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Clinical Study

Pulse Width Programming in Spinal Cord Stimulation: A Clinical Study

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Background: With advances in spinal cord stimulation (SCS) technology, particularly rechargeable implantable, patients are now being offered a wider range of parameters to treat their pain. In particular, pulse width (PW) programming ranges of rechargeable implantable pulse generators now match that of radiofrequency systems (with programmability up to 1000μs). The intent of the present study was to investigate the effects of varying PW in SCS.

Objective: To understand the effects of PW programming in spinal cord stimulation (SCS).

Design: Single-center, prospective, randomized, single-blind evaluation of the technical and clinical outcomes of PW programming.

Setting: Acute, outpatient follow-up.

Methods: Subjects using fully-implanted SCS for > 3 months to treat chronic intractable low back and/or leg pain. Programming of a wide range (50-1000μs) of programmed PW settings using each patient's otherwise unchanged 'walk-in' program.

Outcome Measures: Paresthesia thresholds (perception, maximum comfortable, discomfort), paresthesia coverage and patient choice of tested programs.

Results: We found strength-duration parameters of chronaxie and rheobase to be 295 (242 – 326) μs and 2.5 (1.3 – 3.3) mA, respectively. The median PW of all patients' 'walk-out' programs was 400μs, approximately 48% higher than median chronaxie ($P = 0.01$), suggesting that chronaxie may not relate to patient-preferred stimulation settings. We found that 7/19 patients selected new PW programs, which significantly increased their paresthesia-pain overlap by 56% on average ($P = 0.047$). We estimated that 10/19 patients appeared to have greater paresthesia coverage, and 8/19 patients appeared to display a 'caudal shift' of paresthesia coverage with increased PW.

Limitations: Small number of patients.

Conclusions: Variable PW programming in SCS appears to have clinical value, demonstrated by some patients improving their paresthesia-pain overlap, as well as the ability to increase and even 'steer' paresthesia coverage.

Key words: Spinal cord stimulation, pulse width, paresthesia, dermatome, implantable pulse generator, neurostimulation, chronic pain, neuropathic, dorsal column, dorsal root, chronaxie.

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In 1965, Melzack and Wall proposed the gate control theory of pain, which paved the way for Shealy et al to introduce spinal cord stimulation (SCS) as a treatment for chronic neuropathic pain in 1967 (1,2). Over the past 4 decades, improvements have been made in both the clinical and technical aspects of SCS, including patient screening and follow-ups, and equipment design and functionality (3). With advances in technology, SCS has evolved from bulky single-channel external devices to small, programmable, fully-implantable multi-contact systems (4). Before fully-implantable systems became the primary method of SCS, radio frequency (RF) systems were commonly used. RF systems consist

of an implanted receiver that communicates with a transmitter worn outside the body (5). These systems had the disadvantage of requiring cumbersome external equipment, but they possessed easily-replaceable battery power to allow for higher stimulation energy requirements. When fully-implantable primary cell stimulators (which included an internal, non-rechargeable battery) became the predominant device type used for SCS, concerns for battery life were heightened because the stimulator power source was now implanted and replacement required surgery (6). In these primary-cell devices, lower stimulation rate and pulse width (PW) values became standard.

However, some published reports suggested that there was therapeutic value to having higher parameter ranges than were available on previous primary cell IPGs. In the case of stimulation rate, higher values available only on RF devices at the time were implicated in 'rescued' therapy, where pain relief was recovered in regions of concordant paresthesia only when the rate was increased above 250 Hz in some 15% of implanted patients (7). In addition, longer PWs have been anecdotally described as achieving better pain-paresthesia overlap and comfort for the patient, thus potentially more effective at relieving pain (8). Gould and Bradley reported in a retrospective analysis of patient-preferred programs that over 50% of the programs used PWs in excess of 450μs (9).

Although PW is mentioned in many SCS investigations, it has been the primary focus of very few studies. Several decades ago, research was conducted into the technical aspects of SCS, including PW. In a study of SCS in multiple sclerosis patients, Jobling showed that different patients required widely varying amplitudes of stimulation, and concluded that 200μs was the optimum pulse duration, because it was the most energy-efficient (10). In 1980, Davis and Gray concurred that 200μs was the preferred PW to deliver adequate amplitude while conserving energy (11). However, the introduction and widespread adoption of rechargeable IPGs for SCS has diminished the importance of energy-efficient programming to prolong time between revision surgeries. Investigation into the clinical and technical effects of PWs may be important in the continued effort to more fully understand the mechanisms of SCS. In other neurostimulation applications, varied PW has been shown to provide large and small fiber neural selectivity, where shorter PWs maximized the difference between large and small fiber thresholds (12).

With advances in SCS technology, particularly rechargeable IPGs, patients are now being offered a wider range of parameters to treat their pain. In particular, PW programming ranges of rechargeable IPG's now match that of RF systems (with programmability up to 1000μs) (13). The intent of the present study was to investigate the effects of varying PW in SCS.

Objectives

Using a single-blinded, prospective clinical approach, our objective was to better understand the effect of PW programming in SCS upon technical (strength-duration threshold parameters, paresthesia coverage) and clinical (patient choice of PW setting) outcomes for patients with chronic low back and/or leg pain and fully-implanted stimulation systems.

Methods

Screening and Enrollment

Patients already implanted with the Boston Scientific Precision SCS device and 1 or 2 mid-thoracic (T7-T9) leads were screened for inclusion and exclusion criteria (see below) and those that met the necessary criteria underwent the informed consent process. Upon enrollment, subjects were scheduled for the protocol testing.

Inclusion Criteria:

- Have chronic low back pain following spine surgery (e.g., Failed Back Surgery Syndrome).
- Have been permanently implanted with a Precision SCS system within the last 6 months, or be an appropriate candidate for SCS and for the surgical procedures required for SCS as determined by the physician and have independently selected SCS with Precision for treatment.
- Be 18 years of age or older.
- Be willing and able to comply with all study related procedures and visits.
- Be capable of reading and understanding patient information materials and giving written informed consent.

Exclusion Criteria:

- Have any significant medical condition that is likely to interfere with study procedures or likely to confound evaluation of study endpoints. For example, the inability for a subject to draw on the pen tablet used to capture the paresthesia drawings due

to upper extremity weakness of the writing hand would be considered an exclusion. Another example of such an exclusion would be a subject's inability to verbally communicate the perception of paresthesia, due to a speech impairment from a stroke.

- Have any other chronic pain condition likely to confound evaluation of study endpoints. An example of this exclusion might be a subject with a demyelinating condition that would result in the intermittency of paresthesia perception, despite a constant delivery of SCS.

