Instructions for Use

Caution: Federal (USA) Law restricts this device to sale by or on the order of a physician.

1. SYSTEM DESCRIPTION

The LINX® Reflux Management System is comprised of the following components:

- LINX® Reflux Management System Implant (LINX device)
- LINX® Reflux Management System Esophagus Sizing Tool (LINX Sizing Tool, packaged separately)

Refer to the LINX Reflux Management System Esophagus Sizing Tool Instructions for Use.

The LINX device consists of a series of titanium beads with magnetic cores that are connected with independent titanium wires to form an annular shape. The attractive force of the magnetic beads is designed to provide additional strength to keep a weak LES closed (Figure 1). During swallowing, the magnetic beads slide away from each other on the independent titanium wire "links" to allow esophageal distention as the bolus passes by (Figure 2).

The LINX device is offered in multiple sizes to accommodate variation in esophagus size. The sizes are denoted by the model number (e.g., LXMC14 = 14 Bead Implant). The LINX Sizing Tool, is utilized to associate the esophagus size to an appropriate LINX device. An illustration of a "14 Bead" size LINX device is provided in Figures 1 and 2.

Figure 1 – Illustration of Implant, Closed

Figure 2 – Illustration of Implant, Open

2. INDICATION FOR USE

The LINX® Reflux Management System is a laparoscopic, fundic-sparing anti-reflux procedure indicated for patients diagnosed with Gastroesophageal Reflux Disease (GERD) as defined by abnormal pH testing, and who are seeking an alternative to continuous acid suppression therapy (i.e. proton pump inhibitors or equivalent) in the management of their GERD.

3. CONTRAINDICATIONS

3.1. Do not implant the LINX Reflux Management System in patients with suspected or known allergies to titanium, stainless steel, nickel, or ferrous materials. Please note nickel is not a metal component of the LINX device, only the LINX Sizing Tool contains nickel, which is a single-use instrument used only during surgical placement of the implant.

4. WARNINGS

4.1. The LINX device is intended to be placed around the esophagus, to include the anterior and exclude the posterior vagus nerve bundle. The device should never be placed outside both vagus nerve bundles.

4.2. The LINX device is considered MR Conditional. Please refer to Section 6, MRI Conditional Guidelines. Exposure to an MRI environment above the MR Conditional guidelines could cause serious injury to the patient and/or interfere with the magnetic strength and the function of the device. The device is NOT safe when exposed to a 3T MRI magnetic field. In the event alternative diagnostic procedures cannot be used and MRI is required beyond the MR Conditional guidelines, the LINX device can be safely removed utilizing a laparoscopic technique that does not compromise the option for traditional anti-reflux procedures.

4.3. Failure to secure the LINX device properly may result in its subsequent displacement and necessitate a second operation.

4.4. Laparoscopic placement of the LINX device is major surgery and death can occur.

4.5. The packaged LINX device should not be exposed to temperatures above 60°C (140°F) as this could adversely affect the function of the package/device.

5. PRECAUTIONS

5.1. Implantation of the LINX device should only be performed by a surgeon who has experience in laparoscopic anti-reflux procedures and has received product specific training.

5.2. It is the responsibility of the surgeon to advise the patient of the known risks and complications associated with the surgical procedure and implant.

5.3. Patients should be advised that the LINX device is a long-term implant. Explant (removal) and replacement surgery may be indicated at any time. Management of adverse reactions may include surgical explantation and/or replacement.

5.4. The sterile package and LINX device should be inspected prior to use. If sterility or performance of the device is suspect or compromised, it should not be used.

5.5. The LINX device is intended for single use only. Do NOT re-sterilize the device. Functionality and sterility of the device cannot be assured if re-used.

5.6. The LINX device is magnetic and will be attracted to ferrous objects in the surgical field and other surgical instruments that are ferromagnetic.

5.7. The LINX device has not been evaluated in patients with a hiatal hernia larger than 3 cm. Use of LINX device in patients with a hiatal hernia larger than 3 cm should be considered on the basis of each patient's medical history and severity of symptoms.

5.8. The safety and effectiveness of the LINX device has not been evaluated in patients with Barrett's esophagus or Grade C or D (LA classification) esophagitis.

5.9. The safety and effectiveness of the LINX device has not been evaluated in patients with electrical implants such as pacemakers and defibrillators, or other metallic, abdominal implants.

