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International Congress on Gastroenterology & Hepatology  
**RECENT DEVELOPMENTS IN THE FIELD OF  
GASTROENTEROLOGY & HEPATOLOGY**

Chicago USA October 09-12 2017

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A thank you to the Conference Organizers, Moderators and Co-Moderators, Speakers of this session and the whole Audience.

**The gastroesophageal reflux disease: a  
focus on endoscopic therapy. A clinical  
review and scientific literature.**



Different clinical presentations of gastric reflux disease: dysphagia, cough, rhinitis, burning in the jugular region, burning mouth, chest pain that mimics a heart attack, otitis, post nasal drip, bronchitis, asthma, mucous dryness, headache, exhaustion.

# Definition of GERD\*

A condition that develops when the reflux of stomach contents (in esophagus) causes troublesome symptoms and/or complications

\*Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R. **Global Consensus Group**, *Am J Gastroenterol.* 2006; 101(8):1900.

As a clinical consequence of this correct and practical definition, **the best therapy should be one that prevents any kind of reflux**

My colleagues, Internist and Physiopathologist, explain how to define the type of gastric reflux and try to combat the disease with dietary, behavioral, pharmacological and also physiotherapeutic methods.

My colleagues surgeons have the possibility of performing a laparoscopic fundoplication and have some therapeutic novelties as the magnetic collar, which minimizes the alteration of the anatomical structures. However, all those are surgical procedures, with a 3-4 day stay in Hospital and with the difficulty of re-intervention within a short period of time.

I will talk about endoscopic techniques and critically expose the techniques known and applied so far.

**Endoluminal therapies**

# Techniques

## A) Radiofrequency energy

### **Stretta System**

## B) Injection or implantation techniques (obsolete?)

- **Gatekeeper** Reflux Repair System
- **Plexiglas** (polymethylmethacrylate) and **Durasphere**
- **Enteryx** procedure

## C) Mucosal resection

- Antireflux mucosectomy (**EARMS**)

## D) Endoscopic plication suturing (transoral incisionless fundoplication procedure)

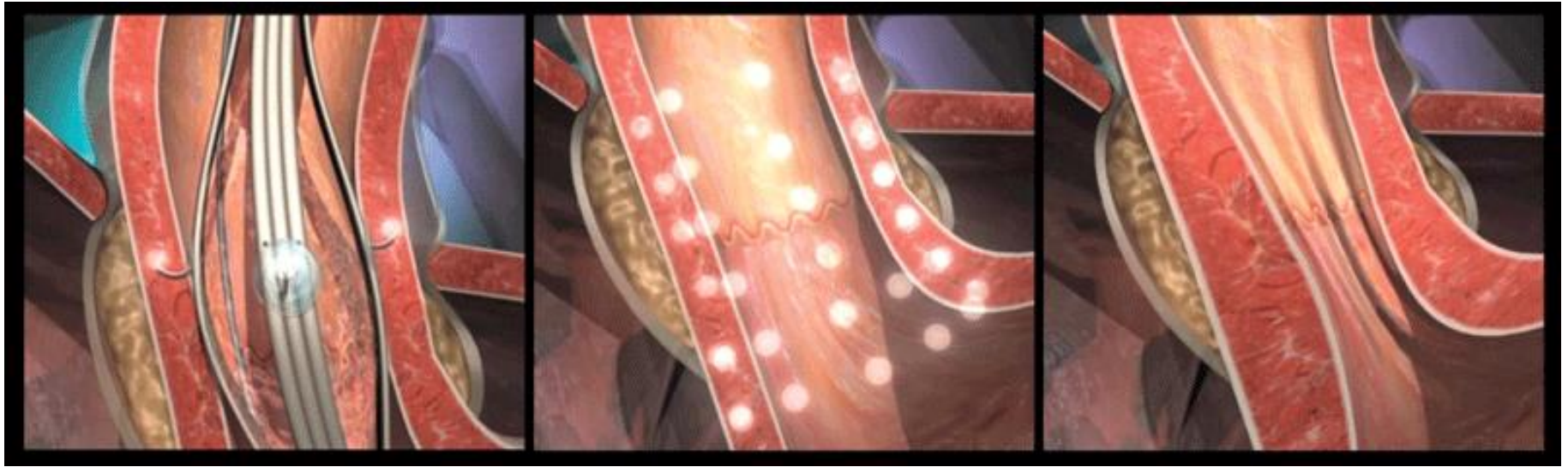
- **EsophyX™** System with SerosaFuse™ Fastener
- Bard **EndoCinch** Endoscopic Suturing System
- **MUSE** (Medigus Ultrasonic Surgical Endostapler)
- **GERD-X** Method

