Spinal cord stimulation for chronic abdominal pain

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Conflict of Interest:

Scientific Advisory Board: Abbott, Nevro, Saluda, SPR Therapeutics, Neuros, Halyard

Consultant: Gimer Medical, Best Doctors

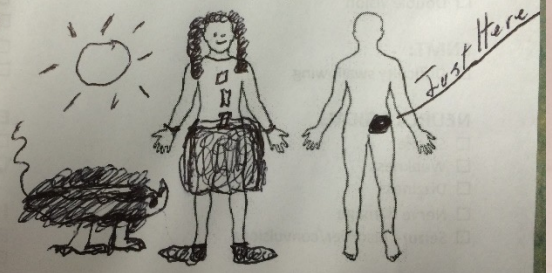
Research: Stimwave, Nevro, Neuros, Halyard, SPR Therapeutics, Boston Scientific, Medtronic, Saluda

Content: treatments for abdominal disorders

- Target population
- Algorithm; other treatment options
- SCS for chronic abdominal pain; basis for therapeutic use
- SCS for chronic abdominal pain: indications, efficacy
- SCS for chronic dysmotility disorders: a first evidence
- Novel SCS modalities and waveforms: useful for chronic abdominal pain?

Sharp	Constant
Stabbing	Occasional
Shooting	Frequent
Stinging	Rare

Shade your painful areas:



9 10 Worst Pain

NO CHANGES: _____

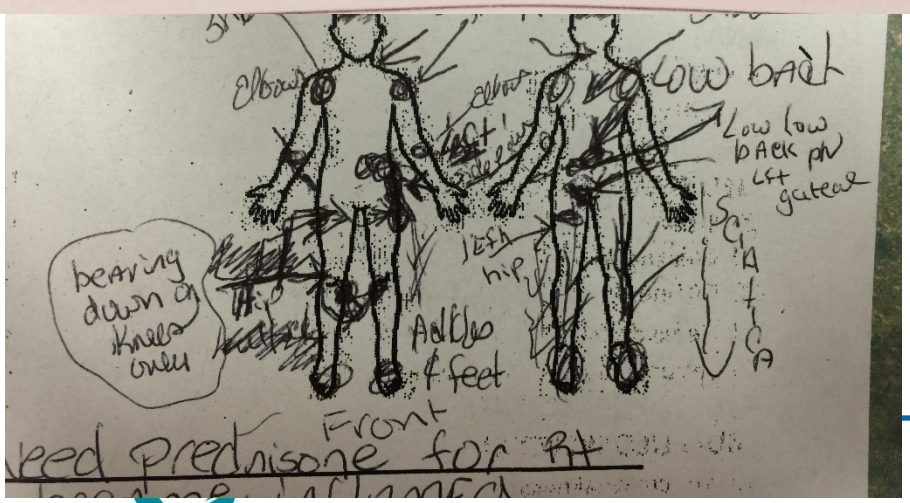
I was born

Was there an inciting event? (Car accident, fall, etc.)

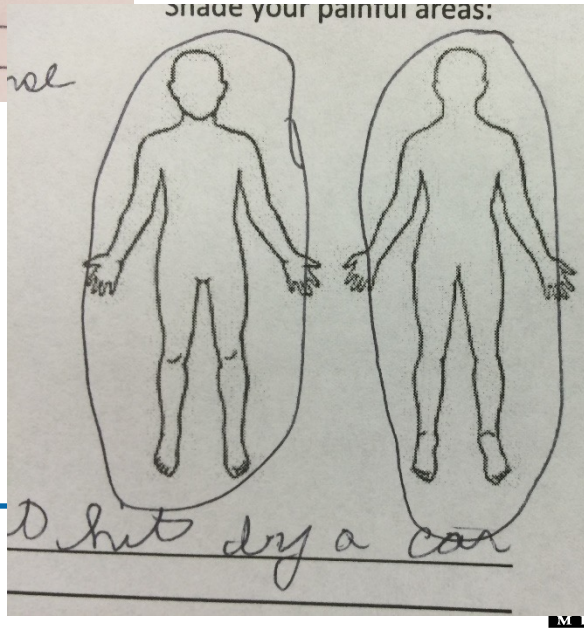
Life

POS/NEG	
1. BZO	Neg
2. BAR	Neg
3. COC	Pos
4. THC	Pos
5. MET	Pos
6. OPI	Pos
7. MTD	Pos
8. TCA	—
9. OXY	Neg
10. BUP	Neg

MDMA - Neg
PCP - Neg
Amp - Neg



Shade your painful areas:



Shit dry a cow

Target population for SCS

Problem

- Approximately 2 million patients in US with severe abdominal pain
- Pain-most prevalent symptom in any GI clinic
- Multitude of imaging studies and surgeries before referred to a chronic pain specialist
- Etiology of some abdominal pains remains elusive
- Impact on the patient's socioeconomic status
- Burden on our healthcare system

- **Russo MW, Wei JT, Thiny MT, Gangarosa LM, Brown A, Ringel Y, Shaheen NJ, Sandler RS. (2004) Digestive and liver diseases statistics. Gastroenterol 126:1448-1453.**
- **Derbyshire SW. (2007) Imaging visceral pain. Curr Pain Headache Rep 11(3):178-182.**

Referred Pain

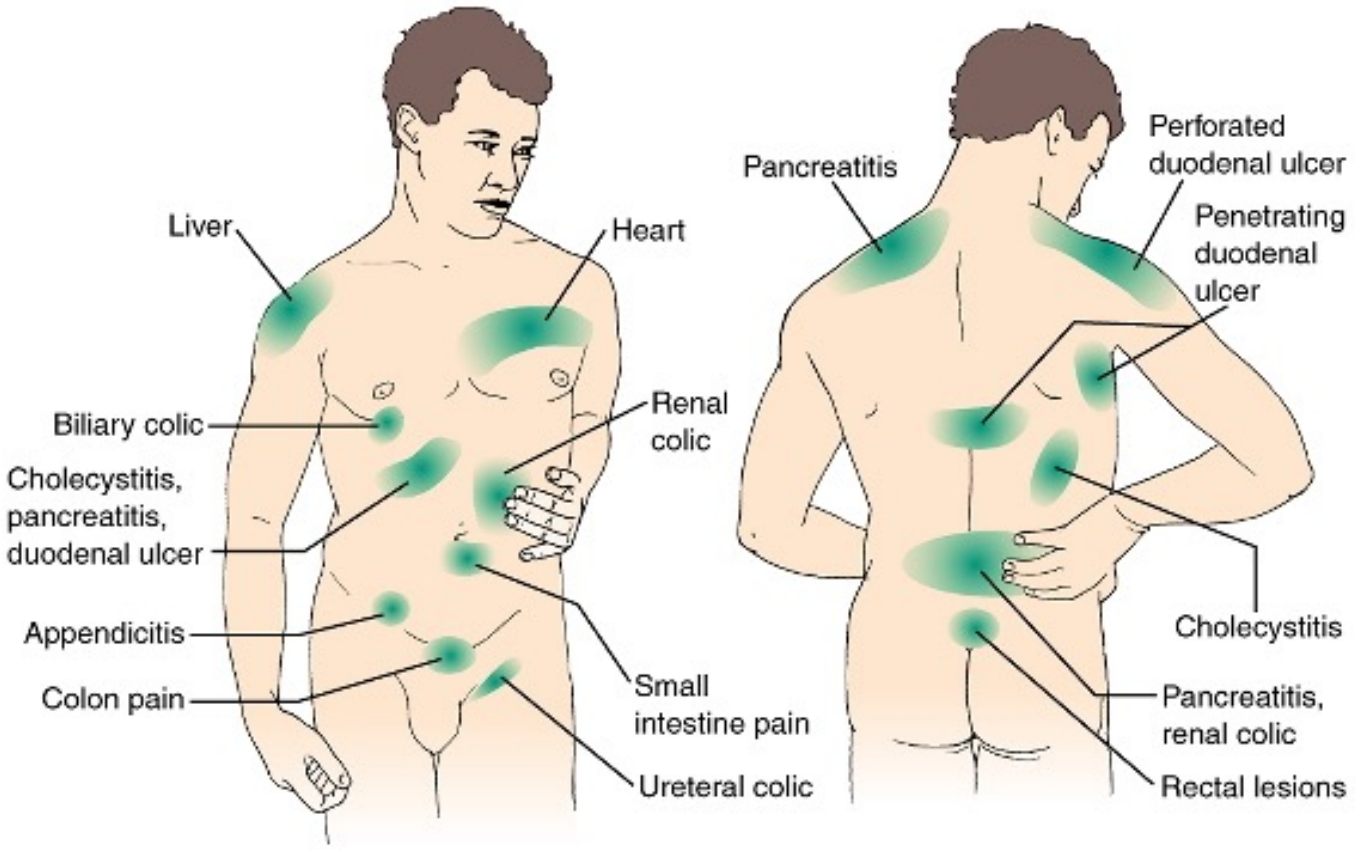
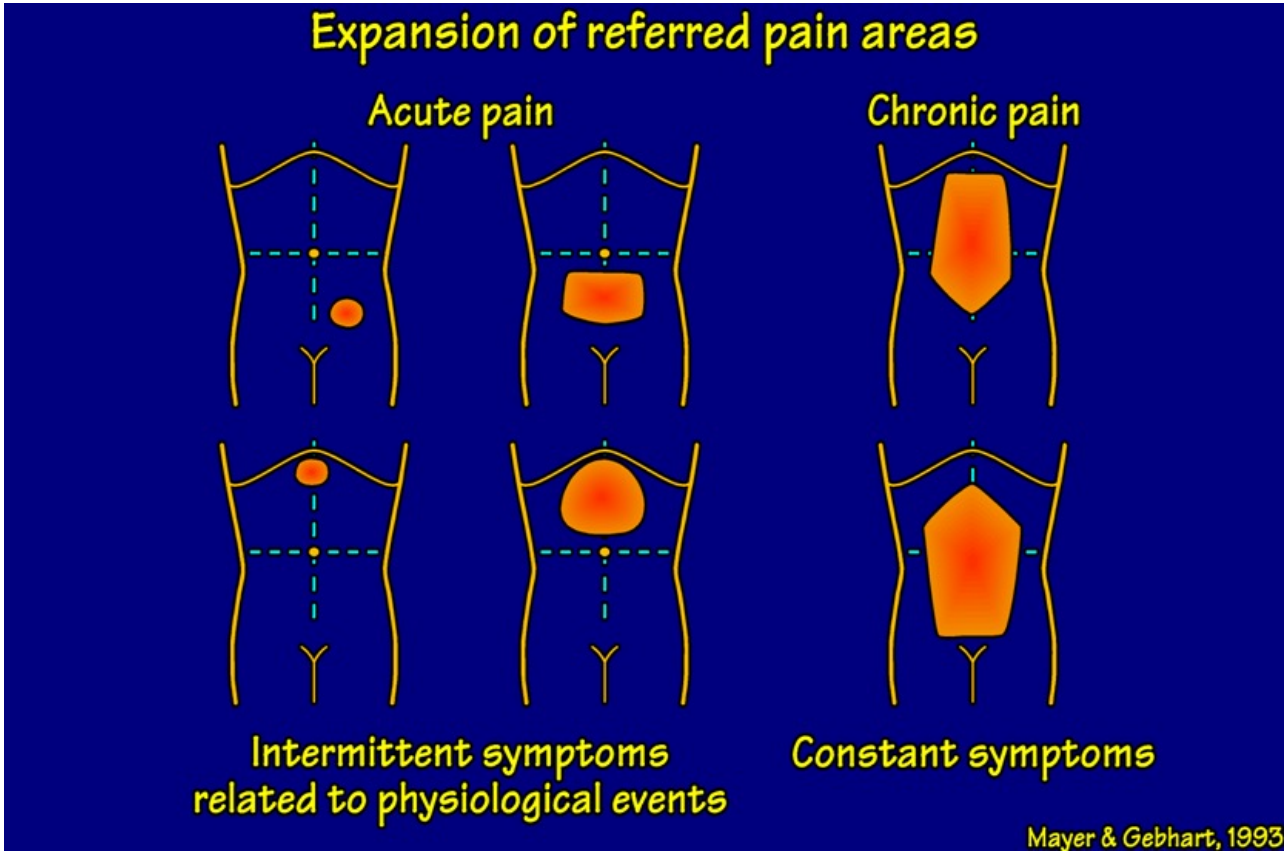


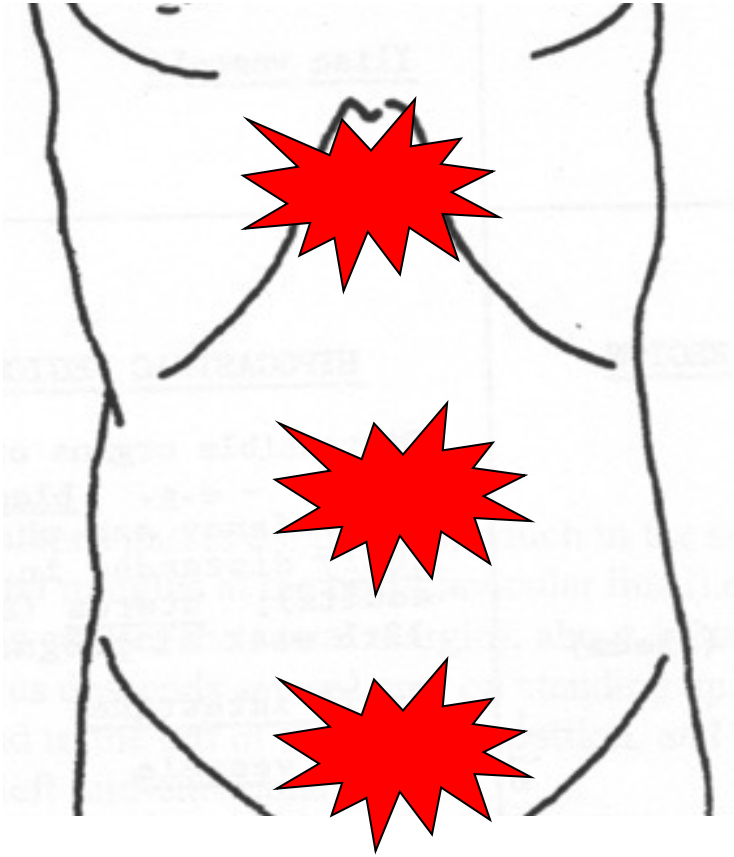
Figure 34-3 Common sites of referred abdominal pain.