5.10. The safety and effectiveness of the LINX Reflux Management System has not been established for the following conditions:

- Scleroderma
- Suspected or confirmed esophageal or gastric cancer
- Prior esophageal or gastric surgery or endoscopic intervention
- Distal esophageal motility less than 35 mmHg peristaltic amplitude on wet swallows or <70% (propulsive) peristaltic sequences or High Resolution Manometry equivalent, and/or a known motility disorder such as Achalasia, Nutcracker Esophagus, and Diffuse Esophageal Spasm or Hypertensive LES
- Symptoms of dysphagia more than once per week within the last 3 months
- Esophageal stricture or gross esophageal anatomic abnormalities (Schatzki's ring, obstructive lesions, etc.)
- Esophageal or gastric varices
- Lactating, pregnant or plan to become pregnant
- Morbid obesity (BMI >35)
- Age < 21

6. MRI Safety Information

Non-clinical testing has demonstrated that the LINX device is MR Conditional. This device can be scanned safely under the following conditions:

- Static magnetic field **1.5-Tesla** (**1.5 T**)
- Maximum spatial field gradient of 1,715 gauss/cm (17.15 T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4 W/kg (First Level Controlled Operating Mode)
- The LINX device contains permanent magnets. The patient may feel pressure around the Lower Esophagus. Should the patient experience pain, immediately discontinue the scan and remove the patient from the MR environment.

RF Heating

In non-clinical testing, with body coil excitation, the LINX device produced a temperature rise of less than 4.0°C at a maximum whole body averaged specific absorption rate (SAR) of 4.0 W/kg, as assessed by calorimetry for 15 minutes of scanning in a 1.5 T Siemens Espree (MRC30732) MR scanner with SYNGO MR B19 software.

Caution: The RF heating behavior does not scale with static field strength. Devices which do not exhibit detectable heating at one field strength may exhibit high values of localized heating at another field strength.

MR Artifact

In testing using a 1.5 T system with gradient-echo sequencing, the shape of the image artifact follows the approximate contour of the device and extends radially up to 10.4 cm from the implant.

Torax Medical recommends that the patient register the MR conditions disclosed in this IFU with the MedicAlert Foundation (www.medicalert.org) or equivalent.

7. ADVERSE EVENTS

7.1. Adverse events that may result from use of the LINX Reflux Management System are both those commonly associated with general surgical procedures as well as those associated with the device specifically.

7.2. Potential adverse events associated with laparoscopic surgery and anesthesia include adverse reaction to anesthesia (headache, muscle pain, nausea), anaphylaxis, cardiac arrest, death, diarrhea, fever, hypotension, hypoxemia, infection, myocardial infarction, perforation, pneumonia, pulmonary embolism, respiratory distress, and thrombophlebitis. Other risks reported after anti-reflux surgery procedures include bloating, nausea, dysphagia, odynophagia, retching, and vomiting.

7.3. Potential risks associated specifically with the LINX Reflux Management System include achalasia, bleeding, cough, death, decreased appetite, device erosion, device explant/re-operation, device failure, device migration (device does not appear to be at implant site), diarrhea, dyspepsia, dysphagia, early satiety, esophageal spasms, esophageal stricture, flatulence, food impaction, globus sensation, hiccups, inability to belch or vomit, increased belching, infection, impaired gastric motility, injury to the esophagus, spleen, or stomach, nausea, odynophagia, organ damage caused by device migration, pain, peritonitis, pneumothorax, regurgitation, saliva/mucus build-up, stomach bloating, ulcer, vomiting, weight loss, and worsening of preoperative symptoms (including but not limited to dysphagia or heartburn).

7.4. Device erosion refers to at least a portion of the LINX device passing through the esophageal wall. Observed events have been reported in clinical literature.[1] Patient consultation with a surgeon who is experienced with LINX procedures and best practices is advised for proper treatment.

7.5. Following are summary safety results (based on 100 subjects) from the pivotal clinical study:

No device erosions, abnormal strictures, or device migrations were reported during the duration of the study as assessed by upper endoscopy and chest x-rays in any of the subjects that were evaluated up to the 60 month time point. The majority of subjects evaluated with barium esophagram had normal swallow function; there were three subjects with abnormal function, one of whom required dilation.

Manometry was performed at baseline and 12 months. At 12 months, 31 out of the 32 subjects who had a hypotensive LES at baseline were evaluated and three remained hypotensive. Fifteen of 93 subjects had <70% effective swallows, and four had distal esophageal amplitude <35 mmHg. One subject was reported to have ongoing complaints of dysphagia and abnormal motility. No other significant differences were seen in measures between baseline and 12 months.