# Radiofrequency (Stretta)

- I have to say that the greater radio frequency application is currently focused on the treatment of Barrett's esophagus, associating it with mucosal or submucosal endoscopic dissection.
- Principle: Radiofrequency energy delivery
- Equipment: **RF control module** and  
**Flexible Stretta catheter**
- Catheter: 20 Fr soft bougie tip and a balloon, which opens into a surrounding basket.
- 4 electrodes deliver 60 to 300 J of RF energy to each needle, heating the surrounding muscle tissue to the target temperature between 65<sup>0</sup>C to 85<sup>0</sup>C



## Stretta procedure



## Stretta Procedure (2)

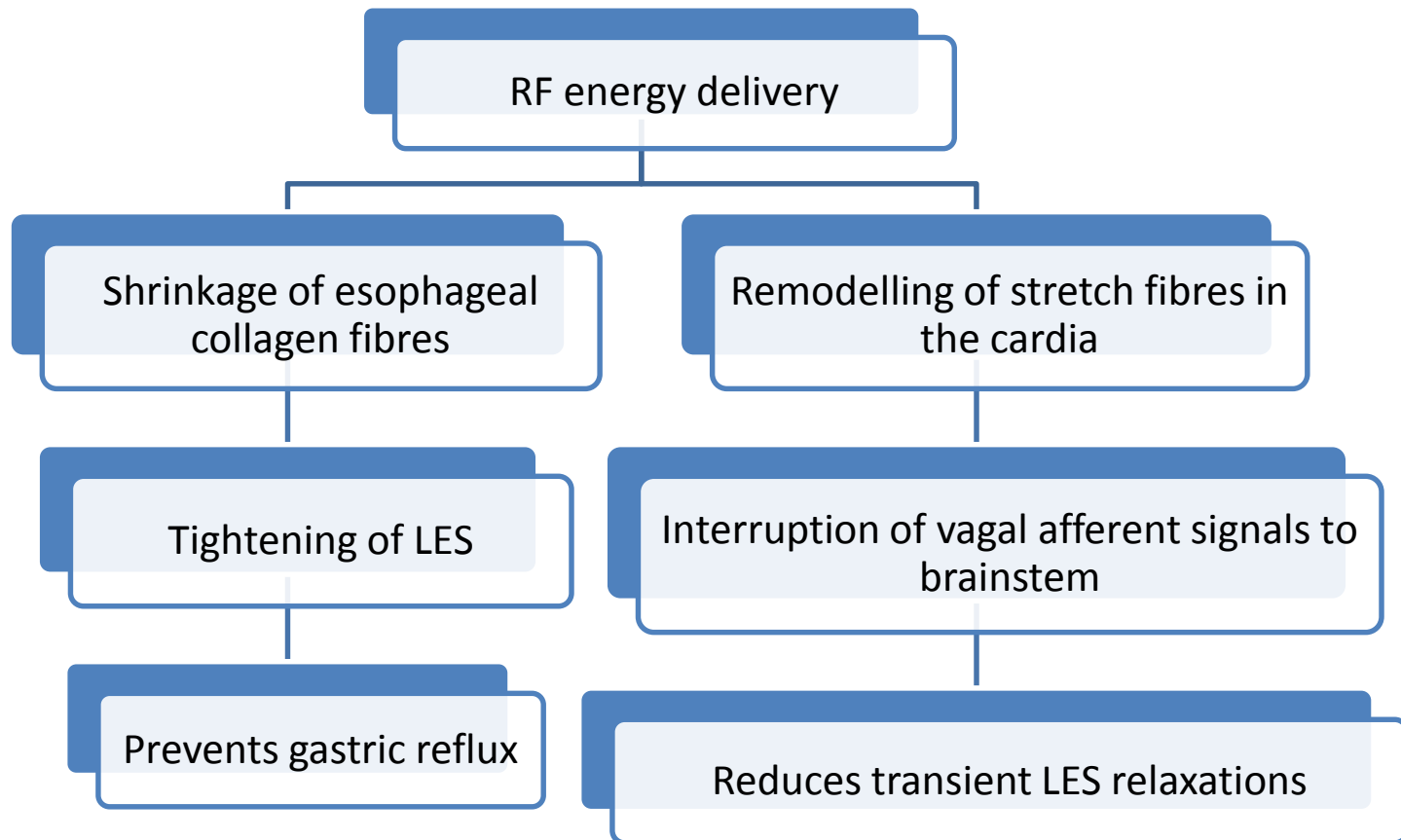
Stretta procedure is based on the use of a device that releases energy in the form of radio frequency, at cardiac level, through needle electrodes inserted in the junctional muscle tissue. This method can be performed with the device in the passage of the endoscope channel or (much more frequent device) inserting it later, under radiological guidance, after taking the measures during gastroscopy