Slide: Thanks to Dr. Arendt-Nielsen

History

- Location
  - Upper abdominal
    - Biliary
    - Pancreatic
    - Ulcer
    - Dyspepsia
  - Mid abdominal
    - Crohn's disease
    - Celiac disease
    - Partial intermittent SBO
    - Chronic mesenteric ischemia
  - Lower abdominal
    - IBS
    - Colitis

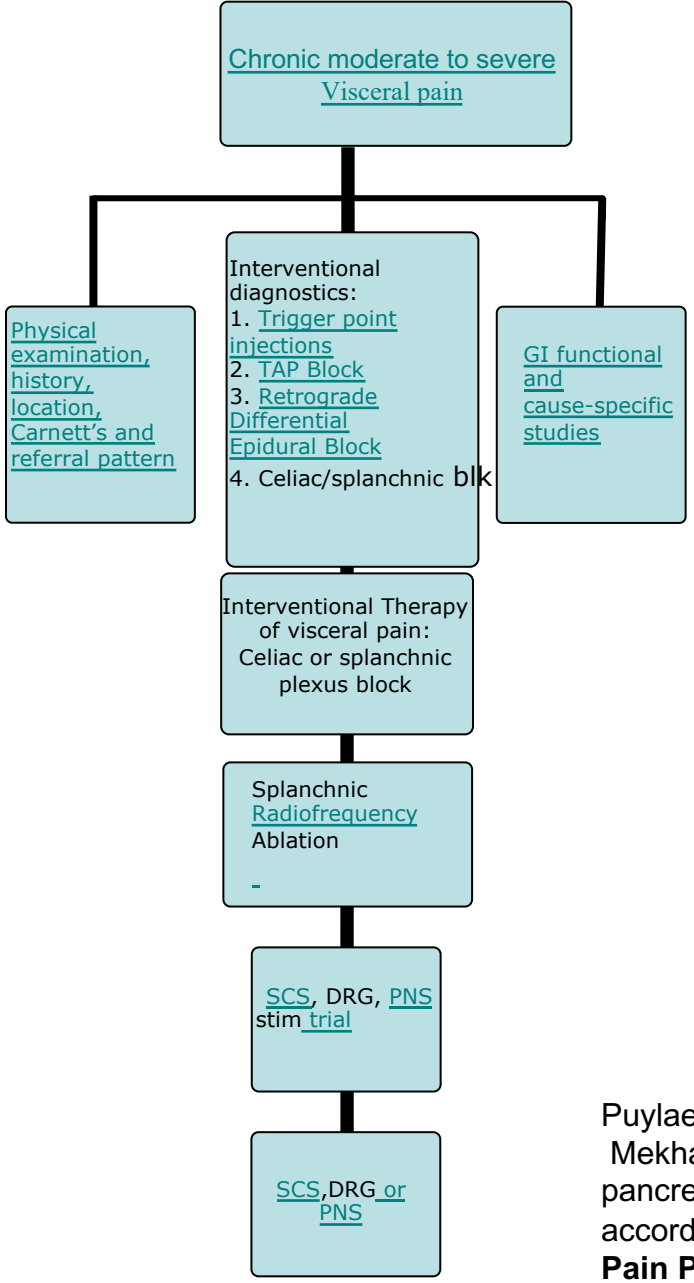


Visceral Pain Syndromes and SCS

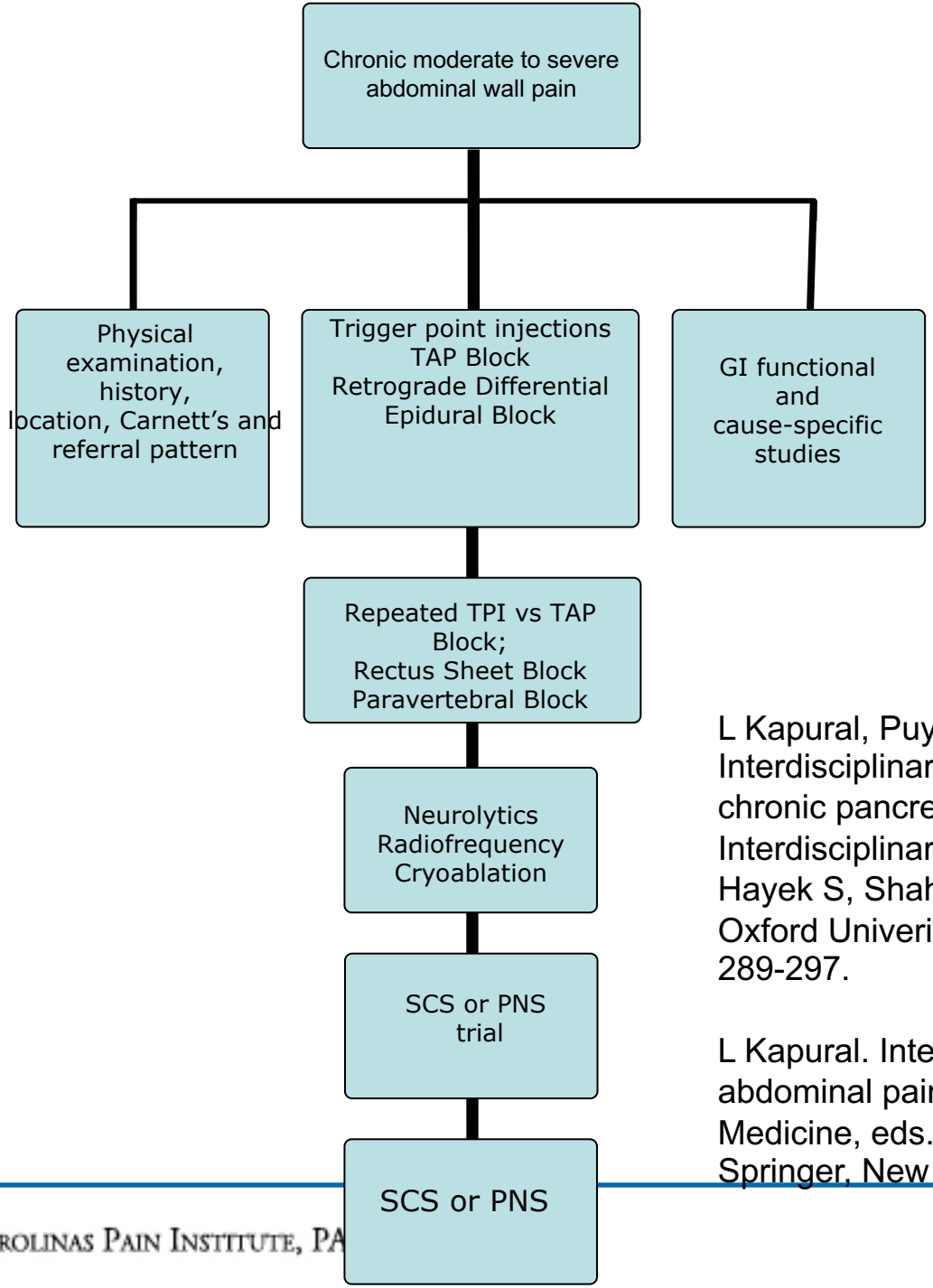
Table 1. Various Causes of Severe Chronic Abdominal Pain Treated With Spinal Cord Stimulation (SCS).

Chronic abdominal pain conditions treated with SCS	Published report/study
Irritable bowel syndrome	Krames and Mousad, 2005 (6)
Mesenteric ischemia	Ceballos et al., 2000 (15); Kapural et al., 2010 (10)
Chronic esophageal dysmotility	Jackson and Simpson, 2004 (16)
Post-traumatic splenectomy	Khan et al., 2005 (7)
Familial Mediterranean fever	Kapur et al., 2006 (17)
Gastroparesis	Tiede et al., 2006 (8); Kapural et al., 2010 (10); Kapural et al., 2010 (11)
Chronic pancreatitis	Khan et al., 2005 (7); Kapural and Rakic, 2007 (9); Kapural et al., 2010 (10); Kapural et al., 2010 (11)
Postsurgical intra-abdominal adhesions	Kapural et al., 2010 (10); Kapural et al., 2010 (11)

Algorithm; other treatment options



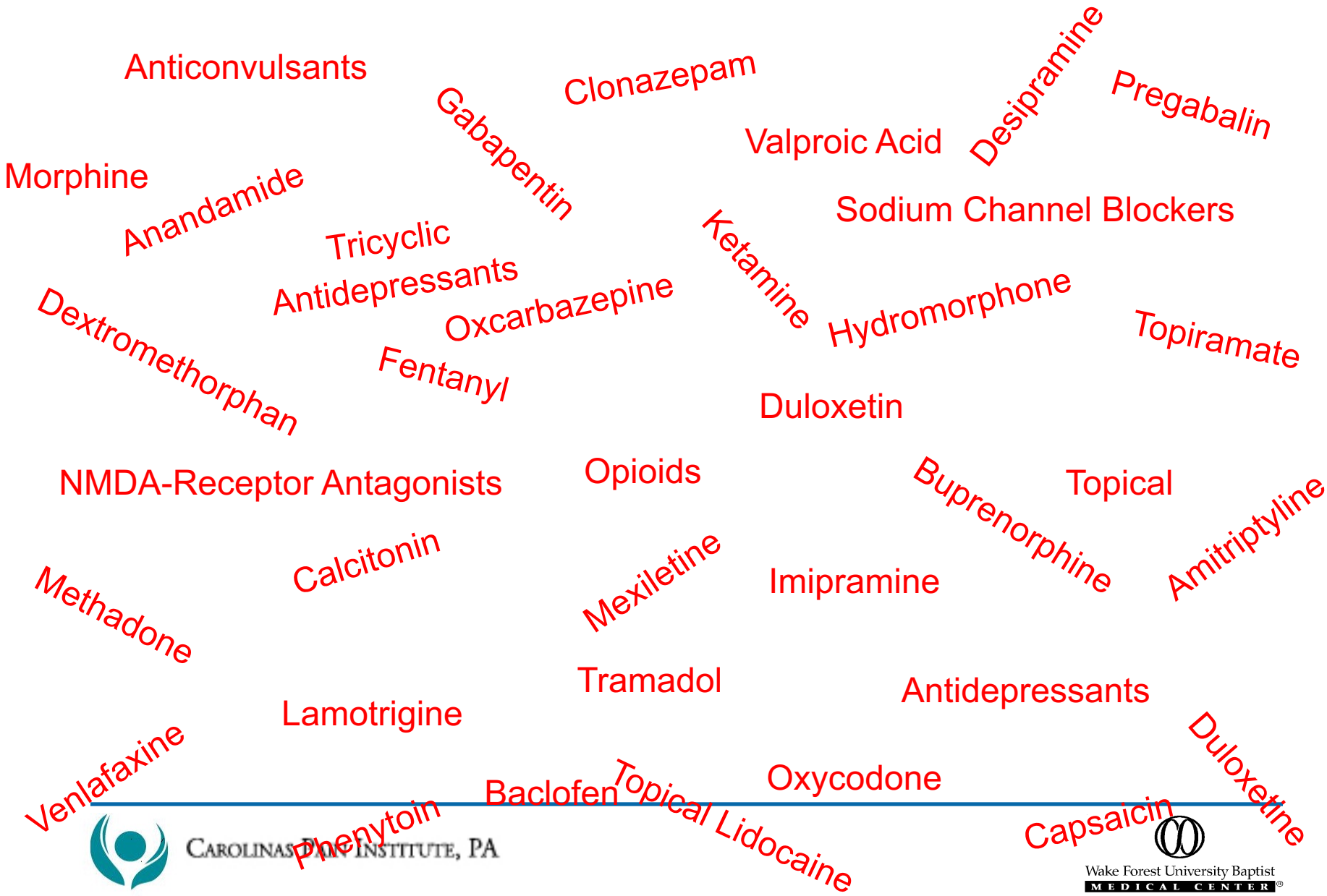
Puylaert,M, Kapural L, van Zundert J, Peek D, Lataster A, Mekhail N, van Kleef M, Keulemans Y. Pain in chronic pancreatitis. Evidence-based Interventional Pain Medicine according to clinical diagnoses.
Pain Practice 2011;11(5): 492-505.



L Kapural, Puyalert M, Walsh M, Sweiss G. Interdisciplinary treatement of the pain from chronic pancreatitis. In Pain Medicine, An Interdisciplinary Case-Based Approach, eds. Hayek S, Shah BJ, Desai MJ, Chelimsky TC, Oxford Univeristy Press, New York,2015, pp 289-297.

L Kapural. Interdisciplinary treatment of chronic abdominal pain. In Fundamentals of Pain Medicine, eds. Cheng J, Rosenquist R., Springer, New York, in press

Pharmacologic treatment

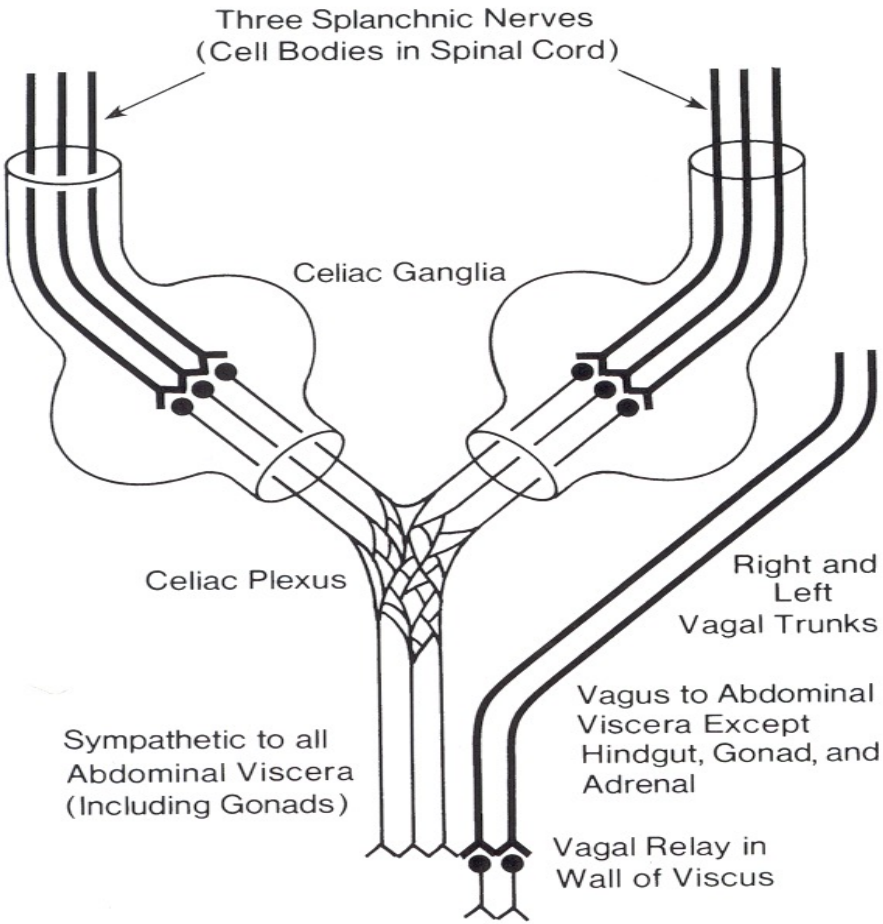


Olesen SS, Bouwense SA, Wilder-Smith OH, van Goor H, Drewes AM. Pregabalin reduces pain in patients with chronic pancreatitis in a randomized, controlled trial. Gastroenterology. 2011;141:536–543.

Olesen SS, Graversen C, Olesen AE, et al. Randomised clinical trial: pregabalin attenuates experimental visceral pa through sub-cortical mechanisms in patients with painful chronic pancreatitis. Aliment Pharmacol Ther. 2011;34:878-887.

Membrane stabilizers for pain control	Starting dose/day	Target dose/day	Side effects
Carbamazepine Tegretol ®	200	600-1200	Sedation, ataxia, diplopia leukopenia, ↓Na^+
Valproate Depakote®	400-500	1000-3000	weight ↑, ↓plt, liver failure
Pregabalin Lyrica ®	75	300-600	weight ↑
Gabapentin Neurontin®	100-300	1800-3600	weight ↑, headache, twitching
Lamotrigine Lamictal®	50	300-500	rash, Stevens-Johnson sdme
Levetiracitam Keppra®	1000	3000	recurring infections
OxcarbazepineTrileptal®	300	600-2400	↓Na^+
Tiagabine Gabitril®	4	32-56	nervousness, flu-like symptoms
TopiramateTopamax®	25-50	200-400	weight ↓, renal calculi
Zonisamide Zonegran®	100	600	weight ↓, renal calculi

Celiac Plexus



- The largest of the SNS great plexus
- Contain visceral afferent and efferent fibers
- Parasympathetic fibers pass through it
- Contain no somatic fibers
- Innervate most of the abdominal viscera
- Three splanchnic nerves - great, lesser and least end up in the celiac ganglion bilaterally