Seventy-eight (78) of the 100 subjects (78.0%) implanted with the LINX device experienced a total of 190 adverse events related to the device and/or procedure, as shown in Table 1.

[1] Lipham JC, Taiganides PA, Louie BE, Ganz RA, DeMeester TR. Safety Analysis of first 1000 patients treated with magnetic sphincter augmentation for gastroesophageal reflux disease. *Diseases of the Esophagus* (2014). DOI: 10.1111/dote.12199.

Table 1: Adverse Events Related to or Relationship to Device or Procedure Unknown

	Related or Unknown		Mild		Moderate		Severe	
Adverse Event	**AEs (n)**	**Subj. % (n)**	**AEs (n)**	**Subj. % (n)**	**AEs (n)**	**Subj. % (n)**	**AEs (n)**	**Subj. % (n)**
Total	190	78% (78)	126	66% (66)	49	32% (32)	15	11% (11)
Dysphagia	80	69% (69)	56	49% (49)	19	17% (17)	5	5% (5)
Pain	32	28% (28)	10	9% (9)	16	14% (14)	6	6% (6)
Stomach Bloating	17	15% (15)	15	13% (13)	2	2% (2)	0	0%
Odynophagia	10	10% (10)	5	5% (5)	4	4% (4)	1	1% (1)
Nausea	8	7% (7)	4	3% (3)	2	2% (2)	2	2% (2)
Hiccups	8	8% (8)	7	7% (7)	1	1% (1)	0	0%
Inability to belch or vomit	7	7% (7)	6	6% (6)	1	1% (1)	0	0%
Decreased appetite	4	4% (4)	4	4% (4)	0	0%	0	0%
Belching	2	2% (2)	2	2% (2)	0	0%	0	0%
Flatulence	2	2% (2)	2	2% (2)	0	0%	0	0%
Weight loss	2	2% (2)	2	2% (2)	0	0%	0	0%
Regurgitation	2	2% (2)	2	2% (2)	0	0%	0	0%
Coughing	1	1% (1)	1	1% (1)	0	0%	0	0%
Dry cough	1	1% (1)	1	1% (1)	0	0%	0	0%
Esophageal pain and discomfort	1	1% (1)	1	1% (1)	0	0%	0	0%
Esophageal spasms	1	1% (1)	1	1% (1)	0	0%	0	0%
Food impaction	1	1% (1)	0	0%	1	1% (1)	0	0%
Globus sensation	1	1% (1)	1	1% (1)	0	0%	0	0%
IBS/Dyspepsia	1	1% (1)	1	1% (1)	0	0%	0	0%
Increased belching.	1	1% (1)	1	1% (1)	0	0%	0	0%
Pinching sensation to mid chest area, sometimes when lying down on right side.	1	1% (1)	1	1% (1)	0	0%	0	0%
Regurgitation of sticky mucus	1	1% (1)	0	0%	1	1% (1)	0	0%
Superficial ulcer found in antrum.	1	1% (1)	1	1% (1)	0	0%	0	0%
Uncomfortable feeling in chest	1	1% (1)	1	1% (1)	0	0%	0	0%
Upper esophageal stricture	1	1% (1)	0	0%	0	0%	1	1% (1)
Linear ulcer at gastroesophageal junction.	1	1% (1)	1	1% (1)	0	0%	0	0%
Pinching sensation on lower esophageal area.	1	1% (1)	0	0%	1	1% (1)	0	0%
Vomiting	1	1% (1)	0	0%	1	1% (1)	0	0%

The most common adverse event experienced by subjects was dysphagia (80 events in 69 subjects). Dysphagia was generally mild in severity and resolved by six months. In many of the patients, dysphagia resolved by six months, however, there were several patients that had prolonged times to resolution (maximum 841 days) and several patients that developed dysphagia after 180 days. The second most common event experienced by subjects was pain (32 events in 28 subjects). Twenty-one (21) subjects underwent esophageal dilation for dysphagia, odynophagia, pain, vomiting, and/or upper esophageal stricture. Unanticipated adverse events included hiccups, belching, food impaction, and pain.

There were 11 serious adverse events in eight (8) subjects reported as related to the device/produce or unknown (Table 2).

