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Prospective Evaluation

Paresthesia-Independence: An Assessment of Technical Factors Related to 10 kHz Paresthesia-Free Spinal Cord Stimulation

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Background: Spinal cord stimulation (SCS) has been successfully used to treat chronic intractable pain for over 40 years. Successful clinical application of SCS is presumed to be generally dependent on maximizing paresthesia-pain overlap; critical to achieving this is positioning of the stimulation field at the physiologic midline. Recently, the necessity of paresthesia for achieving effective relief in SCS has been challenged by the introduction of 10 kHz paresthesia-free stimulation. In a large, prospective, randomized controlled pivotal trial, HF10 therapy was demonstrated to be statistically and clinically superior to paresthesia-based SCS in the treatment of severe chronic low back and leg pain. HF10 therapy, unlike traditional paresthesia-based SCS, requires no paresthesia to be experienced by the patient, nor does it require paresthesia mapping at any point during lead implant or post-operative programming.

Objectives: To determine if pain relief was related to technical factors of paresthesia, we measured and analyzed the paresthesia responses of patients successfully using HF10 therapy.

Study Design: Prospective, multicenter, non-randomized, non-controlled interventional study.

Setting: Outpatient pain clinic at 10 centers across the US and Italy.

Methods: Patients with both back and leg pain already implanted with an HF10 therapy device for up to 24 months were included in this multicenter study. Patients provided pain scores prior to and after using HF10 therapy. Each patient's most efficacious HF10 therapy stimulation program was temporarily modified to a low frequency (LF; 60 Hz), wide pulse width (~470 µs), paresthesia-generating program. On a human body diagram, patients drew the locations of their chronic intractable pain and, with the modified program activated, all regions where they experienced LF paresthesia. Paresthesia and pain drawings were then analyzed to estimate the correlation of pain relief outcomes to overlap of pain by paresthesia, and the mediolateral distribution of paresthesia (as a surrogate of physiologic midline lead positioning).

Results: A total of 61 patients participated across 11 centers. Twenty-eight men and 33 women with a mean age of 56 ± 12 years of age participated in the study. The average duration of implantable pulse generator (IPG) implant was 19 ± 9 months. The average predominant pain score, as measured on a 0 – 10 visual analog scale (VAS), prior to HF10 therapy was 7.8 ± 1.3 and at time of testing was 2.5 ± 2.1, yielding an average pain relief of 70 ± 24%. For all patients, the mean paresthesia coverage of pain was 21 ± 28%, with 43% of patients having zero paresthesia coverage of pain. Analysis revealed no correlation between percentage of LF paresthesia overlap of predominant pain and HF10 therapy efficacy (P = 0.56). Exact mediolateral positioning of the stimulation electrodes was not found to be a statistically significant predictor of pain relief outcomes.

Limitations: Non-randomized/non-controlled study design; short-term evaluation; certain technical factors not investigated.

Conclusion: Both paresthesia concordance with pain and precise midline positioning of the stimulation contacts appear to be inconsequential technical factors for successful HF10 therapy application. These results suggest that HF10 therapy is not only paresthesia-free, but may be paresthesia-independent.

Key words: Spinal cord stimulation, paresthesia, high frequency, 10kHz, pain relief, physiologic midline, paresthesia-free

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For individuals with chronic pain, unrelieved by pharmaceutical, surgical, or other therapeutic methods, spinal cord stimulation (SCS) has offered an effective alternative for pain relief (1-5). Four decades of experience with implantable pulse generators (IPG) delivering low frequency electrical stimulation directly to the nerve fibers in the spine has benefited thousands of people (6-8). Melzack & Wall's Gate Control Theory of 1965 (9) provided a basis for the stimulation strategy in SCS: supra-threshold stimulation of large, myelinated A-beta afferent fiber projections in the dorsal column. Activation of these fibers would, in turn, excite inhibitory interneurons in the dorsal horn through (at least) a monosynaptic connection with local dorsal column collaterals (10). The activated inhibitory interneurons would then pre-synaptically inhibit both small and large fiber connections to pain transmission neurons, thus reducing activity in central pain pathways. Additionally, increased A-beta fiber activity would, through projections to rostral central nuclei in the brainstem, trigger activity in descending circuits, which could further inhibit segmental pain transmission. Inspired by the Gate Control Theory, Shealy et al (11) implanted the first electrodes in humans in 1967, and demonstrated effective pain relief in a small number of patients.

Activation of the particular A-beta fiber collaterals in the dorsal column that communicate with the primary and referred dorsal horn pain circuitry is key to the ostensible pain gating mechanism (12). Thus, the clinical goal of traditional SCS is to induce comfortable paresthesia (defined as any abnormal sensation caused by A-beta stimulation; including what is often perceived by patients as tingling, buzzing, pins and needles, pressure, etc.) that overlaps the existing distribution of pain (13-18). Successful clinical application of SCS has shown to be generally dependent on paresthesia-based outcomes: maximal paresthesia-pain overlap as well as patient acceptance of the induced sensations (16,19,20).

