Enterra® Therapy

FOR CHRONIC NAUSEA AND VOMITING ASSOCIATED WITH DIABETIC OR IDIOPATHIC GASTROPARESIS

enterra medical™

Hope and help for your gastroparesis patients

Enterra® Therapy is the first and only device designed to reduce nausea and vomiting associated with diabetic or idiopathic gastroparesis through Gastric Electrical Stimulation (GES).

Enterra Therapy may be appropriate for patients who:

- **have gastroparesis caused by diabetic or idiopathic origin**
- **have difficulty managing nausea and vomiting symptoms, despite having tried firstline therapies of diet modification and medications**
- **are 18-70 years of age**

More than

patients worldwide

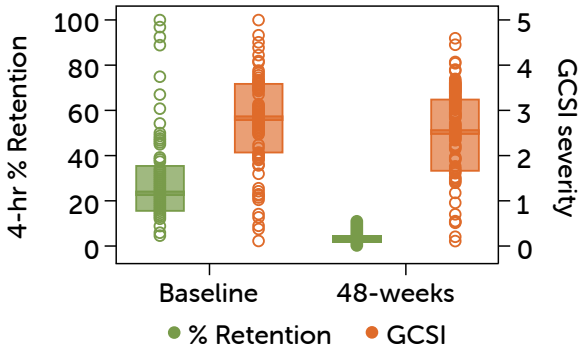
have received Enterra Therapy to help resume everyday activities, like taking their seat back at the table.

Enterra Therapy does not work for everyone. Any combination of diet modification, medication, nutritional support, surgery, and Enterra Therapy may be necessary to control symptoms of gastroparesis.

Gastroparesis is more than a motility issue

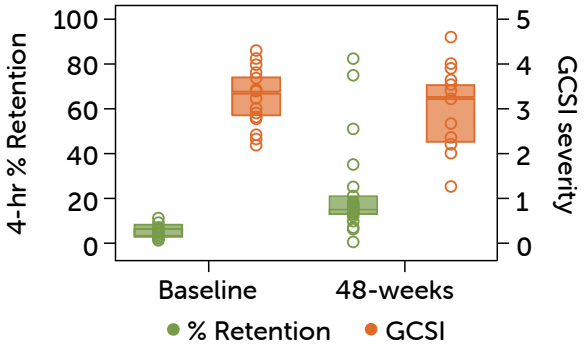
Correlation between delayed gastric emptying and cardinal symptoms are not well established in gastroparesis.[1]

In 2021, a 12-year NIH study of patients with upper GI symptoms found gastric-emptying results are variable and do not correlate with clinical symptoms.[2]



42%

of patients showed emptying improvement without significant improvement in symptoms



37%

of patients showed emptying worsening without significant change in symptoms

Current treatments focused on addressing motility often fail, leaving gastroparesis patients without options focused on relieving nausea and vomiting—the most distressing symptoms of gastroparesis.[3]

Gastroparesis is a quality of life issue

Although it takes an average of 5 years from the onset of symptoms until diagnosis, the journey of gastroparesis hardly ends there — for patients or providers.[3]

Between an evolving understanding of the disease's characteristics and pathophysiology and limited treatment options, gastroparesis remains challenging to treat.

In a recent survey of 1,423 gastroparesis patients, only 4% reported that they were satisfied with available treatment options.[3]

The exhaustion, isolation, and frustration of gastroparesis is real and costly:

68%
Reduction in daily activities[4]

29%
Lower annual income and higher rates of unemployment and underemployment[4]

11%
Medically disabled[4]

24%
Combined anxiety/depression[4]

A different approach to managing gastroparesis

Enterra Therapy is the first and only device designed to reduce the nausea and vomiting associated with diabetic or idiopathic gastroparesis through Gastric Electrical Stimulation (GES).

Implanted in over 15,000 patients, it is an advanced therapy option for gastroparesis patients in their journey to find relief.

