PainWeek®

Peripheral Nerve Stimulation: Indications and Evidence

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Disclosure

- Consultant/Independent Contractor: Abbott, Biotronik, Boston Scientific, Nalu, Nevro, Saluda, SI-Bone, Vertos
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- Advisory Board: Biotras
- Stock Shareholder: Nalu

Learning Objectives

- Describe the history of peripheral nerve stimulation
- Describe the update on mechanism of action of PNS
- Cite indications and current applications of PNS
- List current literature and landmark studies
- Explain advantages and challenges
- Describe emerging trends and future of PNS

Outline

- Evolution of peripheral nerve stimulation
- History of PNS
- Indications for PNS
- Possible mechanism of action
- Innovations in PNS technology
- Recent applications of PNS
- Current literature and studies
- Basics of PNS coding a billing
- Future of PNS

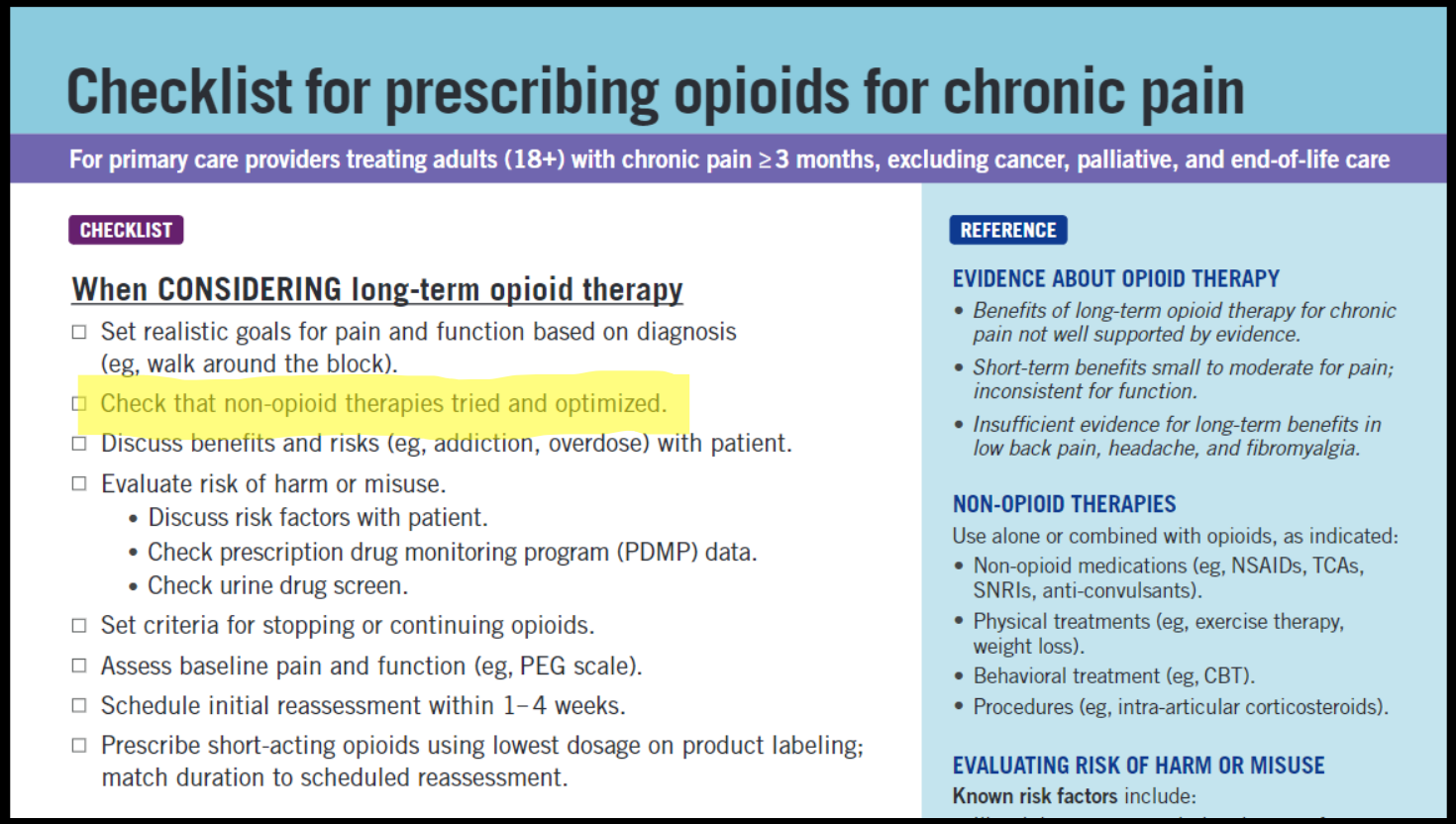
Analgesia

- Sumerians, 3000 B.C. who first cultivated the poppy plant for its opium
- Homer in 300 B.C. Helen of Troy to treat her grief over the absence of Odysseus

Evolution of Opioid therapy

- Lack of long-term efficacy for chronic pain
- Risk for tolerance, dependency, and abuse
- Opioid use disorder
- National opioid crisis
- New CDC opioid prescribing guidelines

CDC Guidelines for Chronic Opioids



Checklist for prescribing opioids for chronic pain

For primary care providers treating adults (18+) with chronic pain ≥3 months, excluding cancer, palliative, and end-of-life care

CHECKLIST

When CONSIDERING long-term opioid therapy

- ☐ Set realistic goals for pain and function based on diagnosis (eg, walk around the block).
- ☐ Check that non-opioid therapies tried and optimized.
- ☐ Discuss benefits and risks (eg, addiction, overdose) with patient.
- ☐ Evaluate risk of harm or misuse.
  - Discuss risk factors with patient.
  - Check prescription drug monitoring program (PDMP) data.
  - Check urine drug screen.
- ☐ Set criteria for stopping or continuing opioids.
- ☐ Assess baseline pain and function (eg, PEG scale).
- ☐ Schedule initial reassessment within 1–4 weeks.
- ☐ Prescribe short-acting opioids using lowest dosage on product labeling; match duration to scheduled reassessment.

REFERENCE

EVIDENCE ABOUT OPIOID THERAPY

- *Benefits of long-term opioid therapy for chronic pain not well supported by evidence.*
- *Short-term benefits small to moderate for pain; inconsistent for function.*
- *Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.*

NON-OPIOID THERAPIES

Use alone or combined with opioids, as indicated:

- Non-opioid medications (eg, NSAIDs, TCAs, SNRIs, anti-convulsants).
- Physical treatments (eg, exercise therapy, weight loss).
- Behavioral treatment (eg, CBT).
- Procedures (eg, intra-articular corticosteroids).

EVALUATING RISK OF HARM OR MISUSE

Known risk factors include:

https://stacks.cdc.gov/view/cdc/38025

Chronic Pain in America

- 1 in 5 Americans suffer from chronic pain
- Large economic impact: ~$600 billion/year
- Loss of productivity: ~$300 billion/year
- Opioid epidemic: #1 health crisis in America
- National health survey by NIH 2012
  - 50 million adults experience pain every day
  - Pain→ worse overall health status
  - Female, elderly, non-Hispanics (Asians less likely)

A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients.
http://jama.ama-assn.org/cgi/content/abstract/274/20/1591

Emergence of Electroceuticals

- Bioelectronics
- Therapeutic devices
- External or implanted
- Delivering electricity
- Neuromodulation
- Alter disease states
- Market prediction of $35.5 billion global market by 2025

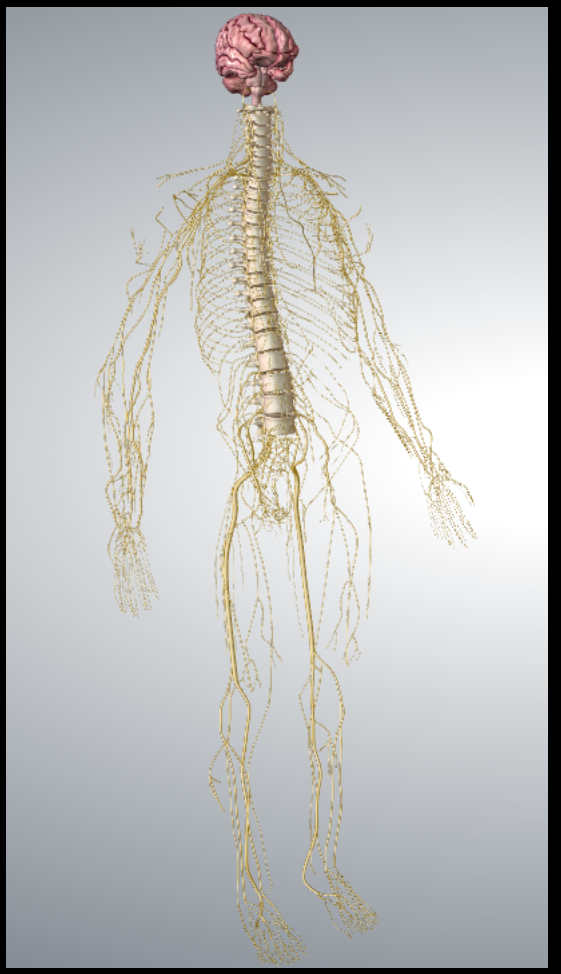
1. Kristoffer Framm, Nature, 2013
2. https://www.grandviewresearch.com/press-release/global-electroceuticals-bioelectric-medicine-market

Innovations in Neuromodulation

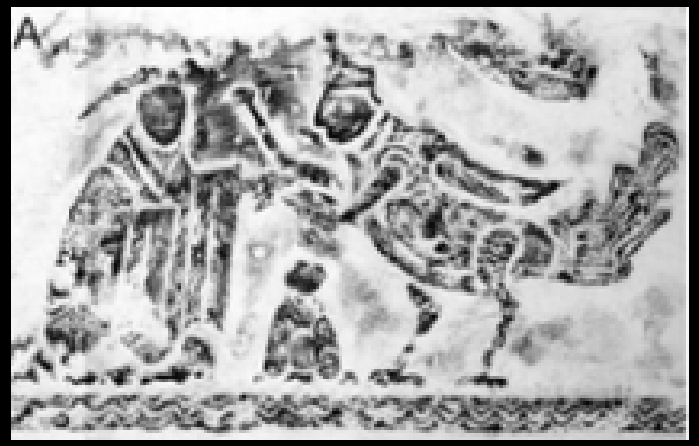
- Adaptive stimulation
- MRI compatibility
- Novel wave forms and targets of stimulation
- *Closed loop technology (not FDA approved)*
- *High Frequency spinal cord stimulation*
- *Peripheral nerve stimulation*
- *Vagal nerve stimulation*
- Micro-dose intrathecal drug delivery

Peripheral Nerve Stimulation

- Form of neuromodulation
- Stimulation of peripheral nervous system
- Direct peripheral nerve stimulation (PNS)
- Peripheral Nerve Field Stim (PNFS)



Ancient Peripheral Nerve Stimulation

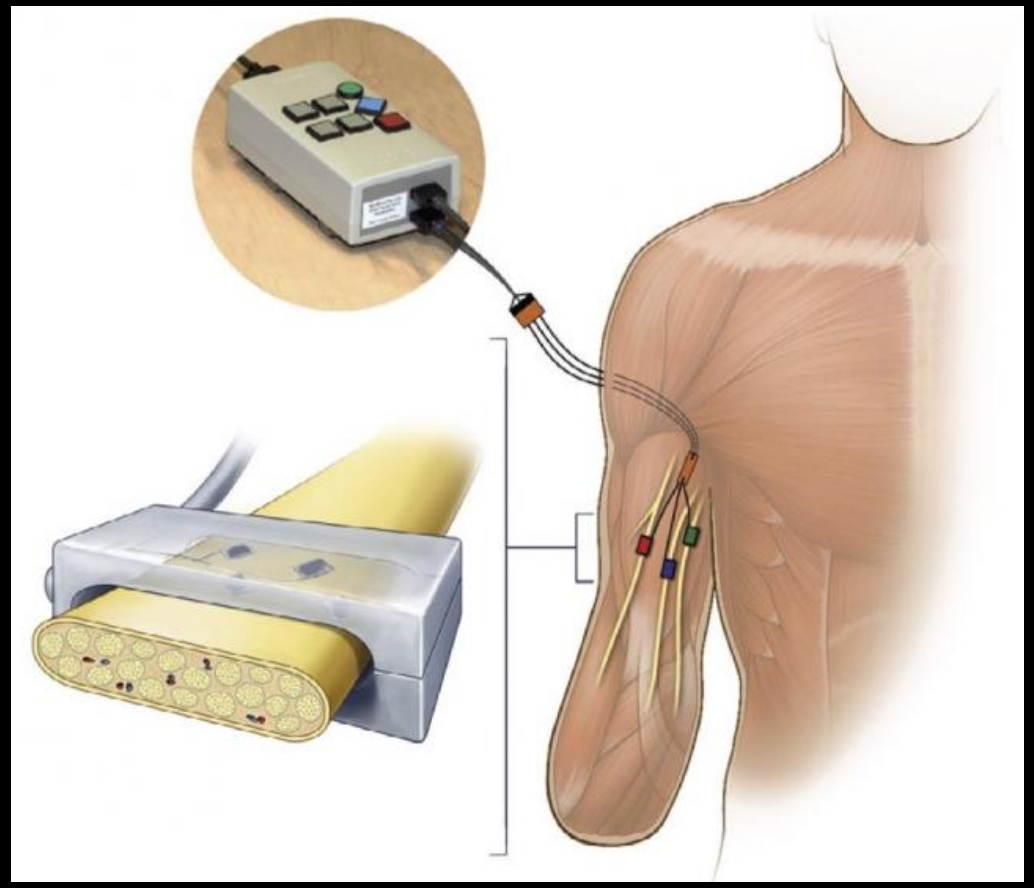


Auricular acupuncture depicted during Han dynasty, 200 BC

Cauterizing the external ear to treat migraine, 12th century Persian surgery text

