

Recent Guideline type papers for PNS:

Natalie Strand, Ryan S D'Souza, Jonathan M Hagedorn, Scott Pritzlaff, Dawood Sayed, Nomen Azeem, Alaa Abd-Elseyed, Alexander Escobar, Mark A Huntoon, Christopher M Lam, Timothy R Deer. **Evidence-Based Clinical Guidelines from the American Society of Pain and Neuroscience for the Use of Implantable Peripheral Nerve Stimulation in the Treatment of Chronic Pain.** J Pain Res. 2022 Aug 23;15:2483-2504.

-recent guidelines and recommendation grades for PNS for various indications, organized by anatomic area, endorsed by ASPN

Table 3 A List of Common Peripheral Nerve Targets Amenable to Percutaneous PNS Treatment

Upper Extremity	Lower Extremity	Trunk/Pelvis	Head/Neck
• Suprascapular** • Axillary** • Radial • Median • Ulnar • Brachial plexus (at interscalene interval)	• Sciatic** • Femoral • Obturator • Lateral femoral cutaneous • Saphenous • Posterior femoral cutaneous • Common peroneal • Tibial** • Sural • Superficial peroneal • Genicular nerves (knee)	• Genitofemoral • Ilioinguinal • Iliohypogastric • Pudendal • Cluneal • Medial Branch**	• Greater occipital

Note: Nerves targets denoted by a double asterisk and are in bold (**) are described in detail below.

Table 1 Hierarchy of Studies by the Type of Design (US Preventive Services Task Force)

Evidence Level	Study Type
I	At least 1 controlled and RCT, properly designed
II-1	Well-designed, controlled, nonRCTs
II-2	Cohort or case studies and well-designed controls, preferable multicenter
II-3	Multiple series compared over time, with or without intervention, and surprising results in noncontrolled experiences
III	Clinical experience-based opinions, descriptive studies, clinical observations, or reports of expert committee

Notes: Reprinted from Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med.* 2001;20(3 Suppl):21–35. Copyright 2001, with permission from Elsevier.¹¹²

Table 2 Meaning of Recommendation Degrees (I.S. Preventive Services Task Force)

Degree of Recommendation	Meaning
A	Extremely recommendable (good evidence that the measure is effective and that benefits outweigh the harms)
B	Recommendable (at least moderate evidence that the measure is effective and that benefits exceed harms)
C	Neither recommendable nor inadvisable (at least moderate evidence that the measure is effective, but benefits are similar to harms and a general recommendation cannot be justified)
D	Inadvisable (at least moderate evidence that the measure is ineffective or that the harms exceed the benefits)
I	Insufficient, low-quality, or contradictory evidence; the balance between benefit and harms cannot be determined

Strand et al

Dovepress

Table 6 ASPN Best Practices PNS Guidelines

ASPN Best Practices PNS Guidelines	Level of Evidence	Grade
Head/Neck Stimulation of occipital nerves may be offered to patients with chronic migraine headache when conservative treatments have failed. The average effect size for relief of migraine symptoms is modest to moderate. There is insufficient evidence to recommend stimulation of supraorbital and infraorbital nerves for neuropathic craniofacial pain.	I II-3	B C
Upper Extremities PNS may offer modest and short-term pain relief, improved physical function, and better quality of life for chronic hemiplegic shoulder pain. PNS for mononeuropathies of the upper extremity may be offered following a positive diagnostic ultrasound-guided nerve block of the targeted nerve and is associated with modest to moderate pain relief.	I II-2	B B
Low Back/Trunk Subcutaneous peripheral field stimulation and optimal medication management may offer moderate improvement in pain intensity for failed back surgery compared to optimal medication management alone. There is evidence that PNS of lumbar medial branch nerves may improve pain intensity, physical function, and pain interference in patients with axial, mechanical low back pain. There is limited evidence that PNS may alleviate pain in neuropathic pain syndrome involving the trunk and back including radiculopathy and post-herpetic neuralgia.	I II-2 III	B B C
Lower Extremities PNS may be considered for lower extremity neuropathic pain following failure of conservative treatment options and is associated with modest pain relief. PNS may be considered for lower extremity post-amputation pain following failure of conservative treatment options and is associated with modest to moderate pain relief.	I I	B B
Other Considerations As a less-invasive modality compared to SCS therapy, PNS may be offered to patients with CRPS Type I or Type II, and may be associated with modest improvement in pain intensity and functional outcomes. However, high-quality evidence is limited and other neuromodulation interventions such as dorsal root ganglion SCS are recommended for CRPS. PNS carries a low-to-intermediate risk for bleeding complications and depends on the proximity of the targeted nerve to critical vessels and invasiveness of PNS implantation.	III III	C I

Jijun Xu, Zhuo Sun, Jiang Wu, Maunak Rana, Joshua Garza, Alyssa C Zhu, Krishnan V Chakravarthy, Alaa Abd-Elseyed, Ellen Rosenquist, Hersimren Basi, Paul Christo, Jianguo Cheng. **Peripheral Nerve Stimulation in Pain Management: A Systematic Review.** Pain Physician. 2021 Mar;24(2):E131-E152.