Pulse Width Testing

At presentation, the subject's self-identified favorite existing program ('walk-in' program) was recorded including PW, amplitude, rate, and contact combination, where 'favorite' was defined as either most-used in past month or best at covering painful area. VAS pain rating was recorded with the 'walk-in' program off and on. The subject was also asked to "paint" their painful areas on a human figure with a stylus on a tablet PC.

The subject was told that a number of stimulation settings were going to be programmed into their stimulator. The subject was not told that the PW of their stimulator program was being modified, nor was any subject aware of the actual PW values during testing. The subject was told that if they preferred any of the programmed settings, that setting's index would be noted and following the testing the subject could opt to have those settings saved into their stimulator. Eleven PW settings were programmed during the course of the study: 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, and 1000μs. To minimize potential sequence bias, PW testing order was randomized for each subject.

The anode-cathode combination and stimulation frequency of each subject's walk-in program were held constant throughout the experiment. For each PW setting, the following protocol was used: stimulation was turned off and the PW was programmed at zero amplitude. To obtain an accurate measure of perception threshold, a modified 'method of limits' technique was used: the amplitude was increased slowly from zero mA until the subject reported first perception of paresthesia and that amplitude was recorded as P1 (14). Stimulation amplitude was decreased slowly until the subject reported a complete loss of paresthesia. This was recorded as P2. The amplitude was then increased until first perception and that was recorded as P3. The subject was then asked to paint all areas of paresthesia on the human figure with the stylus on the tablet PC. Stimulation amplitude was then increased from perception threshold until the subject reported discomfort and that amplitude was recorded as the discomfort threshold (M). Immediately, the amplitude was decreased until the subject reported that it was at a maximum comfortable level (M-). At M- the subject was given the tablet to draw the extent of paresthesia on the human figure on the tablet PC. The amplitude was returned to zero and the next PW was programmed. Approximately 1 minute of 'no stimulation' was administered between PW settings.

All pain and paresthesia drawings were captured on a Toshiba Portege M500 tablet PC running Windows XP. Open-source image analysis software (The Gimp, GNU) was used for the 'paint' application to capture subject drawings. A template of the anterior and posterior aspects of a human was used as the background image for all subject drawings.

After testing all PWs the subject was given the opportunity to choose a favorite PW value from among those tested to be saved into their stimulator. If the subject chose a new PW from among those tested, then that setting was defined for the 'walk-out' program for that subject. If no new PW setting was chosen, then, for the purposes of our analysis, the PW setting for the 'walk-out' program was the 'walk-in' value.

Data Analysis

Strength-Duration Curves

To determine the composite strength-duration curve for each subject, the relationship between perception threshold and PW was plotted. Perception threshold amplitudes acquired using the method of limits were averaged to yield Pav. The Lapicque curve-fit method was used to generate a strength-duration (SD) curve for each subject (15). That technique includes plotting pulsatile charge (PW*Pulse Amplitude) versus duration (PW) and applying a linear curve fit (16). The slope of the linear fit is the rheobase current in mA and the y-intercept is rheobase*chronaxie. Dividing the y-intercept by the slope yields the chronaxie in μs. Using the linear-fit-derived chronaxie and rheobase, curve-fit versions of the SD curve were generated and generally showed good agreement with the raw data SD curves.

Image Processing

To analyze the amount and location of paresthesia that could be generated at each PW, we processed the

drawings made at M-, which likely represented a typical patient-use amplitude setting. From the M- drawing at each PW, the background template image was removed leaving only the foreground drawing (i.e., the actual 'painting' that the subject drew over the background template). Those data were exported to individual JPEG images using standard image compression rates. To determine the distribution of paresthesia by dermatomal segments, the background image was manually segmented according to a single dermatome standard (C2 through S5) and each dermatome image was exported as a JPEG mask (17).

All regions and dermatome images were imported into the Matlab software environment (The Mathworks, v.R13, Natick, MA), converted to binary masks and saved to disk. A custom graphical user interface developed using Matlab's GUIDE UI development tool was written to aid in the analysis of the subject drawings. Features included image import, binary morphological operations, color thresholding, filtering, and image spatial segmentation with pixel counting according to body regions and dermatomes. The images were imported into the UI and preprocessing was applied as necessary, including image registration and binary morphological operations (multiple dilations followed by an equal number of erosions) to correct for intra-subject variability in painting technique. The registered and corrected images were segmented according to dermatomes and body region masks. The number of pixels in each dermatome and body region was summed and written to file.

Pain-Paresthesia Overlap

Paresthesia overlap with each subject's pain was calculated by first calculating the total number and location of pixels in each subject's pain drawing. Then, paresthesia pixels concordant with pain pixels were summed and divided by total pain pixels. This gave the percentage overlap of paresthesia with pain. These calculations were used in comparisons of walk-in and walk-out PW programs.

Total Paresthesia Coverage

Total paresthesia coverage was calculated by summing the number of pixels in all dermatomes for each PW setting. To assess the paresthesia coverage as a function of PW across subjects, the total paresthesia coverage at each PW was normalized for each subject as follows. It was assumed that the maximum paresthesia coverage would be achieved at the highest PW settings, so the number of coverage pixels for the 800, 900, and 1000μs settings were averaged to form the normalizing factor. Then, the total coverage pixels at each PW setting was divided by the normalizing factor for each subject. This normalized data was combined for all subjects and used for across-subject analyses. Linear regression (http://www.statistixl.com) was used to assess changes in total paresthesia coverage with PW.

Paresthesia Coverage by Dermatome

In addition to total paresthesia coverage, the distribution of the paresthesia across dermatomes at each PW was investigated. The outcome of this analysis was paresthesia 'dermatomal focus' defined as the median of the plot of normalized pixels-per-dermatome versus dermatome index (e.g., T11, T12, L1, etc). The pixels in each dermatome drawn by the subject were collected into a histogram of pixels per dermatome. The amount of coverage of that dermatome was then normalized by the total number of pixels in that particular dermatome. Then, the median of each normalized distribution became the 'dermatomal focus' for that PW setting. A graphical example of this analysis technique is shown in Fig. 1.

To allow for fractional dermatomal focus values, the dermatomes were converted to indices from 1 (at C2) to 29 (at S5). For example, dermatomal index 20.3 is 30% between L1 and L2, e.g., L1.3. To assess the change in dermatomal focus of the paresthesia across subjects, regression was performed.

Statistics

Given the relatively small number of patients, and the generally non-linear and asymmetric distributions of the variables, non-parametric measures and tests were used. Unless otherwise indicated, data are shown as median (25% quartile – 75% quartile). Two-group comparisons were performed using a non-parametric test (Mann-Whitney, Wilcoxon paired-sample). For linear regression analyses, variables appearing to have a logarithmic/exponential relationship were transformed prior to regression (18). A p-value of < 0.05 was considered significant.

