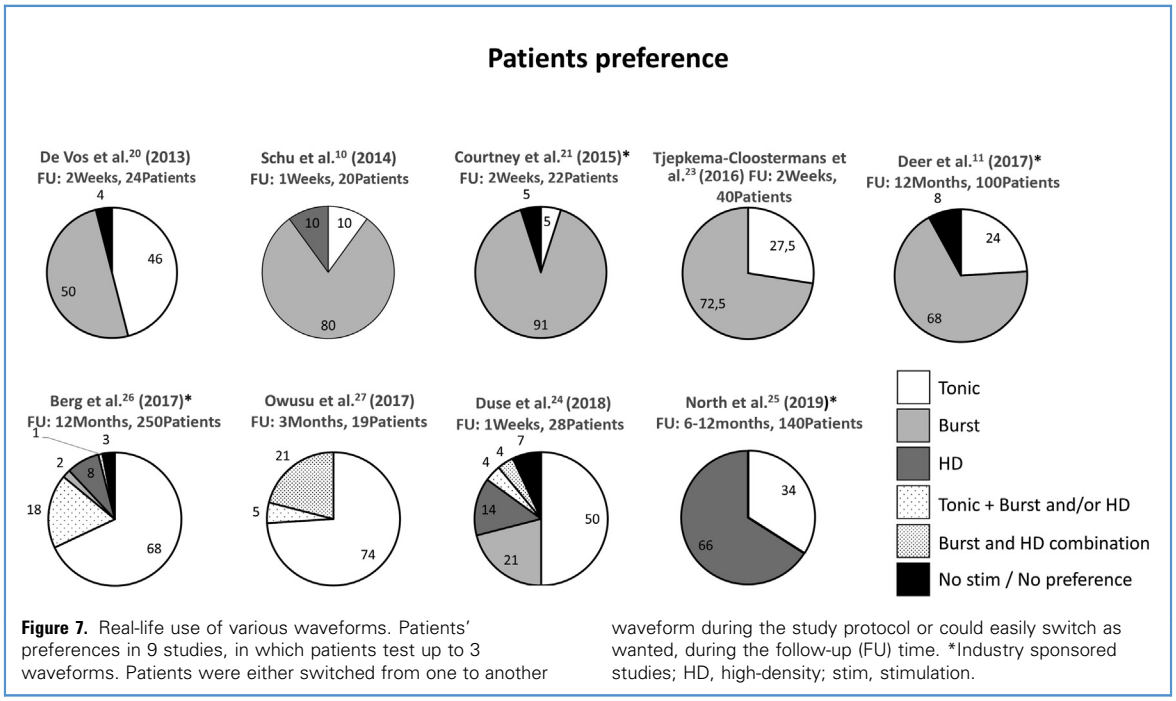


Figure 7. Real-life use of various waveforms. Patients' preferences in 9 studies, in which patients test up to 3 waveforms. Patients were either switched from one to another waveform during the study protocol or could easily switch as wanted, during the follow-up (FU) time. *Industry sponsored studies; HD, high-density; stim, stimulation.

SCS candidates. Long-term effects of high energy delivering modalities on the spinal cord are unknown, and therefore, a precautionary principal approach should motivate us to start with low to moderate energy delivering frequencies, setting aside high energy delivering frequencies for unsatisfactory results only.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Jean-Baptiste Peeters: Conceptualization, Methodology, Investigation, Data curation, Writing - original draft, Validation. **Christian Raftopoulos:** Conceptualization, Methodology, Supervision, Writing - review & editing, Validation.

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Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 16 June 2020; accepted 18 August 2020

Citation: World Neurosurg. (2020). https://doi.org/10.1016/j.wneu.2020.08.128

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