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Six Month Outcomes from Randomized Clinical Trial for Efficacy of Spinal Cord Stimulation at 10 kHz to treat Non-Surgical Refractory Back  
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–Scott M. Fisher, DO

**Overall Scientist**

Differential Target Multiplexed SCS using reduced energy parameters in an Animal Model of Neuropathic Pain  
– David L. Cedeno, PhD

**Oustanding Abstract Achievement**

– Alex D. Pham, MD

# Spinal Cord Stimulation at 10kHz for Non-Surgical Refractory Back Pain: Multicenter RCT Six-Month Results

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## Introduction

Chronic refractory back pain has a major negative impact on mental health and quality of life (QOL), and a high societal cost in terms of lost productivity and health care utilization.<sup>1</sup>

Few treatment options exist for chronic back pain patients who have failed conventional medical management (CMM) and who have not had and are not candidates for back surgery<sup>2</sup>, a condition we refer to as non-surgical refractory back pain (NSRBP).

A long-term (36 month), though small feasibility suggests 10 kHz SCS is effective in NSRBP but more evidence is needed<sup>3</sup>

## Study Objectives and Design

The objective of this multicenter, randomized controlled trial (RCT) is to produce evidence comparing 10kHz-SCS plus CMM (10kHz SCS+CMM) to CMM alone for treatment of NSRBP in terms of clinical- and cost-effectiveness.

NSRBP patients, as defined above, were enrolled if ineligible for surgery based on surgical consultation, as described by Patel et al.<sup>4</sup>

Subjects randomized to 10kHz-SCS+CMM underwent permanent implantation if ≥50% pain relief was achieved during a temporary trial.

Both groups received CMM per standard of care, and crossover was optional for both arms at 6 months.

Primary endpoint: proportion of subjects in each group achieving >50% pain relief at 3 months compared to baseline

Five secondary endpoints were assessed at 6 months and evaluated in a hierarchical manner, comparing the two arms in terms of pain relief (VAS), proportion achieving 10 pts or more reduction in Oswestry disability index (ODI), quality of life (EQ-5D-5L), patient's global impression of change (PGIC), and change in opioid use from baseline.

## Results

Fifteen sites enrolled 211 subjects with 52 screen failures resulting in randomization of 159 subjects (Table 1). Four subjects (10kHz-SCS+CMM = 3, CMM = 1) withdrew prior to treatment. Eighty of the 10kHz-SCS+CMM proceeded to trial, and 74(92.5%) were deemed successful. Five 10kHz-SCS+CMM withdrew for various reasons following a successful trial, and 69 proceeded to implant. In per-protocol analysis, the responder rates were 80.9% and 80.0% for 10kHz-SCS+CMM arm and 1.3% and 2.7% for CMM arm at 3 and 6 months respectively (p < 0.001).

Table 1. Demographics

	10kHz SCS + CMM n=83	CMM n=76
Age in years, median (range)	53 (29.0 to 87.0)	58.50 (26.0 to 77.0)
Sex (female/male), n	(50/33)	(40/36)
Years since diagnosis of CLBP, median (range)	8.50 (0.0 to 52.0)	8.00 (1.0 to 59.0)
Back Pain VAS, Mean (SD)	7.4 (1.2)	7.2 (1.0)
Pain Etiology <sup>a</sup> , n (%)		
Degenerative disc disease	60 (72.3%)	52 (68.4%)
Internal disc disruption / annular tear	8 (9.6%)	6 (7.9%)
Spondylolysis	55 (66.3%)	49 (64.5%)
Lumbar facet-mediated pain	24 (28.9%)	25 (32.9%)
Radiculopathy	34 (41.0%)	35 (46.1%)
Mild/mod spinal stenosis	23 (27.7%)	24 (31.6%)
Spondylolisthesis	7 (8.4%)	9 (11.8%)
Sacroiliac dysfunction	3 (3.6%)	5 (6.6%)

Figures 1 - 5 summarize the primary and secondary endpoints which were met, with superior outcomes in the 10kHz-SCS+CMM group (p < 0.001).

Figure 1. Primary endpoint: Responder Rate

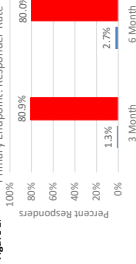


Figure 3. ODI Responder Rate (≥ 10 pt reduction)

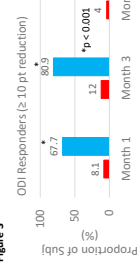


Figure 2. VAS - Change from Baseline

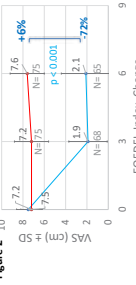
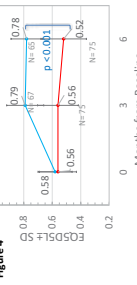


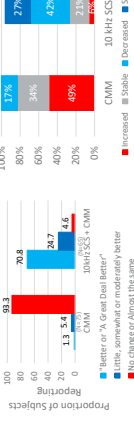
Figure 4. EQ-5D-5L Index Change



Mean change in opioid daily dose was -17.7 vs. +1.0 MME for the 10 kHz SCS and CMM group respectively, p = 0.001. Sixty-nine percent of 10kHz SCS group decreased or stopped opioids vs 17% decreased and 0% stopped in CMM group (Figure 6).

Two procedure related SAE in the 10kHz SCS + CMM arm, osteomyelitis, and severe lethargy due to post operative meds, both resolved. No study related SAEs occurred in the CMM Alone group.

Figure 5. PGIC - Change in Daily Opioid Dose



## Conclusions

- All primary and secondary endpoints were met, verifying that adding 10kHz SCS to CMM results in significant improvement in pain relief, function, quality of life, awareness of positive change, as well as reduction in daily opioid use.
- The 10kHz SCS arm achieved changes in measured outcomes that were multiple times the minimum clinically important difference for each outcome
- The outcomes reported here at 6 months are not different from that reported in the pivotal trial for 10 kHz SCS in a predominantly FBSS population
- The other dimensions of response, including disability (ODI), and quality of life (EQ-5D5L), mirror the response seen in pain relief (VAS).

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Study is funded by Neuro Corp.

# No Differences in Pain Scores and Treatment Response in Patients from Different Socioeconomic Areas in the City of Chicago

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Advocate Illinois Masonic Medical Center

## Introduction

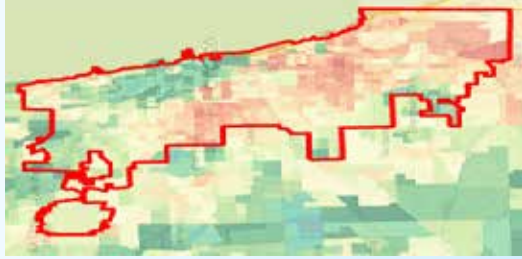
- Racial/ethnic differences in chronic pain experience are evident but poorly understood.
- It is apparent that racial and ethnic minorities are undertreated for pain as compared to Caucasian counterparts<sup>1</sup>
- Socioeconomic status has been linked to worsened pain and disability independent of race.<sup>2</sup>
- Provider biases have been shown to contribute to disparities in healthcare among minorities and patients of low socioeconomic status.<sup>2</sup>
- Chicago has vast variability in race/ethnicity as well as socioeconomic status and serves as an adequate population to study pain outcomes.
- The aim of our study was to find if there were any differences in pain scores or treatment responses between patients with different socioeconomic status estimated by median income by zip-code.

## Methods

- After IRB approval, a retrospective analysis of 1,149 patients treated for different chronic pain conditions at Advocate Illinois Masonic Medical Center Pain Clinic was performed. 207 patients in zip codes with median income <\$51,294, 515 with income \$40,083 and \$51,294, 332 with income \$30,625 and \$40,083, and with income between \$0 and \$30,625.
- Pre and post treatment pain scores, as well as subjective percentage improvement were recorded.
- Various treatment modalities were identified including interventional pain procedures and pharmacologic therapies.
- Opioid utilization at any time throughout treatment was identified and Milligram Morphine Equivalents (MMEs) at first and last visit were calculated using MIDCalc.
- Patients were stratified into quartiles determined by median income by zip-code according to Zip Atlas.

Quartile	Average Age	Average BMI	Total	Female	Male
75-100%	64.7	29.2	207	123 (59.5%)	84 (40.5%)
50-74%	62	30.5	332	200 (60.2%)	132 (39.8%)
25-49%	61.1	31.2	95	59 (62.1%)	36 (37.9%)
0-24%	62.1	30.7	118	71 (59.9%)	47 (40.1%)
Total			752	453 (60.2%)	299 (39.8%)

Quartile	Pre-treatment VAS (mm)	Post-treatment VAS (mm)	Pain Interference (mm)	Percent Improvement (%)	Subsequent Medication (mg)	Number of Visits (n)
75-100%	55.5	7.6	4.1	3.5	46.3	619
50-74%	43.8	13	4.3	3.7	43.5	533
25-49%	47.1	8	4.2	3.8	46.6	624
0-24%	43.9	13	4.3	3.5	44.7	507
Total						2183



Quartile	Opioid	Membrane Stabilizer	NSAID	Muscle Relaxant	TCA	Benzodiazepine	Other Psych
75-100%	130 (22.8%)	64 (30.5%)	119 (54.6%)	55 (26.6%)	9 (4.3%)	47 (22.7%)	59 (28.5%)
50-74%	249 (56.3%)	208 (46.4%)	207 (55.7%)	142 (37.6%)	30 (5.8%)	202 (59.8%)	188 (53.8%)
25-49%	229 (27.2%)	148 (14.6%)	161 (54.5%)	108 (32.8%)	17 (5.1%)	78 (23.5%)	84 (25.3%)
0-24%	63 (53.2%)	37 (35.9%)	50 (52.6%)	33 (33.7%)	3 (2.9%)	19 (18.8%)	25 (25.3%)
Total							

Quartile	Low Back Pain	Neck Pain	OA	Other/Multiple
75-100%	122 (58.5%)	24 (11.6%)	4 (1.9%)	58 (28%)
50-74%	223 (67.7%)	130 (39.3%)	71 (4%)	132 (35.6%)
25-49%	228 (55.7%)	28 (4.4%)	3 (0.4%)	89 (25%)
0-24%	67 (70.5%)	7 (7.4%)	2 (2.1%)	19 (20%)
Total	720	112	15	282

Quartile	MME First Visit (mg)	MME Last Visit (mg)	MME First-MME Last Visit (mg)	Special Injection	Other Intervention
75-100%	218	21	18	178 (86%)	56 (27.1%)
50-74%	173	174	-1	461 (85.5%)	137 (26.6%)
25-49%	362	93	269	284 (85.5%)	84 (25.3%)
0-24%	162	171	-9	85 (88.5%)	20 (21.1%)
Total					

## Results

- Significant differences in age, race, and BMI.
- No differences in type of pain or time since pain onset.
- Average pretreatment pain scores were not significantly different between quartiles.
- No differences in post-treatment pain scores or subjective percentage improvement.
- Highest opioid use and first visit MME in third quartile zip codes.
- No differences in non-opioid pharmacological therapy except membrane stabilizers.
- No differences in interventional procedures.

## Conclusions

- Results of our study showed that there were no differences in pain perception or treatment response in patients from different socioeconomic zip codes despite differences between groups in age, race, BMI, utilization of opioid medications, and MME at first visit.
- Patients at this pain practice all appear to have been treated with similar modalities regardless of socioeconomic status.

## References

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- Chicago, Illinois (IL) income map, earnings map, and wages data City-Data.com(21)

# Differential Target Multiplexed SCS using reduced energy parameters in an Animal Model of Neuropathic Pain

ASIPP ANNUAL MEETING 2021  
June 24-26 | New Orleans

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## INTRODUCTION

Spinal cord stimulation (SCS) utilizing a differential target multiplexed programming (DTMP) approach provided significant improvements in pain-like behavior in an animal model of neuropathic pain. DTMP modulated gene expression in pain-related processes toward levels of naïve animals while balancing neuron-glia interactions<sup>1,2,3</sup>. DTMP uses multiplexed signals that differentially target neurons and glial cells in the stimulated tissue. Preclinical work has been translated successfully to the clinic. Although energy demands of SCS treatments are served well by rechargeable devices, patients may also benefit from options that minimize battery consumption.

## MATERIALS AND METHODS

The effect of reduced energy DTMP derivatives (DTM-RE) on mechanical hypersensitivity and gene expression was studied. The IACUC at Illinois Wesleyan University approved procedures. Rats subjected to the spared nerve injury (SNI) model of neuropathic pain were randomly assigned to treatment groups (Table 1). Naïve animals served as a healthy control. Animals in SCS groups were implanted with a four-contact cylindrical lead at L1 level. Figure 1 shows a timeline of experimental procedures. Animals in the Naïve and No-SCS groups were assessed in parallel to SCS groups. Spinal cord ipsilateral to injury and adjacent to the stimulation lead were collected for RNA extraction. mRNA was isolated and sequenced. Weighted gene co-expression network analysis (WGCNA) and gene ontology enrichment analyses (GOEA) were used to determine the effect of SCS on gene expression and pain-related biological processes. Statistical analyses evaluated the effect of treatment.

Table 1. Experimental groups

Group	SNI	Stimulation
Naïve	No	No
No-SCS	Yes	No
Low Rate (LR)	Yes	50 Hz, 150µs, 70% MT
DTM-RE1	Yes	Proprietary, 50% MT
DTM-RE2	Yes	Proprietary, 50% MT

## MATERIALS AND METHODS

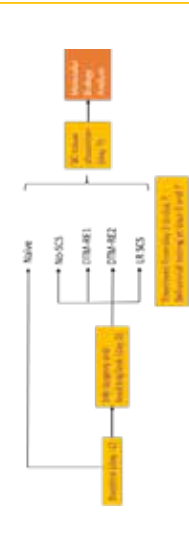


Figure 1. Timeline of Experimental Processes

## RESULTS

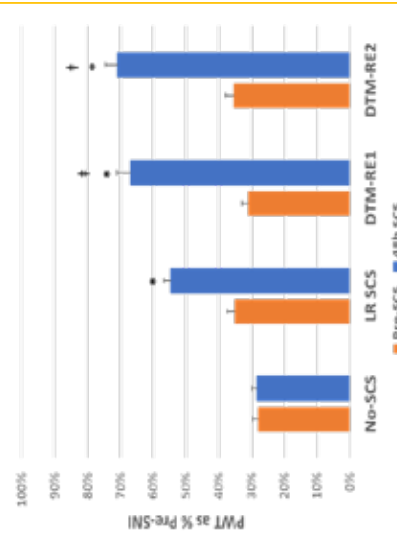
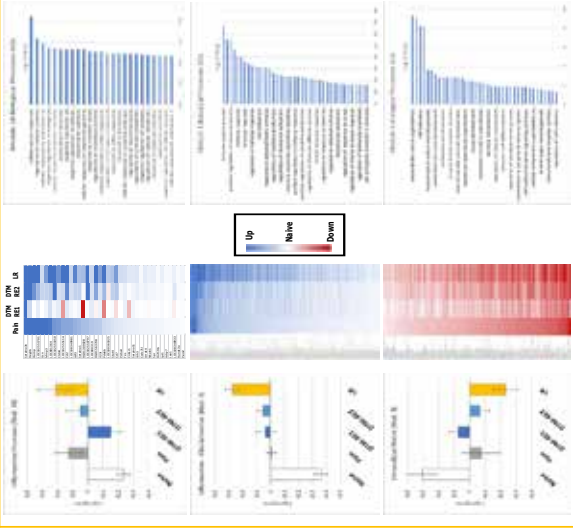


Figure 2. Bar graph showing mechanical hypersensitivity as a result of SCS treatments (LR and DTM-RE) and sham SCS treatment (No-SCS). Errors bars are SEM for N = 12 (No-SCS, DTM-RE2), N = 10 (LR SCS), and N = 9 (DTM-RE1). \* denotes P < 0.001 vs No-SCS; † denotes P < 0.05 vs LR SCS.

8,906 genes were subjected to WGCNA, resulting in 25 modules, of which 14 were significantly modulated by SNI relative to Naïve. Reduced energy DTMP SCS derivatives affected genes in some of these modules differently than LR SCS, modulating expression levels toward the naïve (no-pain) state.

## RESULTS (continued...)



## CONCLUSION

Reduced energy derivatives of DTMP significantly decreased mechanical hypersensitivity in the SNI animal model of neuropathic pain. These derivatives maintained the key elements of DTMP, which differentially modulated neurons and glial cells with multiple electrical signals. Given that they elicited changes in pain-related processes like those previously reported for DTMP in the same animal model<sup>1,2,3</sup> a common mechanism of action is hypothesized. This research has potential benefits if translated effectively to offer multiple effective therapy options that meet the needs of patients.

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## Dorsal Root Ganglion (DRG) and Chronic Pain

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**Background:** Chronic neuropathic pain is among one of the most widespread complaints of patients, as well as one of the most difficult to treat. Many methods and therapeutic targets have been attempted, with most seeming to have limited benefit and similar outcomes. It has been documented that as many as 11.9% of general practice patients suffer from inadequately controlled neuropathic pain[1]. Further evidence demonstrates an increased suicide rate among these patients, defining the need for improved pain control methods[1]. In contrast to existing suboptimal treatment methods, targeting the dorsal root ganglion (DRG) has begun to show promising effects in pain alleviation. The DRG are highly complex structures located on either side of the spinal cord that span the length of the spinal column. Each ganglion is an enlargement of the dorsal roots given off by the spinal cord. These structures are merely the size of a peanut but are able to house up to 15,000 neurons each. The neurons located within the DRG are responsible for sensory transduction and modulation from the periphery, including pain perception[2]. The location of the DRG, which is surrounded by rigid bony structures, leaves little room for expansion of displacement. Herniated disc and osteophytes are common conditions that may cause compression and inflammation at the level of the DRG[3]. The DRG contains clusters of the cell bodies of primary sensory neurons. Each of the axons of these sensory neurons house a variety of fibers with a range of size and excitability. These fibers include the A-beta, A-delta, and C fibers. Compared to the large, myelinated, and high velocity A-delta fibers, the C fibers are unmyelinated, smaller in diameter and have a much slower conduction velocity. Despite these variations, each of these fibers are responsible for conducting sensory signals from the periphery to the DRG and finally the central nervous system[2]. Further research demonstrates C fibers, specifically, play an active role in chronic pain. C-fibers nociceptors have been noted to be involved in aberrant pain signaling within the cell bodies of the DRG[4]. The DRG became a target for pain control, when it was initially hypothesized to be a source of chronic neuropathic pain. Initial therapies targeted towards the DRG were documented as early as 1949. Despite theories of the direct pain control at this location, the difficulty of access or minimal results have limited the progression of DRG pain control. Throughout the years, there have been various methods involving the DRG tested for pain relief. Some of these methods included dorsal rhizotomy or ganglionectomy, dorsal root entry zone (DREZ) lesioning (an adjacent related neural target), conventional radiofrequency denervation, pulsed radiofrequency, and steroid injection[2]. It has only been within recent years that neuromodulation of DRG, a less invasive measure, has gained greater recognition.

**Methods:**

We conducted a systemic comprehensive literature search using a collaboration of existing publications involving studies on DRG stimulation for chronic pain. We displayed existing literature, though limited, displays promising results.

**Results:**

Chronic neuropathic pain is a common condition and carries significant morbidity and impact on the quality of life. Recent evidence supports the use of dorsal root ganglion(DRG) neuromodulation as an effective technique to control chronic pain. Though studies are still emerging, the evidence appears to support this technique. Hunter et al. assessed DRG stimulation with 7 patients experiencing chronic pelvic pain. Results had shown that 4 of the patients reported continues pain relief with no loss of efficacy after one year. Placement of a DRG stimulator at L1 covered abdominal and groin pain while a S2 stimulator covered perineum pain, acting in a synergistic manner. Van Buyten et al. had assessed 11 patients with complex regional pain syndrome with 8 of them undergoing implantation. One month after, patients on a verge reported 62% decrease in pain versus baseline. Mol et al. assessed patients with anterior cutaneous nerve entrapment syndrome (ACNES) who had undergone DRG implantation. Results were not promising in this study as entrapped sensory nerves in the abdominal wall were difficult to treat. Petladé et al. had assessed 20 patients with post herpetic neuralgia (PHN) and had found that placing the electrodes of DRG stimulation on overlapping dermatomes adjacent to the affected DRG suppressed 5 PHN pain. Out of 20 patients sampled, 18 were approved for permanent stimulation implantation. After three months, 77.8% of the patients reported greater than 50% pain relief. Of note, implantation in the cervical region increased risk of complications. Chapman et al. assessed 17 patients with chronic lower back pain. 78% of the patients reported pain relief at 8 month follow up and more than half of the patients reported >80% pain relief from baseline. Deer et al assessed 152 patients diagnosed with complex regional syndrome or causalgia in lower extremities. It was found that 81.2% of subjects receiving DRG stimulation reported > 50% pain relief at 3 months compared to 55.7% of subjects having spinal cord stimulation. Subjects using DRG stimulation reported less postural variation in paresthesia and reduced extraneous stimulation in nonpainful areas, indicating DRG stimulation is superior for targeted therapy to painful parts of the lower extremities. Kallewaard et al had shown that 15 patients with disogenic lower back pain without previous back surgery underwent DRG stimulation and reported >50% pain relief at 1 year follow up. The participants who finished the twelve month study reported significant increases in quality of life, mood, and mobility. A final randomized controlled trial showed promise with the use of DRG stimulation for chronic postoperative inguinal pain. 8 out of the 10 patients reported > 50% reduction in pain from baseline. Chronic neuropathic pain is a common condition and carries significant morbidity and impact on the quality of life. Recent evidence supports the use of DRG neuromodulation as an effective technique to control chronic pain. Though studies are still emerging, the evidence appears to support this technique. Further studies, including large randomized trials evaluating DRG modulation versus other interventional and non-interventional techniques, are needed to further elucidate the efficacy of this method.

**Conclusion:** Chronic pain affects a large part of the population and carries a significant price tag in terms of quality of life, morbidity, and economic loss. Unfortunately, a significant number of patients continue to experience pain with their treatment continues to challenge providers. Many different approaches from multiple disciplines are being researched for the treatment of chronic pain, including conservative, pharmacologic, psychologic, and interventional approaches. Recently, stimulation of the DRG has emerged as a possible technique with positive results. DRG stimulation is a developing scientific technique with little known about the effectiveness and possible complications of permanent implantation devices to treat chronic pain. However, from the limited studies performed, there have been promising results. Chronic pain can be caused by numerous etiologies, including postherpetic neuralgia, lower axial back pain, chronic pelvic pain, anterior cutaneous nerve entrapment syndrome, complex regional pain syndrome, and many more. Dorsal root ganglion stimulation demonstrated greater improvements in quality of life and psychological disposition. An advantage of DRG stimulation is the precision of stimulation at a particular dermatome in contrast to spinal 6 cord stimulation, which affects a broader region. Another benefit of DRG stimulator implantation is a significant decrease in lead repositioning compared to SCS, allowing for more accurate results when reporting pain.



## Spinal Cord Stimulation for Painful Diabetic Peripheral Neuropathy: A Systematic Review

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### Background:

34 million people in the United States have currently been diagnosed with diabetes (10.5% of the US population), according to data from the Centers for Disease Control and Prevention. Additionally, there are 88 million people with prediabetes, which has resulted in the use of \$327 billion in health-care-related costs and lost productivity. It is estimated that 20% of patients with diabetes will develop painful diabetic neuropathy (PDN). Traditionally, patients suffering from PDN are first treated conservatively with medication management. The only treatments for PDN that are approved by the US Food and Drug Administration (FDA) are pregabalin, duloxetine, and tapentadol extended-release. 3 Gabapentin is also commonly prescribed, as are tricyclic antidepressants, opioid analgesics, topical lidocaine, capsaicin cream, isosorbide dinitrate spray and transcutaneous electrical nerve stimulation. These treatments demonstrate various degrees of success, and many times initial treatments are discontinued, indicating low levels of satisfaction or poor tolerability. Thus, at present there is a need to address the treatment gap for patients suffering from diabetic peripheral neuropathy that are receiving incomplete relief from conservative treatment. Neuromodulation with spinal cord stimulation has the potential to address this gap. Spinal cord stimulation has been shown to result in significant pain relief in patients with debilitating neuropathic pain conditions such as failed back surgery syndrome and complex regional pain syndrome. The neurophysiology of how spinal cord stimulation achieves pain relief is not completely understood. Both tonic and paresthesia-free, including burst and high-frequency, stimulation are able to generate highly effective and clinically significant analgesia. There is a growing body of evidence in the literature that spinal cord stimulation is a safe and effective therapy for PDN.

### Methods:

The present investigation was completed with the assistance of a research librarian at University of Colorado Strass Health Sciences Library, Aurora, Colorado. The protocol was designed according to PRISMA guidelines. Relevant literature was identified in the following bibliographic databases: Ovid MEDLINE-ALL (Ovid 1946-current), Embase (Embase.com, 1974-current), and the Cochrane Library (Wiley). No year limits were applied to the searches. The search strategies are based on the concepts of diabetic peripheral neuropathy and spinal cord stimulation using multiple subject headings and text-word terms for each concept. The following keywords were included in the search: "diabetic", "neuropathy", "polyneuropathy", "mononeuropathy", "autonomic", "neuralgia", "PDN", "peripheral diabetic", "diabetic neuropathies", "spinal", "high frequency", "electrical stimulation", "electric stimulation therapy", "spinal cord stimulation." Appendix A shows the full search strategies for all bibliographic databases. Searches were conducted on January 26, 2021. Discovery of the appropriate subject headings involved examining how gold standard articles are indexed, by assessing matches made by the subject heading databases (such as matches to MeSH in Medline), and by using word analysis tools specifically PubMed PubReminer (<https://hgsver2.amc.nl/cgi-bin/miner/miner2.cgi>) and TerMine (<https://naetm.ac.uk/software/terminer/>). All retrieved records were managed with Endnote version 9.3, a citation management application, and with Covidence ([www.covidence.org](http://www.covidence.org)), a systematic review application. Inclusion criteria for this review included randomized controlled trials (RCTs), retrospective, case-control and prospective observational studies assessing spinal cord stimulation for PDN. Exclusion criteria included case reports, case series, historical articles, letters, review articles, foreign language studies, non-human studies, cadaver studies, or conference abstracts. The citations identified were assessed for inclusion in the review using a multi-stage process. Initially, two reviewers (JM and NV) independently screened all study titles and abstracts identified by the electronic searches to identify the potentially relevant articles to be retrieved. Next, full-text copies of these studies were obtained and assessed independently by two reviewers for inclusion using the previously established inclusion criteria (JH and ZB). Any disagreements were resolved through discussion at each stage, and, if necessary, in consultation with a third reviewer (JM). A risk-of-bias assessment was completed for all randomized control trials using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2). Studies were assessed across multiple domains per the specifications of the RoB 2 tool. Studies found to have an overall high risk of bias were judged to be at high risk of bias in at least one domain or were judged to have some concerns for multiple domains. The prospective observational studies were not assessed with this tool, as they were considered to have an implicit risk of bias based on the nature of their study design.

### Results:

Randomized controlled studies: In 2014, de Vos et al. performed the first multi-center randomized controlled trial analyzing the effectiveness of spinal cord stimulation in patients with PDN. Sixty patients with PDN of the lower extremities refractory to conventional medical therapy were randomized 2:1 to best conventional medical practice with spinal cord stimulation or without. Both groups were assessed at regular intervals over a 6-month period using the Euro-Qol 5d, short form McGill Pain Questionnaire (SF-MPQ) and a Visual Analogue Scale (VAS; ranging 0-100). The 5 average VAS was 73 in the SCS group and 67 in the control group. After 6-months of treatment, the average VAS of the SCS group was reduced to 31 (P<0.001) and was 67 (p=0.97) in the control group. Improvements in pain, health and quality of life were also demonstrated in the SF-MPQ and the Euro-Qol 5d questionnaires. There were two adverse events related to the implantation procedure including pain due to the implanted pulse generator in 2 patients, as well as electrode lead migration in 1 patient. There was 1 infection during SCS trial, which resolved and was followed by a permanent implantation. 1 patient had previously undiagnosed ophthalmopathy, which complicated the implantation procedure and resulted in hospitalization. 95% of the patients in the SCS group might or would definitely recommend SCS treatment to other patients with PDN. Slangen et al. also performed a multicenter randomized controlled trial in 36 patients with PDN of the lower limbs. Twenty-two patients were randomly assigned to SCS in combination with best medical treatment while 14 were allocated to a best medical treatment group. Patients were followed over 6 months. Treatment success was defined as greater than 50% pain relief during daytime or nighttime, or "very much improved" for pain and sleep on the patient global impression of change (PGIC) scale at 6 months. Treatment success was achieved in 59% of the SCS and 7% of the best medical treatment group (P<0.05). The mean pain score on the NRS in the daytime was reduced by 3.1 points at 6 months in the SCS group as compared with no change in pain score in the control group (P<0.0001). One SCS patient died because of a subdural hematoma after dural puncture during trial. Another patient developed an infection that resulted in device removal. Prospective observational studies: There were several high-quality observational studies with long-term outcomes. A study demonstrating long-term outcomes of therapy was published by VanBeek et al in 2018. VanBeek followed 48 patients implanted with SCS for PDN over a 5-year period. Treatment success, defined as >30% pain reduction on the NRS scale was observed in 86% of patients after 1 year and 55% of patients after 5 years. 80% of patients with a permanent implant still used their device after 5 years. In terms of adverse events, two patients developed infections that led to device removal. Eight patients required one battery replacement and 5 patients required two battery replacements over 5 years. Four leads were damaged, and replaced during the 5 years, and 5 leads needed to be repositioned to 6 optimize paresthesia coverage. A study by Pliujins et al. of 15 patients demonstrated that 67% of patients experienced greater than 50% decrease in pain intensity at 12 months, while Slangen et al demonstrated 73% of patients had greater than 50% decrease in pain intensity at 12 months (though this dropped to 36% of patients at 36 months). Daoussi et al. demonstrated continued (greater than 50%) pain relief in all patients remaining in their cohort after 7 years.

**Conclusion:** Our review assessing spinal cord stimulation for peripheral diabetic neuropathy demonstrates evidence that it is an effective and safe option for treatment. However, further high-quality research, including a large-scale randomized controlled trial is warranted and would add to the current evidence.

## Role of Oliceridine in Pain Management

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### Background:

Pain is universal, and in its acute form, serves a physiologic response of alerting the body to current or foreseen tissue damage as a protection mechanism. Nociceptors play a key role in sensing pain in the form of high temperatures, pressure, and chemical irritants as well as facilitating its transmission to higher orders of the nervous system, including the brainstem and cortex, for interpretation. While acute pain often progressively resolves with the process of tissue healing, some may become chronic pain through a process called "pain chronification". While the mechanism is incompletely understood, chronic pain is becoming increasingly prevalent. It is estimated that in the United States alone, over 100 million adults are affected at any given time by chronic pain, with the healthcare cost of approximately 560-635 billion dollars per year. With the growing pervasiveness of chronic pain came a search for effective pharmacological products to treat pain, and opioids have been at the forefront of this discussion. With the more recent recognition of the addictive potential of opioids along with the increasing number of opioid-related overdoses came a search for greater control and monitoring, re-licensure of health care providers for prescribing, and even the production of Naloxone for opioid-related overdose. Naloxone is available for intravenous, intramuscular, or subcutaneous use. An autinjector, marketed as Evzio, is available to the general public and delivers a 0.4mg dose. The current labeling of Naloxone recommends an initial dose of 0.4 mg to 2 mg, followed by repeated doses up to 10 mg in the setting of suspected opioid overdose. This information additionally had created a search for effective pharmacological and non-pharmacological treatments of pain. While opioids were a proven and effective method of very successful pain control, particularly in patients with intractable cancer pain, the value of continued research on more effective methods has become clear in the field of medicine. One such potential treatment is oliceridine. Problems with the treatment of acute pain may arise when a patient is opioid-tolerant, such as those on chronic treatment with opioids or on opiate replacement therapy, abusers, and those who are in recovery. While some of the adverse effects of opioid medications are well known, it is also important to recognize the roles of tolerance and hyperalgesia. Oliceridine is the first of its kind by being able to target and to modulate a novel  $\mu$ -receptor pathway. The G protein-biased agonism of oliceridine allows for effective resensitization and desensitization of the  $\mu$ -opioid receptor, which decreases the formation of opioid tolerance in patients. Oliceridine has been demonstrated to be an effective and relatively safe intravenous analgesic for the treatment of postoperative pain, generally well tolerated with a favorable side effect profile when compared to morphine. As the prevalence of pain increases, it is becoming increasingly important to find safe and effective analgesics.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving oliceridine. We present the existing literature in the understanding of the safety and efficacy of oliceridine.

