Non-CME Webinar Series
designed with the trainee in mind

second Tuesdays of odd-numbered months

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Neuromodulation

Tuesday, January 12, 2021

7-8:30 pm ET

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SCS Program, Pulse Trains, and Waveforms: The Science

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Tuesday, January 12, 2021

7-8:30 pm ET

Disclosure

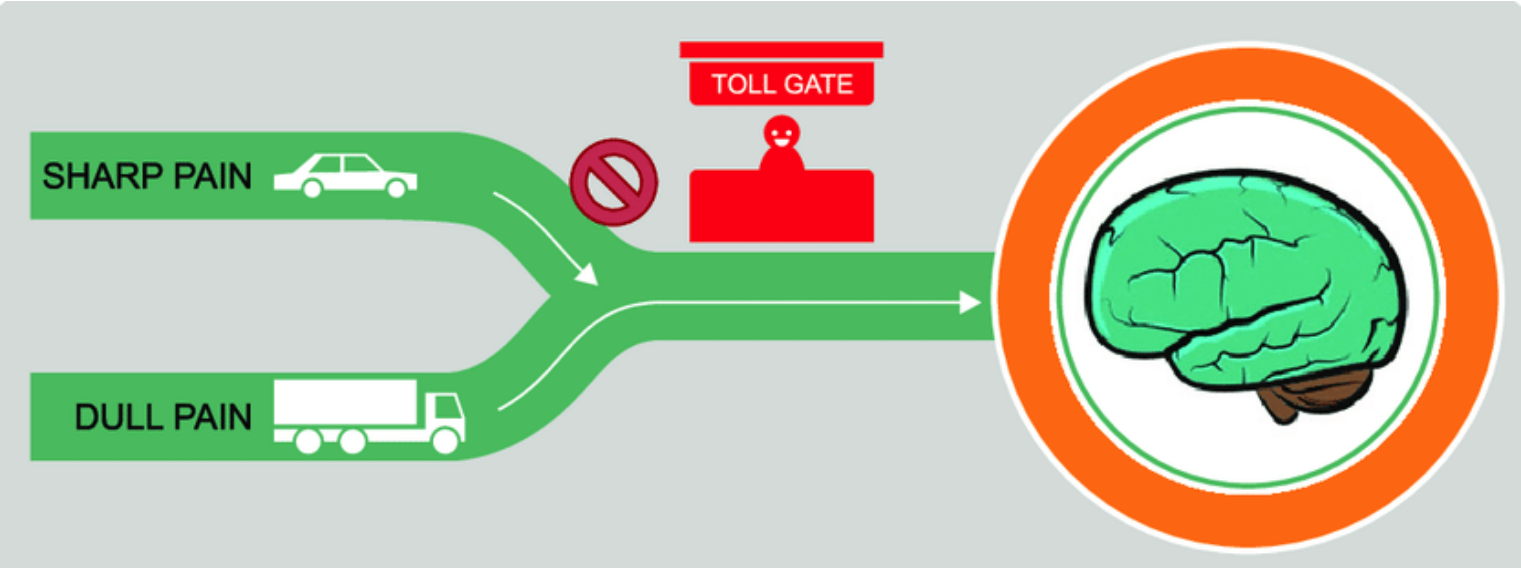
- Consultant fee: Boston Scientific, Medtronic
- Fellowship Grant: Medtronic. Abbott

Outline

- Introduction and historical perspective
- Mechanism
- The device: power source and electrodes
- Indications
- Complications

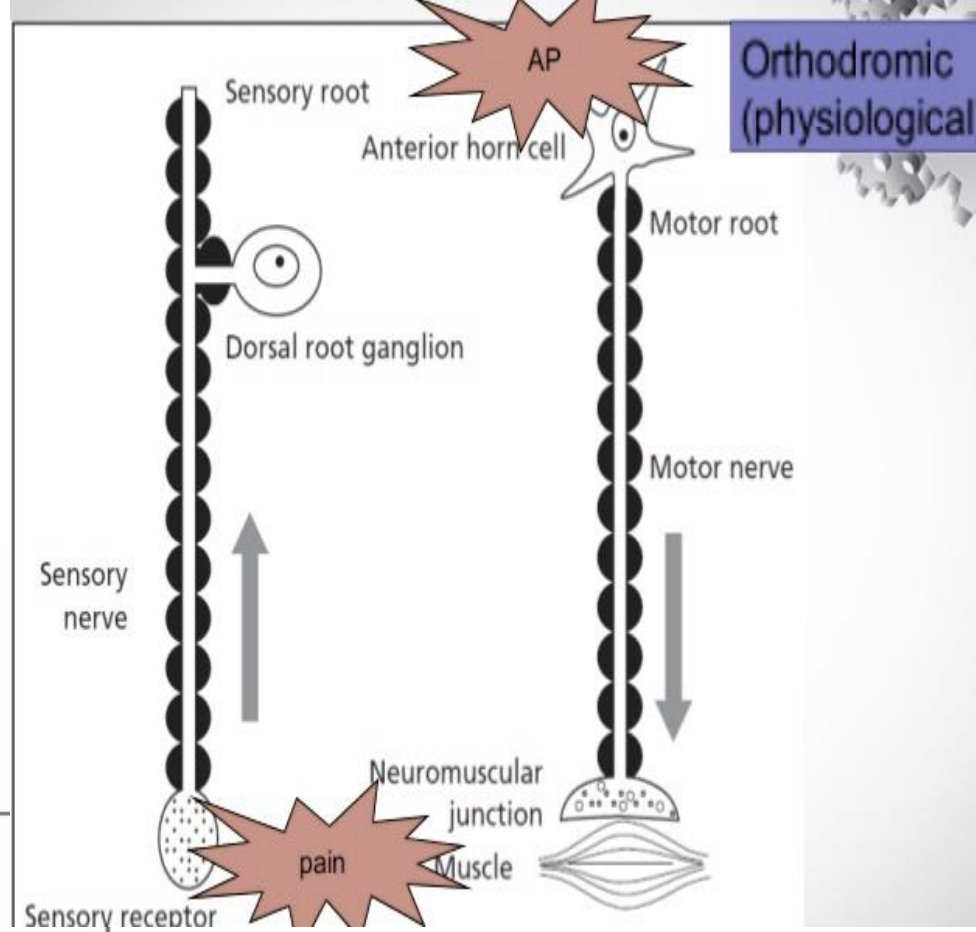
Introduction and history

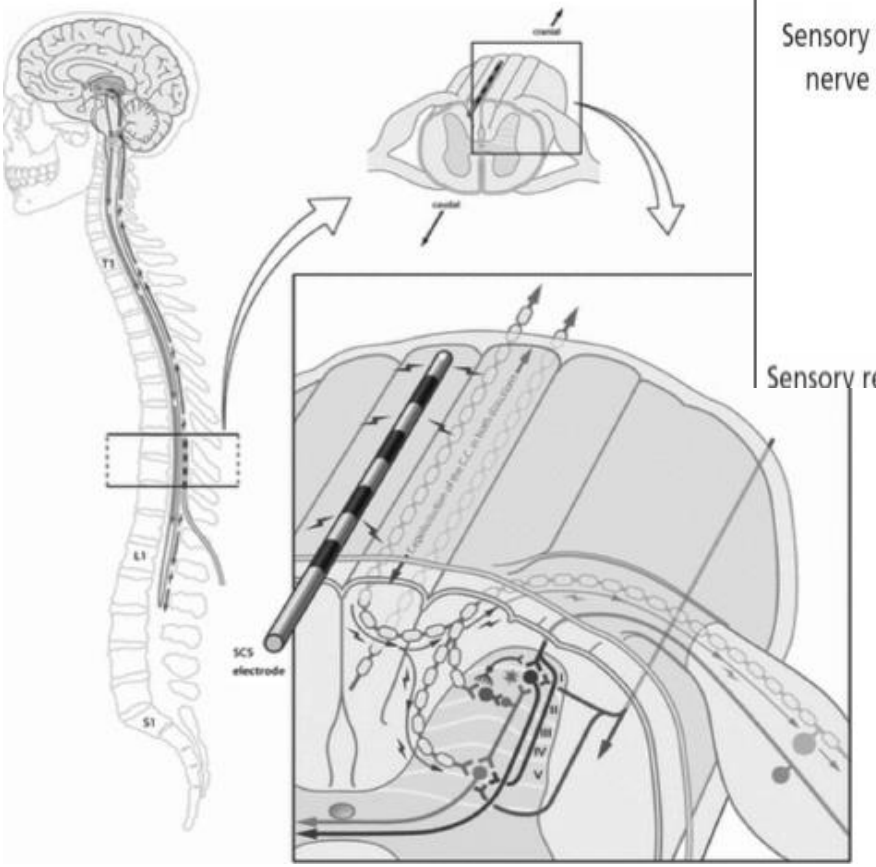
- Based on 1965 gate theory Wall & Melzack
  - Small fibers transmit pain
  - Large fibers electrical stimulation stop pain from being transmitted
- 1967: Shealy placed epidural electrodes in the dorsal (posterior) area in cancer patient- **dorsal column stimulation, later renamed Spinal Cord Stimulator**
- 50,000 implants per year
  - Increase neuropathic pain
  - Alternative to opioids



