

TEXAS PAIN SOCIETY

THE NEUROMODULATION PANEL

PANKAJ MEHTA MD

PETER SIRIANNI, MD

C.M. SCHADE, MD, PHD

BRIAN BRUEL, MD

ADVANCES IN EVIDENCE BASED NEUROMODULATION

- **FIRST RCT IN NEUROMODULATION** : Kemler et al. / Maartin van Kleef , 2000 NEJM
- SCS / PT n= 36
- 6M : VAS decrease in SCS grp ($p < 0.001$)
- In patients with Reflex Sympathetic Dystrophy (RSD) SCS was proven to significantly decrease pain .

ADVANCES IN EVIDENCE BASED NEUROMODULATION

- Kumar et al : (**PROCESS trial**): SCS v/s CMM
- 100 Pts FBSS – SCS PLUS CMM/ CMM , Cross over at 6 months
- ITT @ 6m **48% of SCS pts and 9% of CMM patients (p < 0.001)** achieved 50% pain relief or more. SCS group : Improved leg and back pain relief, quality of life, and functional capacity,
- Equally significant was the observation that **five (9%) SCS patients crossed over to CMM**
- 24m FU : improved leg pain relief (p<0.0001), quality of life (p<0.01), and functional capacity (p < 0.0002).

ADVANCES IN EVIDENCE BASED NEUROMODULATION

- **Over the next two decades** since these studies were actually performed, the techniques, targets, and technologies used for neuro- stimulation have changed dramatically.
- **Novel targets**, such as the DRG, as well as **Novel pulse trains**, such as 10 kHz high frequency(HF) and Burst-DR SCS have forever altered the landscape of neuromodulation.

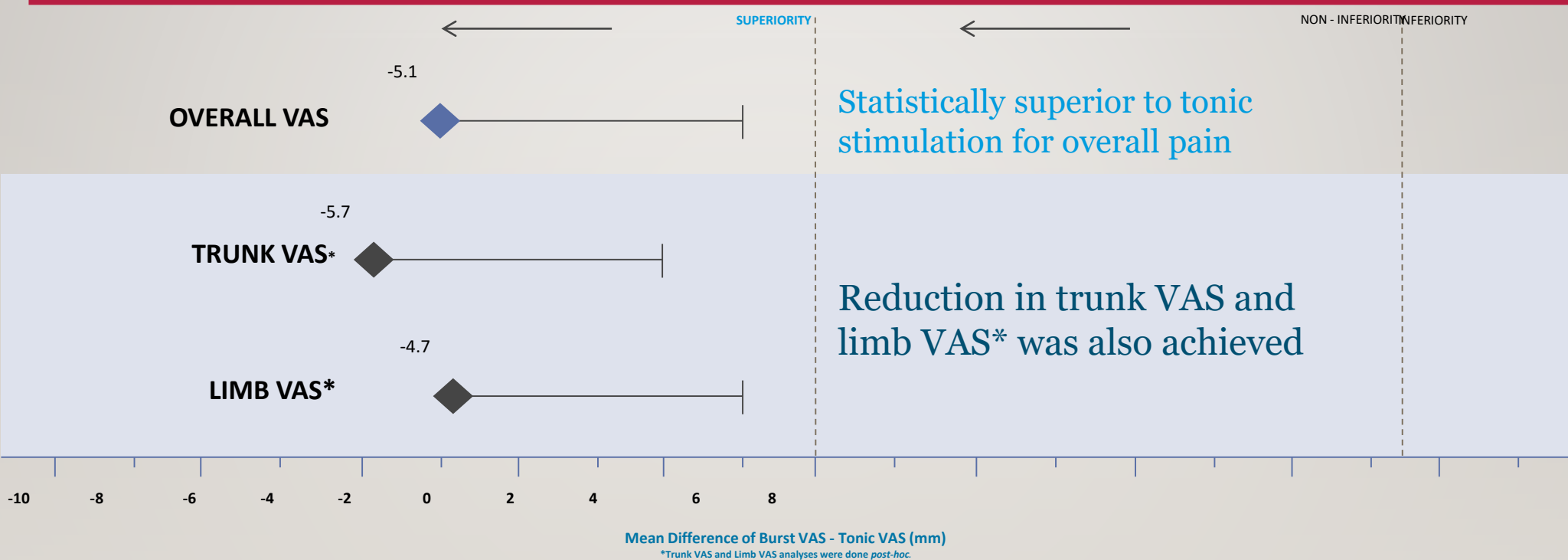
ADVANCES IN EVIDENCE BASED NEUROMODULATION

- **2015 : Kapural et al** : Randomized, parallel-arm, multicenter non- inferiority trial
- Traditional SCS vs. SCS performed at 10 kHz.
- 198 pts 1:1 for SCS and 10K Hz
- **3M** : > 80% HF10 therapy subjects were higher responders for back pain and and leg pain as compared to 40% of traditional SCS ($p < 0.001$ for both back and leg pain comparisons).
- **12M** :The superiority of HF10 therapy over traditional SCS for leg and back pain was sustained ($p < 0.001$)

