

EndoStim® Anti-reflux Therapy

EndoStim is a revolutionary minimally invasive, low-energy, personalized esophageal stimulation device

A smart therapy

Normalizes the function of the lower esophageal sphincter through neuromodulation; therapy can be personalized for each patient

Gentle procedure

Preserves natural anatomy to avoid typical gastro-intestinal side effects of traditional anti-reflux surgery

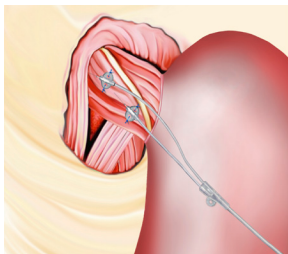
Safe and effective

Excellent clinical outcomes in trials and in standard clinical practice. Most patients experience:

- ✓ Resolution of regurgitation and heartburn
- ✓ Significant improvement in sleep issues related to reflux
- ✓ Elimination of dependency on PPI medication
- ✓ Long-term normalization of acid exposure and sphincter function

EndoStim has been used successfully in Germany and worldwide for several years and is now enrolling patients in a registry clinical trial.

The EndoStim Procedure



1 Attach electrodes by two stitches to the anterior esophagus



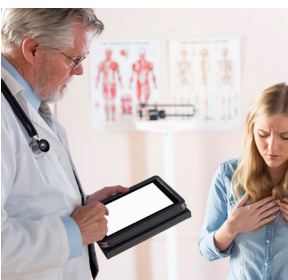
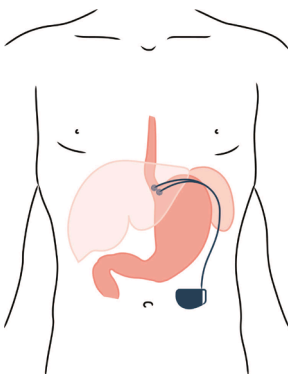
2 Connect the electrodes to the EndoStim stimulator



3 Begin stimulation therapy



4 Annual follow-ups
Wirelessly adjust therapy if needed



The Lost Reflux Patient

Studies recently confirmed that approximately 30% of reflux patients are not adequately treated on PPI therapy alone.

Some of these patients suffer from debilitating symptoms despite PPI use, such as:

- sleep disruption
- ongoing regurgitation
- ongoing heartburn
- vocal impairment
- respiratory complications

Many of these patients have not yet been given the opportunity for specific reflux diagnostics nor additional therapy options aside from their PPI.

Electrical stimulation technology that has transformed cardiac rhythm and pain management is now offered as a new minimally-invasive treatment for reflux that can normalize esophageal function.

Ideal EndoStim Candidate

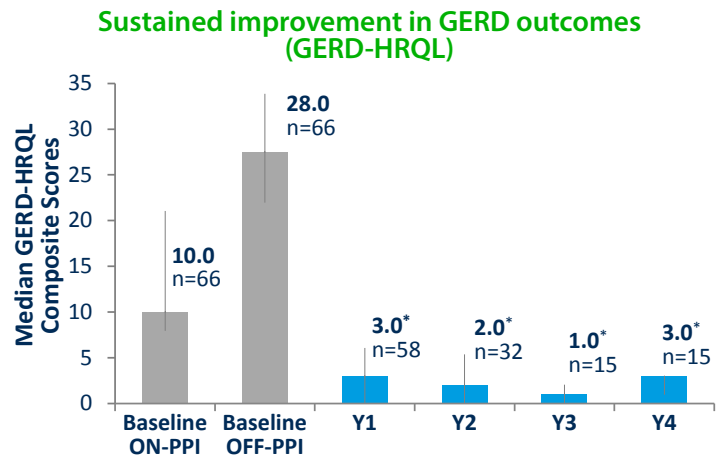
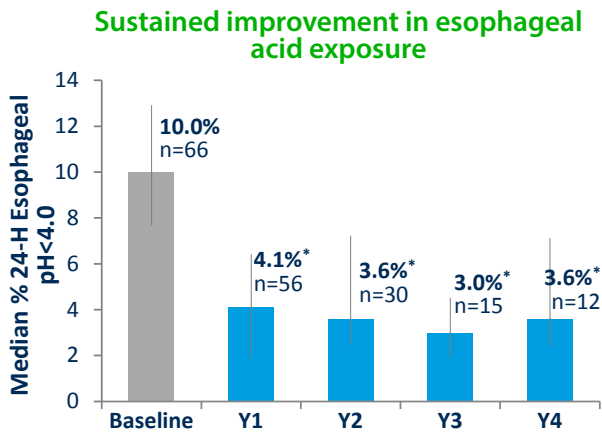
- ✓ On daily PPI therapy for >1 year and dissatisfied with PPI
- ✓ GerdQ Score ≥ 8
- ✓ NERD or esophagitis LA Grade A-C
- ✓ No hernia or hernia which can be corrected during the procedure
- ✓ GERD by pathological pH (24-hour pH <4.0 for >4.0% or DeMeester Score >14 off-PPI)