Splanchnic nerves

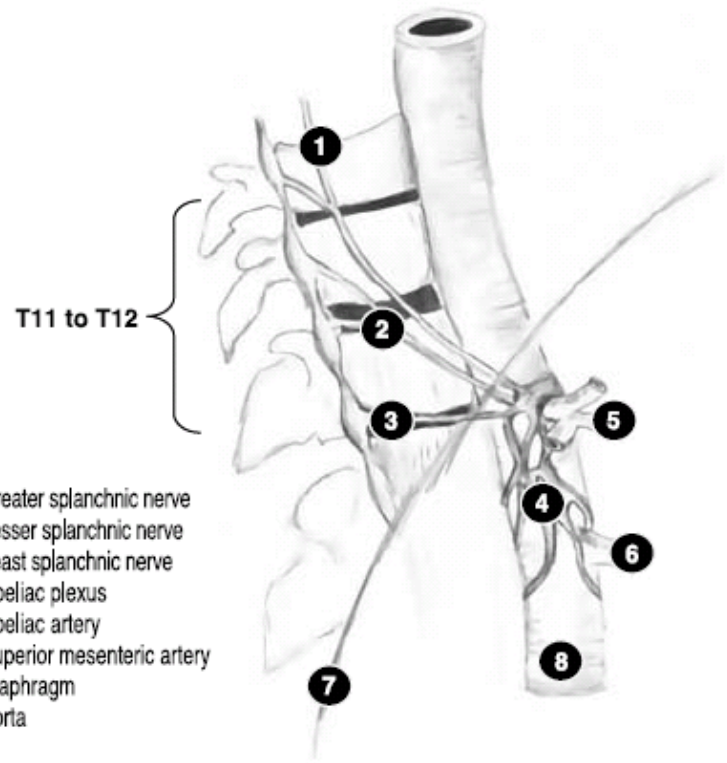
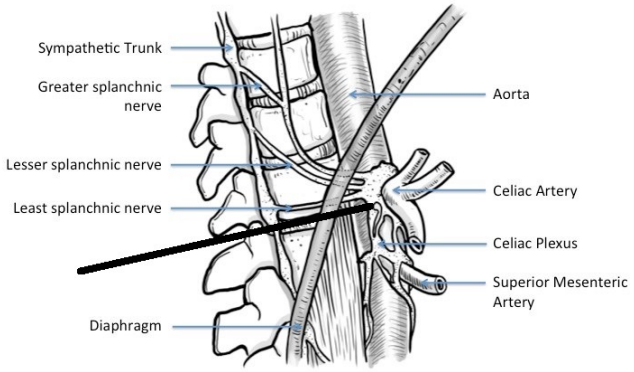
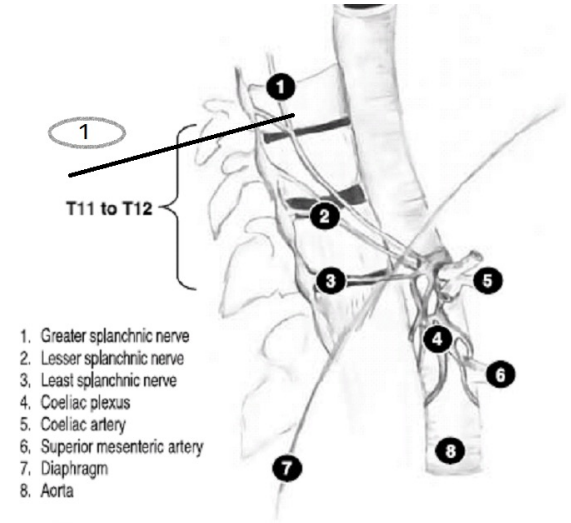
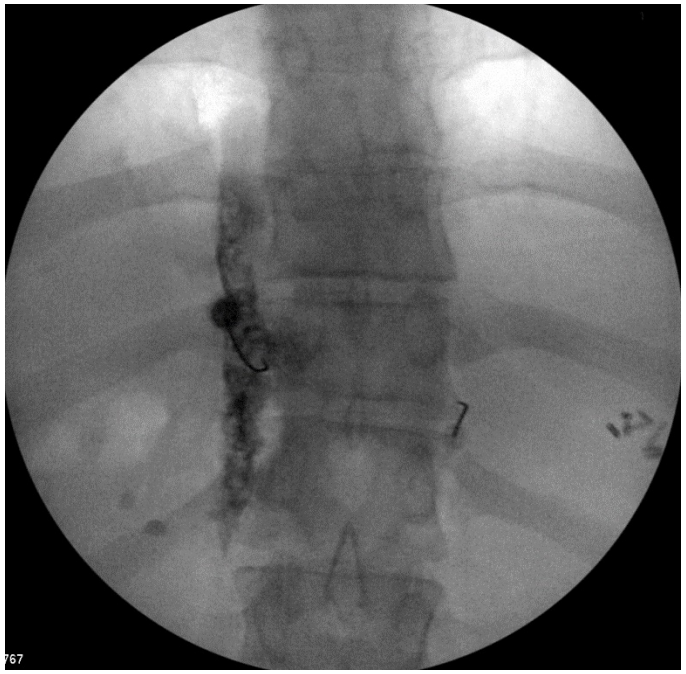


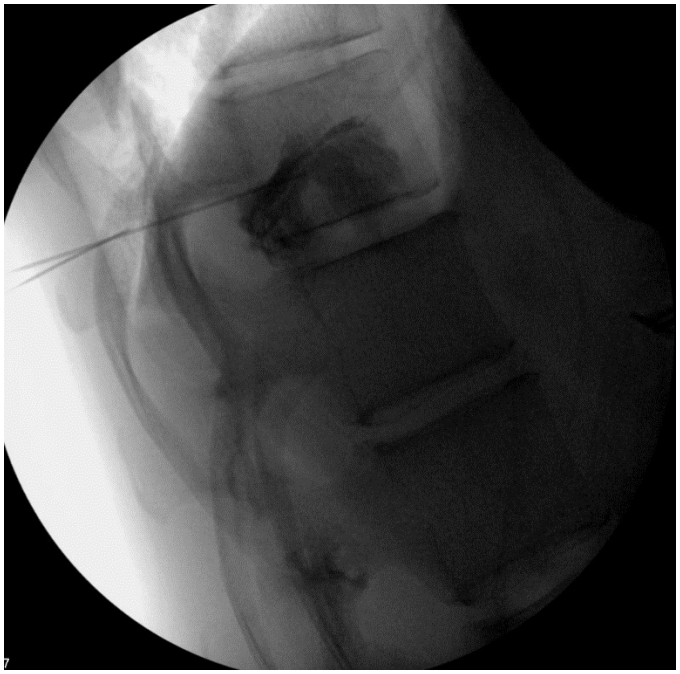
Fig. 1. Anatomy of splanchnic nerves and celiac plexus. Figure adapted from Waldman SD, *Interventional Pain Management*, 2nd ed, Philadelphia, WB Saunders, 2001, p. 503.

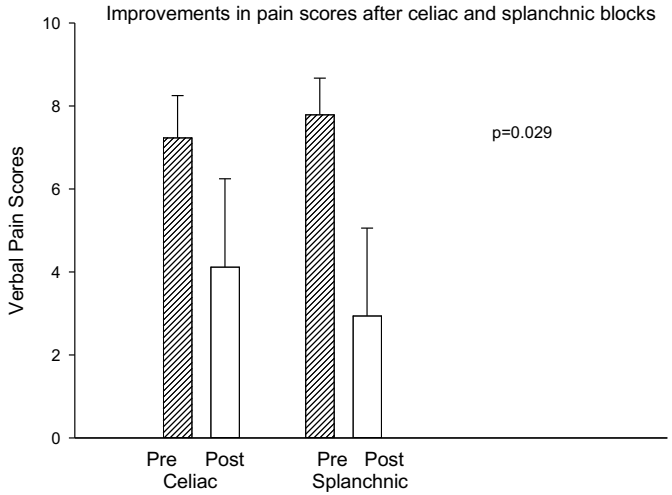


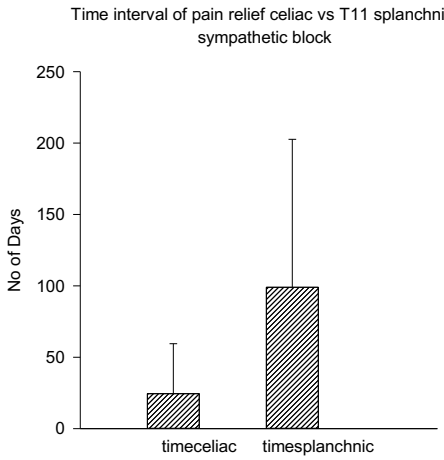


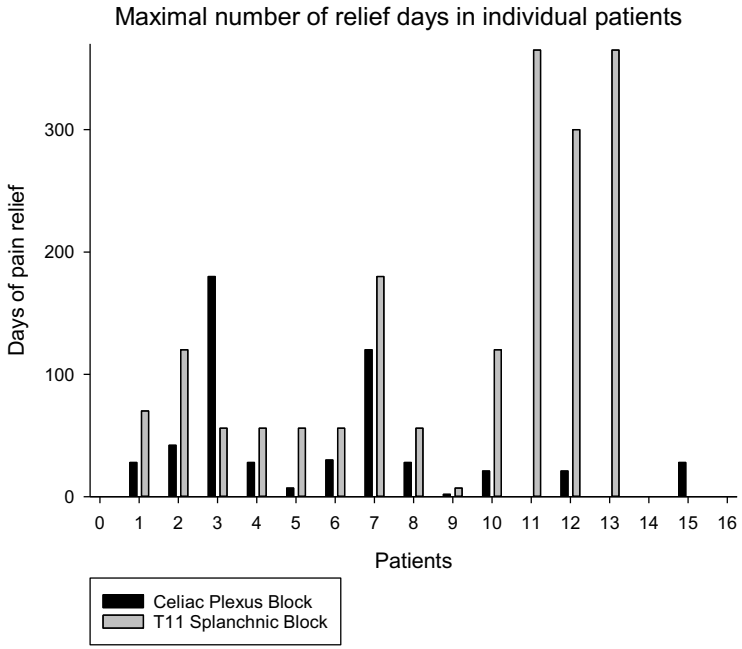
Splanchnic Block





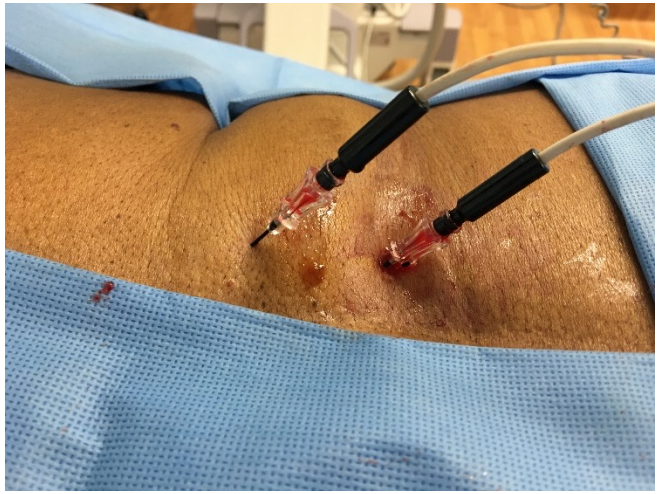


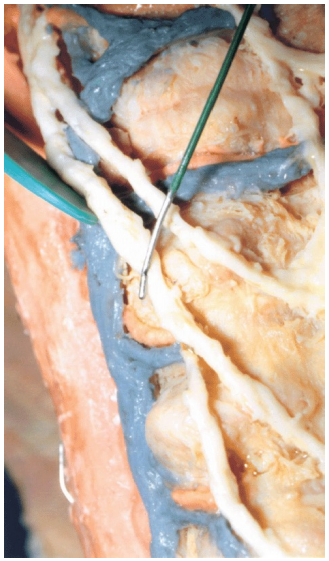


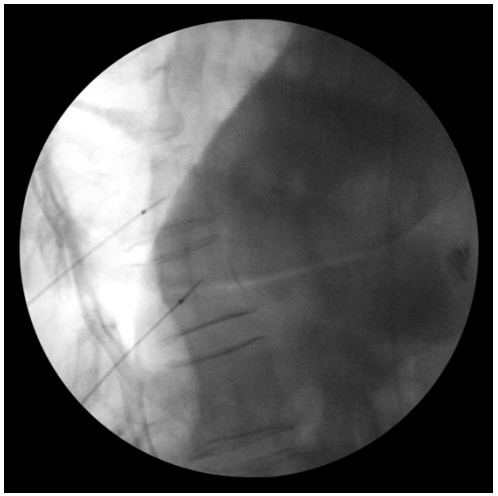


Badhey HS, Jolly N, Kapural L. Bilateral splanchnic block T11 provides longer pain relief than celiac plexus block from non-malignant abdominal pain. ASRA, Miami 2015

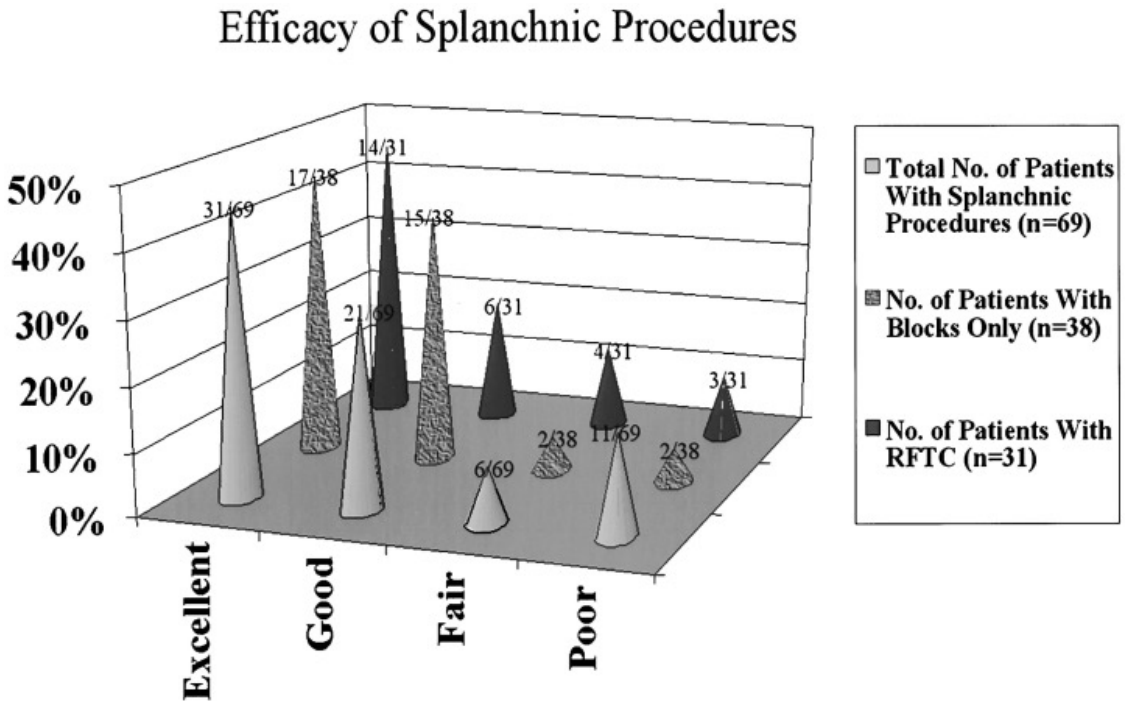
Splanchnic Radiofrequency







Raj et al., 2002



Excellent = ↓75% VAS Pain Scale
Good = ↓50-75% VAS Pain Scale
Fair = ↓10-50% VAS Pain Scale
Poor = ↓0-10% VAS Pain Scale

SCS for chronic abdominal pain; basis for therapeutic use

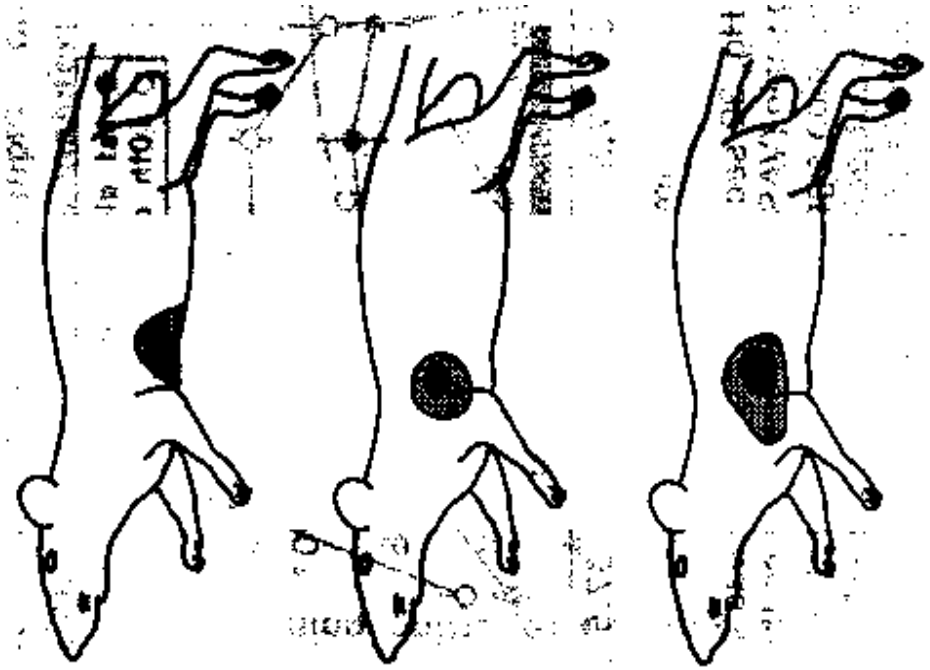
Rat Model

- Measure visceromotor behavioral responses to colorectal distension in rat
- Instillation of inflammatory chemicals will induce increased activity in lumbosacral dorsal column neurons and also potentiate responsiveness to normally non-noxious levels of distention