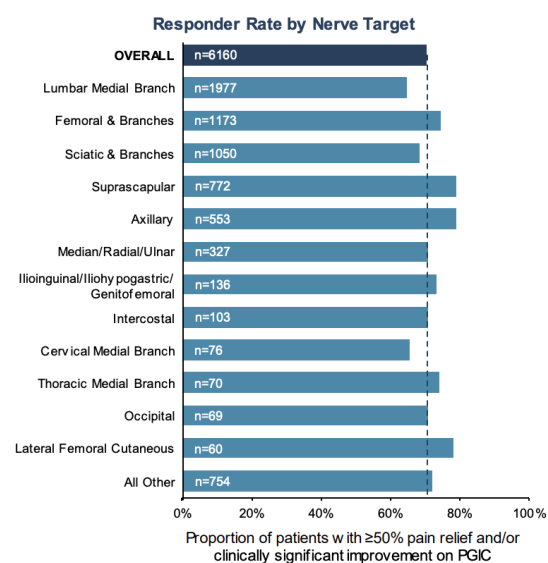
-narrative review of evidence supporting peripheral nerve stimulation for various indications

Marc A Huntoon, Konstantin V Slavin, Jonathan M Hagedorn, Nathan D Crosby, Joseph W Boggs. **A Retrospective Review of Real-world Outcomes Following 60-day Peripheral Nerve Stimulation for the Treatment of Chronic Pain.** Pain Physician. 2023 May;26(3):273-281.

-large review of real-world outcomes using 60 day SPRINT PNS

RESULTS

- Overall, 71% of patients (4348/6160) were responders and pain relief among responders averaged 63%.



-N = 6190, implanted between 2019-2022. 71% overall responder rate, similar across nerve targets in the upper and lower extremities, back/trunk, posterior head/neck (outcomes at end of therapy)

-Limitation: Use of manufacturer's database, retrospective

-For patients whose pain returns soon after 60 day stimulation, this may validate need for permanent system

-While neurostimulation has been historically considered largely for pain of neuropathic origin, PNS has demonstrated both peripheral and central mechanisms of pain relief and has been shown to reduce features of central sensitization regardless of the presence of a neuropathic source. Possible expansion of PNS indication – does not need to be neuropathic pain

-Lead fracture rate during therapy or removal: 8.1%

Table 3. *Medical events.*

	Number of Patients	Number of Events	Percentage of Patients
Overall	369	435	6.0%
Skin irritation	160	163	2.6%
Infection			
Confirmed	7	7	0.11%
Suspected	70	73	1.1%
Painful or uncomfortable stimulation	70	73	1.1%
Change in sensation/ location of stimulation	35	38	0.6%
Pain at lead exit site	18	20	0.3%
Swelling	11	11	0.2%
All other	48	50	0.8%

Important paper prior to development of Reactiv8 (medial branch multifidus stimulation)

Per Kjaer, Tom Bendix, Joan Solgaard Sorensen, Lars Korsholm, and Charlotte Leboeuf-Yde. **Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain?** BMC Med. 2007; 5: 2.

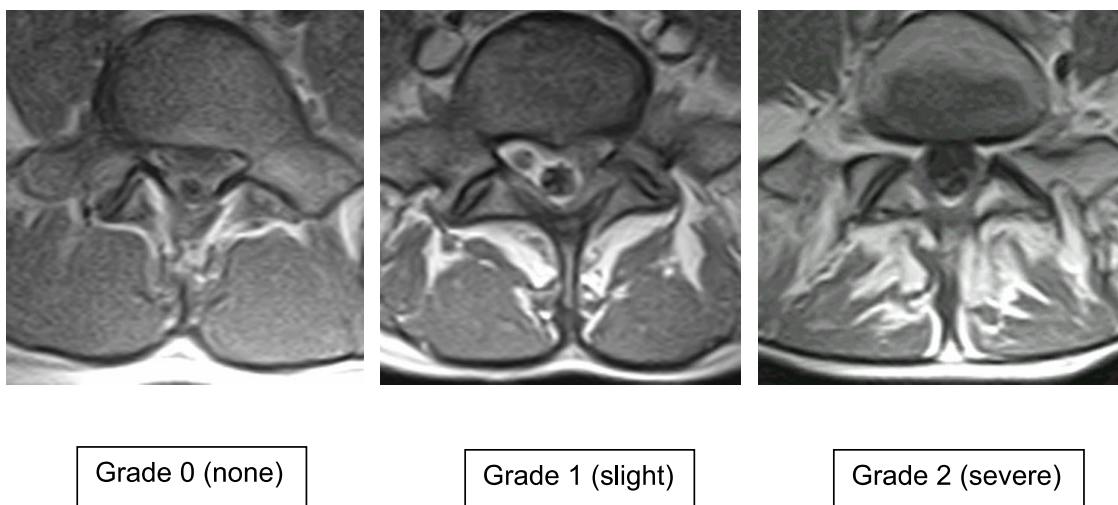


Figure 2

Examples of amounts of fat in the lumbar multifidus muscles as seen on axial T1-weighted magnetic resonance imaging scans. These were rated as grade 0 if normal condition; grade 1 for slight fat infiltration (10–50%), and grade 2 for severe fat infiltration (>50%).

Conclusion: Fat infiltration in the LMM is strongly associated with LBP in adults only. However, it will be necessary to quantify these measurements objectively and to investigate the direction of this link longitudinally in order to determine if the abnormal muscle is the cause of LBP or *vice versa*.

