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A single-center retrospective chart review of percutaneous PNS for treatment of chronic shoulder pain

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A B S T R A C T

Objective: The present IRB-approved retrospective chart review describes the use of a 60-day PNS treatment for shoulder pain at a single center in 60 total consecutive patients.
Background: Chronic shoulder pain affects an increasing number of patients per year and is especially prevalent in elderly populations. Percutaneous peripheral nerve stimulation (PNS) treatment targeting the nerves of the shoulder has been shown to reduce pain in prospective clinical studies and in analysis of real-world data.
Methods: Data were extracted from the electronic medical records of patients who had previously undergone percutaneous PNS treatment for chronic shoulder pain. Demographic data and treatment characteristics were summarized alongside treatment outcomes.
Results: Overall, 84 % (49/58) of patients reported substantial (≥50 %) pain relief at the end-of-treatment. The records for 2 patients did not include patient-reported percent pain relief. The average indwelling period for leads (i.e., treatment period) was 57 days. Findings on treatment effectiveness were consistent when the patient population was stratified by cause of pain, duration living with pain, and presence of pain-modifying comorbidities. Stimulation paradigms were identified and categorized by the nerve target and stimulation frequency (e.g., motor stimulation, sensory stimulation, or bimodal stimulation).
Conclusions: These results indicate percutaneous PNS is an effective treatment for patients with various shoulder pain histories, and while all stimulation paradigms were effective at reducing pain, patients who received bimodal PNS reported the greatest pain relief. Key limitations of the study included heterogeneous shoulder pain etiologies among patients and sparse availability of long-term follow-up data. These data support existing real-world and prospective clinical evidence on the efficacy of 60-day PNS treatment at treating chronic pain and provide valuable insights into its use in clinical practice.

1. Introduction

Shoulder pain can stem from a variety of causes and is exceedingly common with an estimated annual incidence ranging from 0.9 % to 2.5 % and a positive correlation with age [1,2]. For example, osteoarthritis of the shoulder has been estimated to affect up to 32.8 % of the adult population over the age of 60 and imposes a significant economic burden (>$60 billion) each year [3,4]. Shoulder pain commonly adversely affects a person's quality of life, level of activity, and personal independence [1,5,6]. Chronic shoulder pain can arise from vastly different sources and can develop into a centrally mediated pain state (e.g., degenerative joint disease, osteoarthritis, neuropathic pain following surgery, or trauma), and these factors can inform clinical decisions regarding pain management strategies [7].

Common treatment options include physical therapy and over-the-counter or prescription pain medications. However, these therapies may be insufficient, leading to patients pursuing interventional therapies such as corticosteroid or anesthetic injections, radiofrequency ablation (RFA), or surgical intervention [8,9]. Pharmacological pain management can be effective but carries the risk of abuse: a prospective study found 8.3 % of opioid-naïve patients developed prolonged opioid use following shoulder surgery [10]. Non-steroidal anti-inflammatory drugs, a common non-opioid medication used to control pain, can disrupt organ function and produce adverse events such as intestinal bleeding or stroke [11]. Thus, patients suffering from chronic shoulder pain are in need of an effective treatment option that is non-destructive, non-opioid, and can produce substantial relief.

Peripheral nerve stimulation (PNS) is a device-based treatment option that uses implanted leads to deliver electrical pulses to innervating peripheral nerves. Percutaneous PNS treatments, whereby leads are implanted for up to 60 days and stimulation is supplied by an external pulse generator, have been shown to be effective at treating a variety of pain types. In particular, prospective clinical studies [12–18] and real-world evidence [19–24] have demonstrated effectiveness of PNS for

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treating shoulder pain in various chronic pain patient populations. Patient-reported outcomes collected by healthcare providers may elucidate additional details on the efficacy of 60-day PNS for prevalent chronic shoulder pain sources including post-surgical pain, trauma, osteoarthritis, and rotator cuff injuries. Also, although previous real-world studies have highlighted strong effectiveness including for shoulder pain, additional demographic and treatment history would provide insights into patient populations, percutaneous PNS treatment characteristics (including novel multi-modal stimulation paradigms), and therapeutic outcomes. Such data may help inform best clinical practices when treating chronic shoulder pain patients. The present single-site retrospective study reviews the use of percutaneous 60-day PNS in routine clinical practice for the treatment of chronic shoulder pain.

2. Methods

2.1. Study design and intervention

The study was an IRB-approved (WCG IRB) retrospective chart review of patients who previously underwent treatment for shoulder pain using a 60-day PNS system (SPRINT PNS™, SPR Therapeutics, Cleveland, OH). Under an IRB-approved waiver of consent, electronic medical records (EMR) were reviewed for patients who underwent PNS treatment for chronic shoulder pain. Inclusion criteria required patients to have undergone PNS treatment after August 1, 2017, and had completed the PNS treatment at the time the chart review was conducted. Patients with ongoing treatment (i.e., stimulation leads were still implanted) were excluded from the study.

The 60-day PNS treatment has been described elsewhere [17,18]. Briefly, one or two small-diameter, helical-coiled monopolar leads are placed percutaneously and remote (e.g., 0.5–1 cm) from the nerves using a needle introducer. Electrical pulses are applied to the nerve using an external pulse generator (EPG) worn by the patient that are intended to produce comfortable sensations in the patient's area of pain. The device may be programmed such that one or both leads activate sensory afferent nerve fibers and/or motor efferent fibers within the targeted nerve. The device is also capable of delivering concurrent sensory and motor-based stimulation therapies using two leads (i.e., bimodal stimulation).

Common nerve targets for shoulder pain, selected based on patient shoulder history and pain location, included the axillary and suprascapular nerves. Terminal branches of the axillary nerve were targeted with motor stimulation in the middle and posterior deltoid with landmark-based lead placement distal to the acromion. In some patients, the axillary nerve was targeted instead with sensory stimulation at the quadrangular space under ultrasound guidance. The suprascapular nerve was targeted at the suprascapular notch under ultrasound guidance. Final lead placement was adjusted based on patient-reported coverage of the region of pain with stimulation-evoked sensations. Following lead deployment, the patient was instructed on device use (e.g., device charging, stimulation intensity adjustment, etc.). The device is indicated for up to 60 days of treatment, after which the leads are withdrawn.

2.2. Chart review and outcomes

Relevant patient data were extracted by a site clinical coordinator, deidentified, and entered into an electronic data capture system (Merative, Ann Arbor, MI, USA). Baseline data (i.e., before treatment began) were collected, including shoulder medical history, previous shoulder pain therapies (e.g., corticosteroid or nerve block injections, physical therapy, radiofrequency ablations, and spinal cord stimulators/dorsal root ganglion stimulator implantation), medications (e.g., opioid and non-opioid analgesics), and relevant medical history (e.g., diabetes, fibromyalgia, hypertension). Medications affecting pain taken at baseline (e.g., before the start of the PNS treatment period), such as opioids, anticonvulsants, antidepressants, non-steroidal anti-inflammatory drugs, and muscle relaxants, were collected. Opioid doses were identified as "taken regularly" or "taken as needed" (pro re nata, PRN).