**Results:** A 2014 single-site study evaluated the safety, tolerability, and pharmacologic properties of increasing TRV130 doses (0.15 – 7mg IV) in healthy subjects, the impact of poor cytochrome P450 2D6 (CYP2D6) metabolism on TRV130, and the tolerability of short infusions. TRV130 showed good tolerance in all dosing groups, with moderate adverse events occurring only in the 7 mg dosing group. Plasma concentrations were highest at the end of the 1-hour infusion, later declining in multiple phases, indicating more than one distribution compartments. CYP2D6 poor metabolizers had a TRV130 C<sub>max</sub> 1.35 times higher and clearance that was ~50% lower when compared to their normal metabolizer counterparts. 1-, 5-, 15-, and 30-minute 1.5 mg TRV130 infusions were well tolerated. Another study in 2014 showed TRV130 had higher peak analgesia that was generally well tolerated with a reduced side effect profile when compared to morphine. A single-center, double-blind, randomized, placebo-4 controlled, crossover study evaluated  $\mu$ -opioid receptor TRV130 agonism against placebo or morphine IV for analgesia, safety, and tolerability in healthy male individuals. The subjects received single doses of TRV130, morphine IV, or placebo on every odd day for 10 days (day 1, 3, 5, 7, 9). TRV130 infusions were associated with a decreased side effect profile up to the 4.5 mg dosage, whereas the side effects of TRV130 were similar to those associated with morphine IV, while producing an equivalent analgesic effect. TRV130 induced a temporary decrease in respiratory drive that was markedly shorter from the morphine induced decreased respiratory drive that persisted through 4 hour post-infusion. In 2015, TRV130 showed statistically significant pain reduction when compared to placebo and morphine in the treatment of post-operative bunionectomy pain. The phase 2, randomized, double blinded, adaptive-design study assessed the efficacy and tolerability of TRV130 in postoperative bunionectomy patients. The first phase tested 1 mg, 2 mg, 3 mg, or 4 mg IV TRV130 q4h against placebo IV q4h and 4 mg morphine IV q4h. The second phase tested 0.5 mg, 1 mg, 2 mg, or 3 mg q3h against placebo IV q4h and 4 mg morphine IV q4h. In the first phase, 2 mg and 3 mg TRV130 showed better numeric rating scale of pain intensity over 48 hours (NRS TWA0-48) reductions than placebo, similar to morphine. In the second phase, TRV130 3 mg was more statistically efficacious than morphine 4 mg. No severe adverse events occurred in either phase of the study for TRV130, though some side effects were reported (nausea, dizziness, headache, and vomiting). TRV130 showed a smaller effect on oxygen saturation than morphine did. Oliceridine showed to be an effective and relatively safe IV analgesic for the treatment of postoperative pain related to abdominoplasty in 2019. The phase 3, double-blind, randomized placebo- and active-controlled study evaluated the safety and efficacy of oliceridine in treating abdominoplasty-related pain. The patients in the study received a loading dose of oliceridine 1.5 mg, morphine 4 mg, or placebo IV, which was then followed by demand doses of 0.1 mg, 0.35 mg, and 0.5 mg administered either by the patient or clinician. All treatment groups, except for the placebo group, showed markedly decreased need of rescue doses during the treatment course. The placebo group showed the highest occurrence of rescue pain medication use; oliceridine related severe adverse events were limited to syncope and lethargy during the study, while the other observed severe adverse events during treatment were thought to be related to other factors. Gastrointestinal adverse events showed a proportional dose-related relationship with oliceridine use up to the 0.5 mg oliceridine, wherein the incidence of gastrointestinal adverse events was similar to that of the morphine group.

### Conclusion:

Pain is universal and serves a physiological function in its most acute form. While most forms of acute pain resolve with tissue healing, it can also become chronic through the process of pain chronification. The treatment of chronic pain has a remarkable history, altered by drug availability, research, marketing, and even the political climate. Without necessary caution about its abusive potential and side effect profile, opioids entered the forefront of the chronic pain market. Opioids in their natural, semisynthetic, and synthetic forms all serve a similar purpose of analgesia and have proven to be very effective in their realm of pain relief. The search for breakthrough pain relief in patients with chronic pain conditions, most commonly cancer-related, led to considerations of which medications to use and how to administer them. Other concerns, including the various side effect profile and addictive potential of opioids, opened the conversation for medications like oliceridine. Oliceridine is the first drug of its kind that targets and modulates the  $\mu$  receptor's G protein pathway, with the goal of decreasing medication tolerance reducing the incidence of adverse effects. As the prevalence of chronic pain increases, it is becoming increasingly important to find safe and effective medications to treat these conditions. Pain is not only costly in the economic realm but takes a great toll on the quality of life of the patients it affects. Thus, a continued goal of medical research involves extrapolating the effectiveness of opioids in terms of analgesia while simultaneously reducing the side effects and abuse potential.

**Disclosure:** Dr. Kaye served on the FDA Advisory Board on Anesthetics, Analgesics, and Addiction Medicine, which reviewed the application for oliceridine. Dr. Urman has received funding from Medtronic, Merck, and AcelfRx.



**Viable Disc Tissue Allograft Supplementation in the Treatment of Degenerated Intervertebral Discs: One Year Results of a Randomized Control Trial**

**Meredith Langhorst, MD,**  
 Timothy Davis, MD  
 Kasra Amiridelfan, MD,  
 Douglas P. Beall, MD,  
 Michael J. DePalma, MD

**Introduction**

- Chronic low back pain (CLBP) results from internal disc disruption and associated degeneration of the nucleus pulposus.
- A viable disc tissue allograft has been developed to supplement tissue loss associated with degenerated lumbar intervertebral discs and the development of CLBP.

**Materials and Methods**

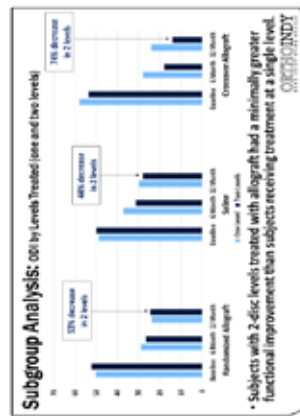
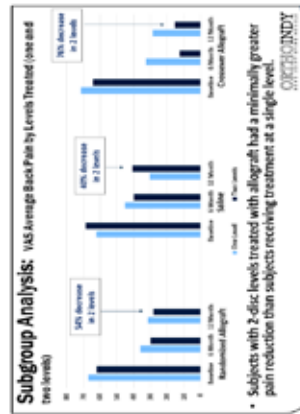
- RCT: 218 patients enrolled, age 19 to 73
- Visual Analog Score (VAS)  $\geq$  40 mm
- Oswestry Disability Index (ODI) Score  $\geq$  40
- Symptoms > than 6 months
- Subjects blinded to receive intradiscal injections of active allograft (AA) or saline (S) or continued non-surgical management (NSM)

- Co-primary clinical outcomes (ODI and VAS) were assessed at 12 months
- Exploratory analysis of Minimal Clinically Important Differences (MCIDs) between groups were assessed for ODI and VAS scores at 12 months

**Discussion**

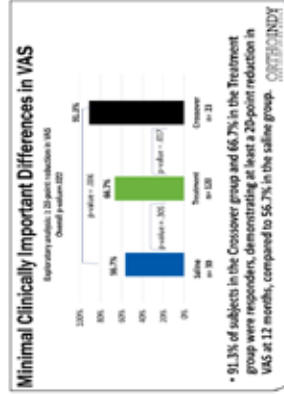
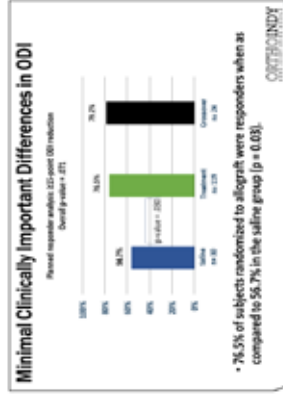
The need for an effective treatment for stable discogenic low back pain is necessary as the existing treatments are marginally effective.

**This prospective blinded RCT suggests that viable disc tissue allograft may be a beneficial and durable treatment for patients with chronically painful lumbar degenerative discs. Both one and two-level treatment produce comparable results with slightly better improvements in pain and function with two-level treatment.**



**Results at 12 months**

- 76.5% of allograft group vs. 56.7% in saline group were responders: ODI  $\geq$  15 pts.
- The planned responder analysis of  $\geq$  50% reduction in VAS, did not demonstrate significant differences.
- 91.3 % of the NSM/crossover group vs 66.7% of the active allograft group and 56.7% of the saline group showed a  $\geq$  20-point VAS improvement.
- VAS scores improved 30.5, 34.0, and 46.7 in the saline (S), active allograft (AA), and the crossover to allograft (COA) groups respectively.
- ODI scores improved 23.9, 27.4 and 36.4 in the same groups, with no statistical difference among groups.



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*Acknowledgement: This clinical study was supported by funding provided by Vivex Biologics, Inc.*





# Real-World Evaluation of an Interspinous Spacer used for the Treatment of Lumbar Spinal Stenosis


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## BACKGROUND

Indirect Decompression Systems (IDS) or Interspinous Spacers are an option in well-selected patients with impaired physical function who experience relief in flexion from symptoms of leg, buttock and/or groin pain due to lumbar spinal stenosis (LSS). A growing body of published clinical evidence has demonstrated excellent long-term clinical benefit with sustained pain relief, improved quality of life and medication reduction up to 5 years post-implant.<sup>1-3</sup> Real-world reports demonstrated excellent long-term clinical benefit for patients including leg pain responder rate and pain severity of 75% and 60% respectively at 12 months post operation.<sup>4</sup> Here, we provide real-world outcomes in patients with severe pain who received an Indirect Decompression System (IDS) for LSS related pain and symptoms as part of an ongoing multi-center observational case series.

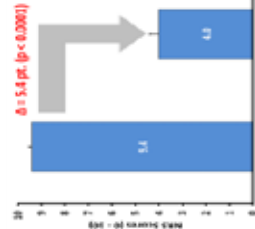
## METHODS

<b>Study Design</b>	Multi-center, observational case-series. Data collected by site personnel only
<b>Study Device</b>	Boston Scientific Superior Indirect Decompression Systems (IDS) 
<b>Patients/Sites</b>	41 patients with severe pain (8 or above) at 7 centers who received IDS for their Lumbar Spinal Stenosis (LSS)

## RESULTS

Gender - Females (%)	56% (23 / 41)
Age [Mean (SD)]	69.7 (11.2) years n = 41
Baseline NRS [Mean (SD)]	9.4 (0.5) n = 41
Follow-up [Mean (SD)]	115.1 (161.8) days n = 41
Diagnosis	Lumbar Spinal Stenosis

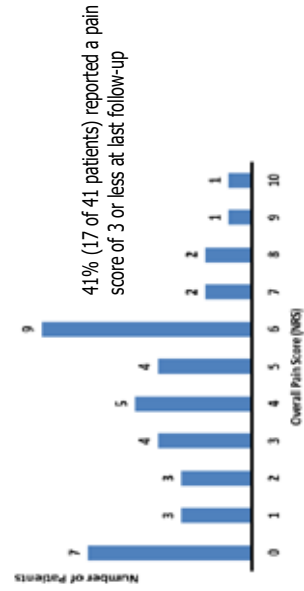
Overall Pain Scores (n = 41)



A 5.4-point improvement (9.4 → 4.0,  $p < 0.0001$ ,  $n = 41$ ) was reported at last follow up (mean = 115 days) among patients with severe pain at Baseline (8 or more)

90% (37 of 42) of patients reported a clinically significant\* improvement in their overall pain at last follow-up  
\*  $p < 0.05$  improvement in pain score (NRS)

Distribution of pain scores at last follow-up (n = 41)



41% (17 of 41 patients) reported a pain score of 3 or less at last follow-up

## CONCLUSIONS

Results from this ongoing real-world observational case-series of severe pain patients (8 or more on NRS scale) who received IDS for the treatment of their LSS symptoms demonstrated at last follow-up (mean = 115 days):

- 5.4-point improvement in overall pain (9.4 → 4.0,  $p < 0.0001$ )
- 90% reported a clinically significant improvement in pain (i.e.,  $\geq 2$ -point improvement)
- 41% reported a pain score of 3 or less

This preliminary evidence aligns with other published reports.

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## DISCLOSURES

This study is sponsored by Boston Scientific. Holly Kaufman, Lilly Chen and Roshini Jain are employees of Boston Scientific.

A 60 Patient Observational Study on the Use of a Patient Navigator to Help Improve Outcomes in Patients on Chronic Opioids



Amol Som, MD, Jae Chen, MD, David Barrell, MD, Amos Wangombe, Am Pollack, Anu Patel



<p><b>ABSTRACT</b></p> <ul style="list-style-type: none"> <li><b>ABSTRACT</b></li> <li><b>Background:</b> In the United States, the prevalence of opioid use disorders has increased in recent years along with an attendant rise in the incidence of chronic pain disorders and prescription opioid use. Patient navigation services have been used to improve health outcomes in cancer and other chronic disease states, but it is unclear whether the implementation of patient navigation services can facilitate improved outcomes among patients receiving chronic opioid therapy.</li> <li><b>Objectives:</b> The objective of this study was to compare the outcomes of patients receiving chronic opioid therapy plus patient navigation services and those receiving chronic opioid therapy as a part of usual care.</li> <li><b>Methods:</b> This was a prospective, observational study conducted at a single independent pain clinic in the United States. Consecutive patients receiving chronic opioid therapy were enrolled, with alternating assignments to patient navigation (n = 30) or usual care (n = 30). Participants in the patient navigation group received support from a non-physician, non-advanced practice provider staff member who initiated frequent contact via telephone, telemedicine, or in-clinic visits to discuss the patient's health goals. The minimum follow-up period was 90 days. Outcomes qualitatively compared across groups included final pain score, final morphine milligram equivalent (MME) per day, and discharge rates. Risk factors for discharge within the navigation group were assessed. Patient feedback was also solicited.</li> </ul>	<p><b>RESULTS</b></p>	<p><b>RESULTS</b></p> <p>❖ <b>Results:</b> Demographic features were similar between the navigator group and the control group. The control group had a higher average initial pain score (7.0/10) than the intervention group (5.9/10) and were receiving a higher initial dose of opioids (23.1 vs 19.0 MME/d). After an average follow-up of 108.7 days, patients in the navigator group had a 16% decrease in final opioid dose compared with a 23% increase in the control group. Furthermore, patients in the control group were discharged from the practice at a higher rate (23.3% vs 6.6%), suggesting increased opioid misuse in the control group compared with the navigator group. In the</p>	<p>Navigator patients demonstrated better compliance and utilized less morphine milliequivalents per day than control group</p> <p><b>Conclusions:</b> Patient navigation decreased opioid use and practice discharge compared with usual care in an independent pain clinic, suggesting a role for patient navigation in reducing opioid misuse and potentially saving lives.</p>
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# A Case of Thoracic T1-T2 Disc Herniation Mimicking Cervical Radiculopathy

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## Introduction

The most common cause of neck pain radiating to the hands is cervical disc herniations. A thoracic disc herniation presenting as neck pain with radiation to the upper extremities is rare. There is a case report of T1-T2 disc herniation by Siven and Karavitis published in 1954.<sup>[1]</sup> In general, thoracic disc herniations are less common, asymptomatic and are usually in the lower thoracic levels. This case reports a patient with T1-T2 disc herniation presenting with T1 radiculopathy, manifesting with neck pain and upper extremity symptoms. The clinical signs and symptoms of T1 radiculopathy are similar to those of C8 radiculopathy.<sup>[2]</sup> The patient had left sided disc herniations which were red-herrings, and a cervical epidural steroid injection at T1-T2 level resolved her symptoms.

## Case Description

A 60-year-old female in need of pain management presented with neck pain radiating to the right upper extremity with tingling and numbness in the inner aspect of the right forearm as well as tingling in the little finger and right finger following a motor vehicle accident. Physical examination revealed decreased sensation in the inner aspect of the hand and the right ring finger and the inner aspect of the right forearm. The deep tendon reflexes were normal; however, there was motor weakness in the right upper extremity. Hoffman's sign was negative on the right side. An MRI study of the cervical spine was obtained which demonstrated disc herniations on the left side at C5-C6 and C6-C7, as well as a right paracentral herniation at the T1-T2 level. The left sided disc herniations could not explain the right sided symptoms. A subsequent MRI of the Thoracic spine confirmed the right paracentral disc herniation at T1-T2. It was deemed that the right sided symptoms were due to T1-T2 disc herniation. The patient underwent an interlaminar Thoracic epidural steroid injection using right paramedian approach at T1-T2 using Dexamethasone under fluoroscopic guidance. The patient tolerated the procedure well and had complete resolution of the right sided paresthesias. This case highlights the importance of looking at T1-T2 disc herniations which can mimic cervical radiculopathy. In these cases, a Thoracic epidural steroid injection at T1-T2 is necessary rather than a routine Cervical epidural steroid injection.

## Discussion

Thoracic disc herniations commonly are asymptomatic with most herniations located below the T8 level.<sup>[3]</sup> The radicular symptoms depend on the level of the root involved. The most common symptom of Thoracic radiculopathy is pain.<sup>[4]</sup> Patients can have chest wall paresthesias and motor weakness in severe cases.<sup>[5]</sup> The incidence of Thoracic disc herniations at T1-T2 is rare because of the relative immobility created by the junction of the first rib and the spine.<sup>[6]</sup> When patients present with cervical radicular pain, a cervical spine MRI typically images C1-T1 vertebra. The T1-T2 level is often inadequately imaged on a Cervical spine MRI. In such situations, disc herniations at T1-T2 level must be investigated. The other differential diagnosis of T1-T2 radiculopathy is Cubital tunnel syndrome involving the ulnar nerve in the ulnar groove and Cervical rib and apical lung pathology involving the lower trunk of brachial plexus. The sensory loss from T1 radiculopathy is mainly to the inner aspect of the forearm and arm. The motor weakness of T1 is limited to the hand muscles namely the abductor pollicis brevis, opponens pollicis, flexor pollicis brevis, lumbricals, interossei and abductor digiti minimi. The muscles commonly evaluated clinically are the abductor digiti minimi and interossei.<sup>[6]</sup> Ipsilateral Horner's syndrome can be seen in T1 radiculopathy due to disruption of fibers destined for supra-clavicular ganglia; however, this can also be seen in C8 radiculopathy. Electrodiagnostic studies may be useful to differentiate T1 radiculopathy, C8 radiculopathy and ulnar neuropathy. The muscle groups associated with a C8 radiculopathy from an electro-diagnostic stand point are the first dorsal interosseus, abductor digiti minimi, abductor pollicis brevis, flexor pollicis longus, and ex-tensor indicis proprius. Paraspinal muscle abnormalities are seen in radiculopathy rather than mono-neuropathy. From an electro-diagnostic standpoint, the muscle predominantly involved in T1 radiculopathy is abductor pollicis brevis. There are case reports of T1 radiculopathy managed by Thoracic discectomy at the T1-T2 level. This case highlights the role of interlaminar Thoracic epidural steroid injection in the management of the T1 radiculopathy mimicking as cervical radiculopathy.

## Conclusion

Upper extremity paresthesias are typically caused by cervical radiculopathy. Routine Cervical MRI can typically miss the Thoracic disc herniation T1-T2. In the clinical setting, it is essential to consider that a T1 Thoracic radiculopathy due to disc at T1-T2 can mimic cervical radiculopathy.

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## A Comprehensive Review of Alternative Therapies for the Management of Chronic Pain Patients: Acupuncture, Tai Chi, Osteopathic Manipulative Medicine, and Chiropractic Care

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**Background:** Pain occurs in 30-7% of adult. Between 9 and 12 million people in the US suffer from chronic pain. Chronic pain is incredibly debilitating. It is associated with decreased function both physically and emotionally as well as a decrease in quality of life. Additionally, the total cost burden due to chronic pain in the US is estimated to be between \$560 and \$635 billion dollars annually. There are many ways to manage pain. Pharmaceutical therapy is usually the first choice with opioid therapy often being considered for severe, chronic pain. Opioids, despite being highly addictive, are still one of the most prescribed pharmaceuticals for this particular issue. There are 5 opioid medications in the top 200 most prescribed drugs in the US, and one within the top 10. The increase in opioid use in the United States is multifactorial. However many attribute the increase over the years to both the introduction of pain as the fifth vital sign in the 90s and the aggressive marketing of OxyContin by Purdue Pharma. A 2019 literature review noted that around 6% of the US abused opioids in some form. Prescription opioids are often described as a "gateway into the drug culture". The rise in prescription opioid abuse has been linked to increases in heroin and synthetic opioid (fentanyl, etc.) related deaths with a 20% and 72% bump in overdose deaths as a result of these substances respectively. Deaths from opioid overdose have risen 156% from 2010 to 2015. There are alternative medications available to treat daily pain. NSAIDs are one of the most common classes of non-opioid pain medication. These drugs may not adequately control pain and are associated with increased risk of gastrointestinal ulcers and bleeding. Several other classes of drugs such as antidepressants and muscle relaxants are often prescribed for pain, but have weak evidence for efficacy against chronic pain. Non-pharmacological alternative therapies for pain have been around for a long time, some for hundreds of years. They have been used throughout history to treat many issues. Currently, alternative medicine is most frequently used to treat musculoskeletal pain and between 59-90% of patients utilizing alternative therapies for chronic pain claimed them to be "helpful". Based on these findings it appears that alternative 4 therapies can serve as an effective adjunctive for the treatment of chronic pain. Some of these alternative therapies that we will discuss include acupuncture, tai chi, osteopathic manipulation, and chiropractic.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving the use of alternative therapies including acupuncture, tai chi, and osteopathic manipulative techniques to treat chronic pain.

**Results:** Acupuncture showed beneficial results for lower back pain. In a randomized controlled trial (RCT) involving 241 patients, patients had a positive effect on SF-36 with increased points - 5.6 points at 12 months and 8.0 points at 24 months. Electroacupuncture has been shown to be effective in the treatment of chronic sciatica. In a study of 100 patients randomized to receive electroacupuncture versus medium frequency electrotherapy, there was a significant improvement in pain based on ODI scores in the electroacupuncture group. Furthermore, results of a randomized double-blind trial illustrated that laser acupuncture using cups with a frequency was 200 Hz and output power of 50 mW resulted in similar pain reduction and quality of life scores as a sham laser cupping control. In the EASE Back pilot trial, 125 pregnant patients were randomized to receive either standard care for back pain, standard care plus sham acupuncture, or standard care plus true acupuncture. After six treatments over eight weeks, patients receiving sham acupuncture and true acupuncture endorsed improvement in pain and physical health. A Cochrane review published in 2011 stated acupuncture used at variety of acuoints resulted in a reduction of labor pain. A 2016 Cochrane review evaluated 22 RCTs with over 4000 participants and found that acupuncture resulted in a 50% reduction of migraines in 41% of the patients. Acupuncture was superior to sham acupuncture in reduction of migraines and a small benefit was found even 12 months after treatment. In a RCT of 320 retired athletes, Tai chi resulted in reduction in lower back pain compared to jogging and no exercise. Furthermore, a RCT of 160 individuals, tai chi was performed 18 times over 10 weeks and led to reduction of pain, bothersome of back pain, and 5 improved self-reported disability based on the Roland-Morris Disability Questionnaire scale. In the 2016 study, patients with LBP were randomly assigned using a computer-generated algorithm to receive either Osteopathic manipulative medicine (OMT) or sham OMT. They then received treatment at weeks 0, 1, 2, 4, 6, and 8, followed by an outcome assessment at week 12. Outcomes were defined by a 100-mm visual analog scale (VAS) and the Roland-Morris Disability Questionnaire (RMDQ). In total, 23 patients enrolled in the study experienced adverse events, but none were determined to have been caused by study interventions. The results of the study showed a statistically significant difference between the two groups. The number needed to treat (NNT) for patients who underwent OMT was 9.9 (95% CI, 5.8-36.2). In this study, patients were assigned to one of three cohorts: medical care only, medical and chiropractic care, or medical and chiropractic care with additional interprofessional collaboration. Patients were required to have experienced at least one month of LBP and needed to rate the pain as at least a 4 on an 11-point scale. One hundred and thirty-one participated in the trial. The results of this study showed improvements in pain and back-related disability in each group. None of the groups appeared to be statistically significant to the others in these measurements.

**Conclusion:** Chronic pain is an issue that affects millions of Americans daily. Current treatments usually include pharmacologic therapies, most notably opioid therapy. However, chronic opioid use carries immense risk given the potential for overdose and addiction with this class of medications. With the current crisis surrounding opioid use and increases in opioid related deaths in the United States there is a clear need for alternative treatment of chronic pain. Many of the pharmacologic alternatives to opioids either are not as effective for chronic pain or carry their own risks and adverse effects such as increased risk of gastrointestinal bleeding. Other modalities for treating chronic pain include therapies such as acupuncture, Tai Chi, OMT, and chiropractic which were all evaluated in this review as alternative and holistic approaches to managing chronic pain. Acupuncture was shown to be effective in reducing chronic low back pain and pregnancy related pain. However, they were ultimately inconclusive in their use towards migraines and CRPS. Tai Chi, similarly, was shown to be useful in chronic low back pain, specifically in the older population. However, it was ineffective for MS related pain and PTSD. OMT was shown to be useful in management of low back pain but 6 not for migraine. Chiropractic was not shown to be effective in management of low back pain, migraine, or neck pain. Overall the evidence for these alternative therapies in the management of chronic pain is mixed. While there is some evidence to claim that specific therapies can be effective for specific types of pain (for example, acupuncture for low back pain), there was also evidence available to refute that claim. At this point in time we cannot conclude that alternative therapies are a replacement for pharmaceutical management of chronic pain. However, they may play a role as adjunct therapies that can potentially reduce a patient's overall opioid need. Additional longitudinal studies are needed to evaluate the role of alternative therapies in the context of chronic pain management.



## A Comprehensive Update of the Current Understanding of Chronic Fatigue Syndrome

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**Background:** Chronic fatigue syndrome (CFS) is a multifaceted illness with a wide array of symptoms, potential etiological causes, and prognosis. Similarly, naming of the condition has proven to be equally as complex, with multiple accepted alternatives such as myalgic encephalomyelitis (M.E.), chronic fatigue immune disorder syndrome (CFIDS), and systemic exertion intolerance disease (SEID). CFS alone tends to oversimplify the complexity of the disease and undermine the constellation of symptoms experienced by patients. Thus, a more recent merging of CFS and M.E., also known as ME/CFS has been described to better encompass the complexity of the disease and its neuroinflammatory components. Individual criteria for CFS and M.E. share overlapping symptoms of fatigue, neurocognitive dysfunction, disturbed sleep, and autonomic dysfunction. In contrast, a required infective agent is unique to M.E. and is a major criteria component. However, this is considered a minor symptom/optional criteria for joint ME/CFS and further proves the merged term to be more encompassing than either CFS or M.E. alone. At the core of ME/CFS is persistent and disabling fatigue that results in a significant reduction in activity for greater than six months. Furthermore, worsening of symptoms after mild physical and/or mental exertion is a key feature of ME/CFS and referred to as post-exertional malaise. Unrefreshing sleep, cognitive dysfunction, including attention or concentration difficulties as well as orthostatic intolerance, are further findings common to ME/CFS patients. In addition to a potential trivialization of the disease, the term chronic fatigue syndrome (CFS) complicates its distinction from idiopathic chronic fatigue (ICF). Fatigue is a common complaint and can be idiopathic or a symptomatic component of various illnesses. An individual's perception of fatigue is subjective and can be perceived differently in relation to not only physical stress but also psychological and social stress. For the same reason that detection and quantification of fatigue are difficult, finding an accurate diagnostic test for ME/CFS has been complicated, as well. Despite seemingly similar features, there are clinical distinctions between experiencing fatigue (CF) and suffering from chronic fatigue syndrome (ME/CFS). According to the Institute of Medicine Diagnostic Criteria, ME/CFS requires the presence of one or more of the following: cognitive impairment and/or orthostatic intolerance. In contrast, little to none of these symptoms are reported in ICF. This suggests that CFS is likely of different etiology with additional clinical features and not simply located on the upper spectrum of general fatigue or ICF. Research into ME/CFS etiology and potential treatment management is important due to its ability to extend beyond the effects on a patient's body. ME/CFS takes a toll on social life, family relationships, and the work-life of the individuals affected. A study of middle school-aged students with ME/CFS was reported to have characteristic symptoms such as irritability and being afraid to go to school. Extending into adulthood, individuals report economic difficulties due to the loss or inability to attain manageable employment. Without more discussion and acceptance in medical research and practice, further misconception, unawareness, and misdiagnoses will persist.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving chronic fatigue syndrome.

**Results:**

Research suggest that the incidence rate of ME/CFS occur at two age peaks: 10 – 19 years old and 30 – 39 years old. Further studies suggest the two-peak pattern was described as more distinct in women, while the second peak was less pronounced in men. Women appear to be more affected than men and represent the majority of the ME/CFS research participants. The studies showed the age of onset to be younger in males in comparison to females and was often triggered by an infectious process. Males reported less muscle, immunological, and neurovegetative symptoms. Both sexes reported similar symptoms of unrefreshing sleep. The clinical presentation of CFS is heterogeneous, with the most common symptoms being mental and physical fatigue, cognitive dysfunction, and mood disturbances. Orthostatic hypotension, malaise after exertion, muscle weakness, cramps, and neuroendocrine abnormalities are common presentations. CFS has also a shared presentation with intracranial hypertension. ME/CFS was first described in reference to post-Epstein Barr Virus (EBV) fatigue. However, infection prior to its onset is not true of all ME/CFS patients; thus, its etiological significance remains uncertain. Infectious triggers are suggested to contribute to the development of ME/CFS through disruption of not only the immune response but also mitochondrial functioning and other cellular processes. Furthermore, it was found that the immune N.K. and B Cells of ME/CFS patients had a reduced expression of the transient receptor potential channel of the melastatin-3 subfamily (TRPM3). TRPM3 gene associated single nucleotide polymorphism SNPs have also been reported in ME/CFS patients compared to controls. Lipid and energy metabolism dysfunction are also thought to contribute to the etiology of ME/CFS. With exercise, ME/CFS patients have shown early activation of anaerobic metabolic pathways, suggesting impaired oxygen consumption. A recent study induced M.E. CFS-like fatigue in mice which has shown that these mice had a decrease in pyruvate dehydrogenase, a critical enzyme for oxidative metabolism. Furthermore, hypothalamic-pituitary-adrenal axis impairment may contribute to symptoms of fatigue and low mood. EBV, HHV-6B, and CMV can disrupt mitochondrial function and may contribute to post-exertional malaise. CFS is a diagnosis of exclusion. Diagnosing CFS vary across countries. At least 6 months of disabling fatigue in adults and 3 months in children/adolescents that affect physical and mental function is an important indicator. The Centers for Disease Control and Prevention established that after discounting any other links for chronic fatigue, diagnostic criteria required fatigue for at least 6 months and 4 of the following symptoms including memory problems, sore throat, post-exertion malaise, tender cervical or axillary lymph nodes, myalgia, multi-joint pain, headaches, and troubled sleep. It has been suggested that using immune-inflammatory biomarkers may help with diagnosis. Cognitive-behavioral therapy (CBT) has shown short term results. Graded exercise therapy (GET) has demonstrated reduced fatigue and improved physical function. Adaptive pacing therapy (APT), has demonstrated inconsistent results. Antidepressants are an option for anxiety and depression. Patients with EBV showed improvement with valacyclovir. Immune modulators have shown inconsistent results. Acupuncture has shown to be efficacious in reducing symptoms of fatigue. Shosholito-based treatment has been reported to provide effective treatment of CFS in a pediatric patient. Probiotic treatment has demonstrated decreased gastrointestinal symptoms, levels of inflammatory markers, and anxiety but failed to alter levels of depression. These studies are limited, and further research is needed to determine efficacy.

**Background:** CFS is a debilitating syndrome that significantly affects the daily lives of those afflicted. Its clinical presentation can vary from patient to patient, making a prompt diagnosis and its management a difficult task. Groups of men and women affected by CFS have shown two peaks of its incidence based on the age group, though women have shown to have a more distinct second peak than men. Many potential etiologies for the syndrome are being considered, ranging from autoimmune, neuroendocrine, and autonomic system dysfunction. Aside from the different clinical presentations of the syndrome, the fact that fatigue is a very subjective symptom makes the diagnosis even more difficult. Thus far, much of the medical management has focused on alleviating the symptoms rather than tackling the syndrome itself. This is partly due to the currently limited understanding of the cause of the syndrome. Given its association with psychiatric comorbidities, such as depression and anxiety, patients have been treated with antidepressants and CBT. The potential infectious trigger of EBV has also led to treatment with antivirals, such as valacyclovir. Many other forms of treatment, including approaching the syndrome with alternative medicine, has been utilized and shown in some studies to be efficacious. Further reliable clinical trials are essential to furthering our understanding of this syndrome. This will provide opportunities in its timely diagnosis and effective management.

## A Comprehensive Update of the Treatment and Management of Bertolotti's Syndrome: A Best Practices Review

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**Background:** Bertolotti's syndrome is a chronic back-pain condition defined by lumbosacral transitional vertebrae. In the spines of patients, the enlargement of the caudal lumbar vertebrae at the transverse process leads to the fusion or articulation of the transverse process with the sacrum or the ilium causing discogenic disease and limited mobility. This congenital lumbosacral transitional vertebra (LSTV) defect, which has a variety of presentations, can begin as asymptomatic but may become a lower back pain syndrome in the mid-20s and 30s of a patient's life. Once the LSTV causes lower back pain syndrome, it is classified as Bertolotti's Syndrome. Pain from Bertolotti's Syndrome is not uniform and originates from many different deformities caused by the LSTV. These deformities include scoliosis, arthropathy of the joints, and muscle strains of the quadratus lumborum and iliopsoas. Also, the deformation of the transitional vertebra may cause nerve entrapment or disc compression and bulging, causing neuropathic pains. Patients, on average, report typical daily pain at above 5/10. Along with significant pain, patients with Bertolotti's syndrome self-report an average of over 36% on the Oswestry disability scale, correlating to a moderate disability that affects many aspects of daily life (3-5). The patients who have LSTV tend to have a more significant spinal degeneration above the deformity than other conditions leading to chronic lower back pain, but they tend to have similar levels of pain and disability to those that have back pain without having LSTV. Bertolotti's Syndrome must be diagnosed in two parts: first, a clinical assessment of pain and then followed by a radiologic exam. Bertolotti's Syndrome can have a variable presentation including symmetrical/asymmetrical pain and tenderness at either the sacroiliac area, hip, or groin. There may be radicular pain due to nerve compression or pseudo-radicular pain related to the bone on bone contact at the pseudo-articulate joint of the transverse vertebra. A clinical exam can include an intra-articular diagnostic block with lidocaine 2% and bupivacaine 0.5% at either the sacroiliac joint or the facet joint under fluoroscopic guidance. Achieving an 80% decrease in pain following these injections is diagnostic and can be followed by many methods of treatment. Bertolotti's Syndrome presents with non-specific back pain; therefore, confirmation of the diagnoses must be made through radiologic examination of the lumbosacral spine. The radiographs of the lumbosacral spine will show unilateral or bilateral enlargement of the transverse processes with possible articulation to the sacrum or ilium. These can be complemented with an MRI of the lumbosacral spine if there is radicular pain drawing suspicion to discogenic bulging and prolapse or nerve entrapment. Bertolotti's Syndrome, lower back pain syndrome in conjunction with LSTV, encompasses many types of LSTV that are defined under the Castellvi system. In 1984, Dr. Antonio Castellvi determined four defining types of LSTV through examinations of myelograms of 200 patients. These four types of LSTV include: Type I-dysplastic transverse process that is at least 19mm wide, Type II-transverse process growth leading to an incomplete sacralization or lumbalization of the transverse process, Type III-complete transverse process sacralization/lumbalization, and Type IV- mixed complete sacralization and incomplete sacralization. Of the Castellvi classifications, the most commonly seen LSTV is Type I (42%), followed by Type II (38%), Type III (8%), and Type IV (5%). Disc herniations are often present and are most common at L4-L5, L5-S1, L3-L4, and L2-L3, although some patients have herniations of multiple discs due to the lumbosacral transitional vertebra. Bertolotti's Syndrome is often an underdiagnosed form of significant back pain that has many modalities of treatment. This review describes possible approaches to alleviating pain and disability in patients with Bertolotti's Syndrome.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving Bertolotti's Syndrome including the epidemiology, pathophysiology, etiology of the syndrome, and treatment.

