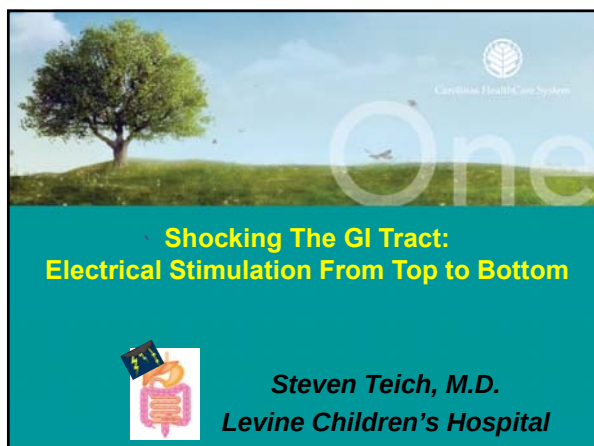




Cardinal HealthCare Systems

Shocking The GI Tract: Electrical Stimulation From Top to Bottom

 **Steven Teich, M.D.**
Levine Children's Hospital

Disclosures

I have the following financial relationship to disclose:

Endostim, Inc*

** Products or services produced by this company are relevant to my presentation.*

9/13/2015 2



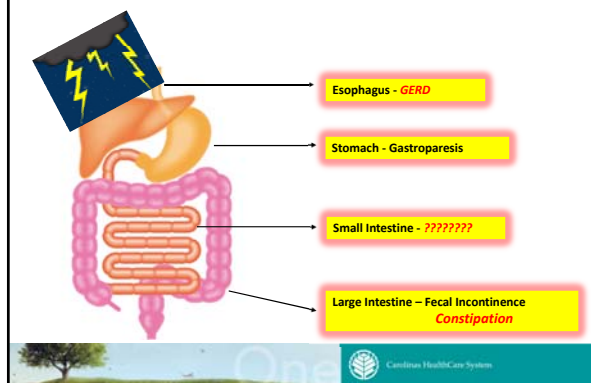
Objectives

1. Upon completion of this session, the learner will understand the history of GI tract stimulation.
2. Upon completion of this session, the learner will be able to state the indications and results of gastric stimulation in pediatric and adolescent patients.
3. Upon completion of this session, the learner will be able to state the indications and results of sacral nerve stimulation in pediatric and adolescent patients.
4. Upon completion of this session, the learner will understand esophageal stimulation for gastro-esophageal reflux disease and its potential use in the pediatric population.
5. Upon completion of this session, the learner will understand the barriers to stimulation of the small intestine.

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What Parts of The GI Tract Can We Stimulate



Gastroparesis Case Study

- 16 year old female who "had the flu" in October 2010
- Persistent nausea & abdominal pain with eating X 3 months
- Evaluated at The Cleveland Clinic
 - Colonoscopy
 - EGD X 2 → food from previous day
 - HIDA Scan X 2
 - Gallbladder Ultrasound
 - Abdominal CT
 - Gastric Emptying Study → "very abnormal"
- Medications
 - Erythromycin
 - Peritactin
 - Zofran
 - Levsin
 - Probiotic
 - Celexa

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Gastroparesis Case Study

- October 2011 presented to GI Motility Clinic for gastroparesis
 - Daily nausea and abdominal pain
 - Emesis once/month
 - No weight gain
 - Occasional blood in the stool
 - Hungry but hurts to eat

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Gastroparesis Case Study

- Botox November 2011 → felt great, gained 10 lbs
- Lasted 5 months then recurrent nausea and abdominal pain
- 4 more botox injections over the next year – decreasing length of clinical efficacy
- October 2012 underwent temporary and then permanent gastric stimulator
- June 2013 – gained 15 pounds
 - occasional nausea and abdominal pain
 - **No medications**

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Gastroparesis

Etiology

- Neuromuscular disorder of the stomach causing persistent symptoms of either nausea, pain, vomiting, early satiety or a combination of these that makes eating unpleasant or difficult
- Measurable abnormalities in electrical or mechanical function of the stomach

Symptoms

- Nausea
- Vomiting
- Bloating
- Early Satiety
- Fullness
- Pain worse after meals
- Weight Loss
- Malnutrition

