Spinal Cord Stimulation for Painful Diabetic Neuropathy

Allen Shoham, MD

Interventional Pain Physician (Anesthesiologist)

Apex Spine Institute Co-Founder & Medical Director

APEX SPINE INSTITUTE

Apex Spine Institute Overview

- Comprehensive Pain Management Center
- Interventional Pain Management
- Spinal Surgery (Dr. Sahota)
- 7 Medical providers (2 physicians, 2 NP's, 3 PA's)
- Imaging center including x-ray and MRI
- Outpatient Ambulatory Surgery Center for Interventional Pain procedures and Spinal Surgery (Overnight 23hr stay)
- Open to new patients for medical pain management including chronic opiate management when necessary

APEX SPINE INSTITUTE

Audience Questions

- Who here has patients with painful diabetic neuropathy?
- Who here has used medications to treat painful diabetic neuropathy?
- Who here has referred patients with painful diabetic neuropathy for spinal cord stimulation?

APEX SPINE INSTITUTE

Objectives

- Painful Diabetic Neuropathy (PDN) is a progressive and debilitating disease.
- Many patients are suffering with conventional medical management (CMM) alone.
- Spinal Cord Stimulation (SCS) is a safe and effective long-term treatment for those with PDN.
- SCS is proven to reduce pain, improve mood and sleep with a high patient satisfaction rate.
- Consider referral for SCS as a treatment option for patients with refractory painful diabetic neuropathy despite conventional medical management.

APEX SPINE INSTITUTE

Painful Diabetic Neuropathy

- 37 Million Americans have diabetes (11% of population)[1]
- 20% of diabetics will develop painful diabetic neuropathy (PDN)[2]
- Distal Symmetrical Polyneuropathy (DSPN) is the most common form of diabetic neuropathy
- Diabetic neuropathy leads to gradual loss of integrity of the longest nerve fibers. Symptoms beginning distally and symmetrically.
- Symptoms include numbness, tingling, and neuropathic pain, appear initially in the toes and feet and migrate proximally in a stocking distribution.

APEX SPINE INSTITUTE

Painful Diabetic Neuropathy

- ~50% of patients with diabetic neuropathy develop painful diabetic neuropathy (PDN).
- PDN is a progressive condition causing extremity pain, paresthesia, burning, and shooting pain that is typically worse at night and disrupts sleep.
- PDN therapies target pain management and glycemic control to mitigate progressive nerve damage
- There are currently no disease-modifying treatments. [8-11]
- Progressive symptoms can be debilitating; extremity numbness increases fall risk
- Loss of protective sensation in feet → associated with foot ulceration, amputation and increased mortality. [3,4]

APEX SPINE INSTITUTE

Conventional Medical Management for PDN

- Typical first-line agents include Gabapentinoids (Gabapentin & Lyrica) and serotonin-norepinephrine reuptake inhibitors—Duloxetine, Venlafaxine.

- Tricyclic antidepressants are commonly prescribed. Refractory pain may be treated with opioids

- A meta-analysis of RCTs on neuropathic pain medication found that the number needed to treat (NNT) for 50% pain reduction ranged from 4 to 11. [12]

- Gabapentin and pregabalin are commonly prescribed for PDN, but long-term adherence is poor, >60% of patients discontinuing by 6 months.

APEX SPINE INSTITUTE

Conventional Medical Management for PDN

- Duloxetine reveals a similar pattern, with 50% discontinuing by 6 months.
- Insufficient pain relief or side effects lead to poor long-term medication compliance
- Most of these patients do not switch to an alternative therapy, leaving their progressive pain condition untreated. This represents a large patient population with significant unmet needs. [13]

APEX SPINE INSTITUTE

Spinal Cord Stimulation (SCS) for PDN

- SCS is effective in treating PDN refractory to med management
- Leads are placed in the epidural space to stimulate the spinal cord electrically
- Various mechanisms of action have been proposed
- Think of electrical stimulation of the spinal cord as a medication that can be dosed by adjusting amplitude, pulse width, rate and electrode selection at various levels along the spinal cord

APEX SPINE INSTITUTE

SCS Animation

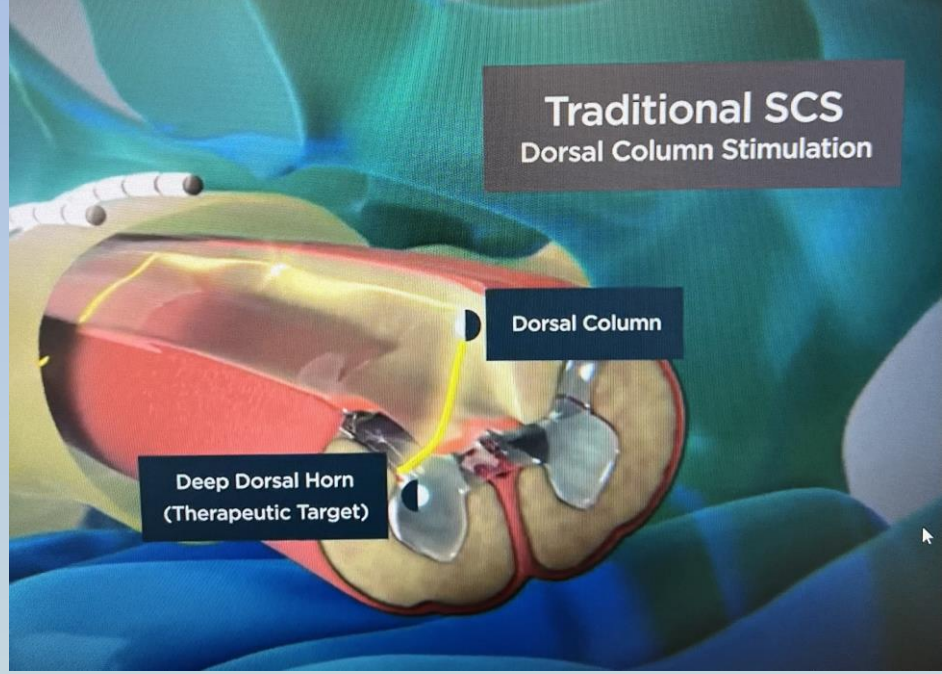
- https://www.youtube.com/embed/mbvdKLORuOs

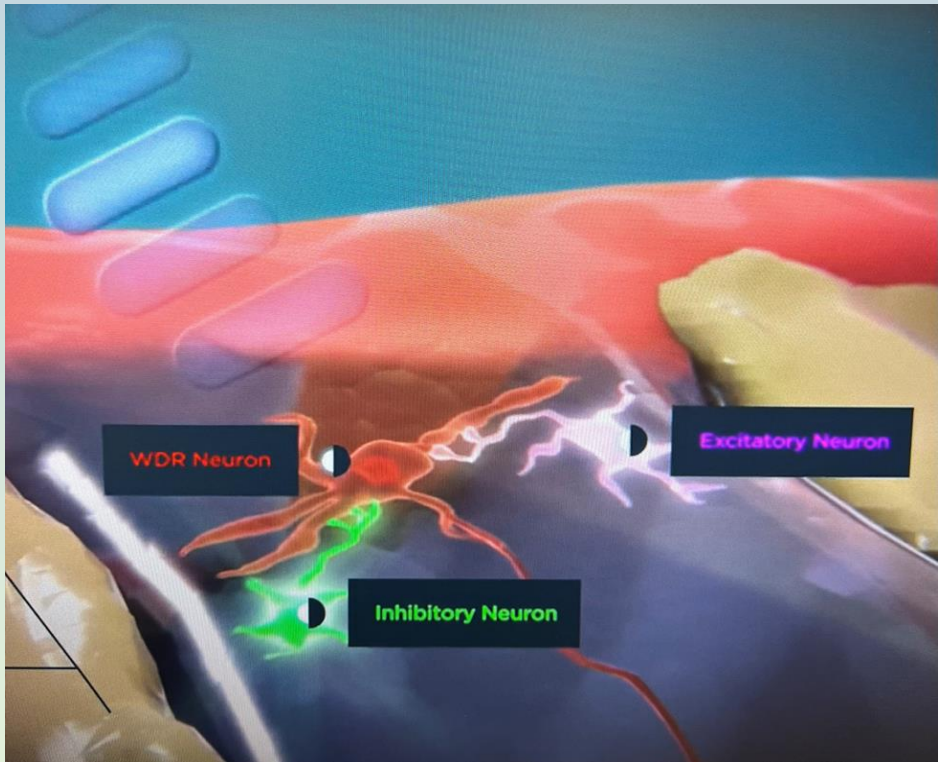
APEX SPINE INSTITUTE

Low vs High Frequency SCS

- **Low frequency** SCS stimulates the dorsal Column→ creates paresthesia in painful area

