

## Neuromodulation for Visceral Abdominal Pain

Leonardo Kapural, MD, PhD  
Clinical Research Director, Pain Management Department,  
Cleveland Clinic  
Associate Professor of Anesthesiology, CCLCM at Case Western

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### Disclosure

- Investigator or co-investigator on multiple neuromodulation studies
- Consultant St Jude Medical and Boston Scientific



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### 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
- Strong affective responses
- 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.

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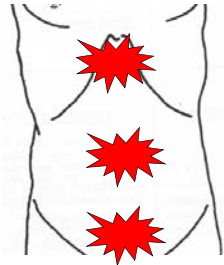
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## History

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




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## Referred Pain

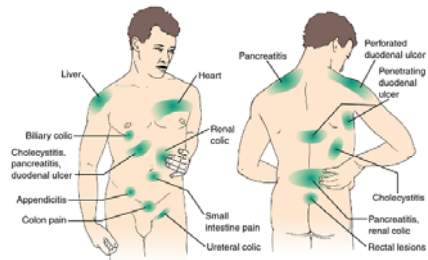


Figure 34-3 Correlation sites of referred abdominal pain.

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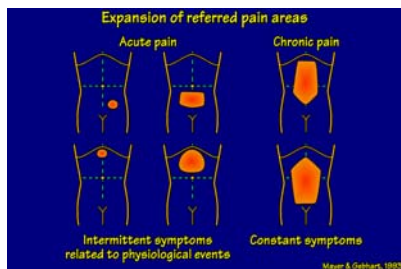
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Slide: Thanks to Dr. Arendt-Nielsen

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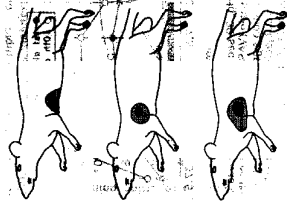
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### Visceral Hyperalgesia

- 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)




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### Manifestations of visceral hyperalgesia

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

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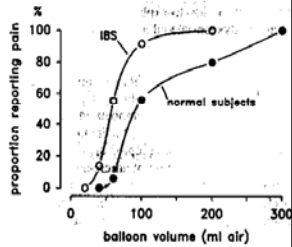
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### Visceral hyperalgesia

- 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




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### 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

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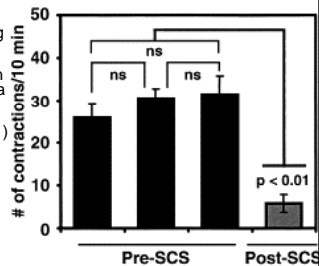
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### SCS strongly suppressed abdominal reflex contractions induced by nociceptive levels of colorectal distention

- 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)



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### 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).
- Recently described 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.

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**Studies-case series:**

- Mesenteric Ischemia (Ceballos et al, 2000)
- Irritable Bowel Syndrome (Krames, 2005)
- Epigastric abdominal pain (Khan, 2005)
- Gastroparesis (Tiede et al., 2006)
- Pelvic visceral pain (Kapural et al., 2006)
- Familial Mediterranean fever (Kapur et al, 2006)
- Non-alcoholic pancreatitis (Kapural, 2008; Kim et al 2009)



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**SCS for visceral pelvic pain**

Kapural et al, 2006

- 6 female patients severe visceral pelvic pains.
- Treated for an average of 14.8 years (from 4 to 38)
- series of hypogastric blocks (in average 5.3)
- All received SCS systems with two leads implanted
- Pain Disability Index (PDI) questionnaires before the implant and recently following implant
- Opioid use calculated as MSO4 milligram equivalents.