Ness TJ, Gebhart GF. Brain Res 1988;450:153-169

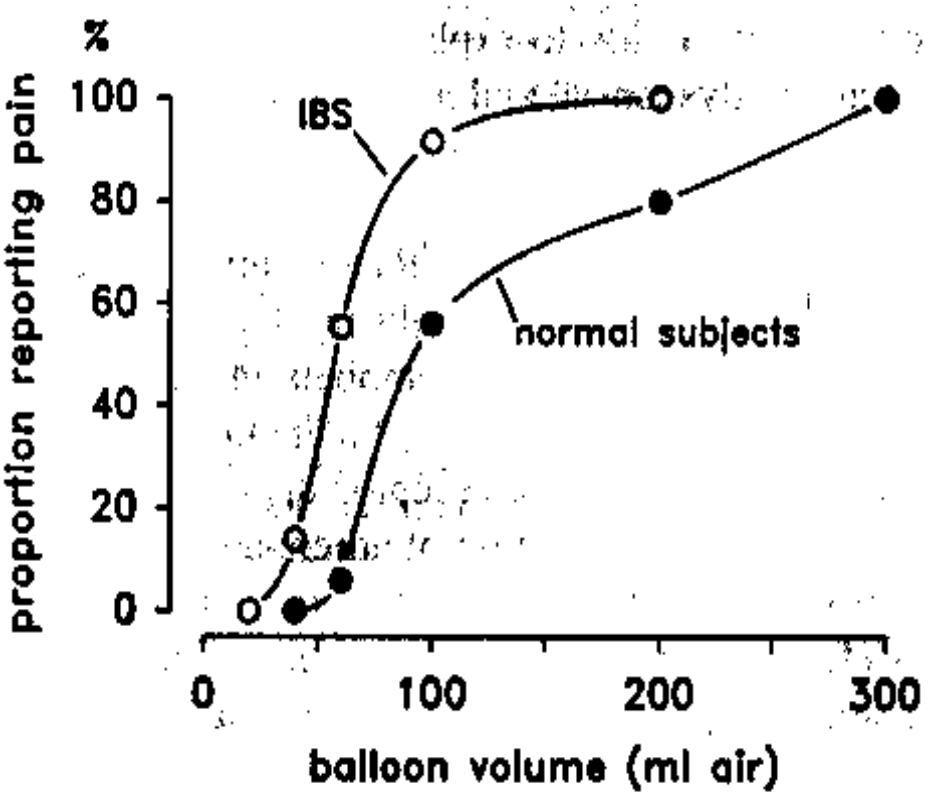
Visceral Hyperalgesia

- Changes-size of cutaneous receptive fields
- Smaller solid areas- originally determined, cutaneous receptive field
- Expanded following 10 to 15 distentions Q6 min (Euchner, Sengupta, Meller, and Gebhart, unpublished)



Visceral hyperalgesia

- Pain from balloon distention of the pelvic colon in normal subjects and those with IBS
- 55% of 67 patients with IBS reported pain with balloon distention -60 mL
- 6% of 16 normal and constipated pain at 60 ml
- 100 to 150 ml, 9 of 16 normals (56%) complained of pain, 90% of IBS reported pain
- Ritchie J. Pain from distension of the pelvic colon by inflating a balloon in the irritable colon syndrome. *Gut* 1973;14:125-132

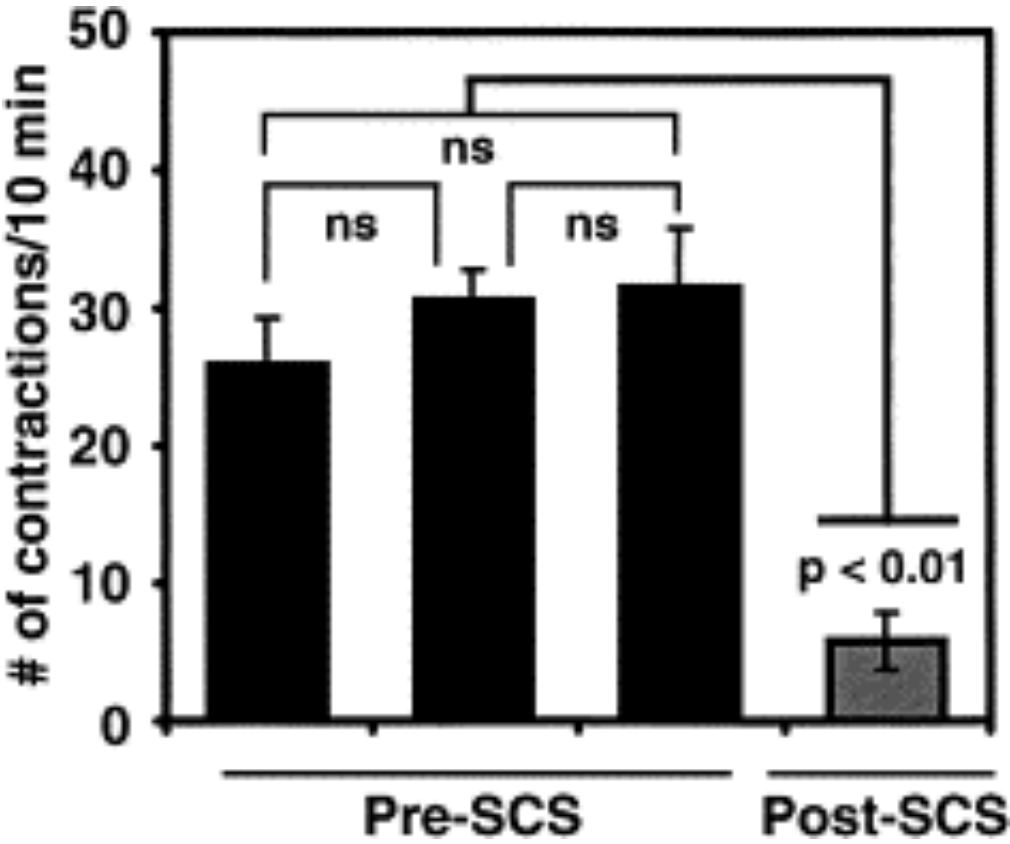


Manifestations of visceral hyperalgesia

- Visceral hyperalgesia
- Viscero-visceral convergence
- Referred visceral hyperalgesia/allodynia
- Viscero-somatic convergence
- Referred cutaneous hyperalgesia/allodynia
- Referred muscle hyperalgesia/allodynia

SCS strongly suppressed abdominal reflex contractions induced by nociceptive levels of colorectal distention

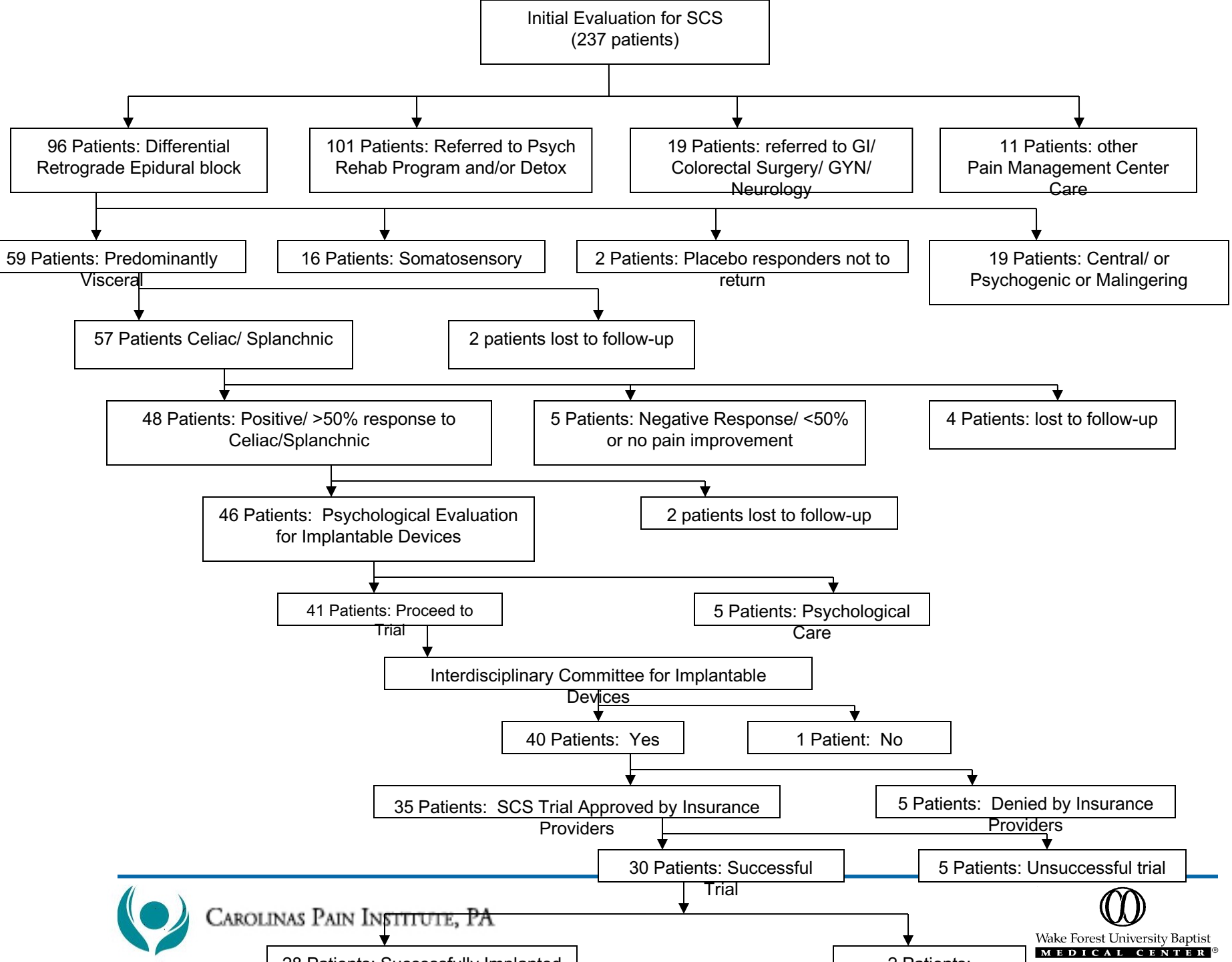
- SCS (90% MT, for 30 min) on the visceromotor response 60 mm Hg distention
- Prior to SCS, colorectal distention 10 min/10-min recovery induced a marked increase in the VMR
- 30-min SCS, significant ($p<0.001$) inhibitory effect in the number of abdominal contractions during a 10-min recording with colonic stimulus in 5 fully conscious rats
- (Greenwood-Van Meerveld et al., 2003)



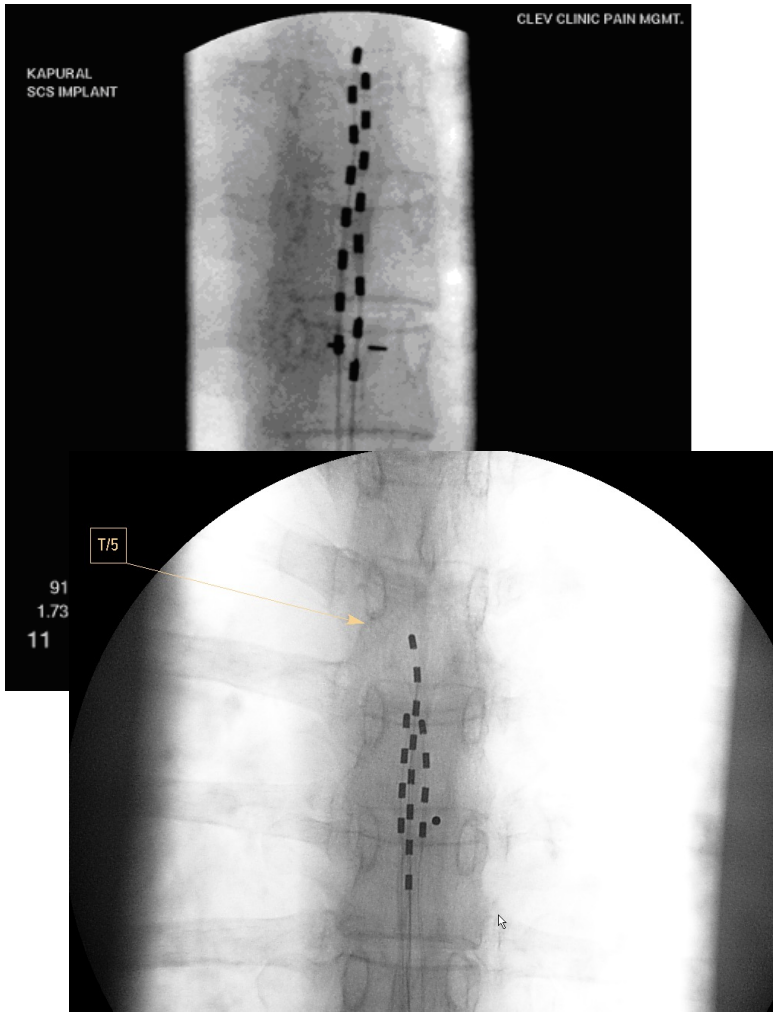
SCS possible mechanisms of action in humans

- Animal studies antidromic activation of primary efferents (Qin et al., 2007).
- Spinal gating mechanisms (Melzack and Wall 1965) -reduction in pain transmission of small diameter visceral fibers by stimulating large afferents (Melzack and Wall, 1965).
- Visceral midline dorsal column pathway- interruption of this pathway relieves visceral pelvic pain in cancer patients (Palecek, 2004; Gildenberg and Hirshberg, 1984; Hirshberg et al., 1996, Nauta 2000; Ness 2000; Palecek and Willis, 2003).
- Suppression of the sympathetic outflow (Steege, 1998). Pain relief with chemical or surgical neurectomy/sympatectomy involving superior hypogastric or celiac plexus (Steege, 1998; Rauck, 1992). Segmental and supraspinal down regulation of sympathetics-important mechanism of pain suppression in intractable angina (Linderoth and Foreman, 2006). Segmental suppression of sympathetic outflow by SCS.

SCS for chronic abdominal pain: indications, efficacy


Initial Evaluation for SCS
(237 patients)
96 Patients: Differential Retrograde Epidural block
101 Patients: Referred to Psych Rehab Program and/or Detox
19 Patients: referred to GI/ Colorectal Surgery/ GYN/ Neurology
11 Patients: other Pain Management Center Care
59 Patients: Predominantly Visceral
16 Patients: Somatosensory
2 Patients: Placebo responders not to return
19 Patients: Central/ or Psychogenic or Malingering
57 Patients Celiac/ Splanchnic
2 patients lost to follow-up
48 Patients: Positive/ >50% response to Celiac/Splanchnic
5 Patients: Negative Response/ <50% or no pain improvement
4 Patients: lost to follow-up
46 Patients: Psychological Evaluation for Implantable Devices
2 patients lost to follow-up
41 Patients: Proceed to Trial
5 Patients: Psychological Care
Interdisciplinary Committee for Implantable Devices
40 Patients: Yes
1 Patient: No
35 Patients: SCS Trial Approved by Insurance Providers
5 Patients: Denied by Insurance Providers
30 Patients: Successful Trial
5 Patients: Unsuccessful trial

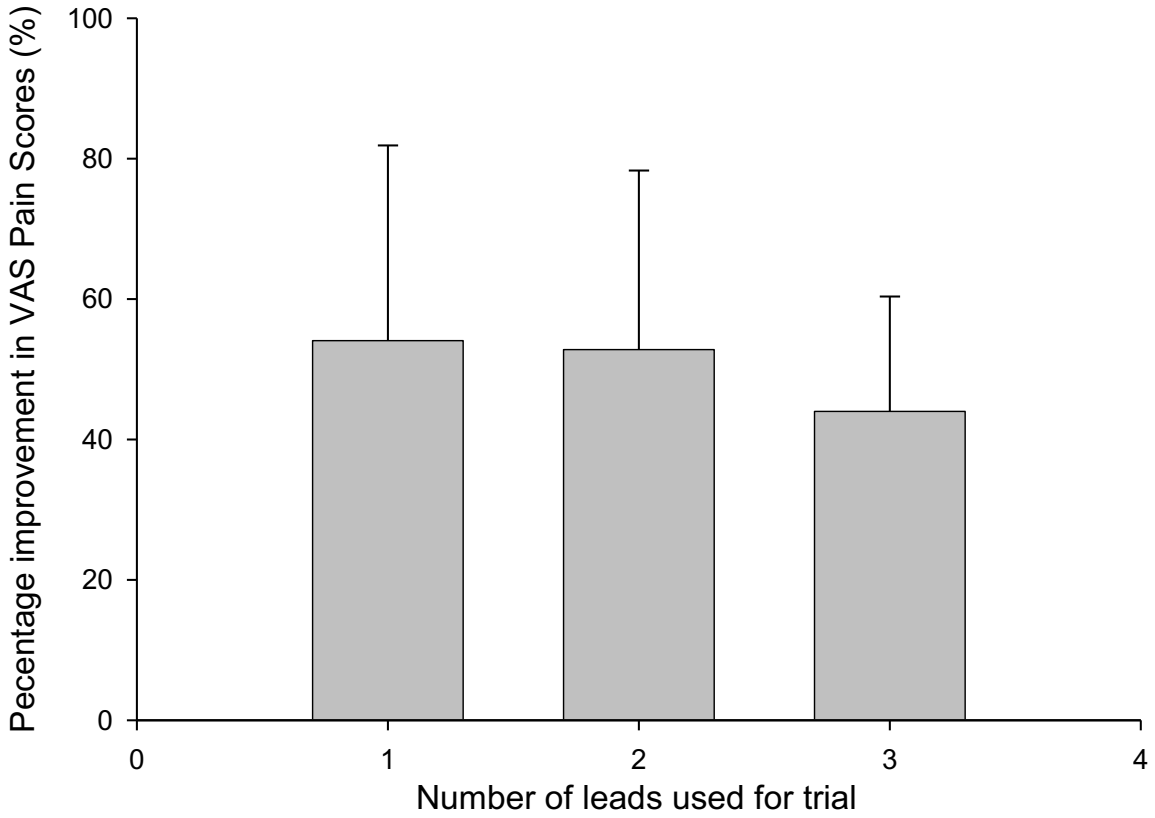
Lead placement



- Entry point T10-11 or higher
- Tip placed at T4 or lower
- We relied on paresthesias over the painful areas
- Midline placement
- (Kapural et al., Pain Medicine, 2010)

Kapural L, Sessler D, Tluczek H, Nagem H. Spinal Cord Stimulation for visceral abdominal pain. Pain Medicine 2010;11(3):347–355.