Patient-reported pain outcomes were collected and categorized based on relation to the PNS treatment: before lead implantation (i.e., at baseline) and at lead withdrawal (i.e., at end-of-treatment, EOT). The primary outcome was patient-reported percent pain relief, based on validated patient-reported outcomes measures asking patients how much pain relief treatment has provided from 0 % (no relief) to 100 % (complete relief) [25,26]. Patients who responded to treatment (i.e., treatment success) were defined as those reporting substantial (≥50 %) pain relief [27] at EOT (e.g., 60 days after implant, but may vary).

The EMR was the primary source of patient data (e.g., medical history and demographics) and outcomes for the study. These data were supplemented by outcomes reported by patients who opted-in at the time of treatment to provide such information to the device manufacturer. In the event data was available from both sources, the data extracted from the EMR was reported herein. To test for potential bias between data sources, a sensitivity analysis was performed to compare percent pain relief reported in the manufacturer's database and the EMR for patients with both available datapoints.

2.3. Statistical analysis

Continuous variables were described as mean (± standard error, SE), and binomial variables were described as population percentages and 95 % confidence interval (95 % CI). The sensitivity analysis comparing data sources (e.g., data reported by the patient to the manufacturer to supplement data extracted from the EMR) was performed using a paired two-sample, two-tailed *t*-Test and a two-tailed Binomial exact test. Analyses were performed using Excel (v16.82, Microsoft, Redmond, WA).

3. Results

3.1. Patient population

Sixty consecutive patients identified as having received 60-day PNS treatment for shoulder pain were included in this chart review and the demographic data was summarized (Table 1). Mean age at the time of treatment was 67.7 (±1.4) years, and a slight majority of patients were female (Female/Male ratio, 1.1). The medical histories were reviewed for selected comorbidities of interest; thirty-three patients (55 % of the total population) had hypertension, 19 patients (32 %) had type I or type

Table 1
Summary statistics of demographics for included patients. Population proportions (%) reported as a percentage of included patients (n = 60).

	Patients included (n)	60	
	Age (years, SE)	67.7 (±1.4)	
	Female/Male Ratio	1.1	
	BMI (kg/m2, SE)	29.6 (±0.9)	
		n	%
Race	**White (%)**	52	87 %
	Black (%)	3	5 %
	American Indian (%)	1	2 %
	Unreported (%)	4	7 %
Ethnicity	**Hispanic (%)**	10	17 %
	Non-Hispanic (%)	43	72 %
	Unknown (%)	7	12 %
Smoking Status	**Current Smoker (%)**	9	15 %
	Past Smoker (%)	8	13 %
	Never Smoked (%)	36	60 %
	Unreported (%)	7	12 %
Key Comorbidities	**Hypertension (%)**	33	55 %
	Diabetes – Type I or Type II (%)	19	32 %
	Fibromyalgia	9	15 %
Military Veterans (%)		4	7 %

II diabetes, and 9 patients (15 %) had fibromyalgia.

Patients' history of shoulder pain was categorized by the side of pain (left, right, or bilateral), cause(s) of pain, prior shoulder surgery(ies), and pain duration prior to PNS therapy (Table 2). Thirty-two patients (53 %) reported pain in their right shoulder while 27 patients (45 %) were treated for left shoulder pain and 1 patient (2 %) had bilateral pain.

All patients had either used at least one non-pharmacological therapy for their shoulder pain or were taking a medication known to affect pain at baseline (e.g., at the start of PNS treatment, Fig. 1 and Table 3). The two most common clinic-based interventional therapies tried before percutaneous PNS were injections (e.g., anesthetic, corticosteroids, etc.) and physical therapy which were used by 29 patients (48 %) and 27 patients (45 %), respectively (Fig. 1). The majority of patients (65 %, 39/60) had pain refractory to at least three treatment options (opioid medication, non-opioid medication, and/or non-pharmacological options) before 60-day PNS, with 90 % percent (54/60) refractory to at least two alternative treatment options.

Fifty-seven patients (95 %) were taking pain medications (Table 3), and 47 patient charts (78 %) reported opioid use on a PRN or regular basis. Of the patients taking opioids at baseline, more patients were prescribed doses to be taken PRN (55 %) compared to patients with regular dosages (17 %) or both (7 %). However, without more detailed medication usage data (e.g., medication diaries) it was unclear how patients were using these medications. Other commonly reported medications that affected pain were non-steroidal anti-inflammatory drugs (58 %), gabapentinoids (53 %), antidepressants (42 %), muscle relaxants (42 %), and anesthetics (23 %).

3.2. Treatment and outcomes

All patients received two implanted leads. The most common nerve target combination was the suprascapular nerve and terminal branches of the axillary nerve near the deltoid (33 patients, Fig. 2) followed by the suprascapular nerve and the axillary nerve at the quadrangular space (15 patients). Other less common nerves targeted for treatment of chronic shoulder pain included the brachial plexus and thoracic intercostal nerves. The average treatment period (e.g., lead indwelling days) was 57 (±2) days. Of the 60 patients included, 58 had an EOT measure for patient-reported pain relief, and the responder rate (≥50 % pain

Table 2
Patient shoulder pain history. Population proportion reported as percent of included patients (n = 60). *Patients may have multiple causes reported (i.e., post-surgical pain and osteoarthritis pain). †One patient previously underwent two types of surgery.

		N	%
Side of Pain	**Left**	27	45 %
	Right	32	53 %
	Bilateral	1	2 %
Cause of Pain*	**Reported Cause of Pain**	35	58 %
	Post-Surgical	*20*	*33 %*
	Trauma	*9*	*15 %*
	Osteoarthritis	*7*	*12 %*
	Rotator Cuff Injury	*2*	*3 %*
	Other Cause	*3*	*5 %*
	No Specific Cause Reported	25	42 %
Surgeries†	**Reported Previous Shoulder Surgery**	*27*	*45 %*
	Rotator Cuff Repair	*11*	*18 %*
	Total Shoulder Arthroplasty	*7*	*12 %*
	Reverse Total Shoulder Arthroplasty	*4*	*7 %*
	Partial Shoulder Arthroplasty	*1*	*2 %*
	Other Surgery	*5*	*8 %*
Duration Living with Pain	**Duration ≤ 1 Year**	11	18 %
	1 Year < Duration ≤ 2 Years	12	20 %
	2 Years < Duration ≤ 5 Years	9	15 %
	Duration > 5 years	10	17 %
	Duration Not Reported	18	30 %