Overlap of pain by paresthesia is dependent upon many factors: patient anatomy, stimulation lead positioning, stimulation program parameters, etc. Certain body regions appear relatively simple to superimpose with paresthesia, while others are more challenging. For example, from a mid- to low-thoracic dorsal epidural position, regions such as the anterior legs and abdomen will frequently be covered by paresthesia, but, due to spinal anatomy and neurophysiology, coverage of the low back is difficult (21,22).

A crucial factor to successful paresthesia targeting is a physiological midline positioning of the stimulation field (23-26). Activation of dorsal root fibers, which can cause uncomfortable, intense segmental sensations, is believed to limit the ability to recruit deeply in the dorsal columns (27). North et al have clinically demonstrated that stimulating contacts positioned precisely on physiologic midline (defined as the mediolateral epidural anatomical position over the dorsal columns which results in left-right balanced body paresthesia) has demonstrated statistically significantly better paresthesia-pain overlap than techniques which generate off-midline stimulation fields (25,28,29).

The sensation of paresthesia is usually well-tolerated by patients, but it can become bothersome or even dysesthetic. Paresthesia can disturb sleep, may be experienced as excessive and uncomfortable, and is sensitive to body position (5,30,31). As a result, stimulator technology has been developed to adapt the paresthesia sensations such that they are less disruptive to the patient experience of paresthesia-based SCS (32,33).

More recently, however, the necessity of paresthesia for achieving effective relief in SCS has been removed by the introduction of 10 kHz paresthesia-free stimulation (34,35). In a large, prospective, randomized controlled pivotal trial, HF10 therapy has been demonstrated to be statistically and clinically superior to paresthesia-based SCS in the treatment of severe chronic low back and leg pain (36,37). This Level 1 evidence was established after prior long-term prospective clinical studies and worldwide clinical experience in thousands of patients had suggested that HF10 therapy provided robust relief of chronic pain (38,39). HF10 therapy, unlike traditional

paresthesia-based SCS, requires no paresthesia to be experienced by the patient, nor does it require paresthesia mapping at any point during lead implant or post-operative programming.

Given the absence of paresthesia in its clinical application, it is not known if HF10 therapy follows the same technical requirements as found historically in traditional, paresthesia-based SCS. Therefore, we measured and analyzed the paresthesia responses of patients successfully using HF10 therapy to determine if 10 kHz paresthesia-free SCS was dependent upon paresthesia-pain overlap and position relative to the physiologic midline.

Methods

Patients

Patients already permanently implanted with a Senza system (Nevro Corp., Redwood City, CA) and receiving HF10 therapy for chronic intractable low back and/or leg pain were enrolled. The system included an IPG and two 8-contact percutaneous leads positioned anatomically at radiographic midline in the dorsal epidural space between the T8-T11 vertebral levels. In the United States, 41 patients already participating in the SENZA-RCT for pain in the trunk and leg (5) were asked if they wanted to participate in this sub-study. Most of the paresthesia measurements were made at the patients' 24-month follow-up visit. In Italy, 20 patients were selected from a single site that was utilizing the Senza system through commercial means to treat back and/or leg pain. These patients were consented to this trial using an ethics committee (St. Chiara Hospital, Pisa, Italy) approved protocol. Paresthesia measurements were made at follow-up visits ranging from 0.25 – 27 months post-IPG implant. Informed consent was obtained on all patients and the study protocol and informed consent forms were approved by each study site's applicable institutional review board.

Pain Relief

Patients provided pain scores using either VAS or verbal numeric rating scale (for any individual patient, the pain score instrument used remained consistent throughout the study) for predominant pain areas. One cohort of patients (N = 20) provided a single pain score for their back and leg pain, whereas the remaining patients (N = 41) provided individual pain scores for back and leg pain. In order to pool the data, in the latter group, the predominant pain region was defined as the region assigned the higher pain score at pre-implant. In 3 of these patients, leg and back pain scores were equal, and so the back region was defined as predominant; this was the more conservative choice in all cases. Scores were obtained at the visit prior to receiving SCS (pre-HF10 therapy) and at the follow-up visit when programming and drawings were obtained (follow-up). Pain relief from pre-HF10 therapy to follow-up was then calculated as 100*(PainScoreBaseline – PainScoreFollow-Up)/PainScoreBaseline.