## Stretta Procedure (3)

- The procedure is a minimally invasive method. The action takes place in two stages: a gastroscopy is performed to measure the patient's esophagus. Subsequently, orally, placing a catheter, until the lower esophageal sphincter, previously located. In this point you dilate the balloon catheter, from which they protrude four needles, with which the radio frequency is applied on the distal esophageal mucosa and cardial junction.
- The procedure lasts about 30 minutes and is performed under general anesthesia, as you need the patient's immobility. The heat should make the lower esophageal sphincter more toned and resistant. Certainly, they are compromised the sensory receptors of the esophagus, so you get the reduction of the pain sensitivity.

## Stretta Procedure (4)

Continuous irrigation of the esophageal mucosa and surface temperature monitoring are utilized to prevent thermal mucosal injury



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## Gatekeeper reflux repair system

The **Gatekeeper** Reflux Repair System utilizes a soft, pliable, expandable prosthesis made of a Poly-Acrylo-Nitrile-based hydrogel (HYPAN). The prosthesis is implanted into the esophageal submucosa, and, with time, the prosthesis absorbs water and expands, creating bulk in the region of implantation. *These agents are not commercially available in the United States and not even in Italy, as far as I can tell.*

***No new studies, that provide substantial new evidence regarding polymer injection and implantation techniques, were identified in the most recent literature search.***

I ask the Endoscopists Gastroenterologists present at the Congress if, in their countries, these endoscopic injection or expandable polymer systems are used.

## Gatekeeper reflux repair system (2)

In a RCT (Randomized Controlled Trial), employing sham controls, Paul Fockens et al. (\*) assessed whether endoscopic implantation of an injectable esophageal prosthesis, the **Gatekeeper** Reflux Repair System (GK), is a safe and effective therapy for controlling GERD.

The investigators concluded that the GK procedure was associated with some serious, but infrequent, complications.

No statistically significant differences in outcomes were observed between the treatment and control groups at 6 months.

“Prospective randomized controlled trial of an injectable esophageal prosthesis versus a sham procedure for endoscopic treatment of gastroesophageal reflux disease”

Paul Fockens, Lawrence Cohen, Steven A. Edmundowicz, Kenneth Binmoeller, Richard I. Rothstein, Daniel Smith, Edward Lin, Nicholas Nickl, Bergein Overholt, Peter J. Kahrilas, Nimish Vakil, Ayman M. Abdel Aziz Hassan and Glen A. Lehman

Surg Endosc. 2010 Jun; 24(6): 1387–1397.

## Gatekeeper reflux repair system (3)

The findings of the Foken study, after inclusion of 143 patients (25 patients enrolled, 75 treated with GateKeeper and 43 control patients), were evaluated with a statistical analysis.

The **GK study was terminated in advance due to the lack of important efficacy data.**

Four serious adverse events (2 perforations, 1 pulmonary infiltration associated with a perforation and 1 chest pain) were reported at the end of the study, without mortality or long-term sequelae.

**Symptoms of stomach burning and exposure of the esophagus to acid have significantly improved at 6 months** in patients treated and in control patients, compared to baseline ( $p < 0.0001$ ), **but** no significant difference was observed in the improvement Patient group among patients treated with GateKeeper and controls ( $p = 0.146$ ).

In summary, this sham-controlled trial of endoscopic implantation of Gatekeeper prostheses for GERD showed that this procedure is associated with serious but infrequent complications and **improves GERD symptoms, quality of life, and drug use for GERD patients at 6 months, with this trend persisting for at least 12 months.**

**BUT**, the **sham group showed many similar improvements**, however. The improvements in esophageal functions (esophageal acid exposure and LES pressure) in the active treatment group were minimal and not clinically meaningful. Overall, no statistically or clinically significant differences in outcomes were observed between the treatment group and the control group at 6 months compared with baseline.