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Etiology of Gastroparesis



- **Diabetes**
- Infection (virus, bacteria, protozoan, Giardia)
- Autoimmune disorder
- Surgery (gastric bypass, Whipple, cancer)
- Chemotherapy
- Pregnancy
- **Idiopathic**

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Gastroparesis

- 500,000 adults with Ulcerative Colitis
- 500,000 adults with Crohn's Disease
- 5,000,000 adults with gastroparesis
- **???? Number of children with gastroparesis**

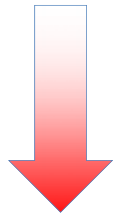
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Gastroparesis Treatments

- Explanation
- Gastroparesis Diet
- Motility agents
- Nutrition
- Pain control
- **Gastric Stimulation**



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Motility Agents

- Metaclopramide (Reglan) - side effects
- Erythromycin - short duration effectiveness
- Domperidone - not available
- Cisapride (Propulsid) - not available
- Zelnorm - not available

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Maintaining Nutrition

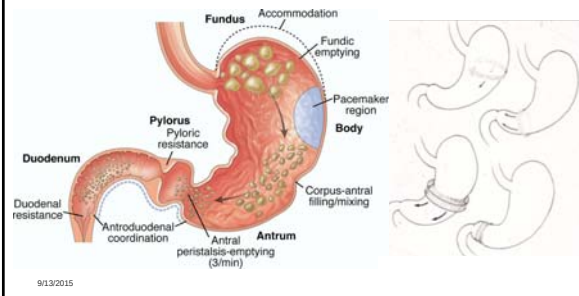
- Gastroparesis Diet
- Surgery
 - Jejunostomy Tube
 - Gastrostomy or Gastro-jejunostomy tubes
 - Central Venous Line & TPN

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Gastric Peristalsis



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Enterra System Components

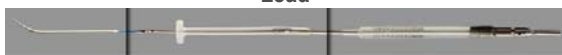
Programmer



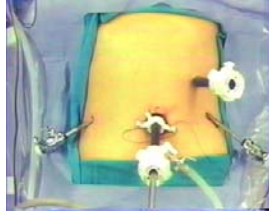
Pulse Generator



Lead



Open vs. Laparoscopic Surgery

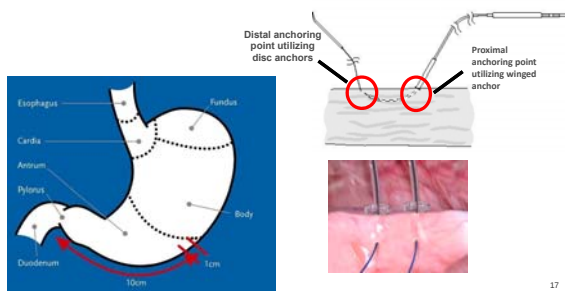


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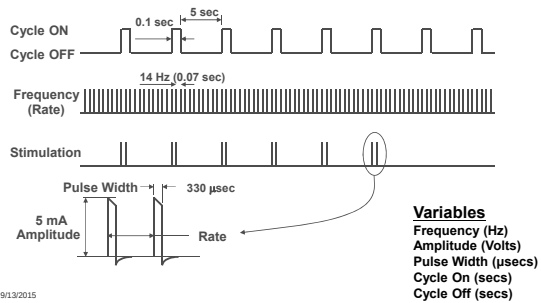
Gastric Stimulator - Lead Implantation



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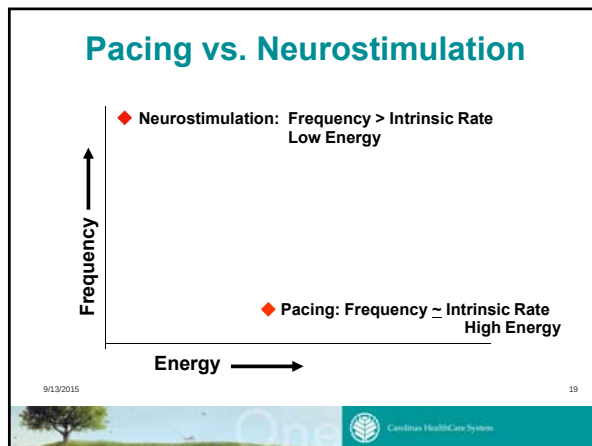