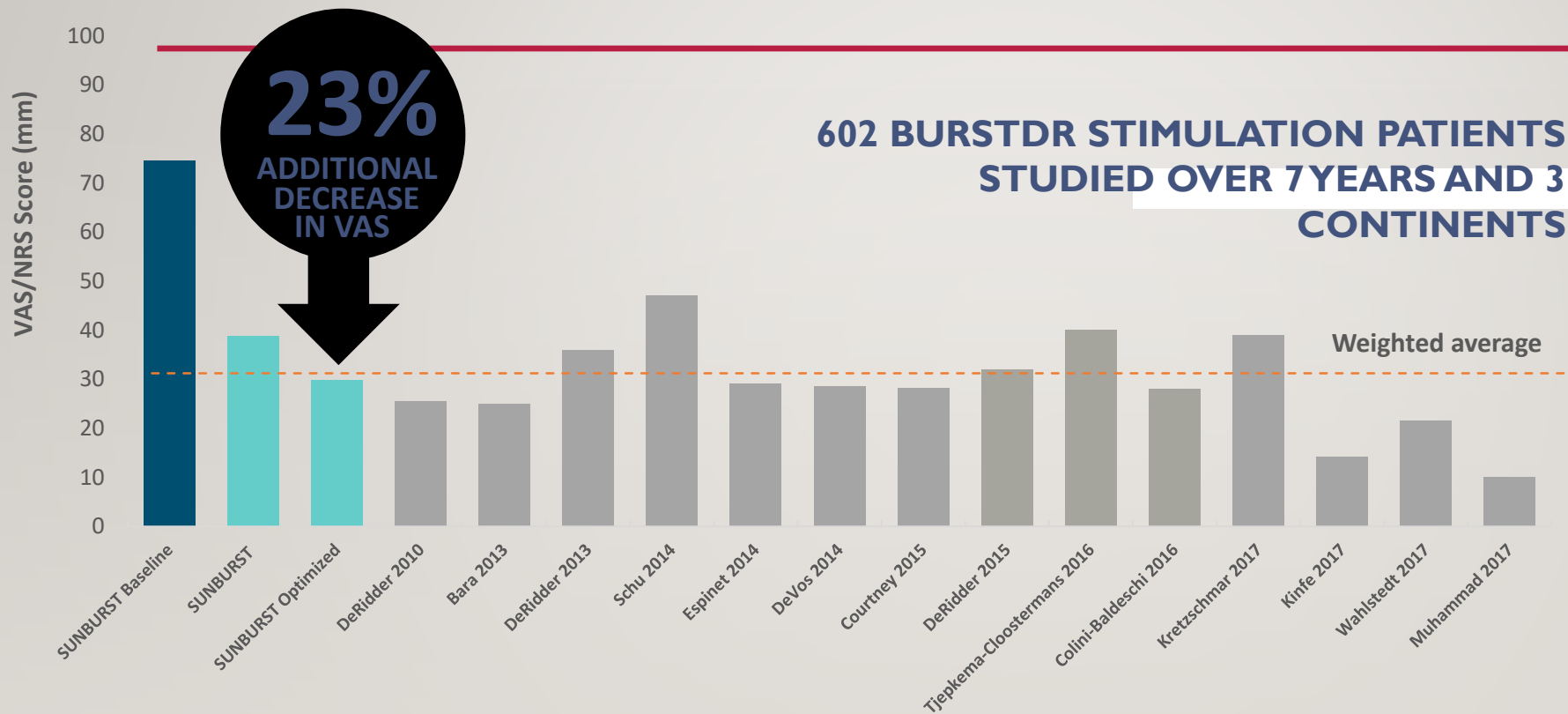
ADVANCES IN EVIDENCE BASED NEUROMODULATION

- **24M:** More subjects were responders to HF10 therapy than traditional SCS ($p < 0.001$ for back pain and leg pain)
- Back pain decreased to a greater degree with HF10 therapy (66%) than traditional SCS ($p < 0.001$ for noninferiority and superiority).
- Leg pain also decreased to a greater degree with HF10 therapy