Contemporary PNS: “Teaching an Old Dog New Tricks”

- Predates dorsal column stimulation
- 1960’s, Wall and Sweet introduced the concept of electrical stimulation of a nerve to control pain
- 1967, Sheldon implanted 8 patients for the treatment of trigeminal neuralgia (14,000 Hz)
- Traditionally, PNS implanted surgically
- 1999, Weiner, PNS implanted for headache
- Recently FDA approved PNS systems



Role of Peripheral Nerve Stimulation

- Chronic refractory neuropathic pain
- Peripheral nerve involvement/distribution
- SCS is not available
- Responsive to local anesthetic block
- LA block or TENS have not shown predictive value

❖Neuropsychological clearance

❖Successful trial

Slavin K., Neurotherapeutics. 2008;5:100-106

PNS: Mechanism of Action

- Based on the Gate Theory of Pain
- Orthodromic stimulation of sensory A-b fibers
- Modulation of inter-neurons within the dorsal horn
- Modulation of local neurotransmitters
- Modulation of local inflammatory mediators
- Reducing ectopic discharge
- Reducing Wallerian degeneration

Deer et al, Bain Sci. 2019
Deer et al, Bioelectronic Medicine, 2020

PNS: Described Indications

- Post-herpetic neuralgia
- Post-traumatic or surgical neuralgia
- Migraine headache
- Occipital neuralgia
- Complex regional pain syndrome (CRPS)
- Cluster headache
- Post-herniorrhaphy pain
- Coccydynia
- Fibromyalgia?

Neurotherapeutics. 2008;5:100-106

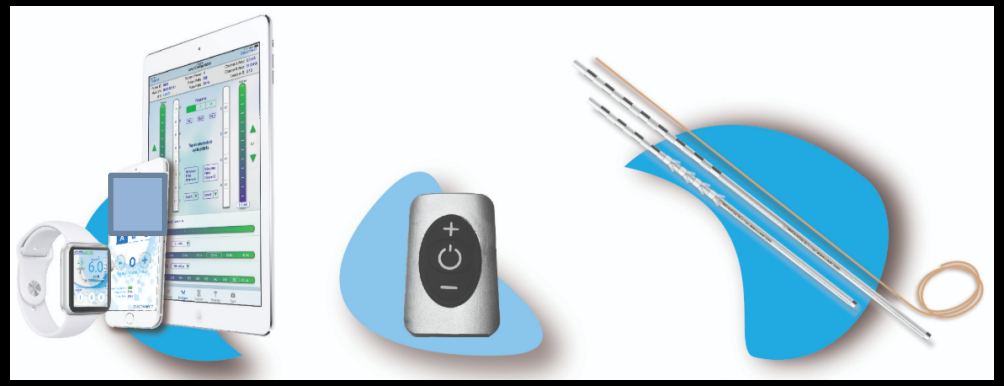
PNS: Challenges and Risks

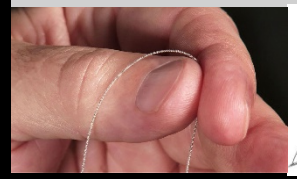
- Limited hardware options (now improved)
- Limited reimbursement (now improved)
- Limited MRI conditional status
- Lead migration/fracture
- Hardware failure
- Infection, hematoma, seroma, skin erosion
- IPG site discomfort (temporary, external IPG options)

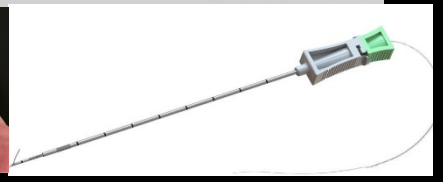
PNS: Implantation Options and Innovations

- Dedicated PNS hardware
- Percutaneous
- Ultra minimally invasive
- Indirect (external) power source
- Non-invasive (example nVNS for headache)
- Implantable pulse generator
- Ultrasound and/or Fluoroscopic guidance

PNS: Commercially Available Systems







Landmark Study: PNS for Chronic Neuropathic Pain

Neuromodulation: Technology at the Neural Interface

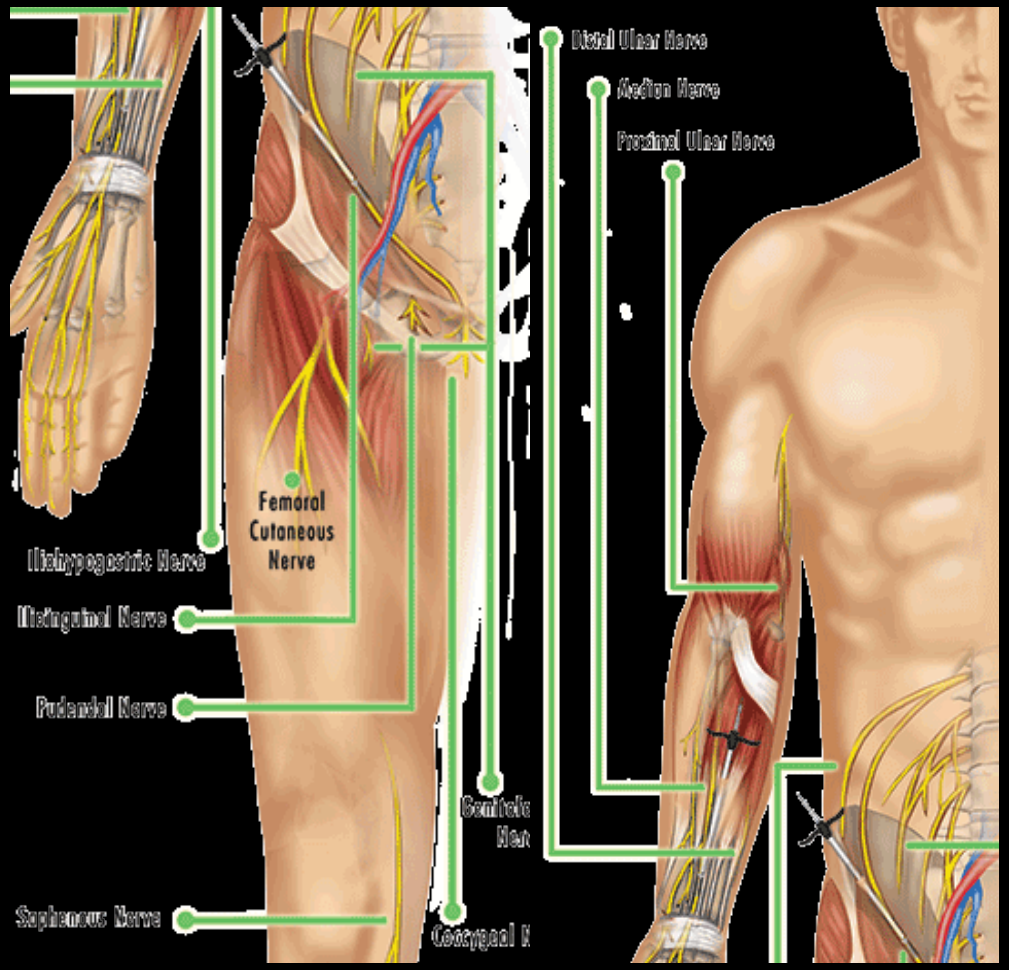
Received: June 23, 2015 Revised: September 10, 2015 Accepted: October 01, 2015

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12381

Prospective, Multicenter, Randomized, Double-Blinded, Partial Crossover Study to Assess the Safety and Efficacy of the Novel Neuromodulation System in the Treatment of Patients With Chronic Pain of Peripheral Nerve Origin

Timothy Deer, MD*; Jason Pope, MD†; Ramsin Benyamin, MD‡; Ricardo Vallejo, MD, PhD§; Andrew Friedman, MD¶; David Caraway, MD, PhD**; Peter Staats, MD††; Eric Grigsby, MD, MBA‡‡; W. Porter McRoberts, MD§§; Tory McJunkin, MD¶¶; Richard Shubin, MD***; Payam Vahedifar, MD†††; Daryoush Tavanaiepour, MD‡‡‡; Robert Levy, MD, PhD§§§; Leonardo Kapural, MD, PhD¶¶¶; Nagy Mekhail, MD, PhD****

Clinical Trial Peripheral Nerve Targets



- **Arm**
  - Ulnar (15), Median (8), Radial (2), Axillary (1), Suprascapular (1)
- **Leg**
  - Peroneal (8), Saphenous (7), Tibial (4), Femoral cutaneous (4), Femoral (3), Sural (1), Genitofemoral (1)
- **Trunk**
  - Ilioinguinal (13), Intercostal (12), Suprascapular (6), Pudendal (3), Iliohypogastric (2), Coccygeal (1), Genitofemoral (1) Superior cluneal (1)

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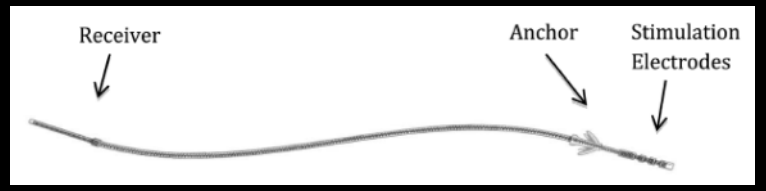
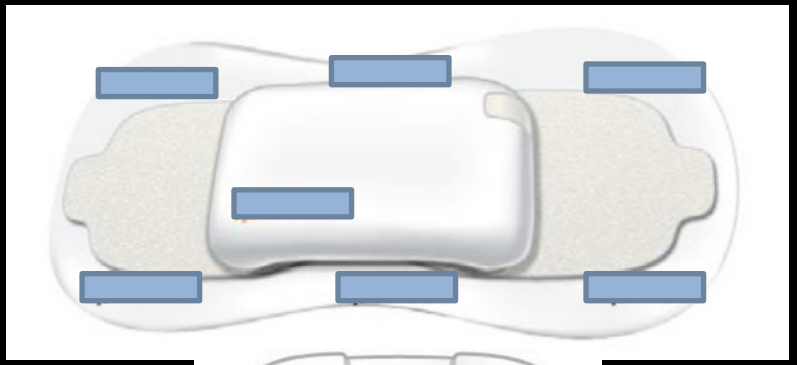
Deer et al. Neuromodulation, 2015

PNS for Chronic Neuropathic Pain

- Prospective, multi-center, randomized, double-blinded, cross-over study
- 147 enrolled, 94 implanted
- 45 treatment, 49 control
- 3 months: 38% vs. 10% responded
- Statistically significant pain relief during cross over, 30% responded
- Treatment group showed improved secondary outcomes
- No serious adverse events





PNS: Post-Stroke Shoulder Pain

NIH Public Access
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Am J Phys Med Rehabil. Author manuscript; available in PMC 2015 January 01.

Published in final edited form as:
Am J Phys Med Rehabil. 2014 January ; 93(1): 17–28. doi:10.1097/PHM.0000000000000011.

Peripheral Nerve Stimulation Compared to Usual Care for Pain Relief of Hemiplegic Shoulder Pain: A Randomized Controlled Trial

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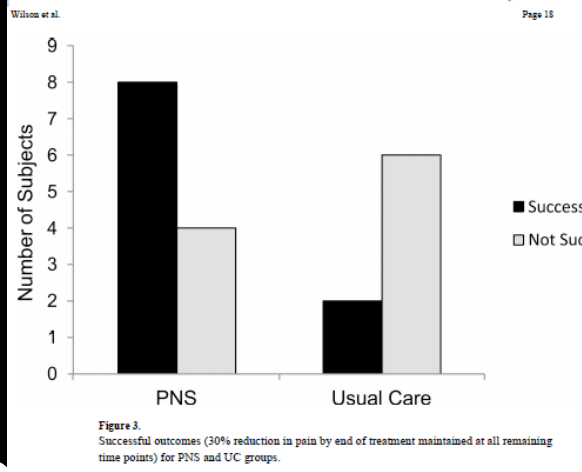
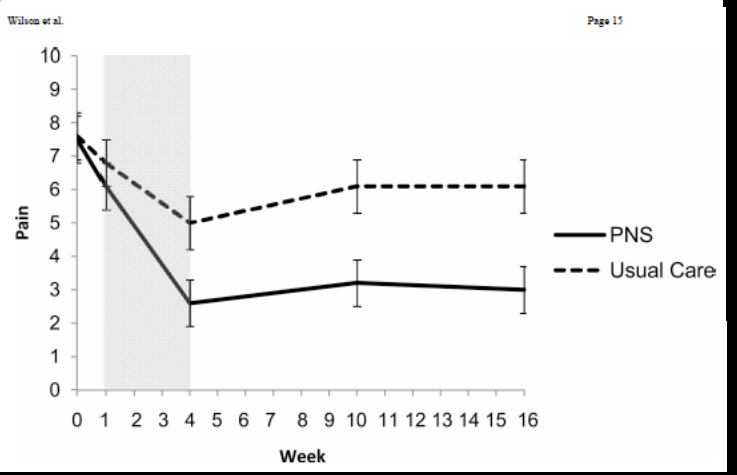


Figure 3.
Successful outcomes (30% reduction in pain by end of treatment maintained at all remaining time points) for PNS and UC groups.