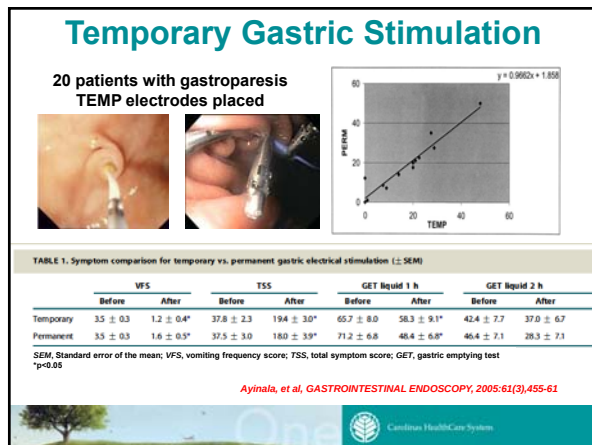
Stimulation Parameters

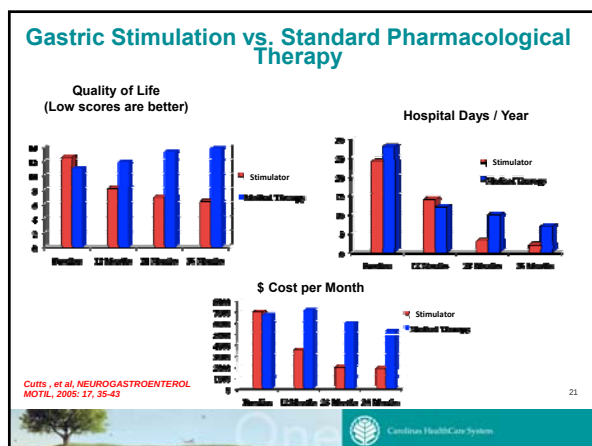


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Symptom Monitor

Symptom	Frequency	Severity
Vomiting	0 = absent	0 = absent
Nausea	1 = rare	1 = mild (not influencing usual activities)
Early satiety	(1 time/week)	2 = moderate
Bloating	2 = occasional	(diverting from, but not modifying activities)
Postprandial fullness	(2-4 times/week)	3 = severe (influencing usual activities, modifies activities)
Epigastric pain	3 = frequent	4 = extremely severe (bed rest)
Epigastric burning	(5-7 times/week)	
	4 = extremely frequent (>7 times/week)	

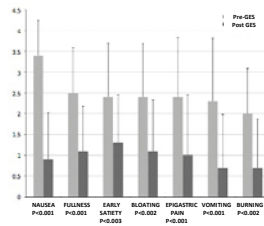
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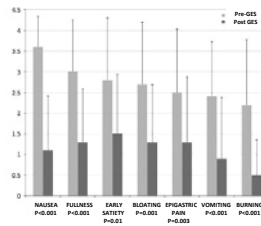


Gastroparesis in Adolescents

Symptom Severity



Symptom Frequency



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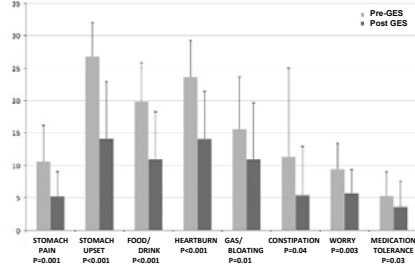
Lu, Teich, et al, *NEUROGASTROENTEROL MOTIL*, 2013; 25, 567-e456

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Gastroparesis in Adolescents

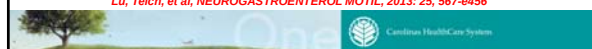
PedsQL GI Symptoms



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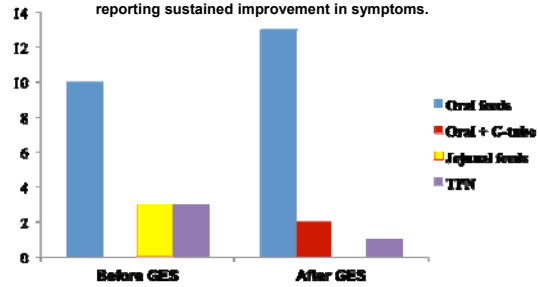
Lu, Teich, et al, *NEUROGASTROENTEROL MOTIL*, 2013; 25, 567-e456