Pain and Paresthesia Drawings

At follow-up, patients were asked to indicate their favorite/most effective HF10 therapy program. The frequency and pulse width pa-

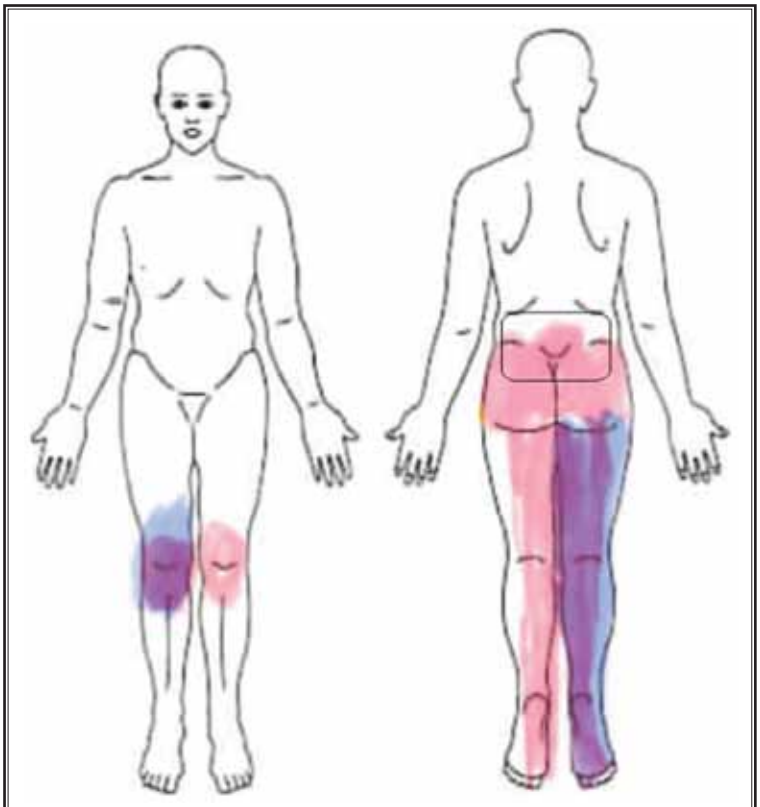

Fig. 1. *Typical body diagram used for pain and paresthesia drawings. Subject 03-112, baseline pain drawing (red) and electronically-superimposed paresthesia drawing (blue) (note: the low back region was not displayed to patients when they drew their pain and paresthesia).*

rameters for this program were then changed to 60 Hz and 467 ± 141 μs, creating a modified program that delivered low frequency (LF) stimulation from sites in the spine where therapeutic HF10 therapy was delivered.

While in a seated position, patients were asked to draw on a commonly used human body diagram printed on paper (Fig. 1) all the regions of pain for which they were using therapeutic SCS. Next, the pulse amplitude of the modified program was increased in 0.1 mA steps to 2 levels: (a) first perception of LF paresthesia, and (b) a drawing threshold (defined in each patient as either 150% of this perception threshold or a maximum comfortable intensity indicated by the patient, whichever was smaller). At the drawing threshold setting, patients were then asked to draw the bodily locations where they experienced LF paresthesia. For patients using multi-area programs, each stimulation area was activated individually and a LF paresthesia drawing was obtained for that area alone.

Analysis

Pain and LF paresthesia drawings were scanned at 300 dpi for each patient. After scanning, all drawings were brought into ImageJ (NIH, Bethesda, MD). At 400x magnification, pain regions, LF paresthesia regions, and overlap were measured by creating closed freeform perimeters surrounding the respective areas; 3 measurements of total pixels contained by each region were made and averaged to form an estimate. For patients using multi-area programs, the paresthesia drawings for all stimulation program areas were first merged before total pixels were measured. Similarly, overlap of LF paresthesia and pain regions was generated by electronically superimposing (as needed; the majority of the drawings collected had pain and paresthesia drawn on separate figures requiring electronic superimposition, though many (43%) drawings did not need electronic image consolidation) the scanned pain and consolidated paresthesia drawings. Overlaid images were co-registered as necessary using rigid translation and elastic registration tools (bUnwarpJ) to correct any offsets or distortion in scanning and to assure body perimeter concordance between drawings. Summary statistics of stimulation current amplitude thresholds were also calculated.

Low back pain is of special interest in SCS, and coverage of this region with LF paresthesia is known to be difficult. As there is no standard definition of the "low back," an aggregate "low back region" was defined based upon several literature sources (22,40-43). The region defined here was bordered rostrally by the bottom of the rib cage, and caudally at the start of the gluteal cleft, centered on the line of the iliac crest, and spreading bilaterally stopping just short of the hips (Fig. 1).

Paresthesia-Pain Overlap

To determine if there was a relationship between LF paresthesia-pain overlap from HF10 therapy stimulation sites and HF10 therapy efficacy, a linear regression analysis (Real Statistics Resource Pack [Release 4.3], Microsoft Excel, Redmond, WA) (44) was performed between estimated LF paresthesia overlap and HF10 therapy pain relief across all patients.