Results

Subjects

Twenty-two subjects provided informed consent. After initial testing, it was determined that one subject (Pt14) was inappropriate for participation (challenged communication about paresthesia intensity and loca-

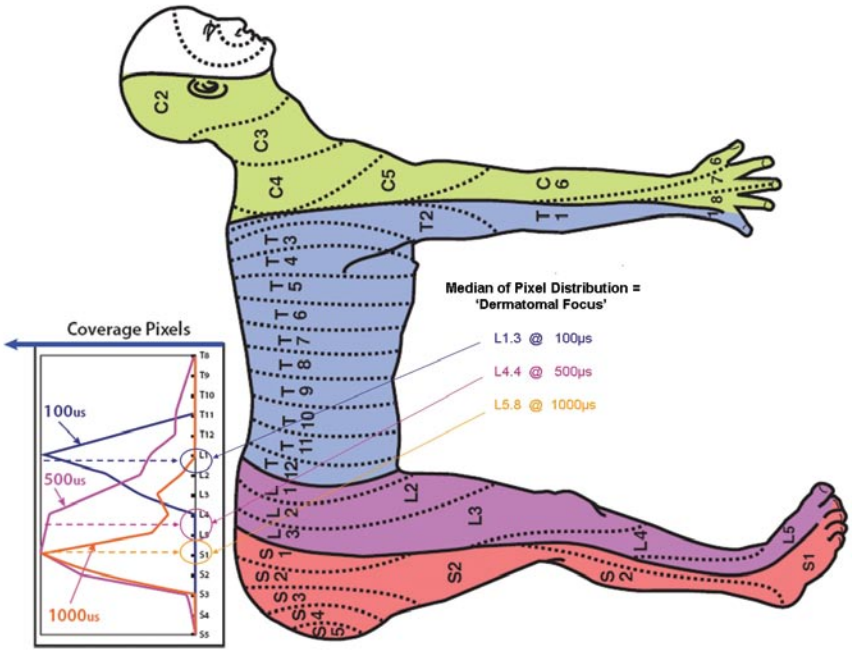

Fig. 1. *Cartoon of Histogram Analysis of Paresthesia Coverage by Dermatome. At each PW setting, a histogram was created of the normalized number of pixels in each dermatome. The median was calculated from each histogram to characterize the 'dermatomal focus.'*

Table 1. *Demographic Statistics of Enrolled Subjects*

Number Tested	19
Gender	11M / 8F
Age	53 (46 – 57) years
Diagnoses (in order of prevalence among enrolled subjects)	Neuropathy/radiculopathy, post-surgical neuropathy (laminectomy, decompression), CRPS
Pain Location	Primary bilateral lower extremity, secondary back pain
Time Since Implant	2.3 (1.3 – 5.1) months

Median (25th –75th quantities)

tion) and this subject was withdrawn prior to completion of testing. Two other subjects rendered consent but were no-shows and were not rescheduled due to logistical reasons. Nineteen subjects fully completed the protocol testing. At the close of the study, it was determined that 4 subjects did not meet a specific inclusion criteria (they had been implanted > 6 months prior to enrollment). Removal of the data from these 4 subjects did not change the gross proportions or the statistical conclusions of the major analysis variables. Therefore, this deviation was not seen as limiting to the goals of the study and data from these subjects was included in the final analysis. Table 1 summarizes the gender, age, diagnosis, location of pain, and time-since-implant of the subjects.

Strength-Duration Parameters

The median Perception threshold strength-duration curve, along with individual curves for all 19 subjects is shown in Fig. 2. The chronaxie and rheobase of all subjects is shown in Table 2. From the plot, it can be seen that 4 subjects Perception threshold exceeded 20mA at 50µs. The chronaxie estimate using the Maximum Comfortable threshold, while trending lower, was not significantly different than the chronaxie estimate using the Perception threshold.

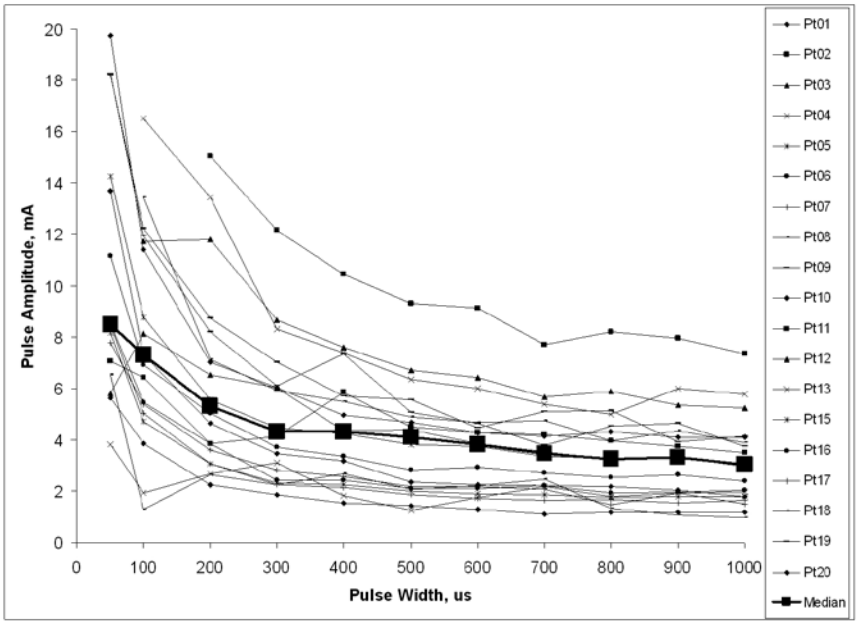

Fig. 2. *Perception threshold strength-duration curves for all subjects.*

Table 2. *Chronaxie and rheobase for perception and maximum comfortable thresholds.*

	At Perception Threshold	At Maximum Comfortable Threshold
Chronaxie	295 μs (242-326)	240 μs (217-284)
Rheobase	2.5mA (1.3 – 3.3)	4.8mA (2.3 – 7.2)

Median (25th –75th quantities)

Patient-Selected Pulse Width

Seven of the 19 tested subjects chose a 'best' PW setting from the applied PW values. The median value of the newly-chosen 'best' PW was 500μs, though this increase from walk-in program was not statistically significant ($P = 0.30$). Across all subjects, the PW testing resulted in a non-significant ($P = 0.49$) median increase of PW setting in the favorite walk-in program, from 350μs (240-470) to 400μs (240-525). The walk-in/walk-out PW values for all subjects are shown in Fig. 3 below.

