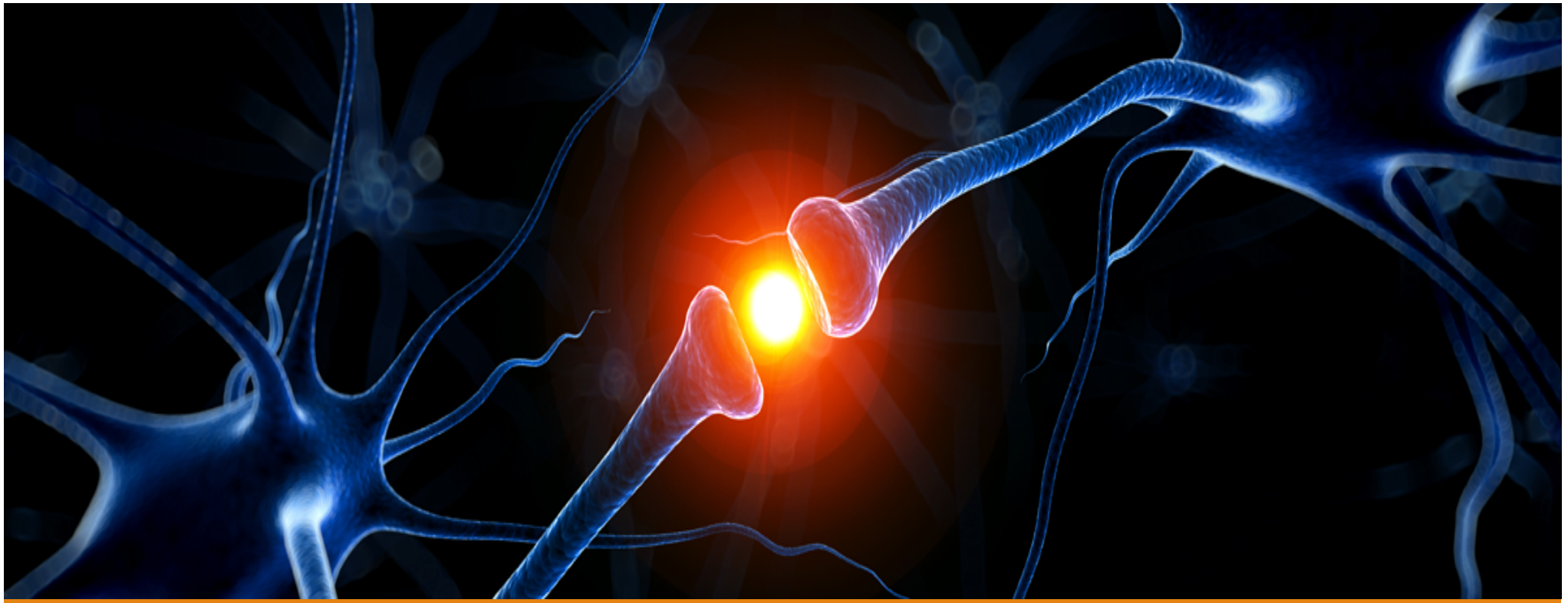


Grupo de Trabajo de Neuromodulaction
Dolor De Espalada Y Estimulacinón Eléctrica

Estimulación Medular con sistema BurstDR

Madrid, 4 Nov 2017

Stefan Schu, MD
Center of Neuromodulation
Sana Klinikum Duisburg, Germany

Disclosures:

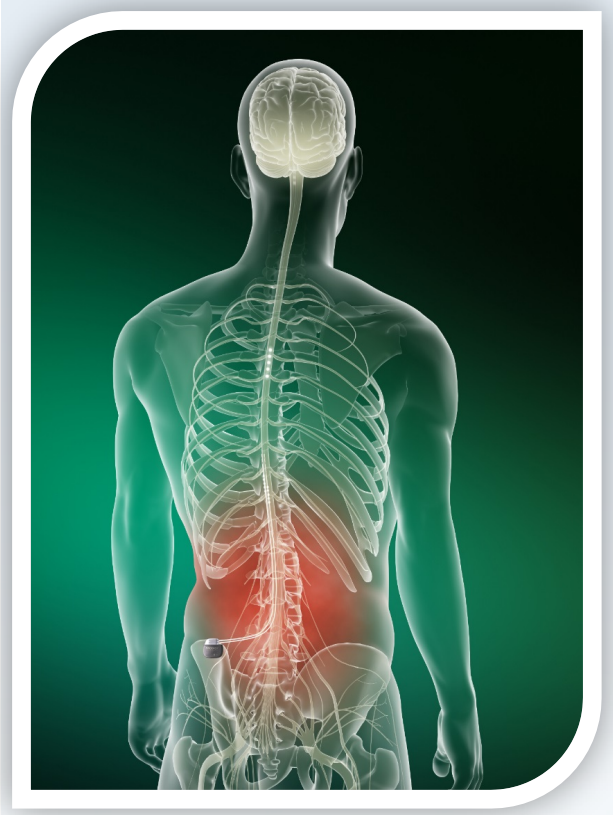
- Dr. Stefan Schu is a paid consultant for

- Abbott

- training and education
- advisory board member

SPINAL CORD STIMULATION –

A STANDARD OF CARE IN THE TREATMENT OF CHRONIC PAIN



- SCS has been an important part of the pain physician's continuum of care since its first reported use in 1967
- Since then, the efficacy of SCS in relieving pain from failed back surgery syndrome (FBSS) has been demonstrated in two randomized, controlled studies.[1,2]
- A recent meta-analysis of spinal cord stimulation studies suggests that up to 77% of patients obtain good pain relief with tonic stimulation.[3]

1. North RB, Kidd DH, Farrokhi F, et al. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: A randomized, controlled trial. *Neurosurgery.* 2005;56(1):98-106; discussion 106–107.
2. Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: A multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain.* 2007;132(1-2):179-88.
3. Frey ME, Manchikanti L, Benyamin RM, et al. Spinal cord stimulation for patients with failed back surgery syndrome: A systematic review. *Pain Physician.* 2009;12(2):379-97.