Mediolateral Distribution of Pain and Paresthesia

The laterality of pain and paresthesia was defined by first bisecting the human figure drawing from groin to cranial apex, and counting anterior and posterior pixels on each body side. The percentage of left-side and right-side paresthesia was calculated as %LeftSide = 100*LeftSidePixels/TotalPixels and %RightSide = 100%-%LeftSide, respectively. The mediolateral distribution, or laterality, of the pain and paresthesia was then defined as the larger of %LeftSide and %RightSide. For example, if %LeftSide(Paresthesia) = 73%, then %RightSide(Paresthesia) = 27%, and then the paresthesia laterality = 73%. With this definition, paresthesia laterality of 50% would be balanced paresthesia to both sides of the body, and paresthesia laterality of 100% would be completely unilateral paresthesia.

Results

A total of 61 patients participated across 11 centers. The mean age and gender was 56 ± 12 years and M28/F33, respectively. Patients had been diagnosed with chronic intractable back and/or leg pain for 14 ± 9 years. The average duration of IPG implant was 19.4 ± 8.6 months.

The average predominant pain score prior to HF10 therapy was 7.8 ± 1.3 and at time of testing was 2.5 ± 2.1, yielding an average pain relief of 70 ± 24%.

Stimulation

Over 75% of patients were tested at pulse width of 500 μs, and the mean LF paresthesia perception threshold for this pulse width setting was 2.7 ± 1.4 mA. The ratio between the mean drawing amplitude and the LF perception threshold was 1.3 ± 0.2.

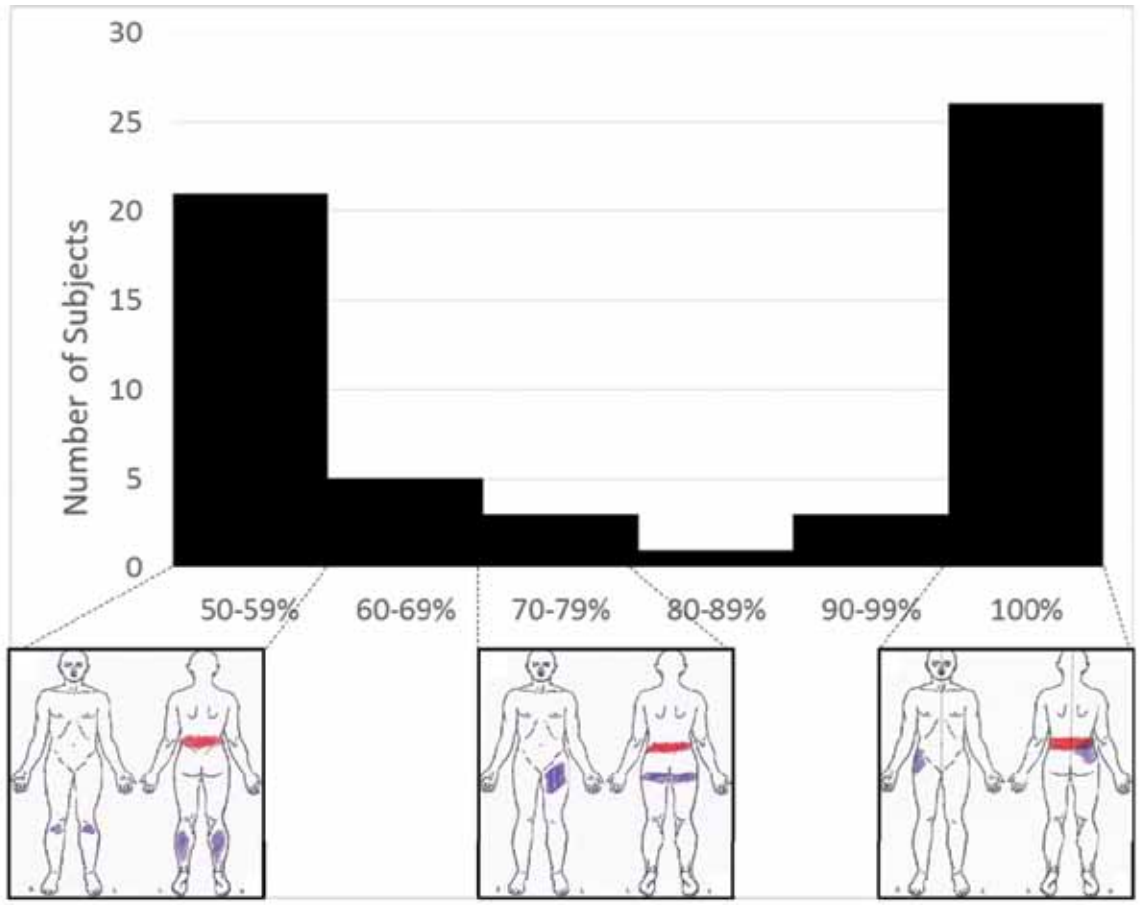

Fig. 2. *Distribution of paresthesia laterality for all patients. The horizontal axis indicates the calculated paresthesia laterality independent of sidedness. Beneath the horizontal axis are shown examples of patient drawings, (where paresthesia drawing is colored blue and pain is colored red) approximately aligned with the axis position of the calculated paresthesia laterality for that drawing: at 50% paresthesia laterality, the far left drawing shows that paresthesia is well-balanced between left and right; the middle drawing shows bilateral posterior paresthesia but asymmetric anterior thigh paresthesia, resulting in a paresthesia laterality of 75%; at the far right, all paresthesia is confined to the right hip, which resulted in a 100% paresthesia laterality.*

