Sub-Perception SCS "neural dosing" parameter relationships

Welcome to NYC Neuromodulation Conference online 2020:

Session Chair: Dr. Simon Thomson
Session Speakers: Dr. Simon Thomson
Session Administrator (Zoom Co-Host): Dr. Simon Thomson

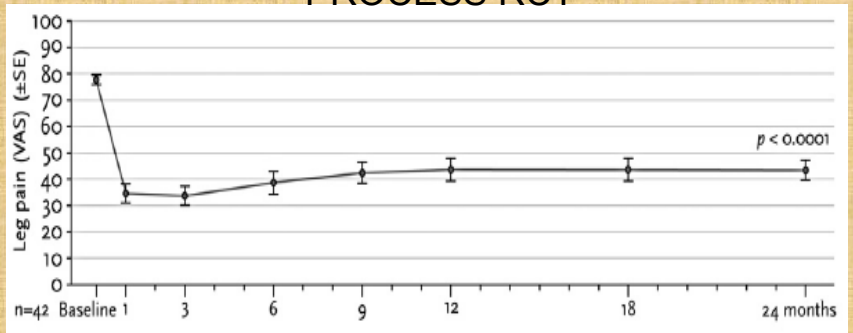
This session is recorded by the host.

Zoom Session Rules
-Chat is open to all for any ongoing discussion. Disrespectful attendees will be immediately removed.
-Questions for speakers through Chat (either public or private message to Session Chair)
-Attendee audio is muted for session (Video optional)
-Logistical concerns can be addressed to Session Administrator (Zoom Co-Host) in private message.

NYC Neuromodulation 2020 Online Conference
A free, self-organized community meeting

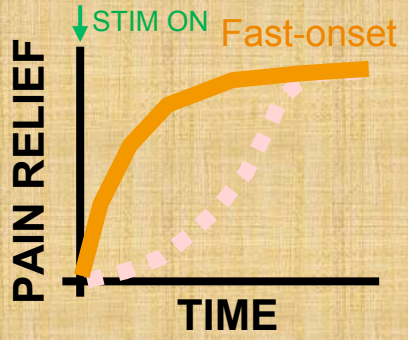
Background: Paresthesia-based SCS

PROCESS RCT[1]



Benefits

- Effective pain relief [1,2,3]
- Low charge burden (~weekly charging)
- Fast-onset analgesia (up to several minutes)
  → Rapid program optimization



Key Challenge: Paresthesia required for pain relief

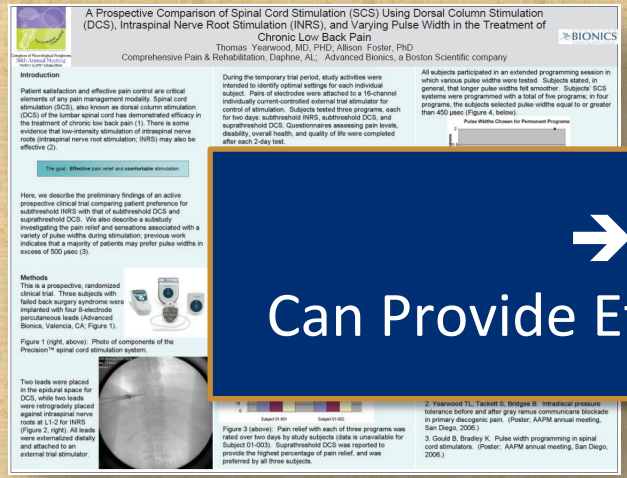
1. Kumar K. *et al., Neurosurgery*. 2008 Oct;63(4): 762-70

2. North R. *et al., Neurosurgery*. 2005;56(1): 98-106.

3. Veizi E. *et al., Pain Med*. 2017 Aug 1;18(8): 1534-1548.

Background: Sub-perception SCS

2006: Early research on sub-perception SCS (Yearwood *et al.*, CNS)

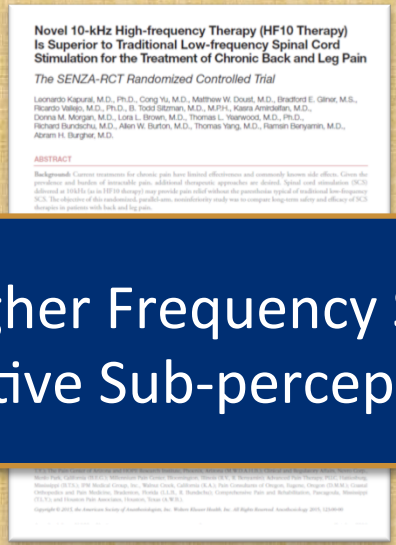


A Prospective Comparison of Spinal Cord Stimulation (SCS) Using Dorsal Column Stimulation (DCS), Intraspinal Nerve Root Stimulation (INRS), and Varying Pulse Width in the Treatment of Chronic Low Back Pain

Thomas Yearwood, MD, PHD; Allison Foster, PhD

Comprehensive Pain & Rehabilitation, Daphne, AL; Advanced Bionics, a Boston Scientific company

SENZA RCT @ 10 kHz (Kapural *et al.*, 2015)



Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain

The SENZA-RCT Randomized Controlled Trial

PROCO RCT @ 1 kHz - 10 kHz (Thomson *et al.*, 2018)

➔ Higher Frequency SCS
Can Provide Effective Sub-perception Pain Relief

The PROCO Randomised Controlled Trial:

Effects of Pulse Rate On Clinical Outcomes in Kilohertz Frequency Spinal Cord Stimulation

A Multicentre, Double-blind, Crossover Study

Dr. Simon Thomson, MBBS
Chief Investigator
Basildon and Thurrock University Hospitals
NHSFT - Sponsor

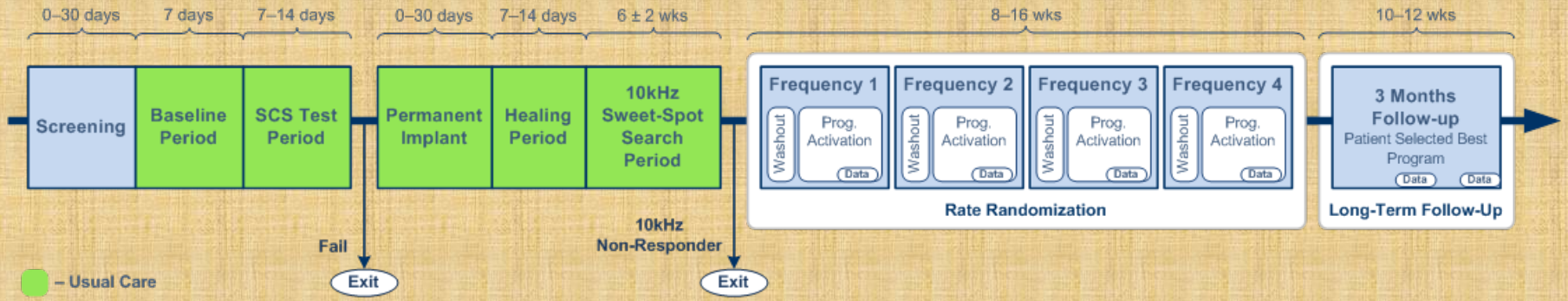
Moein Tavakkoli Zadeh, MD[1], Sarah Love-Jones, MBBS[2], Nik Patel, MD[2], Jianwen Wendy Gu, PhD[3], Amarpreet Bains, PhD[3], Que Doan, BSc[3], Michael Moffitt, PhD[3]