CONCEPT OF SPINAL CORD STIMULATION

Neuropathic pain

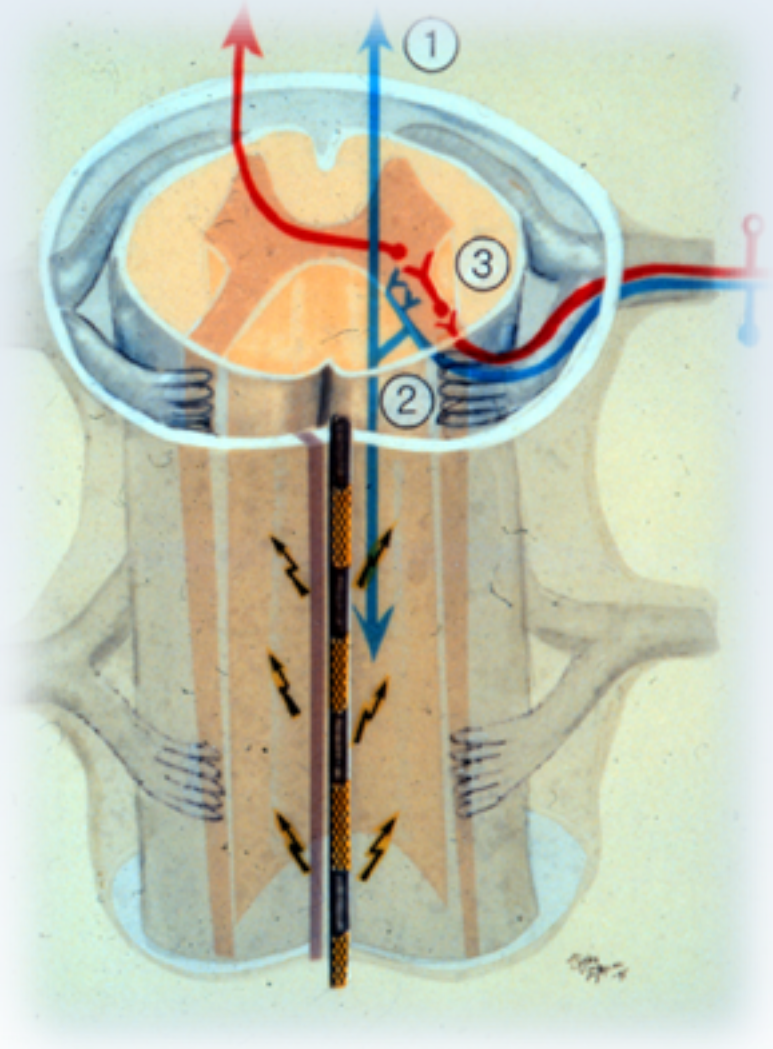
Ectopic or spontaneous discharges in C fibres
(Wu 2002)

Paresthesia and dysesthesia

Ectopic discharges in Aβ fibres
(Ochoa 1980, Nordin 1984)

Spinal cord stimulation

Activates Aβ to suppress C and Aδ fibers
Via inhibitory interneurons (Melzack & Wall 1965)



Cui et al., Neuroscience Letters, 1998.

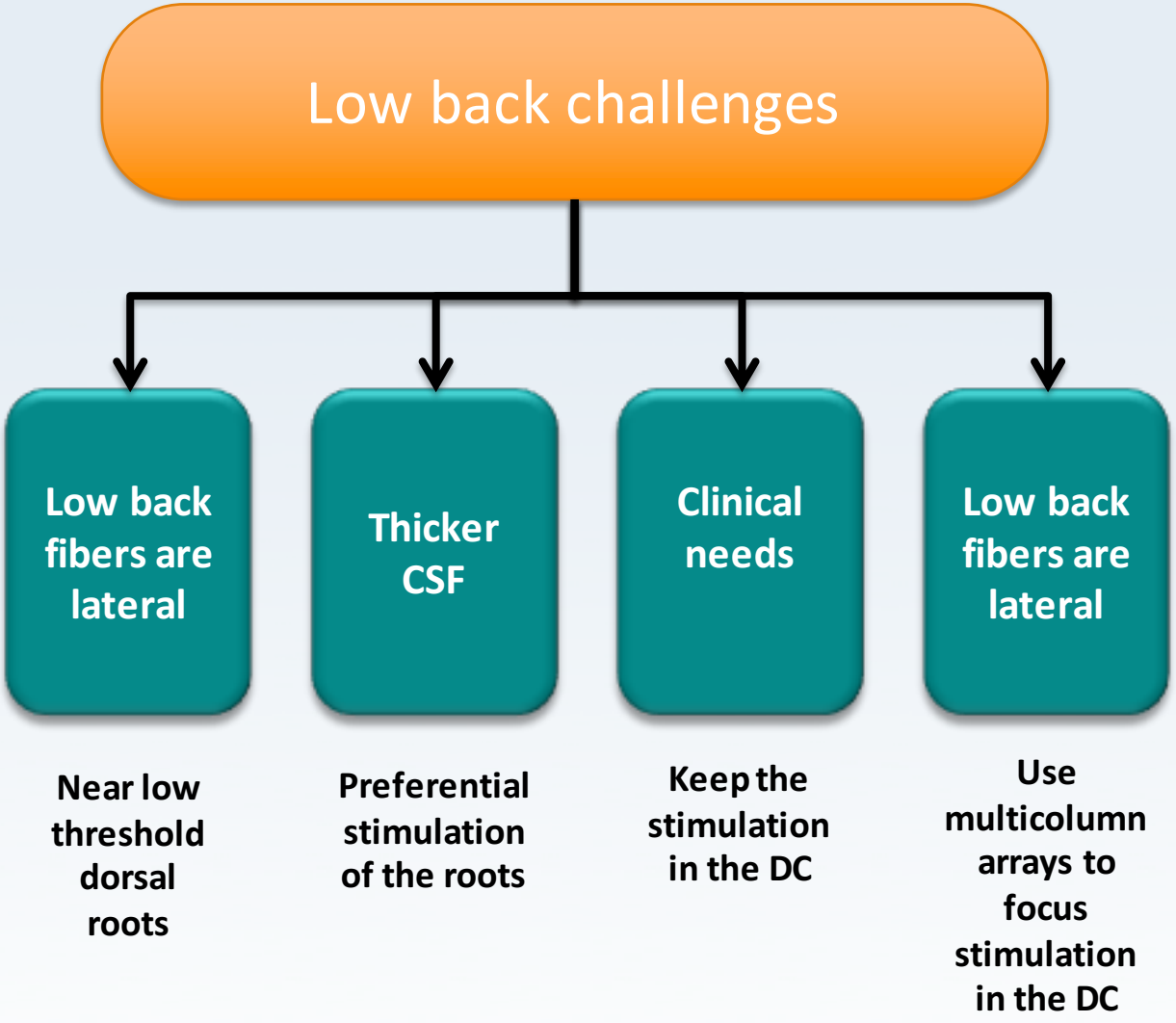
CHALLENGES REMAIN, DESPITE SUCCESS OF SCS