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Patient	Age	Years of pain	Diagnosis	Symptoms	Previous invasive Treatments	Differential block	Trial (days)	Stim (months)
No1	32	12	Vulvar vestibulitis	Pelvic pain, dyspareunia	Surgeries,Hypogastric LA+neurolytic (PHE)	Visceral	14	55
No2	58	38	Endometriosis, pelvic adhesion	Pelvic pain	Surgeries,Hypogastric LA+neurolytic (PHE)	Visceral	10	12
No3	45	14	Utero-vag prolapse, pelvic adhesions	Pelvic pain, rectal pain	Surgeries,Hypogastric LA	none	7	19
No4	31	10	Vulvodynia, endometriosis,pelvic adhesion	Pelvic pain, dyspareunia	Surgeries,TAH, Hypogastric LA	none	7	70
No5	35	11	Endometriosis, pelvic adhesion	Pelvic pain	Surgeries,Hypogastric LA	Visceral	8	18
No6	48	4	Urinary retention, pelvic adhesion	Pelvic pain, urinary urgency	Surgeries,Hypogastric LA+neurolytic (PHE)	Visceral and SS	14	10



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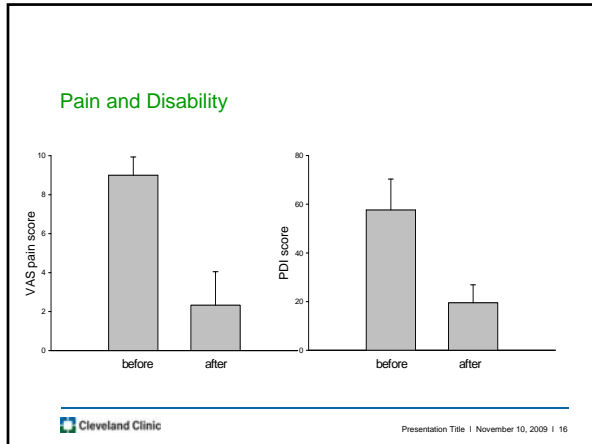
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- ### Results:
- follow-up was 30.6 months
  - Median VAS pain score decreased from 8 to 3.
  - All patients > 50% of the pain relief
  - PDI changed from 58 to 19.7
  - Opioid use decreased from 22.5 to 6.6 mg of MSO4 equivalent per day
  - Two revisions (lead migration) but if calculated per years of SCS- one revision per 2.6 years of stimulation.
- Cleveland Clinic  
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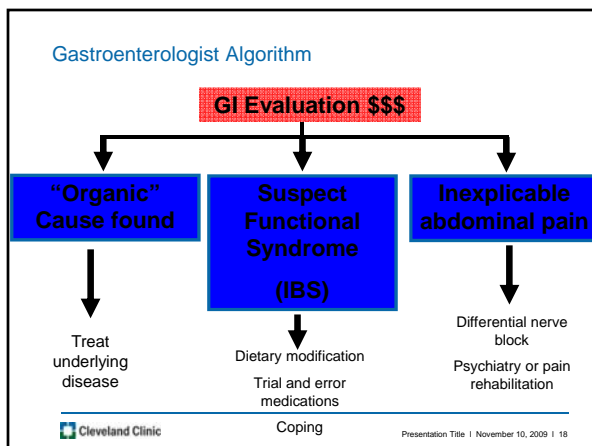
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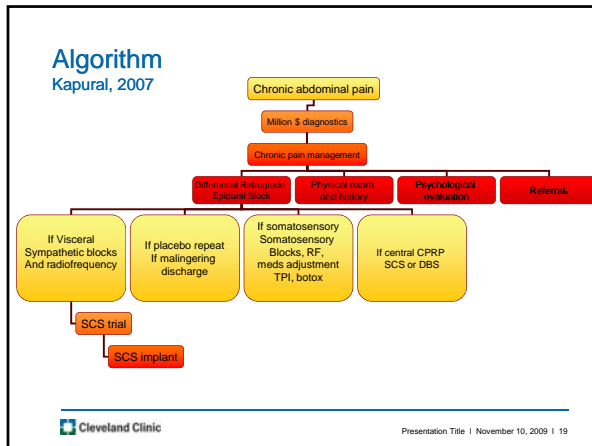
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- ### Establishing diagnosis of visceral abdominal pain
- Differential retrograde epidural block
  - Sympathetic block
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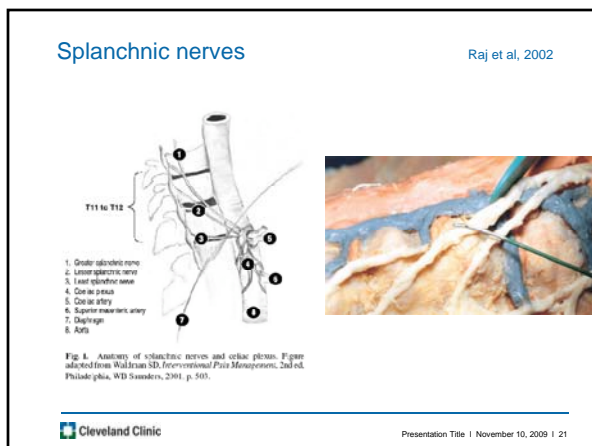
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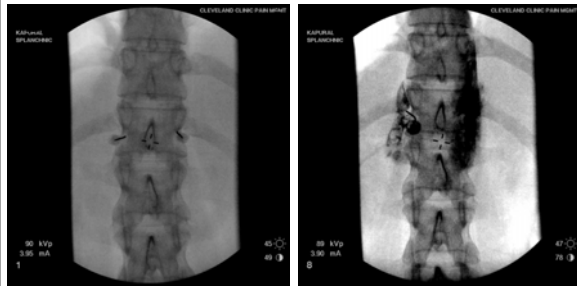
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## Splanchnic Block



