PainWeek

Fundamentals of Neuromodulation

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Disclosure

- Consultant: Nevro, Camber Spine, Vertos

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Learning Objectives

- Explore the use of electrical signals to block pain
- Review the theory of how neuromodulation works, MOA
- Explore the different products that are currently on the market
- Review the application of the devices in clinical practice
- Review data supporting use of products and their role in decreasing opioid use
- Discuss the process of trial and implantation of devices

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History of Neuromodulation

- First used to treat pain in 1967
- Gate theory was published in 1965
- Became more mainstream in 1980s
- 1989 FDA approved use of devices to treat chronic pain from nerve damage in trunk, arms or legs
- Year after year the devices continue to improve upon earlier iterations

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Neuromodulation

- So what is it?
- Application of electrical signals to lessen pain complaints
- Drug/medication = electricity
- Types of neuromodulators
  - Spinal cord stimulators, dorsal column stimulators, dorsal root ganglion stimulators, peripheral nerve stimulators

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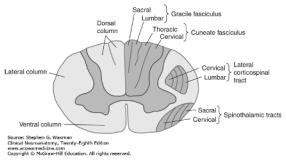
Mechanism of Action

- Continues to be elucidated
- Current thought is that it increases firing of inhibitory neurons in the dorsal spinal horn
  - Decreases transmission/signaling of painful stimulus from reaching brain
  - Gate control theory



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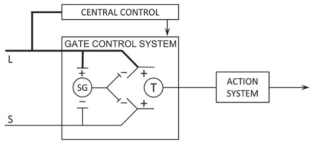
Gate Control Theory

- Published in 1965 in Science by Melzack and Wall
  - "Pain Mechanisms: A New Theory"
- Revolutionized theory of pain control



Katz, Rosenbloom. The golden anniversary of Melzack and Wall's gate control theory of pain: Celebrating 50 years of pain research and management. Pain Research and Management. 2015 Nov-Dec; 20(6): 285-286
Melzack, Wall. Pain mechanisms: A new theory. Science. 1965-150:971-9

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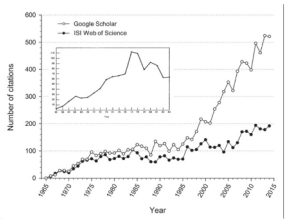
Gate Control Theory



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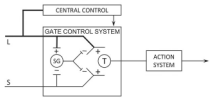
Gate Control Theory

- Gating mechanism in spinal dorsal horn modulates transmission of nerve impulses from afferent fibers to spinal cord transmission cells
  - The gating mechanism is affected by the relative activity in large and small diameter fibers with the former inhibiting transmission (closing the gate) and the latter facilitating transmission (opening the gate)
  - Gating mechanism is also modulated by descending nerve impulses from the brain
  - Burn example



Katz, Rosenbloom. The golden anniversary of Melzack and Wall's gate control theory of pain: Celebrating 50 years of pain research and management. Pain Research and Management. 2015 Nov-Dec; 20(6): 285-286

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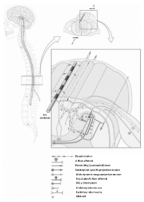
Neuromodulation and the Gate Control Theory

- Conventional SCS devices believed to relieve pain by:
  - Activation of Aβ fibers resulting in variable effects on sensory and pain thresholds
  - Potentiation of inhibition



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Sdrulla, Guan, Raja. Spinal cord stimulation: clinal efficacy and potential mechanisms. Pain Practice. 2018;18 (8):1048-1067

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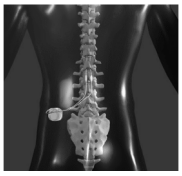
Neuromodulation

- FDA approved
  - Alleviation of pain in trunk, arms or legs
  - Chronic regional pain syndrome
    - AKA RSD or causalgia
- Most common indication/usage
  - Failed back surgery syndrome
    - Post laminectomy pain syndrome
    - Chronic pain syndrome
- Pacemaker companies
  - Developed a lot of the initial technology