- **High frequency** SCS (10kHz) is paresthesia free. It affects deeper into the dorsal horn which stimulates inhibitory neurons, reducing hyperactivity of WDR neurons implicated in chronic pain.





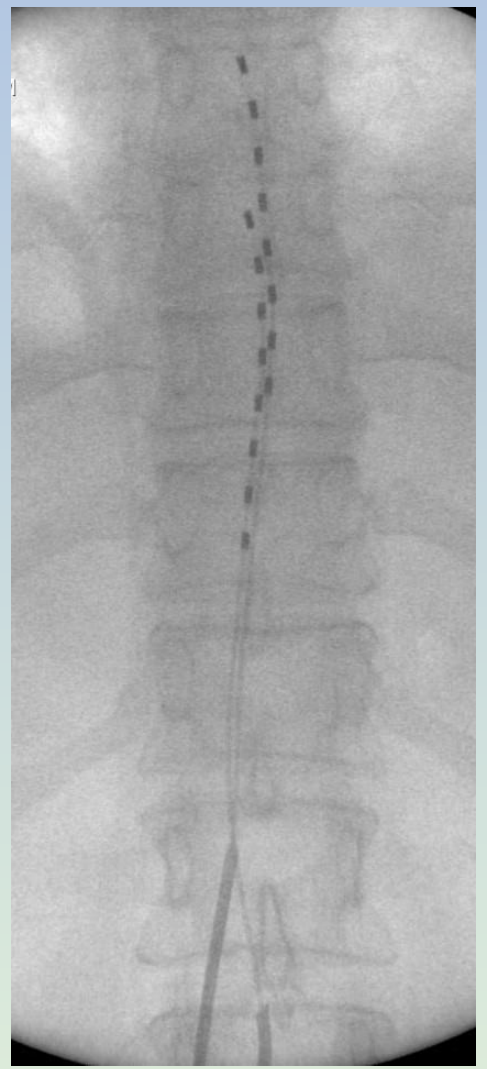
APEX SPINE INSTITUTE

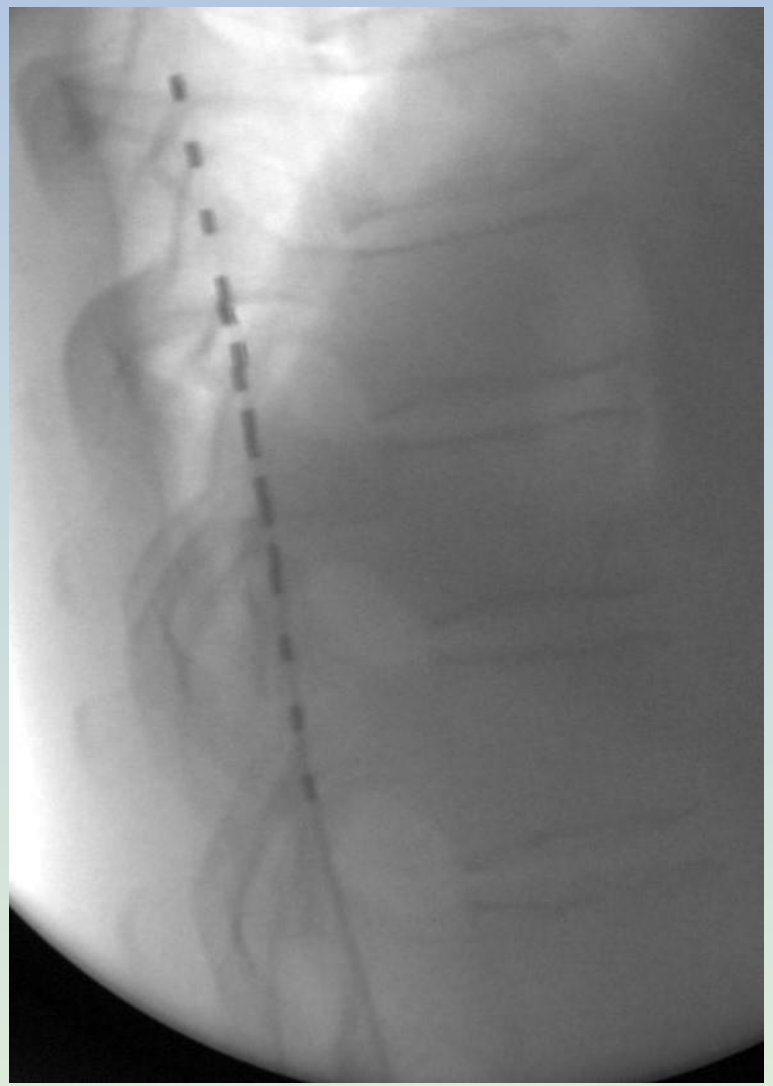
SCS Trial for PDN

- Device is trialed by the patient after a minimally invasive procedure
  - “Try before you buy”
- SCS therapy is evaluated during a trial period to assess efficacy of SCS for painful neuropathy. Trial duration is 5-7 days.
- During the trial period, pain relief and changes in quality of life are noted
- If SCS therapy provides >50% improvement in pain and quality of life→ permanent implantation may be pursued
- Outpatient procedure done under local with minimal sedation, usually takes less than 30 minutes