Table 2: Serious Adverse Events – Related or Unknown

Serious Adverse Event	Events (n)	Subjects % (n)
Total	11	8% (8)
Dysphagia	3	3% (3)
Nausea	2	2% (2)
Vomiting	1	1% (1)
Pain	4	4% (4)
Odynophagia	1	1% (1)

Regarding the time to onset, of the adverse events, there were 150 device or procedure related or unknown adverse events that occurred between 0 and 180 days. After 180 days, there were 40 events considered related to the device/procedure or of unknown relationship. This is shown in Table 3.

Table 3: Days to Onset of Adverse Event

Adverse Event Type	0 – 90 Days	90-180 Days	6M – 1 Year	1 – 2 Years	2 – 3 Years	3 – 4 Years	>4 Years
All Adverse Events	42% (219/517)	6% (32/517)	12% (62/517)	9% (47/517)	8% (40/517)	12% (61/517)	11% (56/517)
Related to device/procedure or unknown relationship	72% (137/190)	7% (13/190)	7% (14/190)	2% (3/190)	3% (5/190)	8% (16/190)	1% (2/190)
Serious	18% (7/38)	16% (6/38)	13% (5/38)	16% (6/38)	8% (3/38)	11% (4/38)	18% (7/38)
Serious related to device/procedure or unknown relationship	55% (6/11)	9% (1/11)	9% (1/11)	0% (0/11)	18% (2/11)	9% (1/11)	0% (0/11)

There were seven (7) subjects who had the device explanted during the conduct of the study. Four (4) subjects had the device explanted for dysphagia. At least three (3) subjects elected to have a Nissen fundoplication following device removal. Details of the seven (7) explants are given below:

- One subject with history of severe heartburn, severe regurgitation, and frequent and prolonged nausea, experienced nausea coupled with dysphagia within two weeks of device implantation. The subject underwent balloon dilation in the region of the gastroesophageal junction without resolution of symptoms and the subject requested to have the device removed at 31 days post-implant. The subject underwent a Nissen fundoplication at a later date.

- One subject with history of GERD started with dysphagia within five (5) days of device implantation. The subject underwent esophageal dilation without resolution of symptoms. Subsequent manometry/motility testing was performed and showed loss of esophageal motility. The device was removed on post-operative day 21.

- One subject started with dysphagia within five days post-implant and odynophagia within seven days post-implant. Esophageal dilations of the GEJ were performed without resolution of symptoms and the device was removed 93 days post implant.

- One subject with recurrent GERD symptoms elected to have the device removed so a Nissen fundoplication could be performed. This occurred 489 days post-implant.

- One subject started with intermittent vomiting within three months of device implantation. The subject was subsequently diagnosed with a Helicobacter pylori infection and started on medication. The vomiting episodes continued and the device was explanted at 357 days post-implant.

- One subject had onset of substernal chest pain 977 days after the implant procedure. Patient was evaluated by barium swallow, which showed no evidence of dysmotility, reflux, or obstruction. A computed tomography scan of chest and abdomen had no significant findings, and an upper endoscopy showed no evidence of erosion of the device into the lumen. Duodenitis and antral gastritis was noted during the endoscopy. A biopsy of the antrum was negative for H. Pylori. Treatment with medication and esophageal dilation did not resolve the pain. The device was removed on post-implant day 1,062 along with a Toupet fundoplication. The pain resolved following device removal.

- One subject was explanted during the course of the study on post-implant day 1,807 for recurrent dysphagia symptoms. The subject continued to report persistent dysphagia symptoms post dilation and a decision was made to remove the device. The patient was seen back at an office visit two months post explant and reported dysphagia symptoms were improving but still ongoing.

Side effects associated with antireflux surgery were minimal after the LINX implant procedure. Additionally, other GERD-related outcomes as assessed by the unvalidated Foregut questionnaire, (bloating, regurgitation, extra-esophageal symptoms) showed long-term improvement (Table 4). Patients that reported daily, bothersome (moderate to severe) heartburn was reduced from 89.0% to 11.9%, and moderate to severe regurgitation was nearly eliminated (57.0% to 1.2%) at 60 months. The frequency (mean/week) of difficulty swallowing at 60 months was comparable to the frequency reported at baseline. Additionally, subjects are able to belch and vomit as needed 60 months post-implant.