**Results:** Bertolotti's Syndrome is chronic back pain caused by transitional lumbosacral vertebra. This transitional vertebra can cause numerous clinical manifestations, leading to many different associated pain types. Most common is a pain in the sacroiliac, groin, and hip regions, with or without associated radiculopathy. Diagnosis is through a combination of clinical presentation with imaging studies and falls into one of four types. The incidence of transitional vertebra is rather high, between 4 and 36%; however, Bertolotti's syndrome is only diagnosed when this is the cause of chronic pain, and the actual incidence is difficult to determine. Initial management with conservative treatment includes medical management and physical therapy. Injection therapy is an effective second line. Epidural steroid injection at the level of the transitional articulation is effective, with either local anesthetics alone or in combination with steroids. Surgery carries higher risks and is reserved for patients failing previous lines of treatment. Options include surgical removal of the transitional segment, spinal fusion, and decompression of stenosed foramina. Recent evidence suggests that radiofrequency ablation (RFA) around the transitional segment may also provide relief.

**Conclusion:** Bertolotti's Syndrome is a back-pain syndrome that is an underdiagnosed cause of back pain. It is caused by a congenital defect of the last vertebra of the lumbar spine that leads to the articulation, pseudo articulation, or full fusion of the transverse process to the sacrum or the ilium. Bertolotti's syndrome, which is present in approximately 7% of chronic lower back pain patients, is defined as a pain syndrome in conjunction with the LSTV. There are many methods to treat Bertolotti's Syndrome, but a lack of research into the syndrome hinders hard evidence of one specific therapy. Outlined in Jancuska et al. is a guideline for the step-based therapy for Bertolotti's Syndrome (10). It is most important to start with conservative therapy methods, including modalities such as steroid injections, anesthetic injections, physiotherapy, and even exercises. Failure of conservative methods signals for a more invasive form of treatment, either surgery or radiofrequency ablation. Surgical methods, which have proved only slightly superior to conservative management, can differ depending on the preoperative degeneration of the spine. Resection and posterolateral fusion are both equally effective methods, but they both hold general surgical risks as well as the risk of repeated surgery and further degeneration of the discs. Radiofrequency ablation in any form (continuous RFA, pulsed RFA, cold RFA, or bipolar RFA) is also an effective method of treatment for patients with Bertolotti's Syndrome. Ablation can address the nociceptive and mechanical pain that is caused by Bertolotti's Syndrome, but there is currently a lack of research into RFA treatment for the variable presentations of LSTV. It is important that when patients present with back pain and LSTV, they are approached in an individualized manner that focuses on treating them conservatively and only moving to advanced therapy, if they fail conservatively.

# A RCT Comparing Traditional Spinal Cord Stimulation (SCS) and Differential Target Multiplexed (DTM SCS) for Chronic Back and Leg Pain



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## INTRODUCTION

DTM™ SCS is a unique programming approach where electrical signals are multiplexed spatially and temporally. DTM SCS was inspired from preclinical research demonstrating that multiplexed signals can differentially modulate neurons and glial cells to balance interactions perturbed by neuropathic pain. A recent randomized controlled trial (RCT) compared the effectiveness of DTM SCS to traditional SCS with a focus on axial low back pain (LBP) relief, a historically challenging population for SCS therapy. This study provides important long-term clinical outcome data for pain relief, quality of life, extent of disability, therapy satisfaction and safety.

## MATERIALS AND METHODS

A prospective, multicenter, post-market, RCT compared DTM SCS to traditional SCS in patients with chronic intractable LBP and leg pain. Key eligibility criteria is shown in Table 1. Consented and eligible subjects were randomly assigned (1:1). Primary endpoint assessed non-inferiority of LBP responder rate (subjects with ≥50% relief) between treatment groups at 3 months post-implant using an intention-to-treat (ITT) analysis. Long-term outcomes measured at 12-month post-implant included pain relief, quality of life (PROMIS Global Health), functional disability (ODI), patient satisfaction and safety.

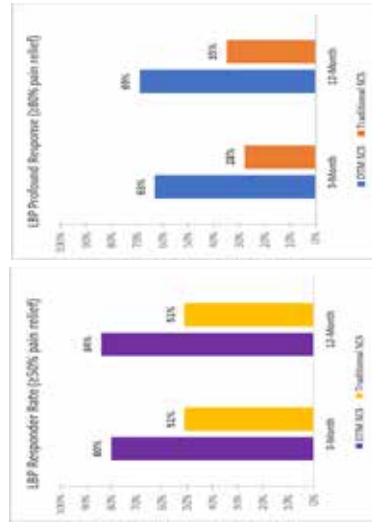
**Table 1.** Key Eligibility Criteria.

Inclusion	Exclusion
<ul style="list-style-type: none"> <li>Adult subjects</li> <li>≥5 cm Baseline VAS in low back pain with moderate to severe leg pain</li> <li>Candidate for SCS</li> <li>Stable pain medication regime</li> </ul>	<ul style="list-style-type: none"> <li>Other active implants</li> <li>Contraindications for SCS</li> <li>Mechanical spine instability</li> <li>Pregnancy</li> </ul>

## RESULTS

**Table 2.** Mean (SD) Baseline Demographics for ITT population.

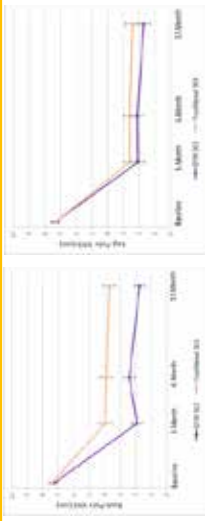
	DTM SCS (n=67)	Standard SCS (n=61)
Age	64.3 (12.2)	60.7 (11.8)
Years of pain onset	12.6 (13.0)	12.9 (11.2)
Number of prior surgeries	1.49 (1.33)	1.41 (1.13)
VAS Low Back Pain (cm)	7.25 (1.49)	7.35 (1.26)
VAS Leg pain (cm)	6.20 (2.58)	6.58 (2.06)



**Figure 1.** Back pain responder rate comparisons at the primary endpoint.

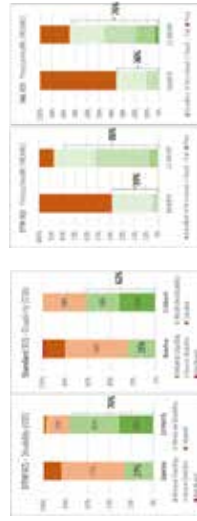
The study met the hypothesis of noninferiority ( $p < 0.0001$ ). DTM SCS provided superior efficacy for LBP ( $p = 0.0010$ , ITT population). LBP responder rate with DTM SCS was sustained at the 12-months follow up. Profound responder rates were also sustained at 12 months (Fig. 1). DTM SCS also provided improved and sustained leg pain relief with a 75.7% mean reduction at 12 months, better than with traditional SCS (67.9%) (Fig. 2).

## RESULTS (continued..)



**Figure 2.** Back pain and leg pain VAS scores.

Both therapies improved functional disability and physical health (Fig. 3) with 76% of subjects with DTM SCS and 62% of subjects with traditional SCS reporting minimal/moderate disability at 12 months compared to 26% at baseline. Eighty-eight percent of subjects with DTM SCS and 76% with traditional SCS reported that the effect of treatment on physical health was fair to excellent.



**Figure 3.** ODI and PROMIS Global Health Measures.

There were 4 study related Adverse Events (non-serious) in the DTM SCS group and 8 in the traditional SCS group (2 classified as serious).

## CONCLUSION

DTM SCS achieved superior responder rate for LBP relative to traditional SCS at the primary endpoint. This study also demonstrated sustained benefits of DTM SCS for LBP and leg pain through the 12-month follow-up. Additional, benefits were observed in quality of life, disability, and subject satisfaction.

**ACKNOWLEDGEMENT:** Study was sponsored by Stimpinger.





## Adjuvant Drugs for Peripheral Nerve Blocks: The Role of Alpha-2 Agonists, Dexamethasone, Midazolam, and Non-Steroid

### Anti-Inflammatory Drugs

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**Background:** Opioids are the most commonly prescribed analgesia in the postoperative period. The overreliance on opioids for pain management has resulted in the quadrupling of deaths from prescription opioids since 1999. Although opioids are an effective treatment in the postoperative setting, the additive potential makes it challenging to transition away from their use during chronic pain management. Alternative pain treatments are necessary because patients with chronic pain have a higher incidence of cognitive decline and early death. Furthermore, the estimated cost associated with chronic pain is \$600 billion annually in the US alone. In an effort to reduce the reliance on opioid treatment and reduce the morbidity of chronic pain, adjuvant drugs for peripheral nerve blocks are a promising solution to acute postoperative pain and the transition to chronic pain treatment. The pathophysiology of pain is complex and involves both peripheral and central nervous system sensitization, ascending and descending nervous system pathways, and overlapping regions within the brain. Current research targets numerous pathways within the complex physiological pathway of nociception. The likelihood of transitioning to chronic postsurgical pain has numerous risk factors, including age, gender, obesity, surgery duration, type of anesthesia, and psychological factors. Genetic mutations involving the COMT, OPRM1, GCHI, and other genes likely play a role in chronic postsurgical pain. Improvements in genetics, neurophysiological characterization of patients, and pharmacokinetics of drugs enable better individualized non-opioid treatments of acute and chronic pain. Individualized selection of adjuvant drugs used with peripheral nerve blocks (PNB) has the potential to improve patient outcomes. Patient outcomes are further improved with advances in ultrasound technology that enables precision-guided techniques for peripheral nerve blocks. PNBs are used in the brachial plexus, lumbar plexus, femoral nerve, sciatic nerve, and many other anatomic locations for site-specific pain relief. However, the duration of action of a PNB is limited without an adjuvant drug. For example, the average duration of lidocaine and mepivacaine is two to three hours. Clonidine, an alpha-2 agonist, increases the duration of the nerve block by two hours in comparison to a local anesthetic alone. For longer-term pain control, continuous peripheral nerve blocks (CPNB) provide site-specific anesthesia and reduce or eliminate the use of opioids. Although CPNBs are effective for longer duration pain relief, the catheter is difficult to insert, it can dislodge, and there is an additional cost. For these aforementioned reasons, a single-shot peripheral nerve block with adjuvant drugs to extend the duration of action is commonly favored. The use of adjuvant drugs for single-shot peripheral nerve blocks (sPNB), such as alpha-2 agonist, dexmedetomidine, midazolam, and non-steroidal anti-inflammatory drugs (NSAIDs), extends the duration of local anesthetics and reduces the dose-dependent adverse effects of local anesthetics. However, dose-dependent effects of local anesthetics are not eliminated with adjuvant drug use. Additionally, adjuvant drugs can also have dose-dependent neurotoxic effects. A severe adverse effect of local anesthetics is local anesthetic systemic toxicity (LAST). Additional risks of the PNB include hematoma, infection, and peripheral nerve injury. Despite these risks, sPNBs are a suitable option for patients who are at high risk of respiratory depression, opioid addiction, opioid-induced nausea, and vomiting or are not responsive to oral medications. Alpha-2 agonists, dexmedetomidine, midazolam, and non-steroidal anti-inflammatory drugs are efficacious adjuvant drugs that require additional research on their safety.

**Methods:** We conducted a systematic comprehensive literature search using a collaboration of existing publications involving adjuvant drugs for peripheral nerve blocks. We present the existing literature in the understanding of the safety and efficacy of adjuvant drugs for peripheral nerve blocks including alpha-2 agonists, dexmedetomidine, midazolam, and non-steroidal anti-inflammatory drugs.

**Results:** Pöpping et al.'s meta-analysis found that 30-300µg of clonidine used as a perineural adjunct with local anesthetics (LA) in PNB prolonged the duration of postoperative analgesia by about 2 hours, while this increase is independent of LA type, the relative gain was markedly higher with intermediate-acting LAs (56% over long-acting LAs (18%). The study found the motor and sensory blocks to be prolonged by 2.5 hours and 1.25 hours, respectively. Evidence for dexmedetomidine as an adjunct for PNB is the strongest for a brachial plexus block (BPB). As supported by a meta-analysis of 34 trials, perineural dexmedetomidine adjunct use in BPB effectively prolonged duration of analgesia by 4.5 hours and motor and sensory blocks by 3 and 4 hours, respectively, and decreased onset time of sensory block by 9 minutes and motor block by 8 minutes. A 2018 meta-analysis showed significant prolongation of postoperative analgesia by 5 hours and motor blockade by 4 hours in 25 to 150 µg perineural dexmedetomidine administration with long-acting LA in PNB. A Cochrane review of 35 trials determined that perineural dexmedetomidine adjuvant increased sensory block 6.7 hours (95% confidence interval) in comparison to a placebo. Similarly, intravenous dexmedetomidine increased sensory block by 6.2 hours versus placebo. The Cochrane review also determined that the cumulative 24-hour opioid consumption was significantly reduced for both the perineural and intravenous dexmedetomidine (19.25 mg reduction and 6.58 mg reduction, respectively). The Cochrane review showed a significant decrease in pain with perineural administration of dexmedetomidine at 12- and 24-hour post-surgery (no significant difference between placebo and dexmedetomidine adjuvant at the 48-hour mark). In contrast, the De Oliveira review showed that a dexmedetomidine adjunct is ineffective, in comparison to the placebo, beyond 24 hours post-surgery. Due to potential neurotoxicity and an inadequate understanding of the mechanism of action of dexmedetomidine, intravenous administration is preferable (23). In a 2021 meta-analysis, when compared to dexmedetomidine, dexmedetomidine reduced fentanyl analgesic consumption by about 29 µg. In another study, it was found that dexmedetomidine's ability to enhance analgesia duration by more than 6h is better than that achieved by adjuvants like clonidine. A 2005 study by Jarbo et al. is primarily cited in support of efficacious perineural adjuvant use of midazolam, where 50 µg/kg of the drug was used with 30 mL of 0.5% bupivacaine LA for a supraclavicular BPB. The authors reported enhanced onset of sensory and motor blockade, reduction of pain scores, and postoperative analgesia without any adverse effects. There has however been animal studies demonstrating intrathecal midazolam to be neurotoxic. Tramadol's effectiveness and safety as an adjuvant to LA for PNB are inconsistent. Reviews by Koyyalamudi et al. and Kirksey et al. investigated tramadol with different local anesthetics (like bupivacaine, levobupivacaine, mepivacaine, and ropivacaine) in various PNBs (interscalene, axillary, and brachial plexus) which revealed the often contradictory nature of the results. A 2019 RCT found that 100mg of tramadol with .5% ropivacaine for interscalene BPB lowered pain scores and morphine consumption 24h post-surgery. Won Shin et al. reported that tramadol prolonged sensory and motor blockade as well as analgesia for BPB with no change in adverse events. Ketorolac prolongs local anesthesia action in regional anesthesia and a dosage of 20-60 mg has been shown to benefit postoperative analgesia when used as a part of intravenous regional anesthesia. Using ketorolac with local anesthetic lidocaine in a PNB for foot surgery increased analgesia duration and quality. However, ketorolac as an adjuvant in infraorbicular BPB could not prolong the duration of motor and sensory blocks and quicken their onset versus dexmedetomidine.

**Conclusion:** Pinal stenosis (SS) is the compression of nerve roots by bone or soft tissue secondary to the narrowing of the spinal canal, lateral recesses, or intervertebral foramina. SS may have acquired or congenital origins. Most cases of SS are acquired and caused by hypertrophy of the ligamentum flavum (LF), enlarged osteophytes, degenerative arthritis, disk herniations, and various systemic illnesses (i.e., endocrinopathies, metabolism disorders, inflammatory diseases). Although it is not common, some people are genetically prone to developing congenital spinal stenosis. SS usually affects both men and women equally around the age of 50. SS can manifest as sharp, aching, and/or tingling sensations in the back, buttocks, or thigh. In severe cases, it can also present as numbness, bladder or bowel incontinence, and difficulty ambulating. SS is most commonly observed in the lumbar spine and is rarely found in the cervical and thoracic spine. Epidemiological data suggest that the incidence of lumbar spine stenosis is 5 cases per 100,000 people. Hypertrophy of the LF in the lumbar spine is the most significant cause of lumbar spinal stenosis; the suppression of the cauda equina by the LF is what evokes the symptoms. The LF is a highly specialized elastic ligament that connects the laminae of the spine and fixes it to the facet joint capsules. LF assists with the realignment of the spinal joint after bending and flexion. Mechanical stress, increasing age, diabetes mellitus, obesity, and change of milieu in disk herniation all lead to a mechanism that results in LF hypertrophy and fibrosis. There are a number of cytokines and growth factors that are secreted by LF macrophages, endothelial cells, and fibroblasts associated with the LF and is hypothesized to be one of the main culprits contributing to LF hypertrophy. Before a clinician orders diagnostic imaging to confirm the diagnosis of SS, pertinent physical exam findings such as moderately reduced lumbosacral range of motion, bilateral extremity weakness, diminished deep tendon reflexes, and positive stoop and straight leg raise tests typically arise suspicion of the condition. The gold standard in diagnosing lumbar spinal stenosis is lumbosacral magnetic resonance imaging (MRI) with or without contrast. The MRI can reveal enhanced sensitivity of nerve roots and the intricate detail of soft tissues including the subarachnoid space, epidural fat, ligaments, intervertebral disks, and the spinal cord. There are a number of treatment options available for spinal stenosis. The older treatments include physical therapy with flexion band exercises, nonsteroidal anti-inflammatory drugs, opioids, neuropathic pain medications, and epidural corticosteroid injections. There have been implants and surgical interventions that have emerged in popularity recently and have been shown to be more efficacious: the minimally invasive lumbar decompression (MILD®), Vertiflex®, MinuteMan® procedures. Conservative treatments are recommended before resorting to surgical interventions. Surgery is only indicated for patients who have failed conservative treatments or have shown evidence of severe pain or neurological deficits.



## Adjuvant Drugs for Peripheral Nerve Blocks: The Role of NMDA Antagonists, Neostigmine, Epinephrine, and Sodium Bicarbonate

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**Background:** Much attention has been brought to the use of opioids for both acute and chronic pain in recent years. The overuse of opioids for pain control has quadrupled the prescription opioid deaths since 1999. Although opioids can be beneficial in controlling both acute and chronic pain, the risk for dependence and overdose and numerous side effects, including urinary retention, constipation, and other adverse effects, make the reliance on opioids problematic. The pathophysiology of pain is multi-faceted and involves components of peripheral and central nervous systems. As surgery is noted to be one of the most common causes of chronic pain (22.5% of chronic pain), the transition from acute postoperative pain to chronic pain is the focus of increasing research. Risk factors for the transition to chronic pain include younger age, female gender, obesity, surgical technique, anesthetic type, and other psychosocial factors. Other potential risk factors for chronic postoperative pain include genetic mutations in COMT, OPRM1, GCH1, and others. The complexity of chronic pain necessitates the individualization of genetic, physiologic, and pharmacokinetic properties of nonopioid pain treatments. To decrease the morbidity and mortality due to opioid use, peripheral nerve blocks are a promising answer for acute pain and the transition to chronic pain management. The use of peripheral nerve blocks for surgery has gained wide acceptance as it minimizes peripheral pain signals from the nociceptors of local tissue sustaining trauma and inflammation from surgery. Peripheral nerve blocks have gained popularity as improvements in ultrasound technology enable safe, precise techniques for local anesthetic injection. Despite improvements in technique, peripheral nerve blocks are limited by the duration of action. Continuous peripheral nerve blocks (CPNB) provide long-term pain control via the transcutaneous insertion of a catheter to the targeted nerve or plexus through which local anesthetic can be infused. Although CPNB provides an effective alternative for long-term pain management, disadvantages of cost, difficulty in insertion, and morbidity with catheter-associated infections and incidental dislodgement often outweigh its advantages. Due to these concerns, the use of an adjuvant drug that extends the duration of action of the local anesthetic, which can be given in a single injection, is more favorable. Dose-dependent adverse effects of peripheral nerve blocks are reduced by adjuvant drugs but not entirely eliminated. Local anesthetic systemic toxicity (LAST) is one of the most concerning adverse effects of peripheral nerve blocks due to its systemic effects and long duration of neurologic complications. Other adverse effects include vascular puncture, hemorrhage, peripheral nerve injury, and infection. Despite these complications, peripheral nerve blocks are an effective alternative in postoperative and chronic pain management, especially in patients who are at high risk of opioid abuse or side effects of respiratory depression, urinary retention, and cognitive impairment. NMDA antagonists, neostigmine, epinephrine, and sodium bicarbonate play an important role as potential adjuvants for local anesthetics.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving adjuvant drugs for peripheral nerve blocks. We present the existing literature in the understanding of the efficacy and safety of adjuvant drugs for peripheral nerve blocks including NMDA antagonist, neostigmine, epinephrine, and sodium bicarbonate.

**Results:** Bone et al. conducted a study looking at the addition of neostigmine to enhance an axillary brachial plexus nerve block. 34 participants were assigned to 2 groups. The treatment group was given 500 µg of neostigmine plus 500 mg of mepivacaine, while the control group was given 500 mg of mepivacaine plus saline. The treatment group reported a lower visual analog scale score (VAS: 14.7 ± 9.9 vs. 32.4 ± 23.5; P < .05) 24 hours post-surgery. In addition, this group required fewer additional analgesics in the first 24 hours post-surgery (P < .05). There were no reported side effects and cardiovascular functions remained stable. There was no difference in onset of duration of the block. Saatchi et al. conducted a prospective randomized double-blinded study to examine if buffered (addition of sodium bicarbonate) versus non-buffered lidocaine with epinephrine would be effective as a buccal infiltration during inferior alveolar nerve blocks (IAN). There was a statistically higher success rate using the buffered solution using a buccal infiltration (buffered group: 78% non-buffered group: 44%; P < 0.05). Success was defined as having no or mild pain on VAS. It was concluded that the efficacy of an IAN block in mandibular first molars with irreversible pulpitis was improved with sodium bicarbonate buccal infiltration. In a 2015 systematic review looking at 39 studies, researchers aimed to identify the safety of epinephrine in healthy individuals and those with poor peripheral circulation at a concentration of 1:100,000-200,000. Of the studies examined, one identified complication in healthy individuals, which included hypertensive crisis and infection. However, these complications did not occur at an increased rate compared to the control group, who did not receive epinephrine. No complications were reported in thousands of digital nerve blocks. The review concluded that not only was epinephrine safe for healthy individuals but that it also accelerated and prolonged anesthesia and analgesia, decreasing the need for additional local injections. In addition, it was found that adding epinephrine to tetrodotoxin (TTX) plus chemical permeation enhancers (CPEs) greatly increased the duration of sciatic nerve block in rats compared to any combination of two of the nerve blocks alone. The use of epinephrine reduced the risk of systemic adverse reactions, including mortality associated with TTX. It was also found that a dilution of 1:200,000 epinephrine with 1% lidocaine had increased efficacy and duration as a peripheral nerve block compared to the 1% and 2% lidocaine treatments alone with no adverse reactions. Zhu et al. conducted a randomized control trial that aimed to evaluate the effects of mixing ketamine with local anesthetics in a combined femoral and sciatic nerve block during anterior cruciate ligament reconstruction. Patients were randomized into three groups which received either a single perineural 40 mL dose of 0.375% ropivacaine, a 40 mL dose of ketamine 40 mg and 0.375% ropivacaine mixture, or a 40 mL dose of 0.375% ropivacaine preoperatively in addition to 40 mg of ketamine intravenously during the operation. No significance was found between the three groups for time to motor block, but the group with the mixture of ketamine and ropivacaine displayed significant reduced post-op pain, more time to first request for analgesics, and longer sensory block. IV-administered ketamine during the operation did not produce the same effects as preoperative administration. In addition, a case series was published describing the effects of ketamine on three patients with complex regional pain syndrome (CRPS) after gunshot wounds. They found that the addition of ketamine to the sympathetic blocks resulted in dramatic and long lasting relief of heat allodynia.

**Conclusion:** Local anesthetics are often limited in their motor and sensory block durations and the potential for negative side effects in the cardiac and central nervous systems. Some adjuvant drugs have been well studied to recommend use in various environments such as perioperative, acute, or chronic use setting with no reported adverse side effects. The use of adjuvants such as NMDA antagonists, neostigmine, epinephrine, and sodium bicarbonate have shown safety and efficacy in increasing the duration of a peripheral nerve block, increasing the onset of action, improving pain post-op with need for rescue analgesics, or limiting the required needed dose. However, more research should go into showing the efficacy of these adjuvants for nerve block prolongation as studies have been either mixed or have small sample sizes.

## Calcitonin (FORTICAL, MIACALCIN) for the treatment of vertebral compression fractures (VCFs)

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**Background:** Osteoporosis is a disorder characterized by decreased bone strength that predisposes individuals to fractures of the spine, hip, and other sites. The condition has a prevalence of more than 10% in the United States in 2010, and the CDC estimates that nearly 25% of women over the age of 65 have findings of osteoporosis. There are many risk factors associated with osteoporotic fractures, including older age, cigarette smoking, use of certain drugs (e.g., corticosteroids), low peak bone mass, low physical activity, low intake of vitamin D and calcium, hormonal factors, and personal or family history. Vertebral compression fractures (VCFs) are a hallmark and common sequela of osteoporosis, representing one the most common types of fragility fractures with an annual incidence of up to 1.4 million. They affect about 25% of postmenopausal women overall, and the prevalence increases with age, reaching 40% in women of 80 years of age. Acute fractures occur when the vertebral body is unable to support the load of the upper body, with severe cases of osteoporosis, inclining incidents can be minor (e.g., vigorous sneezing or stepping out of a bathtub). More force is required in cases of moderate osteoporosis (e.g., attempting to lift a heavy object or falling out of a chair). The majority of damage is normally within the anterior vertebral column; therefore, the fracture is typically stable and rarely causes neurologic compromise. However, multiple fractures can result in significant loss of height through thoracic kyphosis and lumbar lordosis while shortening paraspinous musculature, requiring active contraction to maintain posture and causing pain. VCFs increase the risk of secondary fractures 4-fold, impede respiratory function, and increase overall mortality risk. Conservative treatment is nonoperative and includes physical therapy and pain control with analgesics, while more interventional procedures (e.g., vertebroplasty, kyphoplasty) are considered in those who are unresponsive to conservative treatment. Meanwhile, adequate diagnosis and treatment of osteoporosis itself reduces the incidence of VCFs. One pharmaceutical treatment that holds promise in management and treatment of vertebral compression fractures (VCFs) in patients with osteoporosis is Calcitonin.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving calcitonin (FORTICAL, MIACALCIN) for the treatment of vertebral compression fractures. We present the existing literature in the understanding of the safety and efficacy of calcitonin (FORTICAL, MIACALCIN) for the treatment of vertebral compression fractures.

**Results:** Osteoporosis had a prevalence of more than 10% in the United States in 2010. The CDC estimates that nearly 25% of women over the age of 65 have findings of osteoporosis, which include low spinal bone mass. This condition is highly prevalent and, in an aging U.S. population, quite clinically relevant. Risk factors for this development include advanced age, cigarette smoking, medications, 4 reduced physical activity, as well as low calcium and vitamin D intake. Family history may also play a role. Diagnosis is made based on bone mineral density. Standard therapy for vertebral compression fractures in the setting of osteoporosis include analgesic medications, such as NSAIDs and bisphosphonates, and surgical intervention. NSAIDs address the chronic pain that is a common long-term effect of VCFs. Bisphosphonates have recently been used to attempt to halt the progression and provide prevention. Surgical interventions such as balloon kyphoplasty and vertebroplasty are typically reserved for patients who have failed other methods. Calcitonin is a peptide naturally produced by the human body that is released from the parathyroid gland. It binds to osteoclasts, inhibiting them from inducing bone resorption. By relatively unknown mechanisms, it also appears to induce endorphin release and mitigate pain. Clinical data has shown safety and efficacy for exogenous calcitonin in reducing bone turnover and reducing VCF-induced pain. In a prospective double blind, randomized placebo-controlled clinical trial, 40 patients with recent non-traumatic osteoporotic vertebral fractures either received calcitonin versus placebo suppository once daily with or without also taking paracetamol (500mg) tablets. The calcitonin group experienced less spinal pain early, early mobilization, sitting, walking, and standing with less bone turnover compared to the placebo group. In a multicenter prospective randomized controlled trial had shown positive results for calcitonin. This included osteoporotic women with acute lumbar pain after a new VCF were divided into two treatment groups: 114 received 20 units of calcitonin injected once weekly, and 114 women received NSAIDs daily for 6 weeks. It was found that there were statistically significant differences between the two treatment groups measured through the VAS of pain intensity, and quality of life measured by the IQ22 and RDQ. The mean difference between the calcitonin group and the NSAIDs group in each measure at 4 and 6 weeks were -4.8 and -8.3 for the IQ22, -1.3 and -2.6 for the RDQ, and -11.3 and -11.5 for the VAS, in favor of calcitonin. Binkley et al. conducted a study involving 565 women randomized into 3 groups to receive: oral recombinant salmon (RS) calcitonin with placebo nasal spray, synthetic salmon (SS) calcitonin nasal spray with placebo tablets, and placebo tablet and placebo spray. It was found that women in the oral rSCT group had a greater increase in lumbar spine BMD from baseline than the other two groups and a greater bone mineral density (BMD) in trochanteric and total proximal femur when compared to just the sSCT group. There were significant reductions in 2/3 bone resorption markers in the rSCT group when compared to the sSCT group, and reduction in 3/3 markers when rSCT compared to the placebo group. 80% of the participants experienced at least 1 adverse event and less than 10% in each group experienced a serious adverse event.

**Conclusion:** Osteoporosis and its associated complications, such as vertebral compression fractures, impact large portions of the population and represent a significant clinical burden to the healthcare system. Continued investigation into the management of VCF aims to provide pain and symptom relief. Traditional conservative therapies aim to manage pain through oral analgesics and physical therapy. More invasive procedures, such as kyphoplasty or vertebroplasty, may be pursued for patients requiring further management of pain and fracture complications. Calcitonin is a safe and effective option for patients, especially for those who are unable to tolerate more traditional methods of pain management or who 5 have failed initial treatment. Its added benefits of increasing bone mineral density makes it particularly important for treating VCFs in addition to addressing pain management, and it poses few serious side effects. Further research is needed to fully understand calcitonin's potential role as a preventative therapy in reducing the incidence of future fracture, which would offer another critical advantage in the treatment of osteoporosis and associated VCFs.

# Caspase-Apoptosis Signaling related to Inflammation is Modulated by SCS with Differential Target Multiplexed Programming in an Animal Model of Neuropathic Pain

ASIPP® ANNUAL MEETING 2021  
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## INTRODUCTION

Caspases are proteases that activate intracellular stress signaling in response to neuroinflammation. Neuropathic pain might induce caspase-mediated neuronal apoptosis in the spinal cord<sup>1</sup>, and pain-related behavior can be alleviated by deactivating the caspase-apoptosis signaling pathway using caspase inhibitors<sup>2</sup>. We have demonstrated that the multiplexing of electrical signals to differentially target glial and neuron cells in the spinal cord is effective at relieving pain-like behavior and modulating gene expression in neuroinflammatory processes using an animal model of neuropathic pain.<sup>2</sup> Current efforts in our group aim to demonstrate that this differential target multiplexed programming (DTMP) also modulated expression levels of proteins associated with neuroinflammation.

## MATERIALS AND METHODS

The IACUC at Illinois Wesleyan University approved all procedures. Figure 1 shows a scheme of the experimental design. Bioinformatic tools and online databases identified proteins from the mass spectra of peptides. Statistical methods were used for protein identification. Normalized spectral intensities were used to obtain expression levels and fold changes (No-DTMP/No-SNI and DTMP/No-SCS). Phosphorylated proteins were identified in a separate experiment in which phosphopeptides were enriched and separated using immobilized metal-ion affinity chromatography followed by identification and quantitation via liquid chromatography/tandem mass spectrometry.

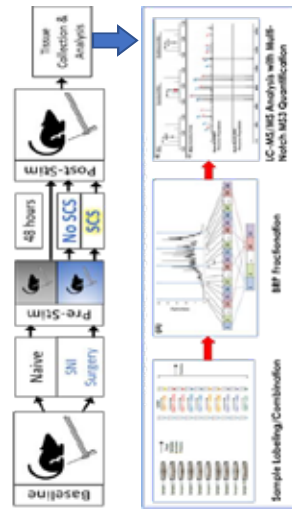


Figure 1. Scheme of experimental design and proteomic analysis.

## RESULTS

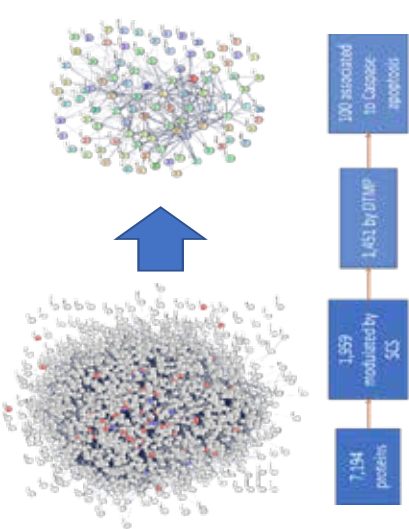


Figure 2. Protein interaction maps for all proteins significantly modulated by DTMP (n = 1,451) and those that were associated to caspase-apoptosis signaling (n = 100).

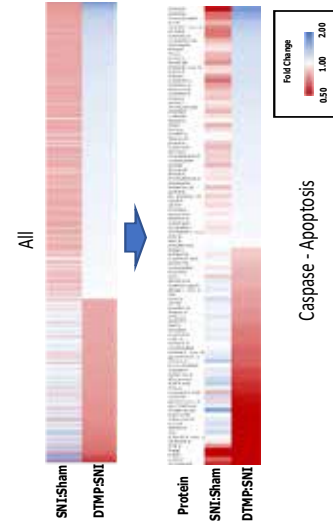


Figure 3. Heat maps showing fold changes in expression levels for all proteins and those involved in caspase-apoptosis signaling that were significantly modulated by DTMP.