Additional Patient Groups

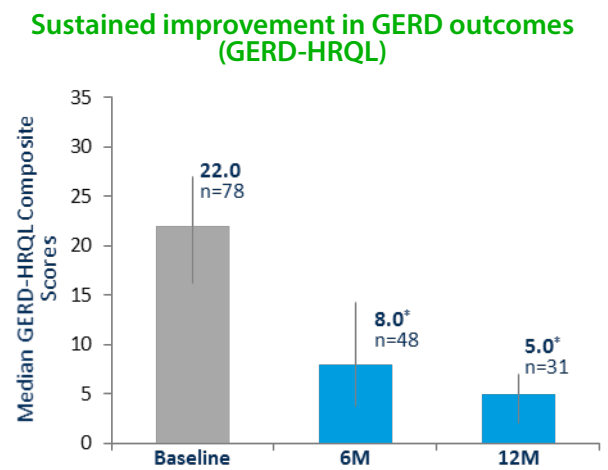
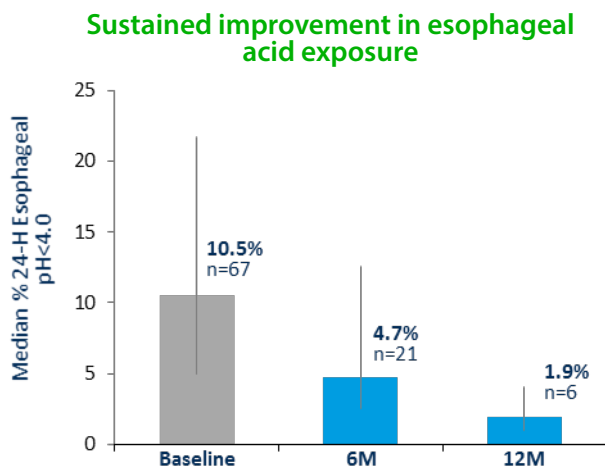
- GERD in bariatric sleeve patients
- Extra-esophageal symptoms
- Esophageal dysmotility

International clinical results

Meta analysis of 2 published trials: Significant Improvement in GERD Symptoms and Esophageal pH 66 patients from 11 centers in 2 long-term clinical trials up to 4 years of follow-up



Outcomes from ongoing multicenter commercial patient registry confirm results of the 2 long-term studies
Data from ongoing post-market patient registry including 11 sites in Germany, Denmark, Netherlands, Mexico, Argentina, confirm results of the clinical trials (accepted for presentation)



*p<0,01 vs. of life in patients with refractory

Select Publications, LES Stimulation Therapy

Soffer E, Rodriguez L, Rodriguez P, Gomez B, Neto MG, Crowell MD. Effect of electrical stimulation of the lower esophageal sphincter in gastroesophageal reflux disease patients refractory to proton pump inhibitors. *World J Gastrointest Pharmacol Ther.* 2016;7(1): 145-155.

Rodriguez L, Rodriguez P, Gómez B, Netto M, Crowell M, Soffer E. Electrical stimulation therapy of the lower esophageal sphincter is successful in treating GERD: long-term 3 year results. *Surg Endosc.* 2015; DOI 10.1007/s00464-015-4539-5.

Kappelle W, Bredenoord A, Conchillo J, Ruurda J, Bouvy N, Van Berge Henegouwen M, Chiu P, Booth M, Hani A, Reddy N, Bogte A, Smout A, Wu J, Escalona A, Valdovinos M, Torres-Villalobos G, Siersema P. Electrical Stimulation Therapy of the Lower Esophageal Sphincter for refractory gastro-esophageal reflux disease – Interim Results of an International Multicenter Trial. *Aliment Pharmacol Ther.* 2015 Sep;42(5):614-25.