ADVANCES IN EVIDENCE BASED NEUROMODULATION



BURSTDR™ STIMULATION DELIVERS CONSISTENT, POSITIVE RESULTS^{8,16-30}

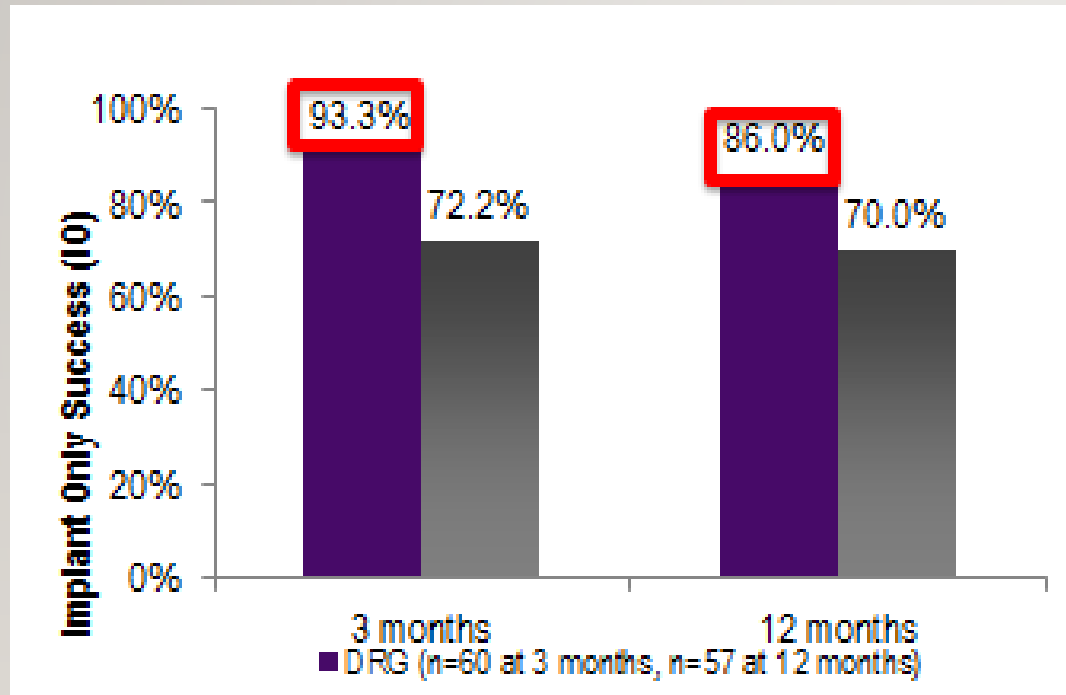


BURSTDR STIMULATION has not only proven to have superiority over tonic stimulation in a large RCT, but it has shown consistent and replicable results across diverse clinical settings around the world over the last 8 years.

- Weighted average score represents an average in which each quantity to be averaged is assigned a weight and that weight is determined by the number of patients in that study.
- Based on the collection of final VAS/NRS scores from publications using BurstDR™ Stimulation.
- Not all real world data came from randomized controlled multicenter clinical studies.

ACCURATE STUDY¹

A PROSPECTIVE, RANDOMIZED, CONTROLLED CLINICAL TRIAL ASSESSING DRG STIMULATION



STUDY SUMMARY

- 152 subjects enrolled
- Randomized 1:1 ratio
- DRG vs. Control (SCS)
- Subject population
- Complex Regional Pain Syndrome (CRPS) Type I (RSD) and Type II (Causalgia)

CONCLUSION

- Superior Pain Relief
- Improved QOL and Functionality
- Improved Targeting of Therapy
- Reduced Paresthesia

DRG stimulation is designed to address limits of conventional SCS



UNSTABLE STIMULATION



LIMITED CEREBROSPINAL FLUID (CSF) around the DRG allows the leads to be closer to the anatomical target: potentially producing less postural effects (compared to conventional SCS)^{1,2}



UNSPECIFIC STIMULATION



SEPARATION OF SENSORY & MOTOR NERVE FIBERS may prevent unintentional stimulation

WELL MAPPED & organized to corresponding anatomies – allowing for highly focused treatment of pain



HIGH ENERGY USAGE



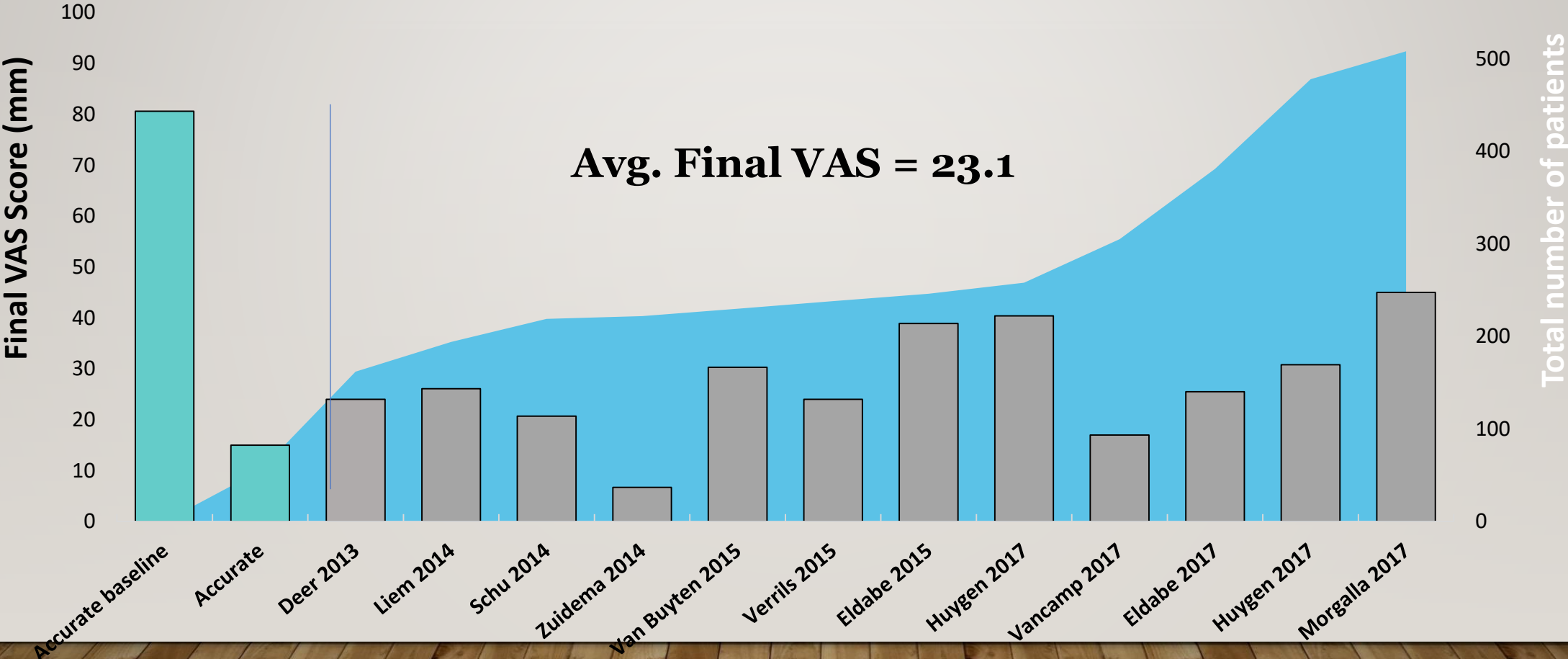
LIMITED CEREBROSPINAL FLUID (CSF) around the DRG allows the leads to be closer to the anatomical target: potentially less energy needed to stimulate sensory fibers (compared to conventional SCS)