In order to determine if those subjects who chose a new PW achieved better paresthesia-pain overlap with the new setting, we compared the paresthesia-pain overlap for their 'walk-in' versus 'walk-out' programs. There was no significant difference ($P = 0.86$) in paresthesia concordance using the 'walk-in' program between subjects who chose a new PW and those who did not. Still, subjects who chose a new PW obtained a significant ($P = 0.047$) 56% (14 – 89%) increase in paresthesia pain overlap, from 27% (23 – 60%) to 48% (41 – 81%) (Fig. 4).

Total Paresthesia Coverage

The variation in total paresthesia coverage with PW is shown in Fig. 5. It can be seen that across all subjects, there was a significant, logarithmic increase in paresthesia coverage with increasing PW ($P < 0.001$).

We noted that the response to PW in some of the subjects was clearly an increasing function (Fig. 6a) of paresthesia with PW, where in others there appeared to be less change (Fig. 6b) as the PW was increased. We therefore established arbitrary criteria for a 'growth responder' by artificially dividing the subjects into two groups based upon the slope of their total paresthesia coverage with PW: if they had a slope greater than the mean population slope, they were a 'growth responder'; if the slope was less than the mean population slope, they were categorized as a 'growth non-responder.' Per this criterion, 10 of the 19 tested subjects were growth responders. Figure 7 shows the different curves for these 2 subject sets.

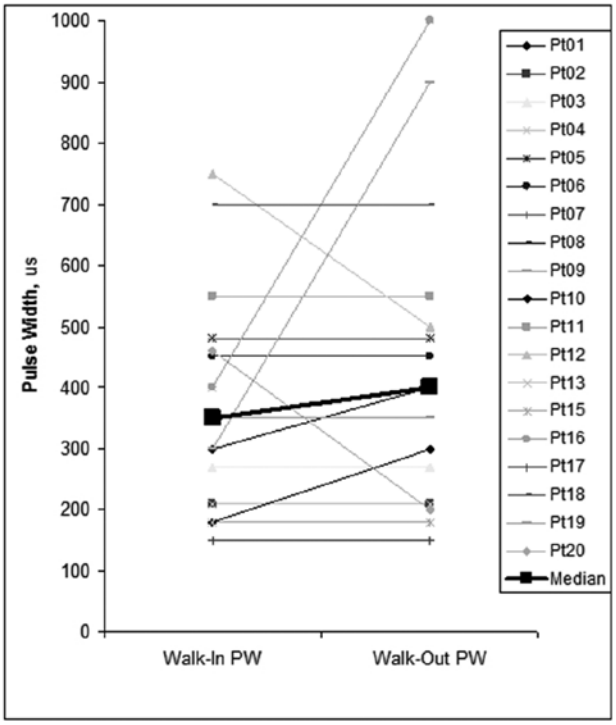

Fig. 3. *Change in PW Settings for Favorite Walk-In Program, All Subjects*

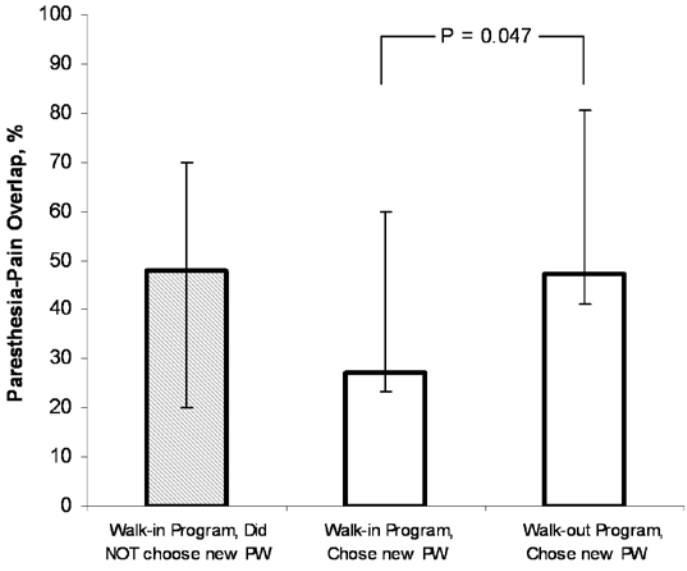

Fig. 4. *Paresthesia-Pain Overlap Ratings for All Subjects. Data is median, error bars are 25% and 75% quartiles.*

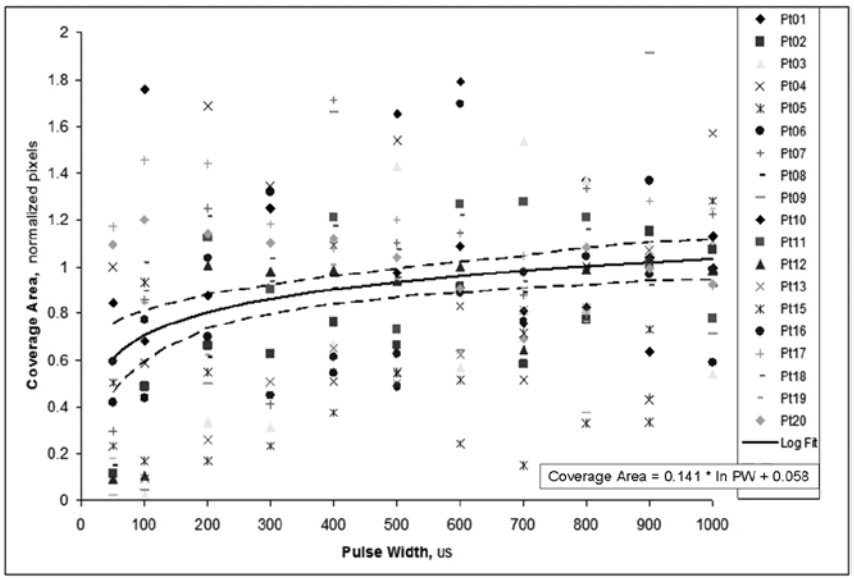

Fig. 5. *Increase in Paresthesia Coverage with PW across Subjects. Significant trend shown as log regression fit with ± 95% confidence intervals.*