APEX SPINE INSTITUTE

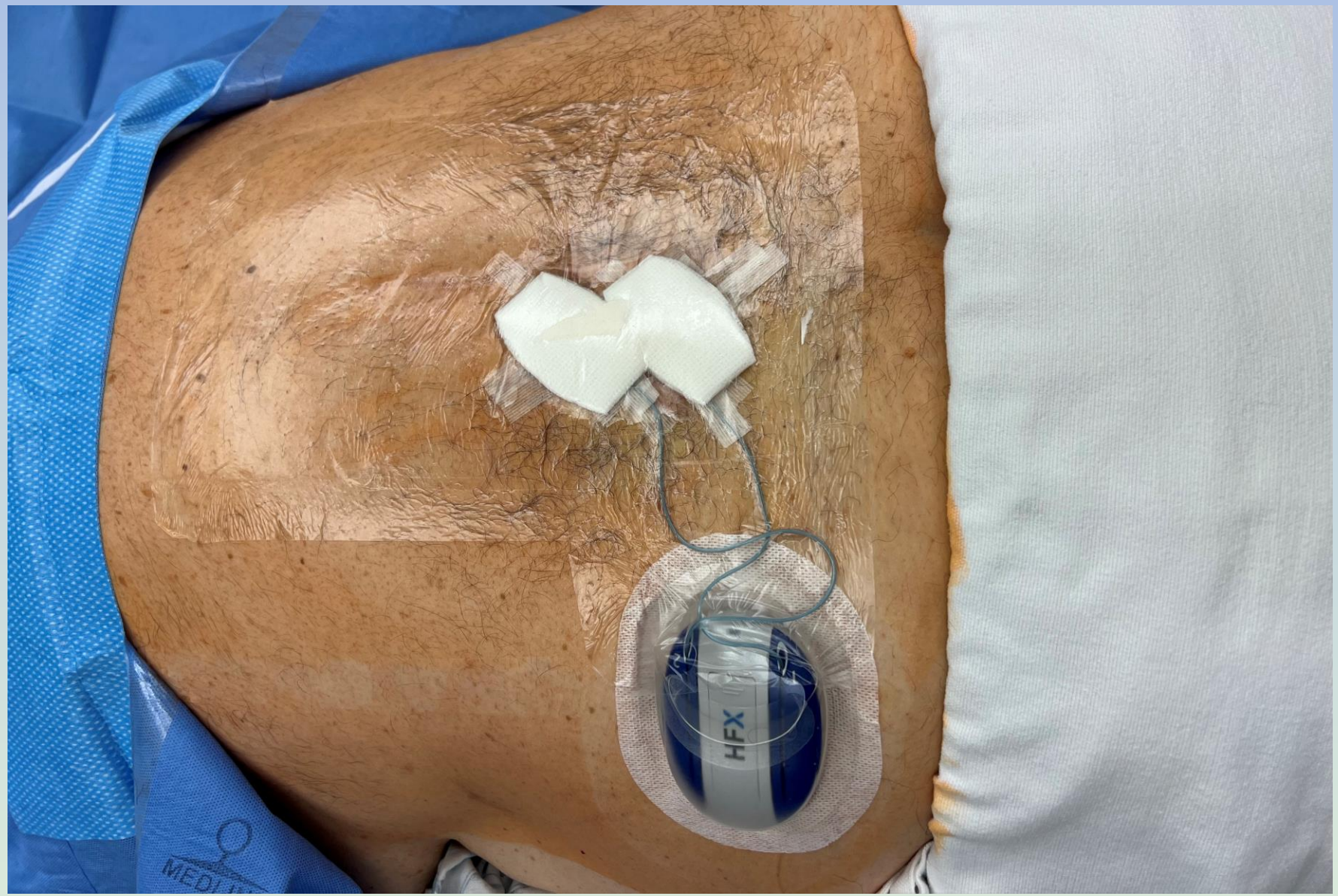
Spinal Cord Stimulator (SCS) Trial





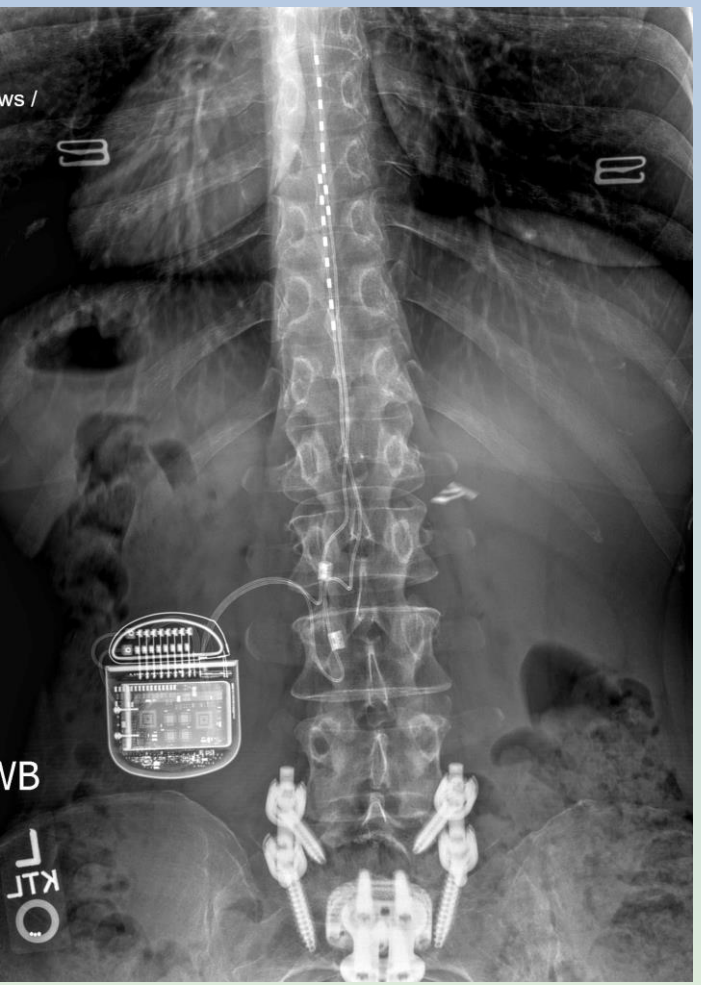
- Fluoroscopic guided with sterile surgical conditions after prophylactic antibiotics
- Using LOR technique, a 14g epidural needle is advanced into epidural space
- SCS Lead is then advanced into the posterior epidural space to desired vertebral levels (T8-T11 for PDN)
- Needles are then removed and leads anchored to skin with steri-strips→leads attached to external pulse generator

APEX SPINE INSTITUTE



APEX SPINE INSTITUTE

SCS Permanent Implantation



- Outpatient surgical procedure under sedation/MAC or general anesthesia with SSEP neuromonitoring
- Leads are placed in same manner through introducer 14g epidural needle using LOR technique under live fluoroscopic guidance
- Leads are anchored to fascia then tunneled under the skin to pocket where IPG is implanted, usually above iliac crest

APEX SPINE INSTITUTE

Contraindications for SCS

- Uncontrolled psychiatric disorders
- Unable to stop anticoagulation
- Systemic Infection
- Coagulopathy
- Thrombocytopenia

APEX SPINE INSTITUTE

SCS Complications/Risks

- Rare, but possible risks of bleeding, infection and neurologic injury are discussed with all patients
- Lead migration (most common) 2-12%
- Infection (2-5)% in most SCS literature
- Key PDN study with diabetic population of HbA1 <10 showed a 5.6% wound complication rate. [14]
- Pocket site discomfort
- IPG failure, electrode fracture

APEX SPINE INSTITUTE

What SCS Works Best For PDN?

- Many companies offering SCS devices (NEVRO, Boston Scientific, Medtronic, Abbott)
- NEVRO has exclusive patent on paresthesia-free therapy at 1,500Hz or higher, no other companies allowed to use high frequency stimulation until patent expires
- Both low and high frequency SCS have been shown to give clinically meaningful improvements in pain, but high frequency (10 kHz) has proven superiority

Data Review: High Frequency (NEVRO 10 kHz) vs Low Frequency SCS for Treatment of PDN

Systematic Review

Indirect Comparison of 10 kHz Spinal Cord Stimulation (SCS) versus Traditional Low-Frequency SCS for the Treatment of Painful Diabetic Neuropathy: A Systematic Review of Randomized Controlled Trials