1. Van Buyten, J. P., et al. Pain Practice 2015.

2. Liem, L., et al. Neuromodulation 2015.

CONSISTENT CLINICAL BODY OF EVIDENCE¹⁴⁻²⁶

508 DRG STIMULATION PATIENTS STUDIED OVER 4 YEARS GLOBALLY



THE PENDULUM HAS SWUNG

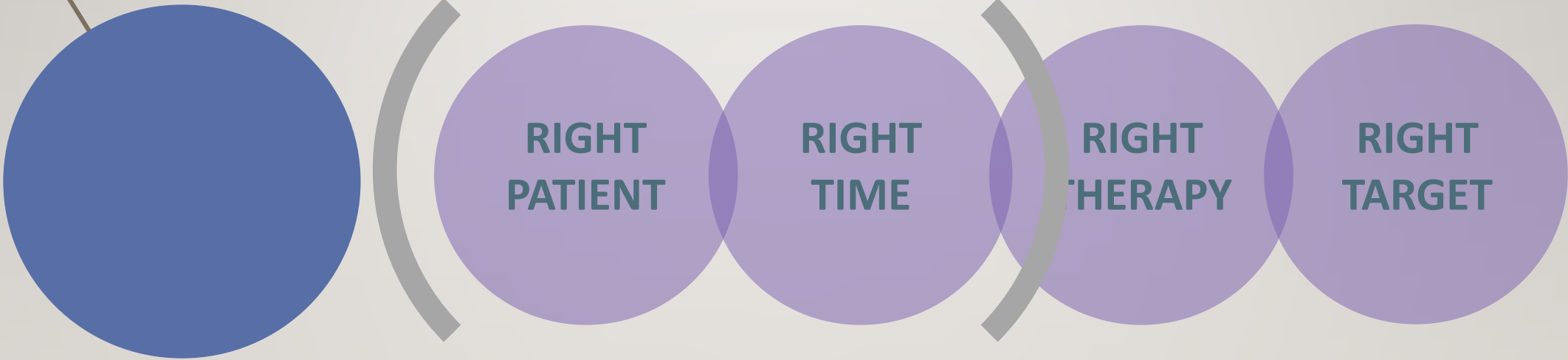
**RIGHT
PATIENT**

**RIGHT
TIME**

**RIGHT
THERAPY**

**RIGHT
TARGET**

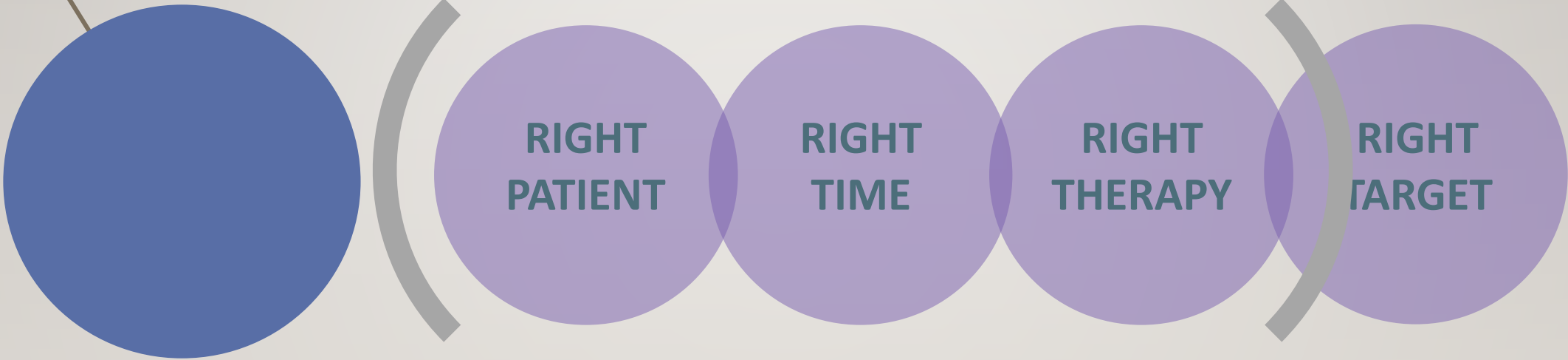
THE PENDULUM HAS SWUNG