1: University College London Hospitals, London, UK
2: Southmead Hospital, Bristol, UK
3: Boston Scientific Neuromodulation, Valencia, USA

All R&D departments at participating hospitals and the Multicentre Research Ethics Committee (MREC) approved this study

Thomson SJ. et al. *Neuromodulation.* 2018 Jan;21(1):67-76

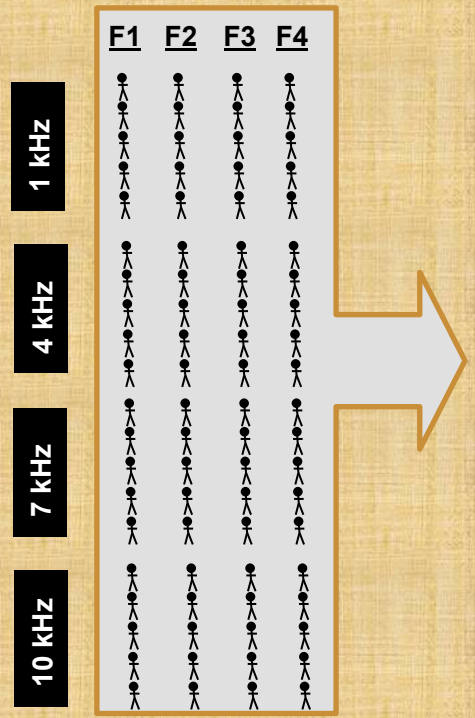
Study design: Multicentre, double-blind, randomised, crossover



- Lead placement: Spanning T9 to T10 vertebral region
- Paraesthesia-based trial
- Over the course of the study, patients experience high rate stimulation for 8–9 months

1: Stubbs et al. 2000
2: Whybrow 2006
3: Hampton & Middleton 2011

Randomized Crossover Increases Statistical Power



Advantages

- Each blinded patient experiences all 4 frequencies
- Patients act as their own control
- The crossover design of the PROCO RCT has the equivalent statistical power of a parallel design study with over 100 patients.

Importance of electronic real-time diary

- Compliance with paper diaries is only 11%[1]
- Many studies just collect VAS or NRS at clinic visit → 1 data point per patient per evaluation period
    - Memory of pain intensity is unreliable[2]
- Real-time E-diary prompted each patient for 180 pain scores over the rate randomisation phase
    - Larger sample size → More accurate results[3,4]

CamNtech Ltd.

Validated[5,6,7] e-diary

1: Stone et al. 2013
2: Broderick et al. 2008
3: McCollough et al. 1963
4:Walpole et al. 2002
5: Stubbs et al. 2000
6: Whybrow 2006
7: Hampton & Middleton 2011