Mechanism

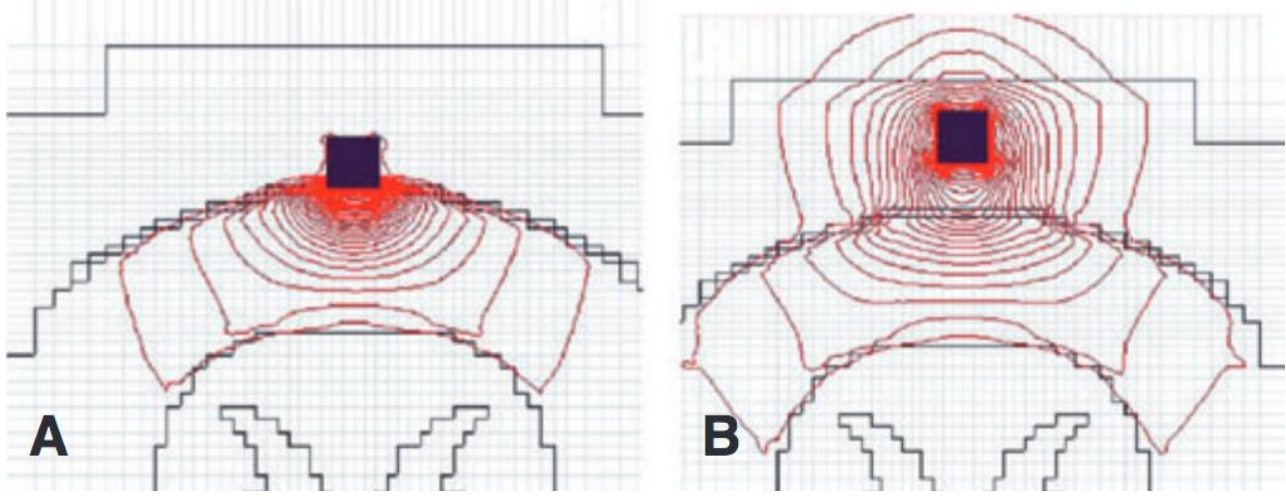
- Electrical current-Activate dorsal root columns axons
- Initiates impulses with transmission
  - Orthodromic (away from soma)
  - Antidromic (towards the soma) transmission
- Placement-epidural space





Location matters

- The electrodes are placed close to dura, as close to midline as possible
- Low resistance: CSF (90% current), white matter
- High resistance: epidural fat, bone
- Types
  - Conventional: exchange unpleasant sensation of pain to ”paresthesia”-tonic
  - “Paresthesia” free stimulation-burst, high frequency
  - Directional: dorsal root stimulation
  - Closed loop stimulators
  - Non-neuronal/alternate fibers stimulation



Chronic pain and SCS

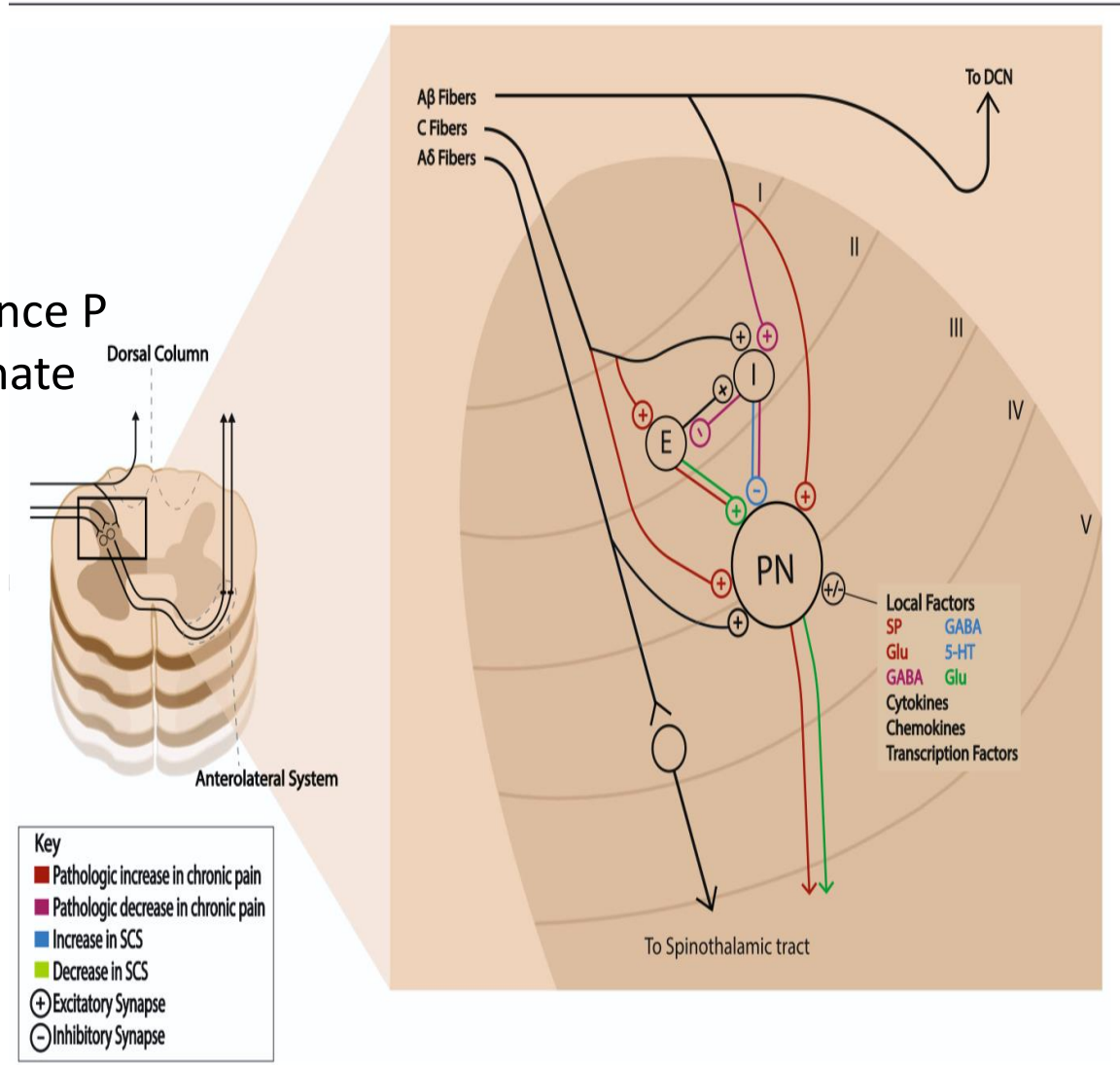
- Chronic pain-neural circuitry rewired
  - Loss inhibition/abnormal enhancement excitatory paths
  - Nociceptive transmission to sub-threshold stimuli.
  - Increased excitatory interneuron input,
  - Decreased inhibitory interneuron input
  - Pathologic destabilization of normal input balance to the projection neuron.
- SCS-balance of nociceptive and antinociceptive inputs
  - Activation: local segmental + descending supraspinal paths
  - Restore balance to the network.

Substance P
Glutamate

Gaba

Gaba
5HT

Glutamate



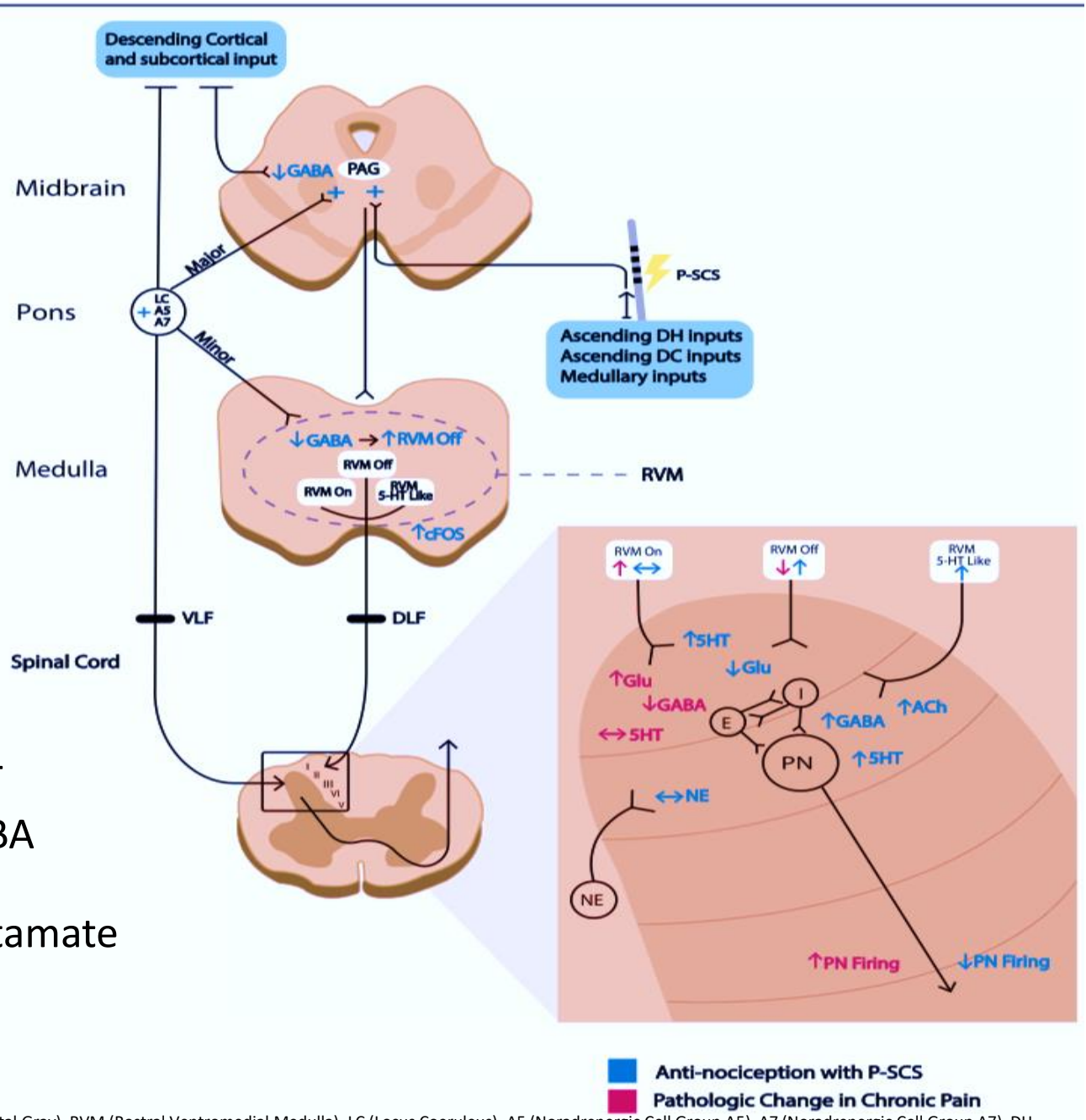
Acronyms: DCN (Dorsal Column Nuclei), E (Excitatory Interneuron), I (Inhibitory Interneuron), PN (Projection Neuron), SP (Substance P), Glu (Glutamate), GABA (Gamma Aminobutyric Acid), 5-HT (5-Hydroxytryptamine, Serotonin)