PNS: Chronic Shoulder Pain

Novel Lead Placement for Suprascapular Nerve Peripheral Nerve Stimulation

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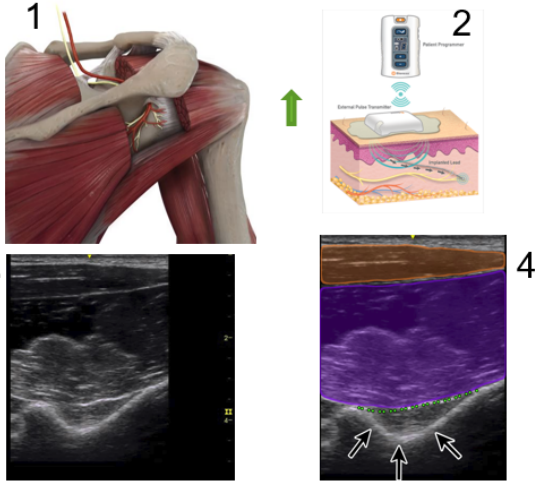
Icahn School of Medicine at Mount Sinai

Introduction

Peripheral nerve stimulation is often times used more for chronic musculoskeletal and nerve related pains. Peripheral nerve stimulation of the suprascapular nerve is one of the most common nerves targeted for shoulder pain. Here we demonstrate a new novel lead placement technique for suprascapular nerve stimulation.

Images



1. Anatomical entry of inferior spinoglenoid notch approach
2. Bioness Peripheral nerve stimulator
3. Coronal Suprascapular nerve US imaging
4. Orange: Trapezius: Purple: supraspintus, arrows: supraspinatus notch green: suprascapular ligament

Case Description

An 82 year old male with chronic right shoulder pain, multifactorial in origin due to osteoarthritis, chronic rotator cuff tendinopathy and post herpetic neuralgia was evaluated for peripheral nerve stimulation. His pain is chronic in origin, having been present for over 10 years, was described as intense burning sensation, and rating a constant 8/10 on a numeric pain rating scale. Physical therapy, multiple medication trials with tricyclic antidepressants, antiepileptics, NSAIDs, platelet-rich plasma injections as well as stellate blocks have not provided any long lasting relief.

Diagnostic axillary and suprascapular nerve blocks significantly relieved different areas of his shoulder pain so a decision was made to place both an axillary and suprascapular nerve StimRouter lead. Theoretical discussion for the inferior approach through the spinoglenoid notch discussed first by Dr. Michael Gofeld.

With the patient sitting in a beach chair, the area over the posterior shoulder was evaluated under ultrasound using a 5 mHz curved array transducer. The probe was placed in the axial plane over the posterior glenohumeral joint, glenoid and medially the spinoglenoid notch over the scapula. The suprascapular nerve was identified along the suprascapular artery. Using an out-of- plane approach, from caudal to cephalad, an 18 gauge spinal needle was inserted 4 cm from the ultrasound probe. Once the tip of the needle was confirmed in the spinoglenoid notch.it was passed superiorly into the suprascapular notch, the ultrasound probe was re-positioned to identify the suprascapular notch and the needle tip was visualized underneath the superior transverse ligament. At this time, the guidewire was then passed through the spinal needle and confirmed in the suprascapular notch. Nerve stimulation reproduced a tingling sensation into the shoulder. The dilator was then placed along with the StimRouter lead. Repeat stimulation confirmed shoulder coverage and the lead was release. The receiver was tunneled laterally over the deltoid.

Patient returned for follow up appointment and continues >50% relief in his shoulder pain without any noted changes in function.

Discussion

Shoulder pain is very important and prevalent in western society with a one-year prevalence of 4.7 - 46.7% (1). The etiology of chronic shoulder pain is very diverse and can include orthopedic conditions but also non-orthopedic causes such as cervical radiculopathy, and in our patients case also post herpetic neuralgia. This can limit a patient's ability for his daily activities and causes burdens on both the patient and society around him. The suprascapular nerve is considered one of the important nerves in the shoulder region. It contains both the motor fibers to the supraspinatus and infraspinatus muscles, and is a major part of sensory innervation of the shoulder which also includes the axillary nerve. These two nerve are important targets for chronic shoulder pains which can cover various pathologies including orthopedic causes, iatrogenic causes as well as hemiplegic shoulders.(2,3). Pain relief of the shoulder can be achieved by nerve blocks (using bupivacaine and methylprednisolone acetate) for a short term effect, as well as radiofrequency for a longer term effect (4). A percutaneous approach for peripheral nerve stimulation seems to be an ideal approach to provide pain relief coverage to the proximal branches to acromion and subacromial regions. Using ultrasound, the usual site of entry involves visualization and scanning at the superior medial border of the scapula and identifying the suprascapular fossa with imaging of the supraspinatus muscle and finally the suprascapular nerve underneath it. (5)

In our patient, a novel ultrasound guided inferior approach through the spinoglenoid notch was performed.Using this technique, potential complications of suprascapular nerve block may be avoided, based on using ultrasound as well as by staying on the scapula. Pneumothorax has been reported following suprascapular nerve block and is a concerning source of litigation (6). A technique described to stimulate the distal branches of the suprascapular nerve (7) was postulated to create a more stable lead position without migration and this may also be another benefit to using this posterior inferior approach.

Conclusion

Based on a literature search on Pubmed we have not been able to find a similar case of using an inferior approach through the spinoglenoid notch as a feasible effective technique for suprascapular nerve lead placement. This case study shows the viability of an inferior spinoglenoid notch approach for supraspinatus nerve peripheral nerve stimulation and may achieve better stability.

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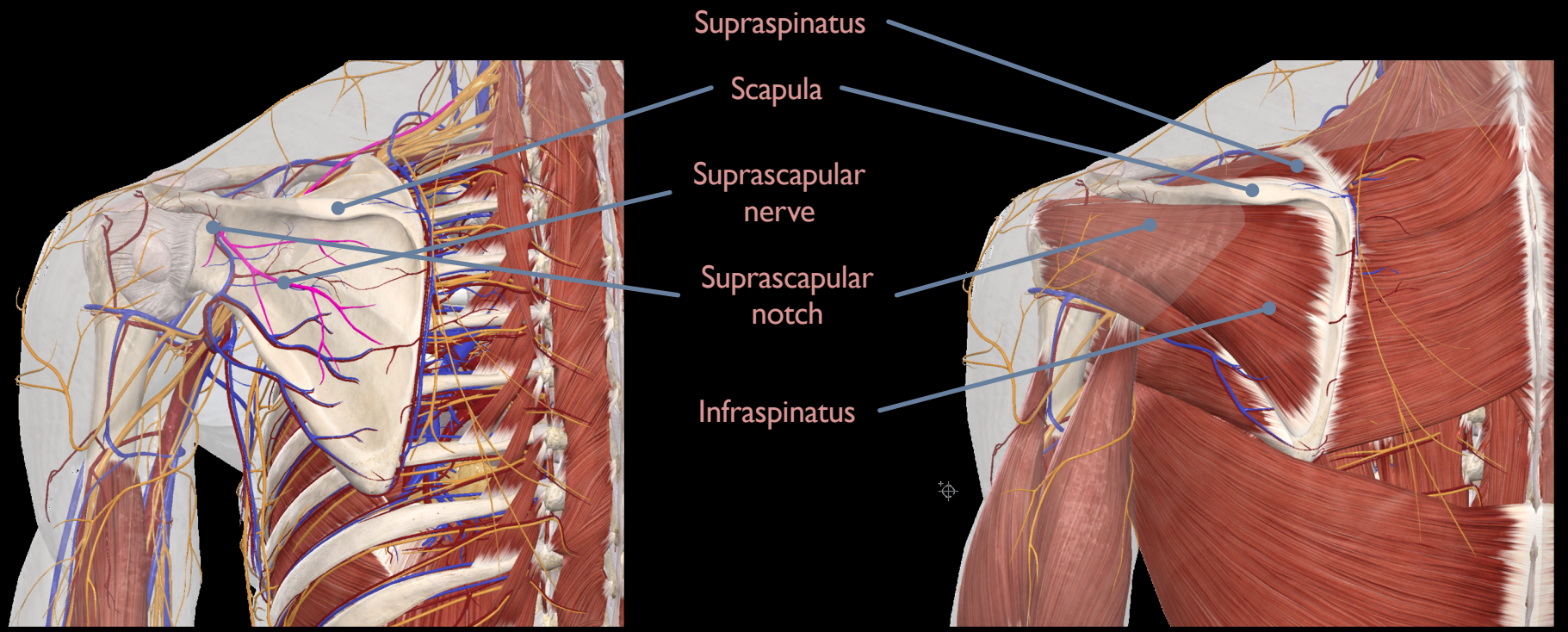
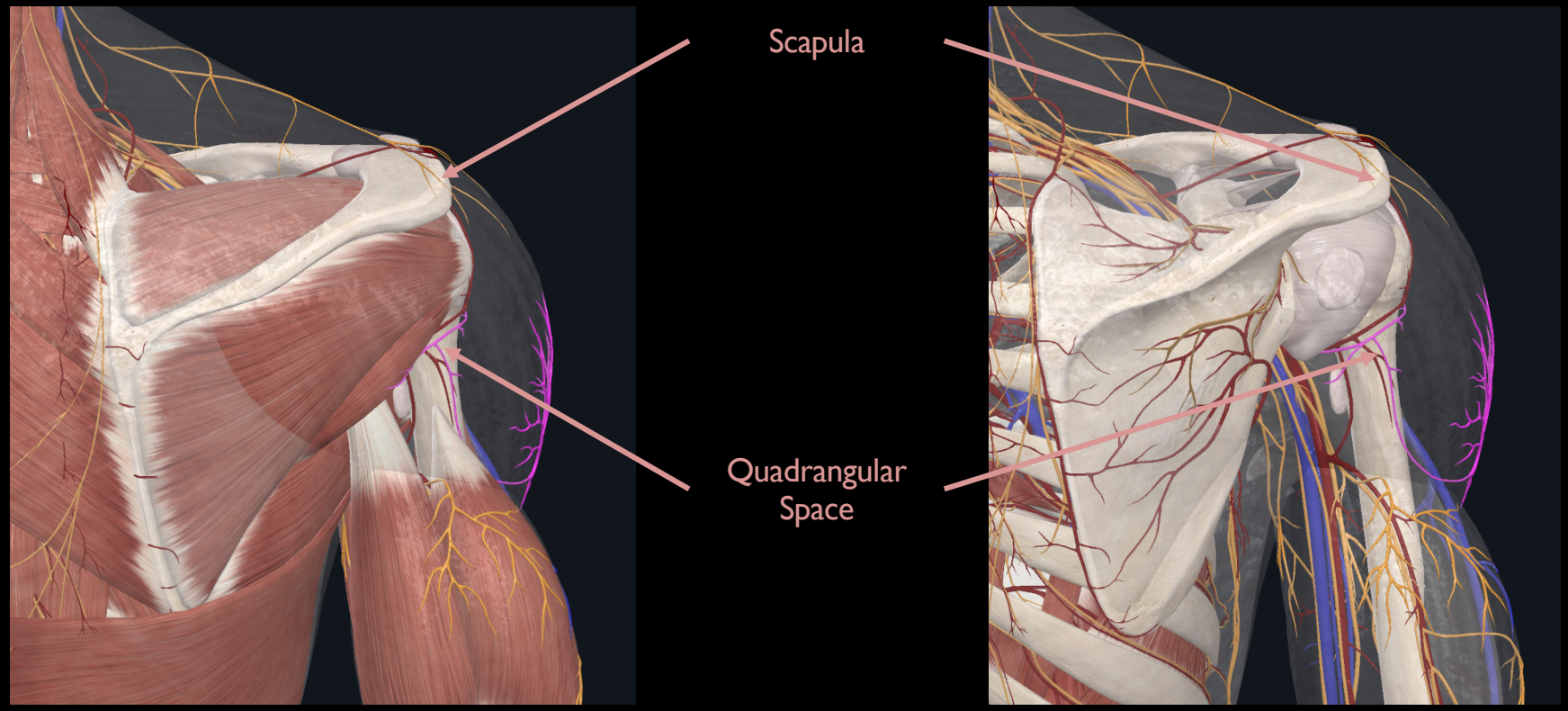
Suprascapular Nerve