## RESULTS (continued..)

The pain model also increased expression levels of p-MST1, which phosphorylates YAP, an inhibitor of apoptosis when is dephosphorylated (net pro-apoptotic effect). We found that the pain model increased expression levels of 4 phosphorylated YAP (p-YAP) isoforms. DTMP decreased expression levels of 3 of the p-YAP isoforms as well as p-MST1 toward levels in uninjured animals with a net anti-apoptotic effect.

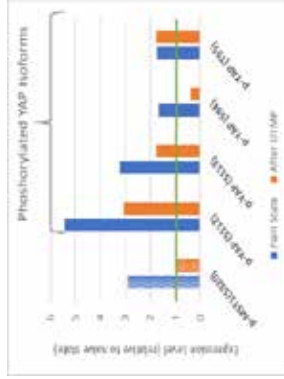


Figure 3. Bar graphs illustrating expression levels of phosphorylated proteins p-MST1 and p-YAP relative to naive animals (green line) due to the pain model (blue bars) and after DTMP treatment (orange bars).

## CONCLUSION

DTMP modulates expression levels of proteins and phosphoproteins known to be associated with neuronal death via the caspase-apoptosis pathway toward expression levels found in uninjured animals. The results support the modulatory effect of DTMP on the apoptotic process, which is known to occur slowly during the evolution of chronic neuropathic pain.

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# Cervical Spinal Cord Stimulator Lead Migration down to the Generator: A Case Report

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## Case Description

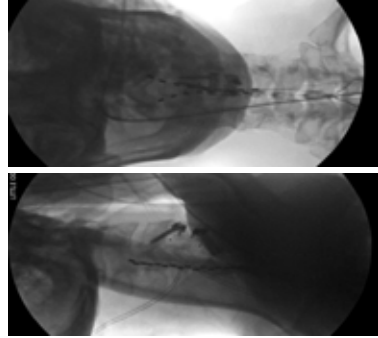
This is a case of a 42-year-old female with a history of a motor vehicle accident in January of 2018. From the accident, she sustained pelvic fractures and a non-displaced C4 vertebral fracture with resulting neck and shoulder pain. She underwent C4 corpectomy and anterior cervical fusion in January 2019. Despite having surgery, she continued to have posterior neck pain and paresthesia down her right shoulder and arm. Due to the persistent pain, she was consulted for a spinal cord stimulator (SCS) trial, and had greater than 50% pain reduction and near complete resolution of her paresthesia. She eventually had the device implanted in June 2020. As time progressed, her pain and paresthesia started to slowly return. On a clinic visit in January 2021, she noted that her pain continued to increase, but attributed it to being more busy at work. We recommended the patient undergo reprogramming in March 2021. However, she noted the stimulation was primarily felt in her buttocks near the implantable pulse generator (IPG). The patient was brought back to the clinic, and a fluoroscopic image (image 1) was taken, which showed the leads wrapped circumferentially around the IPG. After further consultation, given great success of the initial cervical spinal cord stimulation, the patient elected to have a SCS revision and re-implantation. In April 2021, she had a successful operation, and her pain was again improved greater than 50%.



Image 1. Fluoroscopic image of the cervical SCS leads wrapped around the generator.

## Methods

The patient was taken to the operating room, and using standard surgical technique, the pocket where the IPG was implanted was opened, and the IPG was found to have leads wrapped around it circumferentially without any lead fracture. An incision was made in the cervical region and the lead anchors, which were found to be still sutured into the fascia were removed. Using a 14 gauge Tuohy needle, we accessed the epidural space at T1-2 and new leads were threaded up into the epidural cervical space (images 2 and 3). Unfortunately the leads were unable to be advanced past the inferior border of C2 (prior implantation leads were placed at the top of C2). Leads were tunneled to the original IPG pocket and the original generator was used. However in post-programming and 2 week follow up, the patient noted the stimulation still covered her area of pain and was satisfied with the final results of the revision and implantation.



Images 2 and 3. Displaying the new lead placement under fluoroscopy.

## Discussion

SCS is an implantable device that sends a therapeutic electrical current to the spinal cord. The implantation is done in the operating room as a minor surgical procedure. Since its inception around 1967, SCS has undergone multiple advancements. Nonetheless, it is not without risks. In a 2011 retrospective review of 707 SCS cases, hardware-related complications were common and occurred in up to 38% of the cases of SCS implantation. These complications included lead migration (22.6%), lead connection failure (8.5%), and lead breakage (6%).<sup>1</sup> According to a 2006 review of 410 patients over a 22-year period, lead migration was reported in 21.4% of the patients, with cervical being twice as likely as thoracic. This is thought to be due to the higher mobility of the cervical spine.<sup>2</sup> While lead migration is common, in our patient it is unclear exactly what led to this. Per standard protocol, we placed a pressure relief loop as always. The patient notes that when she sat down, she would feel rubbing against the IPG. Perhaps, each time she sat down the leads moved more and more until wrapping themselves completely around the IPG.

## Conclusion

In conclusion, this case highlights a unique situation of lead migration from cervical lead placement with circumferential wrapping of leads around the generator. Since tolerance and other complications are seen with SCS, it is important to start by reprogramming the generator. If the patient still has significant pain, it is warranted to obtain fluoroscopic images to assess for lead migration, which is a common complication. Successful re-implantation can lead towards positive outcomes and patient experiences with SCS.

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# Cooled Radiofrequency Ablation Provides Prolonged Pain Relief Compared To Traditional Radiofrequency Ablation: A Real-Life, Large Retrospective Clinical Comparison From A Single Practice

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## Background:

Knee osteoarthritis (OA) pain is the most common cause of chronic knee pain with a lifetime prevalence of almost 45 percent.<sup>1</sup> Radiofrequency ablation is a commonly used treatment for non-surgical treatment of knee OA. Traditional radiofrequency ablation (TRFA) involves a simple electrode emitting radiofrequency energy, resulting in ionic heating and thermal lesion creation. Cooled radiofrequency ablation (CRFA) involves circulating water through the probe tip which carries the heat away from the tissue-tip interface which reduces desiccation and charring of tissues.<sup>2</sup> CRFA creates spherical lesions that are larger than TRFA and has been shown to deliver significantly more energy to surrounding neural tissues.<sup>3</sup> A head-to-head comparison of CRFA and TRFA in this indication has yet to be conducted.

## Objective:

We completed a large retrospective comparison (n=340) between TRFA and CRFA when used for treatment of chronic knee pain in very heterogeneous patient population.

## Demographic Table:

Characteristics	TRFA (n=170)	CRFA (n=170)	Statistics
Patients Age	Mean 63.3 Median 63.5	Mean 61.77 Median 61	P=0.297
Patients sex	Female 111 Male 59	Female 108 Male 62	P=0.95
BMI	35.9	33.9	P=0.066
Baseline VAS (cm)	Mean 8.3 Median 8	Mean 8.4 Median 8	P=0.505
Diagnostic block VAS (cm)	Mean 2.6 Median 3	Mean 2.2 Median 2	P=0.011
Opioid daily dose (mg)	Mean 48.6 Median 25	Mean 53 Median 35	P=0.05
Other chronic pain sources	Median 2	Median 2	P= 0.624

Table 1. Patients cohorts who were well balanced in most of baseline characteristics.

## Results:

Figure 1: Improvements in VAS pain scores at the first visit (4-6 weeks after procedure) after either TRFA or CRFA were profound. For TRFA VAS pain scores decreased to 5.07±2.8 cm (median 5 cm) and for CRFA to 4.26 ± 3.2 cm (median 3) (p<0.001 for both from baseline). CRFA provided better immediate improvements in VAS pain scores (p=0.010; Figure 1) than TRFA.

Figure 2: Time interval of pain relief (>50% of pain decrease) was in an average only 2.6 months for TRFA and 11.1 months for CRFA group. The difference was profound and significantly better in the favor of CRFA (p<0.001). There were 35 out of 170 patients in TRFA group who maintained > 50% of pain relief for 6 months or longer (or 20.6 %) and only 15 out of 170 patients (8.8 %) who continue receiving > 50 % of pain relief at 12 months, as opposed to 107 out of 170 (63%) patients in CRFA cohort who received >50 % of pain relief at 6 months and 78 (46%) at 12 months.

There was no significant change in opioid usage in either patient cohort (p=0.054 and p=0.954 respectively), but also there was no intended effort to wean the patients off opioids in this diverse patient group who had in an average two other chronic pain sources.

## Discussion:

We compared an initial outcomes and long-term maintenance of pain relief between sub-cohorts of the patients who received TRFA using either 22G (n=92), 20G (n=14), 18G (n=51), 16G (n=13) or CRFA (n=170) (Figure 2). While an initial outcome was similar disregarding the electrode diameter, a long-term outcome (>50% of pain relief) was much longer for the bigger lesion size treatment groups, with CRFA providing the longest pain relief (see Figure 2). Moreover, we found that the long-term positive outcomes (>6 months) depended mainly on the size of the lesion as CRFA and a larger TRFA treated patients received a longer time interval of pain relief (Figure 1 and 2). It is theorized that the amount of energy delivered to neural tissue may play a role in the clinical durability of CRFA.

## Conclusion:

This large retrospective analysis of a heterogeneous real world population indicated that better outcomes were achieved at the first follow up visit (4-6 weeks post RF) and much longer time interval of > 50% of pain relief when CRFA used during geniculate denervation as opposed to TRFA (Figure 1 & 2). The usage of CRFA does provide better long-term outcomes.

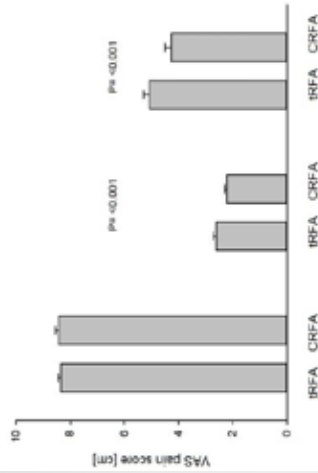


Figure 1. Initial (4-6 weeks) pain relief after TRFA vs CRFA. Improvements in pain scores after the diagnostic blocks, and then either TRFA or CRFA. Blocks and both RFAs showed significant improvement with improvements after CRFA being somewhat better than TRFA (p=0.010) 4-6 weeks after the procedure.

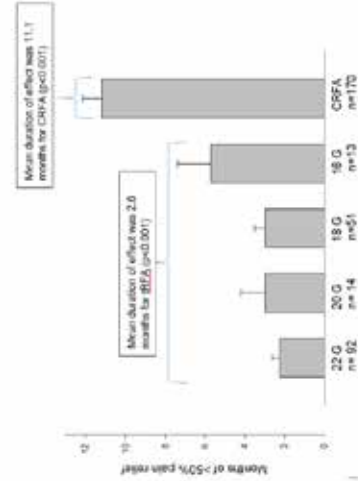


Figure 2. Long-term maintenance of pain relief after TRFA vs CRFA, based on probe gauge. Notice that a significant pain relief was maintained in average after the CRFA (11.1 months, while only 2.6 months for TRFA (p<0.001) n=170 for both).

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## Efficacy of acupuncture in the treatment of chronic abdominal pain

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**Background:** Acupuncture is the practice of applying sterilized needles into specific body points designed to rebalance a patient's qi. Based on the principles of Confucianism and Taoism, health complications are thought to arise when there is an imbalance in a patient's qi, or equilibrium of ying and yang. In modern medicine, acupuncture is defined as a nonpharmacological option used to treat symptoms ranging from tobacco use to abdominal pain. Abdominal pain is a chief complaint that plagues patients of all demographics. In 2002, abdominal pain as a chief complaint accounted for over 13.5 million patient visits in primary care clinics. Abdominal pain can further be classified into two categories: acute abdominal pain and chronic abdominal pain. Chronic abdominal pain has varying definitions, but the most prevalent definition is three episodes of abdominal pain severe enough to disrupt the daily routine for a patient within a three-month period. Common causes for chronic abdominal pain include complications to organs such as gastrointestinal tract organs, digestive organs, and even genitourinary organs. Chronic abdominal pain is sometimes associated with the presence of a functional syndrome. In a meta-analysis, abdominal pain disorders were found to have a prevalence rate of 13.5%. Abdominal pain was reported more frequently in South America (16.8%) and Asia (16.5%) as opposed to Europe (10.5%). Abdominal pain was reported significantly higher in girls (15.9%) than boys (11.5%). The burden of chronic abdominal pain looms large in healthcare around the world. In the Netherlands, over \$623 million is spent yearly on chronic abdominal pain outpatient visits, which equates to over \$720 million. GI and digestive tract organ complications are common causes for chronic abdominal pain. These issues burden the United States by accounting for over 200,000 deaths, 10 million ambulance calls, \$140 billion dollars in cost, and 14 million hospitalizations nationally. The issue of abdominal pain becomes more urgent as the elderly show a mortality rate of 10% due to abdominal pain. In an era in which the population of the elderly (age 65 and older) are growing at a rapid rate with projections of 83.7 million elderly people by 2050 in the United States alone, the healthcare system could soon be overwhelmed. This paper aims to investigate the efficacy of using acupuncture methods to treat abdominal pain.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving the use of acupuncture in treating chronic abdominal pain.

**Results:** Chronic abdominal pain is a common complaint causing significant morbidity and disability and has a hefty price tag attached. Recent studies show it may be prevalent in as much as 25% of the adult population. It is defined as three episodes of severe abdominal pain over the course of three months. Chronic abdominal pain could be the result of chronicity of acute pain or of chronic pain syndromes, most commonly IBD syndromes and IBS. While a plethora of treatments usually fall short of complete symptom control, and there is a need for complementary measures to curb disability and increase the quality of life in these patients. Acupuncture is a form of integrative medicine that has long been used in Chinese and traditional medicine, based on the rebalancing of the patient's Qi, or Ying/Yang balance. It has been shown to be effective in treating several other conditions, and novel evidence may expand its use into other fields as well. Clinical trials studying acupuncture in chronic pain conditions have been promising, and recent evidence supports the use of abdominal pain in chronic abdominal pain conditions as well. Though not curative, acupuncture is a complementary approach that helps reduce symptoms and improved quality of life.

**Conclusion:** Chronic abdominal pain is a common complaint causing significant morbidity and disability and has a hefty price tag attached. Recent studies show it may be prevalent in as much as 25% of the adult population. It is defined as three episodes of severe abdominal pain over the course of three months. Chronic abdominal pain could be the result of chronicity of acute pain or of chronic pain syndromes, most commonly IBD syndromes and IBS. While a plethora of treatments usually fall short of complete symptom control, and there is a need for complementary measures to curb disability and increase the quality of life in these patients. Acupuncture is a form of integrative medicine that has long been used in Chinese and traditional medicine, based on the rebalancing of the patient's Qi, or Ying/Yang balance. It has been shown to be effective in treating several other conditions, and novel evidence may expand its use into other fields as well. Clinical trials studying acupuncture in chronic pain conditions have been promising, and recent evidence supports the use of abdominal pain in chronic abdominal pain conditions as well. Though not curative, acupuncture is a complementary approach that helps reduce symptoms and improved quality of life.



## Efficacy of Electrical Spinal Cord Stimulation with Neuromodulating Medications

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**Background:** Chronic pain is an issue that affects a staggering percentage of Americans—by some measures, more than 30%. Conventional medical treatment of chronic pain comes in a variety of forms including NSAIDs, antidepressants, anticonvulsants, muscle relaxants, gabapentinoids, and opioids. Spinal cord stimulation (SCS) is a newer treatment modality that holds significant potential given their neuromodulating properties. Spinal cord stimulation is used for a spectrum of chronic pain conditions including radicular pain after failed back surgery syndrome, inoperable painful peripheral vascular disease, complex regional pain syndrome, and diabetic neuropathy. SCS leads are placed in the dorsal epidural space and the adjacent 3 tissue receives electrical stimulation. While short term stimulation yields no significant change, long term stimulation of the dorsal column was found to significantly change the threshold of areas inside the area of induced paresthesia. The precise mechanism is not well understood, but there is evidence to support action through stimulation of the dorsal column, dorsal root, and dorsal horn. The landmark paper by Melzack et al. in 1965 proposed that “a gate control system modulates sensory input before it evokes pain perception,” offering an explanation for why not every touch invokes pain. This study was used as the foundation for SCS, however it does not adequately explain why noceptive pain is poorly controlled by SCS. Jensen et al. performed an excellent review of the current understanding about the potential mechanisms for SCS and point out that none of the proposed mechanisms are adequately nuanced to fully explain the analgesic properties. They also put forward their own hypothesis that the pain modulation may be mediated by electrical fields via stimulating dendrites of the dorsal horn islet neurons. Additionally, it has been shown that in rat models of chronic pain, SCS depresses hyperexcitability of dorsal horn neurons, acting as a membrane stabilizer. Membrane stabilizing drugs reduce the electrical excitability of neurons. This diminishes the propagation of action potentials along nerve cells. Gabapentinoids are excellent membrane stabilizers for treating some forms of chronic pain. Both gabapentin and pregabalin are structural analogs of GABA, however they do not act through GABA receptors. Instead they function through binding presynaptically to the  $\alpha$ -2-A subunit of voltage-gated calcium channels found in the spinal cord and brain. This binding inhibits trafficking of the  $\alpha$ 1 pore-forming unit of the calcium channels to the pre-synaptic plasma membrane. They are commonly used for treatment of postherpetic neuralgia, painful diabetic neuropathy, and fibromyalgia. Antidepressant medications are also commonly used for chronic pain indications. The precise mechanism of action for tricyclics remains unclear, however medications in the group such as amitriptyline are well established in the treatment of chronic pain. Likewise, SNRIs such as venlafaxine, desvenlafaxine, and milnacipran are staples of treatment in many types of chronic pain including painful diabetic neuropathy, fibromyalgia, and musculoskeletal pain including back pain. With chronic pain being so prevalent, it is not uncommon for a person to use multiple modes of action to attempt to alleviate their pain. In particular, the possibility of a synergistic effect of neuromodulation via SCS combined with the membrane stabilizing properties of the gabapentinoids is intriguing. This literature review aims to assess the efficacy of using adjunctive medications and SCS simultaneously.

**Methods:** A systematic computerized search of the literature was conducted using PubMed (www.ncbi.nlm.nih.gov/pubmed), the Cochrane Library (www.thecochranelibrary.com), and EMBASE (www.embase.com) for articles published in English. Search terms included “spinal cord stimulation AND gabapentin,” “spinal cord stimulation AND pregabalin,” “spinal cord stimulation AND gabapentinoid,” “spinal cord stimulator AND gabapentin,” “spinal cord stimulator AND pregabalin,” “spinal cord stimulator AND gabapentinoid,” “spinal cord stimulator AND SNRI,” “spinal cord stimulator AND triicyclic antidepressant,” and “spinal cord stimulator AND SNRI.” Duplicate results were eliminated, and results were further narrowed based on title and abstract. All articles with possible relevance were then reviewed in full. Similar search parameters were used for other medications but did not generate relevant results so the discussion of other classes of medications frequently used in chronic pain is not included, including: alpha-2 adrenergic agents, acetaminophen, NSAIDs, and muscle relaxants.

**Results:** A total of 165 articles with possible relevance were found based on the methods above. Results were narrowed based on title and abstract leaving 21 articles for full review. Of these, 3 were determined to have direct relevance to be included. One article by Jang et al. was a Korean study done as a retrospective evaluation of 100 military veterans who had undergone SCS implantation. Of these, 48 still had the stimulator implanted after 2 years. These remaining patients were evaluated in two groups. One group of 20 patients received opioid only, while the remaining 28 received both opioid and gabapentinoid. Data was collected for 1, 6, 12, and 24 months after implantation and information collected included numeric rating scale pain score, quality of life scale score, and oral morphine equivalents. They found that the patients who received gabapentin in addition to opioids and SCS had a better reported quality of life than those who received only opioids and SCS. However, there was no statistically significant difference in pain scores or opioid consumption, suggesting that addition of gabapentin may be helpful for improving quality of life but not necessarily in reducing reported pain or opioid consumption. They do not speculate as to the reason that there was an improved quality of life even though there was no reduction in reported pain. Animal studies have been performed to determine if combination of medications and SCS might be more useful than SCS alone. Song et al. studied a rat model with sciatic nerve injuries by implanting spinal cord stimulators and introducing an intrathecal catheter to inject medication, and subsequently compared pain responses between groups at different levels of stimulation. Studied drugs included a representative tricyclic, SNRI, and SSRI in the form of amitriptyline, milnacipran, and fluoxetine respectively. Their results showed a statistically significant improved pain response for the SNRI and tricyclic medications, however not for the SSRI medication. Another study was published in 2019 on 108 patients who had undergone SCS implantation. Pain scores were collected preoperatively and again at 12 months postoperatively. Outcomes were compared between patients who received SCS alone compared to duloxetine plus SCS. Notably, no randomization was performed and the specific pain indication for device implantation was not reported. The study also performed subgroup analysis for those patients who received gabapentin or pregabalin. Results indicated that patients who received duloxetine had better pain relief as judged by the McGill Pain Questionnaire (MPQ) as compared to those with SCS alone. The study also found that gabapentin/pregabalin did not have significant improvement in pain outcomes and in fact had a significant increase in perceived pain as measured by the MPQ.

**Conclusion:** Chronic pain is prevalent, and detrimental to the quality of life of many people. Promising interventions such as spinal cord stimulation offer a potential opportunity for improved pain control, and there may be additional benefit by combining both SCS and existing therapies, particularly with TCAs and SNRIs. Studies involving gabapentinoids are quite limited and are not adequate to indicate usefulness of these medications with spinal cord stimulators. The existing literature on interactions between medications and SCS is sparse and the results are too limited to reveal a clear pattern of synergy or interference between these techniques, and therefore further research into combining SCS and other forms of neuromodulation will be required.





# Epidural Steroid Injection for Notalgia Paresthetica and Brachioradial Pruritis

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## INTRODUCTION

Notalgia Paresthetica (NP) is a sensory neuropathic syndrome of the midback skin around T2-T6 distribution that can present with episodes of pruritis or pain. It is a chronic, non-curable condition with periodic remissions and exacerbations, and which demonstrates a female predominance.<sup>1,2</sup> Although common, it is not easily recognized, and is thus underdiagnosed. Other features of NP can include localized burning, pain, tenderness, hyperalgesia, or dysesthesias.<sup>3</sup> NP causes significant discomfort to patients and can lead to decreased quality of life. Brachioradial pruritis (BRP) is a localized pruritis syndrome of the upper extremities, typically of one or both forearms. Like NP, it is chronic, non-lethal and non-curable. Most cases of NP and BRP occur together, likely due to underlying degenerative spine, disc, and muscle disease.<sup>4</sup> Initial therapy for NP and BRP with associated cervical disease may include physical therapy, massage, topical ointments, cervical traction, cervical muscle strengthening, and oral nonsteroidal anti-inflammatory drugs and muscle relaxants. Transcutaneous electrical nerve stimulation and cervical discectomy with fusion have also been utilized. Research on the use of epidural steroid injection (ESI) in patients with NP and BRP is limited.

## CASE PRESENTATION

A 51-year-old female with history of hypothyroidism, depression, and cervical radiculopathy treated with ESI 8 years ago presented with “burning” pain and pruritis of the upper back and bilateral arms for about 8 years. She also noted numbness over medial forearm radiating distally to her 4<sup>th</sup> and 5<sup>th</sup> digits. She had previously seen a neurologist and was diagnosed with BRP and NP. She was taking gabapentin and Duplumab, which provided minimal relief. She had taken steroids, NSAIDs and topical tacrolimus, which also provided no relief. Recent cervical spine MRI showed bulging discs at C4-C5 and C5-C6, with mild C6 canal stenosis. Physical exam was notable for erythema, excoriations, and areas of bleeding and skin in different stages of healing over the upper back and bilateral arms that followed a C5-C6 distribution. There was also cervical paraspinal tenderness with radiation to the lateral arms on palpation. There was a positive Spurling’s test, greater on the left compared to the right.

## PROCEDURES

Patient’s initial treatment plan consisted of fluoroscopy guided right parasagittal C7-T1 intralaminar ESI with catheter directed up the lateral gutter just above the C6-C7 juncture. (Fig.1) Her gabapentin dosage was changed to 600mg po nightly, and she was taken off the Duplumab. Three weeks later, she had similar ESI on the left side. (Fig.2)

## RESULTS

At follow up after initial ESI, she noted significant relief (80%) of her right arm pain and itching. She continued to have itching in the left shoulder and arm. At two months follow up after second procedure, she reported a 70% improvement in overall pruritis with 95% relief of her symptoms distal to both elbows. At most recent follow up, she reported 99% relief of overall pruritis in left upper extremity and 75% improvement in symptoms of the right upper extremity. She continues to have mild pruritis in two isolated spots at the right trapezius.

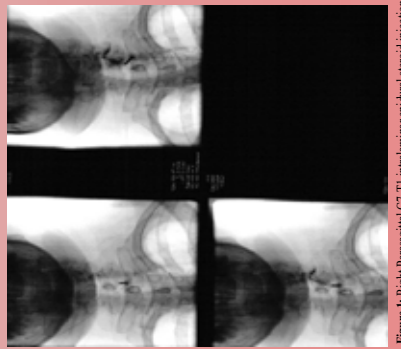


Figure 1: Right Parasagittal C7-T1 intralaminar epidural steroid injection

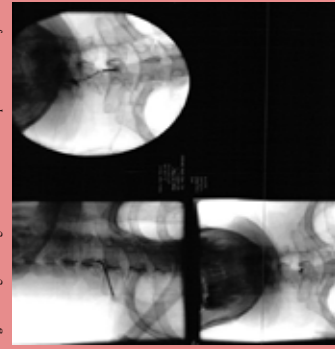


Figure 2: Left Parasagittal C7-T1 intralaminar epidural steroid injection

## DISCUSSION

Multiple mechanisms for NP and BRP have been proposed, including neuropathy or direct nerve impingement from cervicothoracic disc disease and increased localized sensory innervation of the area. NP and BRP are localized pruritic syndromes, and as such there is an association of one with the other. However, the mechanism of the pruritis in both remains unclear. Several studies have shown the association of NP and BRP with significant radiographic changes in the vertebrae corresponding to the patient’s distribution of pruritis and pain.<sup>1,6</sup> Indeed, over 60% of NP patients may have radiographic findings of degenerative vertebral changes or herniated discs in areas that corresponded to the dermatomal distribution of their symptoms.<sup>3,6</sup> Initial therapies for NP discussed above have not shown reliable improvement in symptoms. BRP treatments have shown variable effectiveness, with topical treatments providing minimal relief of symptoms.<sup>5,7</sup> Gabapentin has shown some efficacy in both BRP and NP. A report of NP associated with spinal injury was treated with IV lidocaine which provided significant temporary relief of the patient’s symptoms.<sup>8</sup> One case series showed CT guided cervical nerve root blocks for treatment of BRP provided significant improvement in symptoms; however research on the use of ESI in patients with NP and BRP is limited.<sup>9</sup>

## CONCLUSION

The use of fluoroscopy guided ESI for this patient with refractory pruritis and pain was shown to provide significant improvement in her symptoms. At two months’ follow up, our patient had 70% improvement in overall pruritis with 95% relief of her symptoms distal to the elbows. This interventional approach has not been extensively studied in BRP and NP; however, our results indicate it could provide significant relief, and should be further studied and considered in similar patients for whom conservative management has failed.

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# Erector Spinae Plane Block for Central Pain related to Spinal Cord Ependymoma: A Case Presentation

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## Introduction

Originally described in the management of severe thoracic neuropathic pain by Forero et al in 2016, the erector spinae plane block (ESPB) has gained increasing interest for its high therapeutic efficacy, opioid sparing analgesic benefit and favorable side effect profile [1,2]. Although the ESPB has been reported in the management of acute and chronic refractory pain, particularly of the thoracoabdominal region, the full extent of its use is yet to be completely elucidated [3-5].

The aim of this presentation is to describe the successful use of ultrasound guided ESPB in the management of a patient with central pain related to cervical ependymoma and syrinx of the spinal cord.

## Case Description

A 50-year-old female presented to our pain clinic with a 2-year history of progressively worsening upper back shooting pain radiating to the ribs on her right side with associated pain in her right shoulder, right arm and right leg. She also reported numbness, tingling and weakness particularly of the right lower extremity. Symptoms started after she was found to have a large spinal cord syrinx with a cervical spinal cord ependymoma and metastasis to the conus. Following that diagnosis, she had undergone radiation therapy to the entire spinal cord as well as surgical removal of the ependymoma. Various medications and therapies (such as gabapentin, pregabalin, duloxetine, physical therapy) were tried for the pain with less than satisfactory relief and/or intolerable side effects. On physical exam, there was significant tenderness in the right thoracic region at T8-T11 levels.

Postoperative cervical spine magnetic resonance imaging (MRI) was significant for a large syrinx extending from the distal portion of the medulla into the thoracic region but most significant at C4-C6. Lumbar

## Method

On the day of the procedure, the patient was placed in a seated position with back exposed. Under aseptic conditions, an ultrasound guided right sided ESPB was performed at T8 using a 22G Stimuplex needle. A solution containing 20 ml of 0.125% bupivacaine with 40 mg methylprednisolone was injected into the plane between the erector spinae muscle and T8 transverse process with lifting of the erector spinae muscle observed. She tolerated the procedure well and reported more than 80% pain relief prior to discharge home. This improvement was sustained during her clinic visit 4 weeks later where she reported a sustained 90% improvement of her pain and 90% improvement in functionality of her right side.

## Discussion

Since it was described, studies have been conducted to determine the spectrum of efficacy, mechanism of action and safety/side effect profile of the ultrasound guided ESPB. In literature, it has found encouraging use in postoperative pain management of thoracic and abdominal surgeries in the multimodal approach to analgesia with the aim of reducing opioid consumption [1-5].

Our patient had symptoms and signs of central pain and intercostal neuralgia related to cervical ependymoma and spinal cord syrinx. The goal of the erector spinae block was to reduce her pain severity and improve her quality of life. The ESPB provided our patient with significant and sustained pain relief while improving her functionality. She reported no side effects following the procedure.

To the best of our knowledge, this is the first successful use of the ultrasound guided ESPB, a peripheral nerve block, in the management of pain due to a central nervous system process.

## Conclusion

In conclusion, the ultrasound-guided ESPB may be a beneficial therapeutic option in the management of certain central pain syndrome without causing significant side effects.

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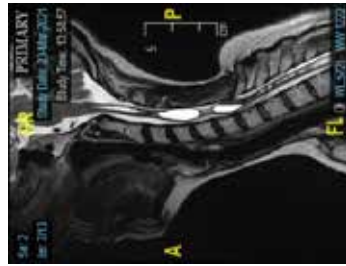


Figure 1: Cervical spine MRI showing a large syrinx extending from the cervicomedullary junction into the thoracic spine. At C4-C5 and C6 levels, the syrinx is much larger in volume. Findings

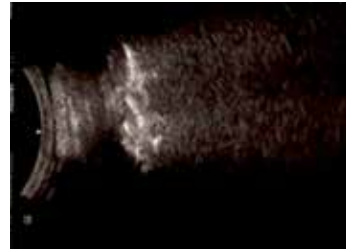


Figure 2: Ultrasound-guided right sided Erector Spinae Block performed at the T8 level.

# Evaluation of a New, Battery-Free Microstimulator SCS System: Comfort and Ease-of-Use Data (AUS-nPower™ study)

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 Affiliations: <sup>1</sup>IPM Medical Group, Walnut Creek, CA; <sup>2</sup>Institute for Neuromodulation, Boca Raton, FL; <sup>3</sup>University of California, San Francisco, CA; <sup>4</sup>Premier Pain Centers, New Jersey, NJ

## Introduction

Miniaturization of electronic components has allowed the creation of a novel externally-powered Spinal Cord Stimulation (SCS) system with a battery-free micro-implantable pulse generator (mIPG; Nalu Medical, Inc., Carlsbad, CA). This system consists of the mIPG (<1.5 cc) that is powered by an external wearable unit (Therapy Disc; TD). The comfort and other ergonomic elements of this system were analyzed in an ongoing first-in-human feasibility clinical study.

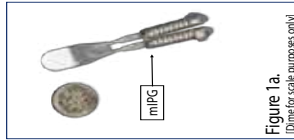


Figure 1a. (Do not use for scale, purposes only)

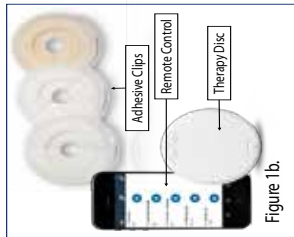


Figure 1b.

Figure 1a. The implanted component of the system consists of a battery-free mIPG (multiple configurations) which connects to leads (not pictured). Figure 1b. The external component of the system consists of the Therapy Disc, secured on the back using an adhesive clip, and a mobile app for remote control of therapy by patient.

## SYSTEM EASE OF USE

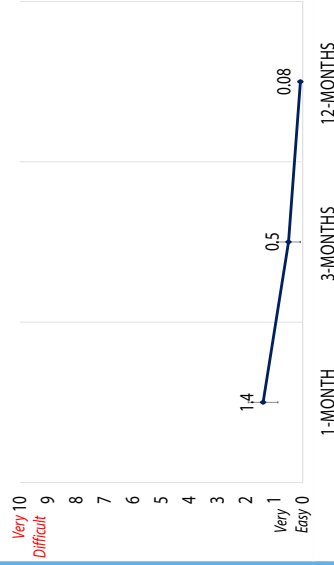


Figure 3: Average system ease of use ratings (0= very easy, 10= very difficult) at 1-month, 3-month, and 12-months post-activation.

## Results

Many patients continued to rate the Therapy Disc "not noticeable" when worn throughout the duration of their participation in the study. On average, patients rated the comfort as 0.8 on the first day, 0.4 after 6-months, and 0.4 after 12-months. The system, as a whole, was rated very user friendly by the patients. Ease-of-use with the system was rated a 1.4 after 1-month, 0.5 after 3-months and a 0.08 after 12-months.