Targets nausea & vomiting

Adjustable

Reversible

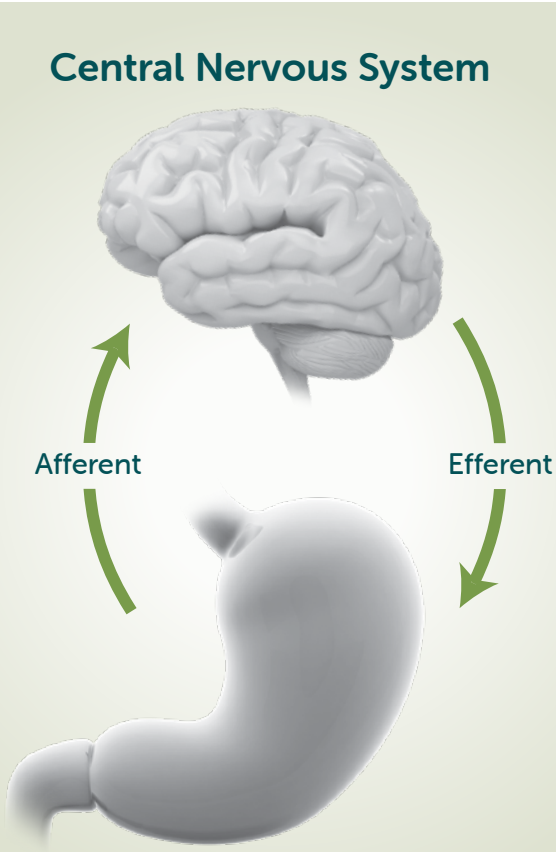
Minimally invasive

Contraindications

The Enterra Therapy System is not intended for patients whom the physician determines are not candidates for surgical procedures and/or anesthesia due to physical or mental health conditions. You cannot have diathermy (deep heat treatment from electromagnetic energy) if you have an Enterra device.

Gastric Electrical Stimulation: Potential Mechanism of Action

The exact mechanism of action of GES is unknown, but the AGA clinical practice update on the potential mechanism hypothesized that Enterra Therapy may impact the afferent (sensory) and efferent (motor) pathways between the stomach and central nervous system, the cell types found in the circular muscle (ICC-CM), and myoneural connections–allowing for the alleviation of symptoms.[5]



How Enterra Therapy works

Enterra Therapy stimulates the nerves and smooth muscles of the stomach by delivering mild electrical pulses, thereby reducing nausea and vomiting symptoms associated with diabetic and idiopathic gastroparesis.

Neurostimulator

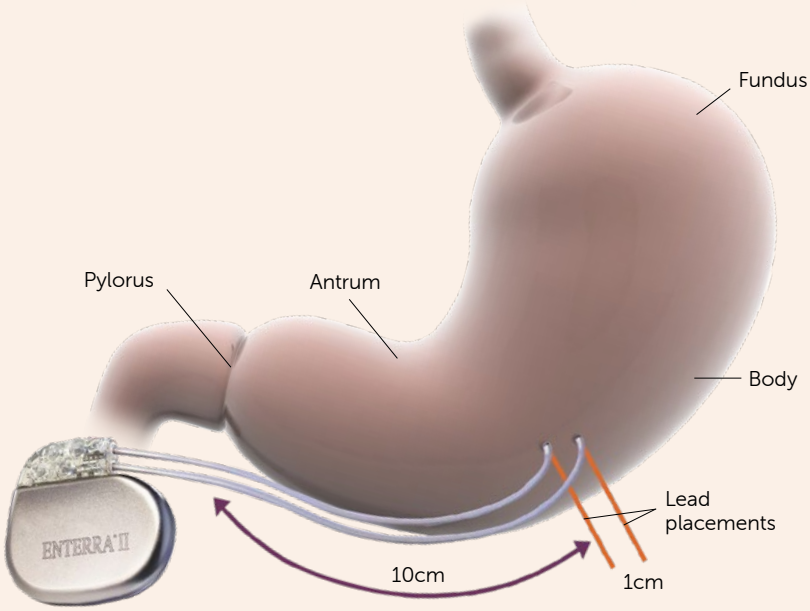
A small, battery-powered gastric neurostimulator is implanted beneath the skin in the lower abdominal region.

Leads

Leads deliver mild, controlled electrical pulses to the antrum portion of the stomach muscle wall.

Programmer

The system is programmed to optimize therapy for the individual patient.