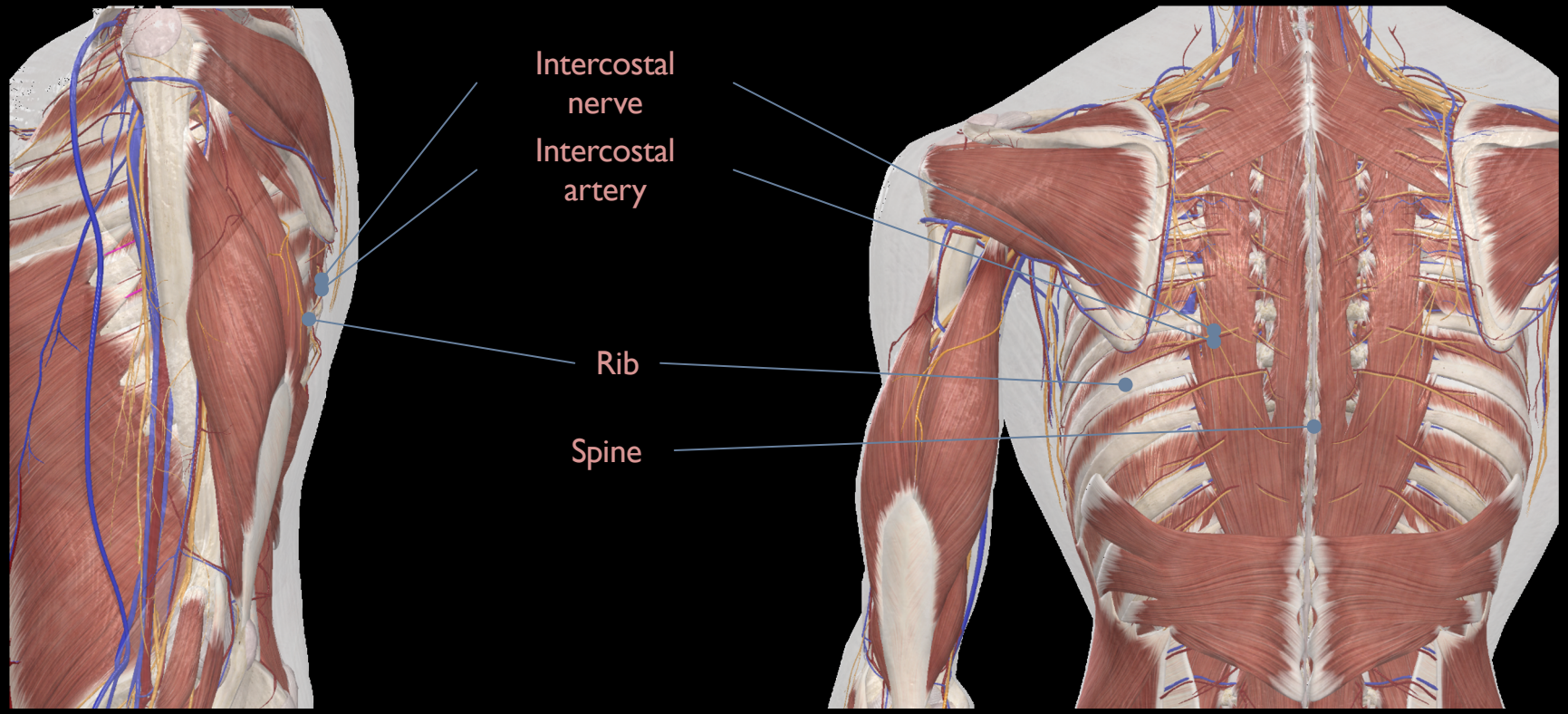
- Upper trunk of brachial plexus (Motor and sensory)
- Supraspinatus muscle and Infraspinatus muscles
- Acromioclavicular and glenohumeral joints

Axillary (Circumflex) Nerve



- Upper trunk, post. division, post. cord (Motor and sensory)
- Deltoid, triceps, teres minor muscles
- Glenohumeral joint, upper arm

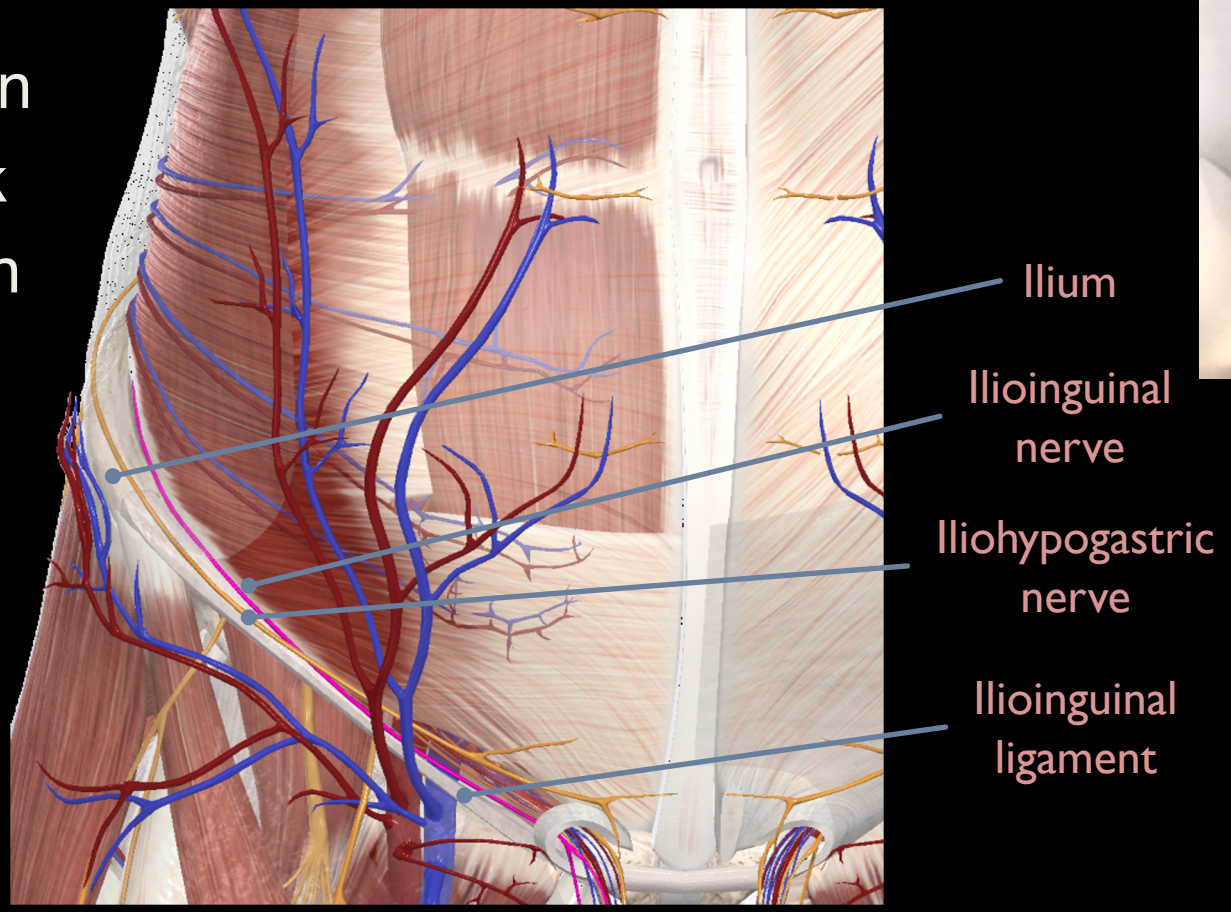
Intercostal Nerves

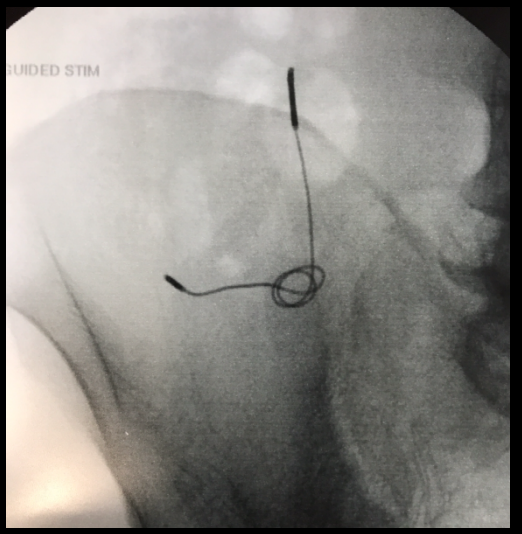


- Anterior rami of thoracic spinal nerves T1-T11
- Intercostal muscles
- Chest wall and parietal pleura

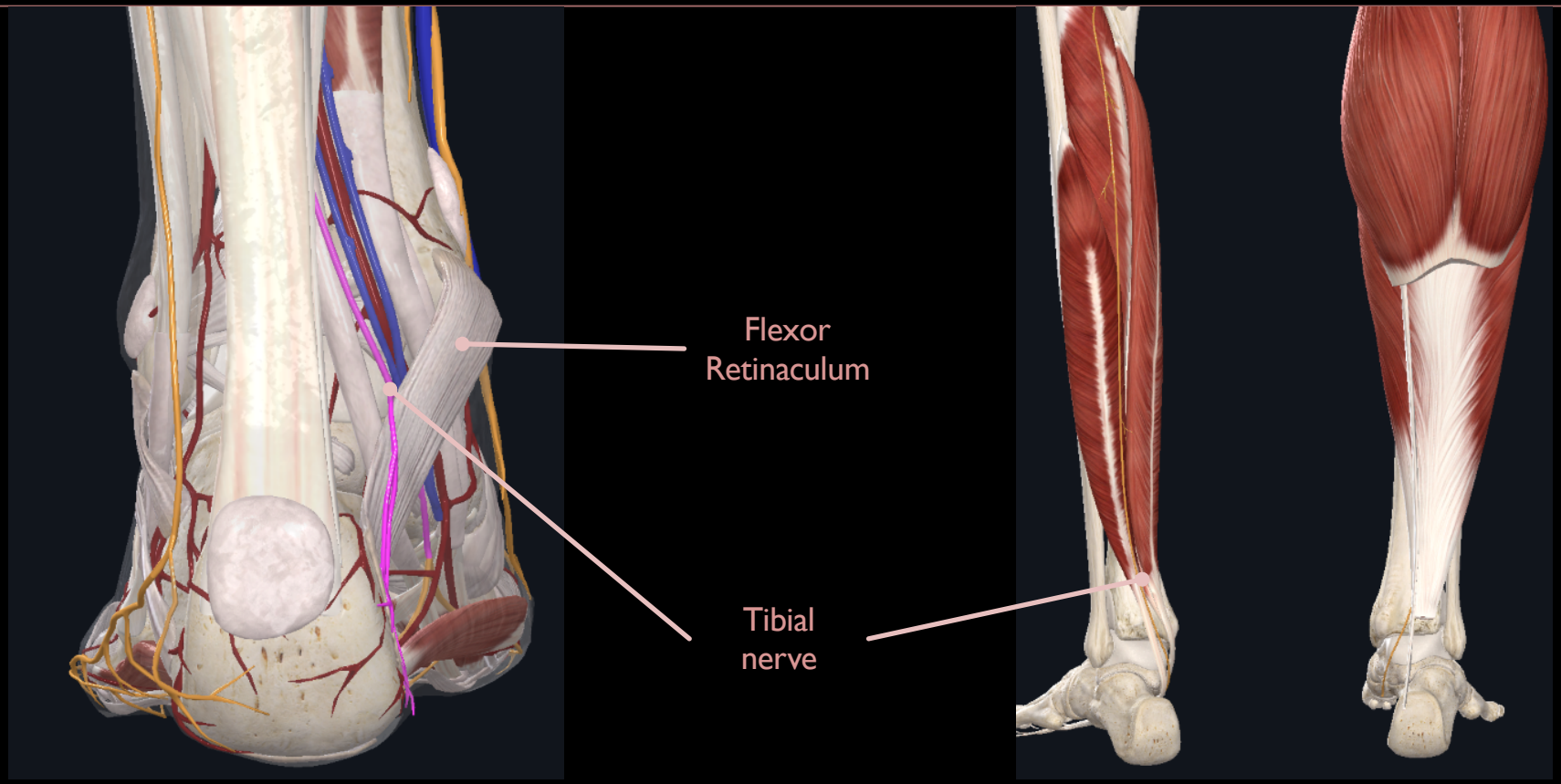
Ilioinguinal and Iliohypogastric Nerves

- T12, L1 (lumbar plexus)
- Motor and Sensory
- Post-herniorhaphy pain
- Peripheral nerve block
- Acute and chronic pain
- PNS target





Tibial Nerve



- Branch of the sciatic nerve
- Motor and Sensory
- Chronic foot and heel pain

PNS for Post-Amputation Pain

Original article

OPEN ACCESS

Percutaneous peripheral nerve stimulation for the treatment of chronic neuropathic postamputation pain: a multicenter, randomized, placebo-controlled trial

Christopher Gilmore,[1] Brian Ilfeld,[2] Joshua Rosenow,[3] Sean Li,[4] Mehul Desai,[5] Corey Hunter,[6] Richard Rauck,[1] Leonardo Kapural,[1] Antoun Nader,[7] John Mak,[4] Steven Cohen,[8] Nathan Crosby,[9] Joseph Boggs[9]