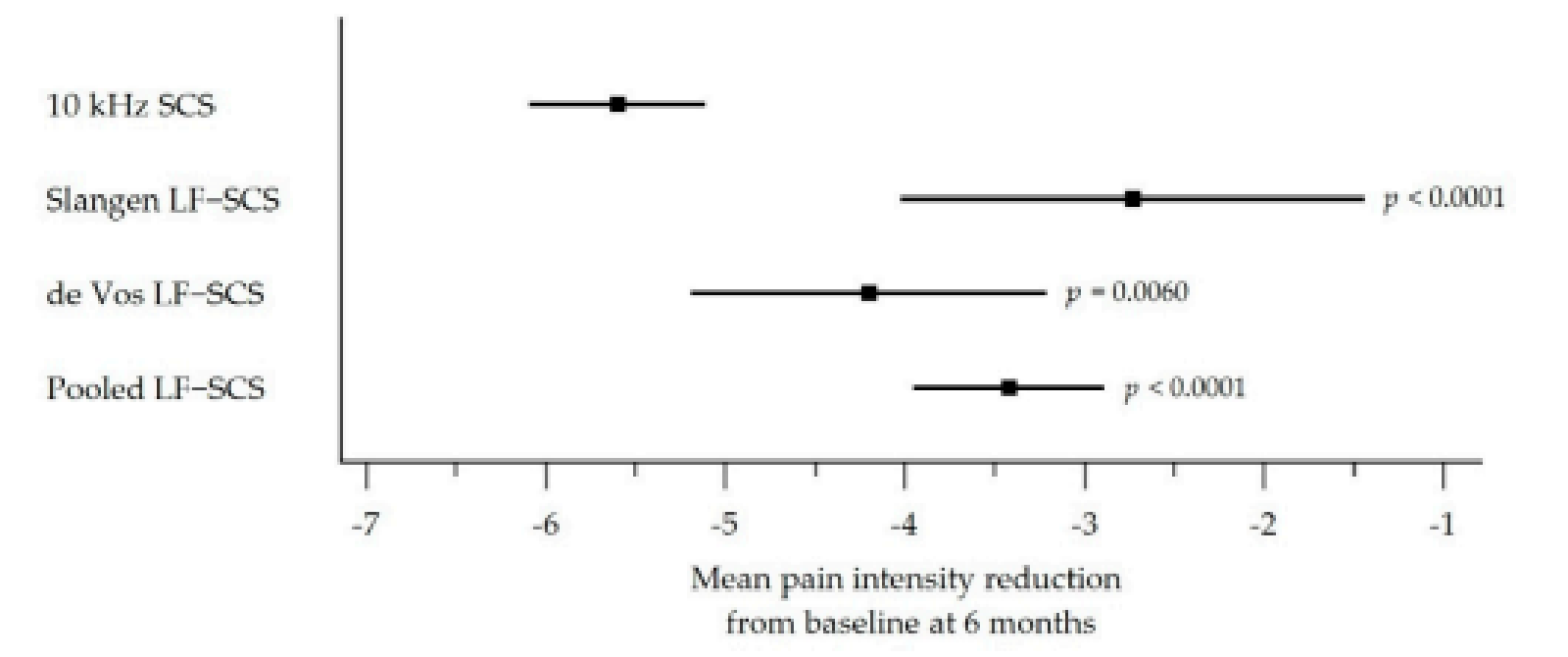
Bryan C. Hoelzer [1], Deborah Edgar [2], Shiao-Ping Lu [3] and Rod S. Taylor [4,5,6,*]

- Data at 6-months comparing 3 studies meeting eligibility criteria (1 HF 10kHz, 2 Low-Freq SCS)
- Clinically meaningful pain relief was seen with each SCS modality
- Average pain reduction in the 10 kHz SCS cohort was 73.7% compared with 47.5% in the pooled LF-SCS group ($p < 0.0001$)

APEX SPINE INSTITUTE

NEVRO Medtronic St Jude

		LF-SCS Group		
Statistic	**10 kHz SCS [38]**	**Slangen LF-SCS ‡ [39]**	**de Vos LF-SCS [40]**	**Pooled LF-SCS † [39,40]**
Percentage reduction in pain relative to baseline	73.7%	38.7%	57.5%	47.5%



APEX SPINE INSTITUTE

PDN Randomized Controlled Trial (RCT)

To determine whether high frequency 10-kHz Therapy improves outcomes for patients with refractory PDN.

- 216 subjects with diabetes
- ≥5 on pain VAS
- A1c ≤10%
- BMI <45
- 18 US centers randomized 216 subjects 1:1
- Crossover at 6 months with 24-month follow-up (93% of those eligible crossed over from CMM)

Treatments

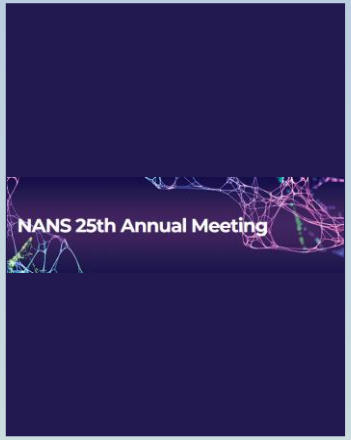
- CMM (Conventional Med Management) vs. 10 kHz Therapy (Nevro Corp.) + CMM.


Effect of High-frequency (10-kHz) Spinal Cord Stimulation in Patients With Painful Diabetic Neuropathy
A Randomized Clinical Trial

6-month[1]
JAMA Neurology
Apr 2021


Durability of High-Frequency 10-kHz Spinal Cord Stimulation for Patients With Painful Diabetic Neuropathy Refractory to Conventional Treatments: 12-Month Results From a Randomized Controlled Trial

12-month[2]
Diabetes Care
Nov 2021



18-month[3]
Presented at NANS
Jan 2022

1. Petersen E. et al. Effect of high frequency (10-kHz) spinal cord stimulation in patients with painful diabetic neuropathy: a randomized clinical trial. JAMA Neurology Apr 2021
2. Petersen E. et. al. Durability of high-frequency 10 kHz spinal cord stimulation for patients with painful diabetic neuropathy refractory to conventional treatments. *Diabetes Care*, Nov 2021.
3. Petersen E. et. al. Durability of 10 kHz spinal cord stimulation for painful diabetic neuropathy: 18-month results. NANS, Jan 2022.
4. Mayo Clin Proc Inn Qual Out n August 2022;6(4):347-360