- However despite the success of SCS, there remains a small but clinically relevant patient population that are SCS non-responders
- This may include:
  - Patients who fail an initial SCS trial procedure
  - Patients who initially respond at trial, and then experience a gradual decline in response (coverage and/or pain suppression) which is not able to be recaptured
  - **Patients with complex back pain of severe intensity, which is inadequately addressed via tonic SCS.**

As a result, some pain practitioners have come to believe that effective pain coverage may require the availability of alternate stimulation options or settings

BACK PAIN – THE CHALLENGE

MAIN FACTORS OF THIS CHALLENGE

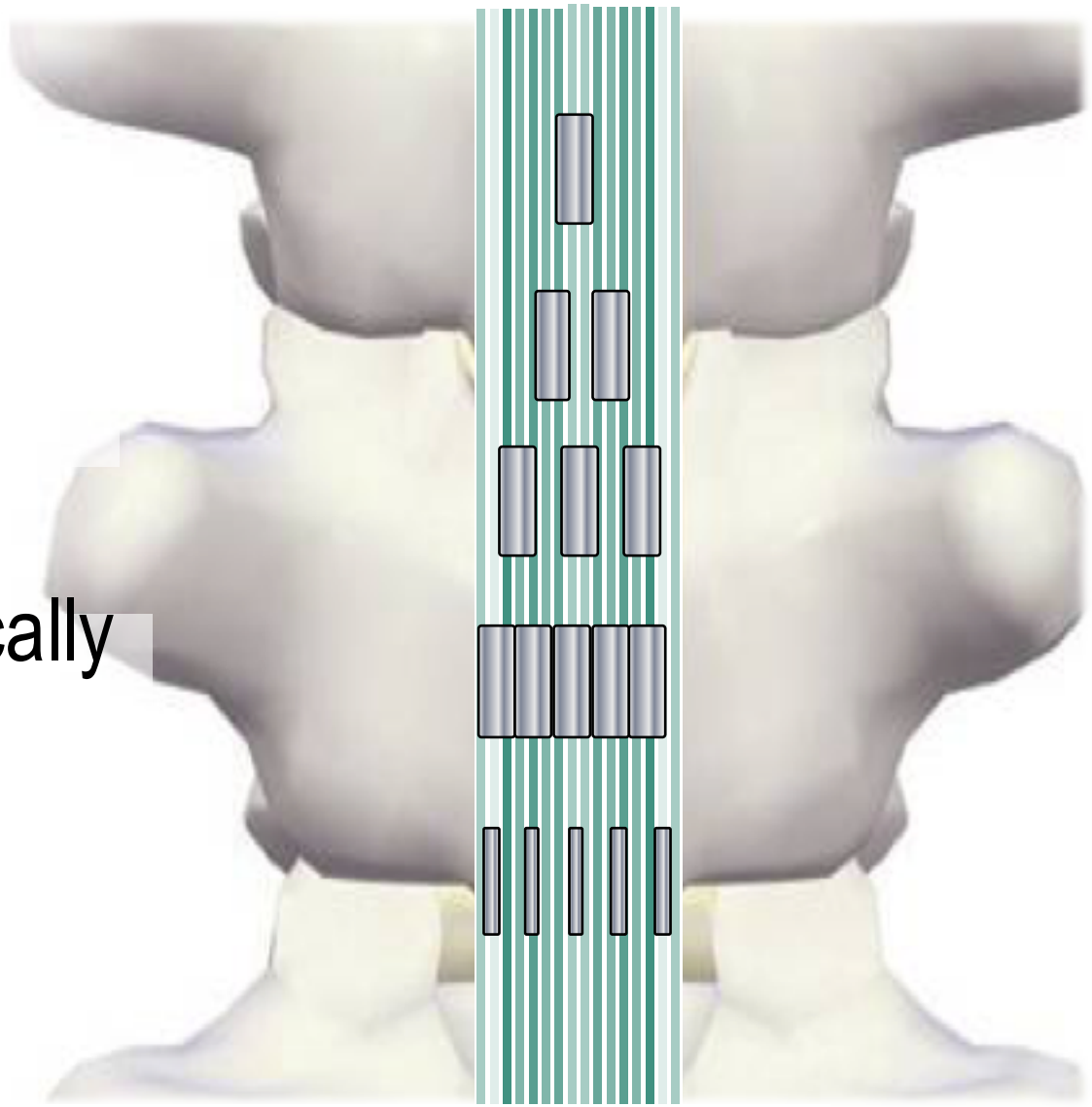


LOW BACK PAIN . . .