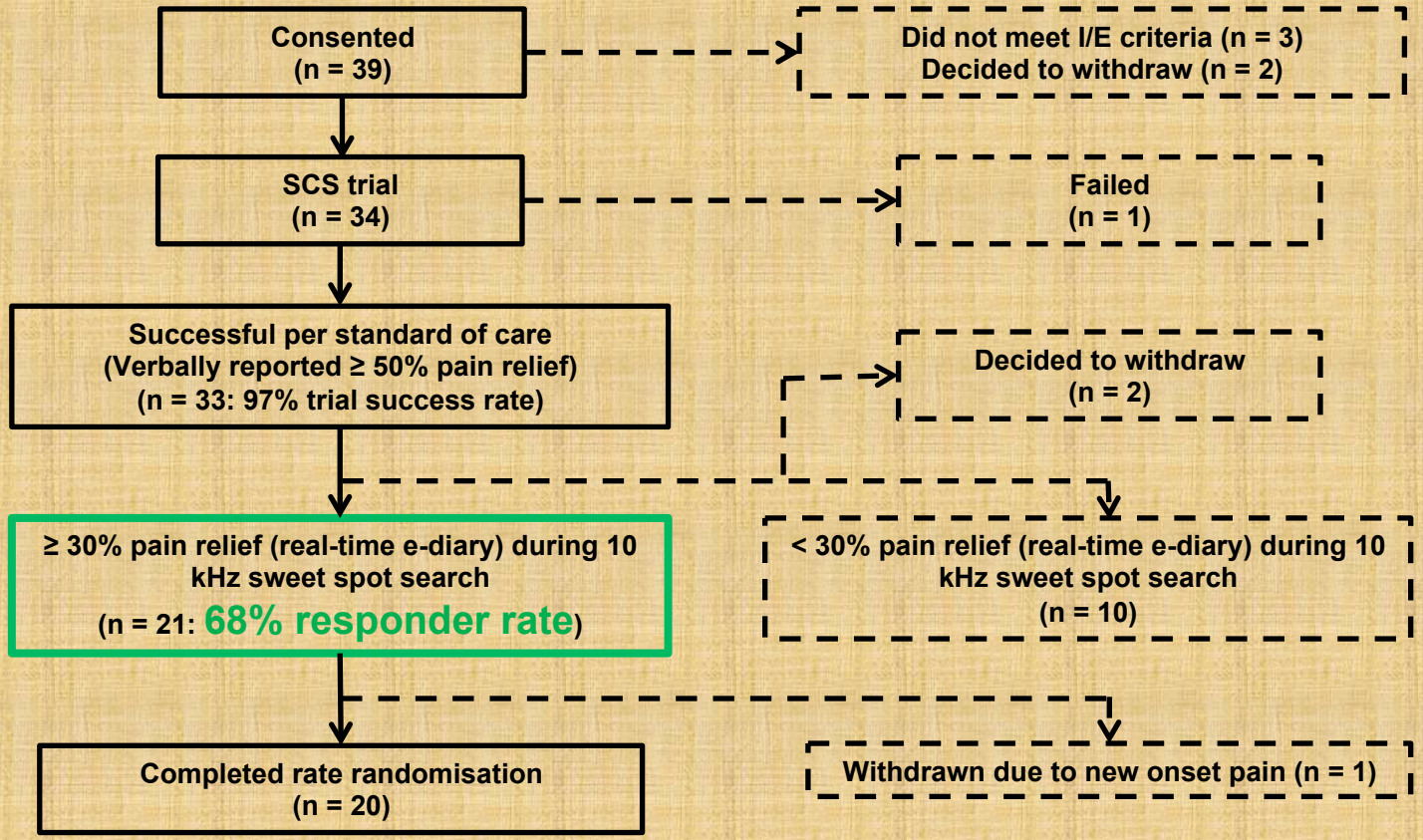
Sweet spot search protocol

- Search done at 10 kHz
- The T9-10 interspace was always tested but was not the most commonly identified sweet spot
- For scientific purposes, the study afforded the opportunity to exhaustively test stimulation locations along both leads
- Multiple bipoles tested to identify best stimulation location
- Best stimulation location used for all frequencies in the randomisation period
    - Only 10 kHz responders continued in the study
    - Potential bias in favour of 10 kHz

Rate randomisation protocol

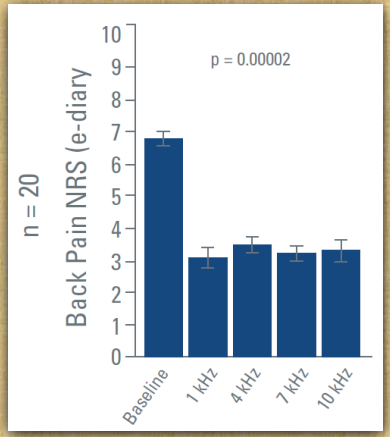
- Rates used: 1 kHz, 4 kHz, 7 kHz, 10 kHz
- Randomised Rate sequencing
- Each rate experienced for 4 weeks (last 5 days was data-collection period)
- Pulse width & amplitude optimised at each frequency for each patient
- Washout period between frequencies

Patient flowchart



PROCO RCT

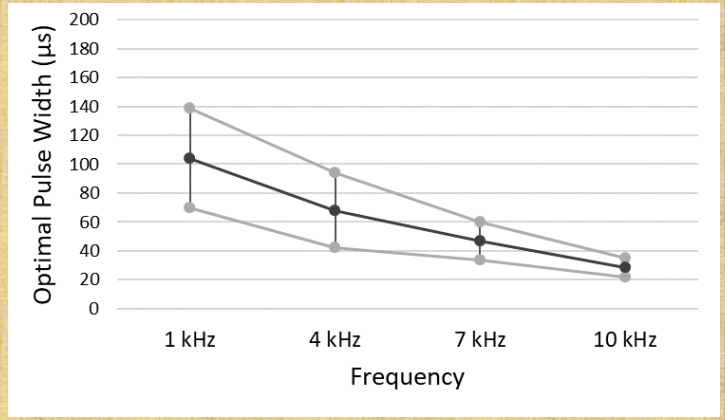
NRS Results



Rule of Neural Dosing

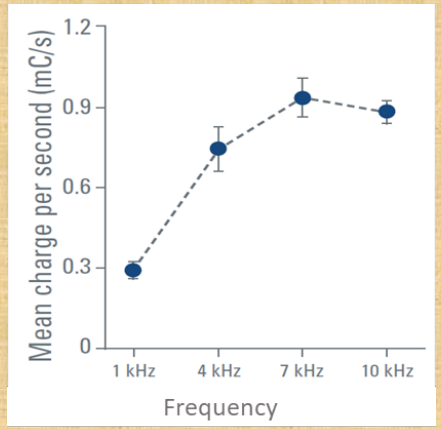
To maintain pain relief, as frequency is DECREASED from 10 kHz to 1 kHz…

(1) Pulse Width must be ***INCREASED***



Thomson SJ. et al. *INS European Chapter* 2018

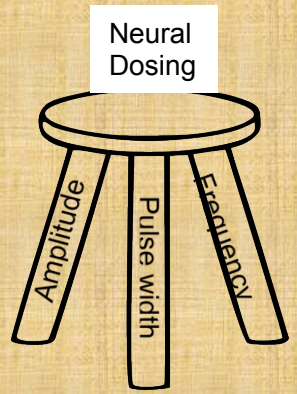
(2) Charge Delivery is ***DECREASED***



Thomson SJ. et al. *Neuromodulation.* 2018 Jan;21(1):67-76

Discussion: Neural dosing

- Achieving pain relief requires delivering the right waveform to the right target
    - Optimal target varied by patient
    - Optimal stimulation at each frequency required titration of pulse width and amplitude to deliver appropriate neural dose
    - Frequency cannot be looked at in isolation
        - Different frequencies required different pulse width and amplitude combinations



Future directions

- What is the best target? Beyond T8–T11?
- Is there a better field shape? Beyond bipole?
- What is the optimal neural dosing algorithm?
  - How low can we go in frequency/energy use while maintaining therapy?
  - What is the minimum effective neural dose?
  - Further analysis of PROCO RCT data in progress…stay tuned

Research into mechanisms and optimization paradigms is accelerating. The future is bright for our field and our patients!