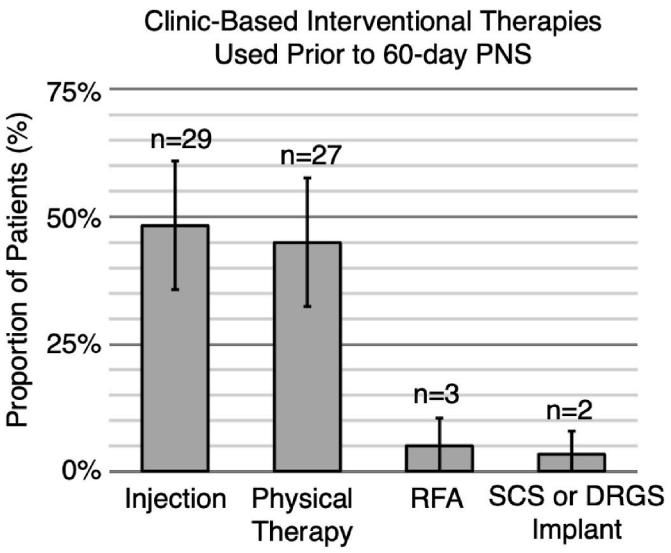

Fig. 1. Clinic-based interventional therapies used prior to 60-day PNS. Data presented as the proportion of patient population ±95 % confidence interval. Abbreviations: PNS – peripheral nerve stimulation; RFA – radiofrequency ablation; SCS – spinal cord stimulation; DRGS – dorsal root ganglion stimulation.

Table 3
Common medications affecting pain taken at baseline (n = 60).

		N	%
Pain Medications	**Any Medications Affecting Pain**	57	95 %
	Opioids	47	78 %
	As Needed Dose	*33*	*55 %*
	Regular Dose	*10*	*17 %*
	As Needed and Regular Doses	*4*	*7 %*
	Non-steroidal anti-inflammatory drugs	35	58 %
	Gabapentinoids	32	53 %
	Antidepressants	25	42 %
	Muscle Relaxant	25	42 %
	Anesthetic (e.g., Lidocaine cream/patch)	14	23 %

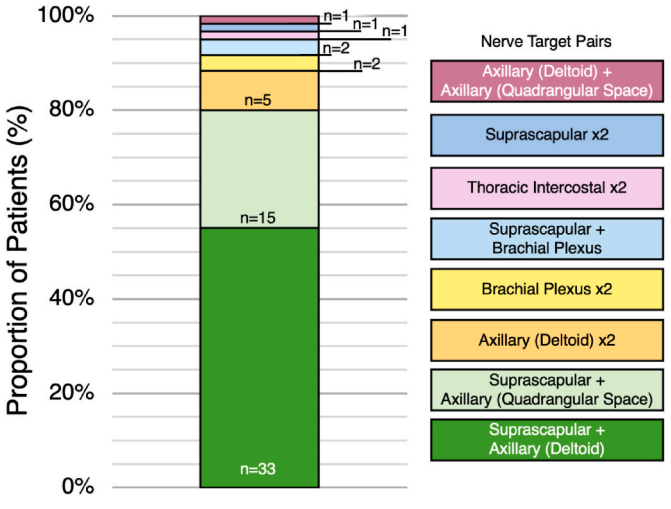

Fig. 2. Proportion of patients receiving stimulation for each nerve target pair. Number of patients per combination presented as numbers within the associated bar section (total n = 60).

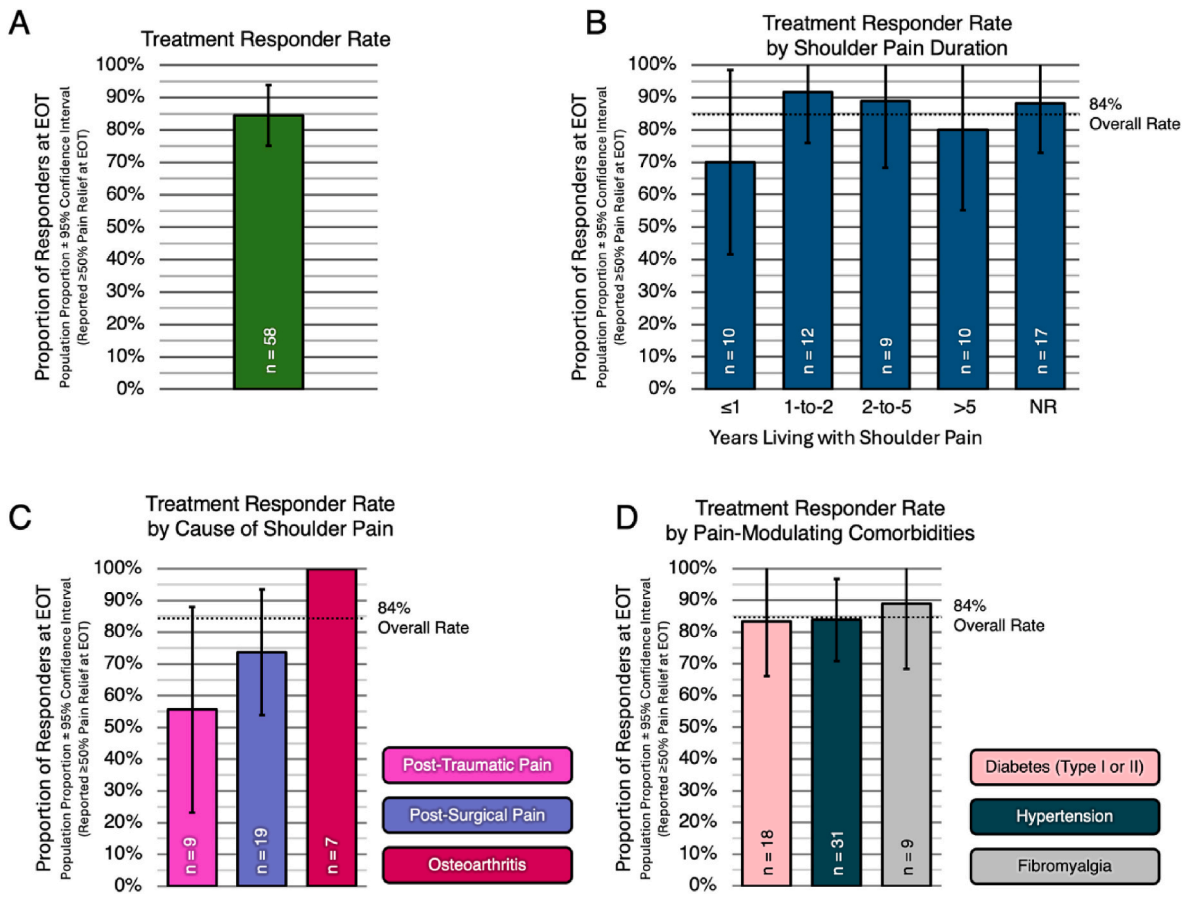

Fig. 3. Treatment outcomes following a 60-day PNS treatment used for shoulder pain. A. Treatment responder rate for all patients included in the study with the primary outcome available (n = 58). B. Treatment responder rate by duration (years) living with pain for patients with available data. C. Treatment responder rate by indicated pain type. Patients were able to indicate multiple pain origins. D. Treatment responder rate by pain-modulating comorbidities. Overall average responder rate (84 %) indicated by dashed black line in panels B–D. Abbreviations: NR – Not Reported.

relief at EOT) among those with data available was 84 % (49/58, 95 % CI: 75–94 %, Fig. 3A). Both patients who lacked primary endpoint data did have other pain scores available in their records; average NRS pain scores indicated one patient was likely a treatment responder (average pain 4 at baseline and 0 at EOT) and one was not (average pain 8 at baseline and 9 at EOT). If these additional outcomes were considered, the overall responder rate for the study population would be 83 % (50/60, 95 % CI: 74–93 %).