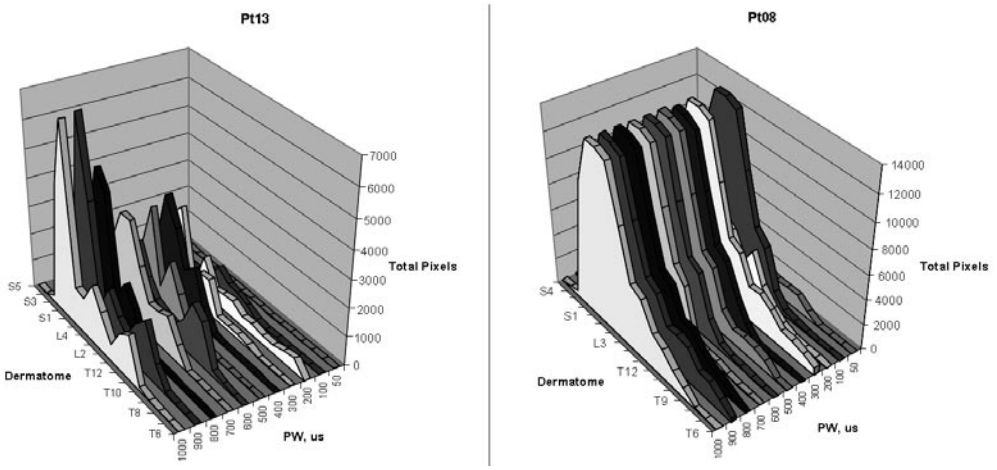

Fig. 6. *Total paresthesia coverage: Pt13: (left chart) paresthesia 'growth responder' showing increase of total coverage with increasing PW. Pt08: (right chart) paresthesia 'growth non-responder' showing little/no paresthesia coverage growth with increasing PW.*

Paresthesia Coverage by Dermatome

The variation in the dermatome focus of the paresthesia with PW is shown in Figure 8. It can be seen that across all subjects, there is a significant caudal shift in the dermatomal "focus" of paresthesia coverage with increasing PW ($P < 0.001$).

As some subjects demonstrated a distinct shift of the paresthesia dermatomal focus with PW (Fig. 9), we performed a similar artificial division of subjects into 'shift responders' and 'shift non-responders.' To identify a shift responder, we established a slope threshold for the paresthesia dermatome focus data (the slope was based upon a regression fit to the transformed data for each subject, where the linearizing transform was

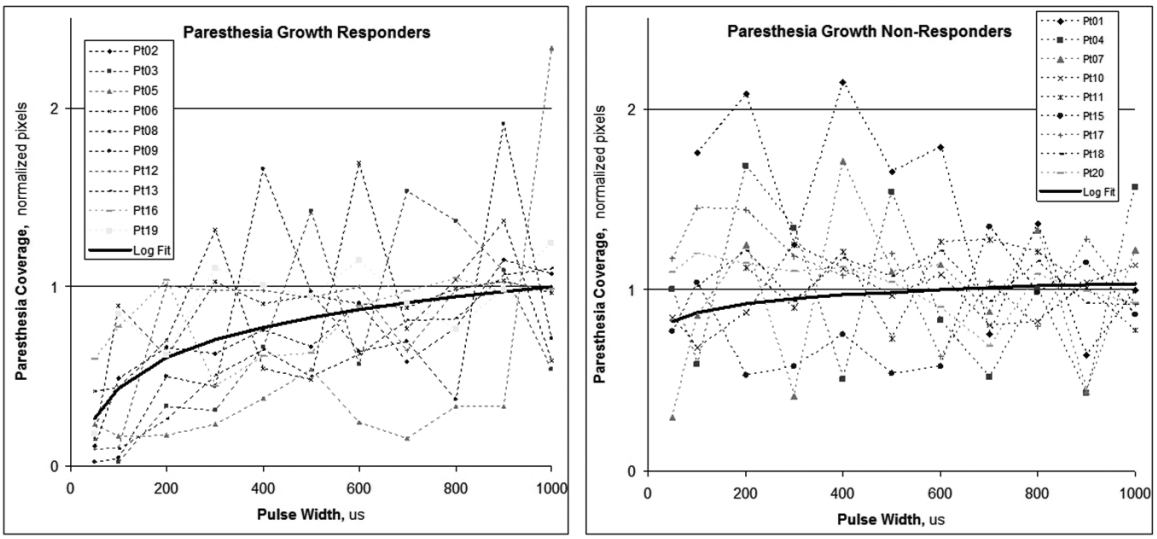

Fig. 7. Change in total paresthesia coverage with PW: Growth Responders (left chart) and Growth Non-Responders (right chart).

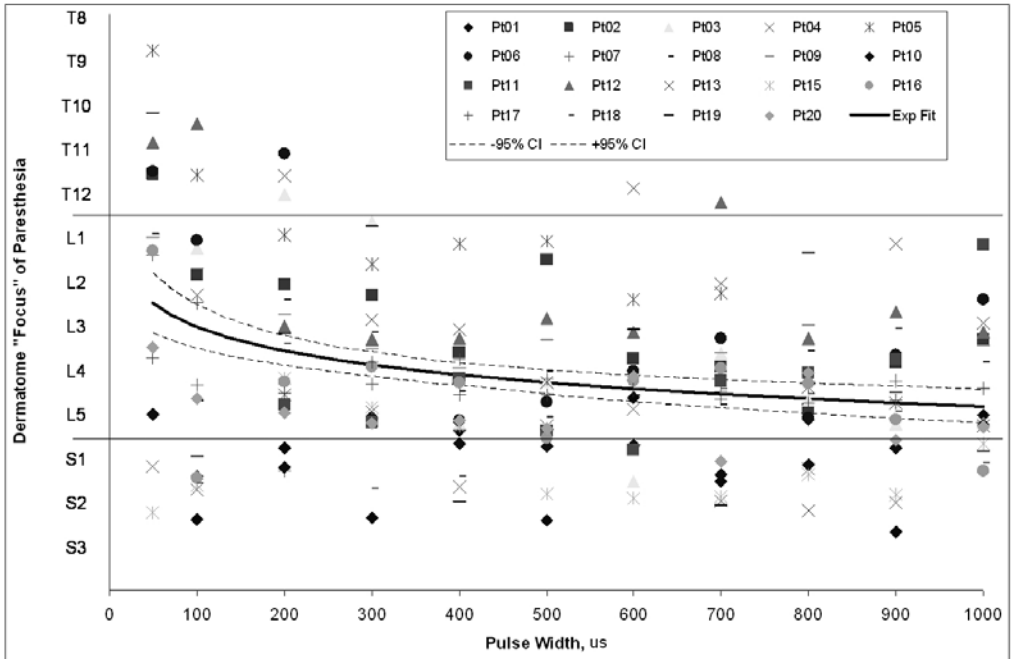

Fig. 8. *Shift of Paresthesia "Focus" with PW across Subjects. Significant trend shown as decaying exponential regression fit with ± 95% confidence intervals.*