Gilmore et al. Reg Anesth and Pain Med, 2019

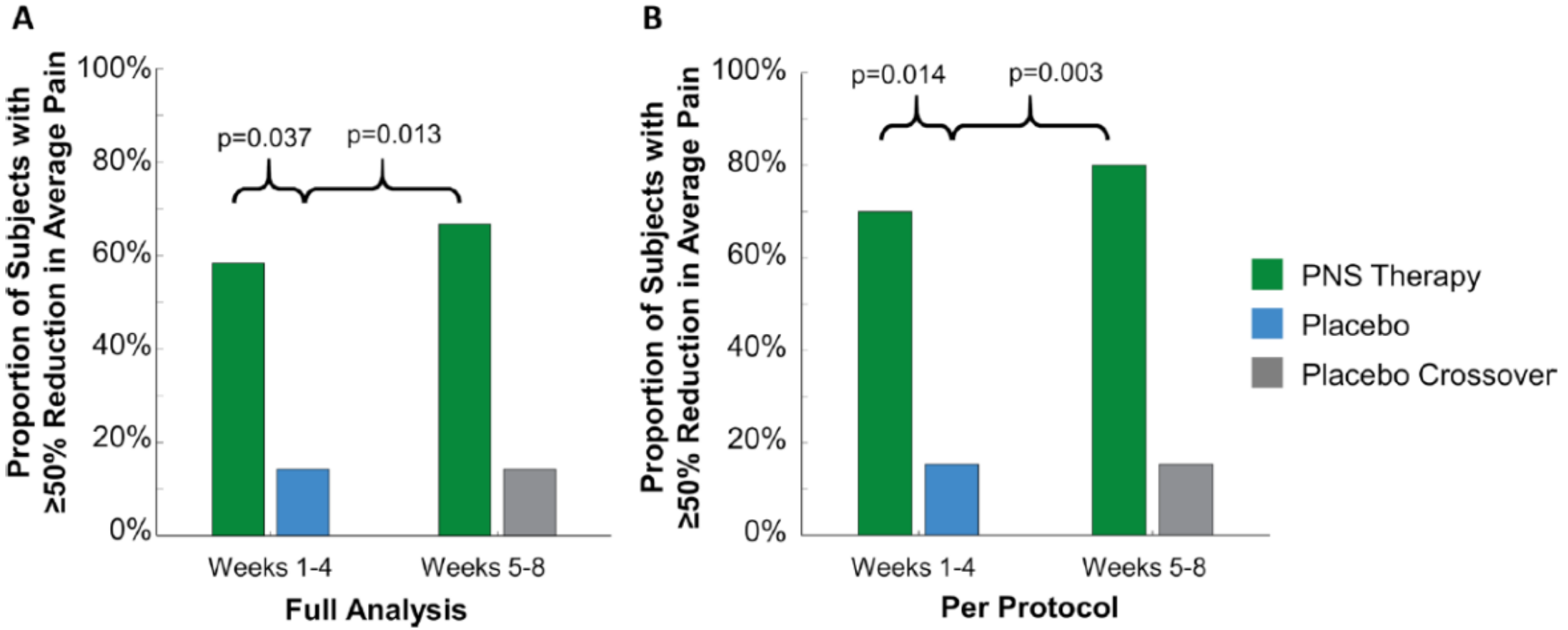


Figure 3 Proportions of subjects with ≥50% reductions in all qualifying regions of residual limb pain and phantom limb pain. Proportions in the (A) full analysis set and (B) per-protocol set during weeks 1–4 and weeks 5–8 of the PNS therapy period were compared with the placebo group at the end of the 4-week placebo period. PNS, peripheral nerve stimulation.

Gilmore et al. Reg Anesth and Pain Med, 2019

Clinical Study: PNS for Post-Amputation Pain

- 60-day PNS for post-amputation pain
- Multi-center, randomized, placebo-controlled, crossover
- N=28 enrolled, 26 implanted
- Weeks 1-4, 58% reported >50% pain reduction vs. 14% in placebo
- Week 8, 67% reported >50% pain reduction vs. 14% in placebo
- 12-months, sustained pain relief, now published
- Reduction of depression at 12-months

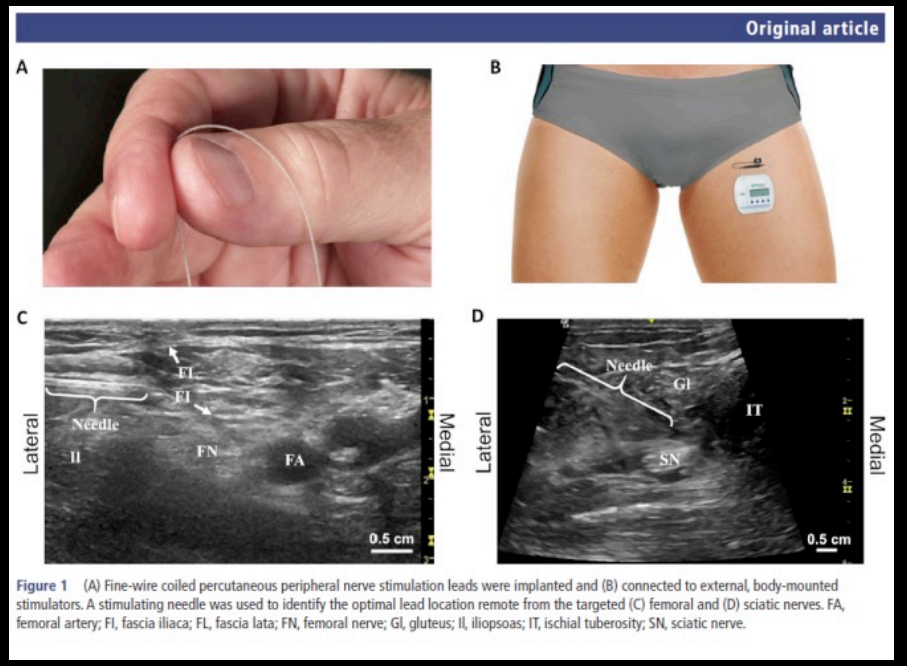


Figure 1 (A) Fine-wire coiled percutaneous peripheral nerve stimulation leads were implanted and (B) connected to external, body-mounted stimulators. A stimulating needle was used to identify the optimal lead location remote from the targeted (C) femoral and (D) sciatic nerves. FA, femoral artery; FI, fascia iliaca; FL, fascia lata; FN, femoral nerve; Gl, gluteus; Il, iliopsoas; IT, ischial tuberosity; SN, sciatic nerve.

U/S Guided Femoral and Sciatic Nerve PNS

Gilmore et al, Reg Anesth and Pain Med, 2019
Gilmore et al, Reg Anesth and Pain Med, 2020

PNS for Chronic Knee Pain

Neuromodulation: Technology at the Neural Interf

Received: November 8, 2017 Revised: March 19, 2018 Accepted: April 9, 2018

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12790

Check for updates

A Feasibility Study of Percutaneous Peripheral Nerve Stimulation for the Treatment of Postoperative Pain Following Total Knee Arthroplasty

Brian M. Ilfeld, MD, MS (Clinical Investigation)*†; Scott T. Ball, MD‡; Rodney A. Gabriel, MD*†; Jacklynn F. Sztain, MD*; Amanda M. Monahan, MD*; Wendy B. Abramson, MD*; Bahareh Khatibi, MD*; Engy T. Said, MD*; Jesal Parekh, PhD‡; Stuart A. Grant, M.B. Ch. B§; Amorn Wongsarnpigoon, PhD¶; Joseph W. Boggs, PhD¶

PNS for Chronic Knee Pain

- Severe OA knee pain
- Post TKA pain
- Failed RF ablation
- Saphenous nerve
- Genicular nerves
- Intrapatellar saphenous
- Alternative to SCS therapy

Pain Physician 2013; 16:E315-E324 • ISSN 2150-1149

Case Report

Infrapatellar Saphenous Neuralgia – Diagnosis and Treatment

Andrea Trescot, MD[1], Michael N. Brown, MD[2], and Helen W. Karl, MD[3]

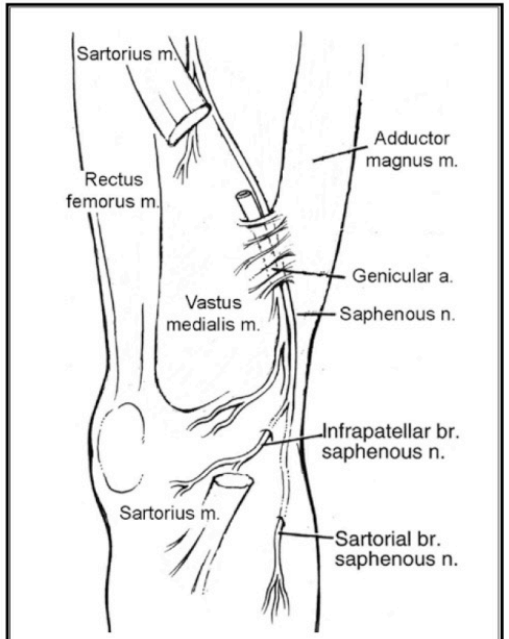


Fig. 3. *The superficial anatomy of the medial knee (modified from Kim by author 1) (58).*

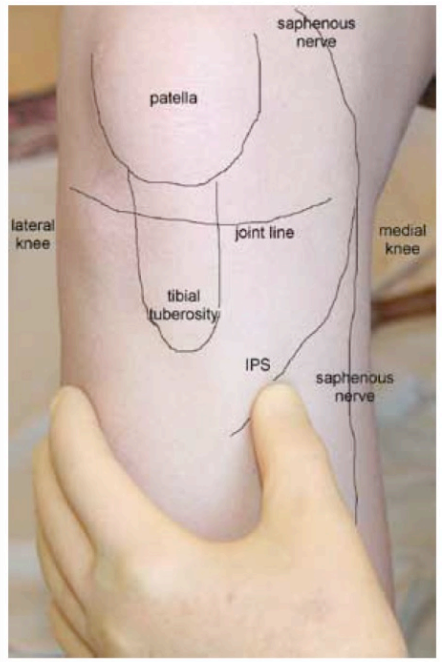


Fig. 5. *Surface landmarks of the IPS .*

- Knee pain
- Post surgical pain
- Infrapatellar saphenous nerve
- U/S guided nerve block
- Cryoablation
- PNS therapy

PNS for Chronic Low Back Pain

Neuromodulation: Technology at the Neural Interface

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New Therapy for Refractory Chronic Mechanical Low Back Pain—Restorative Neurostimulation to Activate the Lumbar Multifidus: One Year Results of a Prospective Multicenter Clinical Trial

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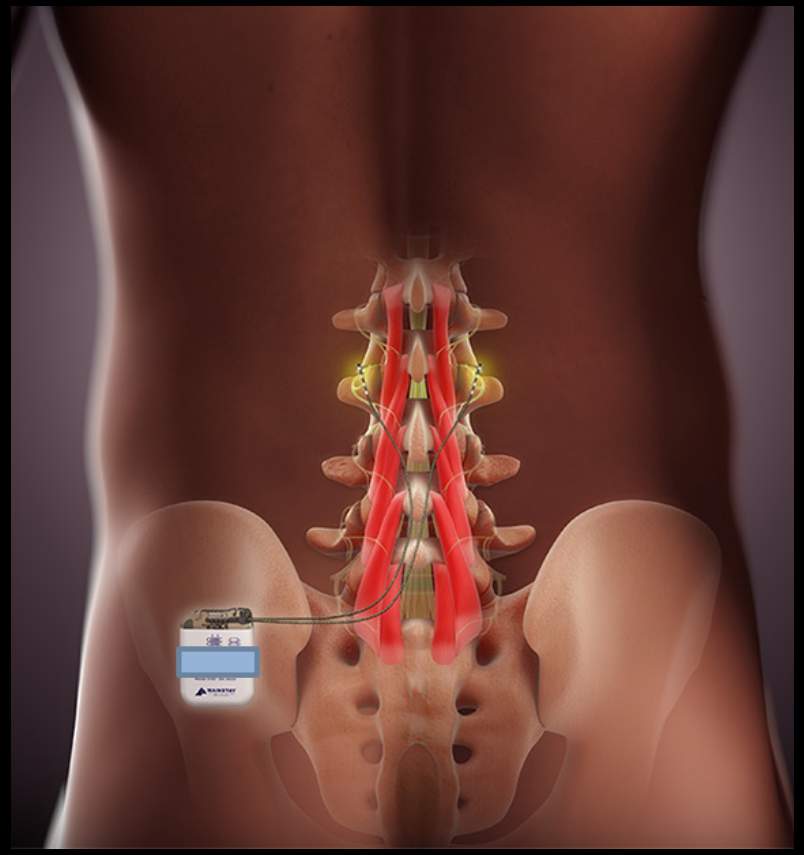

ReActiv8-A

- International, multi-center, prospective trial, single arm
- Austria, Belgium, UK
- Stimulation of the multifidus via medial branch nerve
- At 90 days, N=52, ≥2 on NRS
- Responder rate 58%
- Single arm, no control group

Neuromodulation, 2018

ReActiv8-B

- International, multi-center, prospective, sham-controlled
- Stimulation of the multifidus via medial branch nerve
- USA, Australia, UK
- Randomized 1:1, 14 days after implant
- N=56, at 120 days (responders ≥30% VAS)
- 56% study group versus 47% control
- Not statistically significant
- At 1 year, 60% patients >50% pain reduction
- FDA approval 2020

60-Day PNS for Chronic Low Back Pain

Reductions in Opioid Consumption with Percutaneous Medial Branch Peripheral Nerve Stimulation for Chronic Low Back Pain

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[1] Walter Reed National Military Medical Center, [2] Center for Clinical Research, [3] Duke University, [4] International Spine, Pain and Performance Center, [5] Virginia iSpine Physicians, [6] Premier Pain Centers, [7] Hope Research Institute, [8] The Spine and Nerve Center of The Virginias, [9] Womack Army Medical Center, [10] SPR Therapeutics, Inc.