-long term (2 year outcomes) for multifidus stimulation trial

Christopher Gilligan MD, Willem Volschenk MD, Marc Russo MD, Matthew Green MD, Christopher Gilmore MD, Vivek Mehta MD, Kristiaan Deckers MD, Kris De Smedt MD, Usman Latif MD, MBA, Peter Georgius MD, Jonathan Gentile MD, Bruce Mitchell MD, Meredith Langhorst MD, Frank Huyg

en MD, PhD, Ganesan Baranidharan MD, Vikas Patel MD, Eugene Mironer MD, Edgar Ross MD, Alexios Carayannopoulos DO, MPH, Salim Hayek MD, PhD, Sam Eldabe MD. **Long-Term Outcomes of Restorative Neurostimulation in Patients With Refractory Chronic Low Back Pain Secondary to Multifidus Dysfunction: Two-Year Results of the ReActiv8-B Pivotal Trial.** Neuromodulation: Technology at the Neural Interface. Volume 26, Issue 1, January 2023, Pages 87-97.

Table 1. Baseline Characteristics of the Study Population at Baseline.

Characteristic	Participants Combined group (N = 204) Mean $\pm$ SD or n/N (%)
Age (y)	47 $\pm$ 9
Female sex	110/204 (54)
Body mass index (BMI)*	28 $\pm$ 4
Pain duration from onset of the first occurrence (y)	14.2 $\pm$ 10.6
Percent of days with low back pain in the past year	97 $\pm$ 8
Leg pain associated with back pain	53/204 (26)
Previous medial branch rhizotomy	25/204 (12)
Months from most recent rhizotomy	44.4 $\pm$ 74.7
Previous injection procedure	99/204 (49)
Number of previous physical therapy sessions	31 $\pm$ 52
Medications for low back pain	
At least one medication for low back pain	162/204 (79)
NSAIDs	98/204 (48)
Opioid-analgesics	76/204 (37)
Simple analgesics	42/204 (21)
Muscle relaxants	16/204 (8)
Anticonvulsants	18/204 (9)
Other ($\leq 5\%$)	24/204 (12)
VAS score for low back pain [†]	7.3 $\pm$ 0.7
ODI score [‡]	39 $\pm$ 10
EQ-5D-5L index [§]	0.585 $\pm$ 0.174

-Key efficacy outcomes improved progressively over time

-At 2 years, mean LBP VAS improved by 4.8, with 72% of participants with at least 50% reduction in VAS, with 67% of participants with resolution of CLBP (<2.5 VAS), ODI decreased by 21.4 (started at 39 or marginally severe)

-60% of those on opioids at baseline and completed 2 year follow-up either discontinued or reduced opioid usage

-High rate of continued device use into 2nd year (translates to high level of efficacy)

-No direct comparison with other comprehensive care

Systematic Review of peripheral nerve stimulation mechanism of action: variety of nerve targets, modes of stimulation, human and animal studies