A majority of data points for the primary outcome were extracted from the EMR (31/58) which were supplemented using the manufacturer's database (27/58). A sensitivity analysis was performed using a paired two-tailed *t*-test to compare percent pain relief reported in the EMR and the manufacturer's database for patients with both available datapoints (n = 29). In these patients, the mean percent pain relief from the EMR was 73.1 ± 3.7 % and from the manufacturer's database was 74.7 ± 4.3 % (not significant, p = 0.79, Supplementary Fig. 1A). A Binomial exact test was performed to compare the proportion of these patients with ≥50 % pain relief, and the test did not detect significant difference between the two datasets. The proportion of patients that responded to treatment was equivalent (97 %, 28/29 (95 % CI: 90–100 %)) as calculated from both the EMR and the manufacturer's database, and no patient changed treatment response category depending on the data source (Supplementary Fig. 1B).

Responder rate was also evaluated in patients by duration of pain, cause of pain, and presence of common comorbidities. The duration of shoulder pain prior to PNS treatment was reported in 41 patients with EOT outcome data and categorized into epochs: less than or equal to 1 year, 1–2 years, 2–5 years, greater than 5 years. At least 70 % of patients in each pain duration epoch were responders at EOT (Fig. 3B). A majority of patients reported substantial pain relief (≥50 %) in the three most common causes of pain including post-traumatic (56 %, 95 % CI: 23–88 %), post-surgical (74 %, 95 % CI: 54–93 %), or osteoarthritis pain (100 %, Fig. 3C). Within the post-surgical pain group, 10 patients received PNS for treatment of post-surgical pain following a total shoulder arthroplasty (TSA), reverse TSA, or partial shoulder arthroplasty and had outcomes available at EOT, and a majority (60 %) reported ≥50 % pain relief at EOT. Patients were also categorized based on common comorbidities: diabetes (types I or II), hypertension, and fibromyalgia; the responder rate for all three groups was above 80 % (Fig. 3D).

A majority of patients (54/60, 90 %) continued to have records of pain medication use during the PNS treatment period, and one patient continued use of an existing SCS device (concurrent use of the PNS treatment and other implanted electronics is not contraindicated unless the current paths overlap). Otherwise there were no records of other interventional treatments like injections or ablations during PNS. Of the six patients who did not receive concurrent pain medications or treatment during the PNS treatment period, all six responded to percutaneous PNS treatment.

Of the 16 % of patients who reported <50 % pain relief at EOT, two patients indicated clinically significant (>30 %) pain relief [27] at EOT but did not meet the responder definition of ≥50 %, and seven patients reported less than 30 % pain relief.

Stimulation paradigms included motor stimulation, sensory stimulation, and bimodal stimulation based on the nerve targets and stimulation parameters. Motor stimulation included leads placed in the

deltoid muscle targeting the terminal branches of the axillary nerve and applying lower frequency stimulation (e.g., 12 Hz) with the intention of eliciting comfortable motor contractions. Sensory stimulation included leads placed to target nerves outside of the deltoid (i.e., suprascapular nerve, brachial plexus, or axillary nerve branches in the quadrangular space) and applying higher frequency stimulation (e.g., 100 Hz) with the intention of eliciting comfortable sensations in the shoulder region of pain. Bimodal stimulation used two leads targeting two nerves: one that delivered motor stimulation (e.g., to the axillary nerve terminals in the deltoid) and one that delivered sensory stimulation (e.g., to the suprascapular nerve). A majority of patients received bimodal stimulation (55 %) compared to sensory stimulation alone (35 %) or motor stimulation alone (10 %). All stimulation paradigms achieved a responder rate greater than 65 %. Of patients who received bimodal stimulation and had available primary endpoint data (n = 31, 3 patients did not have available primary endpoint data), 97 % (95 % CI: 90–100 %) were responders at the end of treatment (Fig. 4B). The mean percent pain relief reported by patients in all three stimulation paradigms was greater than 50 % (Fig. 4C), and the mean pain relief among responders in each of the three paradigms was similar (bimodal = 77 ± 4 %, sensory = 78 ± 5 %, motor = 78 ± 3 %).

Percent pain relief was available in follow-up (e.g., after 60 days and post-lead withdrawal) for 18 patients. The mean length of follow-up was 115 days (range: 73–231 days) from the start of treatment (Fig. 5). At these follow-up encounters, 94 % (17/18) patients indicated substantial pain relief (≥50 %) with one patient reporting a return of pain at 85 days. Only one patient had follow-up outcomes at multiple time points (105 and 196 days from start of treatment) and reported substantial pain relief at both timepoints.

3.3. Device safety and performance

Using the manufacturer's product safety and performance database to identify events reported by patients in the present review, 9 events associated with 7 patients were identified. Of the 120 leads implanted in 60 patients, five lead dislodgements occurred in 3 patients (5 % of the study population or 4.2 % of implanted leads). Two patients had both leads replaced and completed therapy. One patient had one lead dislodge and opted to continue treatment with just the remaining lead. All three patients with dislodged leads reported ≥50 % pain relief at EOT. Two lead fractures occurred during therapy in 2 patients (3.3 % of the study population or 1.7 % of implanted leads). Both fractures occurred while using an older lead version before a strengthened lead design was implemented. One patient had the lead replaced and reported <50 % pain relief at EOT, and the other patient opted not to have the lead replaced and reported ≥50 % pain relief at EOT. No serious adverse events or additional sequelae were reported following either lead fracture, and according to the manufacturer's specifications, retained lead fragments are magnetic resonance conditional. Two patients reported suspected infections (e.g., identified redness and/or swelling at the implantation site; 3.3 % of the study population). Both occurred a month into treatment (32 and 35 days) and resolved following administration of oral antibiotics (e.g., 10-day course of cephalexin) enabling both patients to complete PNS treatment.