Supraspinal mechanisms

- Chronic pain: abnormal enhancement of excitatory pathways + loss of inhibition= nociceptive transmission to sub-threshold stimuli.
- SCS: orthodromic activation of supraspinal centers of pain control: antinociception
  - Activation of the Descending anti-nociceptive system (DAS),
  - Recruitment of the PAG, RVM and LC.
  - Changes in spinal neurotransmitters

Ach
5HT
GABA

Glutamate



Acronyms: PAG (Periaqueductal Gray), RVM (Rostral Ventromedial Medulla), LC (Locus Coeruleus), A5 (Noradrenergic Cell Group A5), A7 (Noradrenergic Cell Group A7), DH (Dorsal Horn), DC (Dorsal Column), VLF (Ventrolateral Funiculus), DLF (Dorsolateral Funiculus), RVM ON (RVM On cells projecting from the RVM to the DH), RVM OFF (RVM OFF cells projecting from the RVM to the DH), RVM 5-HT Like (RVM 5-HT Like cells projecting from RVM to DH), cFOS (proto-oncogene), E (Excitatory Interneuron), I (Inhibitory Interneuron), PN (Projection Neuron), Glu (Glutamate), 5-HT (5-hydroxytryptamine), ACh (Acetylcholine), NE (Norepinephrine), GABA (Gamma Aminobutyric Acid)

Evolution of stimulation

- Tolerance to stimulation with time
  - Pulse amplitude needs to be increased
  - Unpredictable, up to 29% in 10 years
  - Causes
    - Neuroplasticity
    - Cellular or fibrotic changes
    - Reframe of pain over time
    - Psychological disorder
- Constant look for improvements

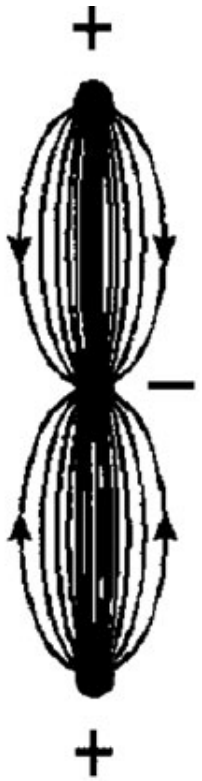
Verrillis et al. J of Pain Research 2016: 9481-92

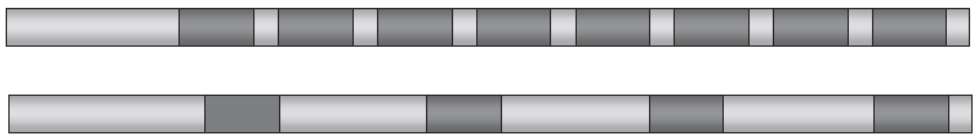
Analgesic effects of neuromodulation

SCS Type	Neurotransmitters	Synaptic Depression	WDR	Glial Cells	Supraspinal	Axonal Conduction
Conventional	Acetylcholine,[108,194] dopamine,[126] cannabinoids,[115,122] GABA,[96,102–105] serotonin[110–112,126,195]	Presynpatic,[196,197] postsynpatic[120,122]	Wind-up,[116,151,198] excitability,[116,117] long-term potentiation[199]	Activation[200]	Descending modulation[125,127,128,150,201,202]	
High frequency			Excitability[152]			Block[147,151,203]
Burst			Excitability[162,163]			
Dorsal root ganglion						Block[171,173]

Sdrulla AD et al. Pain Practice 18 (8), 2018:1048-67

Lead Electrodes





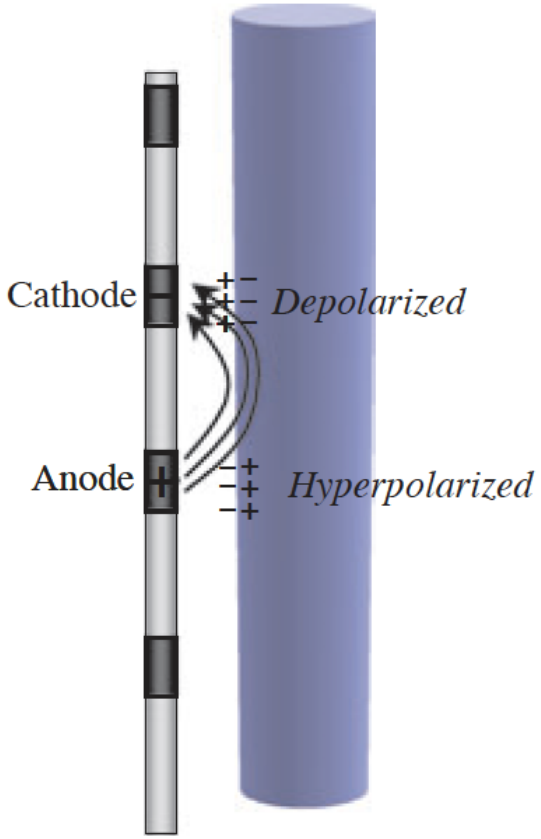
- A nerve fires when the transmembrane potential is driven to threshold

- The transmembrane potential is driven by the spatial gradient of the Electric Field *at the nerve*

- The Electric Field is proportional to the current density *at the nerve*

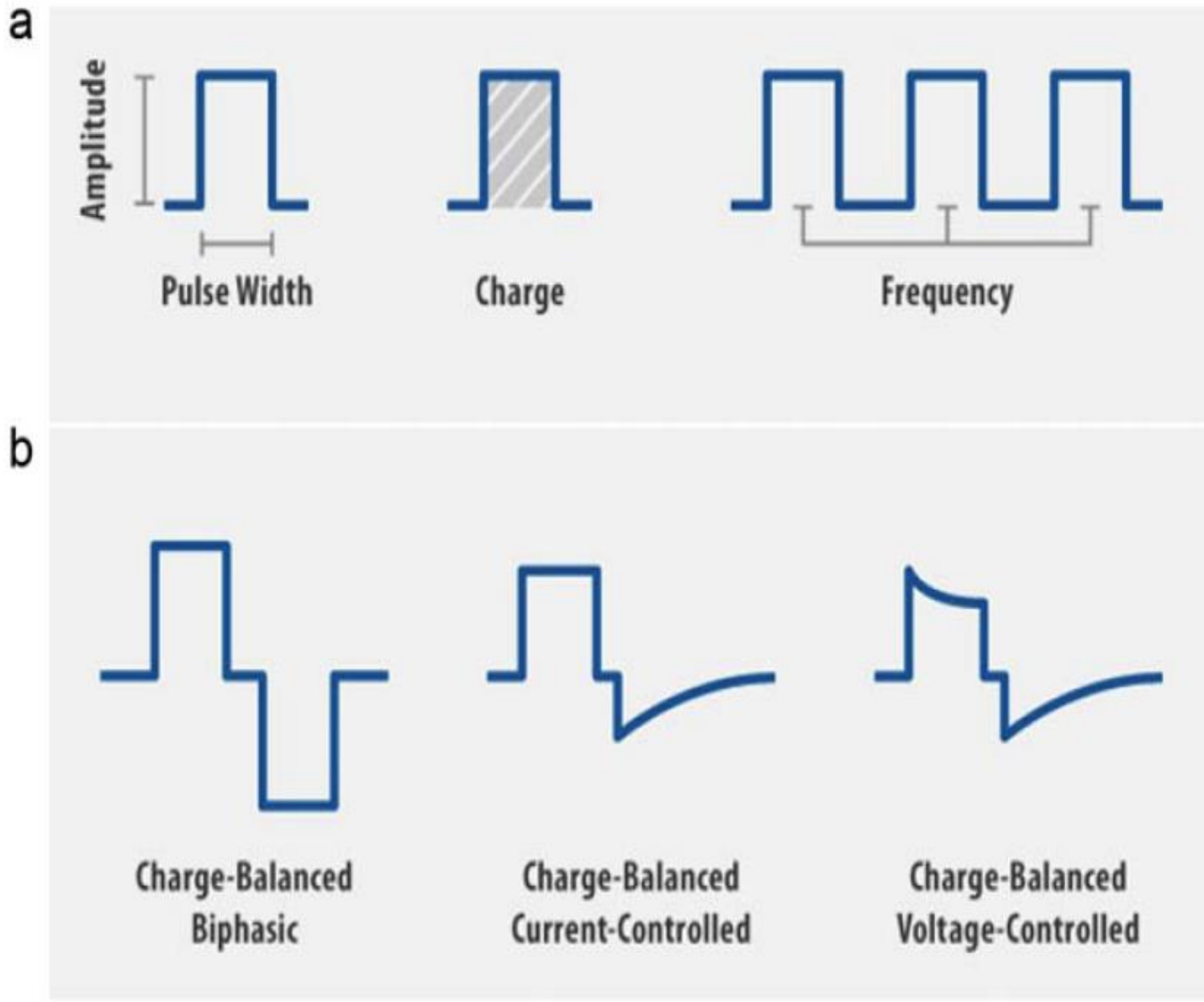
- All geometry being equal, the current density is a direct function of the CURRENT *at the nerve*