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Amplitude, Frequency, Pulse Width

- Parameters we can change with SCS devices
  - Frequency is how often device delivers charge and depolarization
  - Amplitude is relative strength of charge delivered
  - Pulse width is duration of charge delivery
- Tonic or low frequency
  - 20-120Hz range
  - patients perceive individual pulses
- High frequency
  - pulses start to blend so no perception occurs

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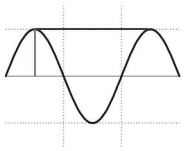
Amplitude, Frequency



Wavelength (λ)
Distance between identical points on consecutive waves

Amplitude
Distance between origin and crest (or trough)

Frequency (ν)
Number of waves that pass a point per unit time

Speed
= wavelength x frequency

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Traditional vs High Frequency vs DRG

- Traditional AKA "low frequency," "tonic"
  - Tens unit sensation, paresthesia present, can go up to 1200Hz
- High frequency, paresthesia not present, 10,000Hz
- DRG (dorsal root ganglion) stimulators
  - Low frequency, used for focal pain locations

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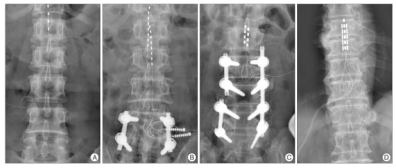
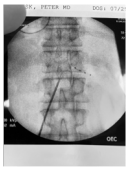
Electrodes

- Typically 8 electrodes per lead with two leads typically used
- Surgeons can place paddle leads with different configurations
- DRG 4 electrodes





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Evidence for Neuromodulation

- Kumar study
- RCT conventional medical management (CMM) vs SCS for neuropathic pain
  - Primary outcome was patients reporting 50% or more relief of leg pain
  - Secondary outcomes were improvement in back pain, QOL, functional capacity, use of medication, patient satisfaction
- Compared with CMM group the SCS group saw
  - Improved back and leg pain, better QOL, greater treatment satisfaction

Kumar, Taylor, Jacques et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomized controlled trial in patients with failed back surgery syndrome. Pain. 2007 Nov;132(1-2): 179-88

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Evidence for Neuromodulation

- Deer study
- Multicenter, prospective RCT
  - Following successful trial 100 patients were randomized after implant to receive 12 weeks of tonic stim followed by 12 weeks of burst
  - Primary endpoint assessed the noninferiorty of the within-subject difference between tonic and burst for mean daily VAS score
    - Burst stimulation is non inferior to tonic stim
    - Significantly more subjects 70.8% preferred burst over tonic; preference was sustained over 1 year

Deer, Slavin, Amirdelfan et al. Success using neuromodulation with burst (sunburst) study: results from a prospective randomized controlled trial using a novel burst waveform. Neuromodulation. 2018 Jan:21(1):56-66

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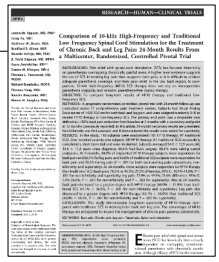
Evidence for Neuromodulation

- SENZA Study
- Head to head study of low vs high frequency
- 24 month outcomes
  - **Sustained, clinically superior outcomes**
  - **Long term, durable pain relief: 24 MONTHS**
    - **76% responder rate**
    - **2.4 cm VAS for both back and leg pain**
  - **Only device labeled as paresthesia-free**
  - **"Top Pain Paper of the Year"**



RESEARCH—HUMAN—CLINICAL TRIALS

Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial

Kapural, Leonardo et. al. 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. Anesthesiology Vol. 123 No 4. October 2015.