4. Discussion

The present retrospective chart review presents data on the efficacy of percutaneous PNS to treat shoulder pain. Sixty patients who received 60-day PNS to treat their shoulder pain were identified at a single center. All patients in the study had failed to achieve adequate relief from prior therapies (Fig. 1) and/or were taking pain medications at the start of PNS treatment (Table 3). The most common cause of shoulder pain reported in this study was post-surgical shoulder pain (Table 2), but the study captured a variety of pain etiologies. Percutaneous PNS produced substantial (≥50 %) pain relief in a large majority of patients with an overall responder rate of 84 % (Fig. 3A). The consistency of treatment efficacy was further explored by subdividing the population by cause of pain and pain duration (e.g., years living with shoulder pain), and a majority of patients in each category were found to have reported

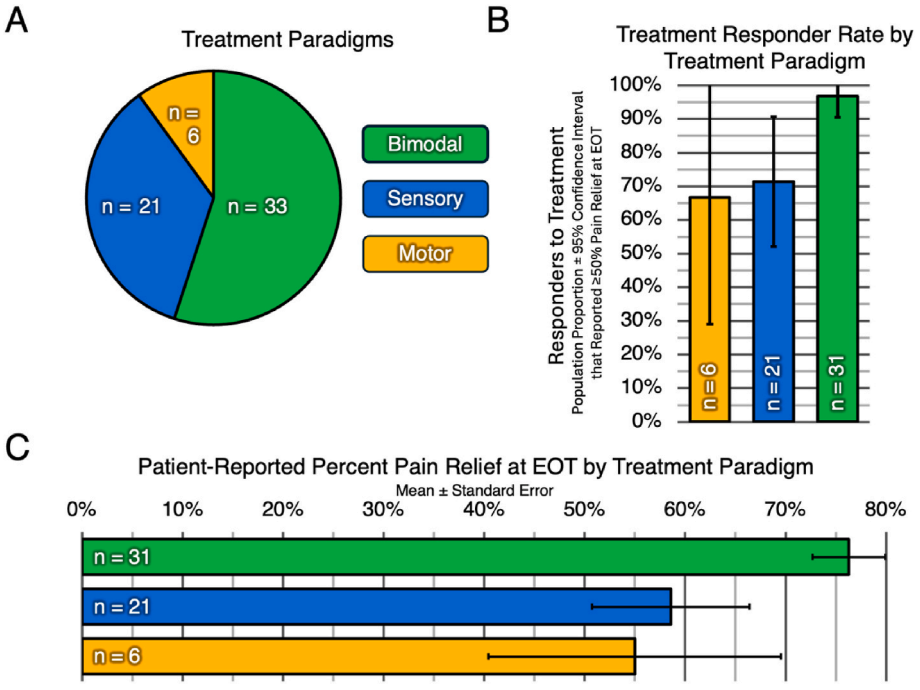

Fig. 4. Stimulation paradigms and treatment outcomes. A. Stimulation paradigms for patients based on nerve targets used during treatment (n = 60). B. Treatment responder rate for stimulation paradigms for patients with available data on patient-reported percent pain relief at end-of-treatment (n = 58). C. Mean patient-reported percent pain relief at EOT (n = 58). Population data presented as proportion ±95 % confidence interval, and continuous variable data presented as mean ± standard error. Abbreviations: EOT – end-of-treatment.

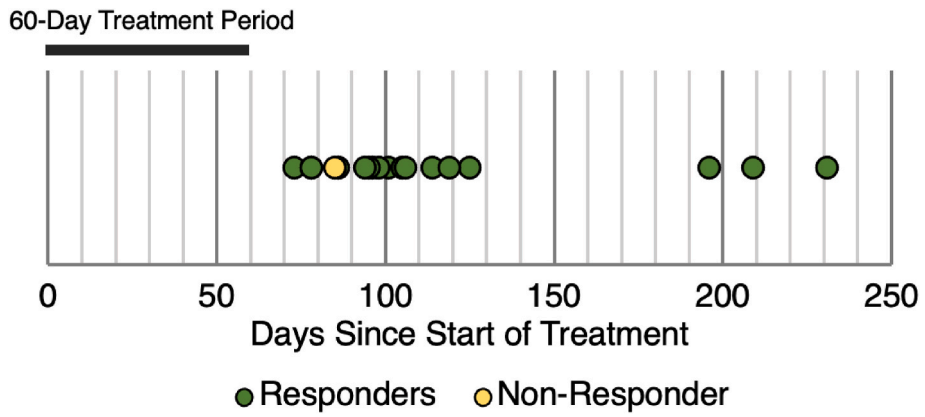

Fig. 5. Follow-up outcomes (e.g., after lead withdrawal) available for 18 patients. Patients reported sustained pain relief at a maximum of 231 days. One patient (orange) reported a return of pain at 85 days. Responders defined as a patient reporting percent pain relief ≥50 %, and non-responders defined as a patient reporting percent pain relief <50 %. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

substantial pain relief. These results indicate consistent treatment effects that may be indicative of a convergent (e.g., centrally mediated) mechanism of analgesia.

Shoulder surgeries can vary greatly in invasiveness to the joint structure, but minimally invasive (e.g., arthroscopic surgery) and more major (e.g., total shoulder arthroplasty, TSA) surgeries can both result in persistent post-surgical pain [28–31]. Surgery can cause nerve injuries that result in neuropathic-type pain, and surgeries like arthroplasty may also disrupt joint innervation altering the perception of interventions like blocks, RFA, or stimulation [32–34]. The results of the present study are therefore notable in patients with post-surgical shoulder pain, including 10 patients with pain following a TSA, reverse TSA, or partial shoulder arthroplasty. A majority of patients with pain following shoulder arthroplasty (60 %) reported ≥50 % pain relief at EOT, suggesting that stimulation of target nerves proximal to the shoulder can still provide adequate pain relief. These findings corroborate evidence demonstrating the effectiveness of percutaneous PNS for treatment of post-surgical pain following orthopedic surgery [35–41].

Osteoarthritis of the shoulder leads to degeneration of the joint and is generally considered to be mechanical in nature, but emerging evidence suggests the chronification of arthritic pain may include the development of an additional central component [42–44]. The current study included 7 patients with arthritic shoulder pain (Table 2) all of whom responded to treatment (Fig. 3). This is notable as the 60-day PNS treatment is not believed to directly address the shoulder mechanics but may provide pain relief through a reconditioning of central pain pathways [44]. Other than an existing case report [21], this finding provides novel evidence that a 60-day PNS treatment may produce pain relief for patients with degenerative shoulder diseases such as osteoarthritis.

All patients had two leads implanted, and a majority of patients (55 %) underwent a bimodal stimulation paradigm (e.g., motor stimulation targeting the terminal branches of the axillary nerve and sensory stimulation targeting the suprascapular nerve). While a majority of patients who received only motor stimulation or only sensory stimulation also reported substantial pain relief (67 % and 71 % responder rate, respectively, Fig. 4), patients who received bimodal stimulation had the highest responder rate (97 %) and reported the greatest mean percent pain relief (76 %). These data indicate that motor and sensory stimulation may act independently to produce pain relief. Furthermore, the convergent effects of each stimulation modality may also be complementary to provide more robust pain relief compared to a single stimulation paradigm (e.g., motor or sensory). Central processing of sensory input from the shoulder has been shown to be altered after traumatic musculoskeletal or neural injury [45,46], surgery [47–49], and osteoarthritis [50]. It is possible that combined sensory and motor PNS treatment drives beneficial peripheral signals from multiple sources surrounding the shoulder that convergently affect this centralized pain state to produce pain relief [44].