APEX SPINE INSTITUTE

Identifying the patient: Inclusion criteria and baseline characteristics

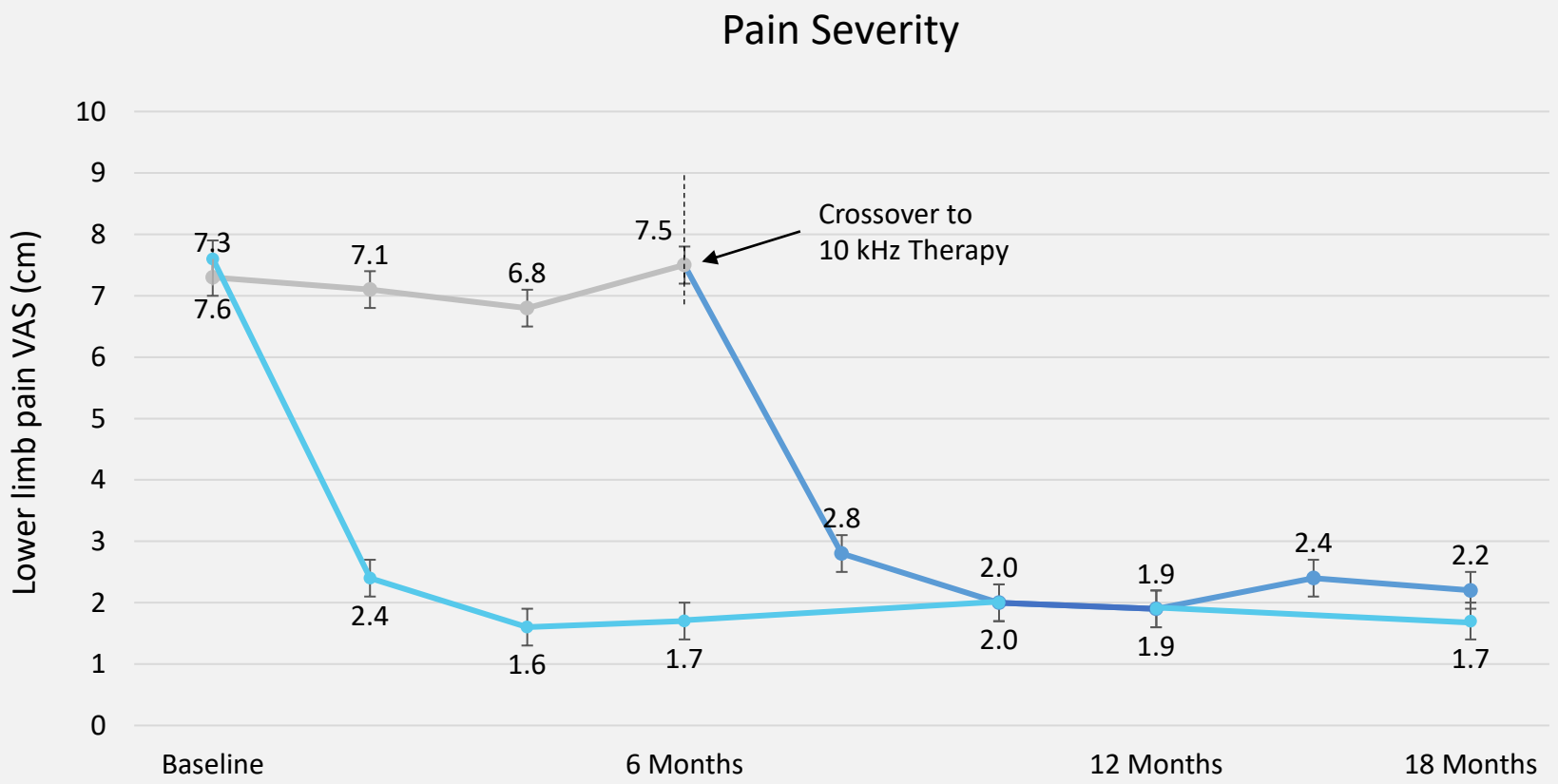
SENZA-PDN RCT Inclusion criteria:

- ☑ PDN diagnosis with symptoms for 12 months or more
- ☑ Refractory to 2 or more pharmacologic treatments (gabapentin or pregabalin and at least 1 other class of analgesic)
- ☑ Lower limb pain intensity of 5 cm or more on a 10-cm visual analogue scale (VAS)
- ☑ Appropriate surgical candidate

Baseline Characteristics	CMM n = 103	10 kHz SCS + CMM n = 113	Standardized Difference*
Age in years, mean (SD)	60.8 (9.9)	60.7 (11.4)	0.01
Male, n (%)	66 (64%)	70 (62%)	0.04
Race			
White, n (%)	85 (82.5%)	87 (77.0%)	0.14
Black or African American, n (%)	13 (12.6%)	18 (15.9%)	
Native Hawaiian or other Pacific Islander, n (%)	1 (1.0%)	3 (2.7%)	
American Indian or Alaska Native, n (%)	0 (0.0%)	2 (1.8%)	
Asian, n (%)	1 (1.0%)	1 (0.9%)	
Other, n (%)	3 (2.9%)	2 (1.8%)	
Diabetes			
Type 1, n (%)	3 (3%)	8 (7%)	0.19
Type 2, n (%)	100 (97%)	105 (93%)	
Duration in years			
Diabetes, mean (SD)	12.2 (8.5)	12.9 (8.5)	0.09
Peripheral neuropathy, mean (SD)	7.1 (5.1)	7.4 (5.7)	0.06
Lower limb pain VAS in cm, mean (SD)	7.1 (1.6)	7.5 (1.6)	0.22
< 7.5 cm, n (%)	57 (55%)	54 (48%)	0.15
≥ 7.5 cm, n (%)	46 (45%)	59 (52%)	
HbA1c, mean (SD)	7.4% (1.2%)	7.3% (1.1%)	0.11
< 7.0%, n (%)	40 (39%)	46 (41%)	0.04
≥ 7.0%, n (%)	63 (61%)	67 (59%)	
BMI, mean (SD)	33.9 (5.2)	33.6 (5.4)	0.06

APEX SPINE INSTITUTE

10 kHz SCS PDN RCT | Pain Relief over 18-Months



No significant benefit to delaying treatment with 10 kHz Therapy for Patients Refractory to CMM

10 kHz Therapy + CMM (n=83)

CMM (n=59)

Crossover CMM + 10 kHz Therapy (n=59)

*Error Bars: 95% CI

APEX SPINE INSTITUTE

10 kHz SCS PDN RCT Individual Pain Relief

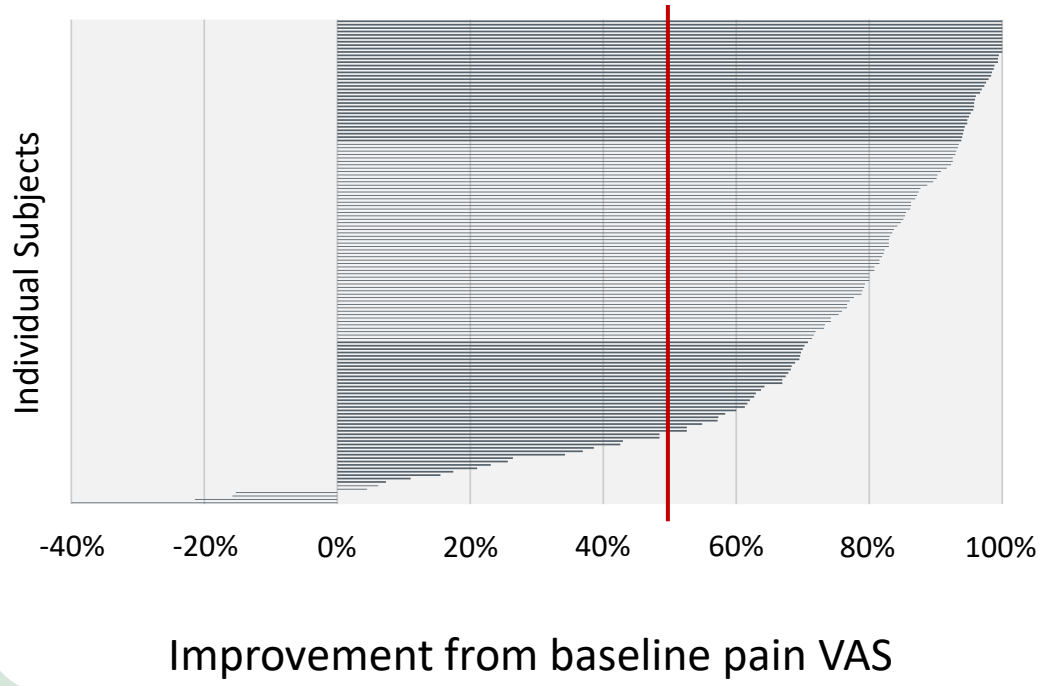
85% Responders (>50% Pain Relief) (121/142)

73% Average Pain Relief

68% Remitters (96/142)