Pain and LF Paresthesia Distributions and HF10 Therapy Efficacy

Thirty patients (49%) had "back only" or "back > leg" pain, 12 patients (20%) had "back = leg" pain, and 19 patients (31%) had "leg > back" or "leg only" pain. Ninety-seven percent of patients drew pain regions that included the axial low back region, while only 44% of patients drew any paresthesia in this region. For all patients, the mean paresthesia coverage of all pain was 21 ± 28%, with 43% of patients having zero paresthesia coverage of pain. Patients who did demonstrate paresthesia coverage averaged 36 ± 29% coverage of painful areas.

To explore the relationship between efficacy of HF10 therapy and the mediolateral position of the spinal stimulation site across all patients, summary statistics of the paresthesia laterality were first compiled for all patients. This resulted in a bimodal histogram (Fig. 2), where it was observed that the 2 prominent modes were medial (generally located between 50% and 79% paresthesia laterality) and lateral (located from 80% to 100% paresthesia laterality). Patients were then categorized into these 2 groups and their mean pain relief was compared. Summary statistics of pain relief were then calculated for both groups and compared (Mann-Whitney U, 2-tailed).

From each patient's paresthesia and pain laterality, it was then determined if they had both a side of ma-

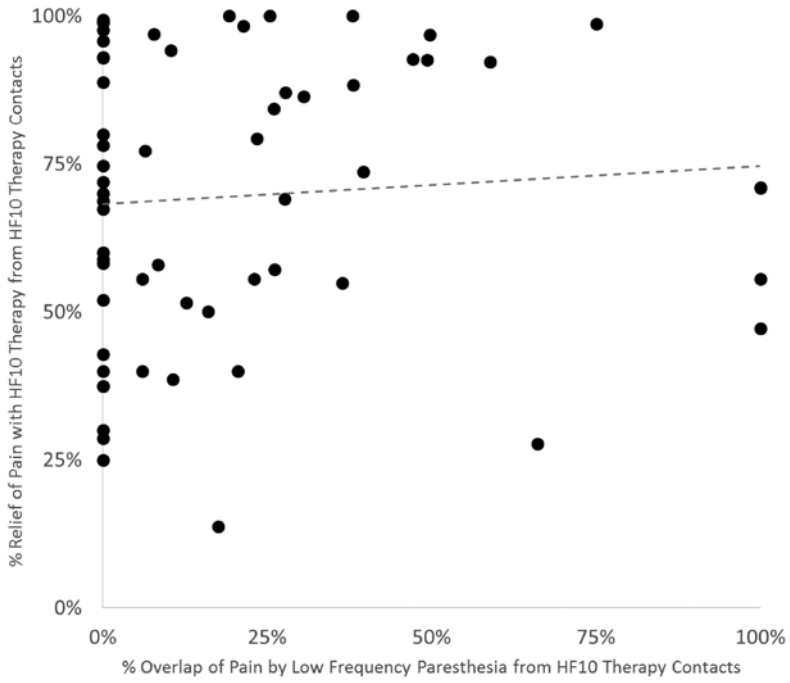

Fig. 3. *Relationship between % low frequency paresthesia overlap of pain regions and HF10 therapy efficacy of predominant pain regions from contacts used for delivery of HF10 SCS. No statistically significant correlation was found between these variables r = 0.08, P = 0.56*

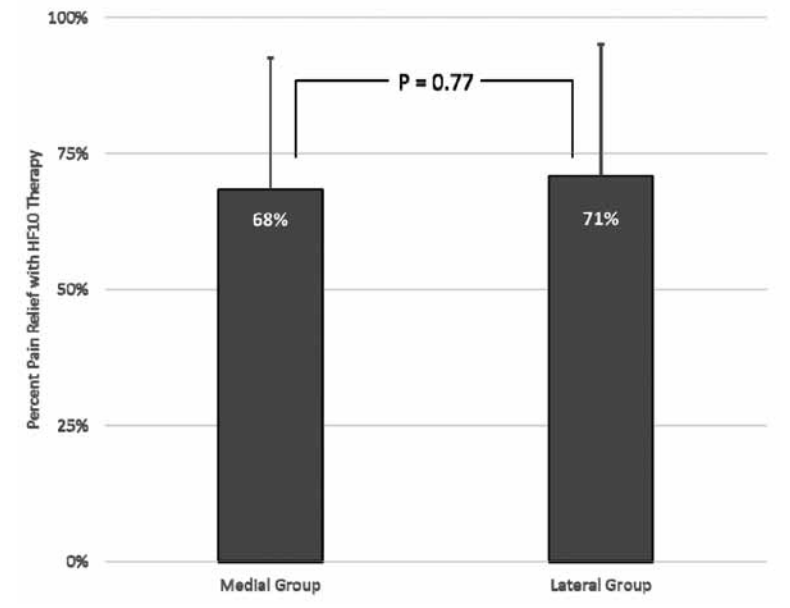

Fig. 4. *Comparison of relief of predominant pain for patients grouped by paresthesia laterality. Pain relief was not significantly different between groups, P = 0.77*