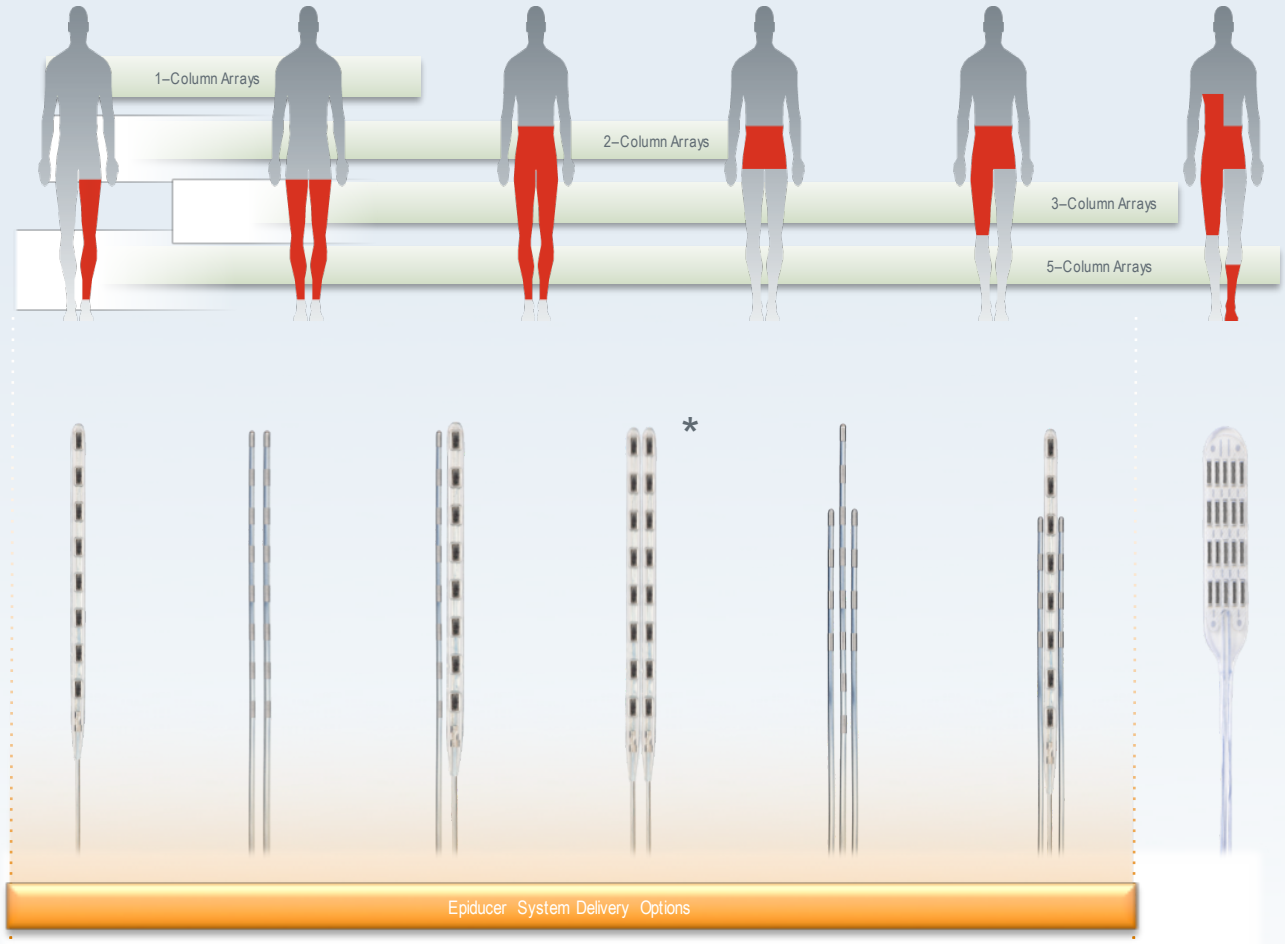
What we had

What we theoretically want

What we need



OPTION I – LEAD CONFIGURATION



Percutaneous Leads

Pros

- Minimally invasive
- Steerable
- Multiple configurations and placements are possible

Cons

- Migration
- 360° energy field

Paddle Leads

Pros

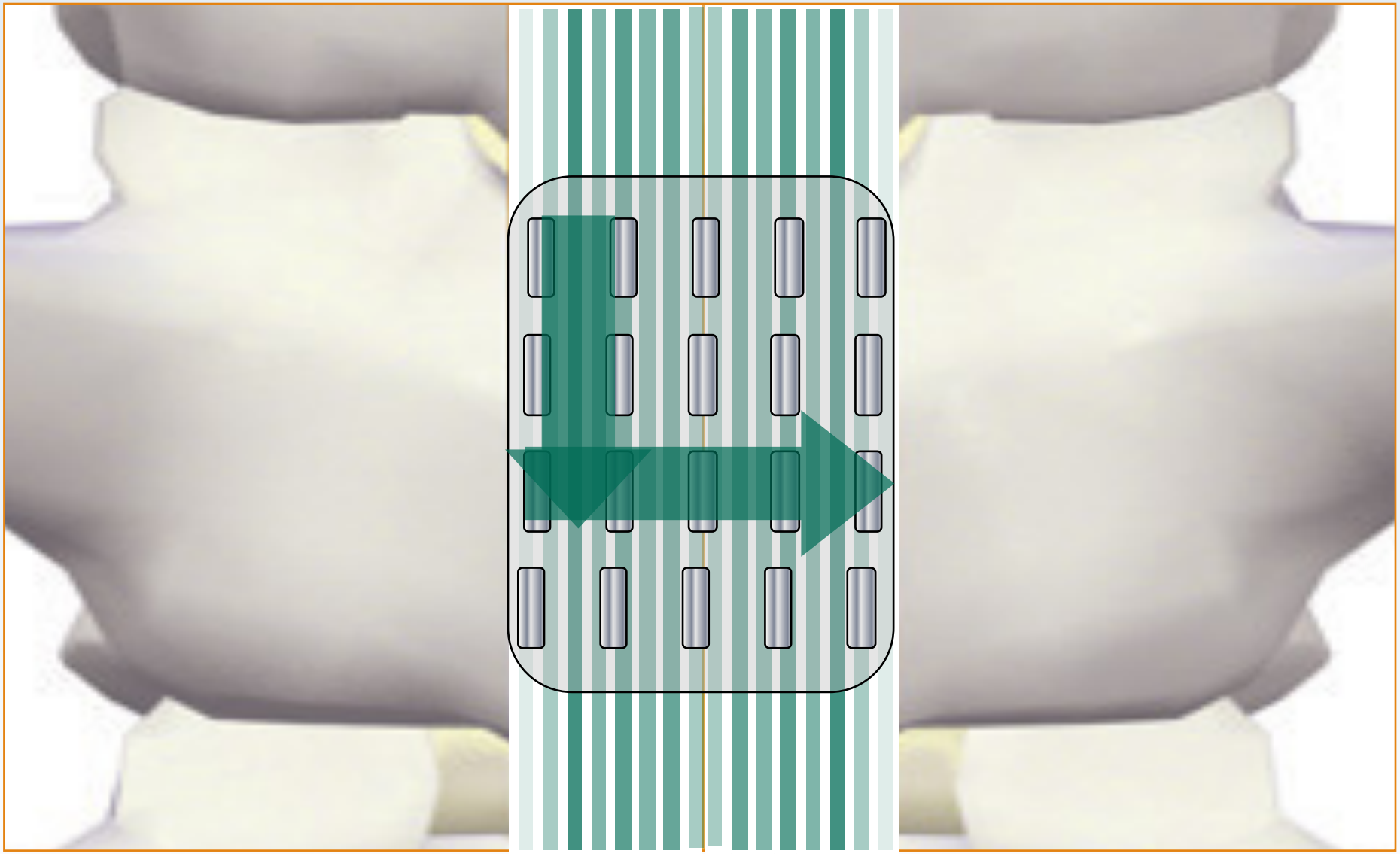
- Almost 60% less migration
- More focused energy delivery
- Potentially require less energy
- Multiple configurations and placements are possible