Table 4: Side Effects and Additional Clinical Outcomes

Parameter	Baseline[1]	12 Months[1]	24 Months[1]	36 Months[1]	48 Months[1]	60 Months[1]
Inability to Belch	0%	1.1%	0%	2.3%	1.2%	0%
Inability to Vomit	0%	0%	1.1%	3.4%	1.2%	0%
Bloating Frequency – Frequently/ Continuously	40.0%	5.3%	6.7%	10.3%	9.3%	8.3%
Heartburn – Severe or Moderate	89.0%	3.2%	5.6%	8.0%	9.3%	11.9%
Heartburn – Mean frequency/week	78.6	2.3	2.0	1.8	11.5	9.1
Regurgitation – Severe or Moderate	57.0%	2.1%	1.1%	2.3%	3.5%	1.2%
Regurgitation – Mean frequency/week	27.9	1.2	0.9	0.4	1.8	5.3
Absence of Extra-Esophageal Symptoms	49.0%	86.3%	87.8%	89.7%	83.7%	76.2%
Chest Pain	69.0%	20.0%	15.6%	17.2%	20.9%	22.6%
Difficulty Swallowing	23.0%	44.2%	46.7%	43.7%	44.2%	45.2%
Difficulty Swallowing – requiring liquids for clearing	4.0%	7.4%	12.2%	8.0%	9.3%	8.3%
Difficulty Swallowing – Mean frequency/week	1.4	1.8	1.2	1.1	1.7	1.7
Patient Satisfied with Present Condition Off PPI On PPI	 0% 13.0%	 94.7% NA	 90.0% NA	 93.2% NA	 87.2% NA	 83.3% NA

[1]Assessments completed off PPI therapy, unless noted

8. CLINICAL STUDIES

The LINX Reflux Management System has been evaluated in two prospective, single-arm, multicenter clinical trials with a combined enrollment of 144 subjects.

Feasibility Study
The first study enrolled 44 subjects at four clinical sites (2 US and 2 OUS) as part of a feasibility IDE trial. Performance outcomes for symptom improvement, reduction of PPI dependence and esophageal acid reduction have been reported through five years (Table 5).

Table 5: Long-Term Feasibility IDE Trial Performance Outcomes

Performance Outcomes[1]	12 Months % (n/N)	24 Months % (n/N)	36 Months % (n/N)	48 Months % (n/N)	60 Months % (n/N)
Improvement in GERD-HRQL scores by ≥50%	97.4% (38/39)	88.9% (32/36)	93.9% (31/33)	96.7% (29/30)	93.9% (31/33)
Reduction in PPI therapy by ≥50%	90.0% (36/40)	82.9% (29/35)	87.5% (28/32)	83.9% (26/31)	93.9% (31/33)
pH normalization or ≥50% reduction in distal acid exposure[2]	79.5% (31/39)	90.0% (18/20)	88.2% (15/17)	87.5% (7/8)	85.0% (17/20)

[1]Compared to the subject's baseline data and assessed while off proton pump inhibitors
[2] pH monitoring is not performed in US subjects beyond the 12-month follow-up.

A total of 29/44 (65.9%) subjects experienced adverse events related to the device and/or procedure. The most common adverse event experienced by subjects was dysphagia (23 events in 21 subjects). Although most cases resolved within approximately three months, two subjects required dilation in the area of the gastroesophageal junction (GEJ), and one subject had the device removed. Other common adverse events included pain, nausea and vomiting. No intra-operative complications, deaths, life-threatening events, device erosions, device migrations or infections were reported. Two subjects had serious adverse events related to the device and procedure that included one device removal for dysphagia and one hospitalization for chest pain <30 days following the device implant procedure. Both events resolved without clinical sequelae. There was one additional anticipated, serious, procedure-related adverse event of post-operative vomiting and nausea resulting in an extended hospital stay after the procedure. The event resolved within five days of onset.

There were three subjects who had the device explanted. Reasons for explant included ongoing dysphagia (serious adverse event reported above), elective removal due to recurrent heartburn and need for an MRI study.

- One subject had persistent dysphagia treated by device removal at 226 days post-implant without incident. The dysphagia resolved and the subject went on to have a Nissen fundoplication at a later time (serious adverse event reported above).

- One subject experienced neurological and vascular symptoms unrelated to the device and procedure. The study subject requested removal of the device in order to undergo this MRI procedure. The Investigator complied with this request and removed the device 468 post-implant without incident.

- Another subject continued to experience recurrent heartburn. A decision was made to remove the device and perform a Nissen fundoplication. The device was removed 1302 days post-implant without incident.