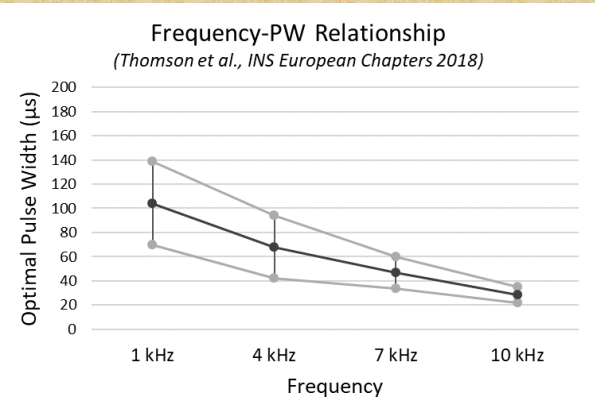
Key PROCO Findings

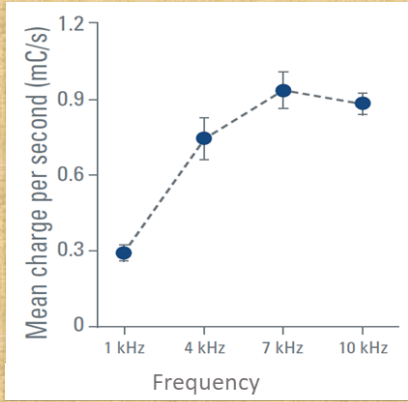
Rule of Neural Dosing

To maintain pain relief, as frequency is DECREASED from 10 kHz to 1 kHz…

(1) Pulse Width must be ***INCREASED***

(2) Charge Delivery is ***DECREASED***

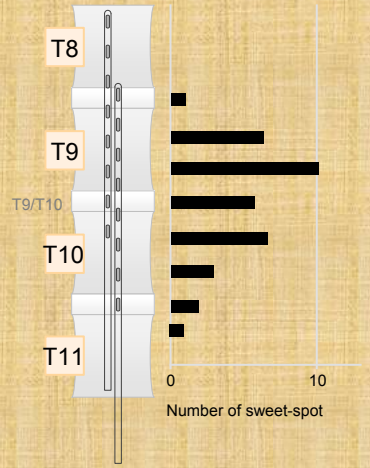




Thomson SJ. et al. *Neuromodulation.* 2018 Jan;21(1): 67-76

Target Variability

Sweet-spot can be anywhere from **T8-11**

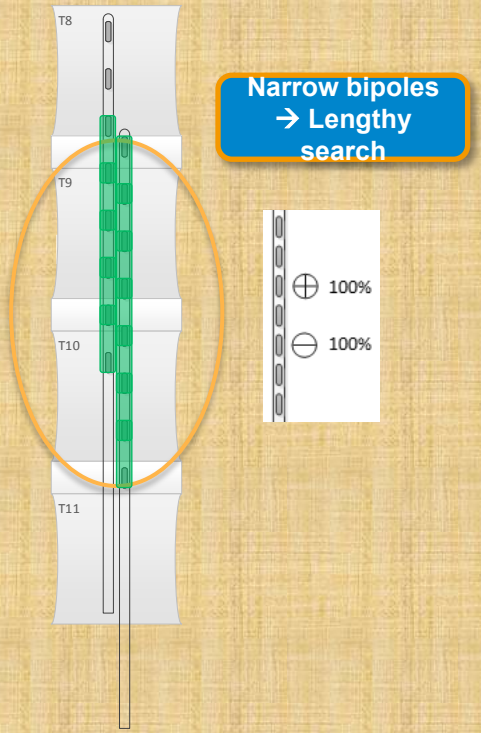


Modified from Thomson SJ. et al. Neuromodulation. 2018 Jan;21(1):67-76.

3 Key Challenges of Conventional High Frequency

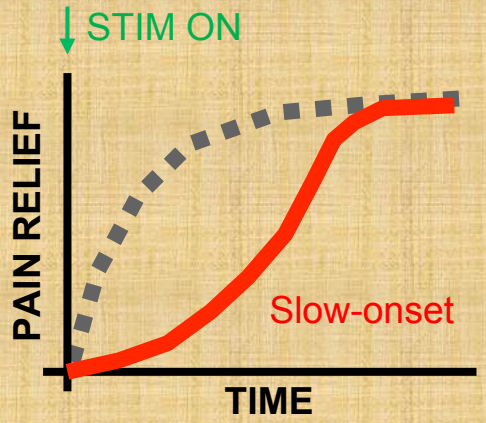
(1) Lengthy "sweet spot" search

Are tight 8mm bipoles the best approach to anatomical sub-p?



(2) Latency of analgesia (1-3 days)

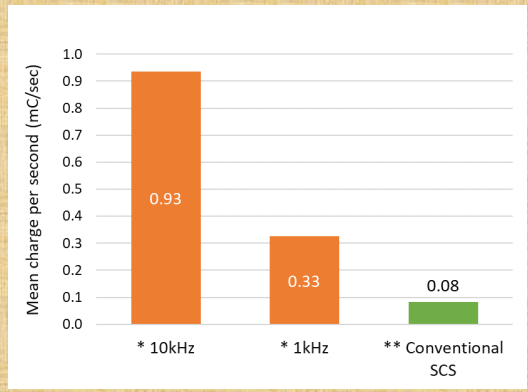
Lengthy program optimization (up to 2 weeks)



Tiede J., et al. *Neuromodulation* 2013; 16:370-375.
Al-Kaisy A., et al. *Neuromodulation* 2015; 18: 18-23.
Thomson S. et al. *Neuromodulation* 2018 Jan; 21(1):67-76.

(3) High charge burden

x10 charge than Conventional SCS



*Thomson S. *et al.* *Neuromodulation* 2018 Jan; 21(1):67-
** 50 Hz, 300 µs, 5.5 mA

EXPLORATION OF HIGH AND LOW FREQUENCY OPTIONS FOR SUB-PERCEPTION PAIN RELIEF:

THE HALO STUDY

José Paz[1], Simon Thomson[2], Roshini Jain[3], Lilly Chen[3], Ismael Huertas[3], Que Doan[3]

1. University Hospital La Paz, Madrid, Spain. 2. Basildon and Thurrock University Hospitals, Basildon, UK 3. Boston Scientific, Valencia, CA USA

Presenter:
Dr. Simon Thomson MBBS FFPMRCA
Basildon and Thurrock University Hospitals NHSFT
UK

SCS modalities scenario

Paresthesia SCS

Sub-perception SCS

HF (10 KHz)

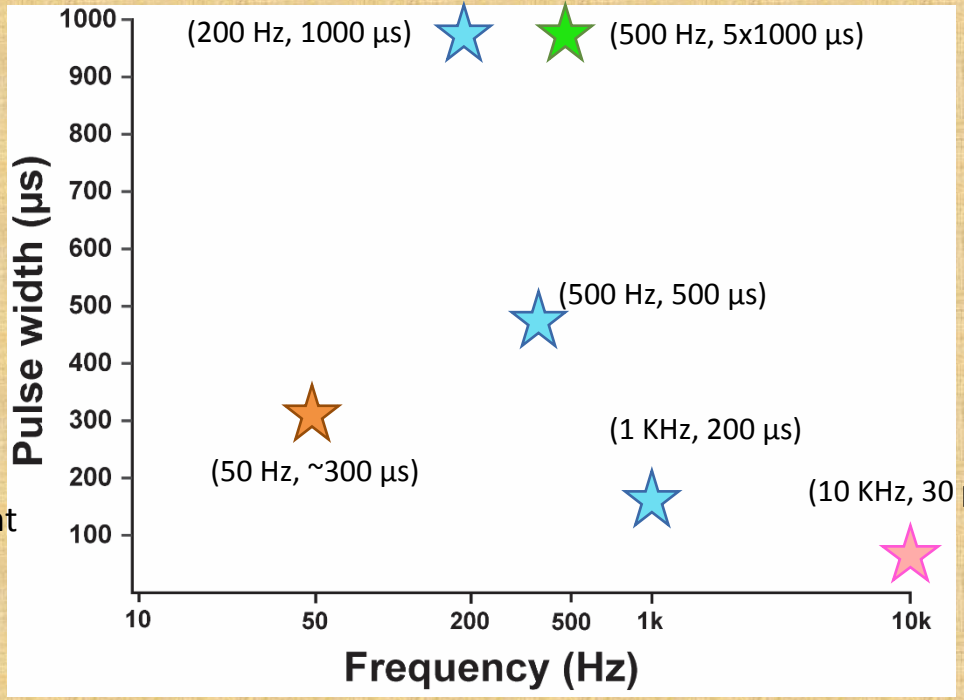
Frequencies below 10 kHz
→ Less/ineffective pain relief?