Patient Selection



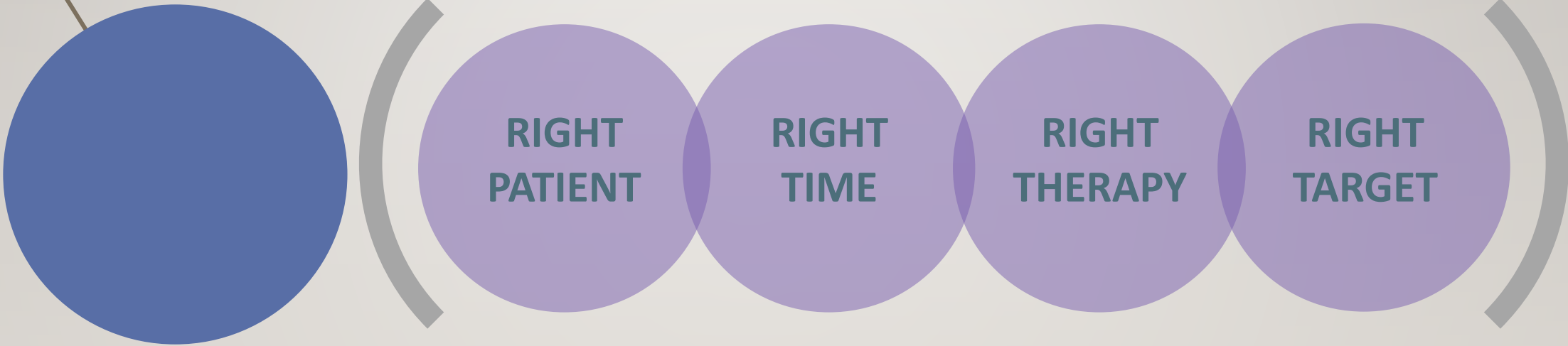
THE PENDULUM HAS SWUNG



Trial to Perm Ratio



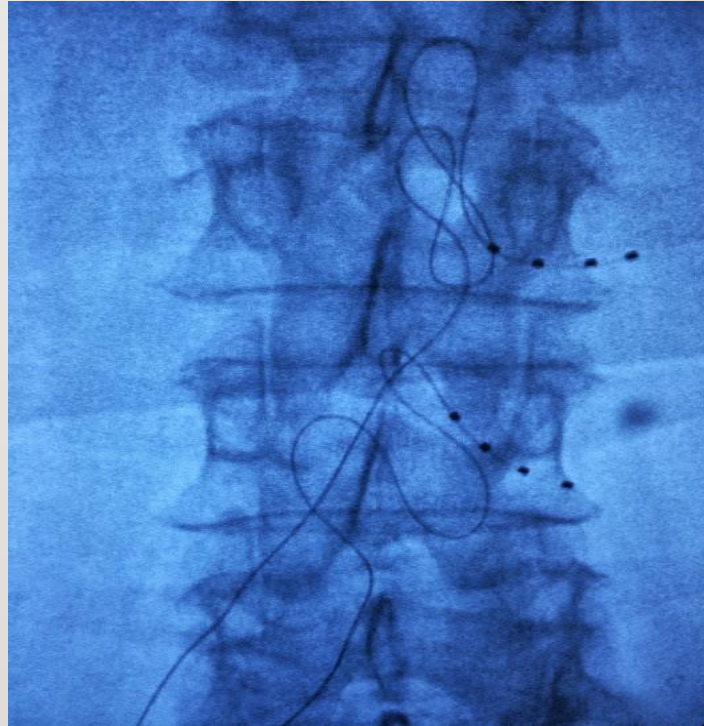
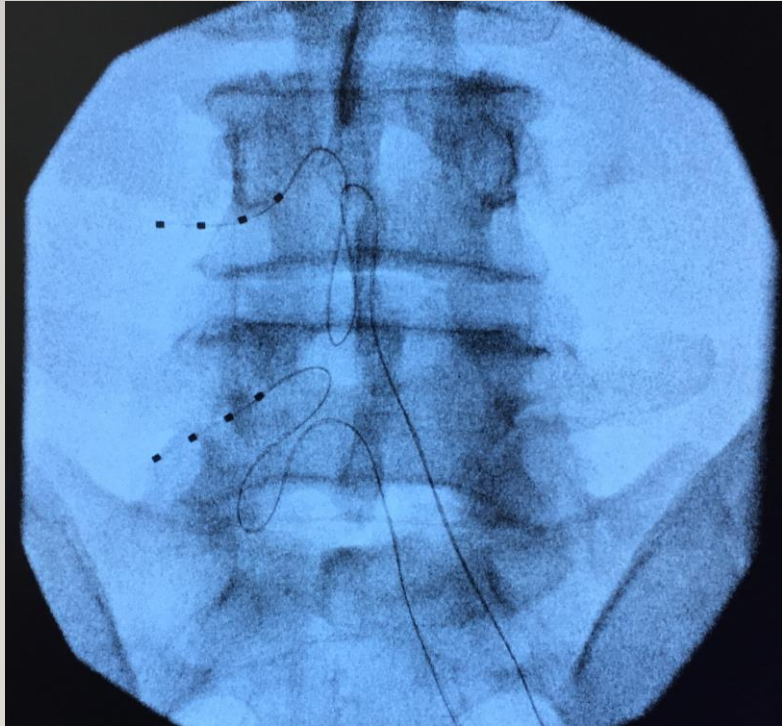
THE PENDULUM HAS SWUNG



Sustainability



DRG THERAPY



THE WAVEWRITER PHILOSOPHY

- Multiple therapies provide superior outcomes when patients are able to choose the most effective therapy.³