jority pain and a side of majority paresthesia (majority defined as ≥ 55% of total pixel counts). This subset of patients were then categorized into 2 groups: IPSILATERAL: majority pain and majority paresthesia on the same body side; CONTRALATERAL: majority pain and majority paresthesia on opposite body sides. Again, summary statistics of pain relief were then calculated for both of these groups and compared (Mann-Whitney U, 2-tailed).

As shown in Fig. 2, correlation revealed no relationship between % LF paresthesia overlap of predominant pain and HF10 therapy efficacy, r(59) = 0.08, *P* = 0.56.

Mean pain laterality was 70 ± 18% and mean paresthesia laterality was 78 ± 22%. When all patients were divided into those with grossly medial paresthesia and those with lateral paresthesia and their outcomes compared, pain relief was not significantly different (*P* = 0.77) between groups (Fig. 4).

A total of 30 patients (64%) could be categorized into groups of either paresthesia ipsilateral (N = 18) or contralateral to predominant pain (N = 12). The average pain relief in the ipsilateral group was 73 ± 22% and 66 ± 25% in the contralateral group, and these were not statistically significantly different (*P* = 0.48) (Fig. 5).

Discussion

In traditional low frequency SCS, paresthesia is known to be the key technical outcome predictive of pain relief (45). Its importance is such that much of the research and technology development of the last 40+ years of SCS has been focused on improving the control of paresthesia.

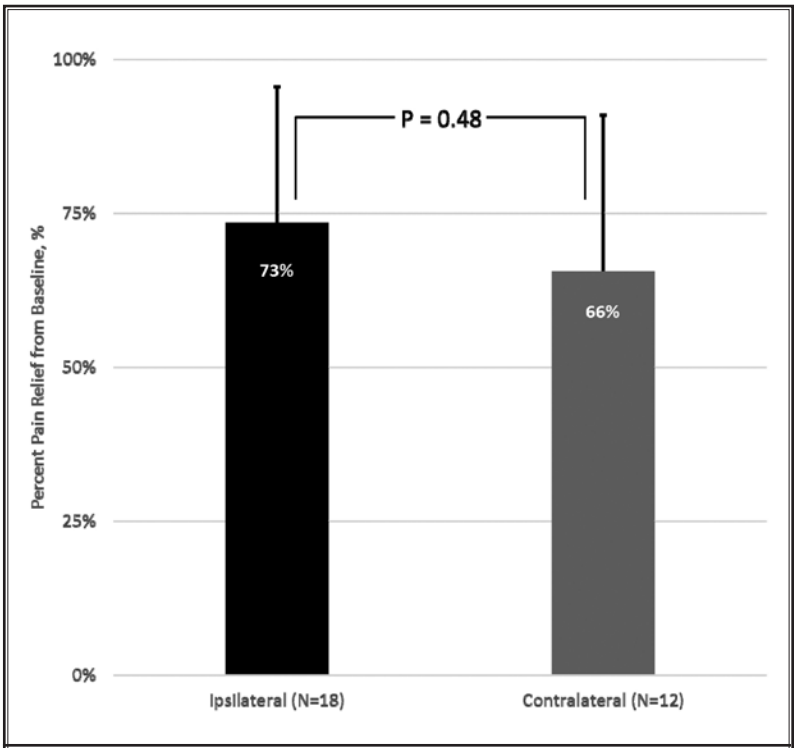

Fig. 5. *Comparison of relief of predominant pain for patients grouped by agreement between majority pain and majority paresthesia. Patients in the ipsilateral group had majority pain and majority paresthesia on the same side of the body. Patients in the contralateral group, who had majority pain on the opposite side of the body as majority paresthesia. The difference in pain relief between the 2 groups was not statistically significant, P = 0.48.*

Research

In the decades following Shealy et al's initial work (11), the nature of paresthesia coverage of pain due to programming, lead placement, lead design, and stimulation technology was investigated. In the 1980s, Law established the value of optimizing the active contact combinations on multiple implanted electrodes when targeting difficult body regions such as the low back (23,46). In the 1990s, Barolat et al (22) created a paresthesia atlas which linked vertebral lead location to the likelihood of paresthesia coverage of particular body areas. In the 2000s, North et al published multiple studies, comparing percutaneous leads to paddle electrodes, single lead vs dual parallel lead implants, as well as demonstrating the efficiencies of patient-interactive programming systems that guided the patient through programming to optimize paresthesia coverage (19,25,42,47-49). And throughout these decades, computational modeling of epidural SCS contributed not only to the understanding of the impact of lead position, contact size, spacing, and orientation on dorsal column activation, but also suggested new lead designs and stimulation architectures that might provide better paresthesia targeting (50-52).