Cons

- Requires surgical procedure

*

OPTION II – PROGRAMMING



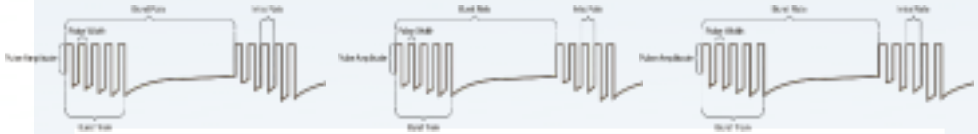
SPINAL CORD STIMULATION WAVEFORMS

Traditional Tonic Stimulation (40 years experience)

•low energy, recharge every 1-2 months

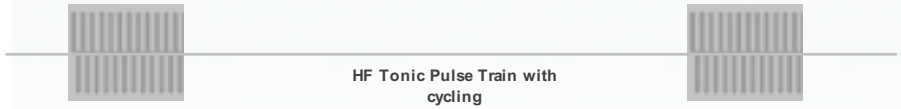
High Frequency Stimulation

- Parameters outside the traditional ranges
- High energy, daily recharge
- **provides tonic stimulation** at programmable frequencies (up to 10,000hz)



BurstDR™

- Parameters within traditional ranges
- moderate energy
- Average recharge 1 week
- Device provides <u>both</u> tonic & burst

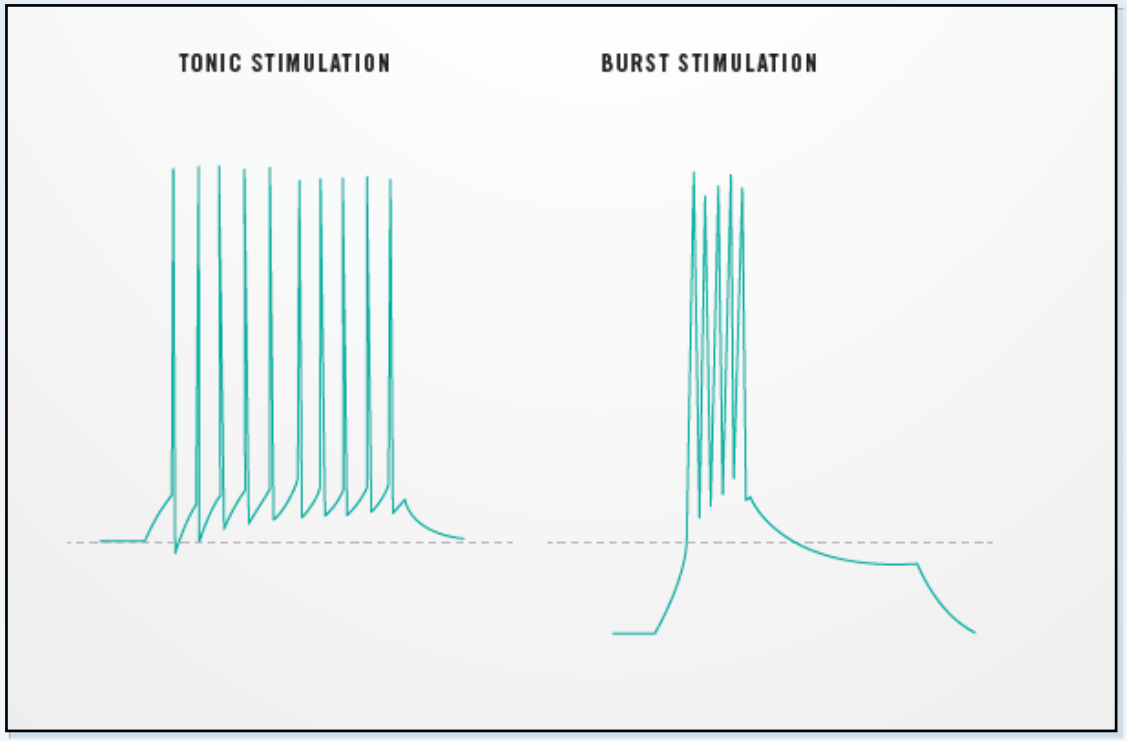


Burst (like) stimulation

provides cycled tonic stimulation at programmable frequencies

BURSTDR™ TECHNOLOGY

A clinically proven stimulation alternative for patients who no longer receive a benefit from tonic stimulation



*As studied by De Ridder D, et al.[4,5]

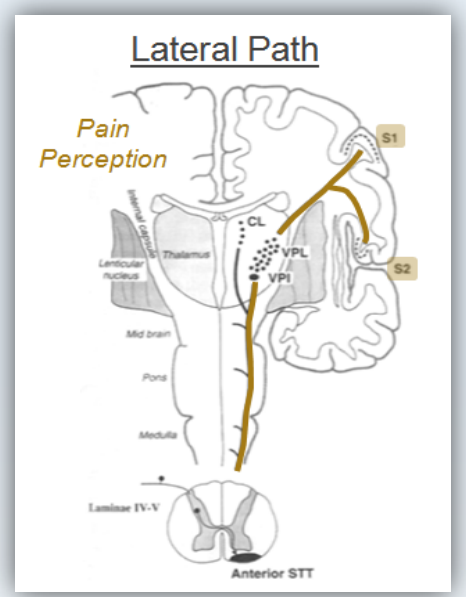
- Burst Technology consists of intermittent packets of closely spaced stimuli.
- 40 Hz burst rate with five intra-burst pulses at 500 Hz
- Each 500 Hz pulse is 1ms in duration with a 1ms interpulse interval.

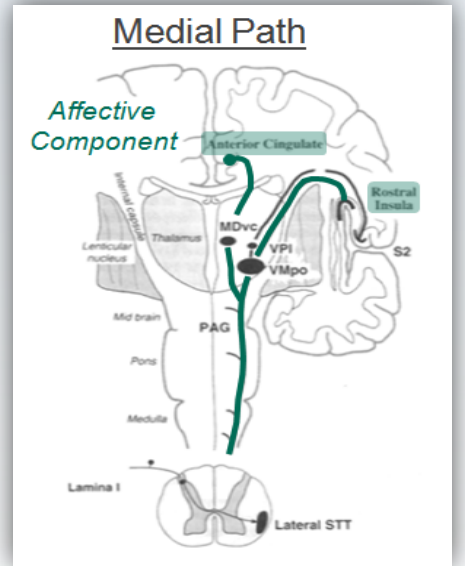
4. De Ridder D, Plazier M, Kamerling N, et al. Burst spinal cord stimulation for limb and back pain. World Neurosurgery. 2013 Jan 12. [Epub ahead of print]. N=15.
5. De Ridder D, Vanneste S, Plazier M, et al. Burst spinal cord stimulation: Toward paresthesia-free pain suppression. Neurosurgery. 2010;66(5):986-90. N=12.