Remission defined as VAS ≤3 for 6 consecutive months

1.3 Number Needed to Treat

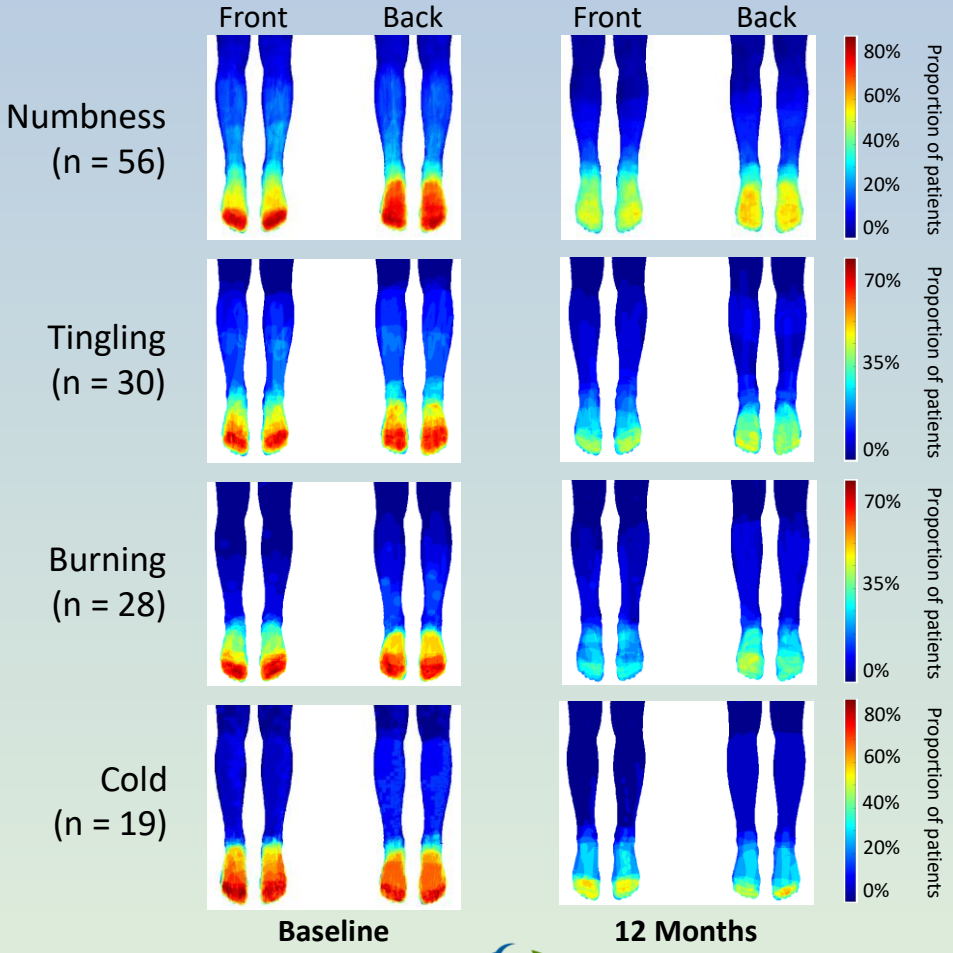


Amirdelfan et al. *Postgrad Med* 2019

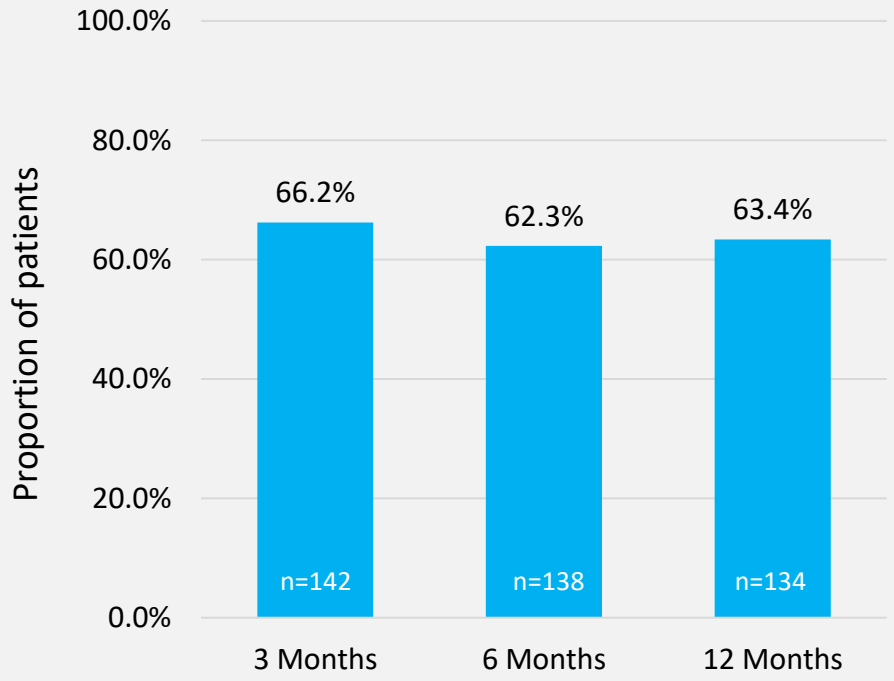
APEX SPINE INSTITUTE

10 kHz SCS PDN RCT: Neurological Improvement with 10 kHz SCS

Patient-reported reductions in dysesthesias



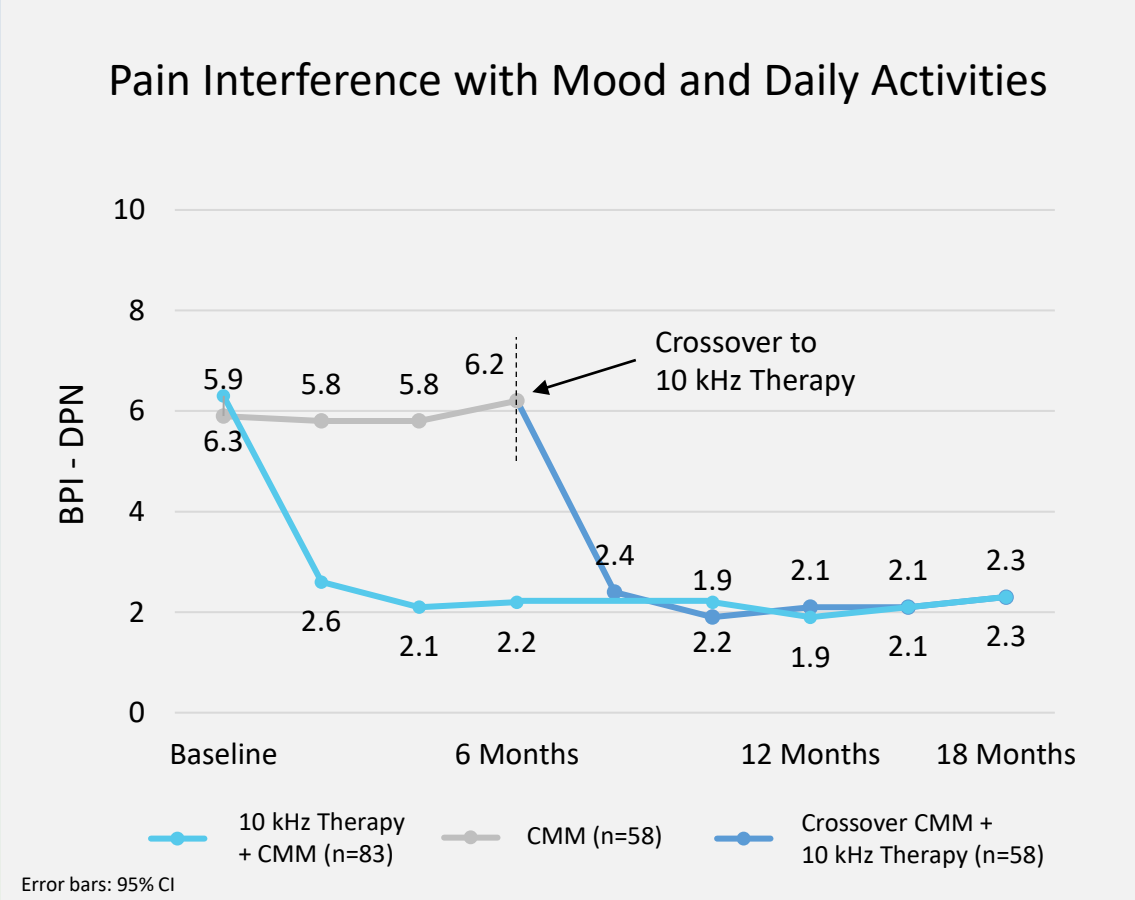
Did the investigator note neurologic improvement compared to baseline neuro exam?
Yes, most improvements seen in sensory exam