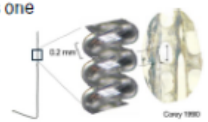
INTRODUCTION

- Chronic low back pain (LBP) is one of the most prevalent and challenging musculoskeletal conditions[1] and is the leading cause of disability in adults.

CONVENTIONAL NEUROMODULATION:

- Requires surgery and permanent implant
- Cost may relegate therapy to use later in the treatment continuum

MINIMALLY INVASIVE, PERCUTANEOUS PNS:



- Wearable stimulator and percutaneous fine-wire, coiled lead (designed to anchor in tissue with excellent safety profile[2]) could overcome limitations of previous systems

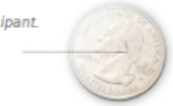
Goal: Evaluate feasibility of 60-day percutaneous PNS to reduce opioid use in patients with chronic LBP.

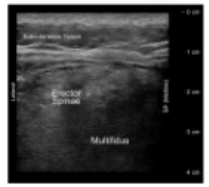
MATERIALS & METHODS

Ongoing IRB approved study; informed consent was obtained from each participant.

Key Eligibility Criteria:

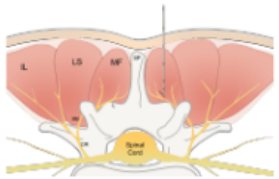
- Participants with chronic LBP (≥ 3 months); no radicular pain
- Stable medication usage at least 1 month prior to baseline
- No prior lumbar surgery or RFA within prior 6 months
- No anesthetic injections within prior 3 months
- Score of ≤ 20 on Beck Depression Inventory





Lead Placement: Bilateral, percutaneous PNS leads, targeting medial branches of the dorsal ramus in the center of the region of pain

- *Image Guidance:* ultrasound and/or fluoroscopy
- *Confirmation:* Stimulation of medial branch confirmed by selective activation of multifidi



PNS Treatment: Stimulation for 6-12 hrs/day for up to 60 days

- Participants continued normal activities
- Leads removed with gentle traction
- Participants return for long-term follow-up visits

Figure Abbreviations: Dorsal Ramus (DR), Iliocostalis (IL), Lamina (L), Longissimus (LS), Medial Branch (MB), Multifidus (MF), Spinous Process (SP).

RESULTS

Participant Demographics (n = 11):

- Average Age: 60.8 years (40.1 – 82.1)
- Average Baseline Pain Score: 6.3 (BPI-5)
- Average Duration of LBP: 17.0 years
- Spinal Level of Lead Placement: L2 (n=1), L3 (n=1), L4 (n=6), L5 (n=3)

Outcomes:

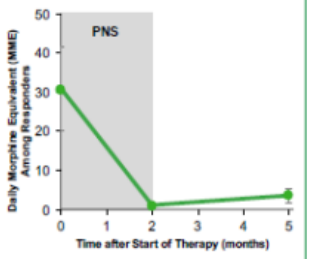
- At End of Treatment (EOT) 64% reported ≥50% reduction in opioid consumption with PNS (n=7/11)
  - *Avg. 29.7 mg morphine equivalent (MME) reduction among responders at EOT*
- At 3 months post EOT, 73% reported ≥50% reduction in opioid (n=8/11)
  - *Avg. 23.1 MME reduction among responders at 3 months post-EOT*
- Majority of participants experienced clinically-significant reductions in average pain intensity, disability, and pain interference.

Safety:

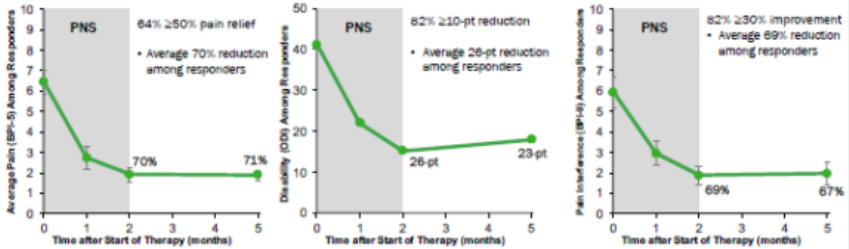
- No serious or unanticipated device-related adverse events

Substantial Reductions in Opioid Analgesic Consumption with PNS:

Participant	Baseline mg Morphine Equivalent (MME)	End of Treatment (EOT)			3-mo Post-EOT		
		MME	MME Reduction from Baseline	% MME Reduction	MME	MME Reduction from Baseline	% MME Reduction
1	80.0	0.0	80.0	100%	0.0	80.0	100%
2	22.1	2.9	19.3	87%	0.0	22.1	100%
3	3.6	0.0	3.6	99%	2.9	0.7	19%
4	13.6	0.0	13.6	100%	6.4	7.1	53%
5	66.4	47.1	19.3	29%	57.8	8.6	13%
6	10.0	9.3	0.7	7%	10.0	0.0	0%
7	3.2	4.3	-1.1	-34%	1.1	2.1	67%
8	1.4	1.4	0.0	0%	0.0	1.4	100%
9	57.9	4.3	53.6	93%	15.0	42.9	74%
10	7.1	0.0	7.1	100%	1.4	5.7	80%
11	31.0	0.5	30.5	98%	5.8	25.2	81%
Average All Participants	26.9	6.3	20.6	62%	9.1	17.8	63%



Clinically Significant[3] Reductions in Average Pain Intensity, Disability, and Pain Interference with PNS:



CONCLUSIONS

- Percutaneous PNS treatment for up to 60 days can significantly reduce usage of opioid analgesic medications in patients with chronic LBP.
- These results support earlier findings that percutaneous PNS delivered for up to 60 days can relieve chronic LBP, which leads to improvement in disability and quality of life, without a permanently implanted device.

REFERENCES & ACKNOWLEDGEMENT

[1] US Burden of Disease Collaborators. The State of US Health, 1990-2010 Burden of Diseases, Injuries, and Risk Factors. *JAMA*. 2013; 310(6):591-606.

[2] Ilfeld et al. "Infection Rates of Electrical Leads Used for Percutaneous Neurostimulation of the Peripheral Nervous System." *Pain Practice* 2016.

[3] Dworkin et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain 2008; 9: 105-121.

Funding:
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Surgical Implant Technique for a Novel, Battery-Free Micro-stimulator for Peripheral Nerve Stimulation System

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St. Charles Spine Institute, Thousand Oaks, CA ;Premier Pain Centers, NJ; University of California, San Francisco, CA; IPM Medical Group, Walnut Creek, CA; University of Florida, Department of Anesthesiology, Gainesville, FL; Nalu Medical

Introduction

- Surgical introduction of leads targeting peripheral neural targets can be challenging
- Often, SCS leads are used for this purpose limiting the utility and stability of the leads
- Large SCS IPGs necessitate significant tunneling
- A novel, miniaturized neuromodulation system has been developed that offers potential advantages for targeting peripheral nerves

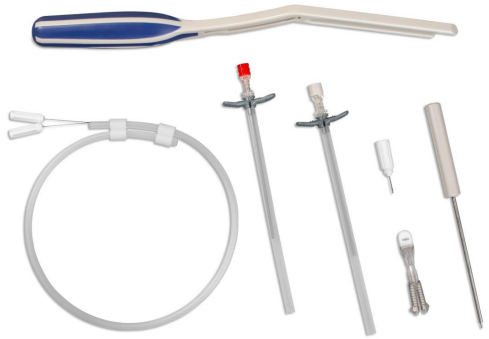
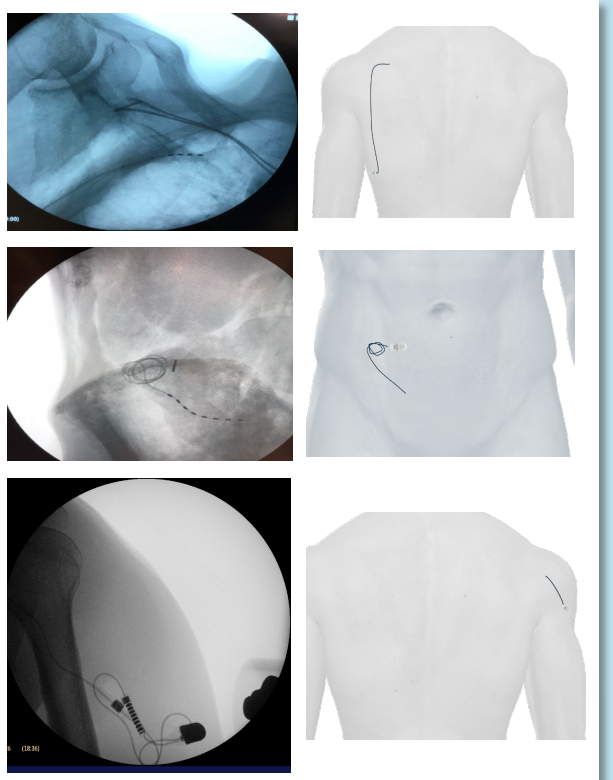


Figure 1. Toolset tested in cadaveric studies.



Place and anchor leads

Create Pocket tunnel

Insert IPG, tuck strain relief, loops and close

Battery-free microstimulators (1.5 cc) come in four configurations

Therapy Disc provides power and system control and can be worn in multiple locations

Methods

- Cadaveric studies were undertaken to develop implantation techniques for suprascapular, Ilioinguinal, and axillary nerves were chosen as implantation targets
- Using a newly developed neurostimulator and implantation tools, we developed surgical approaches for these peripheral nerves

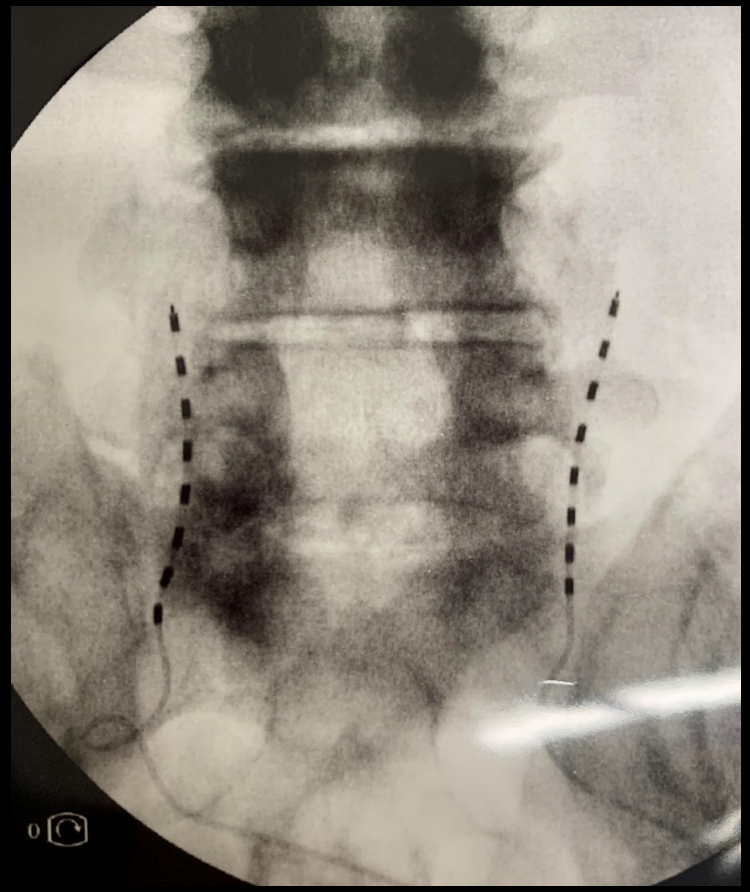
Results

- The miniaturized lead and introducer combination performed well in cadaver studies
- Multiple peripheral nerve targets were easily targeted for lead placement
- The micro-IPG assembly is easily placed subcutaneously close to the initial incision point and neural target