High Density

Must maintain duty cycle constant (20-25%) [Yang, 2019]?

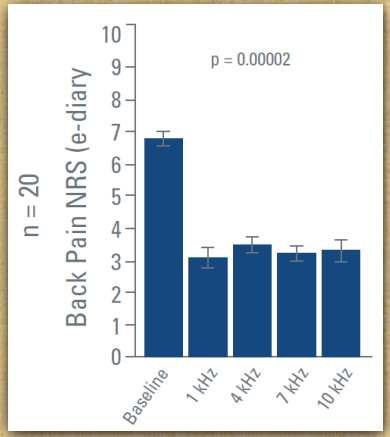
BurstDR

One Fixed burst pattern
(5 x 1000 µs @ 500 Hz) is best?



PROCO RCT

NRS Results



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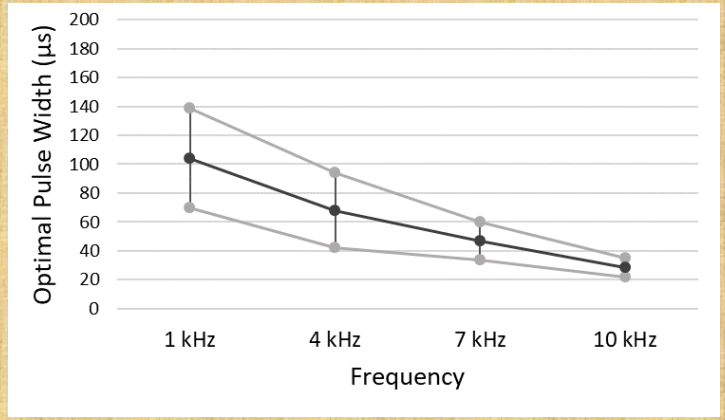

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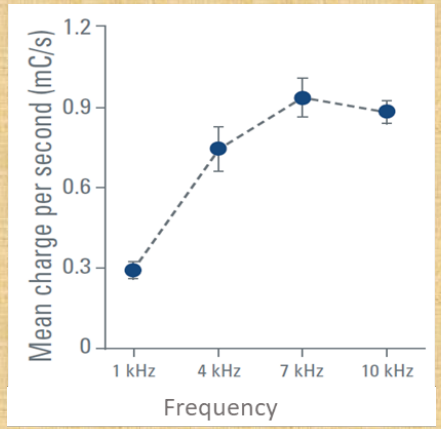


Thomson SJ. et al. *Neuromodulation.* 2018 Jan;21(1):67-76

HALO Study

Motivation

- Does the **Rule of Neural Dosing** hold for frequencies below 1,000 Hz?
- **How low can we go?** Is there a clinical difference in sub-p pain relief from **1,000 Hz to 10 Hz**?
- Can we improve sweet-spot search and targeting in sub-perception SCS with a novel field shape designed to preferentially engage the dorsal horn?

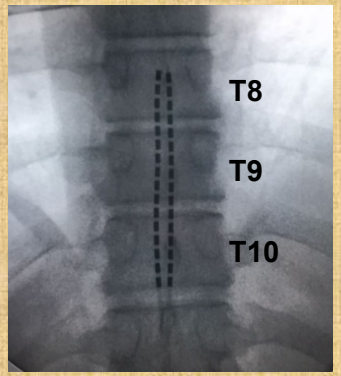
Study Design

- Multicenter, Observational, Real-World, Consecutive, Case-Series (n = 30)
- Program optimization with progressive frequency reduction [1000, 600, 400, 200, 100, 50 and 10 Hz]
- Data collection by site personnel (Retrospective): Pain Scores (NRS/Diary), Satisfaction, Program preference

Programming

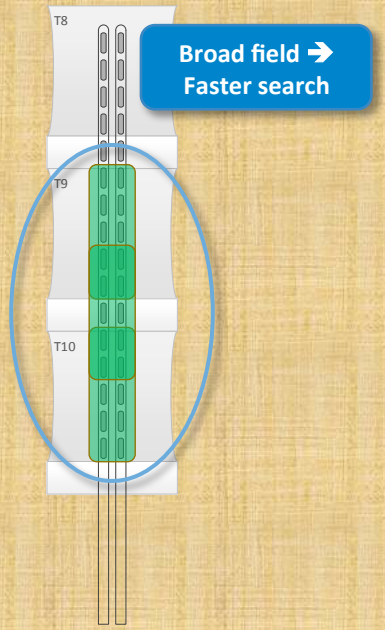
1 Implant

- Dual 16-contact perc leads
- T8-T10 vertebral span
- SCS System: 32 contacts with multiple independent current control capable of calibrated field shape and multiple waveforms



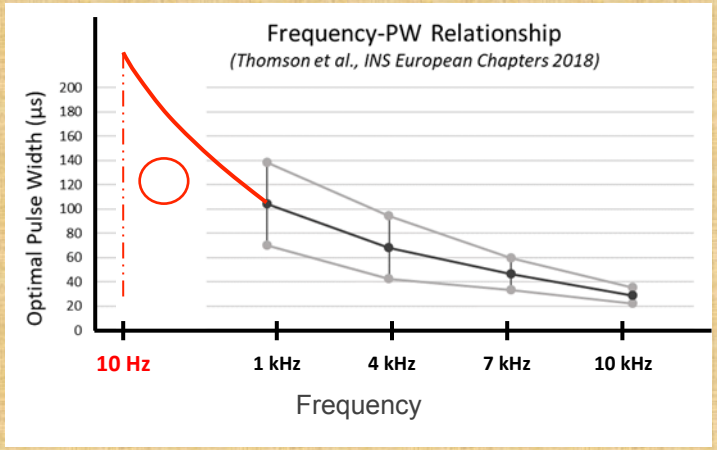
2 Sweet-spot search

- 1000 Hz stimulation
- Broad field covers multiple "sweet-spot"