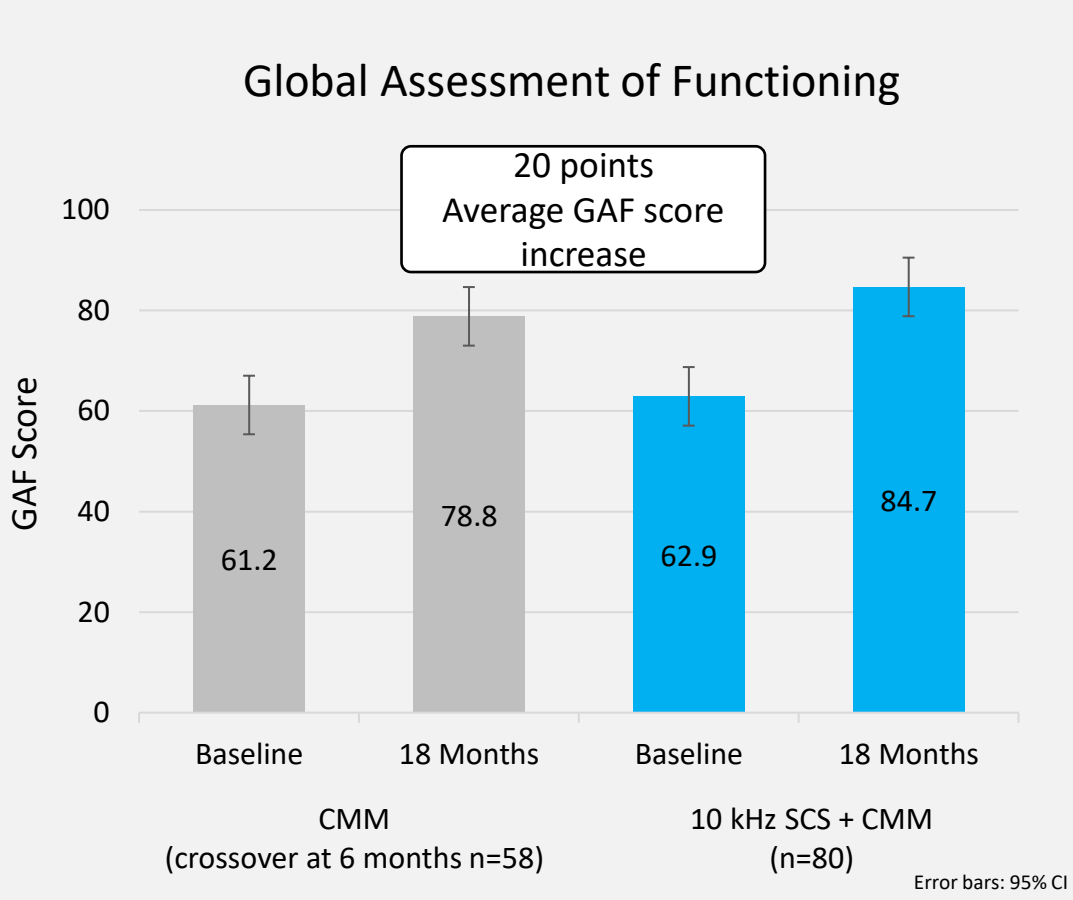


APEX SPINE INSTITUTE

10 kHz SCS PDN RCT | Quality of Life Improvements

Patients reported an average 61% reduction in sleep disturbances due to pain

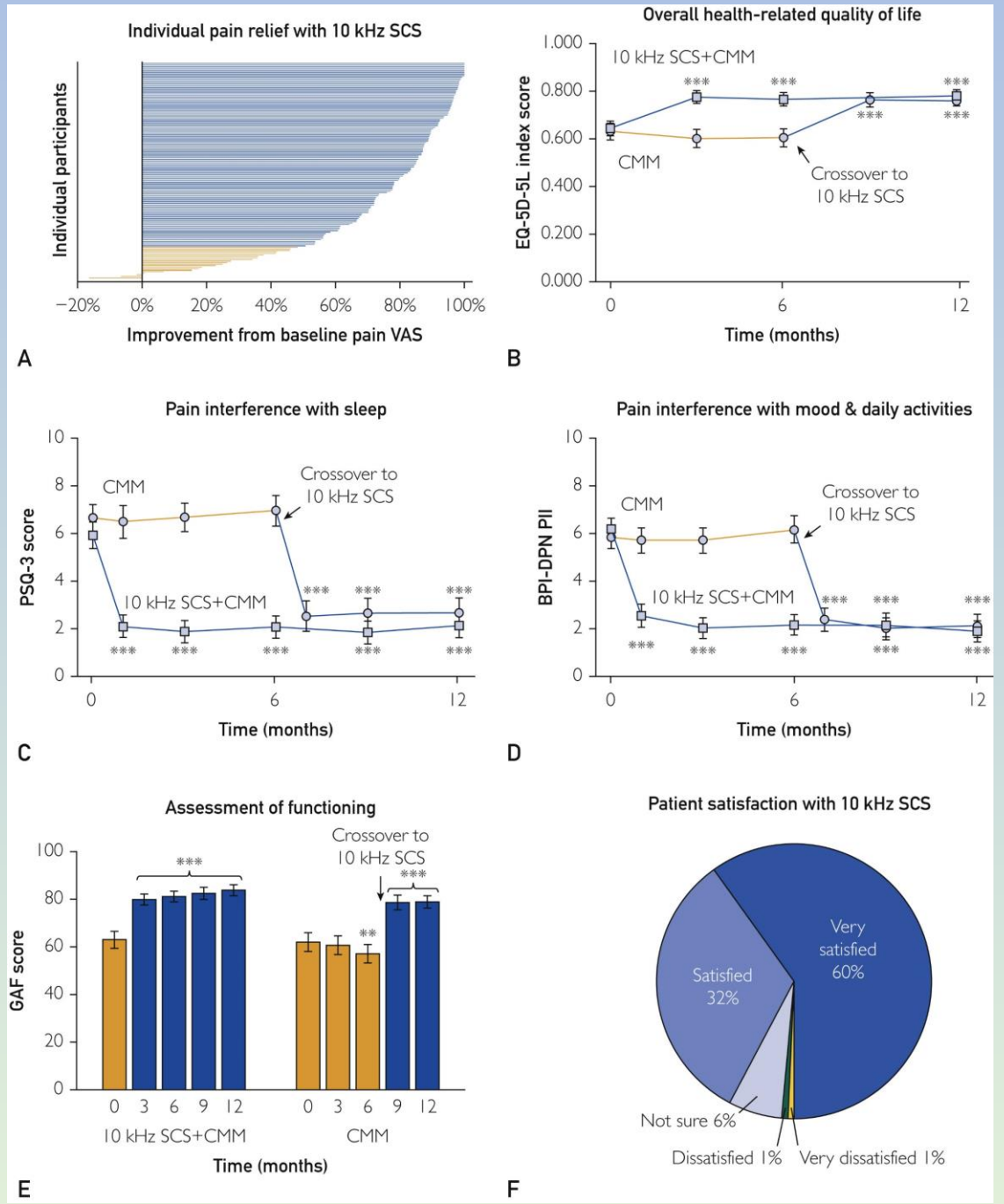




APEX SPINE INSTITUTE

Quality Of Life Improvement

- 61% reduction in pain interfering with sleep



APEX SPINE INSTITUTE

10 kHz SCS PDN RCT | Other Observed Endpoints

6-month: Other observed endpoints reported

Opioid Usage

- Decreased or eliminated: 23% of 10 kHz Therapy subjects vs 8% of CMM subjects
- Increased: 2% of 10 kHz Therapy subjects vs 11% of CMM subjects