Table 1 Studies reporting mechanism of action of peripheral nerve stimulation

Study/year	Subject type	Study type	Location of PNS	Mechanism of action
Ahmed et al. 2018 [13]	Human	Retrospective observational (n=7)	Occipital nerve field in the C2 dermatome	PET scan shows activation of the dorsal lateral prefrontal cortex, and descending pain pathways, specifically the bilateral anterior cingulate cortex and parahippocampal area; EEG evidence of increased cortical activity leading to descending inhibition of pain
Bhadra et al. 2018 [14]	Animal	Prospective observational (n=25)	Sciatic nerve	Duration of kilohertz (kHz) frequency stimulation (10 kHz and above) may significantly affect conduction recovery times. Without continuous application, high-frequency stimulation may lead to carry-over block effects to deliver continuous conduction blockade in peripheral nerves.
Ceccanti et al. 2018 [15]	Human	Prospective observational (n=49)	Median nerve	Increase in MEP amplitude, NMDA-mediated enhanced facilitatory plasticity
Meyer-Frießem et al. 2018 [16]	Human	Retrospective observational (n=13)	Femoral, ulnar, median, radial nerves	Global anti-hyperalgesic effects, endogenous pain inhibition, modulation of central circuits including sensitization (hyperalgesia, allodynia, impaired endogenous analgesia)
Sun et al. 2018 [17]	Animal	Prospective observational (n=254)	Sciatic nerve	Alleviation of bone cancer allodynia and hyperalgesia via upregulation of the Arc protein and decrease of GluA1 transcription in the dorsal horn
Yecies et al. 2018 [18]	Animal	Retrospective observational (n=11)	Pudendal and tibial nerves	Reduction of nerve firing frequency induced by bladder distention which was unaffected with naloxone administration, convergence of inhibitory input on bladder-related interneurons in laminae V–VII of the S2 spinal cord
Bandeira et al. 2019 [19]	Human	Sham-controlled RCT (n=15)	Accessory nerve	Promotion of cortical activation of pain processing cortical areas in the sensorimotor cortex and the dorsolateral prefrontal cortex
Beauchene et al. 2019 [20]	Animal	Case series (n=4)	Sciatic nerve	Response in dorsal horn can be affected and predicted with PNS and can be based on local field potentials and wide dynamic range recordings
Finch and Drummond 2020 [21]	Human	Case series (n=4)	Occipital, supraorbital, and infraorbital nerves	High-frequency biphasic PNS (10 kHz) may cause rapid reversible conduction block, reduce ectopic discharge in neuronal activity, and shift the resting potential of damaged nerves toward hyperpolarization thus making those nerves resistant to depolarization and spontaneous aberrant activity. Frequencies >10 kHz lead to higher rise in conduction block threshold. High-frequency PNS causes outward potassium flow to oppose inward sodium flow, thus making the neuron unexcitable and unable to propagate an action potential.
Franz and Yoo 2020 [22]	Animal	Prospective observational (n=33)	Saphenous nerve	Saphenous nerve PNS leads to bladder-inhibitory responses in a frequency-dependent manner. The hypogastric nerve does not mediate this inhibition.
Garcia-Magro et al. 2020 [23]	Animal	Sham-controlled prospective trial (n=43)	Greater occipital and trigeminal nerves	Greater occipital nerve stimulation facilitates light facial mechanical stimuli in controls, whereas it inhibits the stimuli in animals with infraorbital chronic constriction injury. This is mediated by pathways containing GABAergic and glycinergic mechanisms
Liao 2020 [24]	Animal	Sham-controlled prospective trial (n=40)	Sciatic nerve	Sciatic nerve PNS at low (2 Hz) to medium frequency (20 Hz) may ameliorate inflammation locally and increase recovery through regeneration of nerves, acceleration of regrowth, and improvement of electrophysiological function in taxol-induced nerve injury
Luckey et al. 2020 [25]	Human	Double-blind, sham-controlled RCT (n=30)	Greater occipital nerve	Enhancement of memory by activation of locus-ceruleus-noradrenaline pathways, changes in α -amylase (biomarker for noradrenaline)
Mohapatra et al. 2020 [26]	Animal	Retrospective observational (n=6)	Pudendal nerve	Abnormal afferent activity and prolonged peripheral stimulation could produce central inhibition, which also underlies non-obstructive urinary retention
Tu et al. 2020 [27]	Animal	Sham-controlled prospective trial (n=64)	Sacral splanchnic nerve	Sacral nerve PNS improves colonic inflammation. Sacral nerve PNS increased acetylcholine and anti-inflammatory cytokines such as IL-10; it decreased myeloperoxidase and pro-inflammatory cytokines including IL-2, IL-17A, and TNF- α in the colon

Abbreviations: PET, positron emission tomography; EEG, electroencephalography; MEP, motor evoked potential; Hz, hertz; IL, interleukin; TNF, tumor necrosis factor

Summary of peripheral and central mechanisms (brain and spinal cord)

Periphery

- Reduce ectopic discharges
- Reduction of nerve firing frequency induced by nociceptive input
- Shift resting potential of damaged nerves toward hyperpolarization
- High frequency stimulation affects conduction recovery times, causing continuous conduction blockade in peripheral nerves
- Low frequency stimulation may ameliorate inflammation locally, accelerate regeneration and improve electrophysiologic function
- Increased acetylcholine and anti-inflammatory cytokines (IL-10), decrease myeloperoxidase and pro-inflammatory cytokines (IL-2, IL-17a, TNF- α)

Spinal Cord

- NMDA-mediated enhanced plasticity
- Modulation of central circuits causing anti-hyperalgesic effects, endogenous pain inhibition
- Upregulation of Arc protein, decrease of GluA1 transcription in dorsal horn
- Wide dynamic range neuron activation
- GABAergic and glycinergic mechanisms of inhibition

Brain

- activation of dorsal lateral prefrontal cortex, anterior cingulate cortex and parahippocampal area, leading to descending inhibition of pain
- Cortical activation in the sensorimotor cortex and dorsolateral prefrontal cortex
- Activation of locus ceruleus-noradrenaline pathways

Not PNS, but worthwhile to be aware of this paper on review of pharmacotherapy for neuropathic pain

Finnerup et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurology. 2015 Feb;14(2):162-73.

Table 2

Recommendations for individual drugs or drug classes based on the GRADE classification and for first-, second-, and third-line drugs for neuropathic pain. Drugs pertaining to the same drug class are presented in alphabetical order.

GRADE classification	Drugs	Daily dosages and dose regime	Recommendations
STRONG FOR	Gabapentin Gabapentin ER/enacarbil Pregabalin SNRIs duloxetine/venlafaxine TCAs	1200–3600 mg TID 1200–3600 mg BID 300–600 mg BID 60–120 mg QD (duloxetine); 150–225 mg QD (venlafaxine ER) 25–150 mg qd or BID	First-line First-line First-line First-line First-line ¹
WEAK FOR	Capsaicin 8% patches Lidocaine patches Tramadol BTX- A (SC) Strong opioids	1–4 patches to the painful area for 30–60 min every 3 months 1–3 patches to the painful area for up to 12 hours 200–400 mg BID (tramadol ER) or TID 50–200 units to the painful area every 3 months Individual titration	Second-line (PNP) ² Second-line (PNP) Second-line Third-line ; specialist use (PNP) Third line ³
INCONCLUSIVE	Combination therapy Capsaicin cream Carbamazepine Clonidine topical Lacosamide Lamotrigine NMDA antagonists Oxcarbazepine SSRI antidepressants Tapentadol Topiramate Zonisamide		
WEAK AGAINST	Cannabinoids Valproate		
STRONG AGAINST	Levetiracetam Mexiletine		