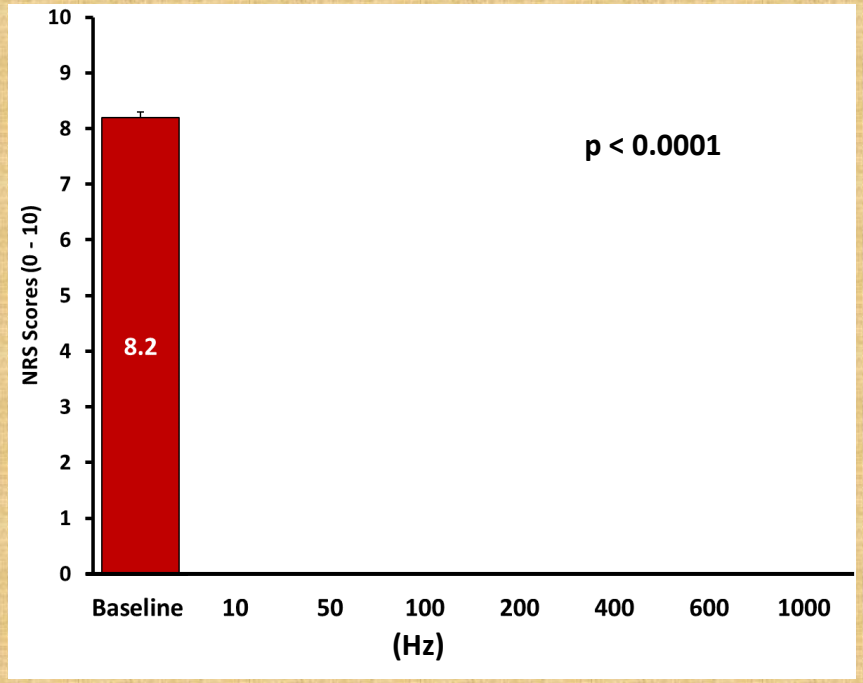
3 Titrate Dosing

- Frequency reduction in sub-p: [1000, 600, 400, 200, 100, 50, 10] Hz
- Pulse width and amplitude adjustment

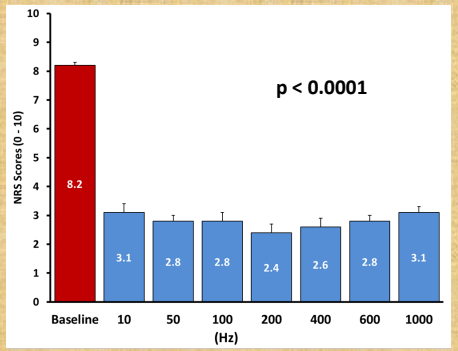


Results

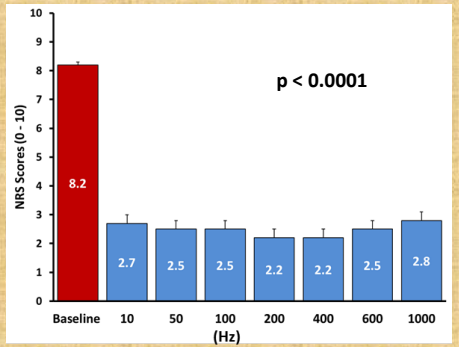
Low Back Pain Scores (n = 30)



Overall Pain Scores (n = 30)



Leg Pain Scores (n = 30)