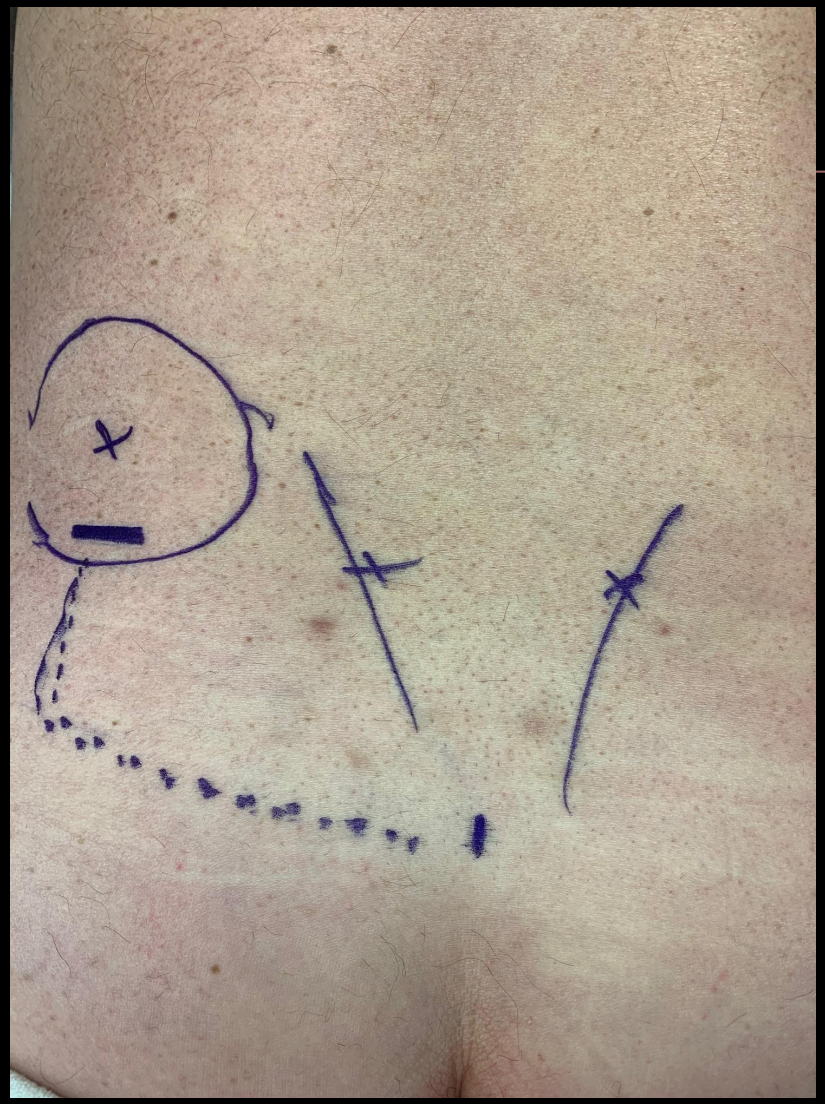
Conclusions

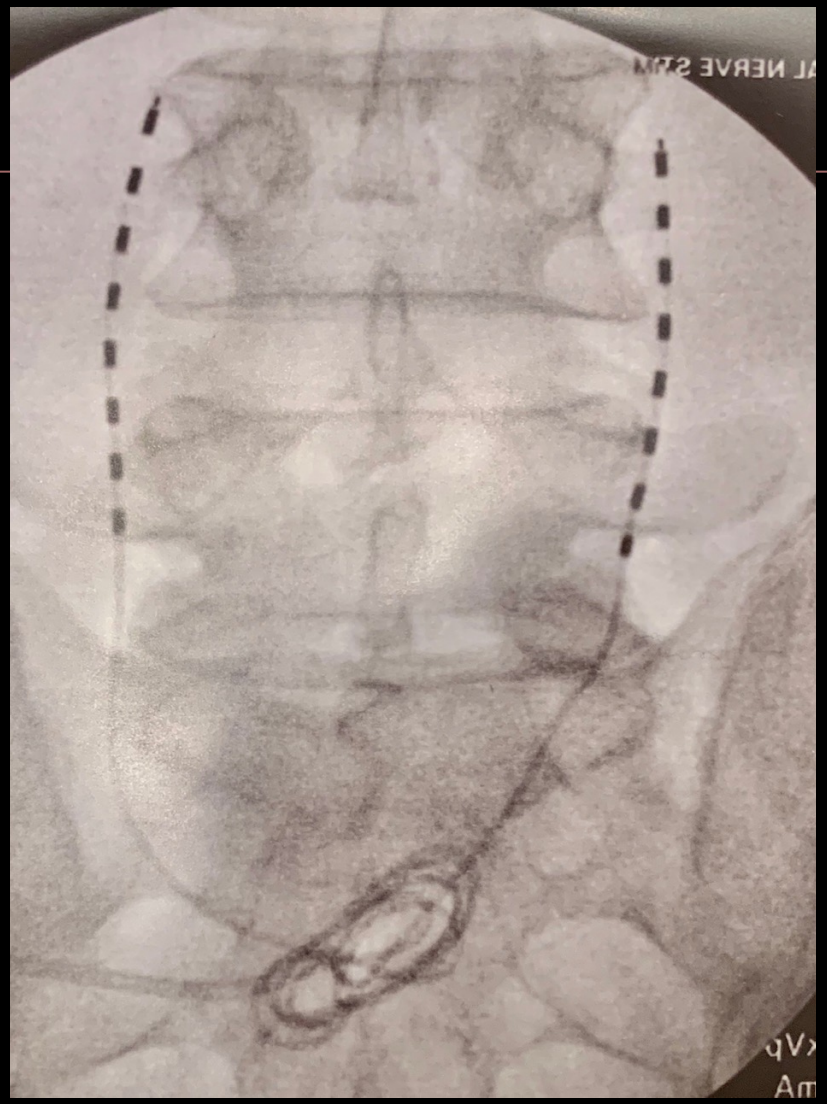
- Multiple peripheral neural targets were easily targeted with the new system
- The battery-free microstimulator IPG allows for close placement near the target
- These findings are encouraging for use in peripheral nerve stimulation

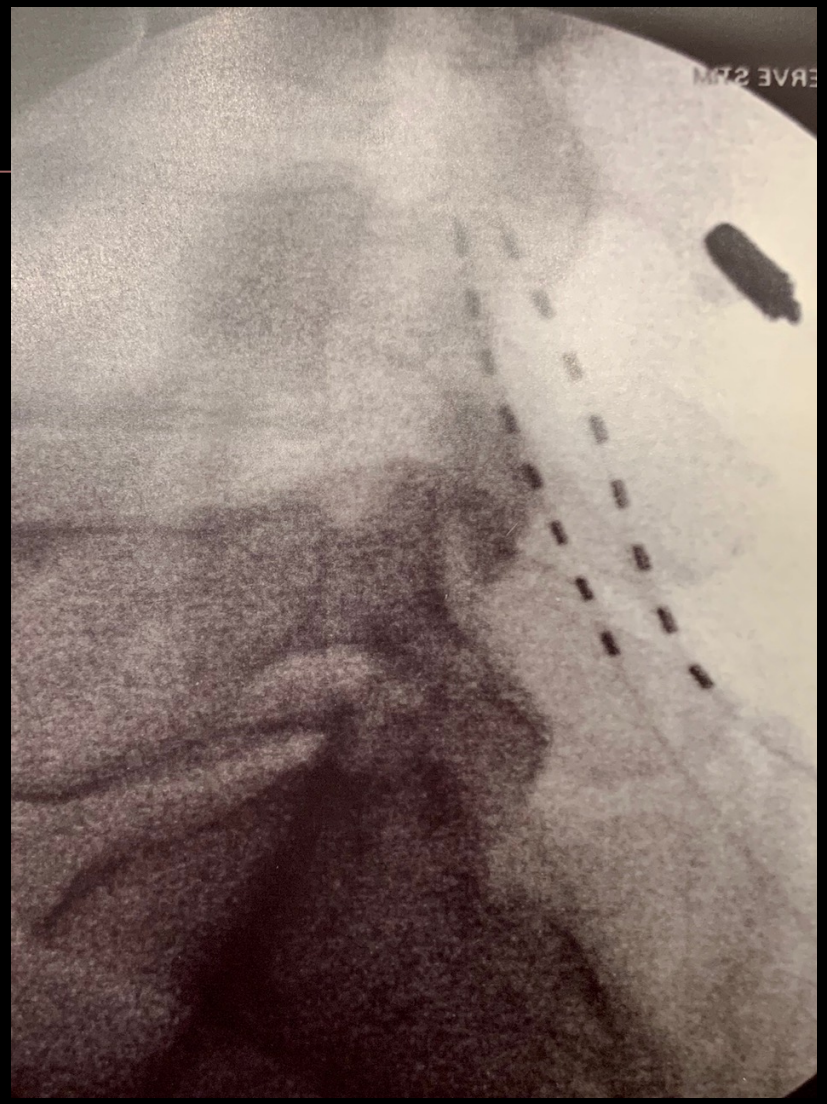
PNS for Failed Back Surgery Syndrome



- 68-year-old male
- Chronic low back pain
- Prior laminectomy and fusion
- Dx: Failed Back Surgery Syndrome (FBSS)
- Failed traditional spinal cord stimulation
- 80% pain relief with 60-day PNS
- Battery-free micro stimulator implanted





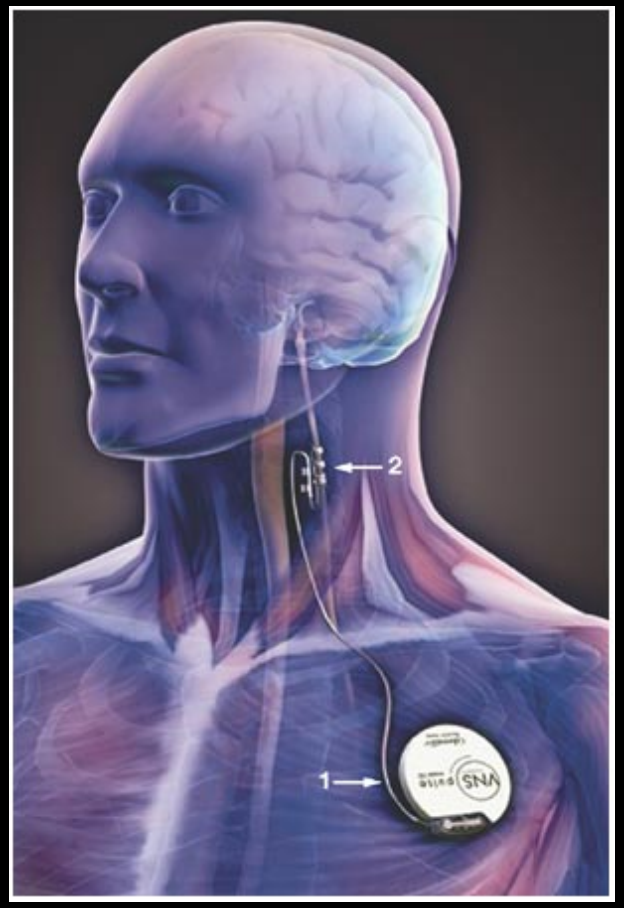


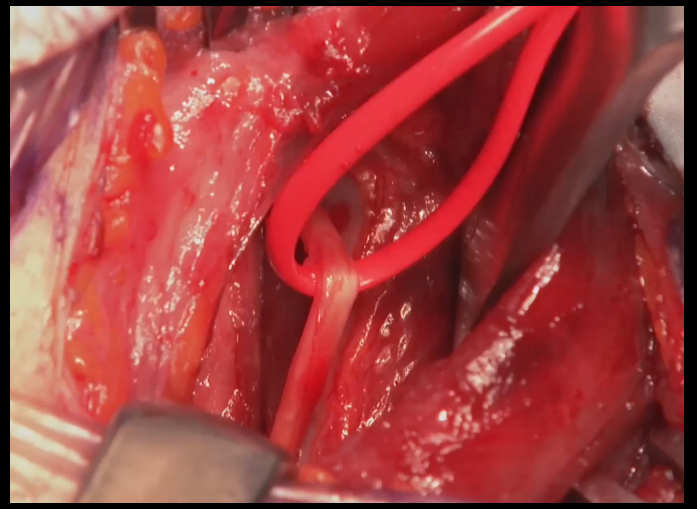
PainWeek®

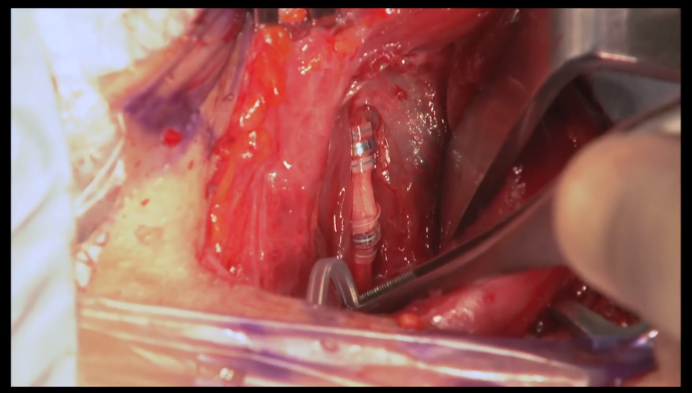
PNS for Treating Chronic Headache

- Migraine HA, 3rd most common disease
- 14.7% prevalence, 28 million Americans
- 3:1 female to male ratio
- Cluster HA, 9.8 per 100,000, 1/25 of migraine
- 4:1 male to female ratio
- 2017 FDA approved: episodic cluster HA
- 2018 FDA approved: migraine HA