Active drug class	Number of comparisons ¹	Participants ²	Pain relief		NNT	Susceptibility to bias ³
			Active	Placebo		
TCAs	15	948	217/473	85/475	3.57 (3.0–4.4)	1973
SNRIs	10	2541	676/1559	278/982	6.40 (5.2–8.4)	1826
Pregabalin	25	5940	1359/3530	578/2410	7.71 (6.5–9.4)	2534
Gabapentin ⁴	14	3503	719/2073	291/1430	7.16 (5.9–9.1)	1879
Tramadol	6	741	176/380	96/361	4.73 (3.6–6.7)	982
Strong opioids	7	838	211/426	108/412	4.26 (3.4–5.8)	1326
Capsaicin 8%	6	2073	466/1299	212/774	10.64 (7.4–19)	70*
BTX-A	4	137	42/70	4/67	1.85 (1.5–2.4)	678

-50% pain improvement in pain as primary measure

-best NNT is between 3-4 (TCA's, opioids)

-NNT for other first line neuropathic medications: 6-7 for gabapentinoids, SNRIs

Worthwhile to be aware of this algorithm of treatment of neuropathic pain (for PCPs) – neuromodulation is 4th line according to these guidelines

Bates et al. A comprehensive Algorithm for Management of Neuropathic Pain. Pain Med. 2019 Jun; 20(Suppl 1): S2–S12.

- The algorithm provides a comprehensive treatment pathway from assessment to first- line through sixth-line therapies for primary care physicians.

- Neuropathic pain assessment: thorough neurologic exam, Diagnostic testing: electroneuromyography (EMG) and nerve stimulation study (NCS), quantitative sensory testing (QST), referral to a pain physician for diagnostic nerve blocks to narrow down pain source, magnetic resonance imaging (MRI) to identify central lesions, skin biopsy for small fiber neuropathy

- No single sign or physical finding is diagnostic of neuropathic pain. Nearly 50% of patients with musculoskeletal pain use words that are commonly associated with neuropathic pain (e.g., “shooting”, burning”, and “tingling”) to describe their pain