## Methods

Twenty-seven (27) chronic, intractable pain patients participating in a prospective, multi-center, open-label clinical study wore the TD, secured on their back via an adhesive clip, continuously throughout their participation in the clinical study. These subjects gave feedback on comfort with the external wearable and system ease-of-use at multiple time-points. Patients rated both metrics on an 11-point rating scale, where 0 was very comfortable/very easy, and 10 was very uncomfortable/very difficult. The study was approved by an independent Ethics Committee and conducted in compliance with local regulations.

## COMFORT OF WEARABLE

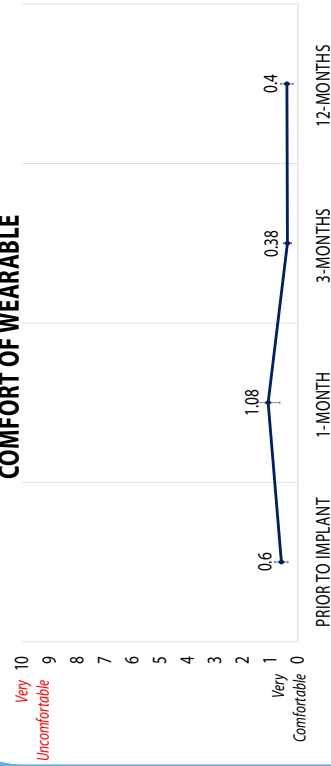


Figure 2: Average comfort ratings (0= very comfortable, 10= very uncomfortable) prior to implant and 1-month, 3-month, and 12-months post activation.

## Conclusion

As shown, patients found the study device comfortable and easy to use. These preliminary results of this ongoing study demonstrate that the externally worn TD is comfortable, requires little effort to maintain, and tends to not be noticeable after a few days of wear. Continued comfort and compliance with wearing the external Therapy Disc is supported by sustained results out to 12-months. Given these preliminary results, this novel system appears poised to provide a solution to common challenges associated with conventional larger SCS systems that use implantable batteries.<sup>1</sup>

<sup>1</sup>Ruchinkas R & O'Grady T. Neuromodulation. 2000.

# Follies of Loss of Resistance – Retrodural Space of Okada

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 Dept. of Family Medicine UIC - Rockford<sup>1</sup>; Philadelphia College of Osteopathic Medicine<sup>2</sup>; Northwest Suburban Pain Center<sup>3</sup>

## BACKGROUND

Interventional pain management physicians utilize epidural injections of corticosteroids under fluoroscopic guidance to treat radicular pain syndromes. The advantage of fluoroscopic guidance is that it allows for the confirmation of the correct spread of medication into the epidural space. There are rare cases in which there is an unexpected spread of contrast into a retrodural and extradural space, known as the Space of Okada. The Space of Okada is a potential space that is dorsal to the ligamentum flavum and can communicate between bilateral facet joints and the extradural interspinous space. It has been described after injections into cervical and lumbar facet joints.

This anatomical structure was initially reported by Okada et al in 1981 when contrast was injected into a cervical facet joint and flowed across to the contralateral facet joint. The space is between the ligamentum flavum and vertebral lamina, and it does not communicate with the epidural space. Contrast spread in this space has been described during facet joint injections and rarely during epidural injections. The injection of contrast showed filling of the interspinous region because the space is contiguous with adjacent facet joints. This pattern is more consistent with a facet joint injection.

## OBJECTIVE

We report three cases in which there has been abnormal contrast spread signifying injection into the Space of Okada during lumbar interlaminar epidural injections. We review the patient backgrounds, the physician's account during the procedures, as well as provide the imaging that shows the abnormal spread of contrast. Our study is able to characterize a false loss of resistance when contrast is injected into the Space of Okada. We also discuss the significance of these findings towards the practical implications of performing epidural injections.

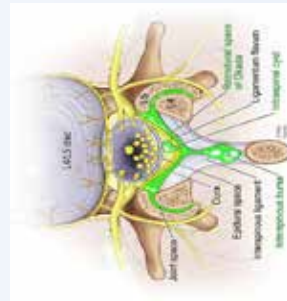
## MATERIALS & METHODS

All three patients were seen in an interventional pain management clinic for chronic low back and radicular pain syndromes. For the procedures, the patients were positioned prone on an X-ray table. The correct interlaminar level was identified using fluoroscopy. The entry point on the skin was infiltrated with 2 cc Lidocaine 1%. A 20 Gauge Touhy epidural needle was introduced as appropriate for the procedure. Anteroposterior and lateral views as well as loss of resistance technique were used to guide the advancement of the needle. 2 cc of Omnipaque 240 mg/ml dye was injected to confirm the final needle position in both anteroposterior and lateral views.

## FINDINGS

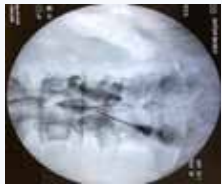
Anteroposterior views that were taken after loss of resistance and contrast injection displayed a spread of contrast into the Space of Okada rather than epidural space. There was an atypical feeling of "pushback" during contrast injection with imaging showing spread along the Space of Okada rather than the epidural space.

In each of the following illustrations, we observe an abnormal contrast spread across extradural interspinous space which is not consistent with standard epidural injections.



## CASE 1

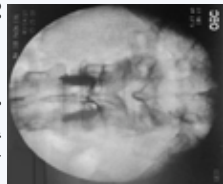
A 55-year-old male presented in 2021 to treat lumbar radiculopathy and spondylosis. The patient received a lumbar epidural steroid injection at interlaminar levels L3/L4.



MRI Impression: diffuse disc bulging, facet degeneration, and ligamentous thickening @ L3/L4

## CASE 2

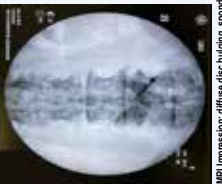
A 61-year-old female with a history of left acoustic neuroma and right hip replacement presented to an interventional pain clinic in 2013 to treat lumbar radiculopathy. The patient received a lumbar epidural steroid injection, performed at interlaminar levels L3/L4.



MRI Impression: diffuse disc bulging, facet degeneration, and ligamentous hypertrophy @ L4/L5

## CASE 3

An 82-year-old female with a history of a CVA and MI presented to the clinic in 2021 to treat lumbar radiculopathy. The patient received a lumbar epidural steroid injection at interlaminar levels L4/L5.

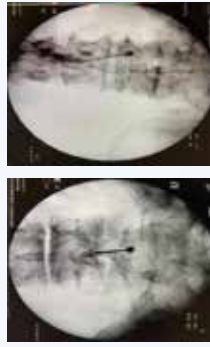


MRI Impression: diffuse disc bulging, spondylosis, facet degeneration, and ligamentous hypertrophy @ L4/L5

Depicted here is a lateral view of the same case 3 patient indicating contrast spread into the Space of Okada.

## CONCLUSIONS

The main significance is that the Space of Okada is an anatomic variant and can have an effect on epidural procedures. Physicians who feel a loss of resistance but are unable to inject medication or thread the catheter into the epidural space are possibly in the Space of Okada. We noted that there is a consistent rebound in the syringe after attempting the injection into that area. In most cases, advancing the needle and feeling a second loss of resistance indicates the epidural space has been entered. The Space of Okada is easily recognizable when contrast and fluoroscopy are utilized but for physicians who do not use these resources, then it is more difficult to identify.



## CASE 2

In both instances above, the pain specialist adjusted needle positioning to avoid similar occurrences of false losses of resistance. The epidural fluoroscopic outcomes as illustrated above demonstrate patterns consistent with standard contrast spreads.

We encourage interventional pain physicians to become educated on the presence of the retrodural space in some patients so that medications can be effectively administered into the appropriate layer.

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# GENITOFEMORAL NERVE STIMULATION FOR A PATIENT WITH INTRACTABLE GROIN AND SCROTAL PAIN: CASE REPORT

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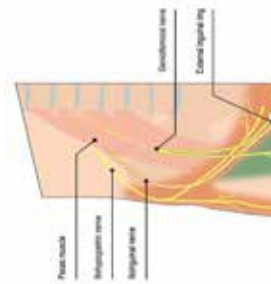
## PROBLEM

Chronic post-operative pain is the most common complication after ilioinguinal hernia repair. With about 800,000 inguinal hernia repair surgeries in the US per year it is one of the most common surgical interventions in general surgery<sup>[2]</sup>. Reports of chronic pain range from 14-54% of all cases<sup>[1]</sup>. Out of that 11% also reported limitations in activities of daily living, work and leisure activities<sup>[1]</sup>.

Current management options include pharmacologic and interventional pain management modalities. Current interventional therapies include nerve blocks to the ilioinguinal or genitofemoral nerves; radiofrequency ablation (RFA) and neuromodulation including spinal cord stimulation (SCS) or peripheral nerve stimulation (PNS). Limitations with treatment can include limited, short term relief from symptoms and risks from procedural therapy including risk for bleeding, risk for infection, and paralysis.

## BACKGROUND

Repair of an ilioinguinal hernia can result in neuropathic pain due to injury to either the ilioinguinal, iliohypogastric or genitofemoral nerves or somatic pain from scarring or tissue damage.



running over the anterior surface of the psoas muscle, it then runs inferiorly separating into the femoral and the genital branches<sup>[6]</sup>. Once the nerve reaches the groin, it goes into the deep inguinal ring through the inguinal canal. This genitofemoral nerve supplies sensation to the anterior scrotal area in men and to the anterior aspect of the thigh. These nerves can be located with ultrasound to perform interventional therapies.

Ilioinguinal nerve blocks have been known to provide temporary relief of pain symptoms, while RFA can be performed by neuro ablation technique and has been shown to provide at least a 75% reduction in pain<sup>[1]</sup>. RFA uses continuous thermal energy to heat the tissue above 45-50 °C resulting in damage to the nervous tissue stopping conduction of the pain signals<sup>[5]</sup>. Limitations with these therapies include nerve regeneration and relief lasting at times less than 6 months before requiring repetitive intervention. Complications are minimal and include risk for bleeding, risk for infection, and paresthesia.

Spinal cord stimulation therapy is another lasting option. This procedure entails the utilization of electrical stimulation using gate control theory to disrupt nerve impulses through the spinal cord<sup>[6]</sup>. Stimulator leads are placed in the epidural space and can be controlled by the patient directly allowing for long term relief. Spinal cord stimulation is shown to be effective in neuropathic pain syndromes including Chronic Regional Pain Syndrome CRPS. With CRPS success with spinal cord stimulation can be 83%<sup>[6]</sup>. Potential complications include risk for hematoma, infection, spinal cord injury, and paralysis<sup>[6]</sup>.

## OBJECTIVE

Utilize ultrasound assistance to implant a peripheral nerve stimulator for a patient experiencing CRPS from post hernia repair for the ilioinguinal and genitofemoral nerve.

A forty-seven-year-old male presented to the clinic suffering from intractable pain of the right groin, radiating to the penis and scrotum for nearly two years. The patient had developed Complex Regional Pain Syndrome of this region after a work-related injury and subsequent hemiorrhaphy. He failed gabapentin 600mg TID, pregabalin 75mg TID, Spinal Cord Stimulator Trial, lidocaine ointment, and oxycodone 7.5mg QID. His urologist suggested a possible orchiectomy and no other urological treatment helped. The patient deferred that option. Diagnostic genitofemoral and ilioinguinal nerve injections using ultrasound and xray were performed in which the patient obtained more than 100% relief. The decision to attempt peripheral nerve stimulation was made jointly with the patient.

## RESULTS

The patient had obtained more than 85% reduction in pain, discontinued all opioids and neuropathic medications. The patient has had this device implanted in him for nearly two years without any complications.



Peripheral nerve stimulation appears to allow for long term therapy and improvement without some of the limitations and risks inherent to other traditional interventions for CRPS related to chronic ilioinguinal and genitofemoral pain. Using PNS, similar to RFA, we are able to target the peripheral nerves directly involved causing the intractable pain of the right groin, radiating to the penis and scrotum. The mechanism of action in some recent papers suggest could be beyond the gate control theory, and actually could be due to Peripherally induced Reconditioning of the CNS, involving stimulation-evoked reversal of the central sensitized state that contributes to chronic pain (7). It is theorized A-alpha and Beta fibers could be activated to help with analgesia from the periphery to the dorsal horn and cortex. PNS use continues to expand to offer alternative interventional treatment options while minimizing risks and limitations of other procedures. PNS seems to be an excellent choice for patients with post ilioinguinal hernia repair pain referable to the groin and testicles.

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# Ketamine-Associated Hemorrhagic Cystitis – A Potentially Severe and Permanent Adverse Effect

Melissa E. Huang, B.S. and Jeffrey A. Wong, M.D. University of California, Irvine

## Background

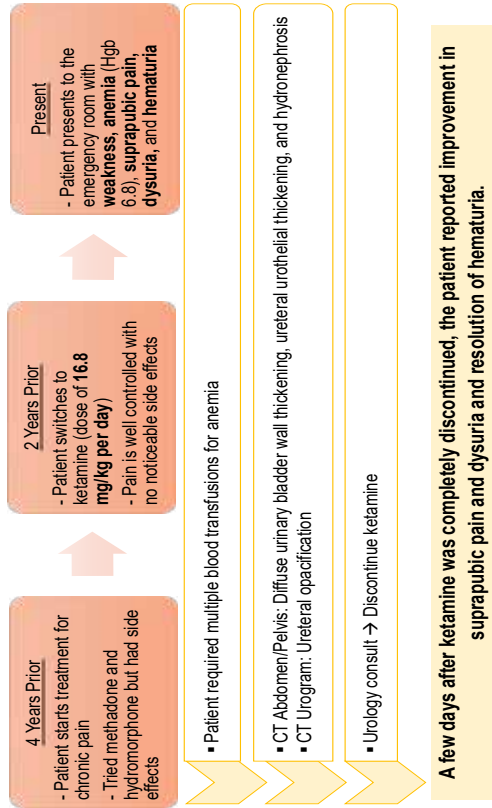
- Ketamine is a phenylcyclohexane derivative and N-methyl-D-aspartic acid (NMDA) receptor antagonist which has seen renewed interest as an anesthetic in perioperative, acute, and chronic pain. It has gained additional use as an opioid alternative and sparing analgesic, and even was recently FDA approved for treatment-resistant depression.
- Ketamine's common adverse effects are often thought of as infrequent, dose dependent, and transient. These include psychomimetic effects, such as hallucinations, euphoria, agitation, anxiety, and nausea. In street drug ketamine users, it has been found that ketamine can cause serious damage to the urinary tract, causing a condition known as "ketamine cystitis."

### Ketamine Cystitis, or "K-Bladder"

- Estimated to develop in ~20-30% of street ketamine users. First reports were published in 2007. To date, there is one report of ketamine cystitis in a pediatric patient using oral ketamine for neuropathic pain at a dose of 6 mg/kg per day for nine days. Her symptoms resolved after lowering the dose to 3 mg/kg per day.
- Symptoms include urinary frequency, urinary urgency, bladder pain, and hematuria. In some cases, these symptoms may persist even after discontinuation of ketamine.
- In severe cases, ketamine toxicity may lead to irreversible bladder damage, including decreased bladder capacity and compliance. The upper urinary tract may also be involved.

## Case Presentation

**Case Description:** 66-year-old female with chronic abdominal pain on ketamine PCA for 2 years develops anemia, dysuria, and suprapubic pain consistent with hemorrhagic cystitis



## Discussion

- Despite its allure as an emerging non-opioid analgesic and a well-tolerated medication, ketamine may cause permanent ketamine-associated cystitis in those taking it for medical therapy.
- First, ketamine is associated with hemorrhagic cystitis and may even be life-threatening, which was seen in this case as the patient required multiple blood transfusions.
- Second, the damage caused to the urinary tract from ketamine is potentially irreversible and may require surgical intervention.
- As more patients are prescribed ketamine for medical purposes, both physicians and patients should consider discussing the potential risks and harms that ketamine may cause and encourage careful monitoring of those taking ketamine in higher doses or for an extended duration.

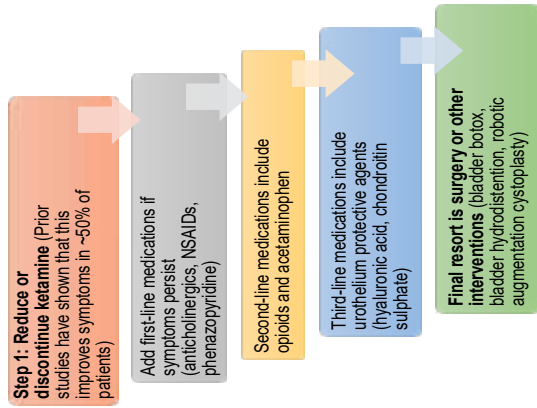
## Diagnostic Approach

The workup of ketamine cystitis serves to exclude other pathology and assess the extent of damage to the urinary tract.

- Laboratory Tests/Imaging:**
- Complete blood count
  - Renal panel
  - Liver function tests
  - Bladder/kidney ultrasound
  - CT urography or CT abdomen/pelvis
- To evaluate and track symptoms:**
- Pelvic pain, urgency, and frequency questionnaire (PUF)
  - Voiding diary
- Findings Indicative of Ketamine Cystitis:**
- Voided volumes < 200 mL
  - Bladder capacity < 150 mL
  - Increased bladder wall thickening
  - Hydronephrosis, ureteral wall thickening (if upper tract involvement)
  - Bladder tenderness and bleeding

A urology consult should be offered, and cystoscopy may be performed to exclude other causes.

## Treatment Algorithm



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UC Irvine Health

# Manifestation of Occult Intrathecal Granuloma at High Altitudes During Commercial Flights

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## ABSTRACT

**INTRODUCTION:** Catheter-tip granulomas are a complication of continuous intrathecal infusion with  $\mu$ -opioid agonists. These granulomas may cause intense pain symptoms. We review a case where a patient receiving intrathecal narcotic infusion had unusual symptoms during flights only. We discuss the likely mechanisms which may have precipitated the patient's symptoms. **MATERIALS AND METHODS:** A 50-year-old female with a remote history of multiple central and lumbar laminectomies, fibromyalgia, arachnoiditis, and an occipital neuralgia. She had a long history of chronic pain and was treated with intrathecal morphine, hydromorphone, and allopurinol in the lower extremities at high altitudes during commercial flights. However, the patient's pain always resolved upon landing. **RESULTS:** Thoracic spine MRI and CT myelogram revealed an ovoid mass in the spinal cord (T12-L1) close to the catheter tip. An exploratory laminectomy was performed and the presence of a catheter-tip granuloma was confirmed, but not removed as the mass was attached to critical spinal cord tissue. However, a portion of the catheter was separated from the granuloma and repositioned distally. Multiple follow-up MRI imaging studies have displayed the persistence of the catheter-tip granuloma, but the patient has not had a relapse of symptoms during flights. **CONCLUSION:** Patients with active intrathecal opioid infusion therapy who demonstrate intense pain exclusively during flights should be evaluated with suspicion for catheter-tip granulomas. Surgical removal of the intrathecal catheter-tip granuloma without granuloma removal may yield effective results. We postulate that the patient's symptoms occurred from aggravation of the nerve entangled granuloma by the catheter tip due to changes in cerebrospinal fluid (CSF) flow at higher altitudes. Given the patient's medical history, it is possible that pre-existing changes to cerebrospinal fluid (CSF) flow could have contributed to intracranial pressure changes, although no evidence of other potential causes was found on imaging and during the exploratory laminectomy.

## BACKGROUND

Intrathecal (IT) drug infusion therapy is an implantable method of targeted drug delivery that was originally designed to provide pain relief for cancer patients that has expanded to be implemented as an intervention for patients with chronic, debilitating non-malignant pain conditions. The intrathecal drug administration system can provide significant pain relief for patients with chronic pain. Despite the obvious improvement in pain control that can be achieved through intrathecal drug delivery, intrathecal pain pumps carry the risk of complications such as catheter-tip granulomas.

## Catheter Tip-Granulomas

Catheter-tip granulomas are a rare complication that form in less than 3% of patients who undergo chronic intrathecal infusion therapy for pain control. Granulomas are globular collections of fibroblasts, macrophages, plasma cells, eosinophils, and lymphocytes whose formation is incited by an infectious or non-infectious agent. Granulomas are known to create a more permanent, stable structure through fibrotic encapsulation. Catheter-tip granulomas are a type of catheter-tip granuloma that has been reported to be associated with specific pain medications, such as  $\mu$ -opioid agonists, in a dose-dependent fashion.

## Uniqueness of Case:

We investigate an atypical case in which a patient reported increased pain from an intrathecal catheter-tip granuloma only at high altitudes during flights. This presentation of symptoms occurring exclusively in the context of a high-altitude setting has not yet been reported in the literature.

## CASE PRESENTATION

### History of Present Illness

A 50-year-old female presented with unusual and severe pain symptoms, particularly during air travel. The patient's symptoms of heightened pain began in 2006 and occurred only at high altitudes during commercial flights. She flew three times during September and October 2006 and while in flight, she experienced muscle spasms in the bilateral lower extremities, worse on the right anterior thigh, as well as severe pain in the right sacral area. The patient reported "electrical shocking-like" sensations, as well as extreme pressure, burning, and allodynia in this distribution. However, the patient's symptoms quickly resolved every time after the plane landed. She reported that she was able to ambulate and even assist her friend in moving luggage despite these episodes.

### Past Medical History:

The patient has had multiple spinal surgeries including a lumbar laminectomy in 1979, cervical laminectomy to treat spondylosis centered at C3-4, and a laminectomy in 1988 status post motor vehicle accident, and surgery to treat fibromyalgia syndrome in 1981. Subsequently, she underwent fusion surgery in 1983 and received posterior fixation rods and vertebral body screws at L4, L5, and S1. The patient continued to have severe low back pain and was subsequently diagnosed with fibromyalgia, neurogenic bladder, and arachnoiditis. Eventually, the patient had an intrathecal drug infusion system implanted in 1985. The patient was on a stable regimen of hydromorphone 20 mg/ml (6.1 mg per day) and 40 mg/ml bupivacaine for several years.

## DISCUSSION

### Risk Factors for Intrathecal Catheter-Tip Granuloma Development

- More predisposed to developing a granuloma due to dosage of narcotic infusion and the location of the intrathecal catheter tip.
  - Intrathecal concentration of 20.0 mg/mL hydromorphone at a dose of 6.1 mg/day for several years.
  - In the 2012 Polypharmacologic Consensus Conference, the panel reported that concentration and dose of intrathecal hydromorphone should not exceed 10 mg/ml and 4 mg/day respectively.
  - Catheter tip was next to the conus medullaris – the most common location for intrathecal granulomas.
  - The history of arachnoiditis as well as multiple spinal surgeries are other potential risk factors.
- Reasons Why Intrathecal Catheter-Tip Granulomas Cause Pain**
- Since the repositioning of the intrathecal catheter during the T12 laminectomy, the patient has not reported any new episode of unusual symptoms, which raises further suspicion of the catheter-related granuloma being the causative agent of the intense pain which patient had for during flights.
  - Sensory abnormalities and increased pain are common presentations of a granuloma that can occur if it affects any part of the central spinal neurons.

### Barometric Pressure Changes as the Trigger for Pain Symptoms

- Changes in barometric pressure as well as the specific location of the granuloma in relation to the adjacent, vulnerable nerve roots may have contributed to the patient's sensory abnormalities.
- However, in the cabin of an airplane during typical commercial flights at cruising altitudes (30,000-40,000 feet), the barometric pressure becomes approximately 610 mmHg. When there is a decrease in barometric pressure, there is an increase in intracranial and lumbar CSF pressure.
- When there is an increase in intracranial pressure, the conus medullaris and the granuloma potentially move with spinal alignment in caudad direction with cerebrospinal fluid flow, thus impinging on various nerves.
- If the conus medullaris moves downward while the granuloma is fixed, the patient may feel increased pain due to nerve irritation.
- Anachonditis likely did not cause episodic pain symptoms because adhesion of the catheter or catheter tip to the aneuridial dura mater was not found on imaging.

## CONCLUSIONS

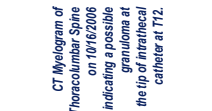
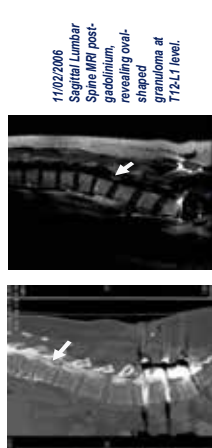
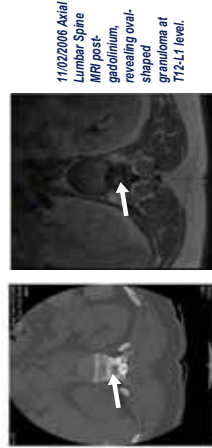
- The main significance is that the patient's symptoms of increased pain appeared only during flights.
- It is important to identify symptomatic cases of intrathecal catheter-tip granulomas early, especially in those with a history of arachnoiditis, extensive spinal surgeries, and chronic pain syndromes.
- MRI and CT myelography may both assist in diagnosis, although exploratory laminectomy may need to be pursued if imaging does not provide a definitive diagnosis.
- Mispositioning of the catheter-tip in relation to the granuloma may precipitate an abnormal continuation of neurological symptoms that patients can experience in response to changes in barometric pressure. The patient's unique presentation of symptoms during flights is a reminder that does not predispose patient to further risk of neurological compromise may be warranted.
- Intrathecal catheter-tip granulomas can be resolved through discontinuing of intrathecal drug infusions into the mass, surgical removal of the granuloma, or replacement/revision of the catheter tip.
- Patient can be symptom-free for many years even with the persistence of an intrathecal granuloma as long as aggravation of the granuloma is clinically managed.

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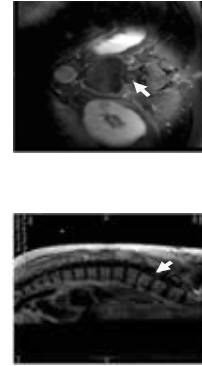


## DIAGNOSTIC IMAGING



## THERAPEUTIC INTERVENTION

- The intrathecal infusion of hydromorphone was stopped and temporarily replaced with saline infusions.
- In November 2006, the patient had an exploratory T12 laminectomy.
- The lesion visualized the granuloma, which was enlarged by the cauda equina and the lateral aspect of the spinal cord.
- The catheter tip was removed from the granuloma and the remaining portion of the catheter was placed 5 cm below the granuloma.
- A culture that was separated from the resected catheter tip did not reveal bacterial growth.
- The pump was continuously infused with saline until January 2007, when the pump was replaced due to end-of-life of battery.
- Hydromorphone infusion was re-started at a concentration of 5.0 mg/mL and a dose of 0.983 mg/day.
- Serial magnetic resonance imaging has been performed every six months since the intrathecal granuloma was detected, indicating no significant change in the appearance of the granuloma at T12 level.
- Despite the persistence of the granuloma seen on imaging for several years after resolution of symptoms, the patient has not experienced a recurrence of such symptoms on subsequent flights.
- Patient continues to have her pain well-controlled through intrathecal delivery of opiates.



MRI Axial Lumbar Spine MRI on 7/20/2015, indicating no significant change in appearance of granuloma from previous MRI images.

**Novel interventional techniques for chronic pain: spinal stenosis, and degenerative disc disease: MILD percutaneous image guided lumbar decompression, Vertiflex interspinous spacer, MinuteMan G3, and Interspinous-interlaminar fusion**

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**Background:** Spinal stenosis (SS) is the compression of nerve roots by bone or soft tissue secondary to the narrowing of the spinal canal, lateral recesses, or intervertebral foramina. SS may have acquired or congenital origins. Most cases of SS are acquired and caused by hypertrophy of the ligamentum flavum (LF), enlarged osteophytes, degenerative arthritis, disk herniations, and various systemic illnesses (i.e., endocrinopathies, metabolism disorders, inflammatory diseases). Although it is not common, some people are genetically prone to developing congenital spinal stenosis. SS usually affects both men and women equally around the age of 50. SS can manifest as sharp, aching, and/or tingling sensations in the back, buttocks, or thigh. In severe cases, it can also present as numbness, bladder or bowel incontinence, and difficulty ambulating. SS is most commonly observed in the lumbar spine and is rarely found in the cervical and thoracic spine. Epidemiological data suggest that the incidence of lumbar spine stenosis is 5 cases per 100,000 people. Hypertrophy of the LF in the lumbar spine is the most significant cause of lumbar spinal stenosis; the suppression of the cauda equina by the LF is what evokes the symptoms. The LF is a highly specialized elastic ligament that connects the laminae of the spine and fuses it to the facet joint capsules. LF assists with the realignment of the spinal joint after bending and flexion. Mechanical stress, increasing age, diabetes mellitus, obesity, and change of milieu in disk herniation all lead to a mechanism that results in LF hypertrophy and fibrosis. There are a number of cytokines and growth factors that are secreted by LF cells that play different roles in activating the fibrotic and subsequent hypertrophic response. Transforming growth factor-beta (TGF-β) is markedly upregulated in the macrophages, endothelial cells, and fibroblasts associated with the LF and is hypothesized to be one of the main culprits contributing to LF hypertrophy. Before a clinician orders diagnostic imaging to confirm the diagnosis of SS, pertinent physical exam findings such as moderately reduced lumbosacral range of motion, bilateral extremity weakness, diminished deep tendon reflexes, and positive stoop and straight leg raise tests typically arise suspicion of the condition. The gold standard in diagnosing lumbar spinal stenosis is lumbosacral magnetic resonance imaging (MRI) with or without contrast; the MRI can reveal enhanced sensitivity of nerve roots and the intricate detail of soft tissues- including the subarachnoid space, epidural fat, ligaments, intervertebral disks, and the spinal cord. There are a number of treatment options available for spinal stenosis. The older treatments include physical therapy with flexion band exercises, nonsteroidal anti-inflammatory drugs, opioids, neuropathic pain medications, and epidural corticosteroid injections. There have been implants and surgical interventions that have emerged in popularity recently and have been shown to be more efficacious: the minimally invasive lumbar decompression (MILD®), Vertiflex®, MinuteMan® procedures. Conservative treatments are recommended before resorting to surgical interventions. Surgery is only indicated for patients who have failed conservative treatments or have shown evidence of severe pain or neurological deficits.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications and current data involving novel interventional techniques for chronic pain associated with spinal stenosis and degenerative disc disease. **Results:** MILD® has shown to be efficacious and safe. One randomized study looked at the 2-year safety and efficacy profile of 145 patients who had undergone the MILD® procedure. No major adverse events were noted. It was concluded that MILD® was superior in efficacy versus epidural steroid injection (ESI) at one year. At the 2-year mark, efficacy was statistically significant with improvements in pain, claudication, and disability index scores. In another retrospective review of 42 patients who underwent the MILD® procedure, patients reported decreased pain scores with improved ability to ambulate. 86% of participants would recommend this to others. In another study involving 17 patients undergoing the MILD procedure, patients reported improved pain and ambulation at 1 year postoperatively. These authors advocated for MILD® to be used as a bridge in therapy between ESI and more advanced surgical procedures. In a double-blind, randomized, prospective study of 38 patients comparing the MILD procedure (n=21) versus ESI (n=17), it was concluded that the MILD procedure was superior to ESI in efficacy with no difference in safety as neither group experienced adverse outcomes. Efficacy was based on reduced pain and improved mobility over 12 weeks. These patients showed greater improvement in VAS and ODI compared to ESI. Superior® has shown to be efficacious in decreasing pain and opioid use. In one study involving 53 patients undergoing the Superior® interspinous spacer, there was significant improvement 2 years postoperatively for axial and extremity pain severity, ZCQ, ODI, PCS, and MCS scores. In another study, 88 patients had received Superior® and were followed over five years. The devices showed clinical efficacy at the five-year mark in 88% of patients. Efficacy was determined by improvement in pain, claudication, and disability. Efficacy improved the greatest within the first year. After the first year, the efficacy of the procedure continued to improve as time elapsed, but the change was not drastic as the first year. Another study observed opioid use over the course of 5 years in 190 patients receiving the Superior® interspinous spacer. Results had shown a decreased prevalence of opioid use in the Superior group over 5 yrs. This was drastically decreased in post-op year 1. By post-op year 5, the prevalence had decreased 85% from baseline. In a study comparing patients receiving surgical decompression and Collex (n=215) versus decompression and pedicle screw (n=107), the results showed that 50.3% versus 44% met success criteria, respectively. Success criteria included: 1) >15-point improvement in ODI score; 2) no reoperation, revision, removal, or supplemental fixation; 3) no major device-related complication; and 4) no epidural steroid injection after surgery. In 2018 study, 230 patients (1:1 ratio) were randomized to either decompression alone (DA) or decompression (D) and interlaminar stabilization (ILS). The results had shown that the composite clinical success was superior for the D+ILS arm. There were higher rates of narcotic use at every time points post surgically for DA patients (16.7% for D+ILS vs 23% for DA at 24 months). The risk of secondary intervention was 1.75 times higher among patients in the DA group than among those in the D+ILS group. The DA arm had 228% more lumbar injections versus D+ILS. Currently, there is an ongoing multicenter randomized controlled trial involving the MinuteMan G3® procedure. The initial unpublished results demonstrated equal effectiveness between MinuteMan G3® and open direct decompression in improving overall lumbar spine stenosis symptoms with superiority of the MinuteMan G3 procedure in reducing leg pain. A biomechanical study demonstrated its stability when compared to other devices.

**Conclusion:** SS is related to the narrowing of the spinal canal which can result in the compression of nerve roots. The most common cause is acquired and is the result of a hypertrophied LF. Past treatments involved physical therapy, medications, and steroid injections. New procedures are recently come to light that have shown promise in the treatment of SS that is not complete surgery. The MILD procedure has shown the most promise with regards to lasting pain relief with no documented major adverse events. Superior® has also shown promise in a 5-year study with regards to pain relief. Important to note about this study is that Superior® also helped decrease the use of opioid medications in patients that underwent the procedure. This is a major step forward in reducing the use of opioid medications and the possible adverse effects of the drug such as addiction, tolerance, withdrawal, and overdose. The interlaminar stabilization Collex® has been shown to be safe and efficacious. It owns the advantage of preserving the posterior lumbar motion. However, it does require a surgical decompression before implanting the device and therefore is not a minimally invasive as the other procedures. The MinuteMan G3® is a promising procedure. A biomechanical study demonstrated its stability when compared to other devices. However, more clinical studies are needed to confirm its safety and efficacy. More studies should be done to further look at the safety and efficacy of these novel procedures. The results so far are very encouraging in terms of pain relief. There is hope in the future that treatment algorithms can be modified to include these procedures to allow for better pain relief and less adverse events that can be seen with medication use and/or more invasive surgical procedures.