Therefore, **CURRENT** *at the nerve* is a key determinant of neurostimulation



Parameters

- Basic unit of electrical stimulation=pulse
  - Delivery of a current with constant **Amplitud**e (mAmps)
  - For a specific amount of time, **Pulse width**
  - Repeated with a certain **Frequency**
- Every pulse is followed by equal flow of current in opposite direction, the ‘recharge’ pulse
  - Biphasic
  - Current controlled
  - Voltage controlled



Various waveforms

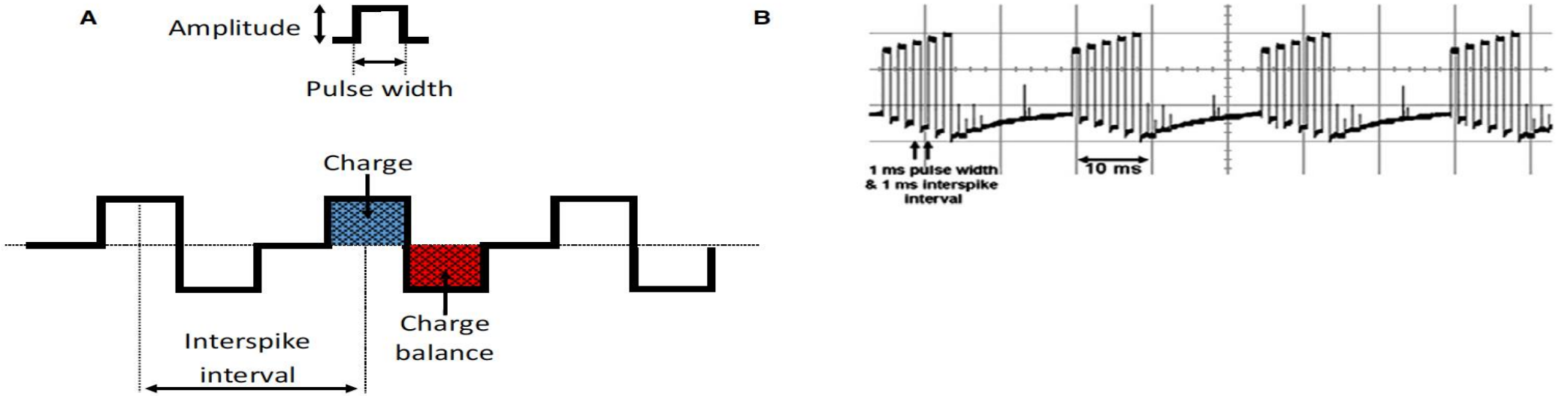


Figure 2. Waveform properties. (A) The amount of charge delivered to tissues depends on pulse properties: shape, amplitude, and duration. The lower panel illustrates the concept of frequency and charge balance. (B) Burst waveform (adapted from De Ridder et al.[3]). The waveform represents five 1-ms-long pulses, delivered at 500 Hz, while the burst frequency is 40 Hz. Charge balance occurs after the 5 pulses.

- Conventional-charge balance every pulse unit
- Burst-charge balance every 5th pulses,

Sdrulla AD et al. Pain Practice 18 (8), 2018:1048-67

SCS and neural mechanisms

	Description	Considerations for neural mechanisms
Amplitude	Current delivered (milliamperes, mA)	• Amplitude and pulse width (charge per pulse) are required to activate neurons. • Axon characteristics (size, myelination) and distance from stimulus will influence activation. • Charge per pulse at the target is lower than the charge at the electrode.
Pulse width	Duration of pulse (microseconds, μs)	• Amplitude and pulse width (charge per pulse) are required to activate neurons. • Axon characteristics (size, myelination) and distance from stimulus will influence activation. • Charge per pulse at the target is lower than the charge at the electrode.
Frequency	Number of pulses (Hertz, Hz)	• Defines the number of pulses delivered in the waveform. • Inversely related to the pulse width. • Neuronal properties define whether the neuron will entrain to each pulse. • With moderate-high amplitude, high frequency may induce axonal blocking mechanisms.
Duty cycle	Amount of "on time" (Percent of time)	• May be a consideration for nonactivating or subthreshold neuronal mechanisms

Miller JP et al. Neuromodulation, 2016; 19:373-384

Parameters among various stimulations

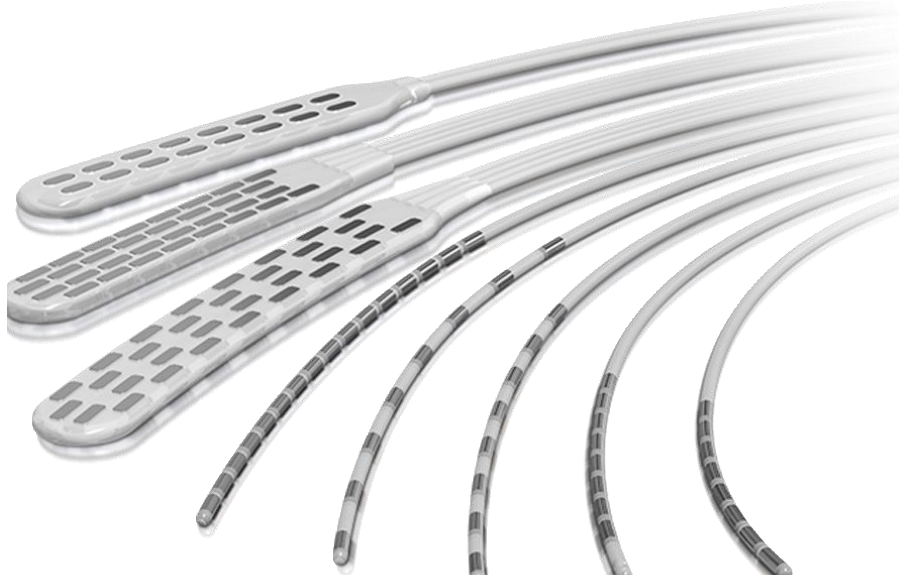
	10 kHz* (Minimum–Maximum)	"Burst"†	Tonic* (Minimum–Maximum)
Amplitude (mA)	1.6–3.8	0.6	3.6–8.5
Frequency (Hz)	10,000	200‡	39–77
Pulse width (μs)	30	1000	347–591
Charge per pulse (μC)	0.05–0.11	0.6	1.2–5.0
Duty cycle (% on time)	30%	20%	1.4–4.6%
Charge per second (μC/sec)	480–1,140	120	49–387
Possible interaction with neurons	Low charge per pulse unlikely to activate fibers or neurons. High charge per second may modulate.	Low charge per pulse unlikely to activate fibers or neurons. High charge per second may modulate.	High charge per pulse likely to activate dorsal column fibers. Modulation is also possible.

Comparison of stimulation waveform characteristics between 10 kHz, burst and tonic spinal cord stimulation.
*Average minimum and maximum parameters reported in Kapural et al., 2015 (15) Calculations characterize the minimum and maximum possible charge per pulse, duty cycle, and charge per second based on the reported values.
†Parameters reported in De Ridder et al., 2010 (20).
‡Average frequency delivered in burst stimulation (5 pulses * 40 Hz).