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## Retrospective study –SCS for abdominal visceral pain (Kapural et al., in press Pain Medicine)

- 35 patients; Age 17-87; 44±15 (median 46) years
- 12 man; 23 women
- Chronic abdominal pain duration from 1-25 years
- Location: 1. epigastric (19)
- 2. RUQ (5)
- 3. LUQ (6)
- Aching, burning, stabbing, sharp

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Patient	Age	Sex	Diagnosis	Years of pain	Location of pain	h/o depression	h/o alcohol abuse	h/o drug abuse	Type of pain (diff)	Response to sym (%)
1	61	F	adhesions	13	LUQ/stab	-	-	-	Visc	100
2	48	M	mesenteric, gastroparesis	10	EP/stab	-	-	-	Visc	80
3	50	M	Pancreatitis	9	EP/ach	Yes	Yes	Yes	Mixed	30
4	50	M	Pancreatitis	25	DIFF/ach	Yes	-	-	Mixed	40
5	30	F	Pancreatitis	2	EP/ach	-	-	-	Visc	100
6	46	M	Pancreatitis	7	EP/ach	Yes	-	-	Visc	100
7	35	M	Pancreatitis	10	EP/ach	Yes	-	-	Visc	100
8	23	F	Pancreatitis	10	EP/sharp	Yes	-	-	Visc	100
9	36	F	Adhesions	5	LUQ/burn	Yes	-	-	Visc	100
10	50	F	Pancreatitis	8	RUQ/ach	-	-	-	Visc	0
11	41	F	Pancreatitis	13	EP/ach	-	-	-	Visc	50
12	35	F	Pancreatitis	3	EP/sharp	Yes	-	-	Visc	80
13	50	M	Pancreatitis	8	EP/sharp	-	-	-	Visc	n/a
14	22	F	Pancreatitis	2	RUQ/stab	-	-	-	Visc	50
15	21	F	Pancreatitis	10	RUQ/sharp	Yes	-	Yes	Visc	80
16	52	F	Pancreatitis	10	EP/ach	Yes	Yes	-	Visc	50
17	21	F	Pancreatitis	10	RUQ/sharp	-	-	-	Visc	50
18	52	F	Adhesions	7	LUQ/sharp	Yes	Yes	-	Visc	100
19	37	F	Pancreatitis	8	LUQ/ach	-	-	-	Visc	100
20	44	M	Pancreatitis	6	EP/ach	Yes	Yes	-	Visc	100
21	35	M	Pancreatitis	10	EP/ach	-	-	-	Visc	70
22	22	F	Pancreatitis	4	LUQ/ach	-	-	-	Visc	50
23	59	F	Pancreatitis	2	RUQ/ach	-	-	-	Visc	50
24	22	F	Pancreatitis	6	LUQ/sharp	-	-	-	Visc	50
25	56	F	Pancreatitis	10	EP/ach	Yes	-	-	Visc	100
26	46	F	Pancreatitis	4	LUQ/sharp	Yes	-	-	Visc	100
27	50	F	adhesions, mesenteric	1	EP/sharp	-	-	-	Visc	100
28	74	F	Adhesions	1	EP/sharp	Yes	-	-	Visc	100