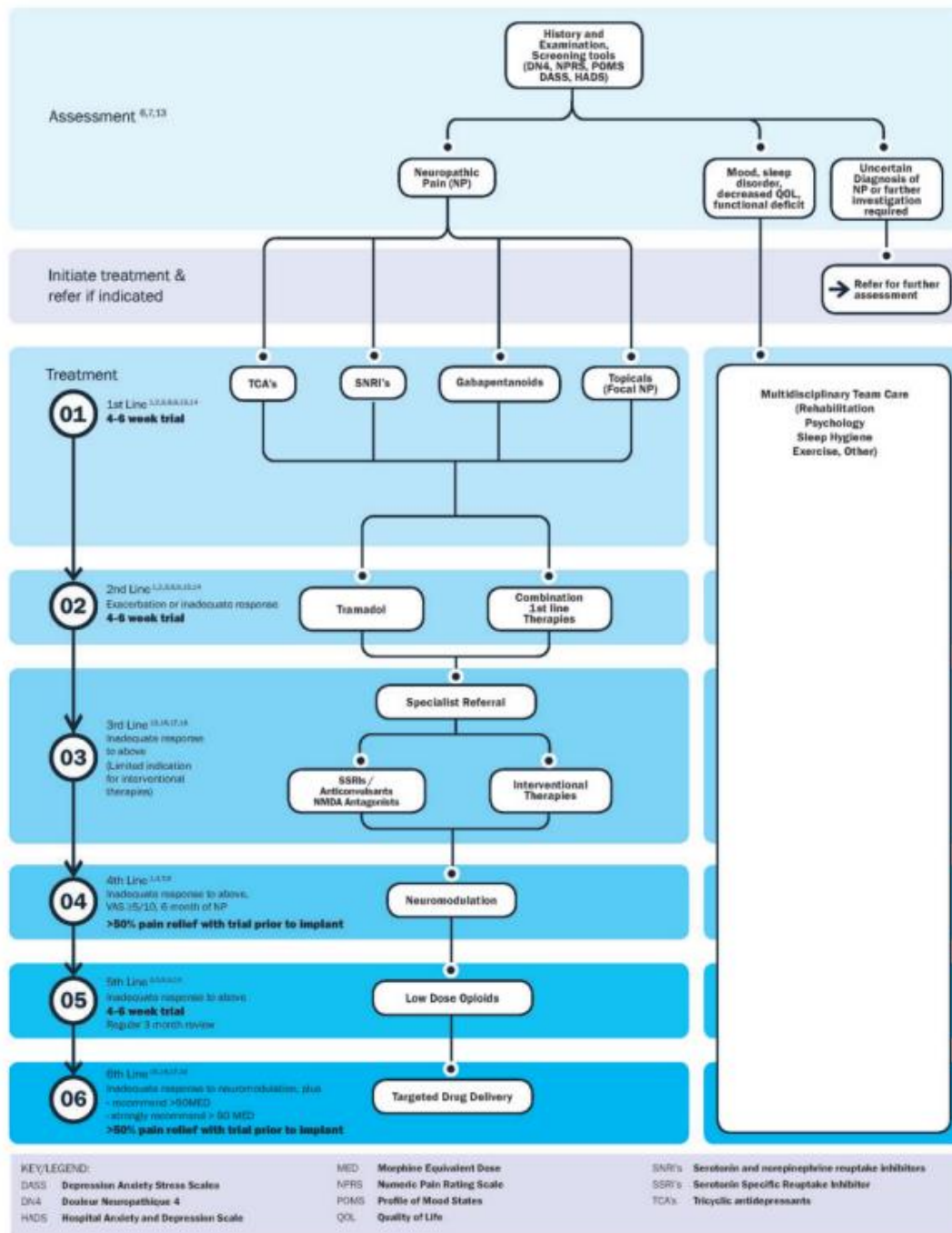


Figure 1. Comprehensive algorithm for the management of neuropathic pain.

Worthwhile to be aware of this paper in Anesthesiology – use of SPRINT temporary PNS for perioperative pain

Brian M Ilfeld, Anthony Plunkett, Alice M Vijjeswarapu, Robert Hackworth, Sandeep Dhanjal, Alparslan Turan, Steven P Cohen, James C Eisenach, Scott Griffith, Steven Hanling, Daniel I Sessler, Edward J Mascha, Dongsheng Yang, Joseph W Boggs, Amorn Wongsarnpigoon, Harold Gelfand; PAINfRE

Investigators. Percutaneous Peripheral Nerve Stimulation (Neuromodulation) for Postoperative Pain: A Randomized, Sham-controlled Pilot Study. Anesthesiology. 2021 Jul 1;135(1):95-110.

-Pilot study, N = 32. Percutaneous lead placed under ultrasound guidance pre-operatively at sciatic nerve for foot/ankle surgery, femoral nerve for ACL repair, brachial plexus for rotator cuff repair. 14 days of nerve stimulation vs sham post-operatively

-Primary outcomes were cumulative oral opioid consumption (morphine equivalent) and mean value of average NRS 0-10 pain scores, during first 7 post-op days

-Median opioid consumption 5 mg in those receiving active stimulation vs 48mg in those receiving sham stimulation during the first 7 days

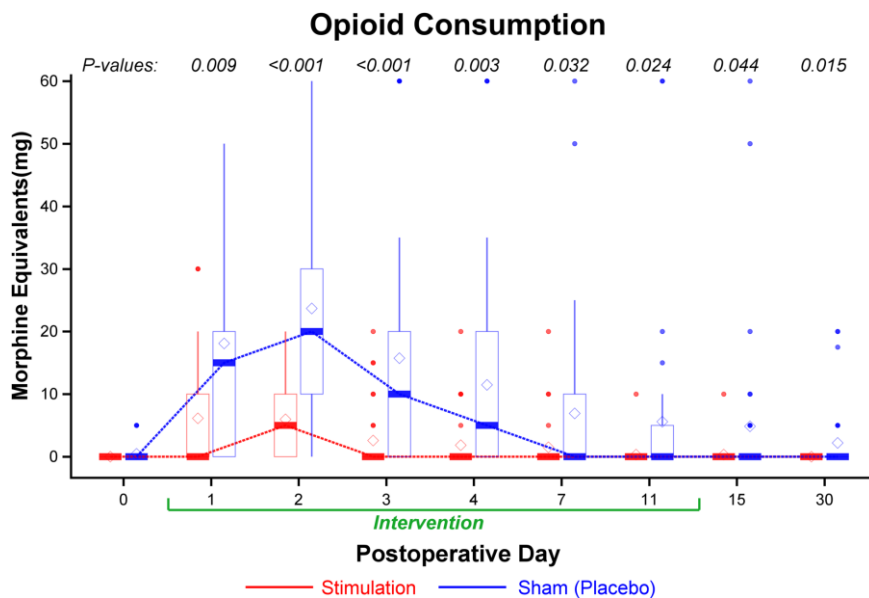
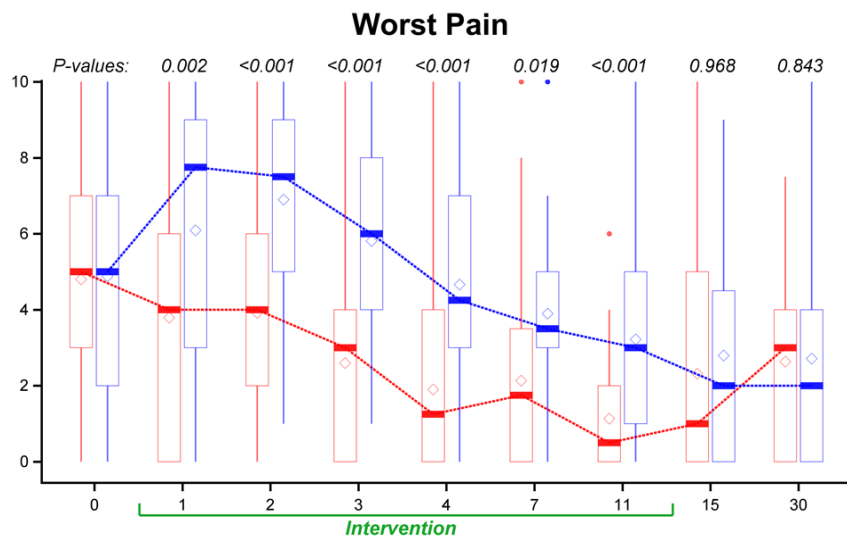
-Mean pain intensity was 1.1 +/- 1.1 in those receiving active stimulation vs 3.1 +/- 1.7 in those receiving sham stimulation during the first 7 days