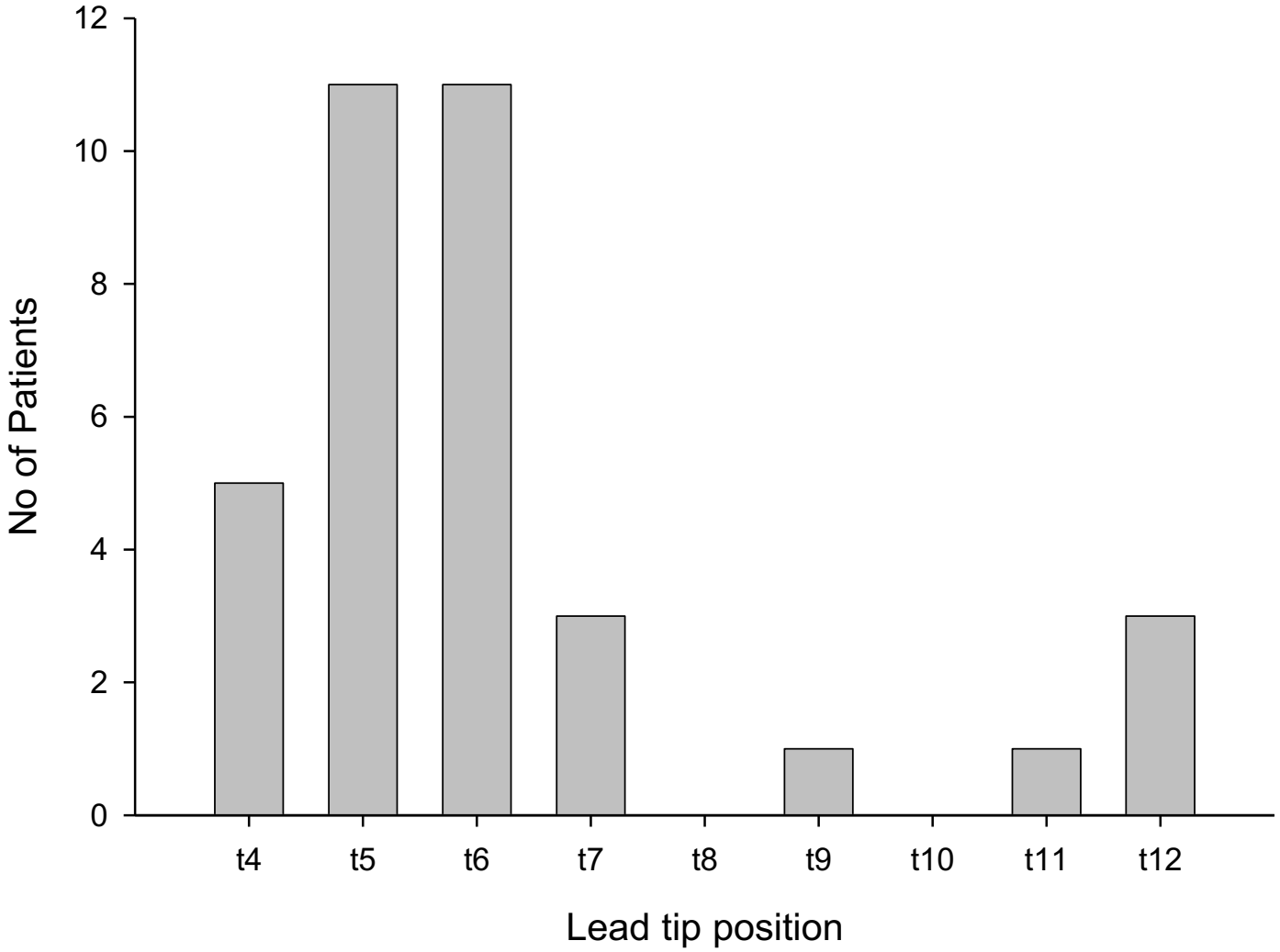
Number of leads during trial and pain relief
(Kapural et al., Pain Medicine, 2010)



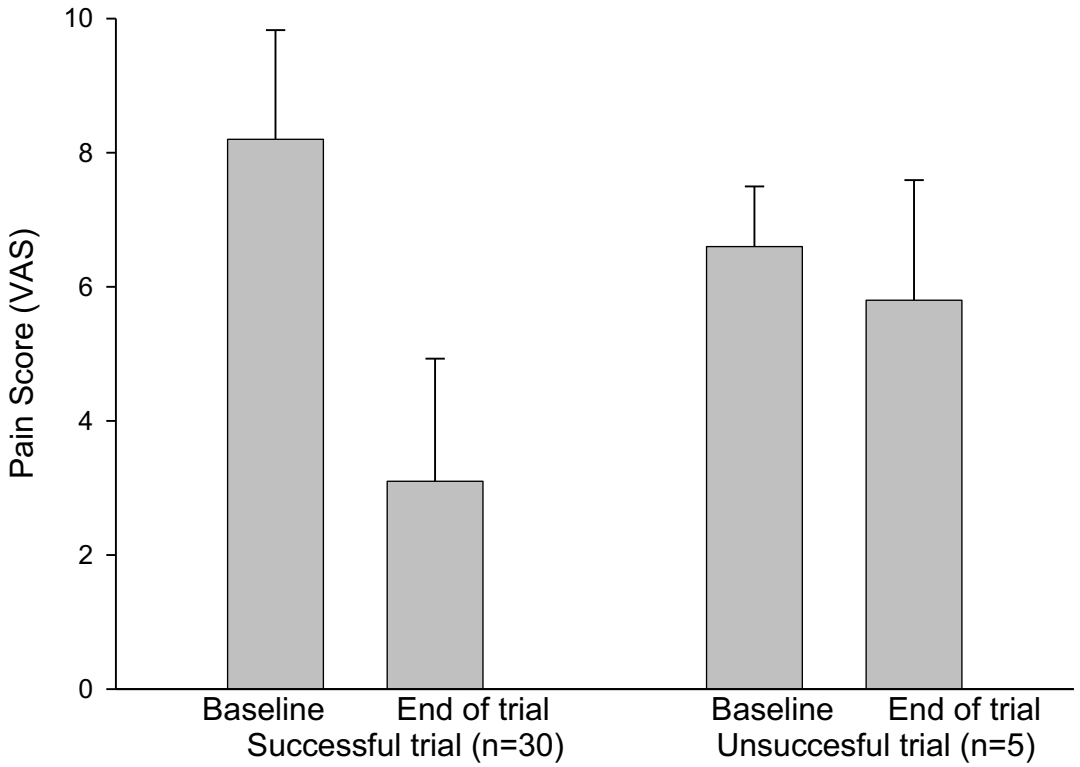
Kapural L, Sessler D, Tluczek H, Nagem H. Spinal Cord Stimulation for visceral abdominal pain. Pain Medicine 2010;11(3):347–355.

Lead tip position

(Kapural et al., Pain Medicine, 2010)



Trial success (Kapural et al., Pain Medicine, 2010)



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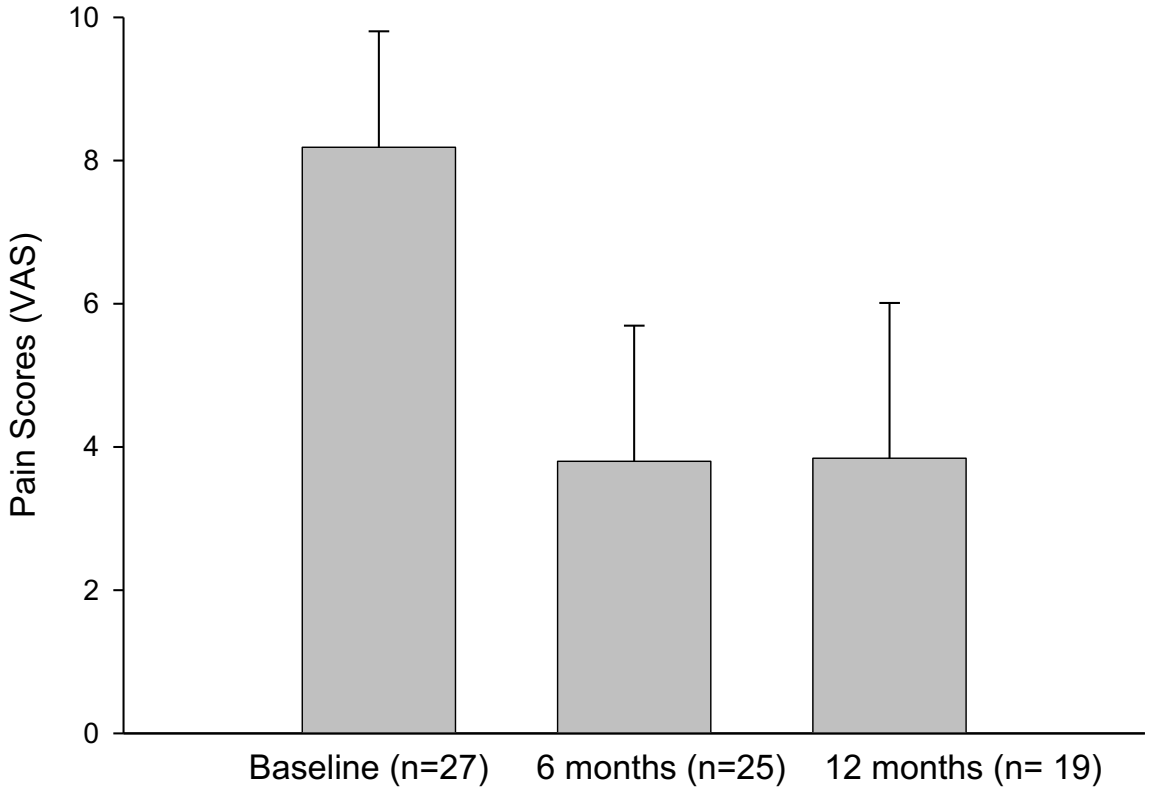
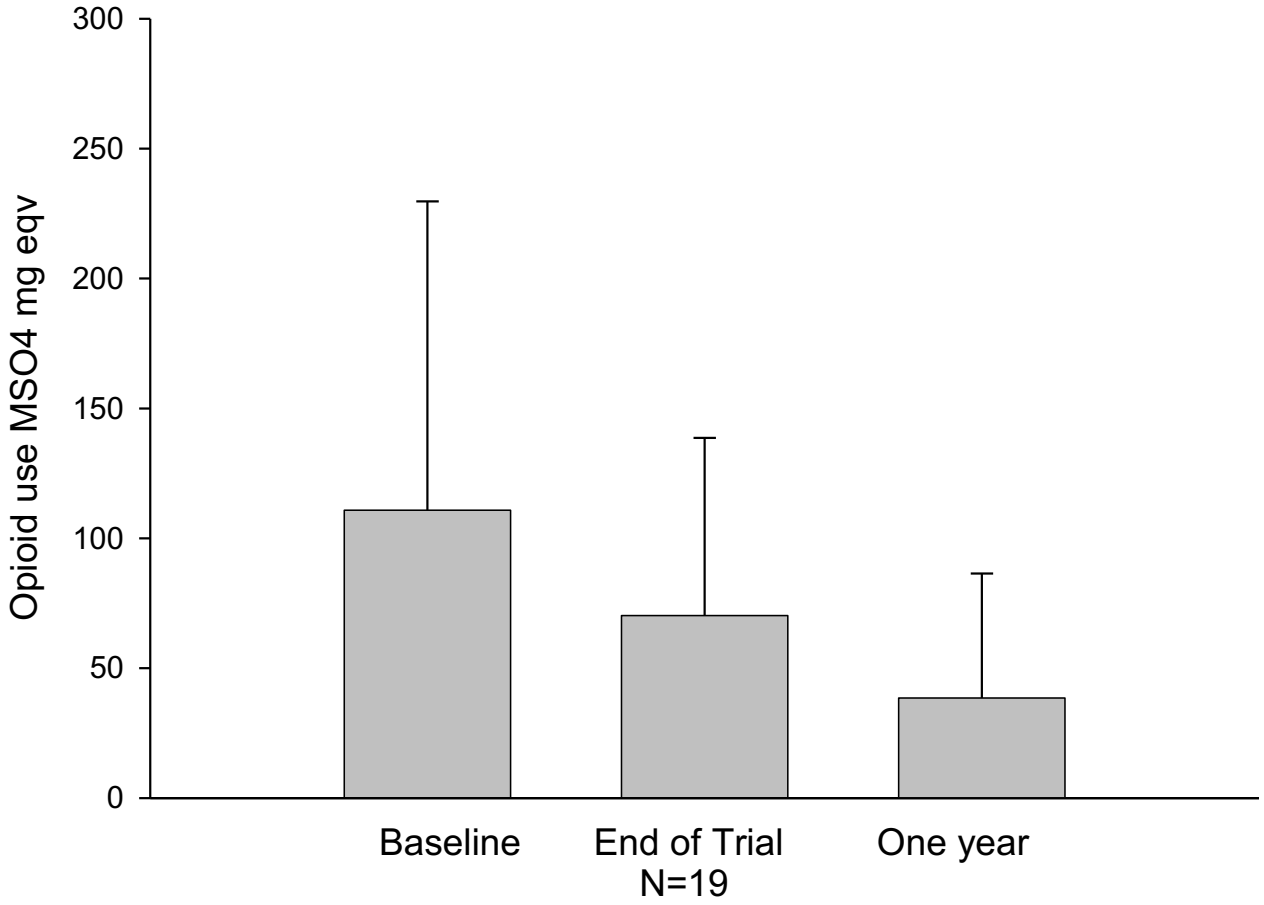
Pain relief (Kapural et al., Pain Medicine, 2010)



- One lost to follow-up after the implant
- 3 patients not completed one year follow-up
- 3 infections
- 1 explant dissatisfied with treatment
- 1 lead migration

Opioid use (Morphine equivalents)



Survey (Kapural et al., Pain Medicine, 2010)

Goal:

- learn on physicians current practices when SCS is used for abdominal pain
- technical aspect of the lead placement
- which abdominal pain syndromes treated

- **Case report-spinal cord stimulation for visceral abdominal and pelvic pain**
- Physician name:_____
- E-mail:_____
- Patients code:_____- Patients age: _____ Patients sex: _____
- Cause of pain (diagnosis):_____
- Pain characteristics:_____
- Pain area (epigastric, periumbilical)_____
- Previous treatments:_____
- _____
- Diagnostic blocks to confirm visceral pain (if any):_____
- _____
- SCS Trial: Psych eval for implantable devices: Yes or No
- Committee eval for implantable devices : Yes or No
- How many leads:_____ Tip at (vertebral level)_____ Type of leads_____
- Leads position (midline, paramedian, lateral):_____
- Days of trialing:_____ VAS or verbal pain score before trial_____ After trial_____
- Opioid use before trial (all opioids)_____
- Opioid use during trial_____
- SCS Implant:
- How many leads:_____ Tip at (vertebral level)_____ Type of leads_____
- Leads position (midline, paramedian, lateral):_____
- Weeks of stimulation:_____ VAS/verbal score before_____ After implant_____
- Opioid use before implant (all opioids)_____
- Opioid use after implant_____
- Patient satisfaction:_____

