Technology Response:
Gastrointestinal System

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**Short term and Long-term** electrical stimulation of the lower esophageal sphincter increases sphincter pressure in patients with GERD

**Short laparoscopic procedure**

Minimal impact on gastro-esophageal junction (GEJ) minimizes GI side effects

**Adjustable treatment algorithms**

Default recommended settings with capability to non-invasively adjust to changes in patient symptoms over time

**Pulse width 200us, frequency:**

20Hz, Amp 5-15mA

Rodríguez L¹, Rodríguez P, Neto MG, Ayala JC, Saba J, Berel D, Conklin J, Soffer E. Neurogastroenterol Motil. 2012-2013 May;24(5):446-50
Gastroparesis: Diagnosis and Treatment Algorithm

Etiologies of Gastroparesis

Mild
- Less than daily symptoms, no hospitalizations, no impact on work and family functioning
- Liquid or soft diet, glucose control, antiemetics prn, review of medications and metabolic state

Moderate
- Daily symptoms, not continuous, occasional hospitalization, and some interference with work and family functioning
- Diet, prokinetics, one or more antiemetics and glucose control, also question addressing pain and psychological aspects

Severe
- Daily, continuous symptoms, multiple ED/hospitalizations, and inability to work and function
- Diet, combining prokinetics, multiple antiemetics, try to minimize or stop narcotics, feeding tube, research
- Inadequate response to therapy
- Gastric electrical stimulation device placement combined with pyloroplasty +/- jejunostomy tube placement

J-Tube Trial
Botulinum pyloric injection trial in post vagotomy and idiopathic
Gastric Electrical Stimulation (GES) / Enterra Device

- Implantable neurostimulator: Medtronic Itrel 3 Model 3116
- Neuromuscular leads (2): Medtronic model 4351

Stimulation Parameters

- Amplitude: 5 milliamps
- Pulse Width: 330 µsec
- Rate: 14 Hz
- Cycle On Time: 0.1 sec
- Cycle Off Time: 5.0 sec
Results of Double Blind Trials with Enterra in Gastroparesis.

Abell T, McCallum RW et al; Gastroenterology 2003; 421-8

McCallum RW et al; Clinical Gastroenterology and Hepatology 2010;8:947-54
McCallum RW et al; Neurogastroenterology and Motility 2013;25:10; 815-e636
Conclusions

- There were no significant symptom differences observed in the double-blind crossover phase between ON and OFF.
  - One explanation is that the initial 6 week ON period rendered the subsequent double-blind data null.
  - The magnitude and duration of symptom reduction suggest that regression to the mean or a placebo effect are unlikely explanations for the overall results.
  - Cross over design is not appropriate for future studies
  - Best trial design is to randomize patients at time of surgery for the gastric stimulator to be turned on or off in a parallel fashion for a period of 3-6 months.
Comparison of Total Symptom Scores (TSS)

Diabetic Group | Idiopathic Group | Postsurgical Group
---|---|---
Baseline: Mean TSS | 1 year of GES: Mean TSS

*P<0.05 compared to baseline
Mechanisms of Action of Enterra

- No effects on gastric slow waves or gastric emptying
- Does not accelerate gastric emptying
- Increases vagal nerve activity
- Relaxes proximal stomach
- Main role is influencing CNS control of nausea and vomiting
Interstitial Cells of Cajal (ICC)

Propagation of slow waves in ICC network

Spontaneous activation of pacemaker current

Electrotonic conduction of slow waves

Depolarization and activation of L-type Ca\(^{2+}\) channels

Neural input to ICC and conduction to smooth muscle

K.M. Sanders et al., Neurogastroenterol Mot. 1999; 11: 331-338
These images were taken at 160 magnification of formalin preserved full-thickness 1 cm² surgically obtained gastric biopsies with staining of CD117. (A) An example of normal numbers of interstitial cells of Cajal (ICC) which is 20 ± 10 (mean ± 2SD) cells per high powered field (HPF). (B) An example of depleted numbers of ICC (less than 10 cells/HPF).
The addition of pyloroplasty as a new surgical approach to enhance effectiveness of gastric electrical stimulation therapy in patients with gastroparesis.

Surgical Pyloroplasty

Gastric Pacing vs. Neurostimulation

- **Neurostimulation:** Frequency > Intrinsic
  - Low Energy (microseconds)

- **Pacing:** Frequency ~ Intrinsic
  - High Energy (milliseconds)

(12 cpm)
Serousal Recording Before, During and After Low-Frequency Stimulation

(3 cpm, 4 mA, 300 ms)

Baseline Tachygastria (>3.5 cpm)

Stimulation initiated

- The four pairs of pacing wires are placed on the serosa of the stomach along the great curvature, at an interval of 2–3 cm.
- The most distal electrodes are placed 2 cm above the pylorus.

Single-channel stimulation electrodes
Depiction of Location of Gastric Electrodes

For multi-channel gastric pacing

Stimulation electrodes

Recording electrodes

1. 15-16 cm from pylorus
2. 11-12 cm from pylorus
3. 3-4 cm from pylorus
4. 7-8 cm from pylorus

Enterra Device

Multipoint gastric pacemaker (MGP)
Example of baseline tachygastric slow waves (4.5 cpm) recorded from 2\textsuperscript{nd} and 4\textsuperscript{th} pairs of serosal electrodes

Slow Waves Normalized to 3.5 cpm after Two-channel Pacing initiated (3.5 cpm, 200ms, 2mA at 1\textsuperscript{st} Channel and 0.5 mA at 3\textsuperscript{RD} Channel) (MGP101D)
Transcutaneous Electrical Acupuncture (TEA) in Gastroparesis - Nausea and Vomiting

Irene Sarosiek¹, Yan Sun², Jiande Chen², Richard McCallum¹

- Neural activity source reconstruction during visual stimulation.
- A large activation of the right inferior frontal gyrus can be seen. Activation of parietal lobe is also evident.

EEG data
Theoretical Approach to Treat Obesity through Electrical Stimulation

Retrograde gastric pacing
6-8 cycles per min
Inhibits Gastric Motility

Pacing duodenum at > 15 cycles per min

Development of innovative techniques for the endoscopic implantation and securing of a novel, wireless, miniature gastrostimulator

What is InterStim® Therapy?

• Electrical stimulation of sacral nerves
• Sacral nerves provide the most distal common autonomic and somatic nerve supply to the pelvic floor, detrusor muscle and lower GI tract.
• Indicated for management of functional disorders of the lower urinary and intestinal tract such as urinary and fecal incontinence.
InterStim® Therapy for Fecal Incontinence

Step 1 - Temporary implant
Simple outpatient procedure

• Evaluate nerve integrity and therapy benefit
InterStim® Therapy for Fecal Incontinence

Step 2 – Permanent implant

• Lead implanted at level S3 or S4

• Stimulator placed in subcutaneous pocket

• Generally one night hospital stay
Follow-Up Results
Fecal Incontinence Episodes (weekly average)

Paired t-test, p<0.05 is considered statistically

Investigational Device: Not Approved in the U.S.
Gastrointestinal Electrical Stimulation
Current and Future Directions

Dr. Richard McCallum
Thank you
Conclusions:

1) In drug-refractory GP the addition of pyloroplasty (PP) to GES substantially accelerated GET;
2) The GET response in post-vagotomy group was the most impressive;
3) GES improves nausea and vomiting by central control effects while PP normalizes gastric emptying which improves the other postprandial symptoms;
4) PP added to GES may sustain better long term symptoms control in gastroparesis.