Advantages:

- avoiding systemic side effects of opioid use (nausea, sedation, respiratory depression),
- avoiding proprioceptive/sensory/motor deficits that may occur with continuous perineural catheter, improving ability to participate in rehabilitation

Disadvantages:

- increased preoperative insertion time
- lack of surgical anesthesia that is attained with local anesthetic nerve block



Historical Studies:

Both of these studies were the initial descriptions of peripheral nerve stimulation, in 1967

C H Shelden, R H Pudenz, J Doyle. **Electrical control of facial pain.** *Am J Surg.* 1967 Aug;114(2):209-12.

- 3 patients treated with implanted peripheral nerve stimulators for trigeminal neuralgia

- electrodes (1¼ by 3/8 inches) were surgically implanted in the substance of the mandibular division of the trigeminal nerve, attached to the bony margins of a temporal craniotomy, distal to the trigeminal ganglion, proximal to the foramen ovale

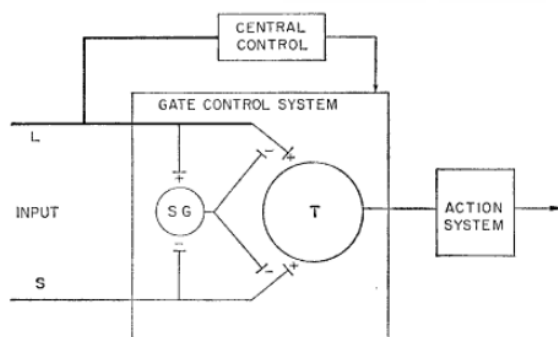
-“We had no idea how often the nerve should be actively depolarized; hence a daily schedule of activation was carried out...each time the power source was applied, numbness developed in the mandibular division lasting several minutes after the power was discontinued”

9“It seems apparent that the initial goal was achieved but, as time passes, we become less certain as to the specific factors responsible for pain relief...It seems that this work is likely to have far reaching impact upon medicine in the future”

P D Wall, W H Sweet. **Temporary abolition of pain in man. Science.** 1967 Jan 6;155(3758):108-9.

-8 patients treated for various neuropathic pain conditions (peripheral nerve injury, diabetic neuropathy, cancer related pain, trigeminal neuralgia), included temporary and permanent stimulators

-“therapeutic implications are at present equivocal because two of the patients, who were stimulated many times per day, reported a decreased effect on their pain after several months”



Nielson KD, Watts C, Clark WK. **Peripheral nerve injury from implantation of chronic stimulating electrodes for pain control.** Surg Neurol. 1976 Jan;5(1):51-3.

--early recognition of various drawbacks of PNS

-“Complications of implantable stimulating electrodes for pain control are becoming recognized. Potential issues are suboptimal outcomes, poor long-term success, complications of nerve injury, fibrosis, lead migration.”

Long DM. **Uses of percutaneous electrical stimulation of the nervous system.** Med Prog Technol. 1977 Jul 15;5(1):47-50

-First mention of a trial period : “Temporary percutaneous electrical stimulation of peripheral nerves and the spinal cord is a valuable screening technique. This approach will provide a much higher success rate for identifying those patients suitable for a permanently implanted stimulation system.”

-“The system appears to be the treatment of choice for chronic, intractable pain caused by nerve injury.”

Many modern day concepts describes in this paper (central mechanism of action, intra-procedure testing, pre-PNS nerve block, pre-PNS psychological evaluation)

J L Goldner, B S Nashold Jr, P C Hendrix. **Peripheral nerve electrical stimulation.** Clin Orthop Relat Res 1982 Mar;(163):33-41.

-40 patients were treated with a follow up period 2-10 years, representing a random sampling of several hundred patients with upper or lower extremity pain associated with peripheral nerve injury. Nerve lesion mechanisms included direct nerve trauma, chemical injection, amputation neuroma, phantom pain, nerve ischemia.

-The earlier electrode implants consisted of a cuff wrapped around the nerve. This sometimes caused constriction and fibrosis of the nerve. The authors used multiple single electrodes sutured to the peripheral nerve epineurium

-Early description of intra-procedure testing: “The patient must cooperate in preparing a motor and sensory nerve map. Accurate electrode placement depends on the patient’s response as to whether pain is alleviated or aggravated by stimulation”

-early description of central mechanisms: “In contradistinction to the antidromic inhibitory theory is a more plausible mechanism concerned with the periventricular gray areas known to inhibit pain. Cells in the (dorsal horn) have large receptive fields that can receive input from widespread areas of the body and can project to all levels of the spinal cord and brain.”

-early mention of psychological evaluation “Prior to peripheral nerve microimplant, history of onset and aggravation of pain, mechanism of injury, as well as social, personal, occupational and emotional history should be assessed. Clinical, psychological, and psychiatric assessment of the patient should be made. The prognosis is affected by a pattern of hysteria, hypochondriasis, or depression.”