Pivotal Study
The second study, a pivotal IDE trial, enrolled a total of 100 subjects at 14 clinical sites (13 US and 1 OUS). All 100 subjects were implanted with the LINX device during a laparoscopic procedure with a mean duration of 39 minutes (range 7 to 125 minutes). Half the subjects (50/100) were discharged the same day as surgery, and the other half (50/100) were discharged the next day. Follow up data is available through 60 months.

The average age of subjects implanted was 50.4 years. Fifty-two percent (52%) were male and 48% female. Fifty-five percent (55%) were overweight (BMI 25-30) and 26% were obese (BMI ≥ 30). Baseline summary statistics for selected demographics and Body Mass Index (BMI) are shown in Table 6.

Table 6: Baseline Demographics

Characteristic	N	Mean ±SD (Median)	Range
Age (years)	100	50.4±12.4 (53.0)	18.3, 74.7
Body Mass Index (BMI)	100	27.9±3.4 (27.9)	19.8, 34.7
Characteristic	**% (n/N)**		
Gender			
Male	52% (52/100)		
Female	48% (48/100)		
Race			
Caucasian/Non-Hispanic	96% (96/100)		
Black	0% (0/100)		
Hispanic	3% (3/100)		
Other	1% (1/100)		
BMI Class			
Normal (<25)	19% (19/100)		
Overweight (≥25 and <30)	55% (55/100)		
Obese (≥30)	26% (26/100)		

In the pivotal IDE trial, a subject met the primary endpoint at 12 months if either of the following criteria were met:

- there was normalization of pH, with normalization defined as pH < 4 for ≤ 4.5% of monitoring time, or
- there was a reduction of at least 50% in total time that pH <4, relative to baseline.

This endpoint would be met if the lower bound of a 97.5% confidence interval for the success rate was at least 60%.

At 12 months, 64% of subjects had pH normalization or a ≥50% reduction in distal esophageal acid exposure, and the mean total acid exposure (percent time pH<4) was reduced from 11.6% at baseline to 5.1%. Since the lower limit of the 97.5% confidence interval fell below the 60% success threshold (53.8%), the primary endpoint of the study was not met. See Table 7.

Table 7: Primary Effectiveness Endpoint: Bravo pH Normalization or ≥ 50% Reduction at 12 months

Primary Efficacy Endpoint	% Successful (Number of Subjects/Total)	Lower 97.5% Exact Binomial Confidence Limit	p-value[1]
Bravo pH ● Normalization (≤4.5%) OR ● ≥ 50% reduction from baseline	64.0% (64/100)	53.8%	0.24

[1] From one-sided, binomial exact test against the null hypothesis of ≤ 60%.

In obtaining the primary endpoint of pH testing, other components of the DeMeester Score as well as the composite score were also able to be examined. It is the composite score, which is made up of these individual components pertaining to acid exposure time, frequency, and duration, that has been reported to be the most reliable measurement of a therapeutic acid suppression regimen or an effective antireflux operation, with sensitivity and specificity for GERD at 96%. There was improvement in the composite DeMeester score in 93% of subjects that had pH testing at 12 months, and 52% had a normalized DeMeester score. This is shown in the Table 8.

Table 8: pH Parameters of Esophageal Acid Exposure

DeMeester Components	Normal Values	Baseline Mean ±SD (median)	12 Months Mean ±SD (median)
Total Time pH <4 (%)	5.3	11.6 ± 4.7 (10.9)N=100	5.1 ± 4.8 (3.3) N=96
Upright Time pH <4 (%)	6.9	14.0±7.2 (12.7) N=100	6.5 ± 5.8 (4.3) N=96
Supine Time pH <4 (%)	6.7	7.8±7.2 (6.0) N=98	2.9 ± 5.8 (0.4) N=95
Number of Episodes pH <4	36.8	175.0±81.7 (161.0) N=100	82.8 ± 67.6 (67.0) N=96
Number of Episodes > 5 min	1.2	12.4±6.7 (12.0) N=99	6.1 ± 6.8 (4.0) N=96
Longest Episode (min)	N/A	37.4±24.4 (29.0) N=99	19.7 ± 20.9 (13.0) N=96
DeMeester Score	<14.72	41 .0±16.3 (36.6) N=97	18.7 ± 17.3 (13.5) N=95
Percentage of Subjects with Normal DeMeester Score	N/A	0%	52%

The 60-month data show sustained improvement in GERD symptoms and reduction in PPI use as evidenced by 89.4% of subjects having sustained a reduction of at least 50% in daily PPI use when compared to baseline. See Table 9.