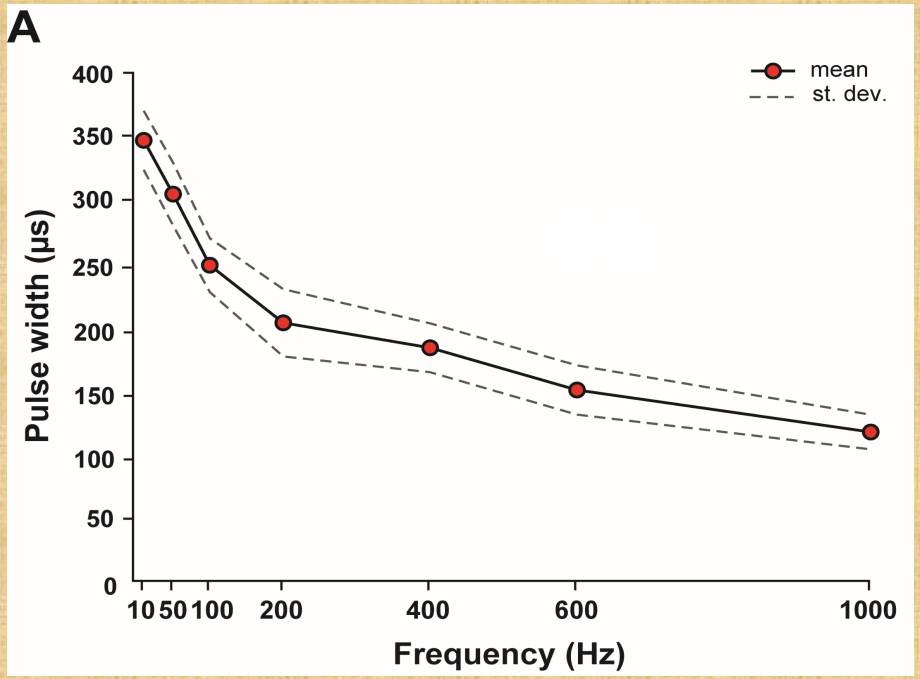


Conclusions

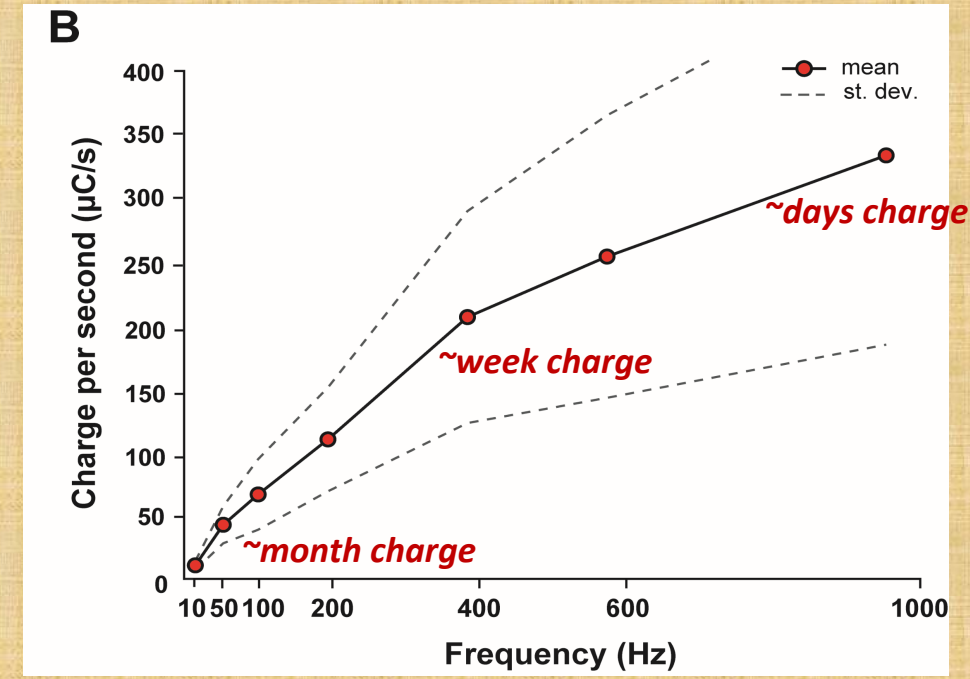
- The **Rule of Neural Dosing** holds for frequencies below 1,000 Hz
  - Effective sub-perception pain relief is achieved for all frequencies (10 Hz-10 KHz) by staying within the neural dosing window
  - Charge-per-second can be drastically reduced, thus enabling patient charging burden to be largely reduced
  - Some known waveforms (e.g. 10 kHz) are just a single point within the neural dosing curve
  - In contradiction with constant duty cycle hypotheses

Results: Neural Dosing Curves

Frequency-Pulse width Relationship



Frequency-Charge Relationship



SCS modalities scenario

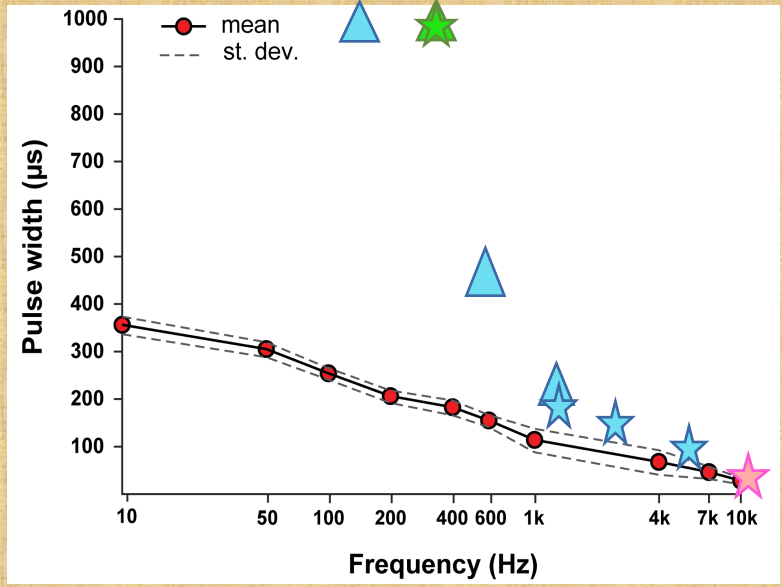
Sub-perception SCS

Neural Dosing

Neural dosing curves define the relationship between:

waveform parameters &

effective sub-p pain relief (10 Hz-10 KHz)



HF (10 KHz) — X — Frequencies below 10 kHz → Less/ineffective pain relief?

High Density — X — Must maintain duty cycle constant (20-25%) [Yang, 2019]?

BurstDR — X — One Fixed burst pattern (5 x 1000 µs @ 500 Hz) is best?

Thomson, 2018 · *Paz, 2019* · *Kapural, 2015* · *Al-Kaisy, 2017* · *Yang, 2019* · *Deer, 2017* · *Vesper, 2019*

Neural Dosing in context of literature

Sub-perception SCS

Neural Dosing

Neural dosing curves define the relationship between:

waveform parameters &

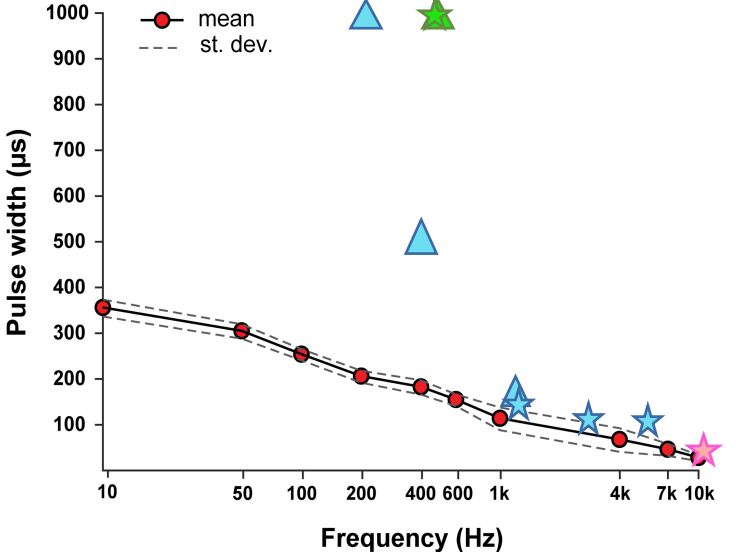
effective sub-p pain relief (10 Hz-10 KHz)

HF (10 KHz) — X — Frequencies < 10 kHz provide effective sub-p pain relief

High Density — X — No need to maintain constant density when reducing frequency

BurstDR — X — Many waveform patterns can provide effective sub-p pain relief

Thomson, 2018 *Paz, 2019* *Kapural, 2015* *Al-Kaisy, 2017* *Yang, 2019* *Deer, 2017* *Vesper, 2019*