-“Nerve block assessment determines if the patient has relief of pain while afferent stimuli are eliminated. This test is helpful in determining prognosis of microelectrode placement on a nerve.”

-“It is our impression that if the patient meets the requirements described, a reasonable amount of pain relief will be obtained by use of the peripheral nerve implant system. Meticulous techniques in applying the implant system, and a mechanical system that accepts stress are essential.”

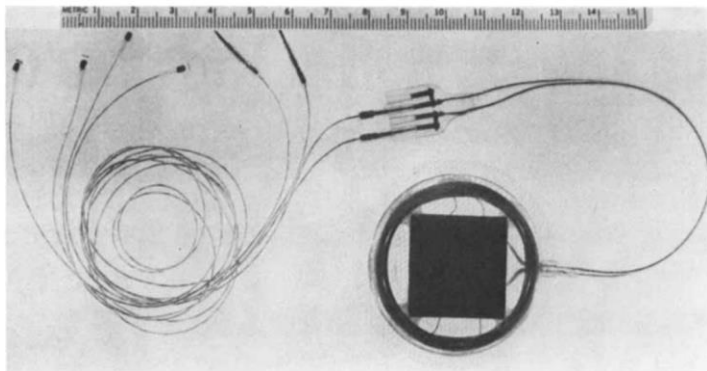
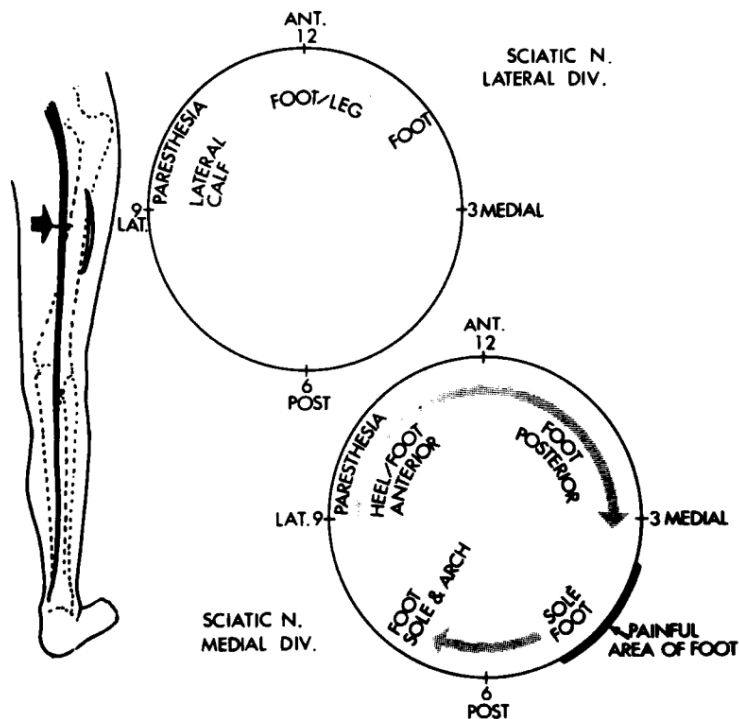


FIG. 1. The multiple electrodes for stimulation are attached to the coiled wire. The interconnecting wires are long enough to allow motion of the extremity and tension on the electrodes without loosening. The implanted radiofrequency receiver is round with an entry zone for the wires and is subcutaneous. An antenna is placed directly on the skin over the receiver and attached to a battery supplied power source. Bipolar platinum electrodes connect the power pack to the antenna which in turn rests over the radiofrequency receiver.

FIG. 3. Nerve map prepared from electrical stimulation of the sciatic nerve while patient was awake. The topography is designated on the map, and the patient's response is recorded after stimulating the lateral division and then the medial division. The area that corresponds to the painful area of the foot is the point on which an electrode is sutured. Electrodes are placed on the sensory fascicles and the motor fibers are avoided. The upper extremity map is prepared in the same way.



R L Weiner, K L Reed. **Peripheral neurostimulation for control of intractable occipital neuralgia.** Neuromodulation 1999 Jul;2(3):217-21.

-one of the earlier descriptions of percutaneous technique using wire electrodes, most similar to today

Excellent description of the difficulties of doing an RCT for PNS

R J Mobbs, S Nair, P Blum. **Peripheral nerve stimulation for the treatment of chronic pain.** 2007 Mar;14(3):216-21; discussion 222-3.

- Retrospective review: 38 total patients with mean symptoms duration 58 months. Implanted median, ulnar, brachial plexus, radial, suprascapular, common peroneal, sural, posterior tibial nerves.

- Largest study at time of publication for implantable peripheral nerve stimulator for chronic pain; 7 studies up to this point had more than 20 patients

- 15% required explant for infection or poor pain relief after initial good result

- “The authors accept that the results are retrospective and not based on a randomized control trial (RCT). Although an RCT of peripheral nerve stimulation would be optimal to evaluate its effectiveness as compared with best medical therapy, this would be impracticable.”

- not feasible as these patients are referred because they have already failed the “best medical therapy” option
- a study that included a “sham” operation as a control group would be unethical
- any trial that attempted to “blind” the patient and/or the surgeon would not be possible, stimulation without the sensation of paresthesia would alert both patient and operator of the assigned study group