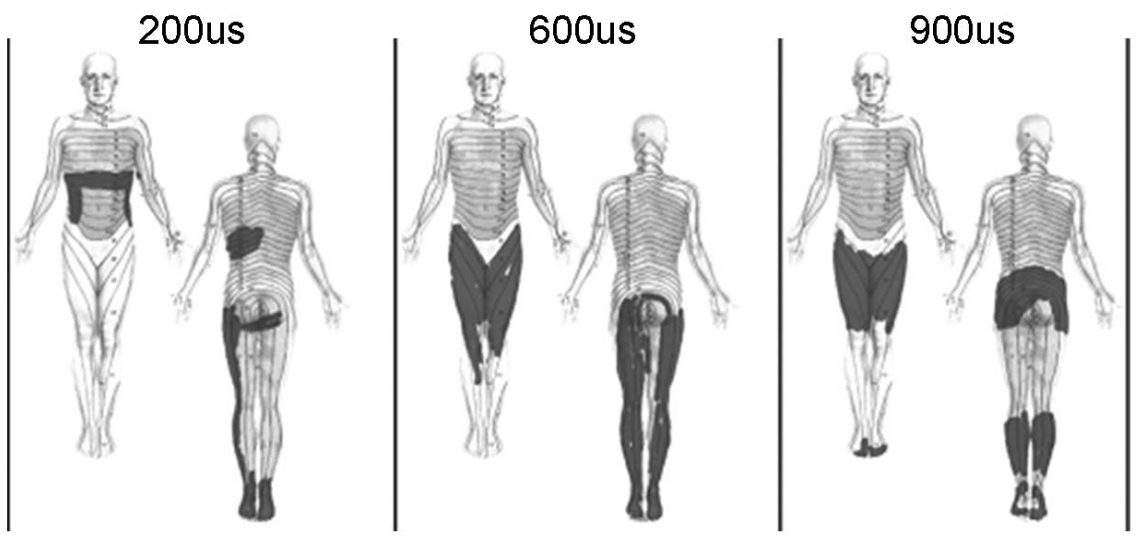

Fig. 9. *Shift of Paresthesia Dermatome "Focus" with PW in Subject 06*

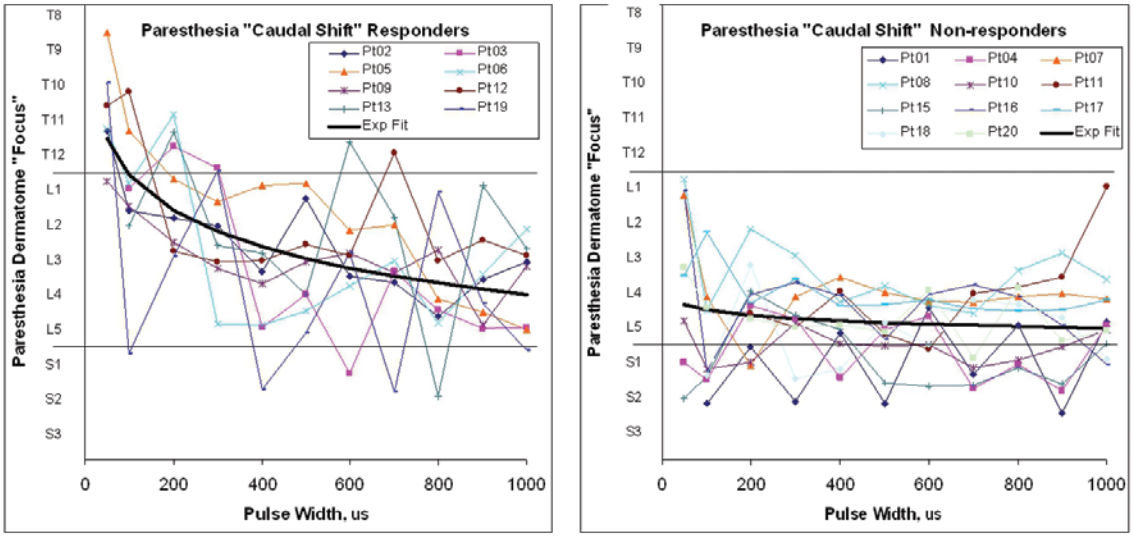

Fig. 10. *Change in Paresthesia Dermatome "Focus" with PW: "Caudal Shift" Responders (left chart) and Non-Responders (right chart).*

based upon the natural log of the PW). The threshold for defining a subject as a responder was having a 'paresthesia focus' slope of greater than the average slope for the population. We determined that 8/19 subjects were responders, exhibiting an exponentially decaying shift (i.e., "caudal shift") of the dermatome focus with increasing PW. Figure 10 shows the different curves for these 2 subject sets.

Discussion

In electrical stimulation applications, pulse generators are most commonly used to stimulate electri-

cally active tissues. Pulse waveforms are used because they are simple to generate and relatively efficient at depolarizing nerves and muscle. In SCS, the pulse amplitude is usually the focus of stimulation control as it is intuitively understood by clinician and patient alike (19-22). The PW, however, may be changed only secondarily, when other parameter adjustments fail to achieve therapeutic goals. In neurostimulation applications, the pulse amplitude and width relate directly to the depolarization of the cell membrane and are therefore critical parameters for determining the locus of excited tissue (23). Thus, to better understand the possible value of PW programming, we investigated the effects of varying the PW in patients using epidural SCS on percutaneous leads for neuropathic pain control.

Strength-Duration Parameters

We found the strength-duration parameters to be grossly in keeping with most previous reports. Jobling et al. found the chronaxie to be approximately 200μs in patients with current-controlled SCS systems (10). We note that those patients were using SCS to treat symptoms from multiple sclerosis and thus may not have had the same underlying pathophysiology as the patients we studied. Davis and Gray anecdotally reported settings of 200μs "delivered adequate levels of charge without compromising the longevity of the power source" in SCS patients (11). This recommendation was based upon data from 20 patients, though chronaxie was not calculated per se. Also, Davis and Gray reported these values for patients with a variety of conditions, none of which was chronic neuropathic pain.

Cameron et al more recently reported a mean chronaxie value of 78μs in 8 patients undergoing SCS for chronic pain conditions (24). This value is much lower than has been reported elsewhere in SCS and the reasons for this discrepancy are unclear. Jobling et al and Davis and Gray report the use of current-controlled stimulators in their work, where Cameron et al. appeared to have used voltage-based RF stimulators for their investigations. This may contribute to the discrepancy; Holsheimer et al and Merrill et al have shown that voltage-based stimulators have a tilted current waveform (Fig. 11) over the course of the stimulation pulse (16,25). This can cause underestimates of the chronaxie because, as the PW value is linearly increased, the delivered charge increases only logarithmically. In effect, using a voltage-controlled stimulator, even a long pulse appears shorter from a delivered charge standpoint.