The study also included collection of treatment outcomes in follow-up after leads were withdrawn. Follow-up percent pain relief outcomes were found to be available for 18 patients, but only one patient reported outcomes at multiple longitudinal follow-ups. The reported percent pain relief values indicated a high degree of sustained relief (94 %, 17/18 with ≥50 % relief) with a range of 73–231 days and a mean of nearly 4 months following start of treatment. However, the sparse availability of long-term data highlights some of the challenges of a retrospective chart review for some types of treatments. The circumstances of the lack of follow-up are largely undocumented and may vary greatly by patient. For example, with no permanent implant requiring maintenance or programming, patients may not have a regular schedule of follow-up unless pain recurs. Patients with long-term sustained pain relief may therefore be less likely to return to a pain specialist. Alternatively, patients with recurring pain may seek treatment at a different clinic or cease pursuing pain treatment altogether. In the present study, other patients had encounters in the EMR for other pain conditions and reported data that were not relevant to or not specific to the shoulder. Therefore, it is difficult to draw conclusions about the long-term outcomes, positive or negative, for patients who lack shoulder-specific data beyond the end of treatment. Nonetheless, the data that are available support evidence from prior prospective clinical studies in shoulder pain, which have reported shoulder pain relief in patients with hemiplegic shoulder pain [14,16,17] and subacromial impingement syndrome [18], as well as case reports in patients with complex region pain syndrome [51] and post-traumatic shoulder pain [23]. Another recent case highlighted a patient with end-stage osteoarthritis of the shoulder who responded well to percutaneous PNS treatment [22]. The patient then had a return of pain and received a permanently implanted system, highlighting the potential benefit of a percutaneous PNS treatment to inform long-term treatment options even if sustained relief is not achieved.

This review included patient outcomes from two sources – EMRs with information collected in routine clinical practice and a device manufacturer's database consisting of outcomes reported by patients to manufacturer's representatives during routine support of therapy. Multiple studies in recent years have utilized patient-reported outcomes from these two sources [52–58], but this is the first study to our knowledge to compare outcomes between these sources for 60-day PNS treatment. The high degree of similarity in quantitative pain relief reported to providers and reported to device representatives points to a consistency in the responses of patients to clinical and support team members, and this quantitative agreement highlights the opportunities to derive confidently insights from real-world data from a variety of

different sources.

4.1. Limitations

A key limitation of the present study was its retrospective nature and reliance on the EMR from a single private outpatient pain clinic. Potentially relevant data from other providers (e.g., treatment and medical history from other providers, including shoulder pain therapies, physical therapy, and medications) were not available for the present analysis. Further, patients may not regularly follow up with the clinic regarding their shoulder pain for various reasons, limiting the availability of longitudinal follow-up data. As a retrospective study performed at a single site, the results focused on the outcomes most commonly recorded in the EMR by the providers, which generally included patient-reported percent pain relief. Additional outcomes of interest for shoulder pain such as physical function, range of motion, or quality of life, were not consistently available. Long-term percent pain relief outcomes (i.e., collected at visits that occurred post lead-withdrawal) were also not consistently available, with data points identified for a minority of patients (30 %, 18/60).

The patient population represented a diverse collection of shoulder histories. Patients had variable diagnoses (e.g., osteoarthritis, post-surgical pain, and post-traumatic pain) and treatment histories. The overall and etiology-specific success rates of PNS treatment imply widespread applicability of this treatment modality for shoulder pain, though the heterogenous mix of cases and sample sizes did not allow for robust comparisons between patient populations.

5. Conclusion

The present retrospective chart review found evidence supporting 60-day PNS as an effective treatment option for different sources of shoulder pain including osteoarthritis and post-surgical shoulder pain. Further, bimodal stimulation was found to be a particularly promising option that utilizes a combination of sensory and motor-based stimulation paradigms, potentially due to complementary effects of stimulation of multiple sources surrounding the shoulder on pain processing in the central nervous system. These data support existing clinical and real-world evidence on the effectiveness of 60-day PNS as a chronic pain treatment and provide insights into its routine use in clinical practice.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Genaro J. Gutierrez reports financial support, administrative support, article publishing charges, statistical analysis, and writing assistance were provided by SPR Therapeutics Inc and a relationship with SPR Therapeutics Inc that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Jacob R. Caylor reports a relationship with Medtronic Inc that includes: consulting or advisory. Pankaj Mehta reports relationships with Abbott, SPR Therapeutics Inc, Boston Scientific Corp, CornerLoc, PainTEQ, Aurora Spine Inc, Spinal Simplicity, Relievant Medsystems Inc, SurGenTec, and Ethos that include: consulting or advisory. William J. Huffman, Joseph W. Boggs, and Nathan D. Crosby are employees of and named on patents assigned to SPR Therapeutics Inc. Nathan D. Crosby and Joseph W. Boggs have stock options in SPR Therapeutics Inc.

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Appendix A. Supplementary data