Technology

In response to these technical research findings, many technologies in SCS were introduced with the goal of selectively stimulating the axons in the dorsal column to provide better paresthesia coverage of each patient's pain. In general, this usually resulted in increased complexity, which required ever more sophisticated systems to tractably manage the massive flexibility of programming these new systems. New SCS system features included increased numbers and orientations of stimulating contacts, increased numbers of stimulation channels within the pulse generators, and programming systems that allowed for steering of stimulation current (5,21,53). Other newer technologies attempt to adapt the stimulation programming to better manage the paresthesia. One such system employs an accelerometer in the IPG which, when it detected postural changes by the patient, would alter the stimulation program parameters to maintain a more stable paresthesia intensity (31,54). More recently, the measurement of evoked compound action potentials (ECAPs) from SCS-activated A-beta dorsal column fibers has been used as a surrogate for paresthesia strength. The amplitude of these ECAPs, measured on the implanted SCS electrodes, provides a servo-like feedback variable to the SCS IPG allowing rapid and sophisticated automatic adjustment of stimulation amplitude to hold paresthesia sensation relatively constant during the patient's activities of daily living (33,55).

HF10 therapy, however, uniquely has paresthesia-free SCS labeling approved by the US Food and Drug Administration. Stimulation leads are placed using only fluoroscopic imaging at radiographic midline spanning empirically established vertebral landmarks, depending upon the pain location. As a result, there is no need to wake patients for paresthesia assessments during intraoperative placement. Paresthesia fitting is not

done and there is no concern for coverage of painful areas with a stimulation sensation. To determine best pain relief, a series of programs are stored in the patient's remote control and the patient is guided to attempt each program over several hours to days to assess the degree of pain relief achieved. Throughout all initial stimulation adjustments and regular clinical use, patients using HF10 therapy for back and leg pain never experience a paresthesia (35).

This contrast between the dependence of traditional LF SCS on paresthesia and the frank absence of paresthesia from any aspect of HF10 therapy provided the impetus to study 2 paresthesia-based technical factors in patients receiving HF10 therapy: paresthesia-pain overlap and mediolateral paresthesia distributions (as a marker of contact orientation to physiologic midline).

Paresthesia-Pain Overlap

Across all patients, we observed very little mean paresthesia overlap of pain (21 ± 28%) using LF stimulation from HF10 therapy contacts. Approximately 40% of patients reported zero paresthesia-pain coverage; those who did report overlap had a low mean value (36 ± 29%). This result is consistent with the observation that most (96%) of the patients drew classic bilateral axial back pain patterns, but only 44% drew any paresthesia in the low back region.

Inference from North et al's Fig. 2 suggests that patients having these low levels of overlap in traditional LF SCS would be expected to achieve no greater than 20% – 30% pain relief (perhaps lower, since a meta-analysis of overlap ratings and pain relief suggests that percent pain relief is often less than percent overlap on a numerical basis) (28,29,45,47). However, the mean pain relief for these patients was approximately 70% using HF10 therapy from these same contacts.

Comparison of percent pain relief versus percent LF paresthesia overlap of pain demonstrated no correlation between the variables (Fig. 2). This again stands in contrast to the weak but significant positive correlation observed by North et al (45) in traditional LF SCS over a similar follow-up period.

Mediolateral Distribution of Pain and Paresthesia

Physiological midline positioning of stimulation leads is considered important in the treatment of patients with low back pain (22,42). The primary rationale is that midline positioning enables a maximal penetration depth of the dorsal columns by the stimulation field prior to activation of dorsal roots (27,56). If the dorsal column is maximally recruited, the patient may report very broad areas of paresthesia perceived in their body and this increases the likelihood of covering complex pain distributions.

Our results suggest that at least half of the patients we studied using HF10 therapy had their efficacious stimulating contacts unilaterally positioned. The distribution of paresthesia in Fig. 2 shows that 26 patients had 100% paresthesia laterality, indicating that their LF paresthesia was completely confined to one side of their body, yet 14 of these patients indicated clear bilateral distribution (≤ 75% laterality) of their pain. When we split our studied population into medial and lateral groups based on their LF paresthesia drawings, and compared the pain relief, we observed no significant difference in outcome. Thus, a physiologic midline position of contact positioning for HF10 therapy appears far less critically important than for traditional LF paresthesia-based SCS.