## Novel Interventional Techniques for Chronic Pain with Minimally Invasive Arthrodesis of the Sacroiliac Joint: (INSITE, iFuse, Tricor, Rialto, and others)

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**Background:** Acute and chronic pain is a public health issues that clinicians have been battling for years. Opioid medications have been the mainstay of treatment for both acute and chronic pain. Deaths from prescribed opioids have more than quadrupled in the USA since 1999, and the same pattern is now occurring all over the world. Chronic pain, which occurs in about 10% of those who have surgery, typically begins as acute pain that is difficult to control but that can persist into a pain condition with neuropathic features unresponsive to opioids. This is where the treatment of pain needs closer attention to what is considered “difficult to control” in terms of pain to stop the progression to chronic pain. It has been proposed that a closer look at genetics and neurophysiological characteristics of patients might favor certain medications. As well, anatomic and metabolizing patterns of individual patients should be taken into consideration. Sacroiliac joint (SI) pain is a common cause of both acute and chronic low back pain. It affects about 15% to 25% of patients with axial low back pain. In the past, a common method to diagnose SI pain was the use of a small dose of local anesthetic. SI joint pain must be distinguished from pain emanating from the lumbar spine, the SI joint itself, and the hip joint. Cluneal nerve pathology as well as soft tissue pathology should also be considered in the differential. Since pain in this region can stem from multiple causes, it is important for clinicians to take a thorough history to try to identify the source of the pain in the SI region and closely evaluate physical examination findings. Recent advances in the treatment of SI joint pain have led to the creation of SI joint fusion devices. These fusion 4 devices seek to stabilize the joints themselves so that they are immobile and, in theory, can no longer be a source of pain. This is a minimally invasive procedure aimed to address the chronic pain endured by patients without subjecting them to lengthy surgery or medications with the potential for addiction and abuse, such as opioids.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving studies on interventional techniques for chronic pain with minimally invasive arthrodesis of the sacroiliac joint

**Results:** The lateral approach for MIS fusion includes SI fusion devices such as iFUSE and TriCor™. A prospective, multicenter, open-label randomized controlled trial that enrolled patients with unilateral or bilateral sacroiliac joint (SIJ) dysfunction related to degenerative sacroiliac and/or sacroiliac joint disruption was conducted at 19 institutions in the United States. The trial compared surgical (iFuse) versus non-surgical management (NSM) of SIJ dysfunction. At six months, 83 of 102 participants in the SIJ fusion cohort met the primary endpoint which was a binary success/failure composite endpoint. The intent to treat in success rate was 54.5%. VAS pain improvement for surgical management was 81.6% versus 12.5% for NSM, ODI scores improved by 72.4% for surgical management vs. 10% for NSM. Patients were allowed to crossover from NSM to surgical management after the 6-month mark. Patients who crossed over had similar improvements in pain (mean decrease of 42.5 points,  $P < 0.001$ ) and ODI (mean decrease of 26.3 points,  $P < 0.001$ ) at the six-month follow-up. The posterior approach for MIS fusion included the CornerLoc™, Rialto™, and PainTeq LinQ™ devices. Prior to February 2021, published literature that evaluated or utilized CornerLoc was not identified. However, a randomized, multicenter, open-label study is currently in the recruitment phase. Currently, CornerLoc is sponsoring the study to compare its device to intra-articular sacroiliac joint steroid injections. A retrospective chart review including 14 patients was performed to assess the Rialto system on its effect on low back pain and narcotic medication changes. Patients receiving the Rialto system reported lower VAS scores and a lower morphine milligram equivalent (MME). In a 24 patient retrospective chart review measuring outcomes with intraoperative stereotactic navigation, the treatment group (Rialto) reported a significant reduction in lower back pain and leg pain. 5. A retrospective case series of sixteen patients who received the LinQ SI reported improved pain and decrease in opioid consumption. A multicenter prospective study of the LinQ system is currently enrolling patients. A retrospective review of patients was performed to compare the clinical outcomes of SI joint fusion between cylindrical threaded implants (CTI) (Rialto, Medtronic) and triangular titanium implants (TTI) (iFUSE, SIBone). It was concluded that there was a significant improvement in pain and disability, but there was no significant difference between the two systems. In a RCT, triangular titanium implant group reported a significant decrease of the referred leg pain component of SI joint pain. Furthermore, another RCT showed that the triangular titanium implant group reported a lower VAS as 6 months and improvement in ODI at 24 months. Adverse events were low in the surgical group, with only three patients undergoing revision surgery within the 24 months follow-up period. A 2-year multicenter prospective study looked at the results of surgical management two years after receiving triangular titanium implants. One hundred seventy-two subjects at 26 US sites were enrolled and underwent minimally invasive SI joint fusion with the triangular titanium implants. Implant group reported a decrease in VAS and ODI which remained low at 24 months. Quality of life scores measured by EuroQOL-5D improved at 12 and 24 months. The percentage of patients that were taking opioids in the study decreased from 76.2% to 55.0% at 24 months. 8 patients had undergone one or more revision surgeries. CT scans at one year showed a high rate of bone adherence to at least 2 implants (97%).

**Results:** The sacroiliac joint is a common cause of both acute and chronic low back pain. It affects about 15% to 25% of patients with axial low back pain, and up to 40% of patients with ongoing pain following lumbar fusion. In the past, SI joint pain was treated with injections of local anesthetics and corticosteroids, physical therapy, and opioid medications. Minimal invasive procedures have been developed to address chronic pain without subjecting patients to lengthy surgeries or long-term use of medications. SI fusion devices were developed to stabilize the SI joint to minimize pain and improve function and quality of life for patients with SI joint pathology. A wide variety of devices have been developed and marketed. Posterior minimally invasive SIJ fusion relies on distraction as a strategy to achieve fusion, tightening and tensioning lax ligaments to stabilize the joint. The lateral approach to minimally invasive SIJ fusion transfuses the joint to provide stability with well-studied biomechanics. Although there is a more robust data set supporting the use of lateral transfuse minimally invasive SIJ fusion, the posterior approach has many potential advantages, and the number of supportive studies is growing. More data needs to be obtained in terms of which fusion system may be better than another when compared head-to-head. In theory, a posterior approach appears to be less invasive, and more readily adopted by spine interventionalists. No studies to the writers' knowledge have been done to look at the difference between the two approaches. SI fusion devices do pose a promising way of treating chronic lower back pain.

## Novel Local Anesthetics in Clinical Practice; Pharmacologic Considerations and Potential Roles for the Future

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### Background:

The treatment of pain, both acute and chronic, has been a focus of medicine for generations. Opiate medications have been the mainstay of pain management, but for the past 30 years, their use and abuse have risen dramatically. Scientists and clinicians have attempted to develop novel ways to battle pain in surgical and post-surgical settings. Chronic pain can result from surgery in about 10% of patients. At present, it is believed that pain can transition from acute post-surgical to chronic if not well controlled after surgery. Research into this transition has led to new pharmacological interventions to try to better control pain after surgery. One intervention used to control pain after surgery is regional nerve blocks. This is the delivery of local anesthetic into the area of interest to block the transition of pain signals by nerves. Sasso et al. looked to see if a regional block could help treat chronic post-surgical pain. They looked at pain at the iliac crest bone graft donor site after anterior lumbar interbody fusion. They found that persistent pain was usually found in about 15-39% of patients undergoing this type of procedure for at least two years. Their prospective study looked at 202 patients, and 43% had persistent pain that only occurred after their surgery at six months, and 33% at one year. Black et al. looked at the use of a transversalis fascia plane (TFP) block to help decrease the development of this chronic pain at the donor site. They found that persistent pain at the donor site was reported in only 4.3% of all patients at six months and 6.5% at 12 months. This raises the question of whether a peripheral nerve block (PNB) can help with acute and chronic pain management. The results of the above studies show that it can be useful, but how long should the block last? In this regard, there are single injection PNBs and continuous PNBs. Continuous PNBs involve the insertion of a catheter to deliver the anesthetic to its intended target. This can be associated with a longer time to discharge, so single injection PNBs are generally preferred. The challenge of single injection PNBs is their length of duration, which is their major limitation. Most have a duration of only 24-48 hours. <sup>4</sup> Researchers have worked to find ways to prolong the length of duration of single-shot PNBs. This has led to looking at adjuvants that could be added to the local anesthetic to increase the length of their block provided. Adjuvants (e.g. dexmedetomidine, clonidine, dexmethasone, ketamine, etc.) are useful at decreasing postoperative pain, rescue opioid requirements, hospital length of stay, and overall health care cost. Many adjuvants are still not FDA approved for use, and more research is needed to determine their safety. Novel preparations of local anesthetics have also been studied. These new preparations allow for the extended duration of action of local anesthetics. One example is the preparation of bupivacaine with a liposomal bilayer, which allows for sustained release of local anesthetic for at least 72 hours after the injection, and this has the potential for decreasing opioid consumption in the postoperative period.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving novel local anesthetics

### Results:

Adequate control of pain in the postoperative period is important for many reasons. One is that adequate control can protect the patient from the development of chronic pain as a result of the surgery. It can also decrease hospital stays, health care costs, and even patient satisfaction scores. The use of single-injection peripheral nerve blocks has been of interest in research. Ways to increase the duration of the block have been important since most blocks do not last a long time. We examined novel formulations of local anesthetics and included Exparel, HTX-011, tetrodotoxin, neosaxitoxin, SABER-bupivacaine and INL-001. In clinical studies, Exparel was not found to improve pain measurements, opioid consumption, PT sessions needed, or time to mobilization. It did, however, do better than its standard formulation in terms of injection site pain. This may be because it is better in terms of pain control when used as a local infiltrate and not as an actual block. The reason that this is the case is unknown. HTX-011 improves pain scores and opioid consumption in groups that received saline or bupivacaine. In one study, 90% of patients that received HTX-011 did not use opioids in the first 72 hours of surgery, which is thought to be when the pain is the most severe. Tetrodotoxin has shown some promise in animal studies as it has been shown to prolong nerve blocks when used with bupivacaine. Neosaxitoxin has shown the same prolonging effects when used with bupivacaine. There was only one published study for SABER-Bupivacaine and even though it has shown good efficacy, it has failed to demonstrate a complete evidence of clinical safety. Bupivacaine collagen matrix INL-001, two independent phase 3 studies have demonstrated statistical and clinical significance in pain intensity reduction in addition to lowering opioids requirement. A third study has shown good tolerability in patients with no major adverse events.

### Conclusion:

These novel formulations show great promise in terms of the ability to prolong the duration of single injection PNBs. This field is still currently in development, and more clinical studies will need to be done to ensure the safety and efficacy of these novel formulations. These formulations could be the future of pain management if more research continues to prove their positive effects and low side effect profiles.

# Novel Use of Candle Gel as Transparent Ultrasound Phantom

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## Background

- Phantom provides an inexpensive method to learn the skills of image-guided needle placement.
- Common materials used to create ultrasound phantoms are blue phantom, water, agar or gelatin-based material, and meat (1,2).
- We propose a new material for phantom, which can be used to teach ultrasound interventions.

## Methods:

- Penreco Versagel® C is a formulation of mineral oils and other hydrocarbons.
- We used the ultrasound to evaluate the feasibility of gel wax as a training phantom.

Figure 1: Photograph of phantom



## Results:

- Gel wax can be poured in layers which combined with its ability to suspend objects of varying density, make it an ideal medium to create complex anatomical models.
- After melting and remolding several times, gel retained its clarity.
- Beginners found that it is easier to learn ultrasound-guided needle handling because of its low intrinsic echogenicity.
- Its transparency makes it an excellent tool for teaching landmark-based, ultrasound-guided blocks side-by-side.
- It can be made more echogenic by changing pouring speed and temperature, which traps small air bubbles.
- Moreover, its microbial resistance makes it a durable material, a property that is lacking in many phantom materials.

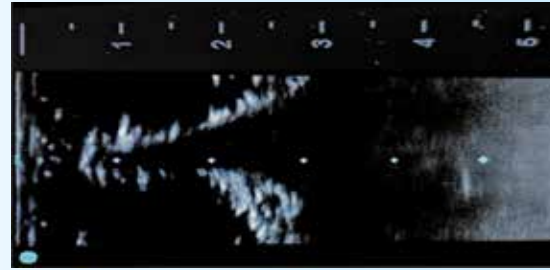
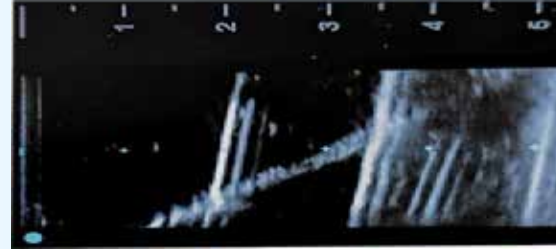
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## Conclusion:

- Candle gel wax is a popular medium for making transparent candles and for embedding items.
- It is also an excellent material for use as both ultrasound and fluoroscopic phantom.
- It is also a cheap material which can be molded using household items.

Figure 2: Ultrasound appearance of phantom and needle placement





## Occipital Nerve Stimulation for the Treatment of Chronic Migraine

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**Background:** Currently, migraine headaches have no cure, and the most common treatments are pharmacologic agents. The goal of acute management is to stop active headache pain, while drugs used for prevention are reserved for those with increased frequency of migraine pain greater than twice a week. Effective drugs to stop active headaches are non-steroidal anti-inflammatory drugs (NSAIDs), triptans, and ergots, and commonly prescribed preventive treatments include beta-blockers (e.g., propranolol), calcium channel blockers (e.g., verapamil or diltiazem), or anticonvulsants (e.g., valproic acid, topiramate). Botox injections, nerve blocks, and surgical decompression have also been attempted with varied success rates among individuals with drug-refractory migraine. The available treatment arsenal does come with medication-related side effects and the possibility of decreased responsiveness and/or lower rates of adherence in some patients. One study revealed that 70.2% of migraine patients treated with medication will be non-adherent to medical therapies within 6 months (25). The need for effective, safe, and long-lasting anti-migraine treatments opened the field to non-pharmacologic neurostimulation. Occipital nerve stimulation (ONS) offers a non-pharmacological alternative treatment for migraine. ONS first found success in the treatment of occipital neuralgia, but is now targeting primary headache disorders like migraine. The mechanism of action of ONS is still under investigation; however, literature suggests that electrical stimulation of C1-C3 nerves, particularly the greater and lesser occipital nerves, reduces the activity of nociceptive fibers in the trigeminocervical complex resulting in pain relief, according to the "gate control" theory. Gate control theory describes the mechanism by which painful sensation can be blunted or reduced by activating a nonpainful sensation. The spinal cord contains the neurological "gate" that allows or blocks the passage of pain signals to the brain. The gate is opened by the activity of pain signals traveling up small nerve fibers and closed by nonpainful stimulation in larger fibers, preventing pain sensations from traveling to the CNS.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving multicenter randomized single-blinded studies, double blinded studies, open-label randomized crossover studies, and open label uncontrolled studies. These studies involved the efficacy and safety of occipital nerve stimulation. Existing data from clinical trials support the overall safety and efficacy of occipital nerve stimulation for the treatment of chronic migraine.

### Results:

Existing data from clinical studies supports the overall safety and efficacy of occipital nerve stimulation for the treatment of chronic migraine, although there are few large controlled, double-blinded studies. Trenman TL et al. assessed the efficacy and safety of ONS through an Open-label, uncontrolled study. Nine participants with medically refractory headache disorders received stimulator implants. At one year, 7 of the 8 patients acquired fair or better results in the reduction of disability with 5 patients rating greater than 90% reduction. There was a mean decrease in the number of headache days at 28.5 (SD = 29.6). Headache severity score on average decreased by 0.88 (SD = 1.36). No major adverse events were reported. ONS showed a clinically significant reduction in headache frequency and severity, although lack of control group precludes conclusions on statistical significance. Low rate of adverse events suggests possible improvements in safety. Lipton R conducted a phase II, randomized, double-blind. Participants (n = 125) were randomly assigned to a treatment group (n = 63) or control group (n = 62). The treatment group received active neurostimulation from the onset of the trial, while the control group received sham stimulation from the onset of the trial to 12 weeks post-activation. The control group received real stimulation following the 12-week follow-up. Treatment group achieved on average a 5.5-day/month (SD = 8.7) reduction in migraine frequency, while the control group achieved a 3.9-day/month (SD = 8.2) reduction. Incidence of adverse events was comparable between treatment and control groups, but merging the control group into the treatment group after 12 weeks limits the data's usefulness. Results from this trial were inconclusive given the merging of treatment and control groups. Additional trials with more statistically sound design are necessary to draw conclusions. Garcia-Ortega R et al. also conducted an Open-label, uncontrolled study. Seventeen participants with chronic migraine (n = 12) or chronic cluster headaches (n = 5) were enrolled. Patients were treated with parathesia-free burst occipital nerve stimulation (BONS). For chronic migraine, patients experienced on average a reduction of 10.2 headache days/month. For chronic cluster headache, cluster attack frequency was reduced by 92%, while intensity was reduced 42%, both representing a significant improvement from baseline. Two patients experienced complications (infection) that required explanation during the course of the study. Finally, Hann S et al. conducted an open-label, uncontrolled study. Fourteen patients with chronic migraine refractory to medical treatment were enrolled. After a 5-day trial, responders received permanent implants. Of the 14 participants, 71% achieved improvement in headache severity and frequency and 50% were able to achieve both normal quality of life and resolution of associated migraine symptoms. Three of 14 participants had previously undergone ONS treatment without success but showed improvement in symptoms when SONS was added. Complications included lead migrations, infections, and discomfort sustained at supraorbital nerve stimulator electrodes. The study gives tentative, preliminary support to the safety and efficacy of dual stimulation. A larger comparative study is necessary to determine if dual stimulation is more effective than ONS alone.

**Conclusion:** Designing randomized, double-blinded trials with sham control for implantable neurostimulators has proven somewhat difficult, for both practical and ethical reasons. Patients with occipital nerve stimulators will almost always feel paresthesia from stimulation, while sham stimulation will not elicit any sensation. Any attempts at masking will soon fail after the onset of treatment. Studies with crossover assignment mitigate this problem by having each subject serve as his or her own control. Further, sham surgeries are considered ethically unacceptable by many, as such a surgery exposes a patient to health risks without any possible benefit. These difficulties in study design may explain why there are currently no FDA-approved implantable occipital nerve stimulators for the treatment of migraine. While ONS is not approved specifically for migraine, neurostimulation is approved by the FDA for the treatment of certain pain syndromes; thus, ONS remains an off-label application of neurostimulation and is still accessible for patients with intractable migraine. Migraine, especially the chronic form, is a debilitating condition that causes profound negative effects on quality of life. Current medications prove effective for some patients but are not always successful and are prone to overuse. Furthermore, patients who overuse acute relief medications have a higher risk of their condition worsening. ONS shows promise and could be recommended as a non-pharmacological alternative treatment for intractable migraine and other chronic headache conditions.

# PAIN, DISABILITY, AND SATISFACTION IN PARESTHESIA REPORTING (PR) AND NON-PARESTHESIA REPORTING (NPR) SUBJECTS USING POSITION-ADAPTIVE STIMULATION AND THE EVOLVE WORKFLOW: A VECTORS STUDY ANALYSIS

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## BACKGROUND

Maintaining optimal spinal cord stimulation (SCS) therapy delivery, in terms of anatomical target and electrical energy delivery, is a key factor in the success of SCS. The position of the spinal cord varies relative to the electrode array with movement or static body position and may cause periodic loss of therapy or uncomfortable sensation that could impact therapy compliance and patient satisfaction. Position-adaptive automatic adjustment of device settings (active electrodes, intensity, frequency, or pulse duration) has been demonstrated to provide more comfortable, convenient, and better pain relief relative to standard, manually-adjusted SCS in a randomized controlled trial as well as in multiple studies of patient-reported outcomes in real-world settings.<sup>1,2,3,4,5</sup> Accelerometer-based closed-loop stimulation has the benefit of being able to maintain consistent stimulation with both paresthesia-based and subperception therapy.

## OBJECTIVES

This analysis characterized pain, disability, and satisfaction in PR and NPR subjects using position-adaptive stimulation in the Vectors study.

## METHODS

The Vectors study was a single-arm, open-label, investigation of the outcomes associated with an algorithmic approach to SCS programming. Subjects were programmed in the clinic to a stimulation setting that felt comfortable to the patient. The subjects could make additional adjustments to stimulation amplitude outside of the clinic as needed. Automatic position-adaptive features were activated in most subjects based on clinical practice decisions. Subjects with AdaptiveStim™ technology ON at the 3- and/or 12-month visits were categorized based on whether they reported experiencing paresthesia since the last visit. ("Since your last visit, have you felt the sensation of paresthesia 'Yes/No'. Visual analogue scale (VAS) scores (overall, back, and leg pain), Oswestry Disability Index (ODI), and subject satisfaction were recorded at baseline, 3-, and 12-month visits. Within-group changes in pain and ODI from baseline to the 3- and 12-month visits were evaluated by whether subjects with AdaptiveStim™ ON reported feeling paresthesia. Post-hoc statistical testing of the within-group changes from baseline were performed using paired t-tests separately within the paresthesia and non-paresthesia reporting groups.

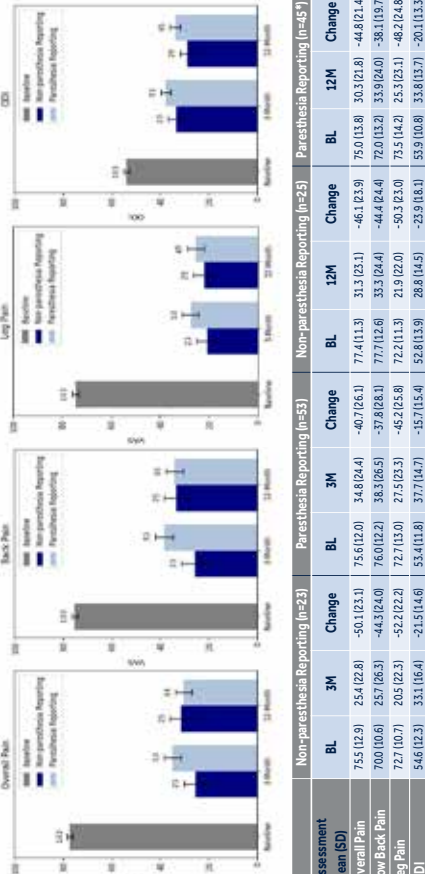
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## RESULTS

The number of subjects for each group are reported above their respective bars in the following graphs.

## VAS/ODI

Changes in pain (VAS) and ODI from baseline to 3-Month and 12-Month are summarized in the table below. A negative change indicates an improvement from Baseline. Subjects with position-adaptive stimulation showed significant reduction in pain and disability, regardless of paresthesia sensation since the last follow-up visit (P<0.0001, all).



\*Paresthesia Reporting group in Overall Pain n=44. Abbreviations: BL=Baseline; 3M=3-Month Visit; 12M=12-Month Visit; SD=Standard Deviation; ODI=Oswestry Disability Index

## SUBJECT SATISFACTION

Overall, subjects with AdaptiveStim™ ON had high satisfaction rates, with subjects who did not report feeling paresthesia trending toward higher satisfaction than subjects who reported paresthesia; however, post hoc testing showed no significant difference between these groups.

Follow-up	Felt Paresthesia			Neutral and Very/Somewhat Satisfied			P-value (Fisher's Exact)
	Total	Very/Somewhat Satisfied	Unsatisfied	Total	Very/Somewhat Satisfied	Unsatisfied	
MONTH 3	N 23	22 (95.7%)	1 (4.3%)	N 33	31 (93.9%)	2 (6.1%)	0.052
MONTH 12	N 25	24 (96.0%)	1 (4.0%)	N 45	43 (95.6%)	2 (4.4%)	0.14

## CONCLUSION

This analysis suggests accelerometer-based, automatically adjusted, stimulation can provide substantial pain relief and improvement in disability regardless of patient perception of paresthesia. Conclusions are limited by the relatively lower number of subjects within the non-paresthesia reporting group at follow-up visit. Further studies of position-adaptive stimulation in subthreshold therapy are needed.

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## DISCLOSURE

This study was supported by Medtronic.





## Percutaneous Endoscopic Lumbar Laminectomy and Discectomy for Revision Open Decompressive Laminectomy

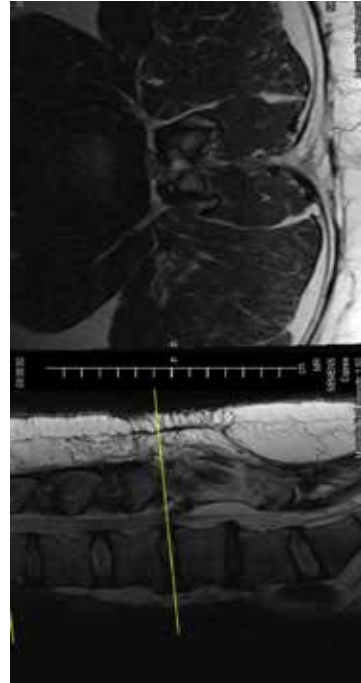
Baher Yanni, MD; Francis Pflum, MD; Salah Eldin Mohamed, MD

### Background:

- Percutaneous endoscopic lumbar laminectomy or laminotomy (PELL) and percutaneous endoscopic lumbar discectomy (PED) is a minimally invasive surgical technique that is utilized to treat lumbar canal stenosis. The procedure is performed through a single port endoscope and has a powerful advantage or structural preservation. It allows for early recovery for patients and faster return to their activities of daily living. The aim for this study is to report the case of a revision of an open decompressive laminectomy at L3-4 via PELL and a discectomy. Scar tissue makes revision laminectomy and discectomy more difficult increasing the risk of dural tear or nerve injury. PELL and PED as revisional surgery for recurrent disc herniation has been thought of as an impossible procedure. Ruetten et al. commented that percutaneous endoscopic discectomy can be conducted using the full endoscopic transforaminal and interlaminar discectomy after the outcomes of endoscopic discectomy as the index operation (1-4). However, there have been few previous studies on the outcomes of endoscopic discectomy for recurrent lumbar disc herniation after open discectomy as the index operation (5,6). The purpose of this study was to determine the feasibility and effects of revisional PELL and PED after open discectomy.
- This is a 53-year-old male who came in with a chief complaint of back pain. The patient had back pain every day radiating down to bilateral lower extremities all the way down to below the knees, however not to the feet. His symptoms were worse on the right than the left. The patient's history goes back to 2011 when he developed back pain and had bilateral lower extremity pain. Patient had a number of epidural steroid injections with only temporarily relief. Patient then proceeded with having a decompressive laminectomy at L3-4, L4-5 in 2011. After review of records, it was noted that patient post-operatively continued to have pain requiring a number of repeat epidural steroid injection that were initially giving him relief, however the pain persisted and continued to increase in intensity.

### Objective:

- Physical exam revealed a longitudinal 3.5 inch scar over his lower lumbar spine. There was not tenderness noted to palpation over the lumbar spine or the sacroiliac joints. He was able to flex forward to a point where he can touch his mid shin with his hands. There was mild decrease in sensation over the lateral aspect of the right leg. Deep tendon reflexes were hypoactive and symmetrical. Motor muscle testing were within normal limits and symmetrical in the quadriceps, dorsiflexors and plantar flexion of the ankle. X-rays of the patient's lumbar spine appeared that the patient had disc space narrowing at L3-4 and L4-5, worse at the L4-5 level. It was evident on the AP view that the patient had a significant laminectomy at L4-5 but the posterior window at L3-4 was essentially unchanged. MRI of the lumbar spine revealed evidence of a laminectomy and posterior surgical changes from the L3 disc level down to the L5-S1 disc space. There was considerable decompression of the spinal canal from the upper body of L4 down to the body of L5. However, there was marked stenosis approximately from the upper body of L4 to the lower third of the body of L3.



### Methods:

- **Surgical indication:** PELL is performed for lumbar canal stenosis. In the case of multiple stenosis, after obtaining consent from the patient, single-level decompression is only performed if it is likely to affect the patient's symptoms; if the patient requests treatment of all the vertebral levels potentially causing the symptoms, microscopic surgery is performed instead. This procedure is used to treat all types of central canal stenosis and lateral canal stenosis.
- **Surgical Instrumentation:** A special single-port endoscope is used for PELL, as with PED. The 7-mm endoscope (VERTEBRIS, Minnova Richard Wolf Medical Instruments Corporation, Germany) has an 8-mm sheath and is easily manipulated, even in a narrow interlaminar space, but is incompatible with some of the instruments that can be used for an 8-mm endoscope. An 8-mm endoscope can be used with drills up to 3.5 mm, which is used for drilling larger areas of bone. The 7-mm endoscope also enables the use of a single leg on patients, as well as a standard table for discectomy. The two Ruyi, Weir Medical, Inc. (Weir Medical, Inc., Canton, MA), the 6-mm endoscope is preferred as a first choice for efficiency; this procedure has been efficient. A special table (Prime 2, Nakanishi, Japan), and a bipolar flexible radiofrequency probe (Eman Trigger-Flex probe; Eman International) are also used.
- **Surgical technique:** The patient was placed under general anesthesia prone on a Wilson-type frame. Preoperative geographical markings were made identifying the L3-4 interspace. In the midline, an injection of lidocaine and epinephrine was made, and then a longitudinal incision was made over L3-4. Thereafter, a blunt dissection was made down through the soft tissues through the fascia down to the posterior window on the right side at L3-4. A scope was inserted, and then the posterior aspect of the lamina was debried with various pluitary forceps and hemostats was controlled with the Bovie. A point object to be the most cephalad and lateral aspect of the lamina on the right side, a burr was used to initiate the laminotomy. This burr was used to thin out the lamina on the right side at the level of L3-4 extending to the posterior aspect of the inferior aspect of the body of L3. The laminotomy proceeded through the tissues down to the anterior aspect of the lamina, and we were able to expose the posterior aspect of the spinal canal, and then with a combination of Kerrison rongeurs, and the burr, a laminotomy was performed to decompress the posterior aspect of the disc space at L3-4. Thereafter, we retraced the dorsal sac and the traversing L4 nerve root medially, and with pluitary forceps performed a discectomy anteriorly to further enlarge the spinal canal. At the termination of this right side, there was free pulsation of the dorsal sac.
- We then proceeded from the posterior incision using the over-the-top technique to the contralateral side. A blunt dissection was made down to the lamina on the left, and then we were able to pass a scope onto the left side and identified the medial and inferior aspect of the previous laminectomy at approximately the level of the inferior aspect of the disc space and the top of the L4 vertebra. Then, with a combination of basket forceps and a Bovie, we debried the same, and then we resected the lamina with a combination of various burrs and the Kerrison rongeur. We brought this hemilaminectomy up to above the level of the L3-4 disc space, at which time, it was noted that the dorsal sac was freely pulsatile. The wound was then copiously irrigated with normal saline and closed in layers of Vicryl. A sterile dressing was applied. Throughout the procedure, spinal cord monitoring was performed and was normal at the termination of the procedure.

### Results:

- First, PELL requires a small skin incision and produces less muscle damage, thereby resulting in a shorter hospital stay. Second, the greatest advantage of this technique is the good field of view on the opposite side, as once the superior lip of the lamina has been drilled, the opposite side lateral recess can be decompressed. After decompression, the transverse root is visible as far as the vicinity of the intervertebral foramen. Drilling of the lateral recess can be carried out relatively easily.

### Conclusion:

Using PELL for the treatment of LCS has some advantages compared with conventional surgery. However, training is needed for this method, because of the limited kinds of operative tools.

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## Peripheral Nerve Stimulation: Techniques and Clinical Efficacy

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### Background:

Chronic pain is a common source of morbidity in many patient populations worldwide. Studies link chronic pain with limitations to mobility, interference with daily activities, dependence on opioid analgesics, and psychiatric illness. With growing concerns about potential side effects of currently prescribed medications and a continued need for effective treatment, the medical community is open to alternatives that provide safe, effective measures to control patient pain. Related to these concerns, peripheral nerve stimulation (PNS) has been regaining popularity as a potential treatment modality. The concept of PNS for the management of pain originated in the first century AD with the discovery that torpedo fish produce electrical discharges that were noted to provide relief of pain. Following this discovery, several attempts were made to produce man-made electrical nerve stimulators that replicate the effects observed from torpedo fish. The earliest concept of peripheral nerve stimulation as we know it today was introduced in 1967. In this study, the authors demonstrated temporary pain relief following a sustained, two-minute electrical stimulation. The first clinical studies of implantable nerve stimulators were performed in 1976 at Johns Hopkins, with the investigators citing reduced opioid requirement, increased ability to work, better sleep, improvements in depressive symptoms, and reduced pain as potential benefits. Several mechanisms have been proposed to explain the effectiveness of PNS. The potential benefits of counterirritation were reported decades prior to Wall and 4 Sweet's landmark publication. Temporary pain relief was observed on withdrawal of many irritating stimuli; irritants used for this study included heat, ice, and vibration. The gate control theory of pain was published later. This theory proposed that pain nerve fibers of different sizes act as "gates" for different types of sensory information and suggested that one can decrease the perception of pain by providing competing, non-painful stimulation through large fiber neurons to close the small-fiber pain "gates." Current thinking suggests that, although the gate control theory is likely involved, it is unlikely to be the sole mechanism by which PNS works. Several additional theories have been proposed, many relating the effects of PNS to changes in various neuromodulators. Despite these lingering questions, PNS continues to be a heavily studied treatment modality for the management of pain. It has shown possible effectiveness in the management of trigeminal neuropathic pain, chronic migraine headaches, complex regional pain syndrome, and many other conditions.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving peripheral nerve stimulation. We present the existing literature on the understanding of the safety and efficacy of peripheral nerve stimulation.