Table 9: Secondary Efficacy Endpoint: ≥ 50% Reduction in Daily PPI Use from Baseline

Parameter	Follow-up Time	Success Rate	Lower 97.5% CI
≥50% reduction in daily PPI use (secondary endpoint)	12 months	93.0% (93/100)	86.1%
	24 months	95.6% (86/90)	89.0%
	36 months	95.5% (84/88)	88.8%
	48 months	94.2% (81/86)	87.0%
	60 months	89.4% (76/85)	80.9%

A validated questionnaire called the GERD-HRQL questionnaire was one method used to assess improvement in GERD-related symptoms. The questionnaire consists of a total of 10 questions that include 6 heartburn questions, 2 swallowing questions, 1 bloating/gas question and 1 question about GERD medications. Each question is scored on a scale of 0 (no symptoms) to 5 (incapacitating). The best possible score is 0 and the worst score is 50. The data show a continued reduction in total GERD-HRQL score with 83.3% (70/84) of subjects at 60 months experiencing at least a 50% improvement from baseline GERD-HRQL total score. See Table 10.

Table 10: ≥ 50% Reduction in GERD-HRQL Total Score from Baseline (Off PPI)

Efficacy Endpoint	Visit	% Successful (Number of Subjects/Total Subjects Evaluate)	Lower 97.5% Exact Binomial Confidence Limit
GERD-HRQL: ≥ 50% reduction	12 months	92.0% (92/100)	84.8%
	24 months	93.3% (84/90)	86.1%
	36 months	88.6% (78/88)	80.1%
	48 months	87.2% (75/86)	78.3%
	60 months	83.3% (70/84)	73.6%

Table 11 shows esophagitis grade by visit as assessed by endoscopy. The percentage of subjects with no esophagitis increased from 60.0% at baseline to 87.6% at 12 months, 88.7% at 24 months and 84.1% at 60 months. Eighteen subjects had Grade B esophagitis at baseline while only a single subject had Grade B at 12 months, and three subjects at both the 24-month and 60-month visits. From baseline to 60 months, 92.7% (76/82) of subjects showed improvement or no change in their esophagitis grade.

Table 11: Esophagitis Grade by Visit

Esophagitis Grade	**Baseline % (n/N)**	**Month 12 % (n/N)**	**Month 24 % (n/N)**	**Month 60 % (n/N)**
None	60.0% (60/100)	87.6% (85/97)	88.7% (79/89)	84.1% (69/82)
Grade A	22.0% (22/100)	10.3% (10/97)	7.9% (7/89)	12.2% (10/82)
Grade B	18.0% (18/100)	1.0% (1/97)	3.4% (3/89)	3.7% (3/82)
Grade C	0.0% (0/100)	0.0% (0/97)	0.0% (0/89)	0.0% (0/82)
Grade D	0.0% (0/100)	1.0% (1/97)	0.0% (0/89)	0.0% (0/82)
Improvement from Baseline	N/A	35.1% (34/97)	34.8% (31/89)	35.4% (29/82)
No Change from Baseline		59.8% (58/97)	58.4% (52/89)	57.3% (47/82)
Worsening from Baseline		5.2% (5/97)	6.7% (6/89)	7.3% (6/82)

Adverse event and safety information for the clinical study is presented above in Section 7.

9. DIRECTIONS FOR USE

9.1. Surgical Access

9.1.1. Gain surgical access through a laparoscopic port to the esophagus at the region of the gastroesophageal junction.

9.1.2. Dissect the soft tissues away from the outside of the esophagus at the location of the gastroesophageal junction. Tissue should be removed to expose the outer muscle of the esophagus. Create a tunnel under the posterior vagus nerve through the peri-neural tissue. The anterior vagus nerve will be included within the implant. Care should be taken to avoid injuring the vagus nerve bundles.

9.2. Sizing of the Esophagus

Refer to the LINX Reflux Management System Esophagus Sizing Tool Instructions for Use.

9.3. Placement of the LINX Device

9.3.1. Bring the chosen LINX device into the surgical field through a laparoscopic port of minimum internal diameter of 10 mm.

9.3.2. Place the device around the esophagus in the same location that was measured, reference Figure 3.

9.3.3. Bring the device ends together, the ends are magnetic and will attract when brought in proximity. Reference Figure 3.