Miller JP et al. Neuromodulation, 2016; 19:373-384

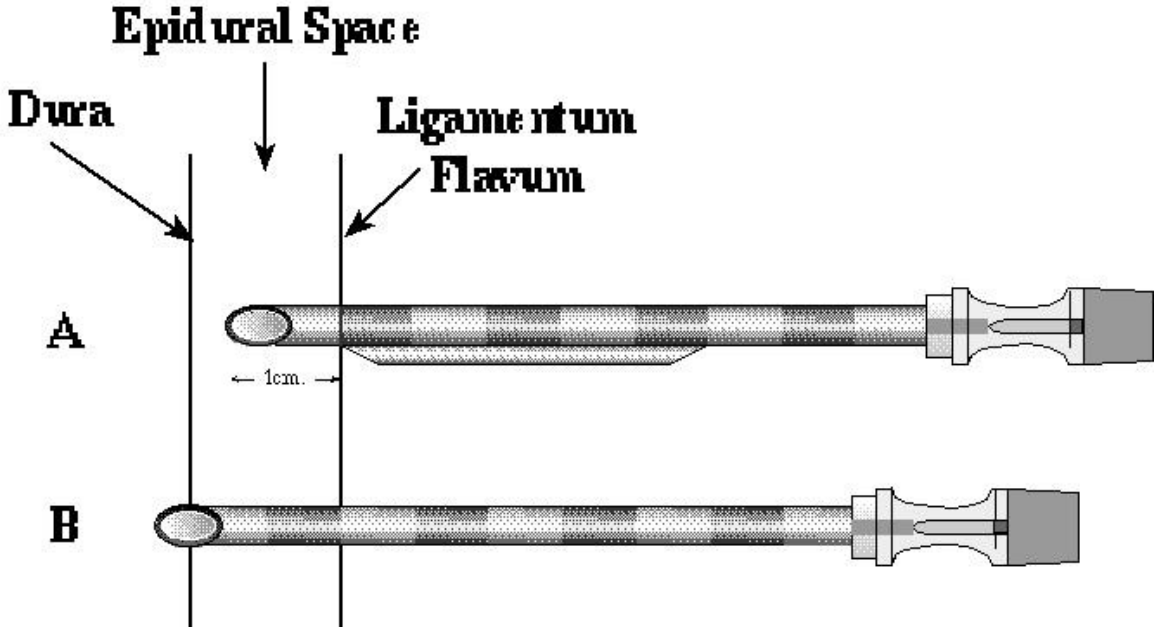
Active elements of the device

- Leads
  - Percutaneous
  - Paddles-via laminotomy
- Power sources
  - Non-implantable
  - Implantable
    - Non-rechargeable
    - Rechargeable



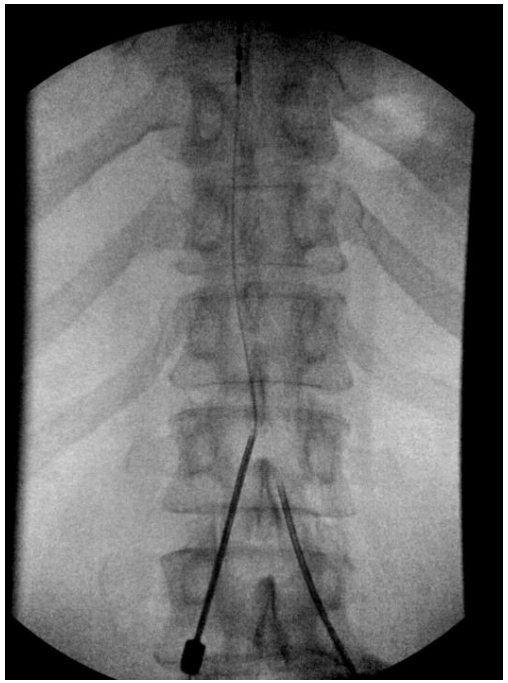
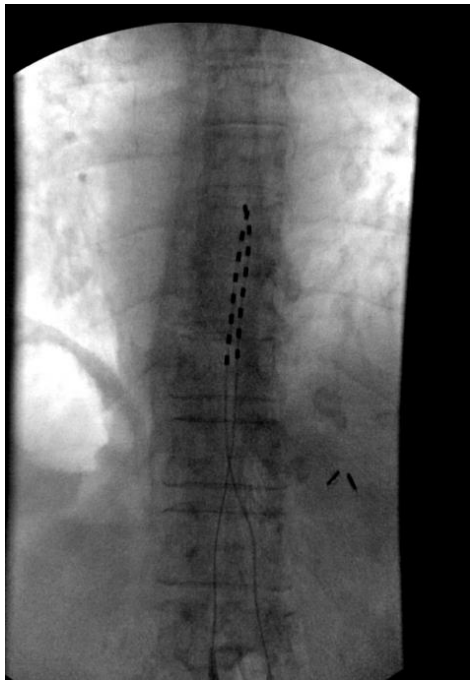
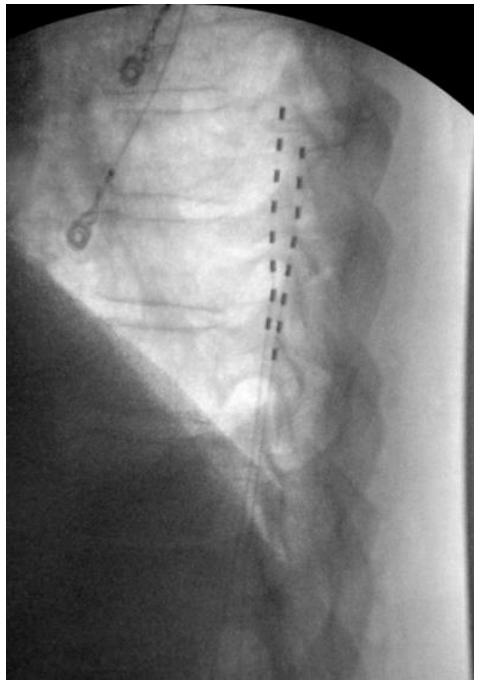
Technique

- Touhy needle in epidural space
- Loss of resistance
- Lead deployed through needle
- Posterior epidural space



Placement

- 2 steps
  - Trial
  - Permanent implant
- Minimally invasive, reversible, miniaturized IPG
- Essential: does not change patient anatomy

Placement of the leads

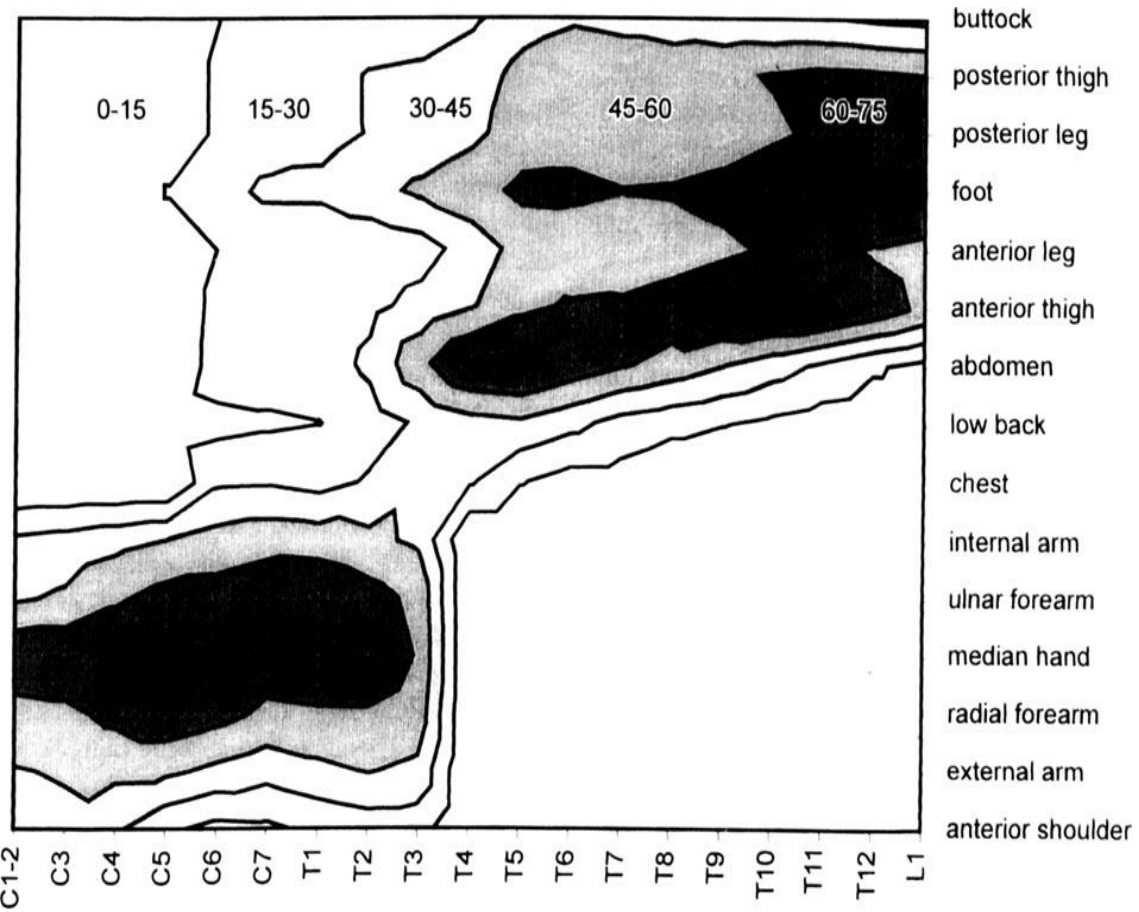


Table 18.1 Barolat paresthesia mapping with anatomic lead placement [12][a]