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References

[1] Luime JJ, et al. Prevalence and incidence of shoulder pain in the general population; a systematic review. Scand J Rheumatol 2004;33(2):73–81. https://doi.org/10.1080/03009740310004667.
[2] Walker-Bone K, Van Der Windt DA. Shoulder pain — where are We Now? Current Treatment Options in Rheumatology 2021;7(4):285–306. https://doi.org/10.1007/s40674-021-00184-z.
[3] Chillemi C, Franceschini V. Shoulder osteoarthritis. Arthritis 2013;2013:370231. https://doi.org/10.1155/2013/370231.
[4] Buckwalter JA, Saltzman C, Brown T. The impact of osteoarthritis: implications for research. Clin Orthop Relat Res Oct 2004;427(427 Suppl):S6–15. https://doi.org/10.1097/01.blo.0000143938.30681.9d.
[5] Gutierrez DD, Thompson L, Kemp B, Mulroy SJ. The relationship of shoulder pain intensity to quality of life, physical activity, and community Participation in persons with paraplegia. The Journal of Spinal Cord Medicine 2007;30(3):251–5. https://doi.org/10.1080/10790268.2007.11753933.
[6] Kemp BJ, Bateham AL, Mulroy SJ, Thompson L, Adkins RH, Kahan JS. Effects of reduction in shoulder pain on quality of life and community activities among people living long-term with SCI paraplegia: a randomized control trial. The Journal of Spinal Cord Medicine 2011;34(3):278–84. https://doi.org/10.1179/107902611x12972448729486.
[7] Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. J Pain 2009;10(9):895–926. https://doi.org/10.1016/j.jpain.2009.06.012.
[8] Mitchell C, Adebajo A, Hay E, Carr A. Shoulder pain: diagnosis and management in primary care. BMJ 2005;331(7525):1124–8. https://doi.org/10.1136/bmj.331.7525.1124.
[9] Millett PJ, Gobezie R, Boykin RE. Shoulder osteoarthritis: diagnosis and management. Am Fam Physician Sep 1 2008;78(5):605–11 [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/18788237.
[10] Gil JA, Gunaseelan V, Defroda SF, Brummett CM, Bedi A, Waljee JF. Risk of prolonged opioid Use among opioid-naïve patients after common shoulder arthroscopy Procedures. Am J Sports Med 2019;47(5):1043–50. https://doi.org/10.1177/0363546518819780.
[11] Bindu S, Mazumder S, Bandyopadhyay U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: a current perspective. Biochem Pharmacol Oct 2020;180:114147. https://doi.org/10.1016/j.bcp.2020.114147.
[12] Yu DT, Chae J, Walker ME, Fang ZP. Percutaneous intramuscular neuromuscular electric stimulation for the treatment of shoulder subluxation and pain in patients with chronic hemiplegia: a pilot study. Arch Phys Med Rehabil Jan 2001;82(1):20–5. https://doi.org/10.1053/apmr.2001.18666 (in eng).
[13] Yu DT, et al. Intramuscular neuromuscular electric stimulation for poststroke shoulder pain: a multicenter randomized clinical trial. Arch Phys Med Rehabil May 2004;85(5):695–704. https://doi.org/10.1016/j.apmr.2003.07.015 (in eng).
[14] Chae J, et al. Intramuscular electrical stimulation for hemiplegic shoulder pain: a 12-month follow-up of a multiple-center, randomized clinical trial. Am J Phys Med Rehabil Nov 2005;84(11):832–42. https://doi.org/10.1097/01.phm.0000184154.01880.72 (in eng).
[15] Renzenbrink GJ, Ijzerman MJ. Percutaneous neuromuscular electrical stimulation (P-NMES) for treating shoulder pain in chronic hemiplegia. Effects on shoulder pain and quality of life. Clin Rehabil Jun 2004;18(4):359–65 (in eng).
[16] Chae J, Wilson RD, Bennett ME, Lechman TE, Stager KW. Single-lead percutaneous peripheral nerve stimulation for the treatment of hemiplegic shoulder pain: a case series. Pain Pract Jan 2013;13(1):59–67. https://doi.org/10.1111/j.1533-2500.2012.00541.x (in eng).
[17] Wilson RD, Gunzler DD, Bennett ME, Chae J. Peripheral nerve stimulation compared with usual care for pain relief of hemiplegic shoulder pain: a randomized controlled trial. Am J Phys Med Rehabil Jan 2014;93(1):17–28. https://doi.org/10.1097/PHM.0000000000000011.
[18] Wilson RD, Harris MA, Gunzler DD, Bennett ME, Chae J. Percutaneous peripheral nerve stimulation for chronic pain in subacromial impingement syndrome: a case series. Neuromodulation Dec 2014;17(8):771–6. https://doi.org/10.1111/ner.12152. ; discussion 776.
[19] Wilson RD, Bennett ME, Lechman TE, Stager KW, Chae J. Single-lead percutaneous peripheral nerve stimulation for the treatment of hemiplegic shoulder pain: a case report. Arch Phys Med Rehabil May 2011;92(5):837–40. https://doi.org/10.1016/j.apmr.2010.11.003 (in eng).
[20] Chitneni A, Hasoon J, Urits I, Viswanath O, Berger A, Kaye AD. Peripheral nerve stimulation for chronic shoulder pain due to rotator cuff Pathology. Orthop Rev 2022;14(3). https://doi.org/10.52965/001c.37494.
[21] Mansfield JT, Desai MJ. Axillary peripheral nerve stimulation for chronic shoulder pain: a retrospective case series. Neuromodulation Aug 2020;23(6):812–8. https://doi.org/10.1111/ner.13096.
[22] Mansfield JT, Desai MJ. Axillary peripheral nerve stimulation for painful end-stage primary osteoarthritis of the shoulder: a case report. Neuromodulation Aug 2020;23(6):878–80. https://doi.org/10.1111/ner.13089.