Procedure overview

Electrodes are implanted in the stomach wall

Enterra Therapy implant procedure typically takes 1-2 hours in a minimally-invasive laparoscopic or robotic surgical procedure, where the leads are placed on the serosal surface of the stomach's greater curvature.

Neurostimulator is implanted in subcutaneous abdominal pocket

The neurostimulator is placed in subcutaneous tissue, typically in the abdomen.

Patient recovery is typically 1-2 days

While some patients leave same-day, a 1-2 day hospital stay is typical.

Therapy is adjusted non-invasively

Post-procedure, Enterra Therapy can be adjusted for symptom control via a programmer in an outpatient clinic.

Gastric electrical stimulation is supported by ACG and AGA guidelines

Gastroparesis care pathway

Evaluation & Diagnosis

Medical History, Physical Exam	Endoscopy no obstruction	Gastric Emptying Test presence of delayed emptying

First line therapies

Dietary modifications	Pharmacologic Management
• Gastroparesis diet • Glucose control	• Prokinetics • Antiemetics • Cessation of narcotics

Advanced Therapies

Gastric electrical stimulation	Pyloric Surgery	Other treatments
		• feeding tubes • gastrectomy • and more

"Gastric electrical stimulation does improve refractory nausea and vomiting in some patients with gastroparesis and may improve glycemic control, nutritional status, and quality of life, while reducing hospitalizations and medication use."[5]

AGA Best Practices Review 2021

Studies demonstrate significant improvements in patient symptoms and quality of life

Clinical evidence documenting the results of GES is found in prospective, controlled, multicenter studies.[6,7] Quality of Life (QoL) improvements are from baseline to 12 months.

*The double-blind 3-month period did not show statistically significant reduction in vomiting in the ON vs. OFF period, the primary outcome variable. Manufacturer Sponsored Studies.

U.S. CONTROL TRIAL

SIGNIFICANT REDUCTION IN **MEDIAN WEEKLY VOMITING*** (AT 12 MONTHS)

68% IMPROVEMENT

DIABETIC GROUP
(N=36, p<0.001)[6]
19.5 TO 4.3 EPISODES

87% IMPROVEMENT

IDIOPATHIC GROUP
(N=18, p<0.001)[7]
17.3 TO 2.0 EPISODES

SIGNIFICANT REDUCTION IN **HOSPITAL DAYS** (AT 12 MONTHS)

75% IMPROVEMENT

DIABETIC GROUP
40 days to 10 days
(N=39, p<0.001)[6]

100% IMPROVEMENT

IDIOPATHIC GROUP
2 days to 0 days
(N=19, p=0.006)[7]

FRENCH MINISTRY OF HEALTH TRIAL

The largest RCT independently conducted on Enterra Therapy to date.

STATISTICALLY SIGNIFICANT IMPROVEMENT IN **VOMITING FREQUENCY SCORE** DURING THERAPY ON PERIOD VS. OFF PERIOD IN GASTROPARETIC PATIENTS.

(N=133, p=0.01)[8]

A TARGETED APPROACH THAT MAY HELP CONTROL THE SYMPTOMS OF CHRONIC INTRACTABLE NAUSEA AND VOMITING DUE TO GASTROPARESIS.*

*Humanitarian Device. Authorized by Federal law for use in the treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology in patients aged 18 to 70 years. The effectiveness of this device for this use has not been demonstrated.

High patient satisfaction

80%

OVERALL PATIENT SATISFACTION WITH GASTRIC ELECTRICAL STIMULATION AT 10 YEARS[9]

N=37

Enterra Medical is dedicated to helping more people with chronic gastroparesis live better lives through advancing technology, bolstering clinical science, and accelerating patient access to Enterra Therapy.