CURRENT WORKING HYPOTHESIS:

BURSTDR™ STIMULATION MAY EXERT ITS MAIN EFFECT THROUGH AN ABILITY TO MODULATE BOTH LATERAL & MEDIAL PATHWAYS

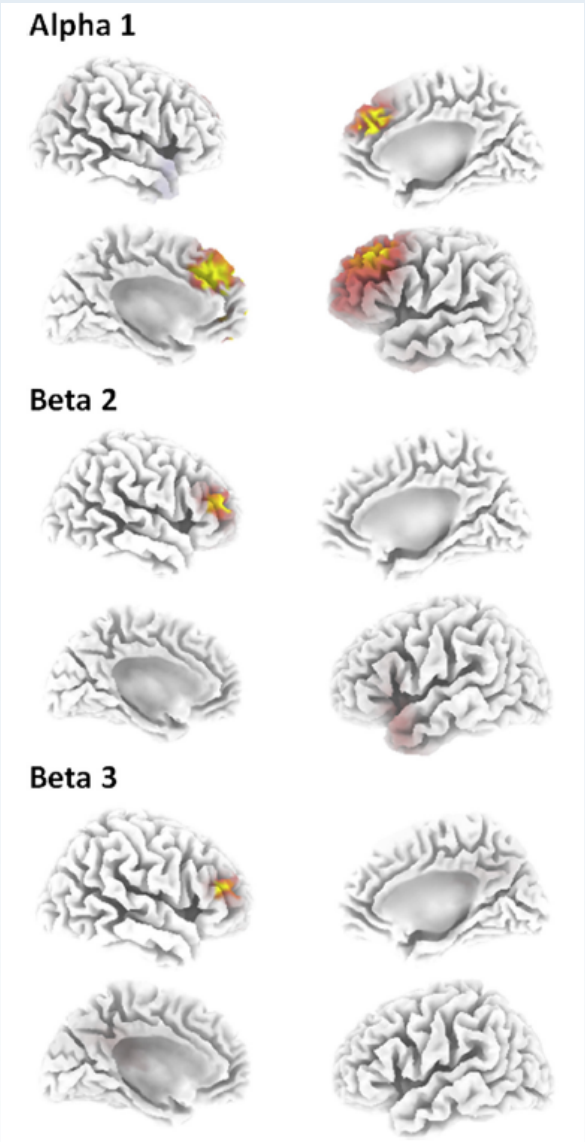
- Pain stimuli are likely processed in parallel by two pathways:
- Lateral discriminatory pathway – helps identify the location, type and intensity of pain
  - Hybrid pathway consisting of
    - WDR neurons firing in tonic → PH (lam. 1, 4-6) → Thalamus (VPL, VPM) → 1 & 2 SSC. Predominant triggering neurons in the lateral pathway
    - Low-threshold neurons firing in burst can also be found in the lateral pathway
- Medial affective/attentional pathway – helps drive attention & salience to the pain
  - Nociceptive specific neurons firing in bursts → PH (lam. 1) → Thalamus (MDvc, VMpo) → Anterior Cingulate, Anterior Insula, Amygdala.
  - Fires in bursts[2].





1. De Ridder D, et al. World Neurosurgery 2013.
2. Lopez-Garcia JA, and AE King. Eur J Neuroscience 1994.
3. Squire L, Berg D, Bloom FE, et al. Fundamental Neuroscience. 3rd Edition, Chapter 25: Somatosensory System, Academic Press (Elsevier), p. 599, 2008.