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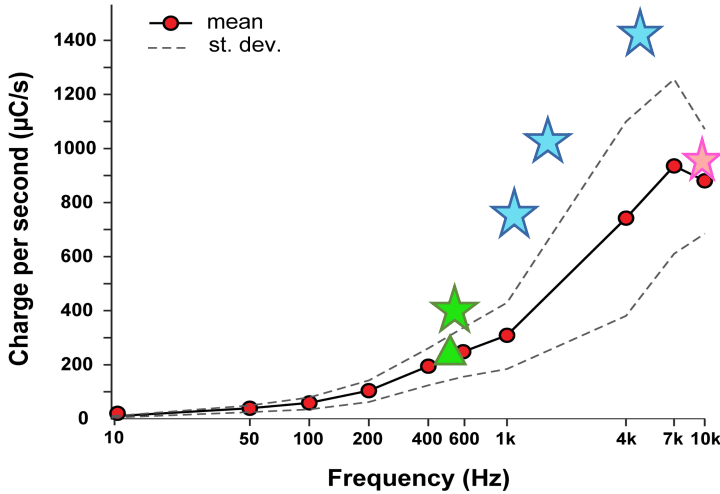
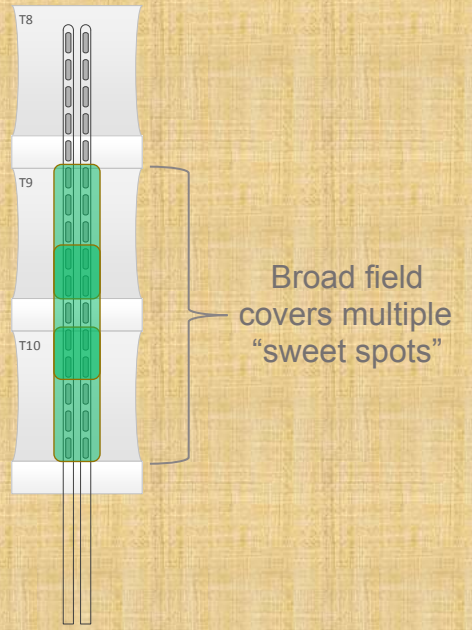


Sub-p Challenges: Current State and Future Directions

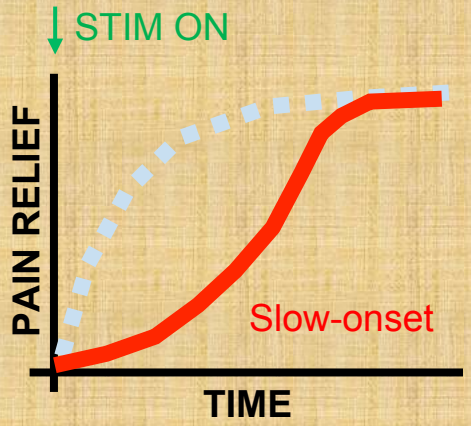
(1) Lengthy "sweet spot" search

→ Faster search



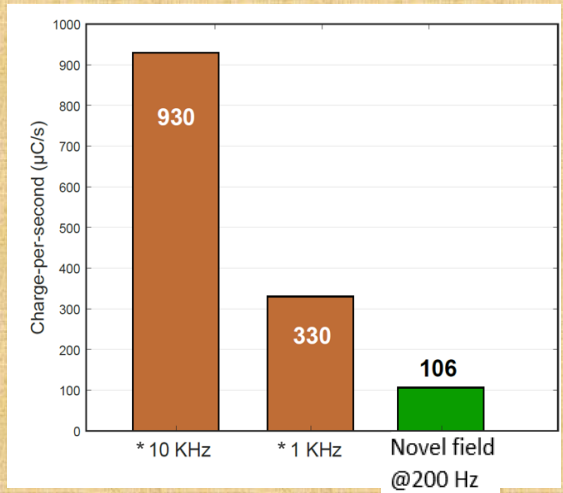
(2) Latency of analgesia (1-3 days)

→ Future study is needed



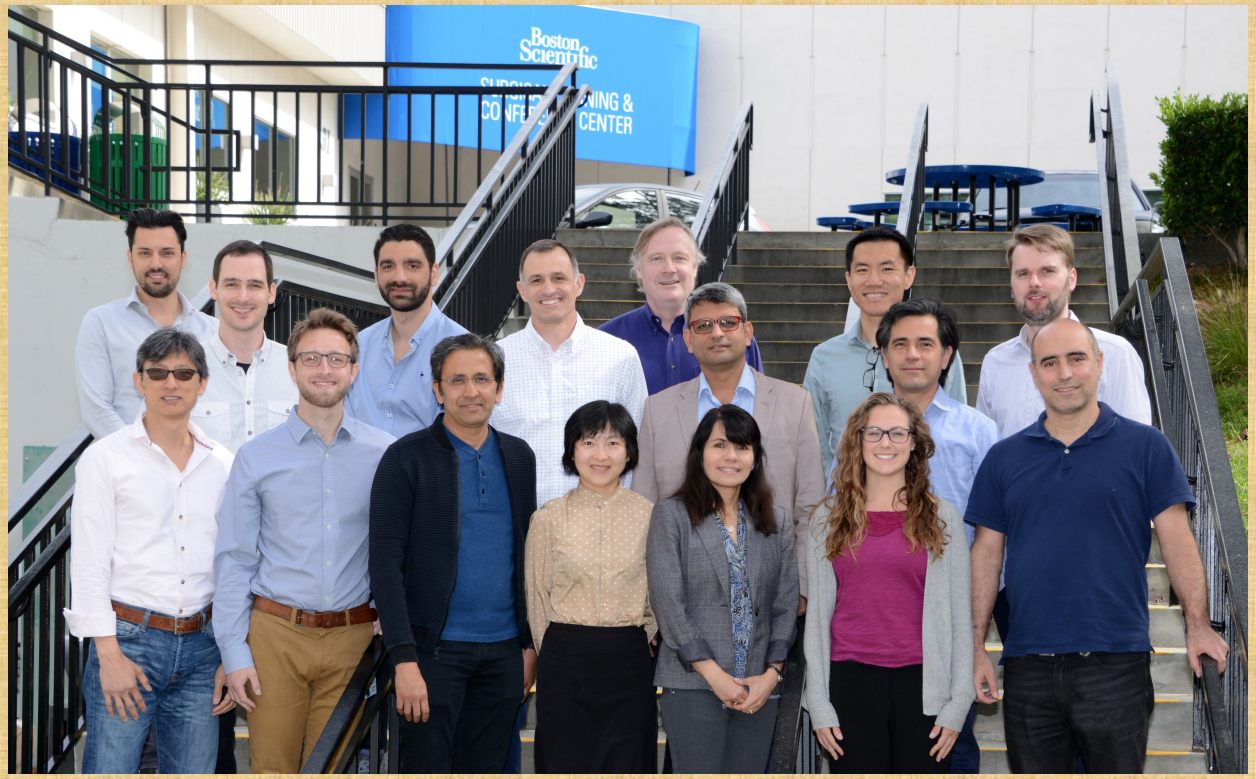
(3) High charge burden

→ Reduced charge burden



*Thomson S. *et al.* *Neuromodulation* 2018 Jan; 21(1):67-76.

NRAC Team 2019; BTUH and La Paz Clinical & Research Teams



Dr. Jose Paz

Dr. Simon Thomson
MBBS

Dr. Ismael Huertas
PhD

Thank You!