To learn more about Enterra Therapy talk to your Enterra Medical representative or visit **www.enterramedical.com/hcp**

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3. Yu D, Ramsey FV, Norton WF, et al. The Burdens, Concerns, and Quality of Life of Patients with Gastroparesis. *Dig Dis Sci* . 2017;62(4):879-893. doi:10.1007/s10620 017 4456-7.
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6. McCallum RW, Snape W, Brody F, Wo J, Parkman HP, Nowak T. Gastric electrical stimulation with Enterra Therapy improves symptoms from diabetic gastroparesis in a prospective study. *Clin Gastroenterol Hepatol.* 2010;8:947-954.
7. McCallum RW, Sarosiek I, Parkman HP, Snape W, Brody F, et al. Gastric electrical stimulation with Enterra Therapy improves symptoms of idiopathic gastroparesis. *Neurogastroenterol Motil.* 2013;25(10):815-e636.
8. Ducrotte P, Coffin B, Bonaz B, et al. Gastric Electrical Stimulation Reduces Refractory Vomiting in a Randomized Crossover Trial. Gastroenterology. 2020;158(3):506-514.e2. doi:10.1053/j.gastro.2019.10.018.
9. Hedjoudje A, Huet E, Leroi AM, Desprez C, Melchior C, Gourcerol G. Efficacy of gastric electrical stimulation in intractable nausea and vomiting at 10 years: A retrospective analysis of prospectively collected data. *Neurogastroenterol Motil.* 2020;32(11):e13949. doi:10.1111/nmo.13949.

Important Safety Information
Enterra® Therapy for treatment of chronic, resistant to medication nausea and vomiting associated with gastroparesis caused by diabetes or an unknown origin in patients aged 18 to 70 years: patients should always discuss potential risks and benefits of the device with their physician. **Indications for Use:** The Enterra Therapy System for gastric electrical stimulation is indicated for use in the treatment of chronic, intractable (drug refractory) nausea and vomiting associated with gastroparesis caused by diabetes or an unknown origin in patients aged 18 to 70 years. **Contraindications:** The Enterra Therapy System is not intended for patients whom the physician determines are not candidates for surgical procedures and/or anesthesia due to physical or mental health conditions. You cannot have diathermy (deep heat treatment from electromagnetic energy) if you have an Enterra device. **Warnings/Precautions/Adverse Events:** This system has not been evaluated for pregnant women, for use in patients under the age of 18, or patients over the age of 70. The system may be affected by or adversely affect cardiac devices. Strong sources of electromagnetic interference (EMI) such as from electrocautery, defibrillation/cardioversion, therapeutic ultrasound, radiofrequency (RF)/microwave ablation, or MRI, can result in serious injury, system damage, or operational changes to the system. EMI, postural changes, or other activities may cause shocking or jolting sensations.

MR The Enterra II System is MR Conditional. This means that patients with the Enterra II System can safely have MRI examinations of some body parts under certain conditions. The conditions for MRI scans will vary with the type of MRI coil. Obtain the latest MRI guidelines by referring to the manuals at www.enterramedical.com/hcp/manuals. Patients on anticoagulation therapy may be at a greater risk for post-operative complications. The use of non-Medtronic components with this system may result in damage to Medtronic components, loss of therapy, or patient injury. There is the possibility of an allergic or immune system response to the implanted materials. When possible, a physician is to identify and treat any infections prior to surgery. Infections at the implant site almost always require the surgical removal of the implanted system. The lead can become entangled with the bowel or perforate your stomach and cause life-threatening blockage or infections that require immediate medical attention and may require surgery. Patients should avoid activities that may put undue stress on the implanted system components (activities that include sudden, excessive, or repetitive bending, twisting, bouncing, or stretching that can cause component fracture or dislodgement). Adverse events related to the therapy, device, or procedure can include: infection, pain at the surgery site, device components may wear through the skin, bruising at the neurostimulator site, bleeding, loss of therapeutic effect, undesirable change in stimulation (described as a jolting, shocking, or burning sensation), gastrointestinal symptoms and gastrointestinal complications (in that the lead may perforate your stomach or device components may become entangled with or obstruct other internal organs, requiring surgery). The system could stop because of battery depletion or mechanical or electrical problems. Any of these situations may require additional surgery or cause your symptoms to return. **Humanitarian Device:** Authorized by Federal law for use in the treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology in patients aged 18 to 70 years. The effectiveness of this device for this use has not been demonstrated. For further information, please contact Enterra Medical at info@enterramedical.com. USA Rx only.

www.enterramedical.com

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