The concept of endoluminal treatment for GERD continues to be appealing because it focuses on gastroesophageal reflux control and not just acid secretory control. *Currently effective medical and surgical therapies for GERD create a relatively high standard for new endoscopic therapies.* To date, the major obstacles against their wider spread use include limited to moderate efficacy for most devices, lack of good reimbursement codes in the United States, serious complications (although less frequent than for surgical fundoplication), and insufficient funding and support for research to develop new technologies to treat GERD. More work is needed before these approaches can be considered a standard of care for GERD.

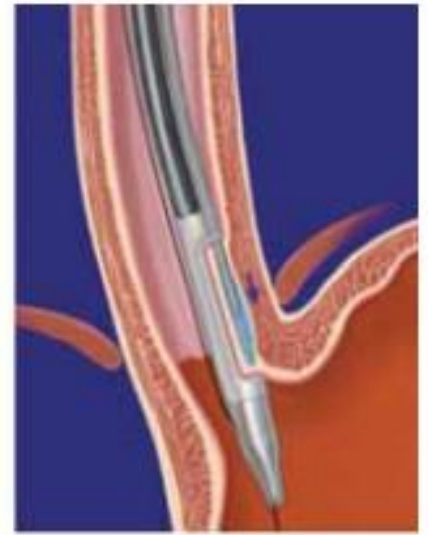




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2



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Gatekeeper reflux repair system

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# Plexiglas technique

The Plexiglas (**P**oly-**M**ethyl-**M**ethacrylate, PMMA) is a procedure which involves **injection of an inert polymer** material into the submucosa of the proximal lower esophageal sphincter zone to provide **bulking support to the sphincter** and **decrease Transient Relaxations** of the **Lower Esophageal Sphincter** (tLESRs).

It is a suspension of poly-methyl-methacrylate **microspheres in gelatin solution**.

Gelatin is **phagocytosed by macrophages** within 3 months and is replaced by fibroblasts and collagen fibres.

# Durasphere

Another bulking agent, pyrolytic carbon-coated beads (Durasphere®), is being evaluated for treatment of GERD. Durasphere is approved by the U.S. Food and Drug Administration (FDA) as a submucosal urethral bulking agent. Use of this product for esophageal reflux would be considered off-label use.

The pyrolysis (or thermal cracking) is a thermochemical process of decomposition of organic materials, obtained by the application of heat and in the complete absence of an oxidizing agent.