When comparing the outcomes of those patients deemed ipsilateral (majority pain and paresthesia on same side of body) to those grouped as contralateral (majority pain and majority paresthesia on opposite sides of the body), there was still no significant difference in the average pain relief (Fig. 5). However, the contralateral group did appear to have approximately 10% less relief than those in the ipsilateral group, suggesting that leads positioned for HF10 therapy should be positioned near the dorsal midline. However, this conclusion needs to be explored in a larger sample in a prospective manner. For the time being, an anatomic midline placement based solely on intraoperative imaging (which ostensibly achieves this goal) has been demonstrated to be highly adequate in achieving excellent long-term pain relief (37,38).

Limitations

Study Design

This was a prospective, non-randomized, non-controlled interventional study of low frequency paresthesia as a correlate to clinical outcome for HF10 therapy. The stimulation contacts employed were located at spinal sites empirically optimized up to 24-months based upon HF10-induced pain relief. The data and analyses presented here do not definitively rule out the possibility that paresthesia mapping could guide HF10 programming; the results published here may provide preliminary data useful in the design of such a study. Nonetheless, the lack of significant correlation between

paresthesia-pain concordance (including approximately 40% of patients with zero overlap) suggest that paresthesia is not correlated to high-kHz SCS pain relief.

Patient Follow-up

We studied patients over a wide range of post-IPG follow-up times in the group using HF10 in typical clinical practice, while nearly all the patients in the SENZA RCT clinical study were assessed at their 24-month follow-up visit. While this variation is not ideal, other researchers have studied patient groups with even greater variation (19,45). Additionally, there are no published definitive assessments of paresthesia coverage over long-term implant, so the impact of capturing paresthesia at different time periods post-IPG implant is unknown.

Lead Position

We did not capture the vertebral lead position via radiographic imaging at the time of paresthesia drawings. However, knowledge of anatomic lead position is not necessarily a precise indicator of paresthesia distributions (22). This is, in fact, the rationale for intraoperative paresthesia programming in traditional SCS; even after anatomic-based placements, lead position adjustments are typically made based upon verbal patient feedback about paresthesia locations (29). In general, we observed leg, abdomen, and (infrequent) back paresthesia in patient drawings, which suggested that the leads were positioned near the dorsal columns and roots in the low-thoracic region, similar to traditional SCS placements to treat pain in these body areas.

Frequency Effects of Paresthesia Coverage

We used low frequency, high PW stimulation parameter settings to map the paresthesia coverage from the HF10 sweet spot. However, HF10 therapy uses high frequency (10 kHz), with a necessarily low PW (30 us). Thus, it might be argued that the paresthesia patterns could be different with these parameter settings. We did not explicitly test paresthesia patterns using HF10-type parameters, because a PW = 30 us yields paresthesia thresholds that are sometimes higher than the maximum current output of the IPG. However, differences in neural recruitment due to higher frequencies are unlikely, as deeper penetration depth into the dorsal columns (ostensibly leading to more neural recruitment) would not be expected since grey and white matter have fairly constant conductivity over the range of 60 Hz – 10 kHz (57). Additionally, the use of a wider PW (250 – 450 us) for paresthesia mapping may have yielded somewhat different paresthesia maps due to fiber steering with changed PW, but more likely the use of a wider PW for mapping increased the paresthesia coverage that would be expected at PW = 30 us (58, 59). Despite this possibility of overestimated overlap, we observed no significant correlation between paresthesia-pain concordance and HF10 therapy pain relief.

Conclusions

In this investigation, we observed no correlation of LF paresthesia-pain overlap with HF10 therapy efficacy. In addition, we also found that mediolateral LF paresthesia distributions from HF10 therapy contacts did not appear to be related to HF10 therapy efficacy. Taken together, these technical factors of paresthesia coverage and stimulation field alignment with the physiological midline, considered important in traditional, LF, paresthesia-based SCS, appear to be relatively inconsequential for successful HF10 therapy application. These exploratory results suggest that HF10 therapy is not only paresthesia-free, but may be paresthesia-independent.

Disclaimer

The sponsor of the study had full control of the data and performed analysis. The study was sponsored by Nevro Corporation. All physician study authors and all study sites received fair market value payments for actual research work done as per the study agreement and no physician author, center or facility received any other incentive or payment. BG, AAP, and KB are full-time employees of Nevro.

Disclosures

Author Contributions

Protocol was prepared by Mr. Bradley with input from investigators and Nevro clinical engineers. The authors were elected based on their contributions to the study. All investigators were involved in the data collection and execution of the study. Mr. Bradley and Ms. Powell conducted a literature search and wrote the first draft of the manuscript. Mr. Bradley and Ms. Powell analyzed the data and managed the study for the sponsor. The sponsor of the study had full control of the data and performed analysis. All authors provided review of the manuscript for intellectual content. All study authors and all study sites received fair market value payments for actual research work done as per the study agree-

ment and no author, center or facility received any other incentive or payment.

Conflict of Interest

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