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Follow-up and Feeding Pattern

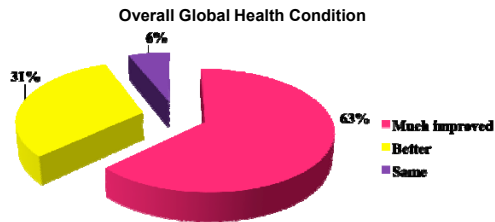
Follow-up ranged from 0.5 to 23 months, with 13/16 pts reporting sustained improvement in symptoms.



9/13/2015 Teich, Mousa, et al, JPEDSURG, 2013:48, 178-183

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Outcome / Complications



GES was complicated with cellulitis in 1 patient and superficial tenderness in 2 patients.

9/13/2015 Teich, Mousa, et al, JPEDSURG, 2013:48, 178-183

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Proposed Mechanisms of Action

- Action on afferent fibers which inhibit the vomiting center or influence symptom perception in the brain or promote fundic relaxation through nonvagal nitrenergic pathways
- Decreases sensitivity to gastric distention and enhances gastric accommodation
- Symptom improvement not due to entrainment of slow waves or correction of underlying slow wave dysrhythmias
- ???????????

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Constipation Case Study

- 16 year old male born with high imperforate anus
- Cecostomy since 6 years of age
- On nightly washouts of NS and GoLyteLy
- Tired of nightly washouts
- Wants to be like other teenagers

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Constipation Case Study

- Underwent temporary then permanent sacral nerve stimulator
- Nightly washouts got much faster
- Within few weeks he could sense when he had to have a bowel movement
- Gradually developed ability to hold bowel movement
- After 6 months he was off all washouts and on NO oral medications
- Cecostomy closed within 1 year of SNS placement

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Treatment Options for Fecal Incontinence

- Conservative treatments
 - Dietary changes
 - Anti-diarrheal medications (e.g. loperamide)
 - Biofeedback
 - “Bowel Regimen”
- Surgical options
 - Colostomy
 - Cecostomy tube with antegrade enemas/washouts

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Indications for SNS

- Intractable bowel or bladder dysfunction
 - Chronic constipation
 - Fecal incontinence
 - Urinary retention
 - Urinary incontinence
- Failure of medical therapy

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Dysfunctional Elimination Syndrome (DES)

- Symptoms associated with
 - Gastrointestinal function
 - Urinary function
- Patients with no known neurologic disorder
- Patients with congenital anomalies have similar presentation
 - Result of the anomaly itself
 - Secondary to surgical repair
 - e.g. imperforate anus, cloacal anomaly

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Sacral Nerve Stimulator (SNS)

- An established therapy that expands treatment options for patients with chronic fecal incontinence who have failed or are not candidates for more conservative treatments.
- Stimulator lead placed within 3rd sacral foramen using the Seldinger technique
 - Placement confirmed with fluoroscopy in OR
 - Signal generator/battery placed in subcutaneous pocket over buttock



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History of Sacral Nerve Stimulation

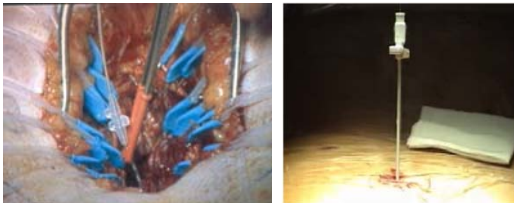
- 1981 – Department of Urology, University of California at San Francisco initiated clinical program.
- 1985-1992 – Multi-center trial conducted by UroSystems, Inc.
- 1994 – Medtronic gets approval to market InterStim in Europe for treatment of urge incontinence, retention and urgency/frequency.
- 1997 – FDA approval of the InterStim System for treatment of urge incontinence in the US.
- 1999 - FDA approval of the InterStim System for treatment of symptoms of urgency/ frequency and urinary retention.
- 2002 – FDA approval of timed lead
- **2012- FDA approval of Interstim System for treatment of fecal incontinence**
- **Over 250,000 implants worldwide**