Reduced hospital & ED visits

- Over 6 months, there were 7 fewer visits per 100 patients in the 10 kHz SCS group vs CMM group

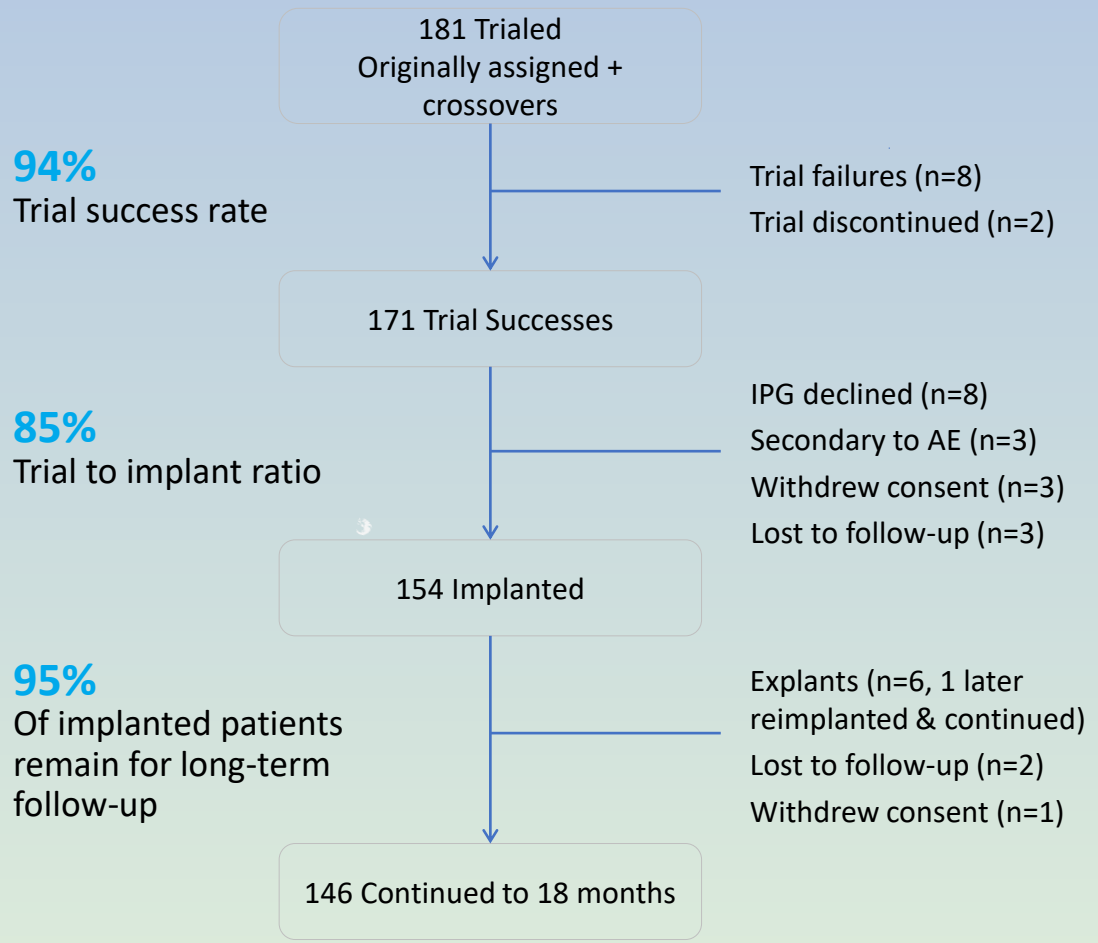
18-month: Other observed endpoints reported

Significant improvement in overall health-related quality of life

- Sleep disturbance due to pain markedly improved by 61% with 10 kHz Therapy.
- Subjects experienced substantial, durable pain relief over 18-months

APEX SPINE INSTITUTE

10 kHz SCS PDN RCT Subject Disposition: 10 kHz SCS



Safety
No stimulation-related neurological deficits
No explants for loss of efficacy
8 procedure-related infections (5.2%) 3 resolved with antibiotics 5 required explant (3.2%, 1 patient reimplanted)
1 explant as a precaution for an unrelated infection
3 IPG revisions (1.9%)
1 IPG replacement (0.6%)
1 lead revision (0.6%)

APEX SPINE INSTITUTE

Nevro SCS – FDA Labeling including recent PDN specific additions

Indications for Use	• The Senza®, Senza II™ and Senza Omnia™ neuromodulation systems are indicated as aids in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain, and leg pain. • **The Senza®, Senza II™ and Senza Omnia™ neuromodulation systems, when programmed to include a frequency of 10 kHz, are indicated as aids in the management of chronic intractable pain of the lower limbs, including unilateral or bilateral pain, associated with diabetic neuropathy.**
Contraindications	The Senza, Senza II, and Senza Omnia Systems should not be used for those patients who: • **Are poor surgical candidates, including those with poor glycemic control in whom the safety of the device has not yet been characterized, i.e. HbA1C >10%.** • Fail to receive effective pain relief during trial stimulation. • Are unable to operate the SCS system.
Warnings	**Patients with diabetes:** This device was only studied in patients with HbA1C up to 10%. In general, patients with diabetes have a higher risk of surgical complications, especially those who are at high risk for ischemic heart disease and those with autonomic neuropathy or renal failure. Appropriate patient selection, pre-operative risk assessment, and reasonable optimization of glycemic control are recommended.

APEX SPINE INSTITUTE

Conclusion

- PDN is an undertreated progressive disease, leaving many with debilitating pain affecting sleep and overall function
- This pain condition is outside of the patient population I typically see
- My goal is to reach community providers about the most effective long-term treatment for PDN refractory to medical management
- Spinal Cord Stimulation is life changing for many of our patients suffering with neuropathic pain
- Please consider a referral to discuss SCS with patients for patients with PDN refractory to medical management

APEX SPINE INSTITUTE

APEX SPINE INSTITUTE

References

- *1.* https://www.cdc.gov/diabetes/data/statistics-report/index.html
- *2. Clin J Pain*. 2002;18(6):350-354
- 3. *Diabetes Care.* 2008; **31**: 1679-1685
- 4. *Diabetes Res Clin Pract.* 2020; **162**108113
- 5. *Clin J Pain.* 2006; **22**: 681-685
- 6. *Diabetes Care.* 2011; **34**: 2220-2224
- 7. Engl J Med. 2004;**351**:48–55
- 8. *Nat Rev Endocrinol.* 2021; **17**: 400-420
- 9. *Diabetes Care.* 2017; **40**: 136-154
- 10. *Curr Diabetes Rev.* 2022; **18**: 42-96
- 11. *Lancet.* 2010; **376**: 419-430
- *12. Lancet Neurol.* 2015; **14**: 162-173
- *13. Pain Med*. 2015;16(11):2075-2083
- 14. *JAMA Neurol.* 2021;78(6):687-698
- *15. Pain Med. 2015;16(11):2075-2083.*

APEX SPINE INSTITUTE