Level	Typical paresthesia coverage
C2-C3	Occipital
C3-C4	Shoulder (SCS leads usually placed more lateral)
C4-C5	Radial
C5-C6	Median (SCS leads usually more mid-line)
C6-C7	Ulnar
T1-T4	Angina
T4-T6	Abdomen/Viscera (SCS leads usually lateral T8-T11)
T6-T8	Low back
T8-T11	Lower extremities
T10-L1	Foot
T5-S3	Pelvic pain (Tripole array/Paddle lead)

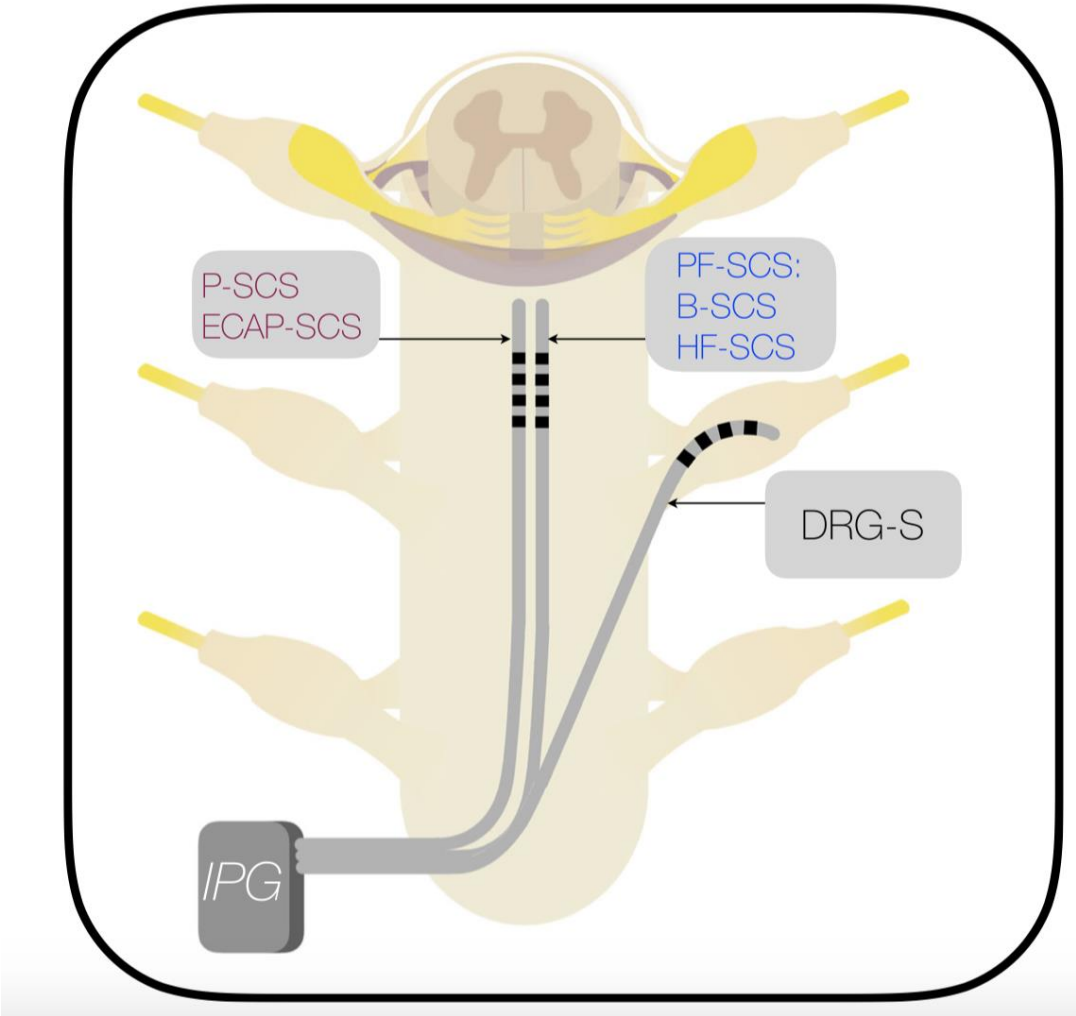
[a]Modified version of neurosurgeon Barolat's paresthesia mapping chart for typical SCS lead placement
SCS spinal cord stimulation