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Advancements in Lead Placement



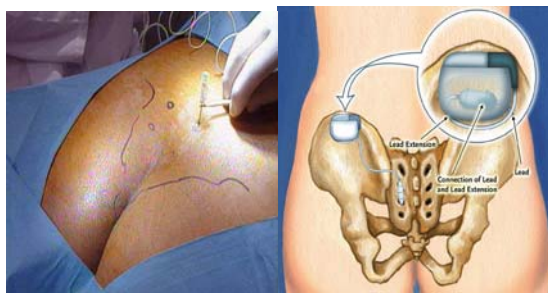
Chronic lead implantation transitioned from requiring a four inch incision to a minimally invasive 0.5 to 1 inch incision using the timed lead and lead introducer

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Implant Procedure



Possible Mechanisms of Action of SNS

- Electrical stimulation of the pelvic floor via the pelvic plexus and pudendal nerve excites the autonomic and somatic nervous systems and cause both direct and reflex-mediated responses to fecal incontinence mechanism
- Increased anal sphincter resting and squeeze pressures
- Increase in colonic peristalsis
- Changes in cortico-anal excitability

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How SNS Works

- Increases external sphincter and pelvic floor tone*
- Increases colonic motility**
- Increases sensory function of rectum and anus***

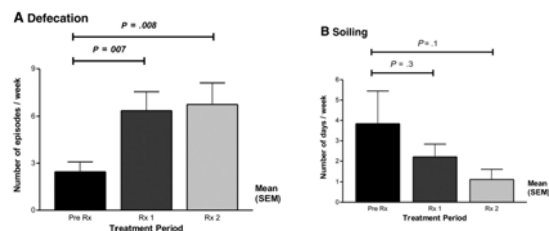
*Rosen HR, Urbarz C. Sacral nerve stimulation as a treatment for fecal incontinence. *Gastroenterology* 2001; 121:536-41.
 **Dinning PG, Fuentetaja SE. Sacral nerve stimulation induces pan-colonic propagating pressure waves and increases defecation frequency in patients with slow-transit constipation. *Colorectal Dis* 2006; 9:123-32.
 ***Brookes SJ, Dinning PG. Neuroanatomy and physiology of colorectal function and defaecation: from basic science to human clinical studies. *Neurogastroenterol Motil* 2009; 21 (Suppl. 2):9-19.

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Transabdominal Electrical Stimulation and Colonic Motility

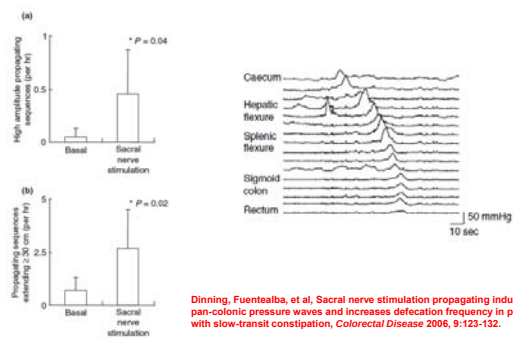


Ismail, Chaso, et al. Daily transabdominal electrical stimulation at home increased defecation in children with slow-transit constipation: a pilot study. *Journal of Pediatric Surgery* 2009; 44:2388-2392.

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SNS and Colonic Motility



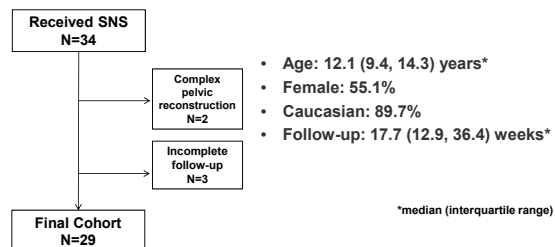
Dinning, Fuentealba, et al, Sacral nerve stimulation propagating induces pan-colonic pressure waves and increases defecation frequency in patients with slow-transit constipation, *Colorectal Disease* 2006, 9:123-132.