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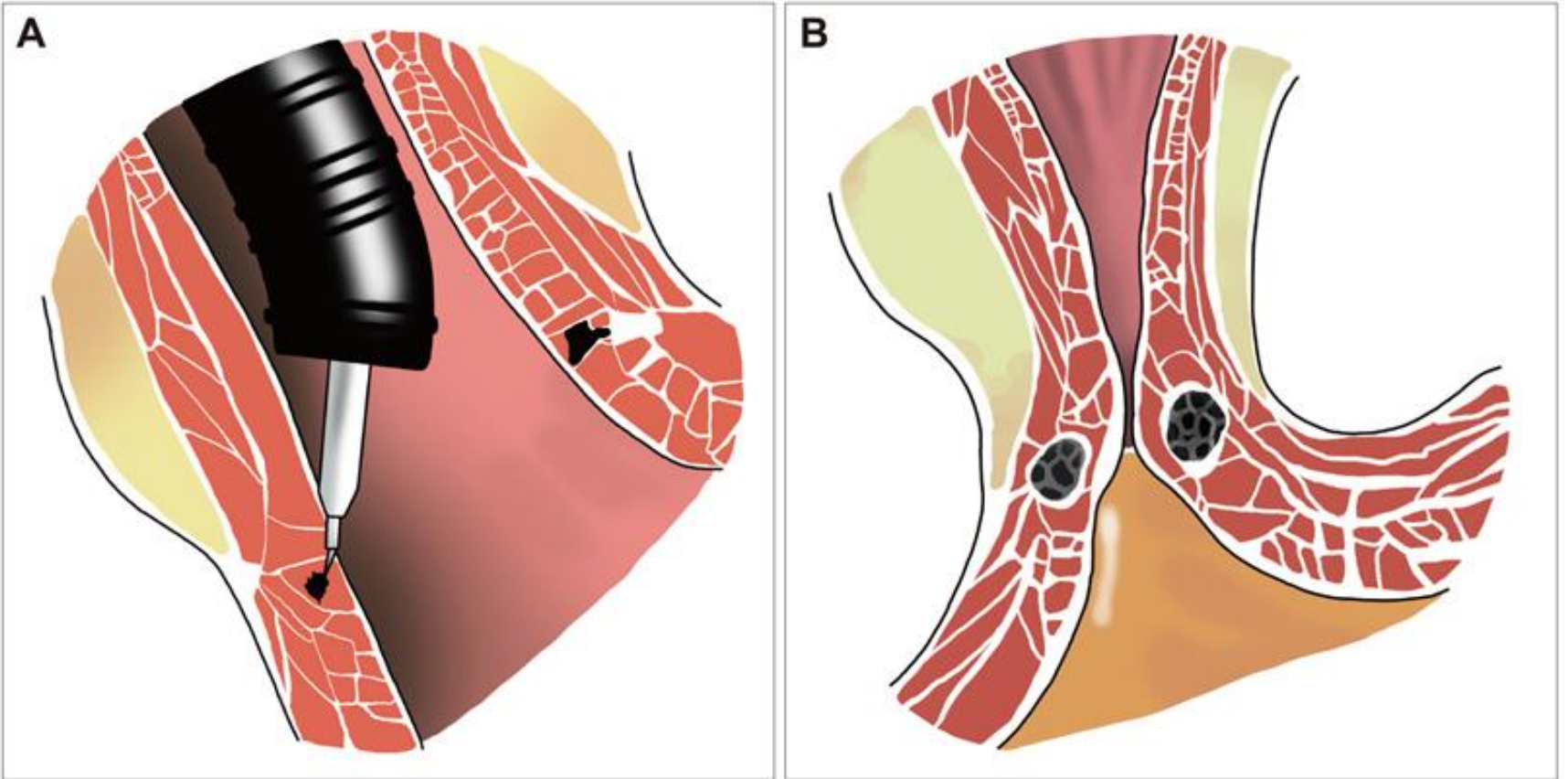
## EnteryX system

**Enteryx** is a co-polymer of **E**thylene-**V**inyl **A**lcohol (EVOH) and tantalum, a radioactive agent dissolved in dimethylsulfoxide (DMSO). A solution of 6-8 ml of ethylene vinyl polymer (EVOH) at 8% is **infused** at a rate of 1 ml/min **in the muscular layer or deep submucosal, 1-2 mm caudally to the Z line**. Although Enteryx does not influence the pressure of the LES, the distency and shape of the GE junction are modified. This solution precipitates in the form of inert mass and reduces the opening of the cardias. **BUT**, in 2005, the Food and Drug Administration ordered the immediate suspension of ENTERYX, as severe adverse reactions, in particular embolization, were reported.

“Complications involving the mediastinum after injection of Enteryx for GERD”.

Wong RF, Davis TV, Peterson KA.

Gastrointest Endosc 2005; 61: 753-756.