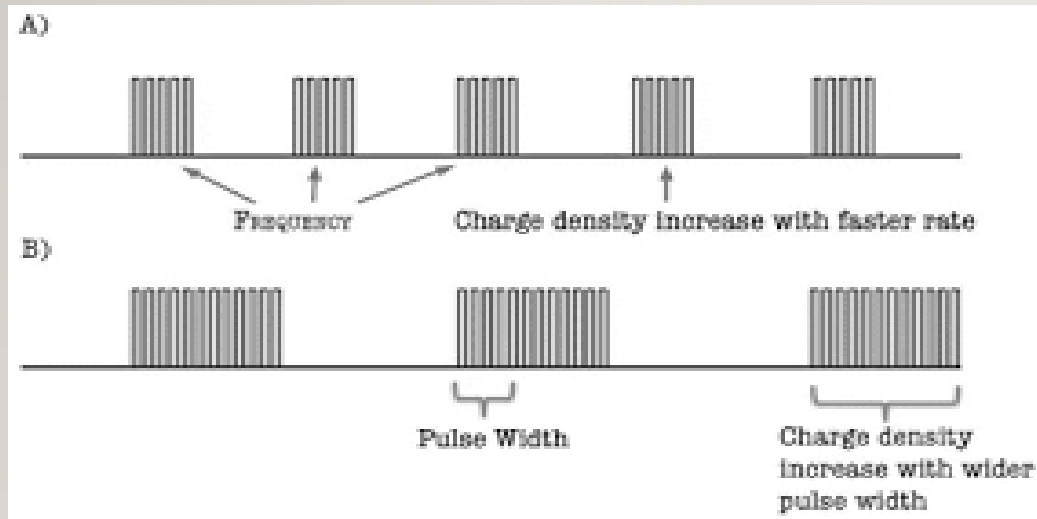


BURST DR THERAPY



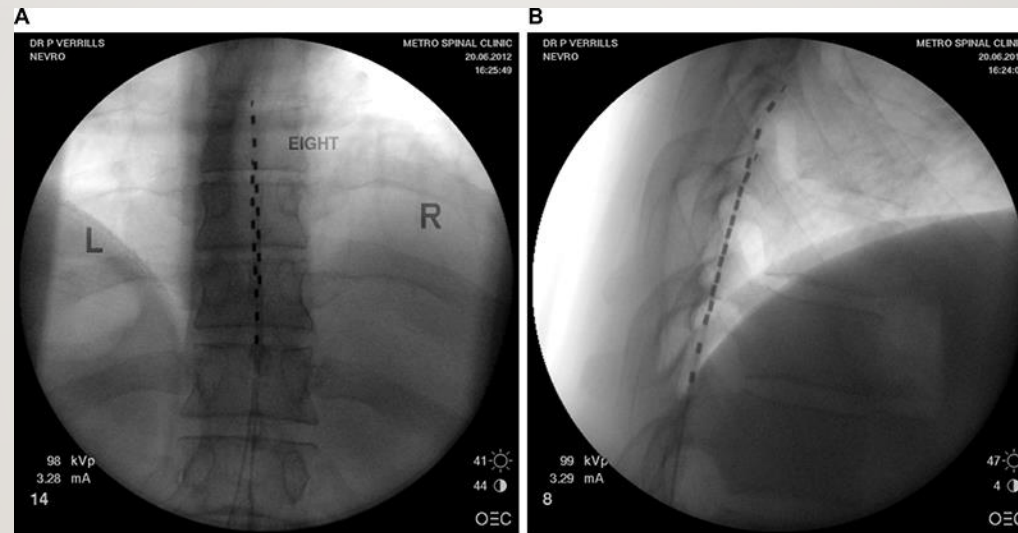
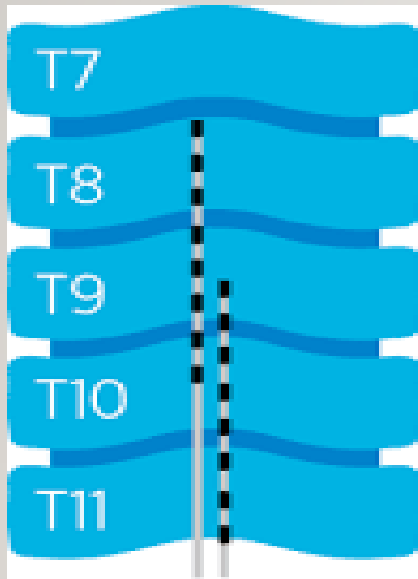
HIGH DENSITY THERAPY

ADAPTIVE STIMULATION TECHNOLOGY



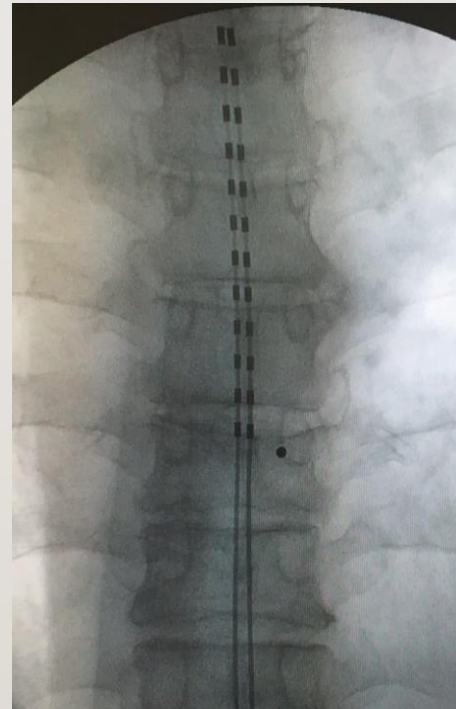
High-Density Spinal Cord Stimulation for the Treatment of Chronic Intractable Pain Patients