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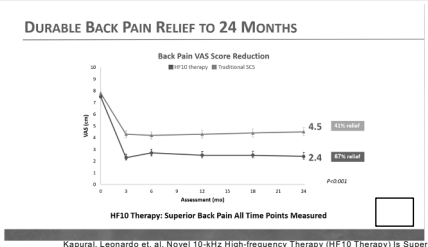
Evidence for Neuromodulation….High Frequency



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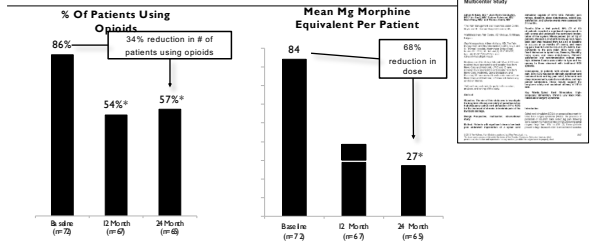
Decreased Opioid Use in SENZA-EU Trial with HF10 therapy After 2 Years



* p-value < 0.001 compared to Baseline

Al-Kaisy A, Van Buyten JP, Smet I, Palmisani S, Pang D, Smith T. Sustained effectiveness of 10 kHz high-frequency spinal cord stimulation for patients with chronic, low back pain: 24-month results of a prospective multicenter study. Pain Med. 2014 Mar; 15(3):347-54.

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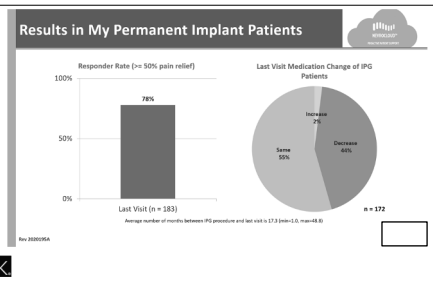
Opioid Reduction in Real World Practice



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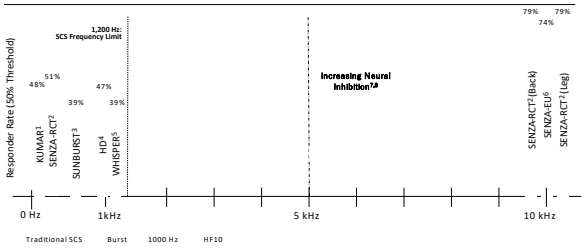
Frequency Matters



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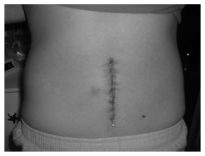
Procedure Overview (Trial)

- Only pain procedure that requires psychiatric/psychological clearance by insurance company
  - Patient is malingering or faking symptoms
  - Patient will call if there is infection or issues with device
  - Most of these patients have undergone previous spine surgery
  - Large scar present on back



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Procedure Overview (Trial)

- Placement of percutaneous electrodes into epidural space
- Just like performing an epidural. Done under xray
  - Rather than injecting medication electrodes are placed
  - Trial leads stay in place for 5-7days and are connected to a battery
    - If >50% pain reduction
    - Implant can be performed

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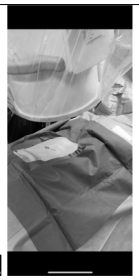
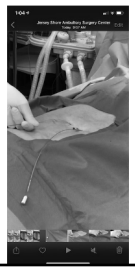
Procedure Overview (Trial)





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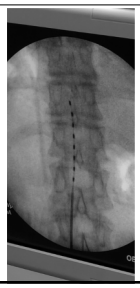
Procedure Overview (Trial)



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Procedure Overview (Permanent Implant)

- Leads are again placed into epidural space and then tunneled under skin to a battery
  - Battery, which powers the device, is placed in the flank
- Battery
  - Rechargeable vs Non-Rechargeable

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Complications/Risks of Procedure

- Infection
  - Epidural abscess
    - Paralysis
- Bleeding
  - Epidural hematoma
    - Paralysis
- Lead migration/lead fracture
  - Loss of efficacy

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Contraindications

- Severe uncontrolled psychological disorders
  - Schizophrenia, depression, bipolar disorder
- Bleeding disorder
- Use of blood thinners or NSAIDs
- Active infection
- Relative contraindication
  - Need for continued MRI studies
    - Most newer devices have MRI approval

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Questions

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