SNS in Children

	SNS placement participants (<i>N</i> = 29)
Male, <i>n</i> (%)	13 (44.9)
Race, <i>n</i> (%)	
White	26 (89.7)
Non-white	3 (10.3)
Age, median [IQR]	12.1 (5.4, 14.3) years
Symptoms, <i>n</i> (%)	
Gastrointestinal	27 (93.1)
Urinary	19 (65.5)
Both	17 (58.6)
History, <i>n</i> (%)	
Idiopathic	19 (65.5)
Hirschsprung's disease	1 (3.4)
Syrinx	1 (3.4)
Imperforate anus	8 (27.6)
With tethered cord	1 (3.4)
With myelomeningocele	1 (3.4)

Teich, Mousa, Sulkowski, et al., Sacral nerve stimulation: a promising therapy for fecal and urinary incontinence and constipation in children. *J Pediatric Surgery* 2015; in press

Cohort



Teich, Mousa, Sulkowski, et al., Sacral nerve stimulation: a promising therapy for fecal and urinary incontinence and constipation in children. *J Pediatric Surgery* 2015; in press

Indications

- 93.1% of patients had GI symptoms
 - 11 had cecostomy
 - 8 born with imperforate anus
- 65.5% of patients had urinary symptoms
 - 11 taking anticholinergic medications
 - 4 performing intermittent bladder catheterizations

Teich, Mousa, Sulkowski, et al., Sacral nerve stimulation: a promising therapy for fecal and urinary incontinence and constipation in children. *J Pediatric Surgery* 2015; in press

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Functional Outcomes

- 6 patients (55%) no longer use cecostomy
 - 1 additional patient with significant decrease in antegrade enemas
- 10 patients (91%) no longer take anticholinergic medications
- **All 8 patients with imperforate anus had cecostomy pre-SNS**
 - **5 (63%) closed or no longer used**

Teich, Mousa, Sulkowski, et al., Sacral nerve stimulation: a promising therapy for fecal and urinary incontinence and constipation in children. *J Pediatric Surgery* 2015; in press

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Patient-Reported Outcomes

Total Cohort (N=29)	Pre-SNS	Post-SNS	P-value
Fecal Incontinence Quality of Life Scale			
- Lifestyle	3.0 (2.2, 4.0)	3.8 (3.1, 4.0)	0.002
- Coping/Behavior	2.8 (1.9, 4.0)	3.8 (3.0, 4.0)	0.001
- Depression/Self-perception	3.3 (2.6, 4.1)	4.1 (3.7, 4.4)	<0.001
- Embarrassment	3.0 (1.7, 4.0)	3.7 (2.3, 4.0)	0.005
Fecal Incontinence Severity Index	15 (13, 17)	18 (14, 21)	0.006
PedsQL™ GI Symptom Scale	13 (7, 21)	8 (3, 14)	0.003
Vancouver DES Symptom Score	17 (8, 26)	10 (7, 21)	0.029

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Conclusions

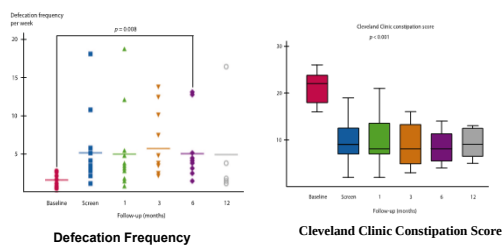
- SNS therapy produces improvements in
 - Bowel dysfunction
 - Urinary dysfunction
- Well tolerated
- Safe, effective treatment

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Clinical Efficacy in Adolescent Constipation

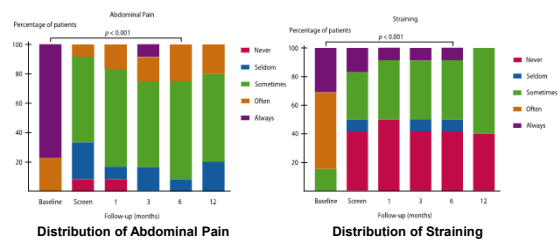


Van Wunnik, et al., Sacral Neuromodulation Therapy: A Promising Treatment for Adolescents With Severe Refractory Functional Constipation. *Dis Colon Rectum* 2012; 55:278-285