### Results:

In a study where 28 lower extremity amputees with post-amputation pain were enrolled, subjects underwent ultrasound-guided implantation of the percutaneous leads, and patients either received PNS or placebo. This was a crossover study in which the placebo group received a PNS for 4 additional weeks. In this study, a significantly greater number of patients who received PNS demonstrated 50% or more reduction in postamputation pain during the 1-4 weeks versus the placebo group. Several studies have shown an overall improvement in pain control, disability, and opioid consumption following PNS implantation for the treatment of chronic lower back pain (CLBP). One case series involving 9 patients underwent PNS with lead placement. This resulted in significant, sustained therapeutic relief of CLBP and disability with clinical reductions of  $\geq 50\%$  in two-thirds of patients for at least twelve months following lead removal. Additionally, a prospective multicenter study involving 118 patients undergoing therapy with PNS showed significant improvement in all pain and quality of life measures and an overall reduction in the use of opioids, non-steroid anti-inflammatory drugs, and anticonvulsants. A third study followed 100 patients with a variety of chronic pain syndromes and measured pain, complications, disability, and depression outcomes following PNS treatment. One cohort of this study showed significant improvement to pain and disability following lumbosacral PNS without any long-term reported complications. In another study with patients who have CLBP, the subjects received percutaneous peripheral nerve stimulator leads that targeted the medial branch of the dorsal ramus in the region of lower back pain. The leads remained in place for 30 days of therapy. Even after the removal of the peripheral nerve stimulator leads, there were sustained long-term benefits of the peripheral nerve stimulator leads in treating CLBP. Patients showed a reduction in pain and disability and sustained reduction in the use of analgesic medication. This continued long term at the four-month follow-up visit. Subjects also reported clinically significant reductions in disability, pain interference, and the patient's global impression of change. In a study of patients undergoing primary, unilateral total knee arthroplasty (TKA), the patients received both a femoral and sciatic open coil percutaneous leads that were placed one week prior to surgery. Although the study was small ( $n = 7$ ), the majority of subjects PNS had well-controlled postoperative pain during the first week following TKA. In 6 out of 7 patients, pain was well controlled even four weeks after TKA. Additionally, 4 out of the 7 subjects studied had such well-controlled pain that opioid use was discontinued in the first week. 1 of the 4 subjects did not even require opioids during the duration of therapy. Another study, patients with greater than 1 year of intractable knee pain following TKA underwent PNS. They showed significant improvement in functional capacity and reduction in pain via visual analog scale scores. Another study reported the effectiveness of PNS in improving chronic knee pain following an eight-week course receiving PNS therapy three times a week. This study showed improvement in pain, stiffness, and physical function. There were no serious adverse events related to the device or the procedure.

**Conclusion:** PNS has shown great promise in the management of a wide variety of common musculoskeletal pains. Several trials have predicted its effectiveness without the side effects and could reduce the need for potentially addictive medications given for management of pain. Further studies are needed as the long-term risks and benefits of PNS have not been well-studied as most information available on the effectiveness of PNS is based on shorter-term improvements in chronic pain. Early investigations suggest that nerve stimulators are safe to use for up to 18 years, with wide differences in biostability noted for stimulators placed in different locations. The utility of newer technology also requires further investigation. New techniques for placement of peripheral nerve stimulation will likely open the possibility of targeting deeper neural structures for PNS. Smaller devices create opportunities to use PNS for smaller nerves that the modern stimulators are able to effectively stimulate. This widens the array of possible chronic pain syndromes for which PNS can provide relief of symptoms not well-managed by traditional medical and physical therapies. PNS can play a large role in the future of chronic pain management. Although there is still much to learn in regard to specific mechanisms, patient selection, and long-term safety, early results have shown promise. Currently, many devices placed for treatment of chronic pain are placed as an off-label use of the device. Obtaining this important safety data is an important next step. More information allows for expansion of the number of relevant diagnoses for which this therapy can be applied. It also allows for standardized safety protocols to be developed to optimize short-term and long-term safety. Through further investigation, a useful adjunct for management of chronic pain can be developed with PNS.


**Peripheral Nerve Stimulation Yields an Unexpected Motor Response in a Patient with Chronic Shoulder Pain**


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**Background**

Peripheral Nerve Stimulation (PNS) serves as an effective form of neuromodulation in patients with focal chronic pain. It represents a viable therapeutic intervention for patients with peripherally originating pain who have exhausted medical and surgical options (1). Electrodes are inserted percutaneously in close proximity to the targeted nerve under image guidance to directly target a discrete neural target. Permanent placement device insertion can often be avoided if prolonged neurostimulation yields long term benefits after application (2).

Mechanistically, it is thought that PNS modulates pain perception via nociceptive activation of large diameter A-beta sensory fibers. These in turn activate inhibitory interneurons in the spinal cord and attenuate ascending afferent pain signals carried by smaller A-delta and C fibers, a hypothesis collectively termed the gate control theory (3,4).

Indications for PNS are relatively broad and its use has been validated in several chronic pain conditions including migraine, low back pain, shoulder pain, Complex Regional Pain Syndrome (CRPS) and pelvic pain (3-5). It is a safe and effective treatment modality supported by moderate to high level evidence-based analysis.

We describe a case of a patient with chronic shoulder pain for several years refractory to both conservative medical therapy and surgical interventions. The patient elected for PNS of the suprascapular and axillary nerves with initial efficacious results requiring minimal electrical amplitude to achieve paresthesia. However, decreasing efficacy resulting in the need for increased amplitude requirements revealed that the threshold for motor response was uncharacteristically lower than the threshold for sensory paresthesia coverage making device dosing challenging secondary to painful muscle contractions. Here we discuss our generalized approach to this unexpected response.



Figure 1: The suprascapular notch on the left side was identified using fluoroscopy for axillary and suprascapular nerve placement

**Case Description**

A 45-year-old female with a pertinent orthopedic history of C5-C7 spinal fusion presented with chronic left sided shoulder pain for several years refractory to surgical intervention and cervical spinal cord stimulation. Additionally, she has tried multiple pharmacologic interventions including anti-inflammatories, antidepressants, anticonvulsants as well as opioids without significant relief. Physical therapy, chiropractic manipulation and acupuncture has provided little to no relief. Her symptoms result in significant functional limitation which interferes with work, sleeping and bathing. Physical exam revealed no impingement and full range of motion is demonstrated in both shoulders. She exhibits no upper extremity weakness but the sensory exam displays allodynia in the shoulder predominantly, but also with some referral to the upper arm down to the wrist level.

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Figure 2: Axillary nerve lead medialized on AP x-ray of the left shoulder

**Discussion**

A PNS with an external pulse generator (EPG) and open coil lead design was used to facilitate fibrosis and scarring to help prevent lead migration (7). This patient appeared to have an altered attenuation of peripheral nerves which exhibited features overlapping with atypical predominant diagnoses such as CRPS. Intraoperatively, she developed attenuation of the sensory nerve fiber response and increased sensitization of motor fibers. Ideally, sensory nerve endings are triggered until a paresthesia is felt and while avoiding thresholds needed to generate a motor response. However, with heightened threshold observed in the motor fibers here, stimulation caused painful muscle contraction prior to any desired paresthesia resulting in difficult neurostimulation titration. Our approach to this paradoxical response was to increase the amplitude to provide both motor and sensory stimulus then the amplitude was decreased until motor response was absent: subthreshold dosing. Unfortunately, her course was complicated by lead migration and both leads were electively removed with plans for re-implantation at a later time.

Since the discovery of peripheral nerve stimulation as a treatment of chronic pain syndromes, the understanding and refinement of techniques has drastically improved (6). Neuromodulation continues to be a fast growing field with widespread clinical application. As techniques are refined its clinical use continues to increase. Also, the development of interventional therapies will prove to be pivotal as alternatives to pharmacotherapy become necessary. Innovation in lead placement has facilitated the use of PNS in several clinical scenarios. Initially, PNS was invasive and completed surgically under direct visualization using hardware adapted, rather than designed for, peripheral use. Less invasive percutaneous placement of leads enhanced by utilization of ultrasound has greatly improved the ease of placement. This has contributed to the expanded use of PNS as it has evolved to become an office based procedure with a low risk profile.

While much is known about PNS there continues to be a gap in the understanding of mechanistic pathways. Gate control theory is the principal foundation upon which PNS is posited, but further studies are needed to clarify the exact mechanism. Current practice deems the perception of sensory paresthesias are necessary to inhibit ascending pain signals from the periphery, but recent studies suggest high frequency imperceptible peripheral stimuli can be effective as an analgesic regimen (6). Additionally, while many retrospective and observational studies have validated the use of PNS there continues to be a paucity of high quality randomized controlled trials supporting its use (7). As modalities develop and further research continues to validate its use, PNS will undoubtedly prove useful in the long term treatment of several chronic pain syndromes.



## Peripheral Nerve Stimulator for Post-sternotomy Pain

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### INTRODUCTION

Post-sternotomy pain syndrome (PSPS) is chronic post-operative pain after median sternotomy lasting ≥ two months after surgery.(1) It affects nearly 40% of coronary artery bypass graft patients for approximately 28 months.(2)

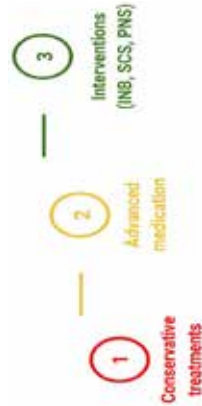


Figure 1. Approach to treating PSPS.

Patients are initially treated with medication, then they are advanced to interventional techniques if pain persists (Figure 1). Intercostal nerve blocks (INB) as well as spinal cord stimulators (SCS) have been utilized for sternotomy-related pain, but peripheral nerve stimulator use (PNS) has not been reported.(3) This is a case of a PSPS patient who received a PNS resulting in 90% pain relief.

### METHODS

- 62-year-old male had aortic valve replacement (AVR) complicated by severe, intolerable chest wall pain along incision site, consistent with PSPS and intercostal neuralgia
- Visited the emergency room twice for pain, was referred to pain management, and failed medication management
- Ultrasound-guided INB of T2-T6 intercostal nerves using 10 mL of bupivacaine 0.5% with 2 mL of dexamethasone 10 mg/mL injected bilaterally = 60% relief for one week
- Second INB using same solution targeting anterior cutaneous branches of the intercostal nerves, closer to the incision site = 100% relief for approximately two weeks



Figure 2. Lead confirmation.



Figure 3. External hardware.

- One year after AVR => implantation of bilateral intercostal PNS. Using fluoroscopy, stimulator probes were positioned in the T2-T6 intercostal nerve fields, parallel to the sternotomy site. Paresthesia overlapping the “pain area” was confirmed before exchanging the probes for indwelling percutaneous leads. These leads were then attached to an external stimulator and paresthesia was again confirmed before anchoring the leads to the skin (Figures 2 and 3)

### RESULTS

Following implantation of the PNS device, the patient reported more than 90% pain relief throughout the 60-day treatment period. He has had regular follow-up with the pain management physician and states that his relief remains sustained until this moment (7 months after implantation).

### CONCLUSIONS

Implantation of a PNS device for PSPS allowed this patient to regain his quality of life to the point that he is functioning normally without requiring the use of any medications for pain.

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## Pharmacological Advances in Opioid Therapy: The Role of Sublingual Fentanyl in Pain Management

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**Background:** In 2019, the Centers for Disease Control (CDC) reported that 20.4% of adults had chronic pain and 7.4% of adults had chronic pain that affected their daily life or work<sup>3</sup> activities. This is also known as high-impact chronic pain. This pain is usually the highest among those 65 years of age and higher. Pain is also a significant concern and one of the most feared symptoms associated with cancer patients. Since pain is subjective, it is often challenging to diagnose and treat appropriately. Furthermore, the timely management of pain is important. Patients whose lives are affected by the pain they are experiencing are often desperate for relief, especially patients whose pain is resistant to other medications. Pain medications can be administered in several ways, including intravenous (IV), intramuscular (IM), and oral. IV and IM injections can be painful upon administration, and IV's can be time-consuming to administer. Furthermore, accessing veins can be difficult in elderly, obese, and burn patients. Oral (PO administration) medications have a slow onset and can take up to 30 minutes to provide relief. However, the sublingual mucosa (under the tongue) is permeable to medications and, depending on the lipophilicity of the drug, can allow for fast onset of drug action. Sublingual fentanyl, used to treat breakthrough cancer pain that is not controlled by other medications, can have an onset of action within 7-15 minutes. Therefore, while not for all patients, sublingual fentanyl can be a useful treatment for qualifying pain patients.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving sublingual fentanyl. We present the existing literature in the understanding of the safety and efficacy of sublingual fentanyl in pain management.

**Results:** Fentanyl is a synthetic opioid that has primarily been used to treat breakthrough pain in patients currently on long-acting pain medications, most commonly cancer patients. The fentanyl patch, marketed as Duragesic, is potent but is not approved for breakthrough pain. The fentanyl patch is also not fast-acting since it has a delay due to issues with absorption. Breakthrough pain is associated with significantly reduced quality of life, even compared to the patients' chronic baseline pain. Thus, finding a medication to treat this type of pain has proven important in the fields of pain management and oncology. Compared to morphine, which can also be used to treat breakthrough pain, fentanyl is more potent and has a faster onset. However, fentanyl is also notable for significant first-pass metabolism in both the liver and GI tract. This has prompted research into a form of fentanyl that could bypass both the liver and gastrointestinal system for a maximal analgesic effect – this was answered by sublingual fentanyl. Sublingual fentanyl comes in the form of a tablet, under the name Abstral and a spray, under the brand name of Subsys. This medication is only intended for patients who are considered opioid-tolerant due to its potency and rapid onset. Sublingual fentanyl's onset of action is approximately 7-15 minutes, making it a suitable medication for breakthrough pain treatment. Sublingual fentanyl has shown to be a good alternative to other forms of fentanyl, such as IV fentanyl citrate, as it overcomes issues with bioavailability. In a 2018 phase I open-label randomized multiple ascending-dose study, the results showed that the mean plasma concentrations increased following repeated doses of sublingual fentanyl spray, while producing a relatively low SE profile in opioid-naïve patients. Several studies have shown great improvement in breakthrough cancer pain (BTCP) with the use of sublingual fentanyl. Minkowitz et al. conducted a multicenter phase 3 open label study testing efficacy and safety of sublingual fentanyl in patients experiencing BTCP who were opioid tolerant. It was found that sublingual fentanyl spray was adequately tolerated and preferred over opioids in opioid tolerant patients with breakthrough cancer pain. In 2014, Shimoyama et al. conducted a study to evaluate the safety and efficacy of varying doses of sublingual fentanyl tablets in managing BTCP. It was found that BTCP was managed well with sublingual fentanyl tablets (SFTs) with no serious adverse events occurring during the study and through the 12-week extended treatment period. Shimoyama et al. also conducted a randomized, phase 3, crossover, double-blinded placebo-controlled and non-blinded active drug clinical trial evaluating the use of disintegrating SFTs in 51 cancer patients experiencing BTCP. The doses of SFTs given in the study were based on a single dose of oral morphine given during the observation phase of the study. This study showed that the use of SFTs at a conversion ratio of 1/50 to oral morphine in the treatment of BTCP was both safe and effective. The 1/25 conversion ratio regimen, while effective in controlling pain, had the highest incidence of adverse drug reactions.

**Results:** Fentanyl is a synthetic drug that is usually used to relieve breakthrough pain in individuals who are taking long-acting analgesics, such as cancer patients. Fentanyl is more potent and has a quicker onset compared to morphine, which can also be used to treat breakthrough pain. However, fentanyl undergoes significant first pass metabolism in the liver and gastrointestinal tract. This knowledge prompted research for a type of fentanyl formulation capable of bypassing both the liver and gastrointestinal system for full analgesic effect. This was met with the production of sublingual fentanyl. Sublingual fentanyl is available as a tablet branded Abstral and as a spray branded Subsys. Due to the medication's potency and rapid onset, it is only indicated for patients who are considered opioid resistant. Sublingual fentanyl is known to have a half-life of about 7-15 minutes, making it an ideal drug for breakthrough pain relief.

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## Regenerative Medicine: Pharmacological Considerations and Clinical Role in Pain Management



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**Background:** Back pain is an extremely common problem that is experienced by people of all ages. Specifically, low back pain (LBP) affects at least 80% of individuals at some point in their lifetime and is the fifth most common reason for physician visits in the United States (U.S.). LBP is a leading cause of activity limitation and work limitation throughout much of the world, second only to upper respiratory conditions. LBP is also now the number one cause of disability in most countries. Analysis of U.S. spending on personal health care, public health, and increases of healthcare costs from 1996 to 2013 showed estimated spending of \$7.6 billion in low back and neck pain, the third-highest healthcare cost among different disease categories. In addition, LBP and neck pain had the second-largest increase in spending associated with it. This is likely to increase with the global aging population. The vast majority of people will be diagnosed with "non-specific" LBP. Once specific causes of LBP (malignancy, fracture, infection) have been ruled out, it is important to differentiate mechanical and inflammatory LBP from one another. Mechanical LBP is an injury or derangement to the anatomic structure of the lower back. When not due to an emergent cause, mechanical LBP is associated with a good prognosis, and management is conservative and includes patient education focused on massage, exercise, and behavioral approaches to minimize injury. Acupuncture and herbal supplements can be effective as well. Inflammatory back pain results from a systemic inflammatory condition, often axial spondyloarthritis. Inflammatory back pain can be distinguished from mechanical back pain due to a younger age of onset, improvement with exercise, pain at night, insidious onset, and no improvement at rest. These patients should be treated with structured exercise, non-steroidal anti-inflammatories (NSAIDs), and should be referred to rheumatology. Regardless of mechanical or inflammatory etiology, it has been seen that most patients with acute or subacute LBP improve over time regardless of treatment, so management should initially be conservative, nonpharmacologic, and non-invasive. Treatment of an acute episode of LBP generally includes rest, activity modification, physical therapy, NSAIDs, and patient education. A small percentage of patients will develop chronic pain lasting 6 to 6 months duration. Clinicians have a very limited ability to detect the exact source of the pathology in this case. This makes a cure unlikely, and care should be supportive, with a goal to improve pain and function. For patients with chronic LBP who have an inadequate response to conservative and pharmacological treatment, a number of techniques have been established. These include complex spinal fusions, image-guided interventional techniques, and regenerative medicine therapies such as injection of platelet-rich plasma (PRP) and mesenchymal stem cells (MSC). The success of PRP and MSC in athletes has brought these into the spotlight.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving peripheral nerve stimulation. We present the existing literature in the understanding of the safety and efficacy of biologics in pain management including the use of platelet-rich plasma and mesenchymal stem cells.

**Results:** Platelet-rich plasma (PRP) has been demonstrated as a viable treatment in several randomized control trials (RCTs). Singla et al. conducted a study involving a 40-patient cohort, comparing the use of steroids versus PRP for the treatment of chronic low back pain secondary to some form of sacroiliac joint pathology. Patients were subdivided into two groups. Group S, the steroid group, received an ultra-sound guided sacroiliac joint injection of 1.5 mL methylprednisolone plus 1.5 mL of 2% lidocaine with 0.5 mL saline. Group P, the PRP group, received 3 mL of leukocyte-free PRP with 0.5 mL of calcium chloride. Group P reported a significantly lower pain score via the VAS at six weeks and three months. Additionally, group P demonstrated both improved MDQ and SF-12 scores throughout the entire three-month study period, while Group S only demonstrated improved scores in the first four weeks. Overall, the study concluded that PRP demonstrated greater efficacy in the treatment of lower back pain when compared with traditional steroid injections. Taiki-Wosomu et al. conducted a RCT involving 47 participants with a history of chronic lower back pain. 29 went to the treatment group and 18 went to the control group. Patients in the treatment group received 3-4 mL of autologous PRP, while patients in the control group received a contrast agent. Overall, the study concluded that patients in the treatment group had significant improvements in their FRI, NRS, SF-36 health survey, and modified NASS outcome questionnaire in the first eight weeks of the trial. No adverse outcomes were reported. Akeda et al. analyzed the safety and efficacy of utilizing autologous PRP in the treatment of discogenic back pain. 71% of patients reported a 50% pain reduction via the VAS. 79% of the patients demonstrated a 50% reduction in their RDQ scores throughout the study period. It was concluded that PRP is a safe and effective treatment for the management of chronic lower back pain with the only adverse events reported in the study period being transient leg numbness that resolved with one week of onset of symptoms. The use of autologous stem cells in the treatment of chronic back pain is currently undergoing rigorous assessment. Kumar et al. conducted a single arm 12-month phase-1 clinical trial involving 10 patients with chronic lower back pain. Patients had undergone a one-time intradiscal injection of hyaluronic acid and autologous adipose tissue-derived mesenchymal stem cells. VAS, ODI, and SF-36 scores were lower in patients who received both high-dose and low-dose AT-MSC injections with no significant difference reported in the two groups. Three of the six patients who reported improved VAS, ODI, and SF-36 scores demonstrated increased water content in their intervertebral discs on MRI. No adverse events secondary to the transplants were noted in the 12-month study period. One RCT conducted by Noriega et al. found that patients injected with allogeneic bone-marrow-derived stem cells demonstrated reduced lumbar pain and disability three months post-transplant, and these results were maintained throughout the entire one-year study period. Amiridellan et al. conducted a multicenter randomized controlled study involving 100 patients with chronic lower back pain with degenerative disc disease. Patients were randomized into four groups: (1) 6 million mesenchymal precursor cells (MPCs) with hyaluronic acid (HA) (2) 18 million MPCs with HA (3) HA vehicle control (4) Saline control (placebo). Both MPC groups showed significant improvements in VAS and ODI scores when compared to the control groups.

**Conclusion:** The strengths and limitations of biologics in the treatment of musculoskeletal injuries and LBP continue to be discovered. Current treatments for chronic back pain include conservative management with exercise, medications such as NSAIDs, surgical fusions, radiofrequency ablation, and spinal cord stimulation, among others. Conservative management continues to be the first-line treatment for LBP. Once conservative options have failed, other treatments have been shown to be effective but also come with considerable side effects and complications. Due to the cost associated with managing these complications, further investigation of alternate treatments remains prudent. PRP and MSCs are used autogenously to help facilitate the healing process, and their injection has been studied in long-term management of discogenic low back pain. PRP has been compared to steroid injections in the sacroiliac joint for chronic LBP, with favorable results. MSCs have also been shown to be useful in intervertebral disc regeneration and treatment of chronic LBP associated with degenerative disc disease. As it currently stands, the price for these treatments is still too high, and thus the standard of care continues to be steroid injections and other treatments. Biologics are often indicated for those who fail corticosteroids or for whom they are no longer appropriate. This could change, however, with more robust data and research on safety and long-term efficacy of biologics compared to other interventional management. Biologics are considered by many to be an economic and fast treatment option, especially for those that fall standard of care treatments. The survival and evolution of biologics into a routine clinical treatment option depends on the standardization of their use, consistency of outcomes, and a decrease in overall healthcare costs. Further high-quality studies can aid in this goal by providing more data and providing more predictability in the use of biologics. This will require commitment from all levels of participants to better utilize biologic therapies and regenerative medicine going forward.



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# Sartorius Chemodenerivation for Chronic Hip Pain: Case of Task-Specific Focal Dystonia

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## Introduction

Task-specific focal dystonia is associated with repetitive motor activities such as playing sports or a work-related maneuver. Patients often have a history of musculoskeletal injury or sustained, non-physiologic postures. Etiology is idiopathic, familial, or post-traumatic. The prevalence of task specific dystonia such as writer's cramp and other focal dystonia occur at a rate of 2.7 and 38.1 in 100,000<sup>1</sup>. The neurologic exam is usually normal. Subtle dystonic postures may develop with motion or spontaneously, thus affecting the person's ability to perform tasks as a result of a loss of fine-motor control, speed, and endurance. Pain is the most associated non-motor symptom that contributes to worsened quality of life. There is limited data related to focal dystonic pain, but it is accepted that it is muscular in origin and associated with an altered processing of nociceptive stimuli at the spinal level due to constant and prolonged afferent input caused by sustained muscle contraction<sup>2</sup>. Botulinum neurotoxin improves quality of life in dystonia by irreversibly inhibiting the presynaptic release of Acetylcholine (ACh), the painful, sustained contractions are alleviated<sup>3</sup>.

## Case Report

20-year-old female with two-year history of worsening anterior hip pain. Pertinent history of repetitive local trauma from pitching five years prior. Her associated pain had resolved until she maintained a fixed, cross-legged posture for a prolonged period while traveling. She failed initial conservative treatments. Over the course of two years, she was seen by Orthopedic Surgery, Physical Medicine and Rehabilitation (PM&R) for trigger point injections and Osteopathic Manipulative Treatment (OMT), and Interventional Pain Management for corticosteroid injections (CSI). Participated in Physical Therapy (PT) and OMT continuously but persistently reported 8/10 pain on the Visual Analog Scale (VAS) and had associated decrease of self-reported functional ability. Bilateral hip X-rays as well as pelvic Magnetic Resonance Imaging (MRI) were unremarkable. Neurological exam was unremarkable. Focal dystonia was suspected in the proximal one-third of the Sartorius muscle. The patient elected to undergo diagnostic and therapeutic injection of botulinum toxin utilizing Ultrasound Guided (USG) Electromyography (EMG) needle.

## Discussion

The case presented in an unusual case of task-specific focal dystonia presenting as chronic hip pain without evident motor findings on exam making the diagnosis more difficult. Key points:

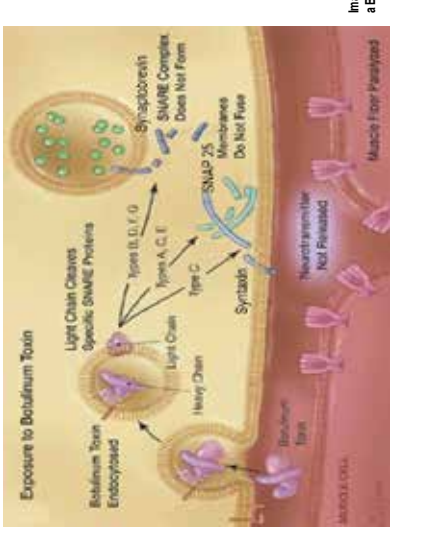
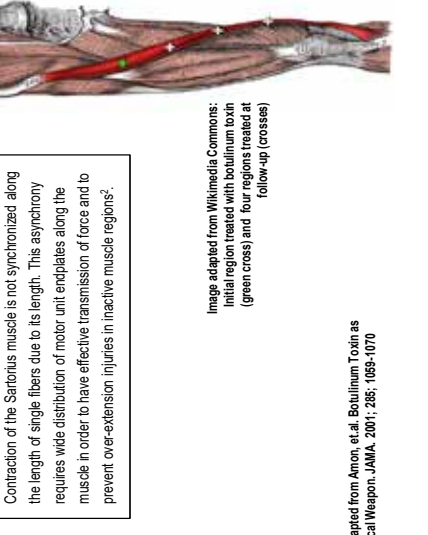
- The Sartorius is a synergistic rather than primary muscle affecting limb movement in multiple planes, across multiple joints.
- Focal dystonia should be considered in refractory pain when history of trauma and maintained postures or repetitive motions are present.
- Length of Sartorius and distribution of motor endplates may require multiple sites to be treated if abnormal muscle activity is present.
- Pain is a significant cause of decrease quality of life in focal dystonia and Botulinum toxin is an effective treatment.
- There is limited data on the pathophysiology of pain related to focal dystonia. More research is needed.

## Procedure and Outcomes

- USG EMG needle was used to identify an area of abnormal spontaneous muscle activity in the proximal third and injected with 20 units of botulinum toxin.
- At two week follow-up, patient reported a decrease in pain from 8/10 on VAS to 2.3/10 and reported significant improvement in her function.
- Discharged from PT with continued Home Exercise Program (HEP).
- Returned for repeat injection of 25 units into four locations along course of muscle for a total of 100 units.
- Three month follow-up pending.

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# The Revision Strategies for Failed Indirect Decompression Accelerated Interventional Orthopedics, PLLC

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## INTRODUCTION

A 72 year old moderately obese female was referred in 2019 for hip pain from her primary care physician. The patient stated the pain decreased her ability to walk and was worse when she tried to walk for long periods of time. She characterized the pain as sharp and shooting and travelled down the posterior hip, anterior thigh and lower leg on both legs. The patient has tried oral steroids and physical therapy with no relief. Her past medical history is hypertension, sleep apnea, hysterectomy, gastric bypass and cataract removal. The patient has never smoked. She is 5'5", 263 lbs with a BMI of 43.

2019 MRI Findings: L4-5 broad based disc bulging abutting the ventral thecal sac with facet hypertrophy causing foraminal stenosis bilaterally.

A trial of one L4-5 interlaminar ESI did not provide any relief. The patient was seen on follow up and a decision was made to place a Superior® implant at L4-5. At follow up the patient reported decreased symptoms and the ability to walk without pain. The patient did not follow up again until 2021, reporting that she had fallen and started noticing sharp shooting pain again that she had before her Superior® implant. A CT scan was obtained (Fig 1), which showed the implant had migrated dorsally at the superior aspect of the device. The patient was then consented for removal and replacement of the Superior® implant. The decision at this time was to implant a fixated Southern Spine Stabilink® Dual Lamina implant. This implant was chosen because of the possibility of bone loss at explant and the need for laminar attachment.

## METHODS & MATERIALS

The patient was placed on the OR table in slight flexion under general anesthesia. Using fluoroscopy, a midline mark and a L4, L5 spinous process line was made. A midline skin incision was made, and using Bovie cautery, dissection was performed down to the thoracodorsal fascia. Staying on midline, the Bovie was used to cut down on the supraspinous ligament. Once the spinous processes of L4 and L5 were visualized, fluoroscopy was used to locate and mark the Superior® implant (Fig 2). This was done because the implant was completely encapsulated by scar tissue. A rongeur was required to clear all of the scar tissue dorsally and laterally. Using the Superior® instrumentation the implant was disengaged. The implant still required to be cleared of scar tissue to be completely removed. Even so, some bone fragment/scar tissue was adhered to the implant (Fig 3). Once the implant was fully removed the interspinous/interlaminar space was sized and a Stabilink® Dual Lamina 10mm implant was placed with good fixation. Fluoroscopic images were obtained to check for optimum placement (Fig 4). The area was then irrigated with bacitracin solution. Demineralized Bone Matrix (DBM) was placed in the interspinous/interlaminar space, as well as, in the posterolateral space to promote fusion of the L4-L5 vertebral segment. The wound was closed in a layered fashion with fascia closed with 1.0 Vicryl, and 2 level subcutaneous closure with 2.0 Vicryl. The surface was closed with staples. The patient was then transferred to the PACU in stable condition.



Fig 1



Fig 2



Fig 3



Fig 4

## RESULTS

The patient was seen 10 days post-op for staple removal. She reported minimal post-op pain and was not requiring any medications for pain relief. She reported complete resolution of her symptoms.

## CONCLUSION

Revision of decompression implants by the interventional pain physician requires an adequate level of surgical skills in order to remove the implant due to the presence of extensive scar tissue. Removal of the decompression implant and placement of an interlaminar fixation device appears to be a successful option for patients suffering from debilitating low back and leg pain.





## The Role of Vitamin D in the Management of Chronic Pain in Fibromyalgia: A Narrative Review



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**Background:** Fibromyalgia (FM) is a combination of prolonged, widespread musculoskeletal pain with associated concomitant fatigue, headaches, stiffness, genitourinary symptoms, disturbed sleep patterns, and cognitive difficulties. The symptoms displayed in a patient can significantly differ throughout the disease from individual to individual. The symptoms also show discrepancies within the same patient throughout the progression of the disease. This makes it critical for the physician to have a reasonable suspicion of diagnosing someone with FM, who presents with the requisite symptoms. With these variable symptoms, the syndrome's presentation must depend on the pathophysiological changes and environmental factors that a person experiences. Fibromyalgia pathophysiology includes genetic and environmental factors that manifest with the human body's neuroendocrine system. There is a central sensitization to pain and limitation to the inhibitory mechanism to pain. The disease's trademark is an overactive central nervous system that results in an increased amount of pain caused by the CNS and perceived by the patient. This syndrome can arise independently and often occurs with other chronic conditions such as continuous inflammation or peripheral nerve damage. With the culmination of symptoms present in FM, managing the syndrome takes a concerted effort by both the patient and the physician. The current treatment for FM includes pharmacologic therapy. The current pharmacological treatment options for FM are pregabalin, duloxetine, and milnacipran, while the non-pharmacologic treatments are physical exercise, cognitive behavioral therapy, and alternative medicine (15). One such alternative medicine is Vitamin D. Low levels of 25(OH)D have been identified as influencing the sensitivity to pain in the central nervous system (CNS) via augmentative properties. In one study, there was an inverse relationship between 25(OH)D levels and mechanical pain sensitivity to mechanical stimuli. This finding is especially notable given that FM has been identified as a central sensitivity syndrome. Furthermore, several studies have identified the role of steroids in modulating neuronal excitability, one of which is vitamin D. These findings indicate that vitamin D can function to influence microglia, astrocytes, and spinal glia in the release of neuroexcitatory substances such as proinflammatory cytokines. By influencing the release of proinflammatory cytokines, particularly tumor-4 necrosis factor-alpha (TNF $\alpha$ ), vitamin D serves a neuroprotective role in reducing the extent of central sensitization to pain. Given this information, however, there has been a large randomized control trial (RCT) conducted in New Zealand which found that there were no significant associations between low vitamin D and chronic pain in older adults. Given these collective results, Vitamin D has shown potential in treating patients with FM.

**Methods:** We conducted a systemic comprehensive literature search using a collaboration of existing publications involving vitamin D in the management of chronic pain in fibromyalgia. We present the existing literature in the understanding of the efficacy of vitamin D in the management of chronic pain in fibromyalgia.