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Causes:

- non-alcoholic, idiopathic, and alcoholic chronic pancreatitis
- long-standing abdominal adhesions from multiple abdominal surgeries
- mesenteric ischemia
- gastroparesis
- post-gastric bypass surgery epigastric pain

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Retrospective study (Kapural et al, in press Pain Medicine)

- h/o depression 18 patients
- h/o alcohol abuse 7
- Psych evaluation and IDC passed
- Differential block visceral (3 mixed visceral/central)
- Splanchnic or hypogastric block (50-100% pain relief)

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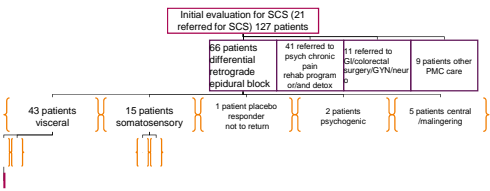
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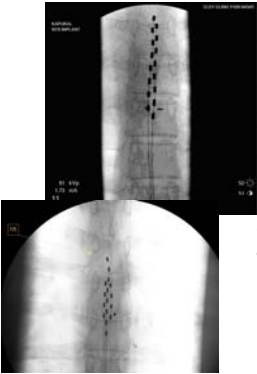
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### Lead placement



- Entry point T10-11 or higher
- Tip placed at T5 or lower
- We regularly achieve paresthesias over the painful areas
- Midline placement

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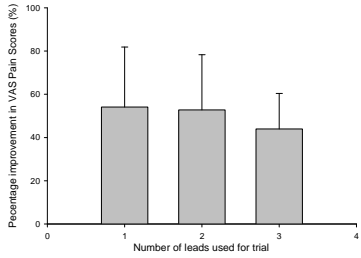
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### Number of leads during trial and pain relief



Number of leads used for trial	Percentage improvement in VAS Pain Scores (%)
1	~55
2	~52
3	~45
4	0

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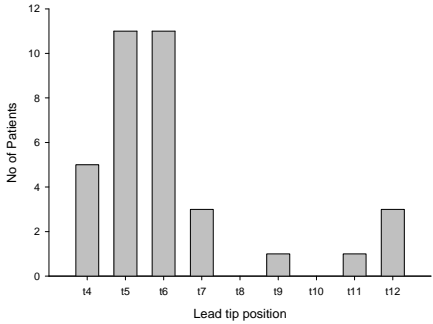
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### Lead tip position



Lead tip position	No of Patients
T4	5
T5	11
T6	11
T7	3
T8	0
T9	1
T10	0
T11	1
T12	3

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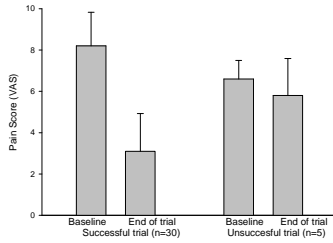
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### Trial success



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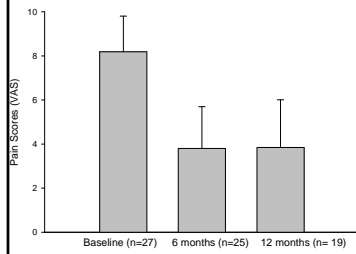
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### Pain relief



- 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

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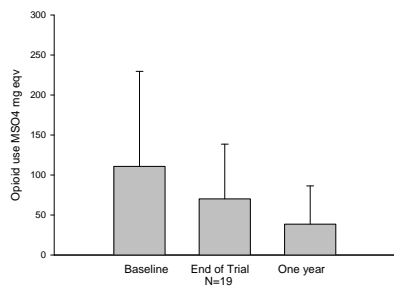
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### Opioid use (Morphine equivalents)



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### Conclusions:

- encouraging -30 out of 35 patients responded to a trial; 28 proceeded to implantation
- 14% failed to improve during trial- much better than trialing in post-laminectomy syndrome, chronic radiculopathy or CRPS
- Patient selection may be a key factor
- Chronic abdominal pain-heterogeneous patient populations including somatization disorders and opioid misuse
- Psychological overlay, secondary gain issues, unexplained source of the abdominal pain and opioid dependence/tolerance, all may be the negative predictors of any treatment success for chronic abdominal pain
- 5 patients failed SCS trial and 1 patient who requested removal of SCS system 6 months into the treatment-few shared group characteristics
- poor response to sympathetic nerve block