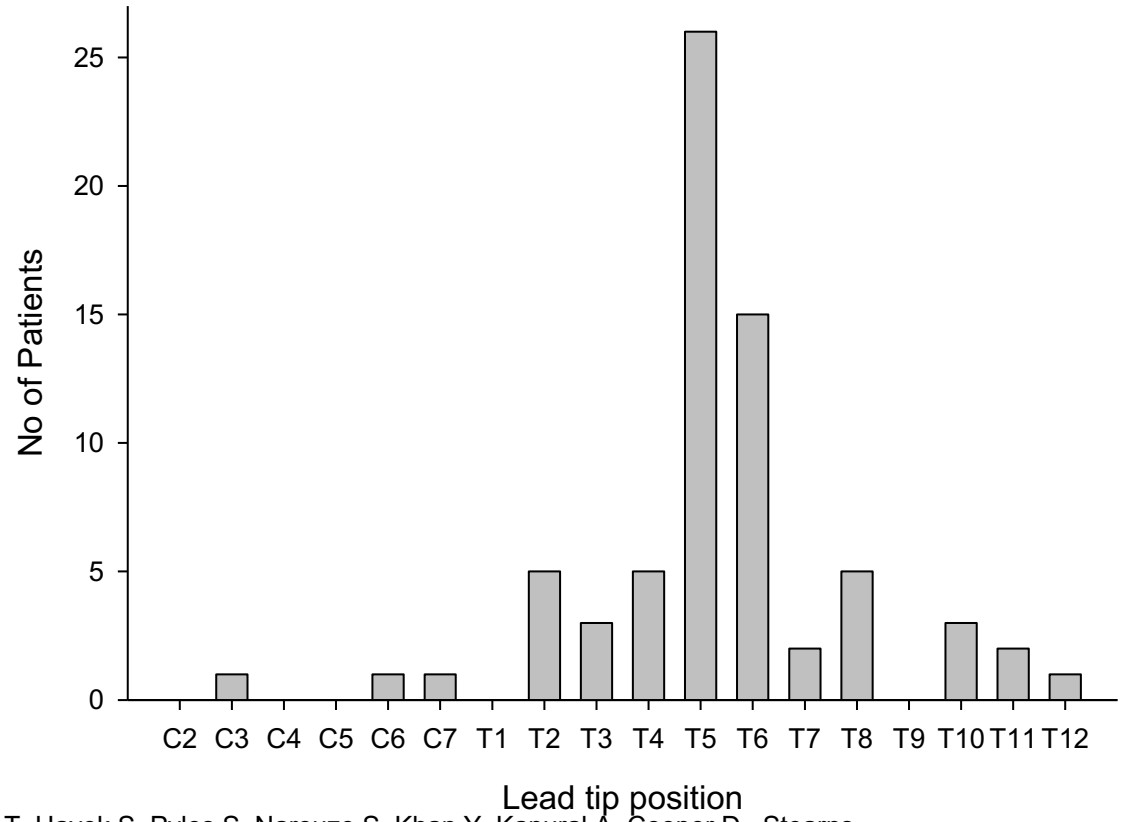
Survey (Kapural et al., Pain Medicine, 2010)

- Patients 16-85 years of age; 47.3 years (median 47)
- **identifiable causes: chronic pancreatitis (23), post-surgical intraabdominal adhesions (20), gastroparesis (9)**
- **post-surgical-following: cholecystectomy, bowel resection, gastric bypass, endometriosis-related surgical procedures and Nissen's**
- 9 patients: no cause could be determined
- Celiac plexus blocks, opoids, anticonvulsants, antidepressants, multiple explorative surgeries
- 76 case reports-23 responding physicians: 6 incompletely filled-excluded; 70 reported
- Characteristics: burning and aching then throbbing, stabbing, cramping, dull and sharp
- Most frequent areas epigastric and periumbilical

Kapural L, Deer T, Yakovlev A, Bensitel T, Hayek S, Pyles S, Narouze S, Khan Y, Kapural A, Cooper D, Stearns LZovkic P. Spinal cord stimulation for visceral abdominal pain: results of the national survey**. Pain Medicine 2010;11(5):685-691.**

Survey (Kapural et al., Pain Medicine, 2010) -trial

- majority leads midline; 21 paramedial
- 50% two leads (mainly octrodes) for trial
- no difference if one or two leads used (p=0.11)
- Trial 4.7 days (median of 4 days); shortest one day and longest 14
- Most patients leads at T5 (26) or T6 (15)
- All physicians reported coverage of the painful area with paresthesias during what was considered above the perception threshold stimulation



Kapural L, Deer T, Yakovlev A, Bensitel T, Hayek S, Pyles S, Narouze S, Khan Y, Kapural A, Cooper D, Stearns LZovkic P. Spinal cord stimulation for visceral abdominal pain: results of the national survey**. Pain Medicine 2010;11(5):685-691.**

Survey (Kapural et al., Pain Medicine, 2010) -permanent implant

- two octapolar leads
- midline
- T5-6
- average follow-up 84 weeks (median 62 weeks)

Kapural L, Deer T, Yakovlev A, Bensitel T, Hayek S, Pyles S, Narouze S, Khan Y, Kapural A, Cooper D, Stearns LZovkic P. Spinal cord stimulation for visceral abdominal pain: results of the national survey**. Pain Medicine 2010;11(5):685-691.**

Chronic pancreatitis- (Kapural et al; Neuromodulation 2011)

- 30 patients
- trials 4 to 14 days (median 9 days)
- SCS lead tip mostly at T5 (n=10) or T6 (n=10)
- 24 patients (80%) reported at least 50% trial
- pre-trial VAS 8±1.6 (SD), PDI=58, opioid use averaged 165±120 mg MSO4 equivalents
- During trial, VAS to 3.67±2 cm ($p<0.001$); opioid to 105±101 mg

Chronic pancreatitis- (Kapural et al, Neuromodulation 2011)

- Six patients failed the trial
- one was lost to follow-up
- 20 followed> year
- SCS removed due to infection or lead migration (n=3).
- 20 patients:
- VAS 4.0±2.1; p<0.001 at one year
- opioid use 54±73mg morphine equivalents.

Kapural L, Cywinski J, Sparks D. Spinal cord stimulation for visceral pain from chronic pancreatitis. **Neuromodulation 2011;14(5):423-427.**

SCS for chronic dysmotility disorders: a first evidence

Basic science

- SCS on gastrointestinal (GI) motility in healthy and diabetic rats
- unipolar electrode at T9/T10
- gastric tone
- gastric emptying
- intestinal transit
- sympathovagal balance
- gastric emptying of solids in diabetic rat

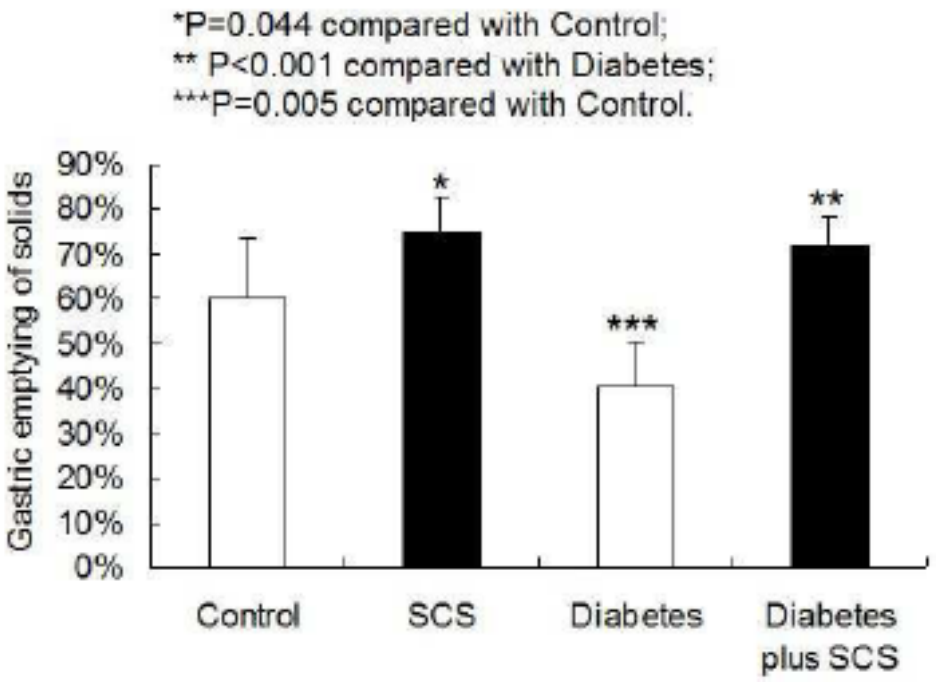
Song GQ, Qin, C and Chen J.Therapeutic Potential of Spinal Cord Stimulation for Gastrointestinal Motility Disorders: a Preliminary Rodent Study; Neurogastroenterology Motility 2014; 26:377-384.

Basic Science: Spinal cord stimulation

- increased gastric emptying of liquids by about 17%
- accelerated small intestinal transit by 20% in healthy rats
- accelerated gastric emptying of solids 24% in healthy rats and 78% in diabetic rats
- decreased sympathetic activity (1.13±0.18 vs. 0.68±0.09, P<0.04)
- sympathovagal balance (0.51±0.036 vs.0.40±0.029, p=0.028)

Song GQ, Qin, C and Chen J.Therapeutic Potential of Spinal Cord Stimulation for Gastrointestinal Motility Disorders: a Preliminary Rodent Study; Neurogastroenterology Motility 2014; 26:377-384.

Song GQ, Qin, C and Chen J.Therapeutic Potential of Spinal Cord Stimulation for Gastrointestinal Motility Disorders: a Preliminary Rodent Study; Neurogastroenterology Motility 2014; 26:377-384.



Physiological Society
Regulatory, Integrative and Comparative Physiology®

Therapeutic value of spinal cord stimulation in irritable bowel syndrome: a randomized crossover pilot study

Göran Lind, Jaleh Winter, Bengt Linderoth, Per M. Hellström

American Journal of Physiology - Regulatory, Integrative and Comparative Physiology Published 15 May 2015 **Vol.** 308 **no.** 10, R887-R894 **DOI:** 10.1152/ajpregu.00022.2015

SCS for IBS

Thanks to Prof Linderoth

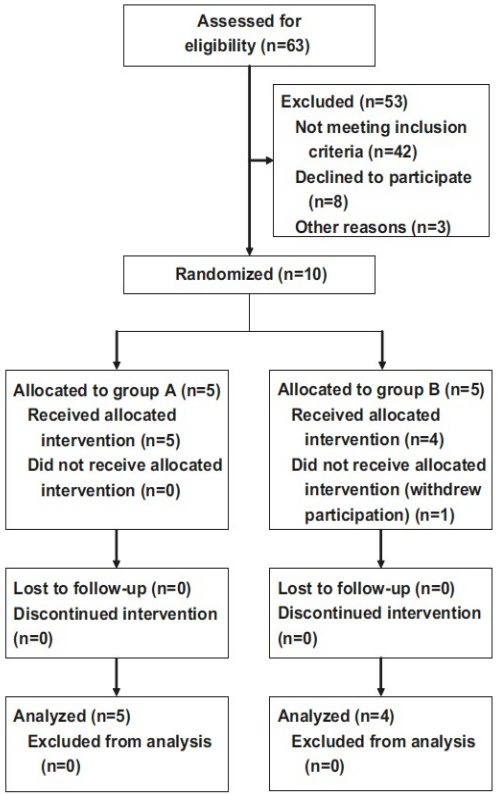


Fig. 3. Flow chart of the study protocol. *Group A* started with spinal cord stimulation upon onset of the study period. *Group B* had delayed start by 6 wk until crossover. The diagram also shows the number of patients available for each step.

SCS-IBS; Fall 2015 (Thanks to Prof Linderoth)

- 9 patients completed the entire program
- 6/9 (66%) considered as Responders
- (the 3 non-responders had their devices removed)
- 2 responders experienced decreasing symptoms and stopped daily SCS but kept the implants
- 1 responder had a malignancy demanding MRI why the device was explanted
- Several batteries were changed
- Still 3-4 pts. (>50% of responders) uses SCS on an almost daily basis
- Longest FU now >> 8 yrs (ie >> 96 months)

Lead positions

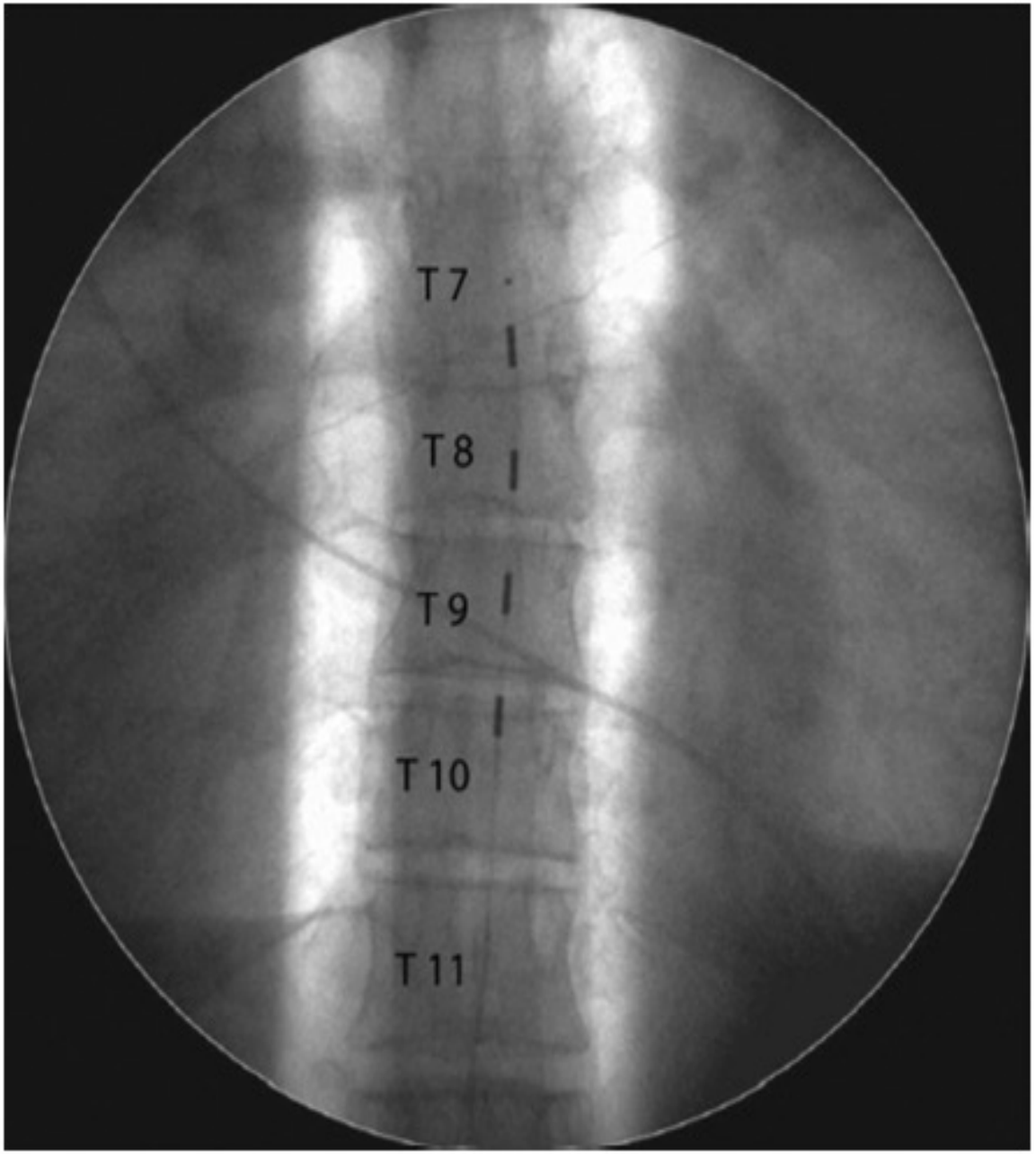
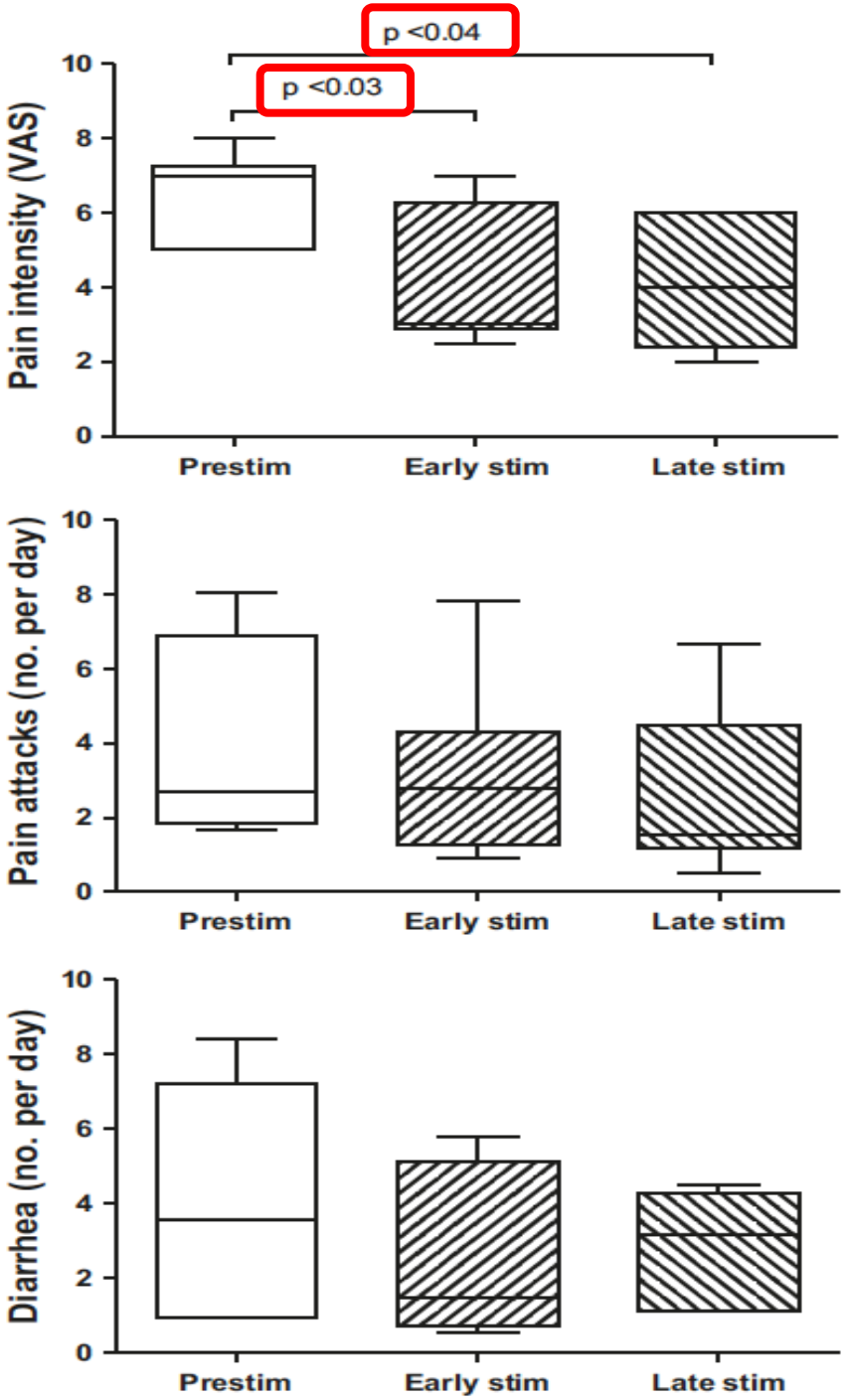


Fig. 1. Spinal cord stimulation system. Anterior-posterior X-ray image of electrode position in a patient (patient no. 9).