Holsheimer J et all, Neuromodulation 1998: L29-36

Advanced Procewdures for Pain management, Springer 2018, Sudir Diwan ed

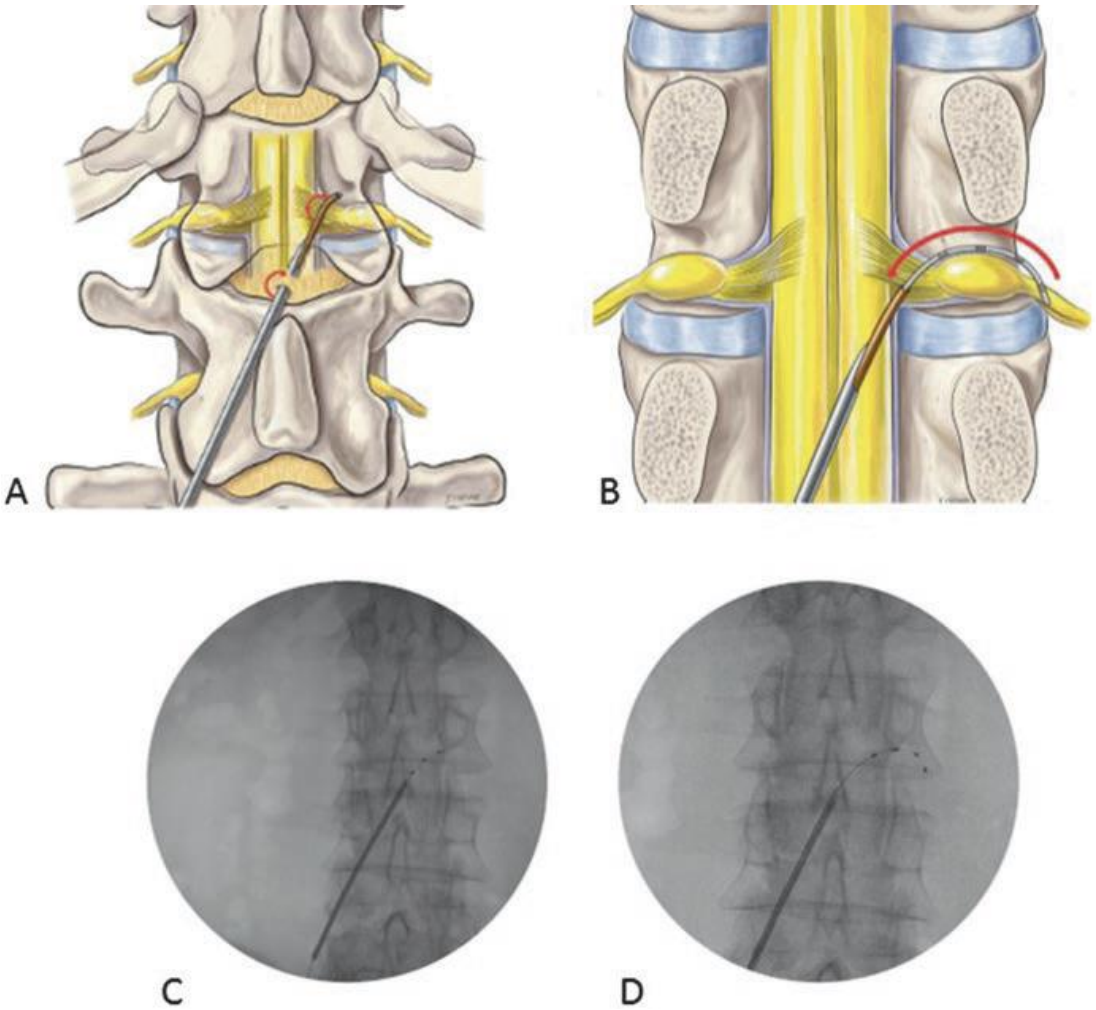
Types of Neuromodulation

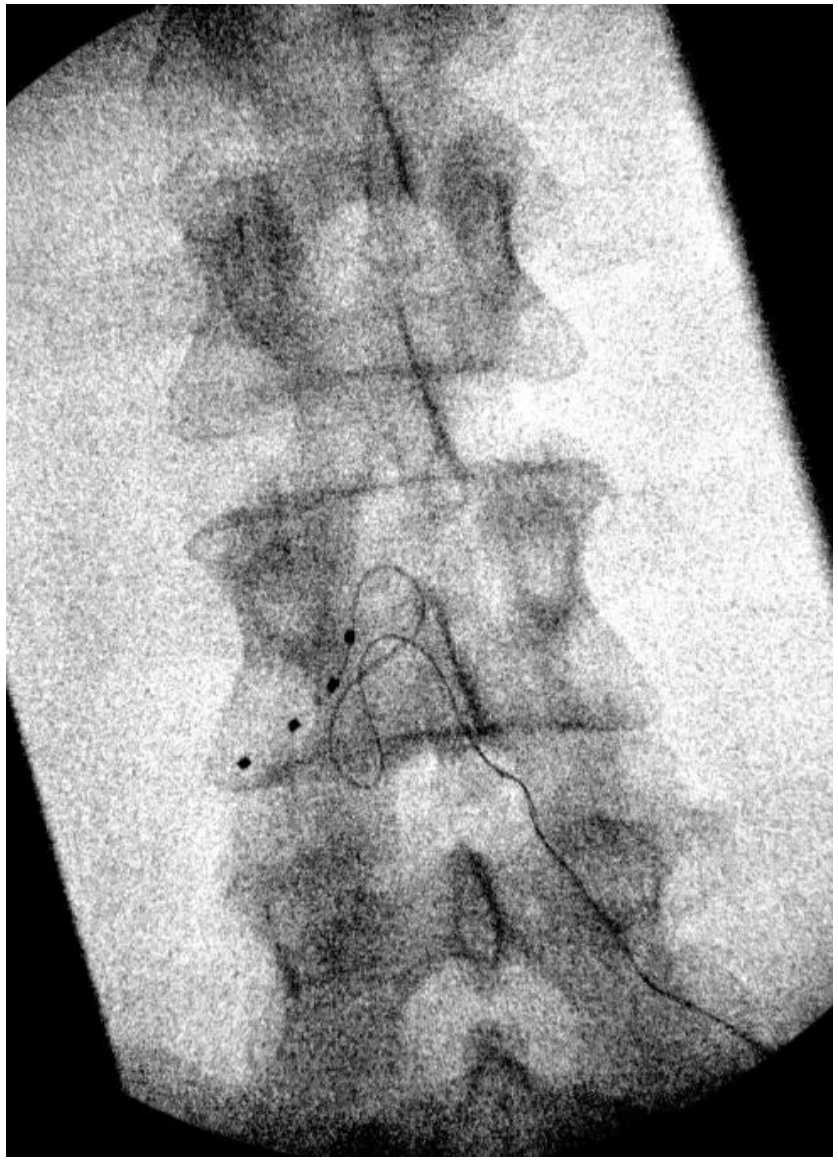
- P-SCS=Paresthesia SCS
- PF-SCS=Paresthesia free SCS
- B-SCS=Burst SCS
- HF-SCS=High Frequency SCS
- DRG-S=Dorsal Root Ganglion stimulation
- ECAP-SCS=Evoked Compound Action Potential SCS
- DTM=Differential Target Multiplex
- Others



Caylor et al. Bioelectronic Med.(2019) S12

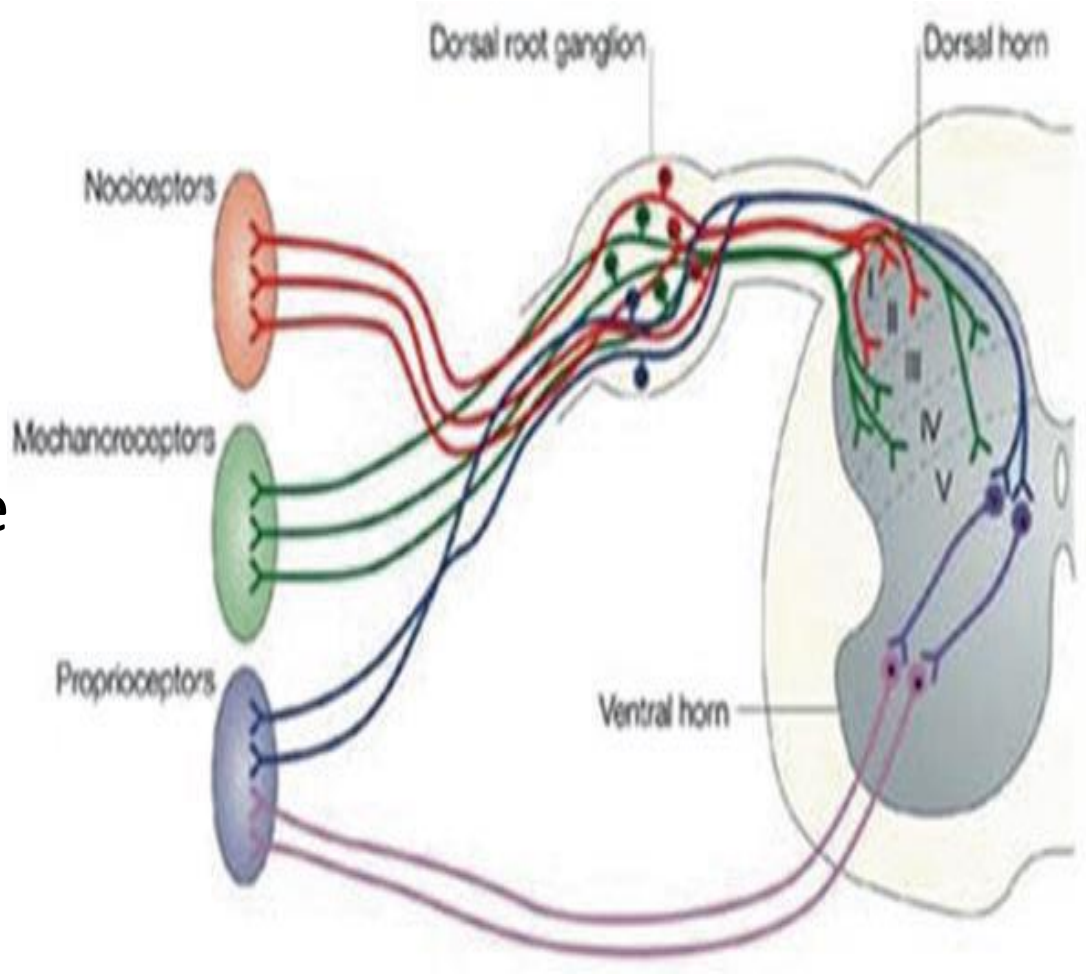
DRG: What does it mean?





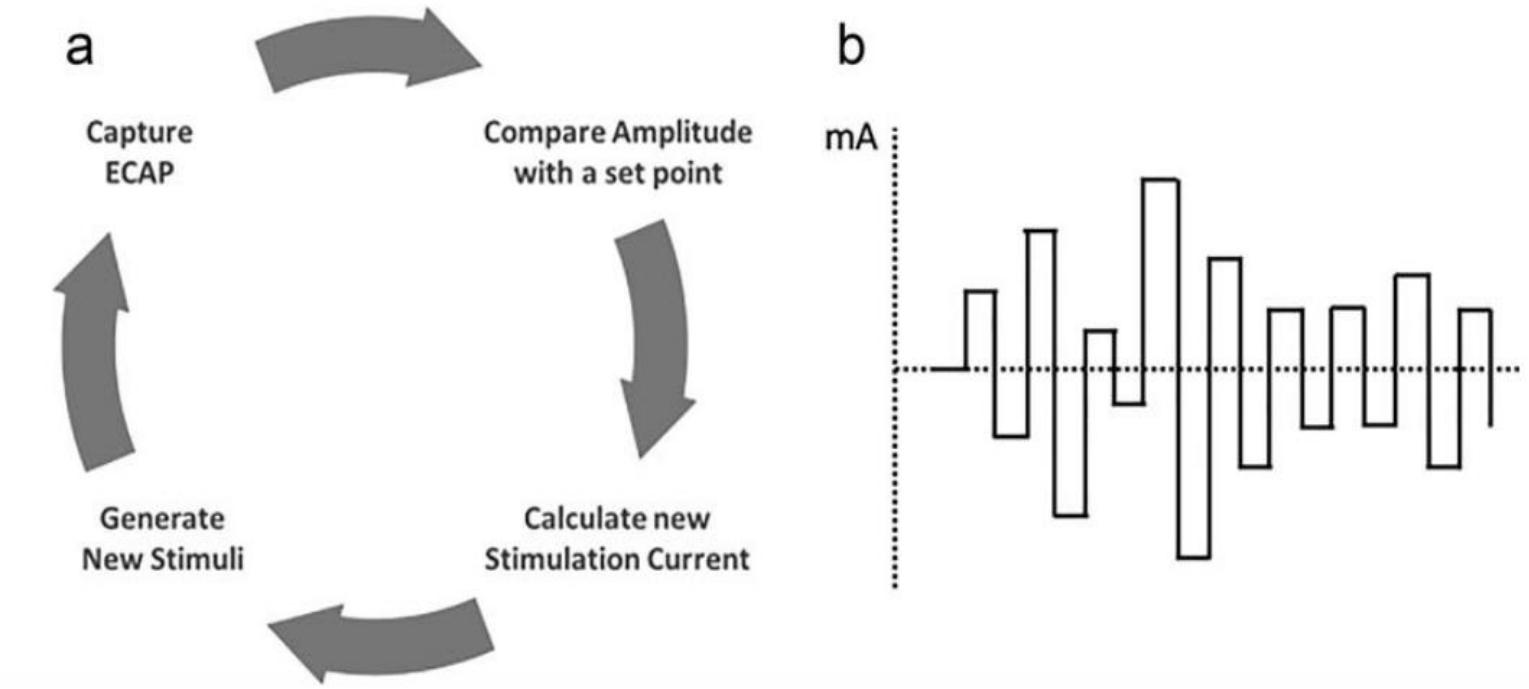
Direct stimulation of the dorsal root

- Electrical field of DRG stimulation affects cell bodies (axons in conventional)
  - More recruitment, less power
- Type of recruitment: small (nociceptive) and large (touch)
- DRG somata projects to the gray matter-wide activation of neurons in the gray matter (wide-dynamic, interneurons, etc.)
- Distribution focal or wide, depending on location of electrode



Closed loop

- Open loop conventional- patients manually adjust stimulator current
- Closed loop-measures evoked compound action potential (ECAP) to maintained automatically the desired fibers recruitment



Russo M et al. Neuromodulation, 2018; 21: 36-47

Indications

- Classical
  - Radiculopathy- from nerve root damage and may be associated with FBSS or a herniated disk
  - Plexopathy
  - Arachnoiditis
  - Epidural fibrosis
  - Painful Peripheral Neuropathy
  - MS – with LE pain
  - CRPS
  - Ischemia
- Expanded to include visceral, pelvic, truncal, mechanical etc.