HF10 THERAPY

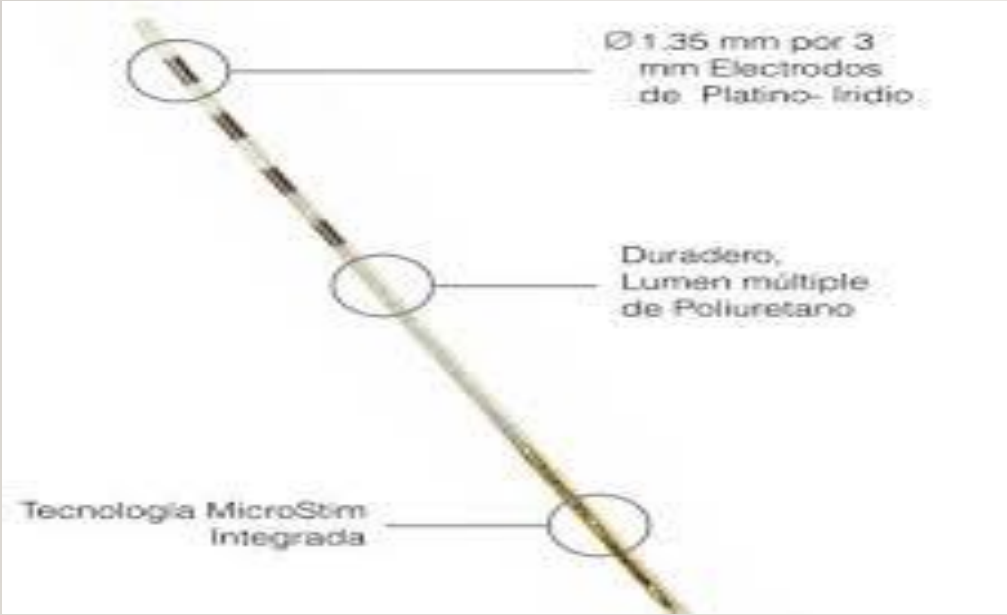


Is HF10 therapy right for you? >

12 CONTACT STRETCHY COVERAGE



STIMWAVE



WHY IS SUSTAINABILITY THE NEW MAIN FOCUS?



Sustainability is in the limelight after 2 major explant studies with similar results^{9,10}

International SCS Effectiveness Study: Long-Term Outcomes of the Therapy in 956 Implants

Jean-Pierre Van Buyten, MD¹, Frank Wille, MD², Iris Smet, MD¹, Jennifer Breel, MPA², Marieke Devos, MSc¹, Carin Wensing, MSc², Edward Karst, MS³, Katja Pöggel-Krämer, RN⁴, Jan Vesper, MD⁴

The largest study of its kind to assess real world outcomes

- International Study
- Retrospective analysis of 956 patients

Multicenter Retrospective Study of Neurostimulation with Exit of Therapy by Explant

Jason E. Pope, MD; Timothy R. Deer, MD; Steven Falowski, MD; David Provenzano, MD; Michael Hanes, MD; Salim M. Hayek, MD, PhD; Jacob Amrani, MD; Jonathan Carlson, MD; Ioannis Skaribas, MD; Kris Parchuri, DO; W. Porter McRoberts, MD; Robert Bolash, MD; Nameer Haider, MD; Maged Hamza, MD; Kasra Amirdelfan, MD; Sean Graham, MD; Corey Hunter, MD; Eric Lee, MD; Sean Li, MD; Michael Yang, MD; Lucas Campos, MD, PhD; Shrif Costandi, MD; Robert Levy, MD, PhD; Nagy Mekhail, MD, PhD

18 sites reviewed explants done over the last 5 years

- National Study (US)
- Retrospective chart review of 352 patients

SALUDA MEDICAL

NOT FDA APPROVED IN USA



Randomized Double-Blind Crossover Study Examining The Safety And Effectiveness Of Closed-Loop Control In Spinal Cord Stimulation

Steven Rosen¹, John L Parker², Milan Obradovic³, Nastaran Hesam Shariati⁴, Robert B Gorman⁵, Leonardo Kapural⁶, Didier Demesmin⁷, Steven Falowski⁸, Michael J Cousins⁹, Ashwini Sharan¹⁰

¹ Fox Chase Pain Management Associates, Trenton, PA, USA
² Carolina Pain Institute, Winston-Salem, NC USA
³ St. Luke's University Health Network, Bethlehem, PA
⁴ Thomas Jefferson University, Philadelphia, PA USA
⁵ Saluda Medical and National ICT Australia, Sydney NSW Australia
⁶ University Pain Management Centre, Somerset, NJ
⁷ Pain Management Research Institute and Kolling Institute, University of Sydney at the Royal North Shore Hospital, Sydney NSW Australia
⁸ CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use.

Introduction

- Traditional spinal cord stimulation (SCS) and therapies such as HF-10 and DRG stimulation attempt to maintain constant pulse amplitudes (voltage or current).
- However, neural fiber recruitment can be dependent on many factors: neural tissue movement, heartbeat, breathing, variability in the excitability of the fibers.
- These factors can have a negative consequence on pain relief, cause overstimulation or understimulation, and as a result patients find it difficult to achieve effective pain relief.
- Paresthesia free technologies, novel neural targets, and sensors can help mitigate the side effects^{1,2,3}; however, these new options ignore the underlying mechanism of action.
- Controlling stimulation dose through a closed-loop system by regulating the amount of current delivered to maintain constant evoked compound action potential (ECAP) amplitude has shown to have advantages⁴.
- We present data from a randomized double-blinded crossover feasibility study with closed-loop control.

Materials and Methods

- This study compared Closed-loop control to traditional SCS (Tonic) for subjects with chronic pain of the trunk and/or lower limbs.
- Data was collected as part of an FDA, IRB approved IDE protocol at 10 sites.
- All subjects were approved for and underwent a commercial SCS trial prior to entering the randomization phase. Subjects who completed the trial and met requirements for undertook an extended trial for up to 20 days with an IDE approved stimulator, Saluda Medical ETS.