Pain Intensity (VAS)

No. of Pain Attacks/day

No of Diarrheas/day



SCS for Painful gastroparesis

21 patients trialed, T4

18 patents went for an implant

2 revised

4 had no improvement in nausea/vomiting

14 > 50% of pain relief

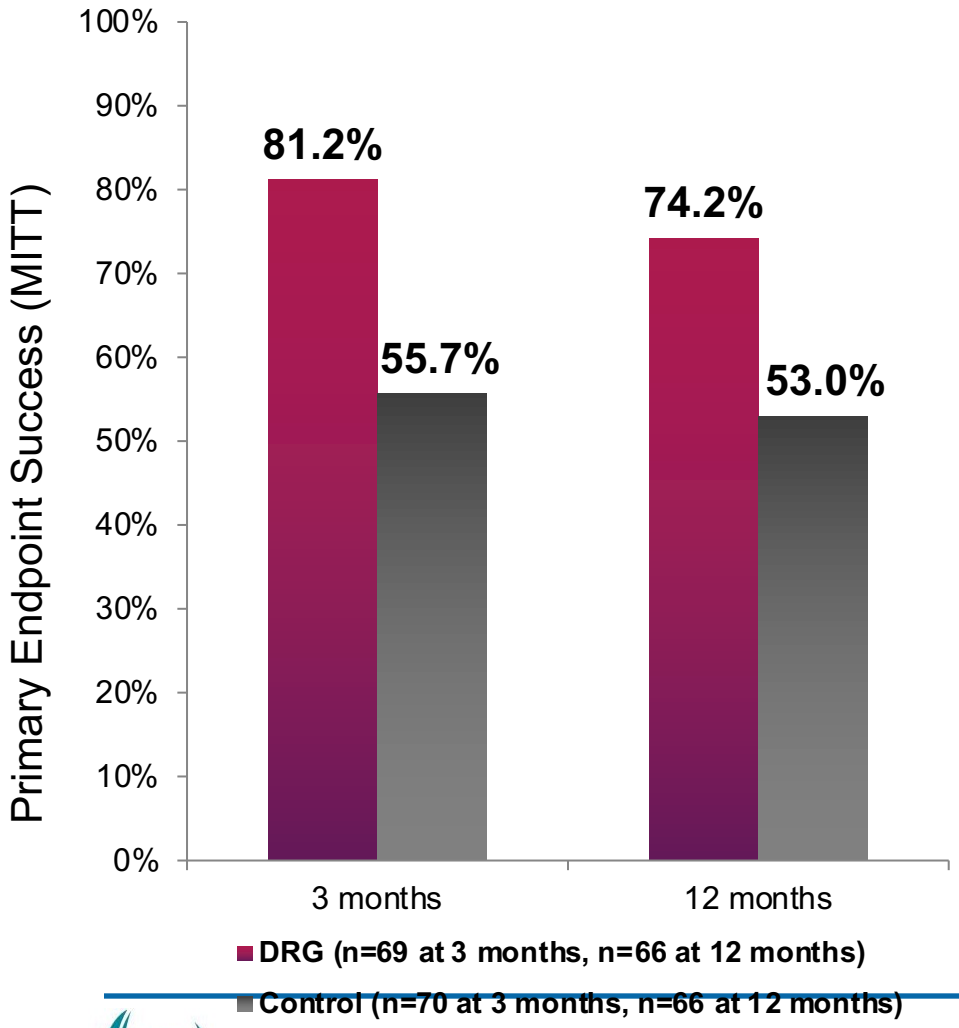
9 minimal nausea/vomiting

All had positive responses to splanchnic blocks

- 6 patients had an objective test before and after: smart pill (1), electrogastrogram with water load (2), gastric emptying (3)
- 5 normalized
- Would require prospective assessment using a single test

Novel SCS modalities and waveforms: useful for chronic abdominal pain?

Accurate study results: ITT Analysis

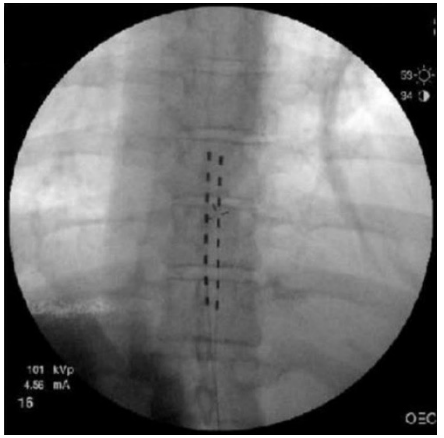


- Prospective, Randomised, Crossover, Controlled, Feasibility Study to Assess the Efficacy of Dorsal Root Ganglion (DRG) Neurostimulation as a Treatment for **P**ersistent **A**bdomi**N**al Refr**A**ctory Vis**CE**ral P**A**in Secondary to Chronic Pancreatitis: **PANACEA Trial** Dr Ganesan Baranidharan, Leeds UK

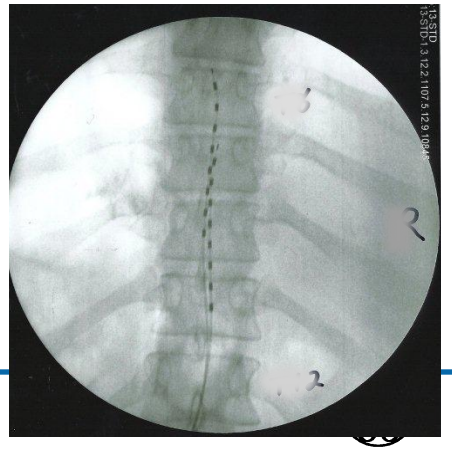
Levy R and Deer T. NANS 2015

Procedure

- Traditional lead placement requires intraoperative paresthesia mapping
  - Goal is to cover areas of pain with paresthesias
  - **Paresthesia based lead placement (T6-T10) for back and leg pain**
  - Requires patient feedback
  - Can lead to wide range in procedure times



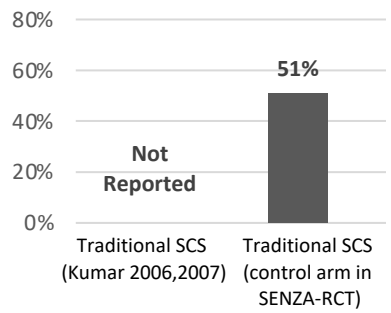
- HF10 leads are placed anatomically
  - Paresthesia mapping not required
  - **Anatomical lead placement (T8-T11) for back and leg pain**
  - No intra-operative programming
  - Consistent procedure time



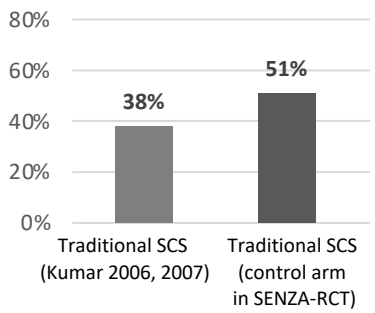
Comparison of Published, Prospective Results

Back Pain — 12-Month Follow-Up — Leg Pain

Responder Rate

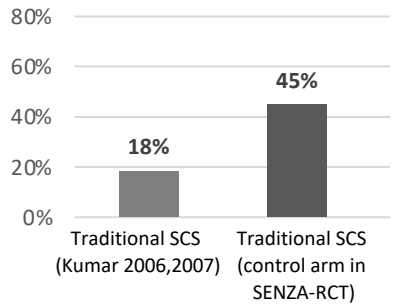


Responder Rate

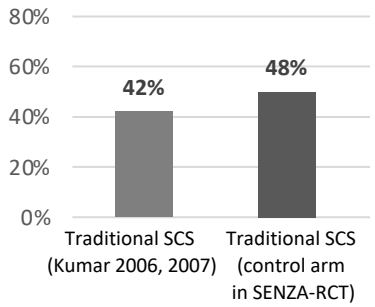


HF10 superiority*

% VAS Reduction



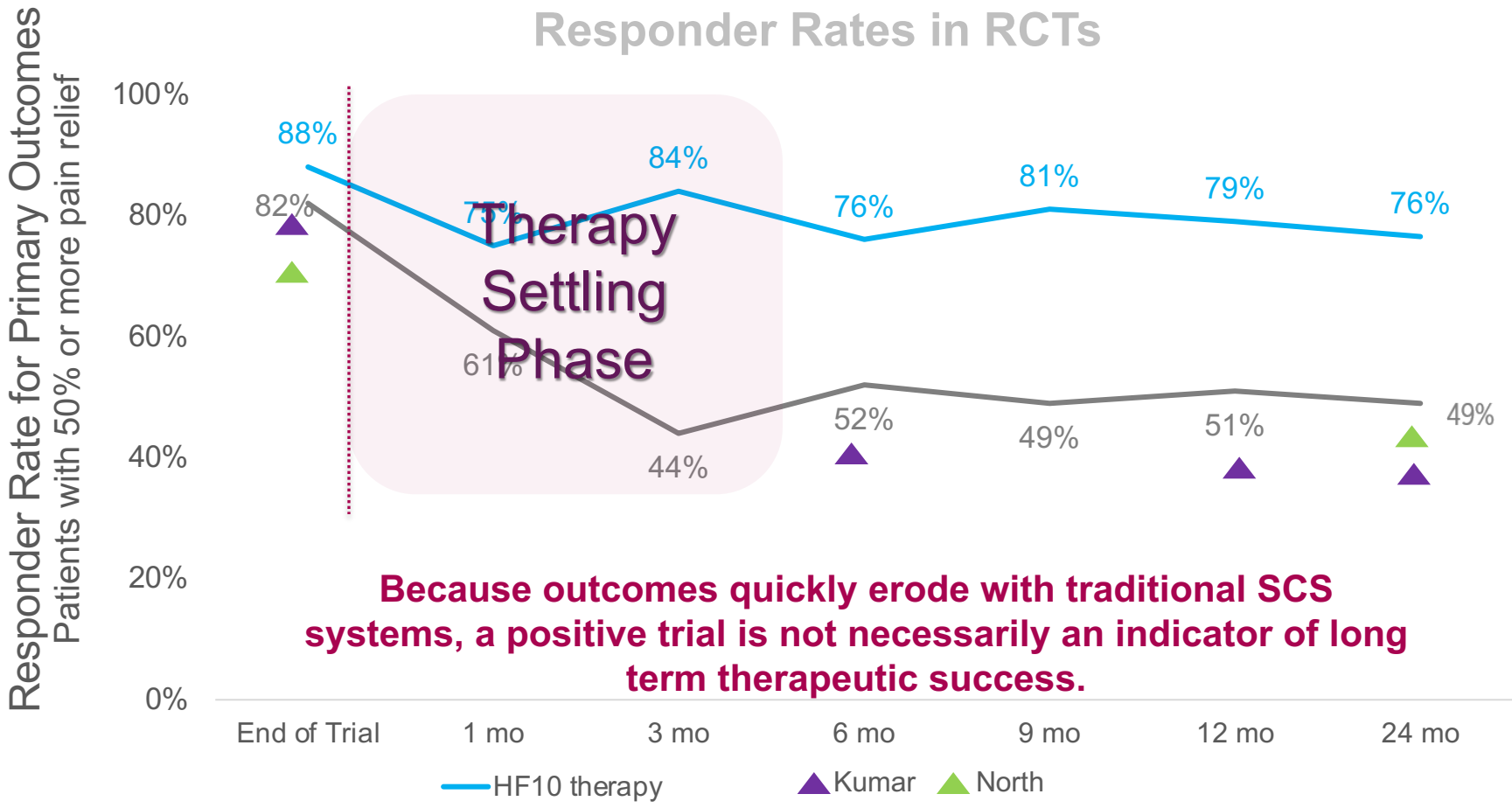
% VAS Reduction



*Based on post-hoc superiority analyses. Analysis of permanent implant population

EU Study: Al-Kaisy, Van Buyten, Smet, et al. *Pain Medicine.* 2013.

Comparison of Response Rates Across Prospective RCTs



n = 171 to 12 months (n = 90 test, n = 81 control); n = 156 at 18 and 24 months (n = 85 test, n =71 control)
p-value < 0.001 at all time points 3 months and beyond

1..Kapural L, et al. 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. Neurosurgery. Published 09 2016 [Epub ahead of Print]. 2. Kumar K, et al. The Effects of Spinal Cord Stimulation in Neuropathic Pain are Sustained: A 24-Month Follow-Up of the Prospective Randomized Controlled Multicenter Trial of the Effectiveness of Spinal Cord Stimulation. Neurosurgery 2008;63:762–770. 3. North RB, et al. Spinal Cord Stimulation Versus Repeated Lumbosacral Spine Surgery for Chronic Pain: A Randomized, Controlled Trial. Neurosurgery 2005;56:98–106.

SENZA-RCT Published in Anesthesiology

ANESTHESIOLOGY
The Journal of the American Society of Anesthesiologists, Inc.

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

Leonardo Kapural, M.D., Ph.D., Cong Yu, M.D., Matthew W. Doust, M.D., Bradford E. Gliner, M.S., Ricardo Vallejo, M.D., Ph.D., B. Todd Sitzman, M.D., M.P.H., Kasra Amirdelfan, M.D., Donna M. Morgan, M.D., Lora L. Brown, M.D., Thomas L. Yearwood, M.D., Ph.D., Richard Bundschu, M.D., Allen W. Burton, M.D., Thomas Yang, M.D., Ramsin Benyamin, M.D., Abram H. Burgher, M.D.

ABSTRACT

Background: Current treatments for chronic pain have limited effectiveness and commonly known side effects. Given the prevalence and burden of intractable pain, additional therapeutic approaches are desired. Spinal cord stimulation (SCS) delivered at 10 kHz (as in HF10 therapy) may provide pain relief without the paresthesias typical of traditional low-frequency SCS. The objective of this randomized, parallel-arm, noninferiority study was to compare long-term safety and efficacy of SCS therapies in patients with back and leg pain.

Methods: A total of 198 subjects with both back and leg pain were randomized in a 1:1 ratio to a treatment group across 10 comprehensive pain treatment centers. Of these, 171 passed a temporary trial and were implanted with an SCS system. Responders (the primary outcome) were defined as having 50% or greater back pain reduction with no stimulation-related neurological deficit.