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### Survey (under review)

#### 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-epinal 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: \_\_\_\_\_

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### Survey (under review)

- 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, opioids, 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

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### Survey (under review)

- Conservative: most of the patients opioids
- membrane stabilizers, antidepressants
- Interventions: sympathetic blocks prevailed (only 53%)
- pancreatic resection, ileostomy closures, ERCP, gastric pacemakers (5 patients) and multiple laparoscopic adhesiolysis
- 62 out of 70 psychological evaluation
- Only 24 out of 70 (34%) evaluated by multidisciplinary committee for appropriateness of implantable devices

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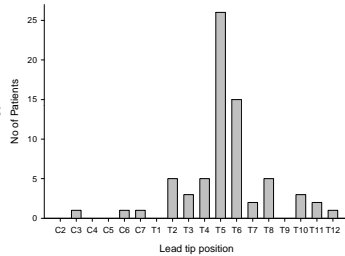
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### Survey (under review)-trial

- 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



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### Survey (under review)-permanent implant

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

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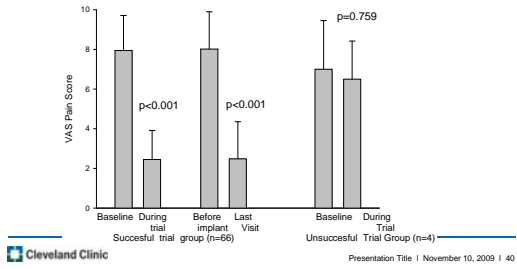
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Survey (under review)

- 4 failed SCS trial: VAS 7±2.4 to 6.5±1.9; p=0.759
- >50% in 66 of 70 patients(94%): 7.9±1.8 to 2.45±1.45 cm (p<0.001)
- Permanent: 8±1.9 to 2.49 ±1.9 cm (p<0.001)




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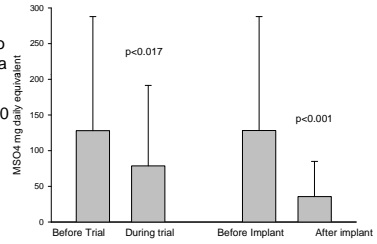
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Survey (under review)

- TRIAL: opioid use decreased from 128 mg to 79mg MSO4 equivalents a day
- PERMANENT: 158 mg (80 mg) to 36 mg (20 mg)



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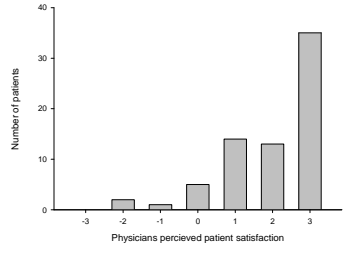
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Survey (under review)

- 8 revisions
- 2 removed-patient dissatisfaction (one diarrhea with SCS and other headache)



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Conclusions:

- SCS rarely used for this indication
- technical aspects consistent with our retrospective study
- Lead midline T5 and T6
- bias for pain physicians to participate in the survey if they had positive responses
- not clear if the sample size of the physicians being surveyed is sufficient enough

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Chronic pancreatitis-abstract

- 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  $8 \pm 1.6$  (SD), PDI=58, opioid use averaged  $165 \pm 120$  mg MSO4 equivalents
- During trial, VAS to  $3.67 \pm 2$  cm ( $p < 0.001$ ); opioid to  $105 \pm 101$  mg

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Chronic pancreatitis-abstract

- Six patients failed the trial
- one was lost to follow-up
- 18 followed > year
- 6 patients less than a year (n=3) or SCS removed due to infection or lead migration (n=3).
- 18 patients:
- VAS  $4.0 \pm 2.1$ ;  $p < 0.001$  at one year
- PDI= 28
- opioid use  $54 \pm 73$ mg morphine equivalents.

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

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Thank you  
[Kapural@ccf.org](mailto:Kapural@ccf.org)



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