Chronaxie is best understood from an energetic standpoint. In a simple stimulation model, where the stimulator is modeled as a pulsed current source, and the tissue is modeled as a lumped parallel resistance and capacitance, the chronaxie is defined as the PW setting that minimizes energy delivery from the stimulator (23). Clinically, however, the value of using chronaxie for determining therapeutic programming is questionable. We found that all subjects who chose a new 'favorite' PW value from among a full range of PW settings chose PW values different than chronaxie. And the median PW setting for subject 'walk-out' programs was 450μs, which is at least 150% larger than the population chronaxie we measured. Finally, the variations in paresthesia coverage and focus we observed with different PW settings suggest that using only chronaxie for programming might result in suboptimal paresthesia coverage.

Chronaxie has been used historically in an attempt to characterize the type of tissue being stimulated. Gross differences are clearly observed (e.g., nerve vs muscle), but chronaxie seems too coarse a metric for fine divisions of nerve fiber types (23). Chronaxie has been shown to depend upon the distance from the electrode to the fibers, the distribution of the fiber diameters near the electrode, the size and shape of the electrode, etc. (26-28). Also, because patient-selected 'favorite' programs were used for testing in the current study, the number, relative location, and distribution of current on cathodes and anodes may be important considerations. For example, a tightly spaced bipole would result in intrinsically higher perception threshold values than a monopole and lower perception threshold values than a tightly guarded cathode. Since chronaxie of relatively large myelinated central nervous system fibers has been determined to be ~100μs, our results suggest that the higher chronaxie in SCS also reflects these other geometric and distributional factors (29).

Patient-Selected Pulse Width

We found that 7 of 19 subjects selected a new PW from among those tested. While relatively high PW values were commonly selected, the median PW of the walk-out programs was not significantly higher than the walk-in program, for those who chose a new value or for all subjects. Those subjects that did choose a new PW, however, demonstrated a significant increase in paresthesia overlap, by over 50% on average. Thus, it appears that optimizing the PW can be useful in achieving the technical result of paresthesia-pain overlap, a critical parameter in optimizing pain relief using SCS (30).

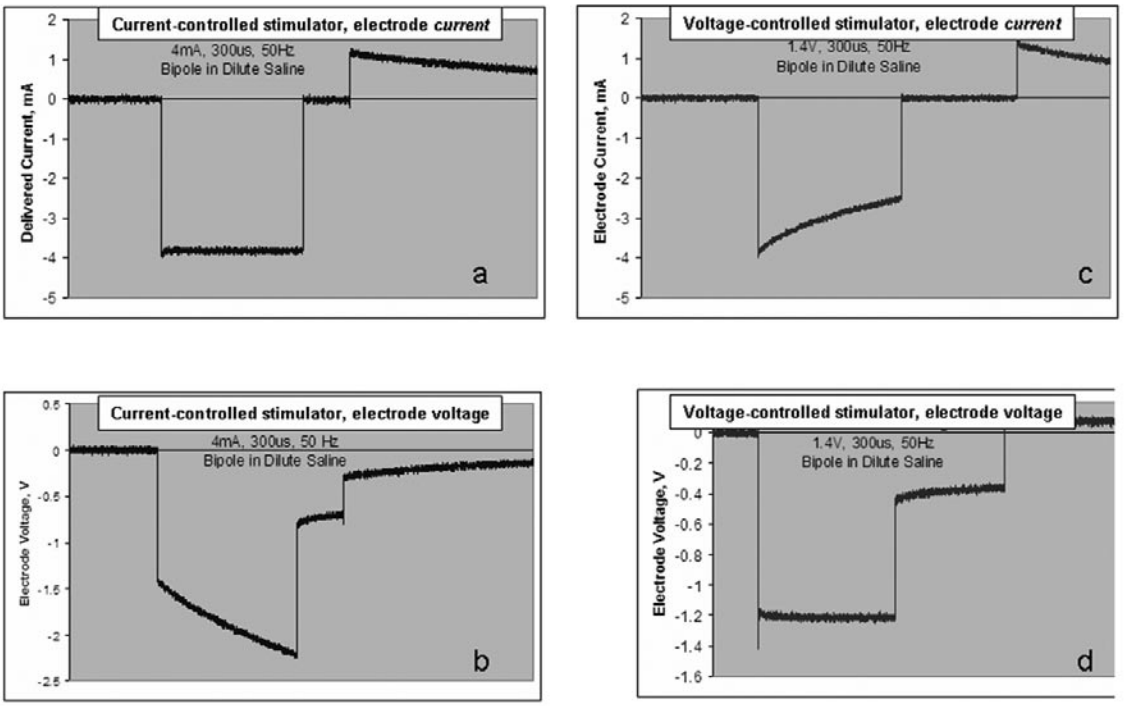

Fig. 11. *Difference in current waveforms between current-controlled (left) and voltage-controlled (right) neurostimulators. Panels a and c show the current flow through the contact for current- and voltage-controlled stimulators, respectively. It can be seen that the current-controlled stimulator has a precisely controlled stimulation current output (panel a); in order to maintain the current constant during the pulse, the current-controlled stimulator must increase the voltage on the electrode during pulse delivery (panel b) to compensate for electrode polarization effects (25). In contrast, a voltage-controlled stimulator holds the voltage on the contact fixed throughout the pulse (panel d) and therefore doesn't compensate for electrode polarization. The effect of this is a decaying electrode current pulse (panel c). Thus, extending the PW of the voltage pulse will not result in a linear increase in delivered charge as is found in a current-controlled stimulator.*

Paresthesia Changes with PW

We observed that approximately one-half of the subjects appeared to show paresthesia coverage growth and caudal shift with increasing PW (all 'shift responders' were also 'growth responders'). These results suggest that, in some patients, increased PW leads to recruitment of more caudal dermatomes and greater overall paresthesia coverage. Our companion mathematical modeling suggested that greater activation of smaller fibers would occur as the PW was increased (31). Since there is a greater relative fraction of smaller fibers in the medial aspects of the dorsal columns, then the modeling results would predict greater paresthesia coverage in the lumbar and sacral dermatomes with increased PW at a mid- to low-thoracic lead placement (32). Indeed, this appeared to be what we observed clinically.