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Clinical Efficacy in Adolescent Constipation

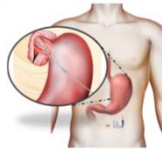
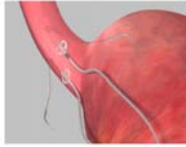


Van Wunnik, et al., Sacral Neuromodulation Therapy: A Promising Treatment for Adolescents With Severe Refractory Functional Constipation. *Dis Colon Rectum* 2012; 55:278-285

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Electrical Stimulation of the LES



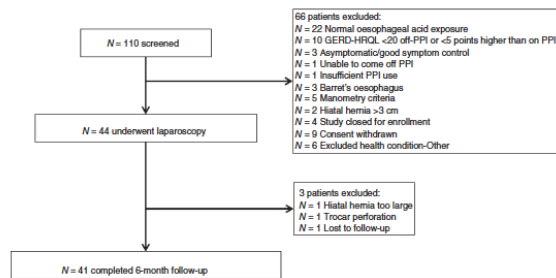
INCLUSION CRITERIA

- Age 21-80 years
- History of heartburn or acid, regurgitation or both
- Continued daily use of PPI for ≥ 12 months prior to enrollment
- Continued symptoms in spite of acid suppression therapy prompted consideration of alternative therapy for GERD
- Baseline GERD-HRQL score of ≥ 20 following 10-14 days off-PPI, and at least 5 points higher than the on-PPI score
- Excessive esophageal acid exposure during 24 hr pH monitoring of acid suppression therapy (pH<4 for $\geq 5\%$ of total time)
- Resting LES end-expiratory pressure ≥ 5 mm Hg

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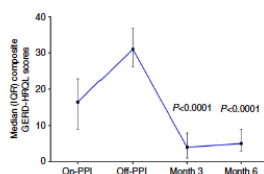
Electrical Stimulation of the LES



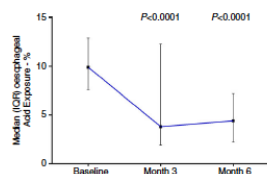
Kappelle WF, Bredenoord AJ, Electrical stimulation therapy of the lower oesophageal sphincter for refractory gastro-oesophageal reflux disease – interim results of an international multicentre trial, *Aliment Pharmacol Ther* 2015; in press

Electrical Stimulation of the LES

Change in GERD Health-Related Quality of Life Composite scores

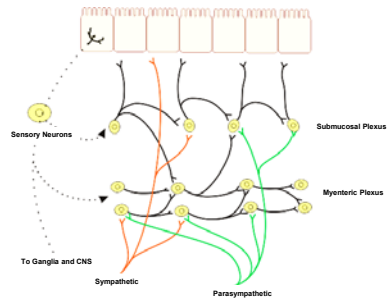


Change in Distal Esophageal Acid Exposure



Kappelle WF, Bredenoord AJ, et al, Electrical stimulation therapy of the lower oesophageal sphincter for refractory gastro-oesophageal reflux disease – interim results of an international multicentre trial, *Aliment Pharmacol Ther* 2015; in press

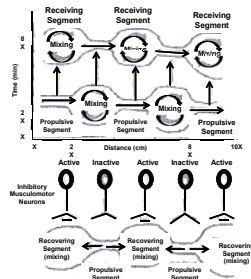
Small Bowel Autonomic Innervation



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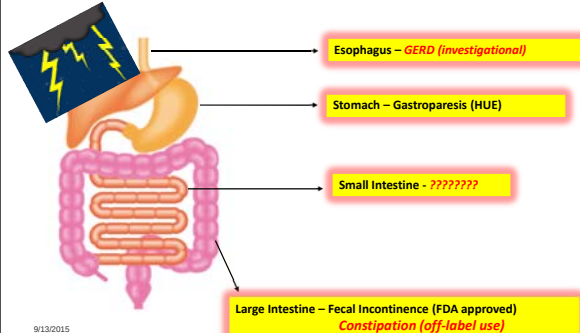
Small Bowel Autonomic Innervation



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What Parts of The GI Tract Can We Stimulate



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Questions????



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