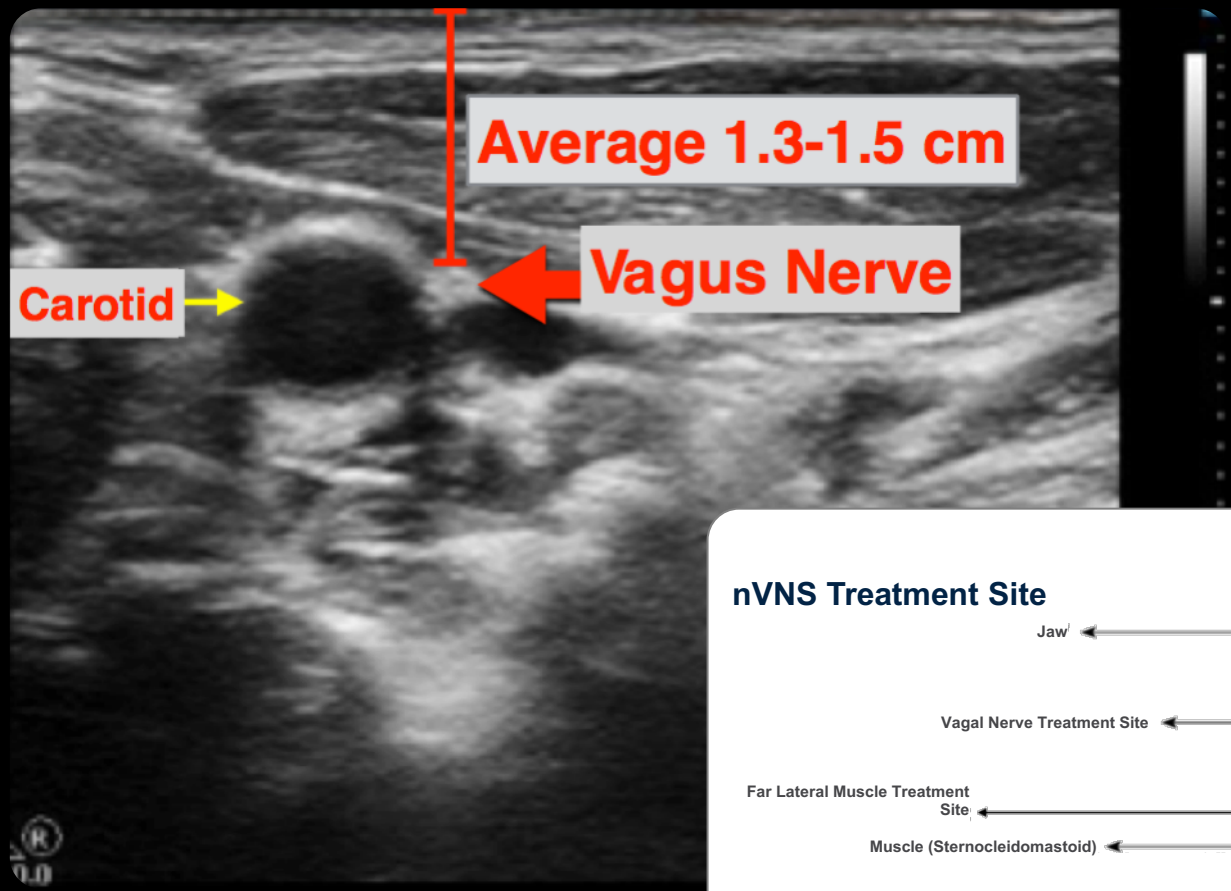
iVNS: Implanted Vagus Nerve Stimulation

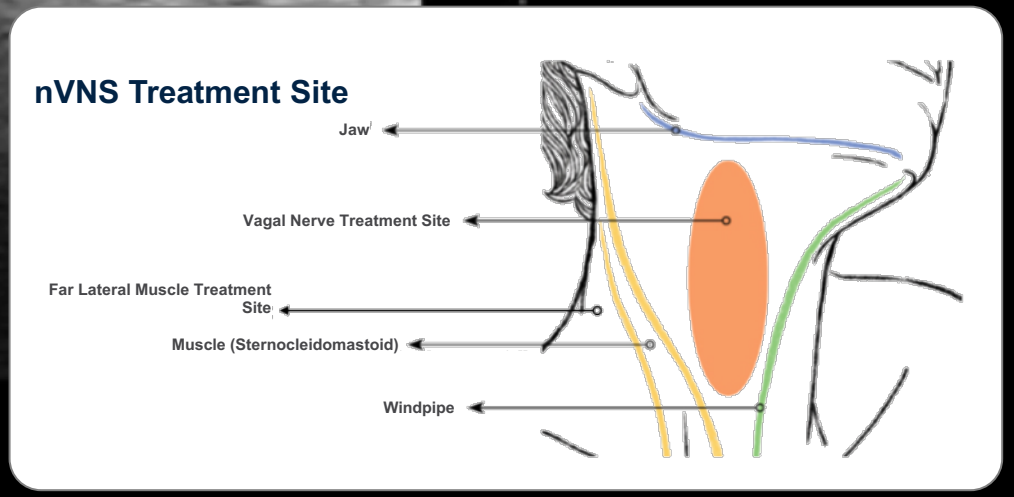






nVNS: Noninvasive Vagus Nerve Stimulation

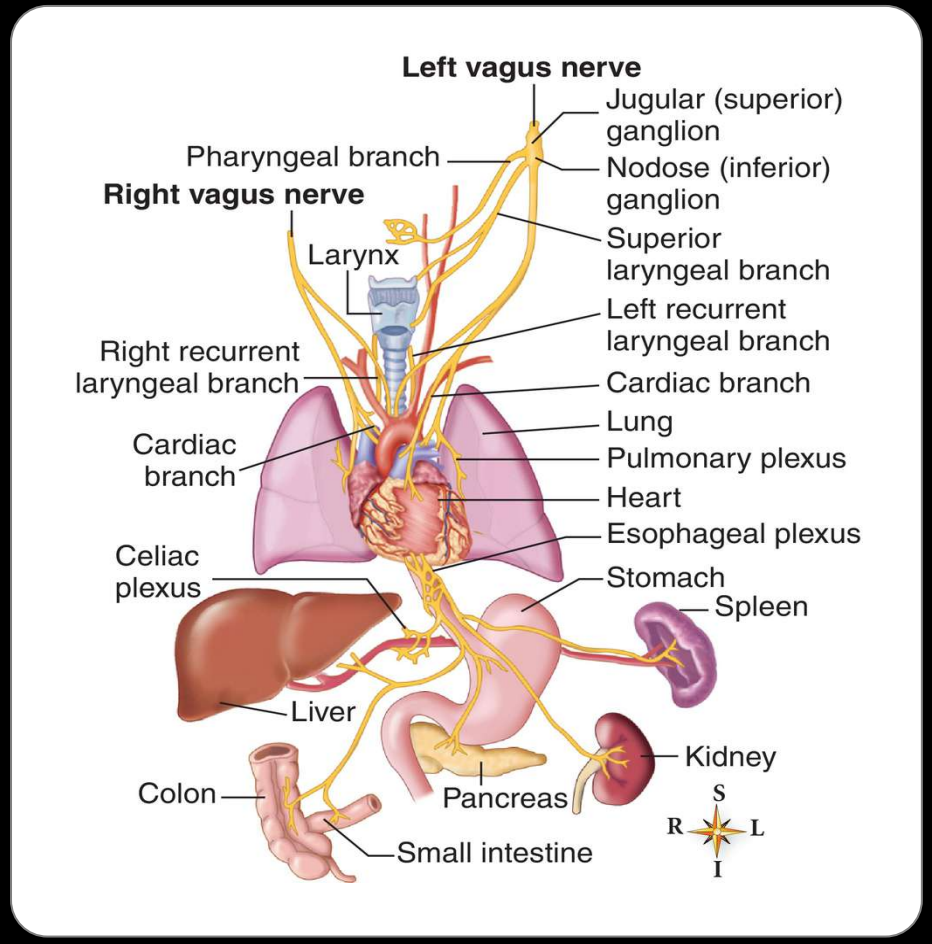




Courtesy of electroCore, LLC.

CN X: *the great wandering protector*

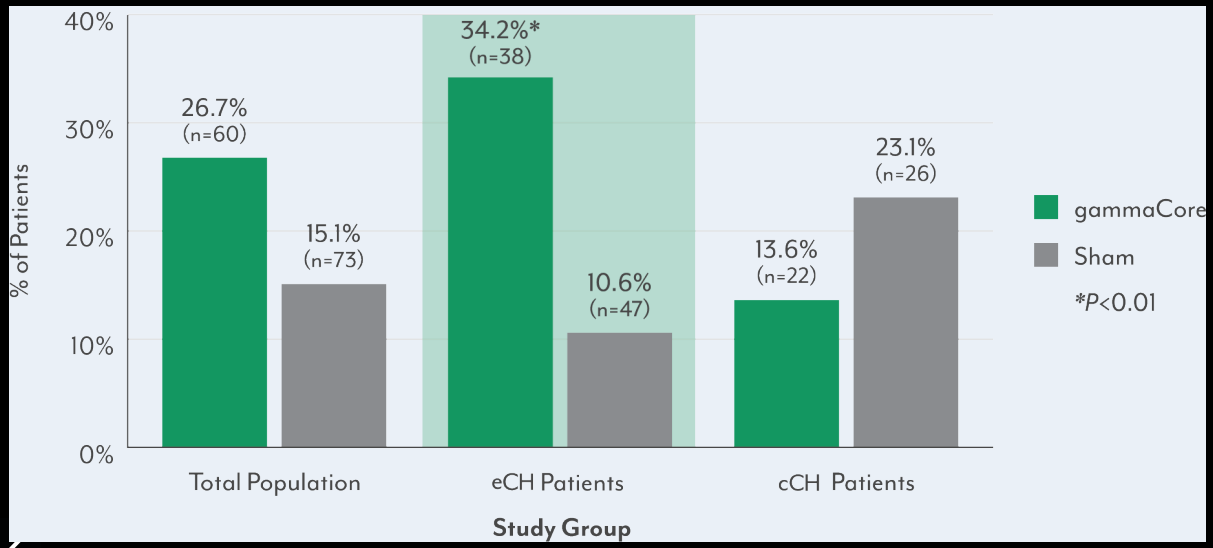
- Longest cranial nerve (CN X)
- Innervates structures of head, neck, thorax, and abdomen
- 80% afferent, 20% efferent
- Involved in autonomic, cardiovascular, respiratory, gastrointestinal, immune, and endocrine systems
- Primarily regulates involuntary (autonomic) functions:
  - Heart rate
  - Blood pressure
  - Respiration
  - Digestion and peristalsis



Silberstein et al. Headache 2015
Yuan et al. Headache 2016

Vagal Nerve Stimulation

- Non-invasive
- Inhibits cortical spreading depressions
- Suppresses the increase in inflammatory cytokines
- Metered dose device
- FDA approved for cluster and migraine HA



Headache. 2016;56(8):1317-1332.

Potential Indications for VNS

- Anxiety – George M, et al. Brain Stimulation.2008(1);112-21.
- Asthma – Hoffman/Emala Staats
- Alzheimer's disease – Sjogren, et al. J Clin Psychiatry, 63:11 Nov. 2002
- Fibromyalgia – Lange, et al. Pain Medicine.2011;12:1406-13.
- Stroke – Mravec, Auton Neurosci.2010 Dec 8;158(1-2):8-12.
  - Acute, Rehabilitation
- Obesity – Pardo, et al. Int J Obesity (Lond). 2007 Nov;31(11):1756-59.
- Diabetes Hypertension
- Irritable bowel syndrome
- Rheumatoid arthritis
- Liver disease (NAFLD NASH)

Neuromodulation: Technology at the Neural Interface

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The Use of Non-invasive Vagus Nerve Stimulation to Treat Respiratory Symptoms Associated With COVID-19: A Theoretical Hypothesis and Early Clinical Experience

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- July 10, 2020
- FDA approves nVNS for emergency use authorization
- COVID-19 related dyspnea and reduced respiratory flow
- Hypothesis: nVNS may suppress the “cytokine storm”

Potential Targets for PNS and PNFS

Disease/Pain State	Nerve Target
Occipital neuralgia	post-gang C2 fibers, occipital
Headache and facial pain	supra/infra orbital, temporo-auricular, trigeminal divisions, vagus
Upper extremity	axillary, suprascapular, median, ulnar, radial
Axial spine	dorsal cutaneous (C/T/L), medial branch
Chest	intercostal
Sacral/pelvic	cluneal, lateral branch, pudendal
Groin	ilioinguinal, ilihypogastric, genitofemoral
Lower extremity	lateral femoral cutaneous, common peroneal, genicular, femoral, sciatic, saphenous, infrapatellar saphenous, tibial

PNS: Coding and Billing

- PNS lead: 64555
- PNS IPG: 64590
- Programming: 95971/95972
- Fluorography: 77002/77003
- Ultrasound: 76942

Summary

- 25.3 million (11%) adults in U.S. experience daily chronic pain
- ~$600 billion/year health expenditure
- Opioid epidemic
- Aging population
- Improved PNS technology
- Cost effective compared to SCS
- Low risk, minimally invasive
- Level 1 evidence
- Favorable reimbursement

A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients.
http://jama.ama-assn.org/cgi/content/abstract/274/20/1591

Thank You