SOURCE-LOCALIZED EEG SUPPORTS SIGNIFICANTLY

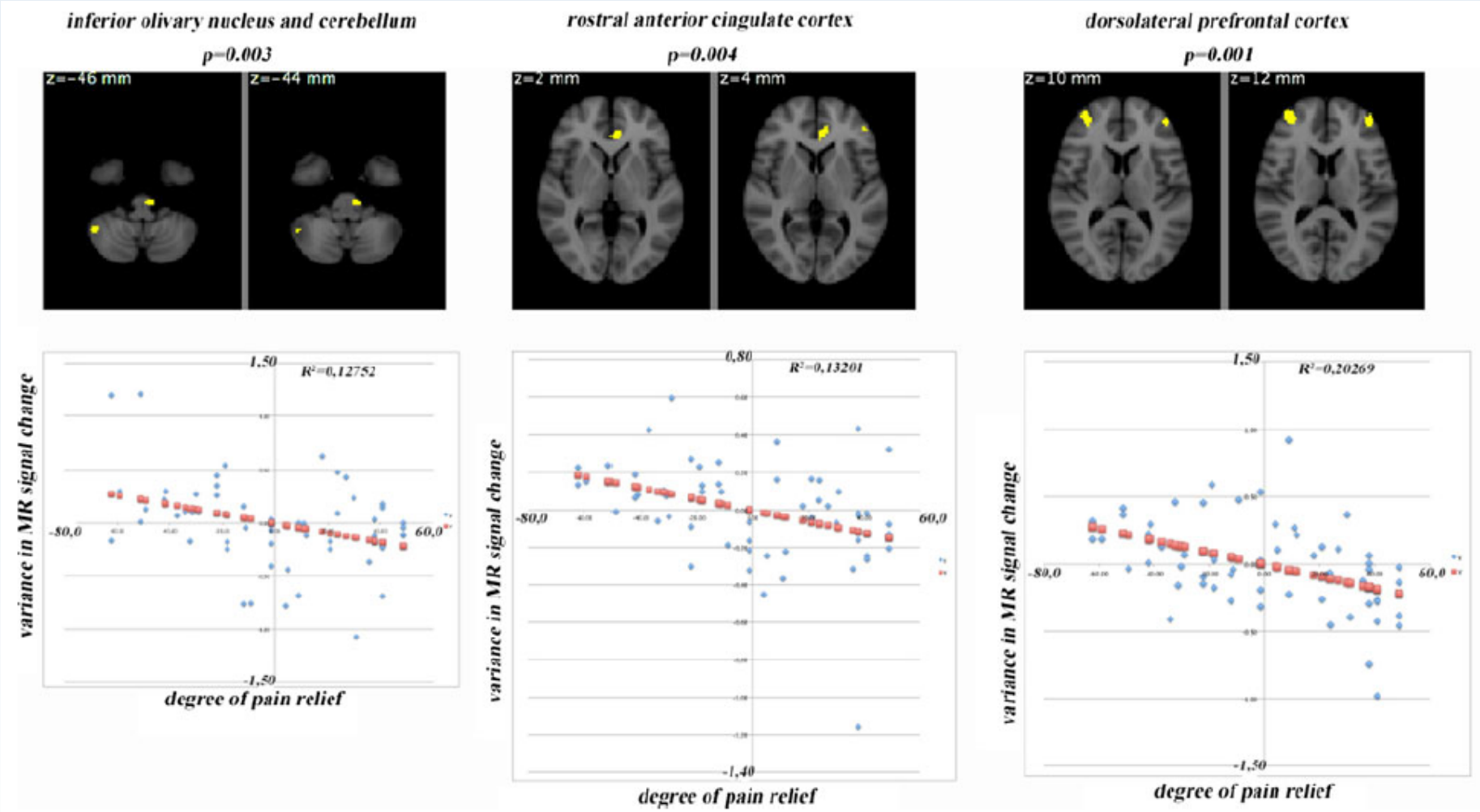


In a subgroup of 5 patients in De Ridder's study, burst stimulation showed more alpha activity in the dorsal anterior cingulate in comparison with tonic, placebo, and baseline.

1. De Ridder D, et al. World Neurosurgery 2013.
2. Lopez-Garcia JA, and AE King. Eur J Neuroscience 1994.
3. Squire L, Berg D, Bloom FE, et al. Fundamental Neuroscience. 3rd Edition, Chapter 25: Somatosensory System, Academic Press (Elsevier), p. 599, 2008.

De Ridder, et al. World Neurosurgery 2013

FMRI STUDY SUGGESTS THALAMUS AND ACC ARE RESPONSIVE TO SCS STIMULATION AND MODULATING PAIN PERCEPTION

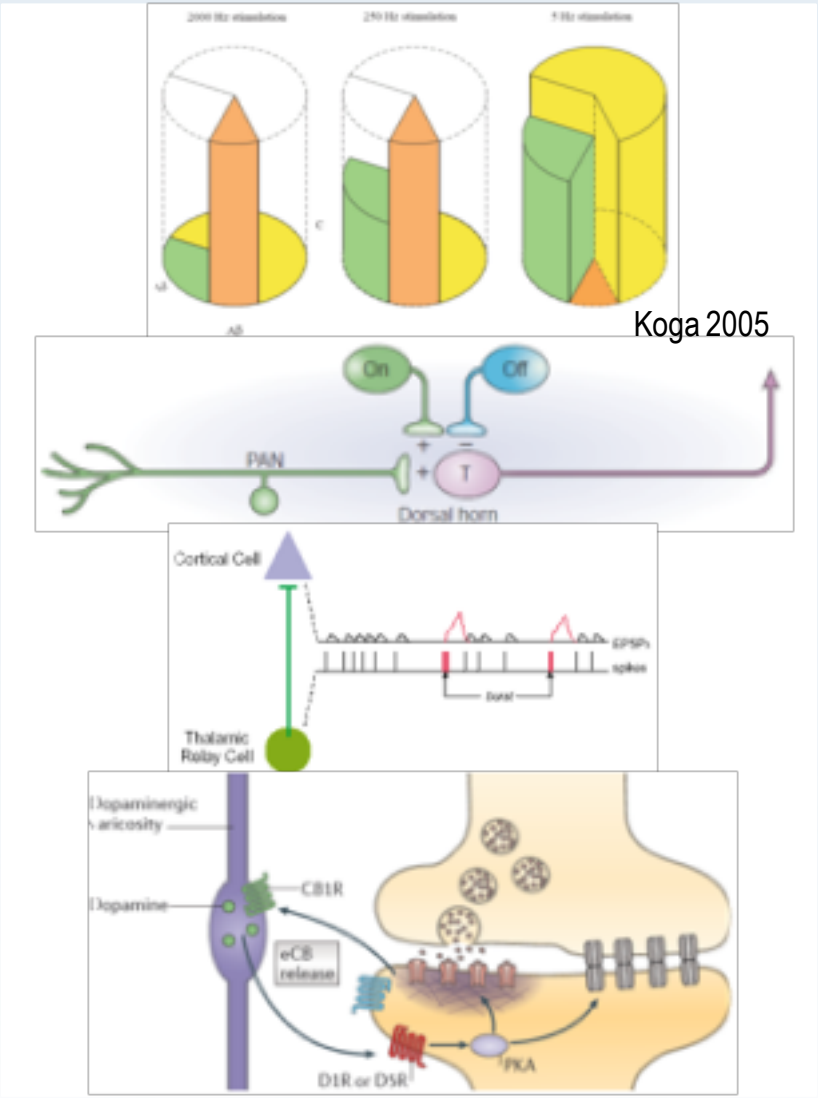


Moens M, et al. Neuroradiology 2012.