Those subjects that appeared to demonstrate a caudal shift in paresthesia coverage (shift responders) typically had a low-thoracic/upper lumbar dermatome focus at low PW. In contrast, those that demonstrated no caudal shift (shift non-responders) had a distribution of paresthesia that was focused primarily in the lower lumbar/sacral dermatomes at low PW settings. Since these 'non-responders' also did not demonstrate much paresthesia growth with increasing PW, it appears that, when there is a paresthesia-changing effect of increasing PW, it is one of 'fiber steering,' where the use of wider PW enables smaller, more medial fibers to be recruited along with or prior to larger, more lateral fibers. Anecdotally, we observed that approximately half of the shift responders were able to eliminate abdomen paresthesia with higher PW settings, when they had experienced rib or abdomen paresthesia at lower PW.

The geometry of the stimulation system may play a role in the observed 'steering' effect with increased PW. We cannot assess this hypothesis, since we did not capture radiographic images of the leads at the time of study, so we cannot assess the orientation of the electrodes with respect to anatomic midline, which can play a significant role in the fibers activated (19,33,34). Under the assumption that the contact combination can influence the laterality of the fibers activated (wider anode-cathode separations have greater likelihood for dorsal root activation), we assessed but did not find any correlation between rostrocaudal anode-cathode separation and a caudal shift of paresthesia (35).

Interestingly, only 3/8 of the 'shift responders' were among those subjects who chose a 'favorite' PW from those applied in our testing. It may be that the newer PW settings chosen by subjects did not require a caudal shift of paresthesia so much as fine tuning of their coverage; i.e., elimination of paresthesia from a sensitive area, rebalancing the intensity within the covered area, improved or added recruitment of a more rostral dermatome, etc. Further study is needed to detail the clinical value of changing the PW setting.

Limitations

This was an acute study of technical outcomes of SCS where only the PW was varied. This study design was chosen to mimic the effect of changing only PW in a clinical setting. Other variables could also contribute to changes in paresthesia coverage, such as lead position, number of leads, contact combination, possibly stimulation rate, etc. To determine the effect of these variables, a multifactorial design would be appropriate to assess not only the univariate effects of these other parameters, but also possible interactions between parameters. There are significant challenges with such a design, such as the limited resolution of each parameter (eg, only two to three values can be tested for each parameter), the extremely large variability of contact combinations possible, the differences in anatomy from subject to subject, requiring different lead positions within the spine, etc. Certainly these could be managed and, in this context, we see the present study as an initial baseline investigation that establishes the expected responses from PW variation alone.

Since this was an acute study, we did not assess the effect of PW on pain relief. We expect that such changes should correlate to coverage, i.e., coverage of a painful region with paresthesia should reduce the perceived pain from that body area (4), but we did not investigate chronic pain relief in these subjects. A chronic investigation into the effect of increased PW over time could be undertaken, with the caveat that the ability to create concordant paresthesia in all studied subjects would have to be available using stimulation parameters other than PW, such as different contact combinations or amplitude. This is not a given: we observed that overall paresthesia was increased in many patients by using a larger PW where a smaller PW did not result in the same coverage, and in both cases the amplitude was determined by the same clinical definition, "maximum comfortable." The implication is that 'increased amplitude' changes cannot achieve the same coverage as increased PW.

We did not perform fluoroscopic or x-ray imaging at the time of follow-up, so precise vertebral lead locations were unknown. The vertebral level and mediolateral position of the lead may be a predictor of paresthesia location (33). Additionally, we did not attempt to assess the relative mediolateral 'balance' of the paresthesia of the given combination. North et al have described a useful technique at implant for assessing the mediolateral position of a single lead intended to be placed 'at midline' (34). Future investigations into PW programming would benefit from knowledge of the mediolateral position and vertebral level of the active stimulating contacts and the resulting electrical field used for testing

While it was the intent of this study to capture paresthesia location and extent at a 'maximum comfortable' stimulation amplitude setting determined individually by each subject, we could have used a fixed criteria for all subjects, e.g., at 90% of the usage range. Such standardization may have allowed for more quantitatively robust comparisons. We felt that an individually-defined 'usage' threshold, however, might be more clinically applicable to the patient's everyday use of SCS, since the upper limit of stimulation is, in our experience, more subjectively defined than initial perception of paresthesia. This patient-specific 'usage' setting for evaluating paresthesia coverage has also been used by others (36).

We used a 'standard' homuncular graphic with displayed dermatome divisions for the paresthesia drawings for all subjects. While this allowed us to standardize our analyses, it is well-acknowledged that such dermatome segmentations can vary from patient to patient and that there is no agreed-upon standard (37). Thus, we cannot infer likelihoods of generating paresthesia in any particular dermatome for a patient for a given PW

setting. With this limitation in mind, we focused our analyses on relative growth and relative shift of paresthesia within each subject when the PW setting was changed. Also, the presence of distinct divisional lines on the graphic may bias the subjects in their drawings.

Finally, the 'standard' homuncular graphic was a 2-D figure. This is a clinical standard for capturing pain and paresthesia sensations but it does have limitations, especially when precise quantitation is needed for technical assessments (38,39). Our analyses likely have erred in actual paresthesia and pain coverage estimates, since the paresthesia distributions on the side of the subject's body may be underrepresented when counting pixels. The use of a four-sided view of the body could likely improve such estimates in future studies. Additionally, the perceived 'depth' of the paresthesia sensation is not easily captured using monochromatic 2-D paresthesia drawings. This could be improved possibly by color-coding the drawings, though this would likely add complexity to the experimental procedures.

Conclusions

In our investigation into programming PW settings for patients using SCS for chronic low-back and/or leg pain, we found that the median chronaxie for subjects with dual mid- to low-thoracic percutaneous leads was 295μs, which was higher than previous reports. We found that over one-third of the tested subjects selected new PW values to improve their walk-in 'favorite' program. The median PW of the walk-out program was 400μs, approximately 48% higher and statistically different than the chronaxie value of our sample. Thus, chronaxie may underestimate the PW program settings that the patients choose for therapy. We observed that subjects who chose a new PW setting showed a statistically significant increase in their paresthesia-pain overlap from their walk-in program.

Approximately half of subjects appeared to demonstrate that increased PW can both increase the total paresthesia coverage, as well as shift the paresthesia focus to more caudal dermatomes, suggesting that PW can have a 'steering' effect. A companion mathematical modeling study suggested that the mechanism behind such paresthesia steering is due to the different selectivity of PW for larger and smaller fibers. The mathematical model incorporates realistic fiber size, density, and distributions in the dorsal columns, based upon human anatomic data. With a greater relative density of smaller fibers located more medial in the dorsal columns, an increase in PW will recruit smaller fibers more readily, and thus result in greater midline axon recruitment. Clinically, this appeared to manifest as a caudal shift in paresthesia.

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