Efficacy and cost

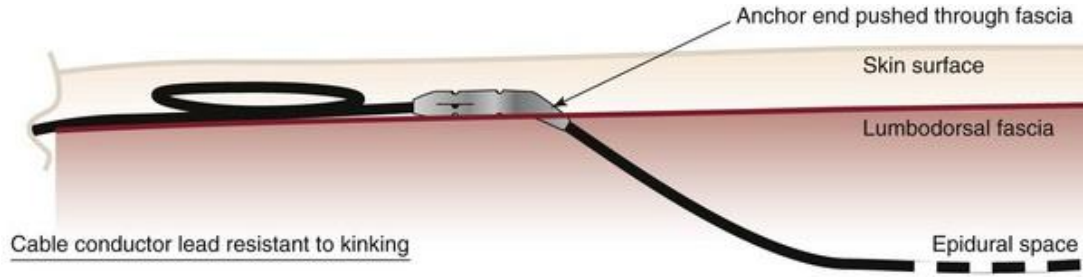
- Target 50-80% pain relief
- Improve function
- Measured success
  - **Reduction in pain intensity** measured on VAS (50% pain reduction in 60-90% of patients),
  - **Decreased use of pain meds,**
  - **Improved function scores**, ADLs, quality of life scores,
  - **Return to work**
  - Confirmation that **Patient would again choose SCS.**
- Cost: high initial, subsequent decrease per year (multiple studies)

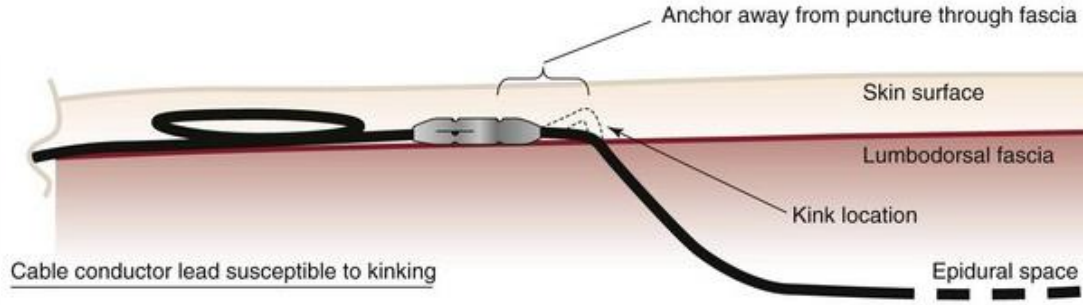
Complications

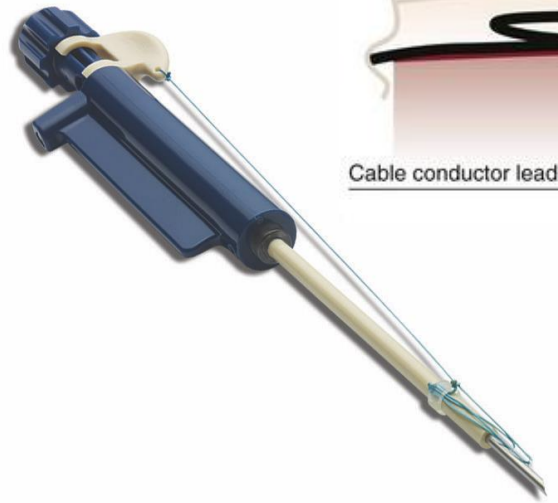
- Mechanical
- Biological
- Technique related

Mechanical and technique related

- Lead fractures 5-9%
- Lead migration 0-27%
- Pulse generator failure 1.7%
- Mitigate them
  - Leads, anchor technique
  - Limited movement for 3 months

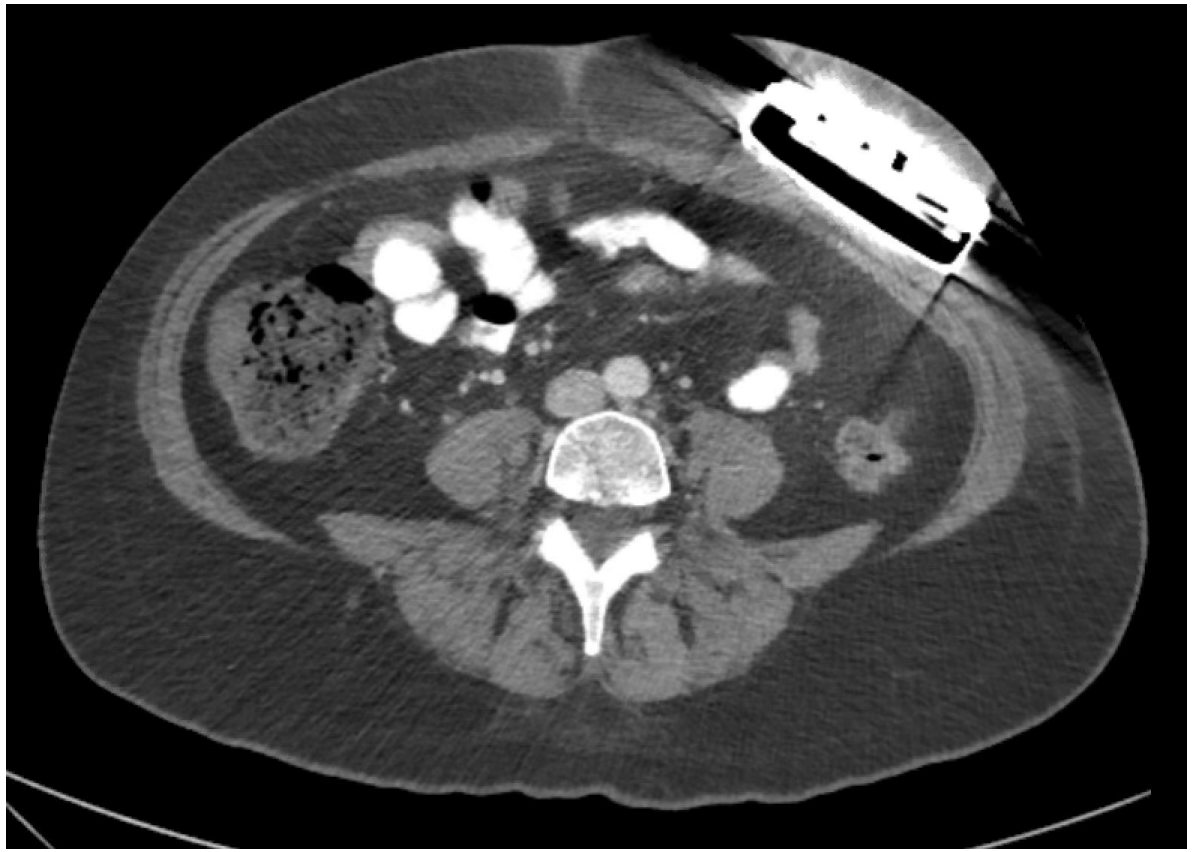






Biological

- Infections 3-8%, usually superficial
- Allergic reactions
- Seromas at generator site
- Epidural fibrosis
- Epidural hematoma
- Dural puncture
- Neurological injury-rare



Aware of…

- MRI compatible, conditional, 1.5 T
- Other devices (pacemakers) compatible as long as distance maintained (generators on opposite parts of body)
- Caution
  - Pregnancy
  - Medical conditions: anticoagulation, immunosuppression, significant co-morbidities
  - Psychosocial-cognitive impairment, unacceptable social, active substance abuse

Practical points

- Trial always-1 week ideal
- Psychological evaluation
- Many types, choose wisely
  - Based on patients signs and symptoms
- Move up in treatment algorithm
- Operating Room cases and strict prevention of SSI

Conclusions

- Spinal cord stimulators have been used effectively for >50years
- Placement: minimally invasive, reversible
- More efficient and smaller devices
- Wide variety of conditions treated and expanding indications
- Emerging technology and sprouting of novel ideas
- Placement still associated with complications but reduced with proper surgical technique.

Thank you