Subject Profile

- 22 subjects finished the study and met the protocol definition for analysis.
- The table to the right lists the demographics of the subjects.

Characteristic	Feedback (FB)	No Feedback (NFB)
Age (Mean ± SD)	54.2 ± 10.1	53.8 ± 11.2
Gender (Male/Female)	12/10	11/11
Height (Mean ± SD)	175.2 ± 8.5	174.8 ± 9.1
Weight (Mean ± SD)	78.5 ± 15.2	79.1 ± 16.0
Duration of Pain (Mean ± SD)	12.3 ± 5.4	11.9 ± 6.1
Baseline Pain (Mean ± SD)	7.2 ± 1.8	7.1 ± 1.9
Baseline Function (Mean ± SD)	45.2 ± 12.1	44.8 ± 13.0
Baseline Depression (Mean ± SD)	15.1 ± 4.2	14.9 ± 4.5
Baseline Anxiety (Mean ± SD)	18.3 ± 5.1	18.1 ± 5.3
Baseline Sleep (Mean ± SD)	3.2 ± 0.8	3.1 ± 0.9
Baseline Quality of Life (Mean ± SD)	28.5 ± 6.2	28.3 ± 6.5

Overall Results: Met the Primary Endpoint for Safety and Effectiveness

Effectiveness

- 14/22 (63.6%, p<0.05) of patients met the primary objective
- Subjects report either less pain or fewer stimulation-related side effects, with no increase in either.

Parameter	FB	NFB
Mean Pain (SD)	3.2 (1.5)	4.1 (1.8)
Mean Side Effects (SD)	1.2 (0.8)	1.8 (1.2)
Mean Sleep (SD)	3.8 (0.9)	3.2 (0.8)
Mean Quality of Life (SD)	32.1 (7.2)	29.5 (7.5)

Safety

- There were no serious device-related adverse events
- Adverse event rate was comparable in not only both arms of the study, but also the commercial trial.
- There were no infections reported in an extended trial of ~25 days.

AE Type	FB	NFB
Blurred Vision	1	1
Constipation	1	1
Dizziness	1	1
Headache	1	1
Nausea	1	1
Rash	1	1
Sore Throat	1	1
Tiredness	1	1
Total	7	7

Secondary Outcomes

- No changes in paresthesia strength with large movements such as sitting to supine in the feedback arm.
- The change in paresthesia strength from sitting to supine was significantly different in the feedback arm (0.25 ± 2.00, 95% CI:0.88) compared to the non-feedback arm (3.45 ± 2.56, 95% CI:1.32)
- The description of paresthesia was significantly different. There was a significant increase in the words "quiet" (59%), "soft" (50%), "constant" (30%), and "gentle" (29%) used to describe the stimulation in feedback over non-feedback.
- No difference was found in the quality of life using the EQ-5D and SF-36 measures
- 26% improvement in VAS in the feedback arm; however, it was not statistically significant.
- In this blinded cohort, 86% of patients preferred feedback to tonic stimulation.
- High satisfaction rate in both arms but skewed to "very satisfied" in the feedback arm

Group Preference

86% preferred Feedback (FB) over No Feedback (NFB). 14% preferred NFB.

Patient Satisfaction

Bar chart showing patient satisfaction scores for FB and NFB across various categories.

Subjects turned off stimulation in the traditional SCS arm to sleep

Subject 05-05

- Therapeutic Window**: Patient was able to sleep with closed-loop stimulation.
- Traditional SCS - Turned off during sleep**: Patient did not sleep with traditional stimulation and turned it off to avoid overstimulation.
- Closed loop - Slept with stimulation on**: Patient maintained stimulation during sleep.

References

- Schultz, et al (2012). Sensor-driven position-adaptive spinal cord stimulation for chronic pain. Pain Physician 15:1-13.
- Parkes, et al (2012). Compound action potentials recorded in the human spinal cord during experimental low pain relief. Pain 153, 389-400.
- Kapural, et al (2015). Novel (20-40) High-Frequency Therapy is Superior to Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain. Anesthesiology 123:600-602
- Winters, et al (2015). Lack of body position effect on paresthesias when stimulating the dorsal root ganglion (DRG) in the treatment of chronic pain. Neurostimulation 16:103-107

With conventional stimulation, patients adjust their stimulation to avoid overstimulation

Subject 05-05

- ECAP maintained at the subject's preferred amplitude with closed-loop
- Stimulation was 67% higher on average than traditional SCS where current was turned down to avoid overstimulation.

ECAP Amplitude

Line graph showing ECAP amplitude over time for Tonic, Closed-loop, and Closed-loop (Initial) conditions.

Conclusions

- Compared to traditional SCS, subjects in the closed-loop cohort reported:
 - Greater reduction in pain with therapy maintained without under or overstimulation.
 - Fewer side effects, with increased convenience (comfortable sleep), and stimulation sensations described more positively.
- Although the therapy needs to be proven in chronic studies, acute results demonstrate the potential for pain relief with reduction in overstimulation, sustained stimulation within the therapeutic window, and fewer programming adjustments.

Effective Relief of Pain and Associated Symptoms With Closed-Loop Spinal Cord Stimulation System: Preliminary Results of the Avalon Study

PANEL DISCUSSION

- How do you chose you the RIGHT THERAPY FOR THE RIGHT PATIENT ?
-

- Is it the Right Neural target ??

- Rechargeable and Non Rechargeable devices ??

- Neuropathic :Axial pain Lumbar and Cervical region

- Other Intractable Chronic Pain syndromes – Abdominal pain , Diabetic neuropathy , Pelvic neuritis