Rodriguez L, Rodriguez P, Gómez B, Ayala JC, Oxenberg D, Perez-Castilla A, Netto MG, Soffer E, Boscardin WJ, Crowell MD. Two-year results of intermittent electrical stimulation of the lower esophageal sphincter treatment of gastroesophageal reflux disease. *Surgery.* 2015; 157(3):556-567.

Hoppo T, Rodriguez L, Soffer E, Crowell MD, Jobe BA. Long-term results of electrical stimulation of the lower esophageal sphincter for treatment of proximal GERD. *Surg Endosc.* 2014; 28(12):3293-301.

Ciotola F, Ditaranto A, Bilder C, Badaloni A, Lowenstein D, Riganti JM, Hoppo T, Jobe B, Nachman F, Nieponice A. Electrical stimulation to increase lower esophageal sphincter pressure after POEM. *Surg Endosc.* 2015; 29(1):230-235.

Rinsma NF, Bouvy ND, Masclee AAM, Conchillo JM. Electrical Stimulation Therapy for Gastroesophageal Reflux Disease. *J Neurogastroenterol Motil.* 2014; 20(3):287-93.

Eypasch E. Electrical stimulation of the lower oesophageal sphincter: an emerging therapy for treatment of GORD. *Eur Surg.* 2014; 46:57–64.

Banerjee R, Pratap N, Kalpala R, Reddy DN. Effect of electrical stimulation of the lower

esophageal sphincter using endoscopically implanted temporary stimulation leads in patients with reflux disease. *Surg Endosc.* 2014; 28(3):1003-9.

Crowell MD. Implanted electrical devices and gastroesophageal reflux disease: an effective approach to treatment. *Expert Rev Gastroenterol Hepatol.* 2013; 7(3):189-191.

Rodriguez L, Rodriguez P, Gomez B, Ayala JC, Oksenberg D, Perez-Castilla A, Netto MG, Soffer E, Crowell MD. Long-term results of electrical stimulation of the lower esophageal sphincter for the treatment of gastroesophageal reflux disease. *Endoscopy.* 2013; 45:595:604.

Rodriguez L, Rodriguez P, Gómez B, Ayala JC, Saba J, Perez-Castilla A, Galvao Neto M, Crowell MD. Electrical stimulation therapy of the lower esophageal sphincter is successful in treating GERD: final results of open-label prospective trial. *Surg Endosc.* 2013;27(4):1083-1092.

Rodriguez L, Rodriguez P, Neto M, Ayala JC, Saba J, Berel D, Conklin J, Soffer E. Short-term electrical stimulation of the lower esophageal sphincter increases sphincter pressure in patients with gastroesophageal reflux disease. *Neurogastroenterol Motil.* 2012; 24(5):446–450.

Nieponice A, Borbely Y, Rodriguez L, Schulz HG, Ortiz C, Talbot M, Martin D, Bouvy N. EndoStim LES Stimulation Therapy Improves GERD in Patients with Laparoscopic Sleeve Gastrectomy (LSG). *Surg Endosc.* 2016; 30:5263.

Attwood SE, Leontiadis GI, Rodriguez L, Siersema PD, Labenz J. Global clinical experience with EndoStim lower esophageal sphincter stimulation therapy: an individual patient data meta-analysis of the open label clinical trials. *UEG Journal.* 2015; 3(5S):A295.

Schulz HG, Leodolter A, Pedersen JB, Eypasch E, Labenz J. Preliminary results of a prospective multi-center observational registry of lower esophageal sphincter stimulation for GERD: the LESS-GERD Registry. *UEG Journal.* 2015; 3(5S):A294-295.

Bouvy N, Rinsma NF, Escalona A, Ruurda JP, Conchillo J, Bredenoord A, van Berge Henegouwen M, Chiu P, Booth M, Hani A, Reddy D, Smout A, Wu J, Siersema P. Lower Esophageal Sphincter (LES) Electrical Stimulation improves sleep quality, work productivity, and quality of life in patients with refractory GERD. *UEG Journal.* 2014; 2(1S):A577.

Additional data on file.