BURSTDR™ SPINAL CORD STIMULATION

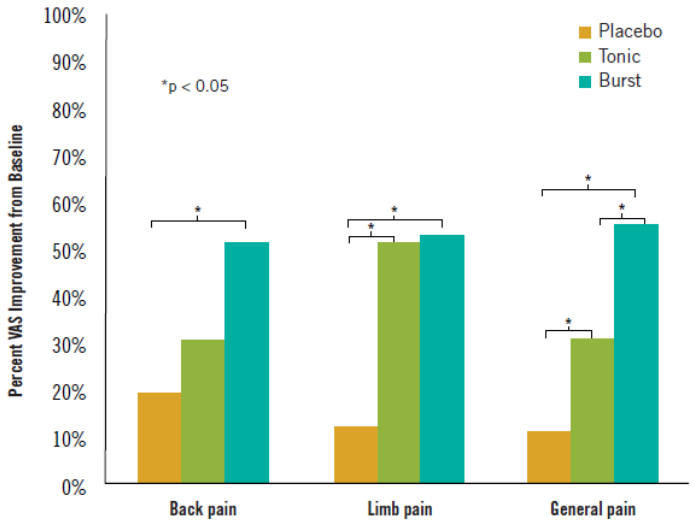
Hypothetical working mechanisms

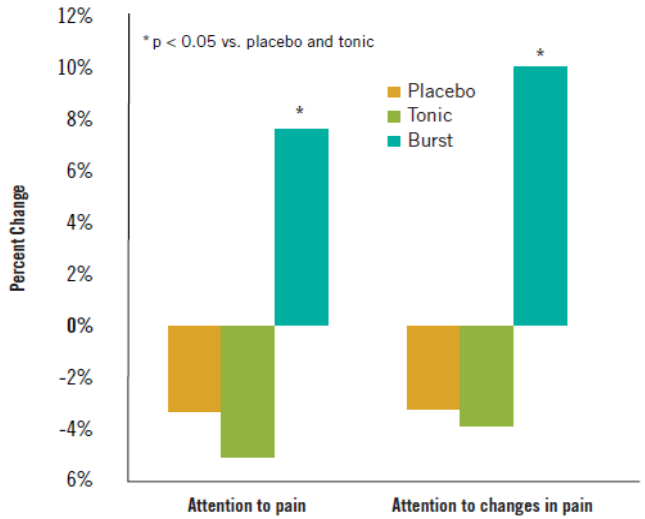
1. Burst firing like high frequency firing selectively modulates Aβ fibers, without activating C fibers (Koga 2005, Sundar 2006)
   Subthreshold stimulation can already suppress pain
2. Frequency dependent opioid release from dorsal horn neurons with maximal release at 500 Hz (Song 2003)
3. Burst modulates medial and lateral system vs tonic only lateral system
4. Burst modulates Off-cells of descending antinociceptive system
5. Burst is stronger activator than tonic
6. Activation of pleasure evoking tactile C-fibers (Liljencrantz 2014)
7. 500 Hz burst induces LTP of mixed electrical and chemical synapses (Yang 1999, Pereda 2014)



BURSTDR™ SPINAL CORD STIMULATION FOR LIMB AND BACK PAIN

De Ridder, et al. *World Neurosurgery*, 2013[3]





- This single-center study compared three stimulation paradigms (Burst stimulation, tonic stimulation and placebo) in a randomized trial on consecutive patients (n = 15).
- Compared to baseline, Burst stimulation significantly reduced back pain by 51.3%, leg pain by 52.7% and general pain by 55.0%. Statistical analysis revealed that Burst stimulation was significantly different from placebo stimulation for back pain, limb pain and overall pain ($p < 0.05$). See Figure 3.
- There were no differences between tonic and Burst stimulation for back pain or limb pain. However, a significant difference was obtained between tonic and Burst stimulation for general pain. See Figure 3.

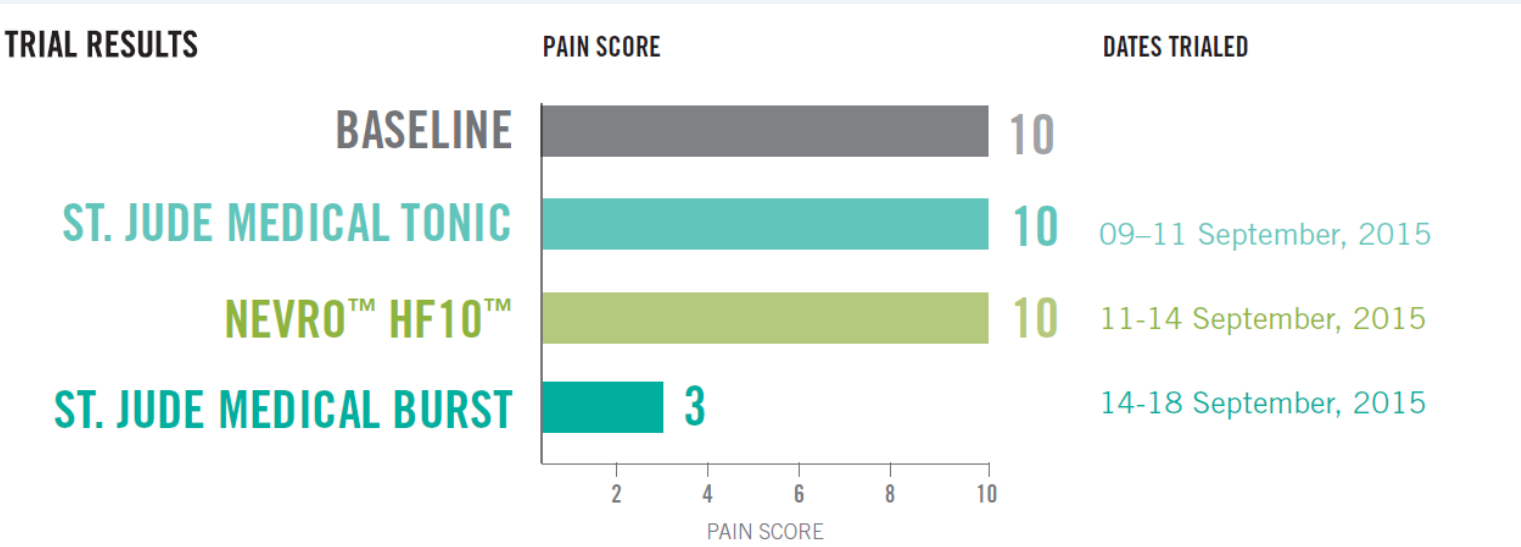
3. De Ridder, D., Plazier, M., Kamerling, N., Menovsky, T., & Vanneste, S. (2013). Burst spinal cord stimulation for limb and back pain. *World Neurosurgery, 80*(5).

CASE STUDY:

BURSTDR™ STIMULATION IS SUPERIOR TO TRADITIONAL TONIC STIMULATION IN A 49-YEAR-OLD PATIENT

Björn Carsten Schultheis, Dr. med.
Hospital Neuwerk, Mönchengladbach, Germany

- 49-year-old female with a history of herniated disc (2011) and epiduroscopy (2013). Following the epiduroscopy, the patient continued to suffer from back and leg pain through September 2015.
- The patient underwent several treatments, including injection therapy, electrical stimulation therapy, manual therapy, rehabilitation sports and transcutaneous electrical nerve stimulation (TENS)—none of which provided effective pain relief long-term.
- The patient cannot work and must rest frequently (every 500 m) when walking due to pain. The pain worsens in the evening and she does not sleep well.
- The patient takes the prescribed 50 mg of morphine 3 times per day.



SUMMARY

- BurstDR™ stimulation lead to a significant improvement of SCS therapy
- BurstDR™ is able to suppress pain equally or even better than tonic stimulation
- BurstDR™ significantly reduces the SCS non responder rate
- BurstDR™ Activation of pleasure evoking tactile C-fibers (Liljencrantz 2014)


Questions?