[23] Pressler MP, Callihan PC, Singla P, Mendelson AM. Novel and effective Use of peripheral nerve stimulation to treat trauma-Induced chronic shoulder pain: a case report. Pain Medicine Case Reports 2023;7(4):197–200.
[24] Chae J, Yu D, Walker M. Percutaneous, intramuscular neuromuscular electrical stimulation for the treatment of shoulder subluxation and pain in chronic hemiplegia: a case report. Am J Phys Med Rehabil Apr 2001;80(4):296–301. https://doi.org/10.1097/00002060-200104000-00014.
[25] Witkin LR, et al. Patient-reported outcomes and opioid Use in outpatients with chronic pain. J Pain May 2017;18(5):583–96. https://doi.org/10.1016/j.jpain.2016.12.018.
[26] Tan G, Jensen MP, Thornby JI, Shanti BF. Validation of the Brief pain Inventory for chronic nonmalignant pain. J Pain Mar 2004;5(2):133–7. https://doi.org/10.1016/j.jpain.2003.12.005 (in eng).
[27] Dworkin RH, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain Feb 2008;9(2):105–21. https://doi.org/10.1016/j.jpain.2007.09.005.
[28] Mouton WG, Bessell JR, Otten KT, Maddern GJ. Pain after laparoscopy. Surg Endosc 1999;13(5):445–8. https://doi.org/10.1007/s004649901011.
[29] Park SJ. Postoperative shoulder pain after Laparoscopic surgery. The Journal of Minimally Invasive Surgery 2020;23(1):3–4. https://doi.org/10.7602/jmis.2020.23.1.3.
[30] Bjørnholdt KT, Brandsborg B, Søballe K, Nikolajsen L. Persistent pain is common 1–2 years after shoulder replacement: a nationwide registry-based questionnaire study of 538 patients. Acta Orthop 2015;86(1):71–7.
[31] Fredrickson MJ, Krishnan S, Chen CY. Postoperative analgesia for shoulder surgery: a critical appraisal and review of current techniques. Anaesthesia 2010;65(6):608–24. https://doi.org/10.1111/j.1365-2044.2009.06231.x.
[32] Vajapey SP, Contreras ES, Cvetanovich GL, Neviaser AS. Neurologic complications in primary anatomic and reverse total shoulder arthroplasty: a review. J Clin Orthop Trauma Sep 2021;20:101475. https://doi.org/10.1016/j.jcot.2021.06.005.
[33] Cheppalli N, Bhandarkar AW, Sambandham S, Oloyede SF. Safety and efficacy of Genicular nerve radiofrequency ablation for management of painful total knee replacement: a systematic review. Cureus 2021. https://doi.org/10.7759/cureus.19489.
[34] Bage T, Power DM. Iatrogenic peripheral nerve injury: a guide to management for the orthopaedic limb surgeon. EFORT Open Reviews 2021;6(8):607–17. https://doi.org/10.1302/2058-5241.6.200123.
[35] Chitneni A, Berger AA, Orhurhu V, Kaye AD, Hasoon J. Peripheral nerve stimulation of the Saphenous and Superior Lateral Genicular nerves for chronic pain after knee surgery. Orthop Rev 2021;13(2). https://doi.org/10.52965/001c.24435.
[36] Fruh A, et al. Peripheral nerve stimulation for the treatment of chronic knee pain. Sci Rep Sep 20 2023;13(1):15543. https://doi.org/10.1038/s41598-023-42608-x (in eng).
[37] Ilfeld BM, et al. Ultrasound-guided percutaneous peripheral nerve stimulation: a Pragmatic effectiveness trial of a Nonpharmacologic alternative for the treatment of postoperative pain. Pain Med Dec 12 2020;21(Suppl 2):S53–61. https://doi.org/10.1093/pm/pnaa332.
[38] Ilfeld BM, et al. Neurostimulation for Postsurgical analgesia: a novel system enabling ultrasound-Guided percutaneous peripheral nerve stimulation. Pain Pract Sep 2017;17(7):892–901. https://doi.org/10.1111/papr.12539.
[39] Ilfeld BM, et al. Percutaneous peripheral nerve stimulation (Neuromodulation) for postoperative pain: a randomized, Sham-controlled pilot study. Anesthesiology Jul 1 2021;135(1):95–110. https://doi.org/10.1097/ALN.0000000000003776.
[40] Ilfeld BM, et al. Percutaneous Neuromodulation of the brachial plexus and Sciatic nerve for the treatment of Acute pain following surgery: Secondary outcomes from a multicenter, randomized, controlled pilot study. Neuromodulation Apr 2023;26(3):638–49. https://doi.org/10.1111/ner.13492 (in eng).
[41] Ilfeld BM, et al. Ultrasound-guided percutaneous peripheral nerve stimulation: Neuromodulation of the Femoral nerve for postoperative analgesia following Ambulatory Anterior Cruciate Ligament Reconstruction: a Proof of Concept study. Neuromodulation Jul 2019;22(5):621–9. https://doi.org/10.1111/ner.12851.
[42] Dimitroulas T, Duarte RV, Behura A, Kitas GD, Raphael JH. Neuropathic pain in osteoarthritis: a review of pathophysiological mechanisms and implications for treatment. in Seminars in arthritis and rheumatism 2014;44(2):145–54.
[43] Thomas M, et al. Glenohumeral osteoarthritis. Shoulder Elbow 2016;8(3):203–14. https://doi.org/10.1177/1758573216644183.
[44] Deer TR, et al. Peripherally Induced reconditioning of the central nervous system: a Proposed Mechanistic theory for sustained relief of chronic pain with percutaneous peripheral nerve stimulation. J Pain Res 2021;14:721–36. https://doi.org/10.2147/JPR.S297091.
[45] Zhu J, Gu R, Shi L, Su Y. Altered intrinsic brain activity in patients with neuropathic pain after brachial plexus avulsion. Brain Res Bull Jan 2024;206:110831. https://doi.org/10.1016/j.brainresbull.2023.110831 (in eng).
[46] Sparling T, Iyer L, Pasquina P, Petrus E. Cortical Reorganization after limb Loss: Bridging the Gap between basic Science and clinical Recovery. J Neurosci Jan 3 2024;44(1). https://doi.org/10.1523/JNEUROSCI.1051-23.2023 (in eng).
[47] Issa CJ, Svientek SR, Dehdashtian A, Cederna PS, Kemp SWP. Pathophysiological and Neuroplastic Changes in Postamputation and neuropathic pain: review of the Literature. Plast Reconstr Surg Glob Open Sep 2022;10(9):e4549. https://doi.org/10.1097/GOX.0000000000004549 (in eng).
[48] Kurien T, et al. Chronic postoperative pain after total knee arthroplasty: the potential contributions of synovitis, pain sensitization and pain catastrophizing-An explorative study. Eur J Pain Oct 2022;26(9):1979–89. https://doi.org/10.1002/ejp.2018.
[49] Pogatzki-Zahn EM, Segelcke D, Schug SA. Postoperative pain-from mechanisms to treatment. Pain Rep Mar 2017;2(2):e588. https://doi.org/10.1097/PR9.0000000000000588.
[50] Iio R, et al. Assessment of prevalence and risk factors for central sensitization related to shoulder osteoarthritis and rotator cuff Tears using the central sensitization Inventory: a cross-sectional study in shoulder surgery patients. J Clin Med Aug 29 2023;12(17):5633. https://doi.org/10.3390/jcm12175633.
[51] Vu PD, Hasoon JJ, Chen GH. Pain relief and Dermatological Changes in complex regional pain syndrome with peripheral nerve stimulation. Pain Med Dec 18 2023. https://doi.org/10.1093/pm/pnad163.
[52] Huntoon MA, Slavin KV, Hagedorn JM, Crosby ND, Boggs JW. A retrospective review of real-world outcomes following 60-day peripheral nerve stimulation for the treatment of chronic pain. Pain Physician May 2023;26(3):273–81 [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/37192232.
[53] Kelly TD, Pazzol ML, Rahimi Darabad R. Peripheral nerve stimulation in chronic knee pain: a case series. Cureus Dec 2023;15(12):e50127. https://doi.org/10.7759/cureus.50127.
[54] Mainkar O, Singh H, Gargya A, Lee J, Valimahomed A, Gulati A. Ultrasound-guided peripheral nerve stimulation of Cervical, thoracic, and Lumbar spinal nerves for Dermatomal pain: a case series. Neuromodulation Aug 2021;24(6):1059–66. https://doi.org/10.1111/ner.13334.
[55] Naidu R, Li S, Desai MJ, Sheth S, Crosby ND, Boggs JW. 60-Day PNS treatment may Improve Identification of Delayed responders and Delayed non-responders to Neurostimulation for pain relief. J Pain Res 2022;15:733–43. https://doi.org/10.2147/JPR.S349101.
[56] Pingree MJ, Hurdle MF, Spinner DA, Valimahomed A, Crosby ND, Boggs JW. Real-world evidence of sustained improvement following 60-day peripheral nerve stimulation treatment for pain: a cross-sectional follow-up survey. Pain Manag Jul 2022;12(5):611–21. https://doi.org/10.2217/pmt-2022-0005.
[57] Sudek EW, Mach S, Huh B, Javed S. Use of Temporary percutaneous peripheral nerve stimulation in an Oncologic population: a retrospective review. Neuromodulation Jan 2024;27(1):118–25. https://doi.org/10.1016/j.neurom.2023.06.009 (in eng).
[58] Vangeison CT, Bintrim DJ, Helms J, Saha AK, Samant AN, Chung M. The role of peripheral nerve stimulation in refractory non-operative chronic knee osteoarthritis. Pain Manag Apr 2023;13(4):213–8. https://doi.org/10.2217/pmt-2023-0025 (in eng).