**Results:** A randomized control trial studied the effects of patients taking 2000 IU of oral cholecalciferol daily for six months. Out of 72 patients diagnosed with FMS, 36 patients received vitamin D treatment while the other 36 received a placebo. At six months, patients in the TG showed decreased VAS scores from  $6.6 \pm 2.5$  to  $2.9 \pm 2.7$  ( $p < 0.001$ ). The scores also showed that lower 25-OH vitamin D levels correlated with higher scores of the FIQ with an  $r$  of  $0.549$  ( $p < 0.005$ ). This study concluded that vitamin D supplementation had a positive effect on pain perception in FM patients. Vepnar et al. conducted a study involving 30 women with FM who were divided into vitamin D group versus placebo. There were significant improvements in the vitamin D group in terms of VAS scores, and SF-36. Yilmaz et al. conducted a study that involved 58 patients to assess the effect of vitamin D supplementation in patients with chronic widespread musculoskeletal pain (CWP), including those with FMS. Patients were given 50000 IU/week oral vitamin D and elemental calcium daily for three months. At baseline, the frequency of meeting FMS criteria within those with CWP was increased in those with severe vitamin D deficiencies, as defined as  $< 0.001$  and a significant decrease in ALP levels ( $p < 0.001$ ). There was no significant change in the Ca or P levels. There were significant decreases in pain and asthma ( $p < 0.001$ ). The study concluded that vitamin D supplementation lead to an improvement in musculoskeletal symptoms and patients' quality of life. Patients with CWP should be investigated for vitamin D deficiencies. In a randomized control trial of 37 patients with FMS, patients received combined vitamin D supplementation with Trazadone for eight weeks and found similar results. Patients were given 50,000 IU of oral vitamin D weekly and 25 mg of trazadone at bedtime daily. Results at the end of 8 weeks showed a significant improvement in both the physical ( $p = 0.001$ ) and mental ( $p = 0.04$ ) component scores of the SF-36 survey in the TG compared with a decrease in the CG. There was a decrease in WPI scores<sup>5</sup> in both the TG and CG but the decrease was more significant in the TG ( $p = 0.007$ ). The TG groups showed improvement in subscores of FIQ including the most improvement seen in morning tiredness, stiffness, anxiety, and depression. Total FIQ scores decreased from  $52.4 \pm 16.6$  to  $29.7 \pm 14.4$  in the TG compared to a decrease from  $50.7 \pm 16$  to  $40.4 \pm 15.3$  in the CG ( $p = 0.064$ ). PSQI scores decreased from 10 to 6.1 in the TG and from 10.4 to 8.1 in the CG ( $p = 0.002$ ). One limitation of this study was the short follow up time of 8 weeks. Despite the data suggesting significant potential in vitamin D, there remains some discordance about the benefit of vitamin D in the management of patients with FM. In a RCT of 50 patients diagnosed with FM, there were no significant differences in pain scores between the treatment arm and the control arm despite there being a difference in serum levels of vitamin D between the two groups.

**Conclusion:** Fibromyalgia is an idiopathic, complex disorder that presents as chronic, widespread pain with fatigue, stiffness, cognitive impairment, and depressed mood. It typically affects women more than men. Most patients who suffer from FM also have other comorbid, chronic medical conditions. Environmental, genetic, and neuro-hormonal factors can play a role in the pathogenesis of this disease. The treatment of FM involves a holistic approach involving pharmacological and non-pharmacological interventions. Delayed diagnoses, expensive cost, insurance barriers, lack of consistency in treatment guidelines, and low treatment adherence heighten the barriers to effectively treating FM. The current pharmacological treatment options for FM are pregabalin, duloxetine, and milnacipran, while the non-pharmacologic treatments are physical exercise, cognitive behavioral therapy, and alternative medicine. One alternative medicine option is Vitamin D supplementation in patients with FM. Vitamin D plays a vital role in maintaining numerous homeostatic processes, regulating hormones, and nociceptor innervation in skeletal muscle. Some studies show that low Vitamin D levels facilitate increased sensitivity to pain in the central nervous system (CNS) of patients with FM; however, some studies refute these findings. Some randomized control studies show that Vitamin D Supplementation helps to alleviate pain, fatigue, and depression in patients with FM. It is still unclear if Vitamin D proves to be fully efficacious because some studies show conflicting results. Vitamin D supplementation is inexpensive, has minimal side effects, and can still provide benefits to patients with FM regardless of its efficacy in pain control. Vitamin D can improve muscular strength, decrease the risk of developing osteomalacia, and improve long-term bone health in patients with FM. Vitamin D supplementation has the potential to improve the quality of life in patients suffering from FM, for a low cost, and thus should continue to be explored.

# Cluneal Neuropathy, commonly missed diagnosis. Case Report.

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## BACKGROUND

Cluneal neuropathy is an underdiagnosed cause of low back pain. This nerve can be trapped under many structures but commonly can be trapped under the long posterior sacroiliac ligament. The middle cluneal nerve is a sensory branch of the dorsal rami of S1 to S3 and travels below the PSIS to give sensation to the posterior thigh to calf. A diagnosis can be made by symptoms with palpation of the iliac crest.

## CASE REPORT

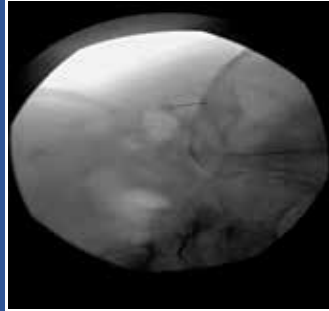
78 year-old female with past medical history of cervical cancer, lumbar scoliosis, and L2/L3 right sided disk herniation with foraminal stenosis presents to our outpatient pain clinic for chronic low back pain with radicular symptoms. Low back pain is 5-6/10, but can get up to 7/10 via VRS. Pain is alleviated with sitting and resting. Pain is exacerbated by bending at the lumbar spine and prolonged standing. Patient is sp trigger points in the RIGHT gluteus medius and iliobial band, multiple LESI, RIGHT SIJ, RIGHT hip IA injections, RIGHT Lumbar L3-L5 MBB RFA. Patient initially had great relief from the RIGHT SIJ however they decreased in efficacy.

Patient has tried topical and oral NSAIDS, acupuncture, physical therapy, opioids (Tramadol), and neuropathic pain medications (Gabapentin).

Patient does not want surgery and requested to move forward with another interventional option. We offered a RIGHT cluneal nerve block on 4/9/2021 for both diagnostic and therapeutic uses.

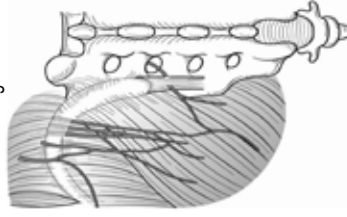
## Discussion

The patient was brought into the procedure room and placed in the prone position on the fluoroscopy table. AP fluoroscopy was used to identify and mark the superior border of the ilium. The skin and subcutaneous tissues in these identified areas were anesthetized with 1% lidocaine. A 25 gauge 3.5 inch spinal needle was advanced toward three points marked along the ilium under fluoroscopic guidance. Once bone was contacted, 1ml of contrast solution was injected. An appropriate pattern without vascular uptake was noted. Negative aspiration was confirmed and 0.5 mL of 2% lidocaine was injected at each level. Patient had 100% pain relief after a RIGHT cluneal nerve block on 4/9/2021 after the procedure which lasted up to 4 hours after the procedure.



## CONCLUSIONS

The middle cluneal nerve is a sensory nerve that innervates the gluteal region that can mimic symptoms of low back pain if it is trapped under the posterior sacroiliac ligament. Management of this condition is via nerve blocks or decompression surgery. We opted to utilize peripheral nerve stimulation as this patient was refractory to medical management.



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# Increased Spinal Cord Stimulation Trial Efficiency and Pain Relief Using Neural Dosing and Precise Targeting of Sub-Perception SCS

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## BACKGROUND

The use of sub-perception based Spinal Cord Stimulation (SCS) modalities including higher frequencies (10 kHz), lower frequencies (1 kHz), and burst have been shown to elicit pain relief in patients with chronic pain.<sup>1-3</sup> However, sub-perception SCS has now been demonstrated to be clinically effective using frequencies down to 10 Hz.<sup>4,5</sup> Additionally, it was noted in these studies that the area of pain at times overlapped with patient perceived paresthesia. Early outcomes in a recently reported real world, observational case-series utilizing paresthesia as a physiological-based marker for precise targeting of sub-perception stimulation fields, used in combination with neural dosing, now demonstrate significant pain relief with rapid onset of analgesia.<sup>6</sup>

Here, we report real-world observations using a novel SCS therapeutic modality now known as fast-acting sub-perception therapy (FAST) either with or without use of a customized field shape programming algorithm during the trial period in a single-center, observational case-series.

## METHODS

<b>Study Design</b>	Single-center, observational case-series. Data collected by site personnel only
<b>Study Device</b>	Boston Scientific Spectra WaveWriter: <ul style="list-style-type: none"> <li>• Illumina 3D Algorithm with Multiple Independent Current Control (MICC)</li> <li>• Paresthesia-Guided Stimulation Field Targeting, Fast-Acting Sub-Perception Therapy (FAST)</li> <li>• Customized Field Shape Programming (CONTOUR)</li> <li>• 16-contact Infinion Leads</li> </ul>
<b>Follow-up Duration</b>	End of trial outcomes only
<b>Key Inclusion</b>	Real-world chronic pain patients who underwent a temporary trial on-label.
<b>Study Design</b>	Single-center, observational case-series. Data collected by site personnel only

## RESULTS

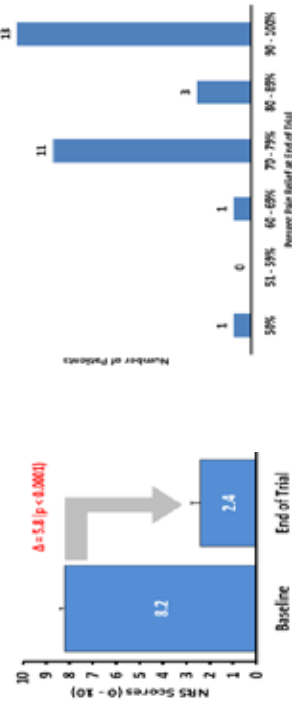
Baseline Characteristics (n = 33)

Gender - Females (%)	66.7% (22/33)
Age [Mean (SD)]	63.5 (13.2) years, n = 33
Pain Location (%) (may have multiple pain locations)	Low Back and Legs (87.9%)
	Lower Limbs (12.1%) Upper Limbs (6.0%)
Baseline NRS [Mean (SD)]	8.3 (1.3), n = 33
Follow-up duration [Mean (SD)]	End of Trial per standard of care

33 patients underwent a temporary trial at a single center July 2020 - Oct 2020

- All patients received fast-acting sub-perception therapy during the trial (alone or in combination with customized field shape programming).
- Of these 33 patients, 29 were FAST responders (≥50% pain relief) at end of trial

Overall Pain Scores at End of Trial [FAST Responders]



- A 5.8-point improvement (8.2 → 2.4, p < 0.0001) was reported at End of Trial compared with Baseline for FAST responders at end of trial (n = 29)
- Among FAST responders (n = 29), 55% (16 of 29) reported ≥ 80% pain relief at end of trial
- A 5.4-point improvement (8.3 → 2.9, p < 0.0001) was noted for all patients who underwent a trial (n = 33)

## CONCLUSIONS

- Preliminary data from this single-center, real-world observational case series (n = 33) demonstrates that significant pain relief (> 5 NRS points) may be achieved with a novel fast-acting sub-perception (FAST) alone or in combination with customized field programming during the trial period.
- Among FAST responders (n = 29)
  - Δ = 5.8-points (8.2 → 2.4, p < 0.0001, FAST responders n = 29)
  - 55% reported ≥ 80% pain relief at end of trial
- The use of customized field shape programming combined with fast-acting sub-perception has the potential to improve the SCS patient experience.

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## DISCLOSURES

Study sponsored by Boston Scientific. Lilly Chen and Roshini Jain are employees of Boston Scientific.



# Long-Term Outcomes of an SCS System Capable of Multiple Neurostimulation Modalities: A Randomized Controlled Trial (COMBO)

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## BACKGROUND

Several published pre-clinical Spinal Cord Stimulation (SCS) studies have shown that stimulation of different neuronal targets (e.g. Dorsal Horn, Dorsal Column, etc.) helps to more robustly modulate neural activity, and in turn, perception of pain.1-4 We hypothesized that therapeutic neurostimulation configured in a manner to allow for stimulation of multiple simultaneous targets (i.e. with dual use of sub-perception and supra-perception based SCS modalities) may help to enhance pain relief outcomes.

Here, we report one-year outcomes from an ongoing randomized controlled trial (RCT) that evaluated the effectiveness of SCS using sub- and supra-perception modalities as a combination therapy for chronic pain.

## METHODS

<b>Study Design</b>	Prospective, multi-center, parallel group, randomized controlled trial
<b>Study Device</b>	Spectra Wavefilter SCS System (Boston Scientific)
<b>Subjects</b>	89 randomized subjects
<b>Primary Endpoint</b>	Proportion of subjects with ≥50% reduction from Baseline VAS in average overall pain intensity at 3-months post-randomization, with no increase in baseline average daily opioid medications used to treat pain
<b>Study Arms</b>	<ul style="list-style-type: none"> <li>Combination Therapy (customized sub-perception-based field shape algorithm [Conour, Boston Scientific] + parasthesia-based SCS; delivered simultaneously)</li> <li>Conventional: parasthesia-based SCS only (monotherapy)</li> </ul>

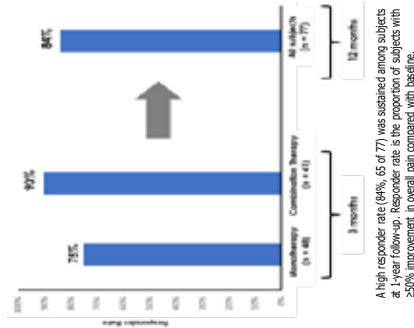


## RESULTS

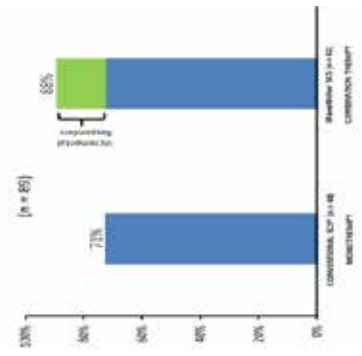
Baseline Characteristics (n = 68)

Age (years) - Mean (SD) n	57.3 (11.86) 89
Gender (Female) - % (n/N)	65.2% (58/89)
Diagnosis for receiving the stimulator (may have multiple diagnosis) - %	
Failed Back Surgery Syndrome (FBSS)	67.4%
Radiculopathy	15.7%
Complex Regional Pain Syndrome (CRPS)	2.2%
Other	14.6%
Average Low Back Pain (VAS) - Mean (SD) n	7.6 (1.0) 89
Average Overall Pain (VAS) - Mean (SD) n	7.4 (1.0) 89
Disability ( Oswestry Disability Index [ODI] - Mean (SD) n)	54.2 (8.9) 89
Duration of low back/pain (years) - Mean (SD) n	16.2 (13.0) 89

Responder Rate (overall pain) up to 1-year



Primary Endpoint Analysis at 3 Months



- The primary endpoint was successfully met based on a pre-specified cohort of 89 randomized subjects (p < 0.001)
- Combination Therapy enabled more subjects to achieve a successful outcome versus monotherapy alone at 3-months (end of randomized phase)

## CONCLUSIONS

- The COMBO RCT met the primary endpoint and all secondary endpoints based on a pre-specified cohort of 89 randomized subjects at 3-months post-randomization.
- Combination Therapy (custom sub-perception-based field shape algorithm + parasthesia-based SCS) enabled a larger number of study participants to achieve a successful outcome versus those using Parasthesia-based SCS (monotherapy) alone at 3-months post-randomization compared with Baseline.
- At 1-year follow-up:
  - High responder rate (94%, 65 of 77) in all subjects
  - 90% of subjects had a successful clinical response based on responder rate, disability improvement, patient global impression of change and treatment satisfaction
  - A programming algorithm designed to provide customized neurostimulation fields clinically applied in combination with conventional, parasthesia-based SCS can produce highly effective outcomes for treatment of chronic neuropathic pain.

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## DISCLOSURES

This trial is sponsored by Boston Scientific. Drs. Wallace, North, Washabaugh, Lee, Phillips, and Trainor have consulting agreements with Boston Scientific. Lilly Chen and Roshini Jain are employees of Boston Scientific.

# Retrograde Spinal Cord Stimulation for Persistent Genital Arousal Disorder

## Arousal Disorder

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### Introduction

First described in 2001, Persistent Genital Arousal Disorder (PGAD) is a rare and painful disorder more commonly seen in females. Some refer to PGAD as an overly sensitive or persistent sexual arousal syndrome (PSAS) or restless genital syndrome (RGS). While the case report will focus on PGAD, collectively, this group of disorders is mainly understood as and made research conditions affecting the daily lives of countless patients. PGAD has mostly been investigated by psychologists with physicians largely unaware of it (1). It is a potentially debilitating disorder of unwanted genital sensation and arousal that is generally spontaneous and unrelated to any feelings of sexual desire (2). There are only 5-10 documented cases of diagnosis and treatment of this condition in male patients. The working definition of PGAD consists of

1. Persistent physical arousal in the genital area lasting hours or days and does not subside completely on its own
2. The symptoms are not diminished or resolved by ordinary orgasm thoughts
3. Symptoms of arousal are experienced in the absence of conscious thoughts of sexual desire or interest
4. Persistent genital arousal can be triggered not only by a sexual activity but also by non-sexual stimuli or by no apparent stimuli at all
5. Arousal symptoms feel unwanted, intrusive, unwanted and the symptoms cause at least a moderate degree of distress (3).

Of unknown certain medical causality, most patients are referred for mental health treatment, but as research suggests, there are associations with neurological symptoms and conditions (1). Some cases are attributed to brain effects of serotonergic and dopaminergic drugs (1). Fregenhann and Komisaruk established the firmest association to date, with sacral T10-L10 cysts forming and can damage sensory ganglia and roots (1). A recently published report associated PGAD with disorders and lesions of the lower spinal cord, roots, and nerves that control sexual arousal and orgasm (1). Hypothesizing that at least some PGAD cases arise from lesions affecting the sacral sensory networks that transmit sexual arousal – that it is a disorder of spinal sensation skin to neuropathic pain and itch. A range of treatments have been explored primarily in case studies, from electroconvulsive therapy to oral medications, with variable success rates and some suggesting a psychosomatic condition (4,5). Our case report highlights on the neuropathic symptoms associated with this debilitating disorder and a successful alternative treatment modality used to treat our male patient.

### Objective

To explore the efficacy of an alternative treatment for persistent genital arousal disorder (PGAD) not yet described in the literature or in any published case reports discovered in our literary search. We hope this provides useful information for others to use as part of their diagnosis and treatment management.

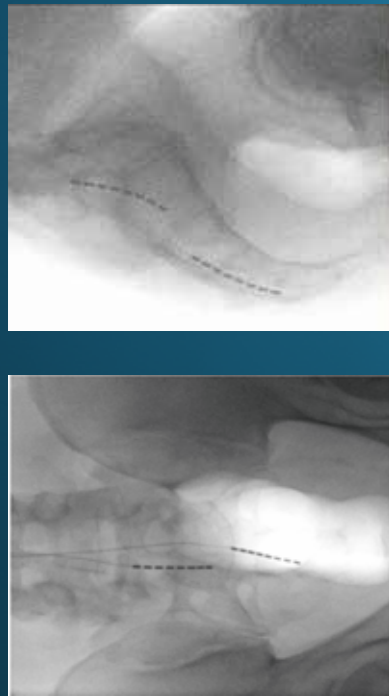


Figure 1: Contact leads placed at S2 and S4; leads were placed retrograde from L1-L2-T11 interlaminar space (not pictured)

### Methods

Our case report describes a 44-year-old male with a past medical history significant for chronic post-traumatic stress disorder, obesity with body mass index of 42, insomniac myalgia after herpes zoster, hypertension, hypertriglyceridemia, degenerative disc disease, difficulty defecating, and testicular hypofunction. His surgical history is significant for left inguinal hernia mass removed in 2010.

Patient reports initiation of symptoms in 2016 which he describes as a sudden, acute left greater than right sided low back pain radiating to his perineum. He rated his pain scale as a seven out of ten. He describes an acute painful tingling sensation that is sharp and burning feeling. He also reports this sensation is associated with left lower extremity dull leg ache during the day and at night. He reports the painful sensations are worse when he is seated or walking. The pain is altered by transcutaneous electrical nerve stimulation (TENS) unit but not normally. He experienced diminishing results over time. He also noted a perineal sensation of ejaculation which was improved by any specific triggers that he could ascertain. Patient's comprehensive review of systems was unremarkable including but not limited to negative for recent infection, bowel or bladder incontinence, weakness or numbness.

Neurologic physical examination unremarkable with bilateral lower extremity strength and sensation intact and equivalent. Bilateral lower extremity pulses intact. Normal deep tendon reflexes in bilateral lower extremities.

Patient with allergies to penicillin and sulfas drugs. Medication list included: acyclovir, amitriptyline, baclofen, duloxetine, gabapentin, mometilast, naproxen, doxycycline, testosterone topical gel.

### Results

The patient presented to interventional pain clinic with the initial complaint of back pain radiating to his perineum with associated PGAD symptoms as described previously. A ganglion impar block was attempted in early 2019, which reliefs of his pain for 5 days and he conveyed the leg seizure-like activity with ejaculation was unchanged. The patient returned to interventional clinic in the summer of 2020 with the same initial complaint at which time he received a caudal epidural injection that provided significant relief of his back pain but still reported constant feeling of arousal. In November 2020, the patient received a bilateral pudendal nerve block. His subsequent perineal arousal sensation had resolved and pain in his tail bone reduced to 50% for 48 hours, however, the pain returned.

One month later, we attempted bilateral S1 transforaminal epidural steroid injections to see if there was improvement in both pain and arousal symptoms. The assessment was made that if positive but short lived or no response to this procedure, SCS (spinal cord stimulator) trial would be considered. In January 2021, the patient received a trial SCS implant with final trial position, right sided S4 posteriorly and left side S2 anteriorly. On his initial postoperative visit patient reports 95% relief with SCS trial leads. Following successful permanent SCS placement, the patient reports 98% reduction in symptoms. S1-S2 on the left and S3-S4 lead on the right in the paramedian region. He reports a return of lower left sided back pain has been unmasked now that his arousal pain has resolved. At his one-month postoperative visit following retrograde SCS placement, the patient reported excellent pain relief as well as healed incisions without signs or symptoms of infection.

### Conclusion

As our case report emphasizes, the presentation of PGAD comes in a variety of etiologies as well as patients. The most important aspect is recognizing this rare condition to ensure optimal management and treatment options can be specific for each patient. It is theorized that his experience was possibly brought on by his transverse myelitis after a herpes zoster. Currently, little is known about PGAD biological correlates, etiologies, or definitive treatments (4). Some research implies the persistent arousal sensation that is temporarily resolved with pudendal block could be suggestive of possible autonomic pudendal nerve etiology. A component of this etiology was likely present in our patient given his complete yet temporary resolution of symptoms following the bilateral pudendal block. Initial treatment attempts with medication management and titration of oral medications did not appear to improve our patients' symptoms. Ultimately, we found the placement of retrograde SCS was largely curative with successful resolution of our patients' arousal symptoms and pain. This highlights the fact that still much research is required in this disorder, as each patient is uniquely responsive to treatment modalities with PGAD.

Of note, following retrograde SCS trial placement the patient did report return of previous left lower extremity weakness that was unchanged. Neurologic assessment remained consistent with previous evaluations in which strength and sensation remained intact bilaterally. After permanent SCS placement he reported a return of lower left sided back pain. We proposed this pain was possibly unmasked following the resolution of his arousal pain.

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# Real-World, Prospective, Multicenter Study Outcomes Using an Interspinous Spacer for Lumbar Spinal Stenosis (LSS)

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## BACKGROUND

The introduction of interspinous spacers, a less invasive treatment option for patients with moderate Lumbar Spinal Stenosis (LSS) symptoms has been increasingly adopted over the last several years.

A growing body of published clinical evidence has demonstrated excellent long-term clinical benefit with sustained pain relief, improved quality of life and medication reduction up to 5 years post-implant.<sup>1-4</sup> Additionally, real-world outcomes with the use of interspinous spacers suggest high patient satisfaction and overall improvement.<sup>2</sup>

Here, we report an ongoing prospective, multi-center real-world outcomes study using an interspinous spacer for LSS.

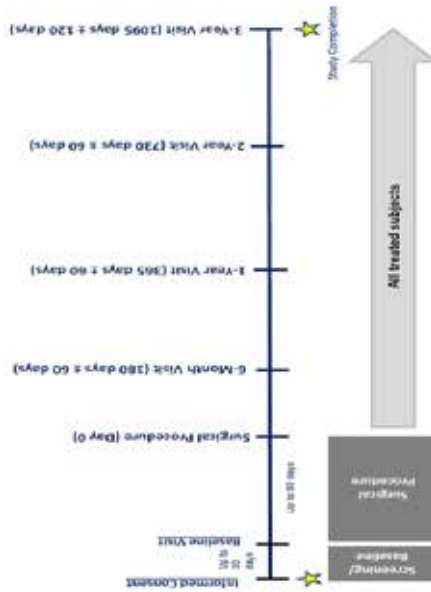
## METHODS



**Boston Scientific Superior Indirect Decompression System (IDS)**

## STUDY DESIGN

Prospective, global, multi-center outcomes study



### Key Clinical Endpoints:

- Proportion of subjects with improvement in low back/leg pain
- Change in mean low back/leg pain intensity and with worse pain along with ambulation
- Change in overall disability, walking and quality of life
- Change in self-defined Functional Objectives

### Key Inclusion Criteria:

- Scheduled to receive or previously received a commercially approved Boston Scientific Indirect Decompression System, per local Instructions for Use (IFU).

## CONCLUSIONS

Real-world outcomes with the use of interspinous spacers suggest high patient satisfaction and overall improvement.<sup>2</sup>

However, long-term, real-world data, beyond 1-year is crucial to further support the clinical adoption of minimally-invasive IDS in patients with neurogenic claudication associated with LSS.

- Study is currently ongoing.
- A total of up to 3000 subjects are expected to be included in the study

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## DISCLOSURES

This study is sponsored by Boston Scientific. Holly Kaufman, Lilly Chen and Roshini Jain are employees of Boston Scientific.

# Real-World Outcomes Using Radiofrequency Ablation for Chronic Knee Pain

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## BACKGROUND

Radiofrequency ablation (RFA) has long been shown to be effective for chronic intractable pain with a wide variety of etiologies. There are numerous studies evaluating RFA for treating chronic pain, including single-arm, randomized controlled studies and retrospective case series. To date, the clinical efficacy of RFA (using thermal or pulsed radiofrequency approaches) for use in various pain indications including (but not limited to): cervicogenic headaches, occipital neuralgia, lumbar radicular pain, cervical radicular pain, zygopophysial (facet) joint pain, disc herniation, discogenic pain, spinal foramen stenosis, radiculitis, knee pain, and pain of the sacroiliac joint has been reported.<sup>1-10</sup> Most studies have shown improvement in outcomes for patients with chronic pain treated with RF compared to baseline, although some control groups also improved correspondingly. Gathering real-world utilization of radiofrequency techniques and impact to outcomes will add to the compendium of existing evidence. Hence, we report here outcomes in patients who underwent RFA procedure for the treatment of their chronic knee pain.

## METHODS

Study Design	Multi-center, Observational, Case-Series (all data collected by site personnel, NCT01550575)
Study Device	Commercially-available Boston Scientific (formerly Cosman) RFA Systems used in the treatment of chronic pain.
Analysis Cohort	68 subjects with chronic knee pain at 6 sites in USA
Key Inclusion	Received RFA with Boston Scientific Systems per local directions for use

## RESULTS

Baseline Characteristics (n = 68)

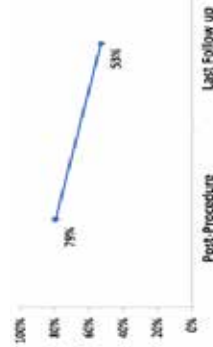
Gender - Females (%)	66.2% (45/68)
Age (Mean (SD))	70.0 (11.0) years n = 65
Baseline Overall NRS (Mean (SD))	7.42 (2.20) n = 68
Follow-up Duration (Mean (SD))	117 (174) days n = 68
Number of Procedures - Single (%)	86.8% (59/68)

RFA Technique (79 procedures)

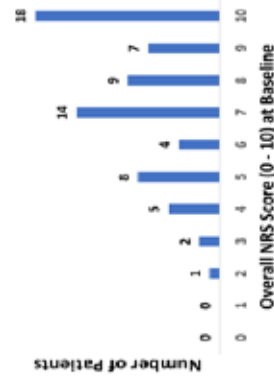
Type of RFA [n = 79 procedures]	Thermal (100%)
Number of diagnostic blocks (%) [n = 58*]	1 (55.2%)
	2 (17.2%)
	≥3 (27.6%)
Number of Burns (%) [n = 76*]	3 (76.3%)
	Other (20.8%)
	80 °C (75.3%)
Burn Temperature (%) [n = 77*]	85 °C (6.5%)
	90 °C (16.9%)
	Other (1.3%)
Burn Time (%) [n = 76*]	60 s (23.7%)
	90 s (59.2%)
	120 s (15.8%)
	Other (1.3%)

Responder Rate (n = 68)

Proportion of patients with >30% pain relief post initial procedure\*



Baseline Distribution of Overall Pain (n = 68)



\*Data as available for 79 procedures in 68 patients

## CONCLUSIONS

- Preliminary analysis based on this real-world multicenter, observational, case-series demonstrated a high responder rate post initial procedure for patients being treated with RFA for knee pain suggesting that thermal RFA can be effective in obtaining knee pain relief
- These results suggest that improvement in pain outcomes with the use of traditional RFA can be achieved in patients with chronic knee pain.

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## DISCLOSURES

Study sponsored by Boston Scientific. Dr. Atallah has a consulting agreement with Boston Scientific. Kristen Lechletter, Lilly Chen, and Roshini Jain are employees of Boston Scientific.

# UTILIZATION OF DIFFERENT ENERGY PROFILES OF DIFFERENTIAL TARGET MULTIPLEXED™ SPINAL CORD STIMULATION

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## BACKGROUND

Differential Target Multiplexed (DTM™) spinal cord stimulation (SCS) is an advanced, proprietary stimulation pattern that has been developed through years of preclinical research, which has expanded our understanding of mechanism of action to include glial cell modulation.<sup>1,2,3,4</sup> This work was then translated into a randomized controlled trial showing superior back pain relief compared to traditional SCS.<sup>5,6</sup> Recently developed stimulation patterns can be associated with higher energy requirements than traditional SCS, which can limit the access of therapy to some patients. Exploring energy profiles has the potential to expand the therapy to meet individualized patient needs. Some waveforms have employed manipulation of stimulation parameters such as frequency, amplitude, pulse width, as well as therapy cycling in attempts to claim sustained efficacy with reduced energy consumption. Additional preclinical and clinical research is needed to demonstrate the physiologic effects of specific parameters as well as their ability to provide sustained pain relief.

## OBJECTIVES

Characterization of efficacy and energy use of a DTM stimulation pattern with a reduced-energy profile.

## METHODS

A prospective, multicenter, post-market feasibility study enrolled a cohort of patients implanted with a rechargeable neurostimulation system to treat chronic intractable back and leg pain consistent with commercial labeling.

The analysis cohort consisted of enrolled subjects who were implanted for at least three months on stable stimulation programming to standard of care (SOC) parameters with a cumulative frequency setting of ≥200Hz and had pain relief (NPRS ≤ 5). After enrollment, subjects went through a therapy washout period of about 1 week following which, subjects were programmed to a DTM stimulation pattern with a reduced-energy profile. An analysis was completed for subjects with available data at baseline and 1-month post therapy adjustment who remained programmed to the reduced-energy stimulation pattern. Outcomes included Numeric Pain Rating Scale (NPRS) scores (recorded in a daily pain diary during the follow-up periods) and patient satisfaction (recorded at the follow-up visits).

## RESULTS

Sixteen subjects were enrolled in the study between October 30, 2020, through March 24, 2021, and met the cohort population definition for analysis. Subjects had an average age of 62.1 years and 62.5% were female. The main etiologies included post-laminectomy pain/failed back surgery syndrome (75.0%), radicular pain syndrome (18.8%), and degenerative disc disease (6.3%). Average time since SCS implant was 1.7 years, with a range from 4 months to 3.3 years.

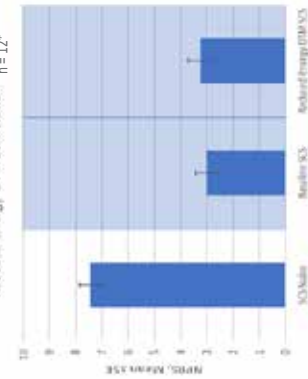
The mean of the pre-SCS pain scores (prior to enrollment) was 7.46 (SE ±0.40). The mean of the baseline active SCS pain scores (at the time of enrollment) was 3.00 (SE ±0.43). Between enrollment and 1-month follow-up, 3 subjects discontinued reduced-energy SCS and returned to SOC programming. One additional subject withdrew from the study for reasons unrelated to the therapy.

The mean NPRS for the subjects who remained on reduced-energy programming at the 1-month follow-up after washout was 3.25 (SE ±0.46) as reported in Figure 1.

All subjects were somewhat to very satisfied with their therapy at baseline and maintained satisfaction after reprogramming to reduced-energy DTM stimulation at the 1-month follow-up.

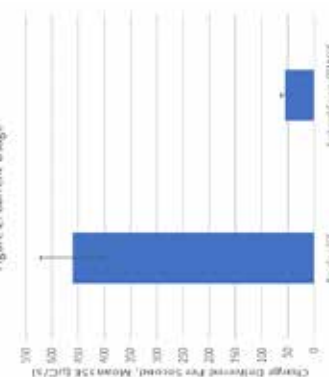
Subjects SOC stimulation parameters resulted in an average current drain of 461 (SE ±60) µC/s. Reduced energy DTM stimulation at 1-month resulted in an average current drain of 56 (SE ±8) µC/s, as reported in Figure 2. This equated to an 86% reduction in current usage.

Figure 1: Overall Pain in Subjects Programmed to Reduced-Energy DTM Stimulation, n = 12\*



\* 1 subject had a missed visit at 1-month (Reduced-Energy DTM SCS). Subject X reported a mean NPRS of 3 at 19 days follow-up.

Figure 2: Current Usage



## CONCLUSIONS

This study provides early feasibility data characterizing the efficacy of a novel DTM stimulation pattern with a reduced-energy profile. After one month of therapy, patients were able to achieve a similar degree of pain relief and maintain therapy satisfaction with reduced-energy DTM SCS compared to their stable, pre-study SCS settings. The reduced-energy DTM parameters used in the study resulted in an 86% reduction in charge delivered per second as measured in microcoulombs per second.

Low-energy stimulation patterns can provide effective pain relief and an opportunity to further tailor therapy approaches for individual patients. Additional potential benefits include extending battery longevity for recharge-free devices and reducing the recharge frequency for rechargeable devices. For some patients, this may help to overcome barriers to therapy adoption.

Further research is needed to demonstrate the sustainable effectiveness and benefits of DTM stimulation with a reduced-energy profile.

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## DISCLOSURE

This study was supported by Medtronic.