9.3.4. While grasping at the distal knots align and mate the interlocking ends. Reference Figure 4.

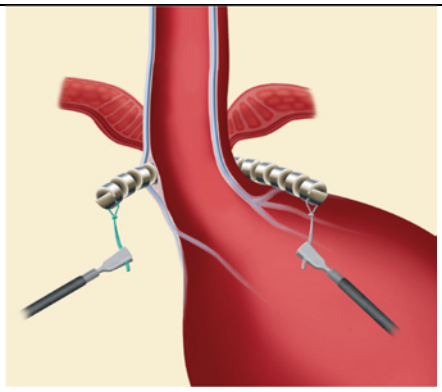

Figure 3 – Implant at Area of LES

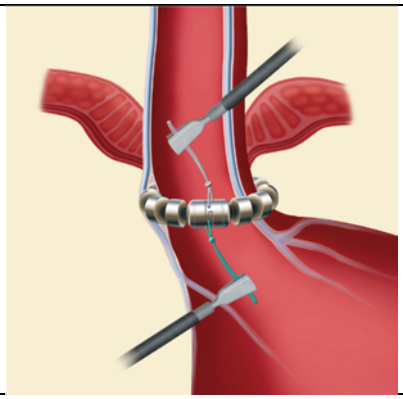

Figure 4 – Ends Interlock

9.3.5. Make sure the ends are fully engaged. It may be necessary to fully close the ends using a grasper. Reference Figure 5.

9.3.6. Trim the suture ends below the proximal knot and remove all excess suture material. Reference Figure 6.

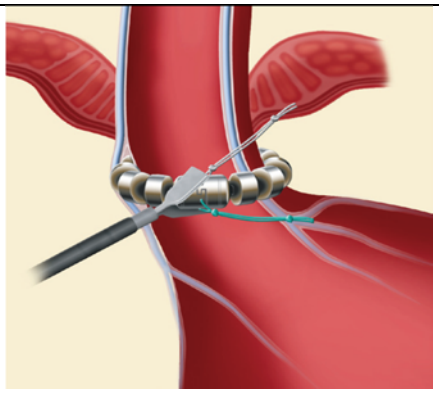

Figure 5 – Ends Fully Engaged

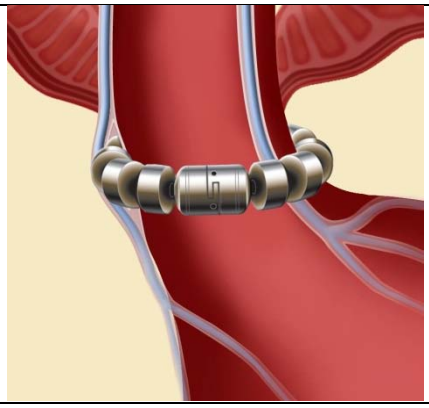

Figure 6 – Trimmed Suture Ends

9.3.7. If a hiatal hernia is observed intra-operatively, repair of the hernia should be considered in conjunction with the LINX implant procedure.

10. PACKAGING/STORAGE

The LINX device is provided sterile and designed to remain sterile unless the primary product pouch has been opened or damaged. Store in a cool, dry place. If opened and not used, discard device or return device to Torax Medical Inc. Do Not Resterilize.

11. LIMITED WARRANTY

(a) Torax warrants that the product shall be free from material defects in materials and/or workmanship, and shall perform substantially in accordance with the written specifications, through the earlier of (i) the expiration of the shelf-life as specified on the applicable product labeling or (ii) the date on which the products are used or implanted.

(b) This limited warranty does not extend to damage caused by (i) abuse or misuse of any product, (ii) accident or neglect by you or a third party; (iii) use of the product other than in accordance with Torax's instructions or specifications; or (iv) any alterations made to the product after shipment.

(c) Torax's entire liability and your exclusive remedies under this limited warranty are, at Torax's option, for Torax to use commercially reasonable efforts to fix or replace the defective product.

(d) EXCEPT AS EXPRESSLY STATED ABOVE, TORAX MAKES NO WARRANTIES, EXPRESS OR IMPLIED, WRITTEN OR ORAL, BY OPERATION OF LAW OR OTHERWISE, OF ANY PRODUCTS OR SERVICES FURNISHED UNDER OR IN CONNECTION WITH THIS AGREEMENT. TORAX DISCLAIMS ALL IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, AND THOSE WARRANTIES ARISING BY STATUTE OR OPERATION OF LAW, OR FROM A COURSE OF DEALING OR USAGE OR TRADE.

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