Results: At 3 months, 84.5% of implanted HF10 therapy subjects were responders for back pain and 83.1% for leg pain, and 43.8% of traditional SCS subjects were responders for back pain and 55.5% for leg pain ($P < 0.001$ for both back and leg pain comparisons). The relative ratio for responders was 1.9 (95% CI, 1.4 to 2.5) for back pain and 1.5 (95% CI, 1.2 to 1.9) for leg pain. The superiority of HF10 therapy over traditional SCS for leg and back pain was sustained through 12 months ($P < 0.001$). HF10 therapy subjects did not experience paresthesias.

Conclusion: HF10 therapy promises to substantially impact the management of back and leg pain with broad applicability to patients, physicians, and payers. (ANESTHESIOLOGY 2015; 123:00-00)

WE present a multicenter, randomized, controlled trial evaluating the safety and efficacy of 10-kHz high-frequency (HF10) therapy, which is an innovative spinal cord stimulation (SCS) system for the management of chronic back and leg pain. This system delivers electrical stimulation pulses at high frequency (10,000 Hz) as compared with traditional low-frequency SCS systems (typically around 50 Hz). Previous work suggests that the higher-frequency system may treat back and leg pain to a greater degree. Moreover, it may be able to do so without producing paresthesias associated with low-frequency SCS, which some patients find uncomfortable.[1–3]

What We Already Know about This Topic

- Spinal cord stimulation (SCS) often relieves radicular pain but is relatively poorly effective for the treatment of back pain
- High-frequency SCS may improve the efficacy of SCS for the treatment of low back pain

What This Article Tells Us That Is New

- This randomized trial involving 198 participants demonstrated that high-frequency spinal cord stimulation (SCS) was superior to conventional SCS for the treatment of back pain and leg pain
- The effects of high-frequency stimulation relative to conventional stimulation persisted for 12 months

This article is featured in "This Month in Anesthesiology," page 1A. Full protocol available at: gliner@nevro.com. Raw data available at: gliner@nevro.com.

Submitted for publication November 13, 2014. Accepted for publication May 29, 2015. From the Center for Clinical Research and Carolina's Pain Institute at Brookstown, Wake Forest Baptist Health, Winston-Salem, North Carolina (L.K.); Swedish Pain Center, Seattle, Washington (C.Y., T.Y.); The Pain Center of Arizona and HOPE Research Institute, Phoenix, Arizona (M.W.D.A.H.B.); Clinical and Regulatory Affairs, Nevro Corp., Menlo Park, California (B.E.G.); Millennium Pain Center, Bloomington, Illinois (R.V., R. Benyamin); Advanced Pain Therapy, PLLC, Hattiesburg, Mississippi (B.T.S.); IPM Medical Group, Inc., Walnut Creek, California (K.A.); Pain Consultants of Oregon, Eugene, Oregon (D.M.M.); Coastal Orthopedics and Pain Medicine, Bradenton, Florida (L.L.B., R. Bundschu); Comprehensive Pain and Rehabilitation, Pascagoula, Mississippi (T.L.Y.); and Houston Pain Associates, Houston, Texas (A.W.B.).

CAROLINAS PAIN INSTITUTE, PA

Wake Forest University Baptist MEDICAL CENTER®

RESEARCH—HUMAN—CLINICAL TRIALS

OPEN

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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

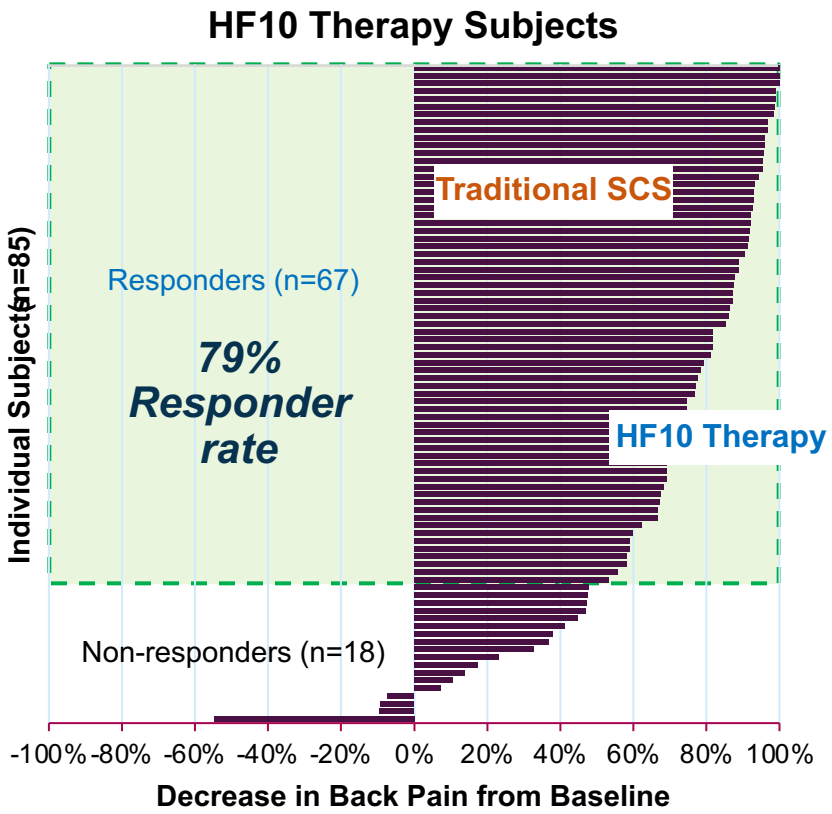
BACKGROUND: Pain relief with spinal cord stimulation (SCS) has focused historically on paresthesias overlapping chronically painful areas. A higher level evidence supports the use of SCS in treating leg pain than supports back pain, as it is difficult to achieve adequate paresthesia coverage, and then pain relief, in the low back region. In comparison, 10-kHz high-frequency (HF10) SCS therapy does not rely on intraoperative paresthesia mapping and remains paresthesia-free during therapy.

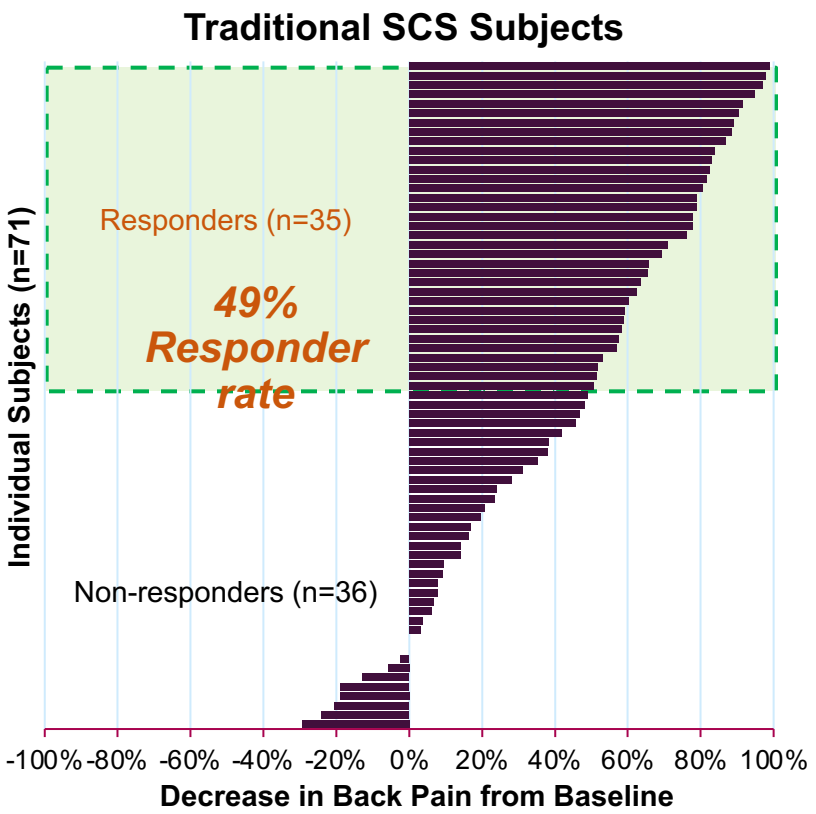
OBJECTIVE: To compare long-term results of HF10 therapy and traditional low-frequency SCS.

METHODS: A pragmatic randomized, controlled, pivotal trial with 24-month follow-up was conducted across 11 comprehensive pain treatment centers. Subjects had Visual Analog Scale scores of ≥5.0/10.0 cm for both back and leg pain, and were assigned randomly (1:1) to receive HF10 therapy or low-frequency SCS. The primary end point was a responder rate, defined as ≥50% back pain reduction from baseline at 3 months with a secondary end point at 12 months (previously reported). In this article, 24-month secondary results are presented. Non-inferiority was first assessed, and if demonstrated the results were tested for superiority.

RESULTS: In the study, 198 subjects were randomized (101 HF10 therapy, 97 traditional SCS). One hundred seventy-one subjects (90 HF10 therapy, 81 traditional SCS) successfully completed a short-term trial and were implanted. Subjects averaged 54.9 ± 12.9 years old, 13.6 ± 11.3 years since diagnosis, 86.6% had back surgery, 88.3% were taking opioid

Individual Back Pain Reduction at 24 Months





Responder rate: P<0.001

- Each horizontal line represents the response of a study subject.
- Responders (colored horizontal lines) are distinguished from non-responders (grey horizontal lines).

Each line represents a patient

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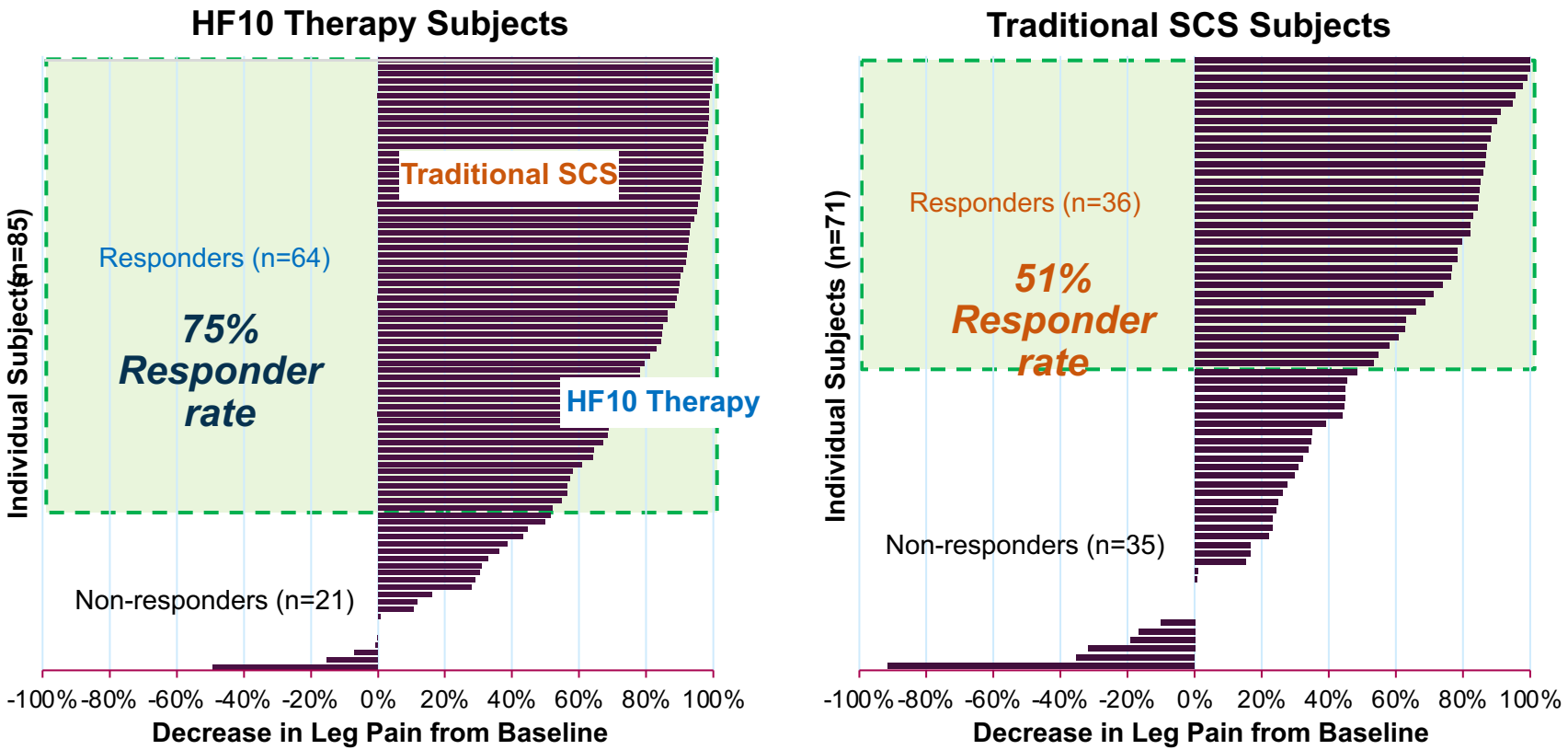
Individual Leg Pain Reduction at 24 Months



Responder rate: P=0.003

- Each horizontal line represents the response of a study subject.
- Responders (colored horizontal lines) are distinguished from non-responders (grey horizontal lines).

Each line represents a patient

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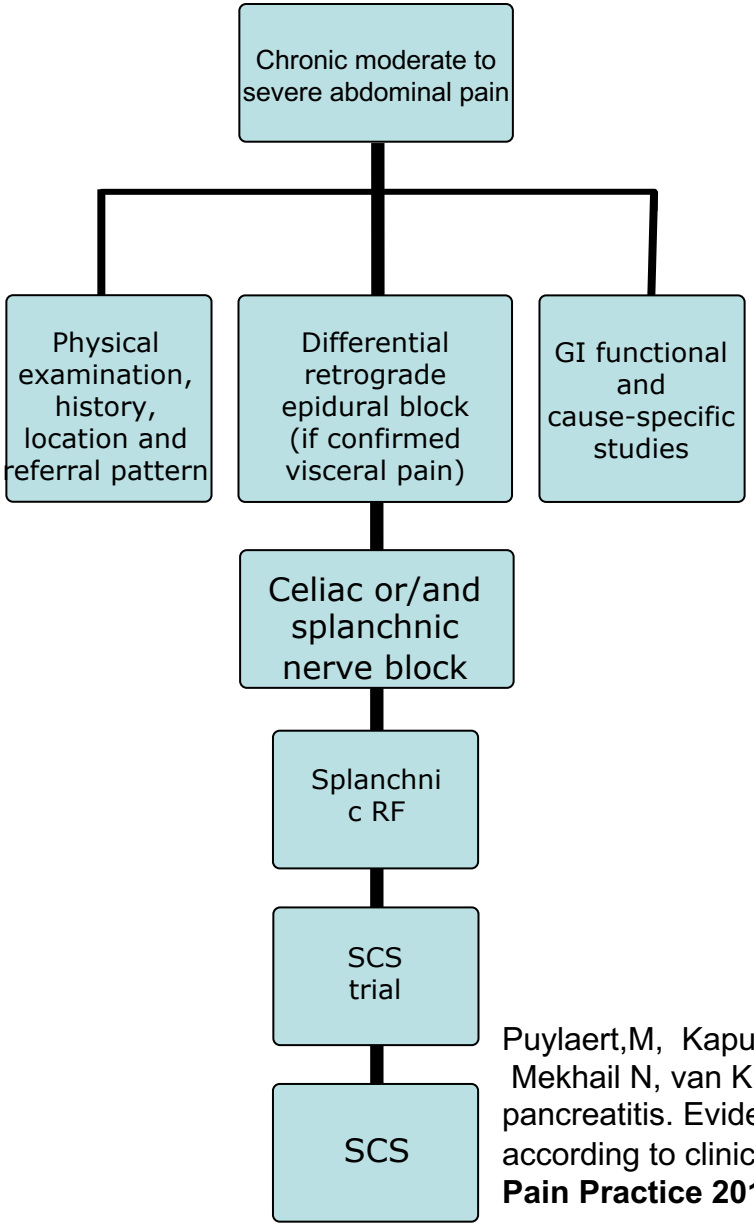

Puylaert,M, Kapural L, van Zundert J, Peek D, Lataster A, Mekhail N, van Kleef M, Keulemans Y. Pain in chronic pancreatitis. Evidence-based Interventional Pain Medicine according to clinical diagnoses.
Pain Practice 2011;11(5): 492-505.

Summary:

- Animal models of colorectal distension and irritant induced colonic sensitization suggest that SCS may ameliorate the effects of visceral hyperalgesia? (Greenwood-Van Meerveld,2003)

- Given the dismal history of conventional treatment for chronic visceral pain, our results suggest that SCS may be a very useful therapeutic optior

- Spinal cord stimulation for visceral pain requires additional research (prospective, randomized) to determine the efficacy and optimize patient selections

Thank you
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