EnteryX system

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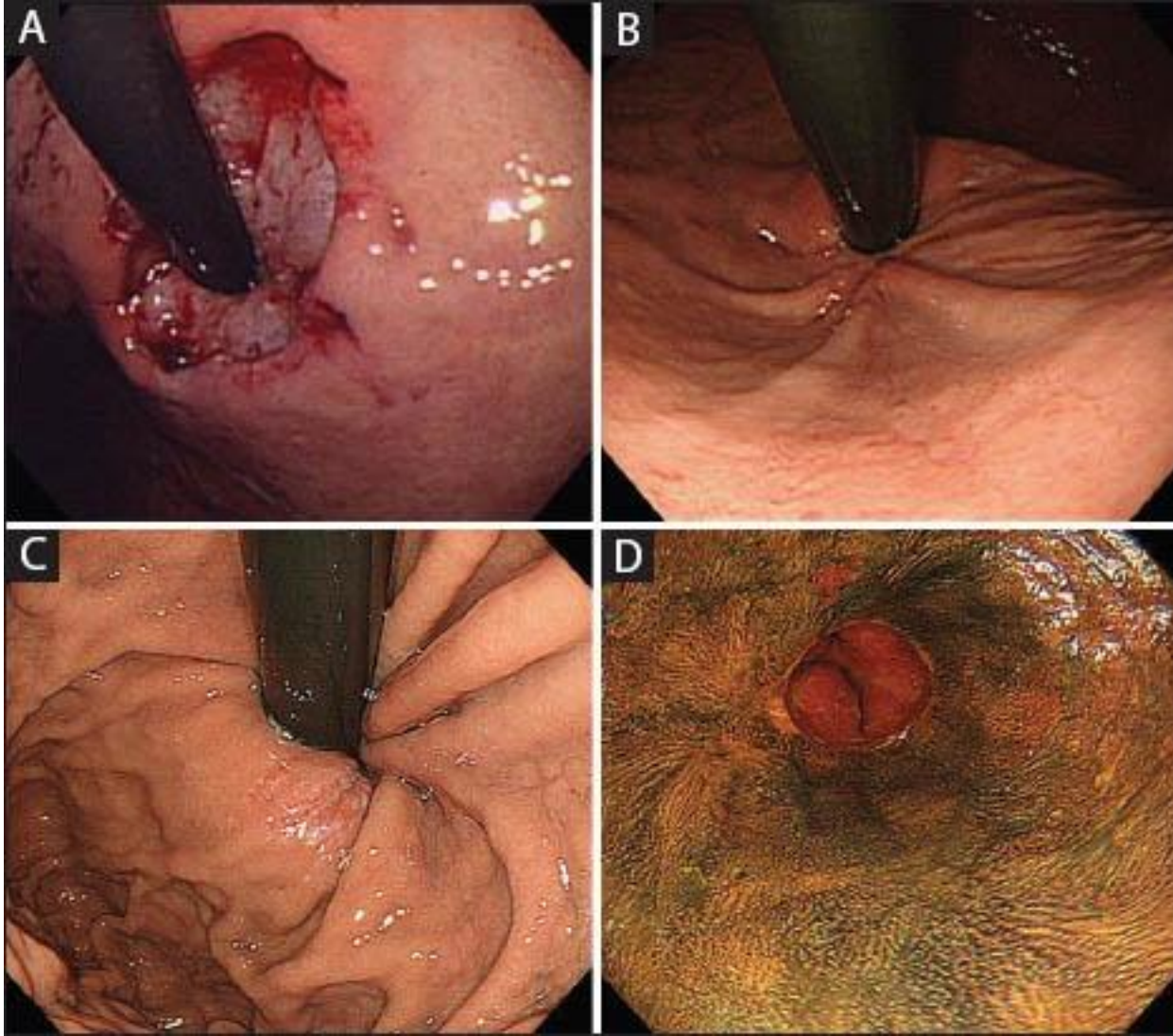


## ANTI-REFLUX MUCOSECTOMY (EARMS)

The **ARMS** (Anti-Reflux Muco Sectomy/EARMS Endoscopic Anti Reflux Muco Sectomy) procedure is based on the principle that, after mucosal resection, mucosal healing causes **scar formation**. This results in retraction and remodeling of the esophagus-gastric junction (similar to STRETTA procedure). This reduces reflux episodes. Although the first case was executed more than a decade ago, the results of the first series were published recently (\*). The technique of the EARMS procedure (as described by Inoue et al.) provides a half-moon resection of esophageal mucosa for 1 cm and gastric mucosa for 2 cm. The resection limit is marked by the endoscopic needle knife. Subsequently, a saline solution, mixed with the indigo-carmin dye, is injected under the mucosa to lift it. In the later phase, mucosal resection is performed along the small gastric curvature by endoscopic resection of the mucosa or submucosa dissection. A space equal to twice the diameter of the endoscope is left along the side of the large curvature. **The circumferential resection is avoided to prevent stenosis, as has been observed in the first cases of this series.** Any bleeding during the procedure is controlled by coagrasper (hemostatic forceps). In the only published pilot study (\*) there was a reduction in EAET (Esophageal Acid Exposure Time) and an improvement in the His angle of the esophagus-gastric junction. In addition, all patients may stop PPI after ARMS therapy.

\* "Anti-reflux mucosectomy for gastroesophageal reflux disease in the absence of hiatus hernia: a pilot study"

Haruhiro Inoue, Hiroaki Ito, Haruo Ikeda, Chiaki Sato, Hiroki Sato, Chainarong Phalanusittheppha, Bu'Hussain Hayee, Nikolas Eleftheriadis and Shin-ei Kudoc. Ann Gastroenterol. 2014; 27(4): 346–351.



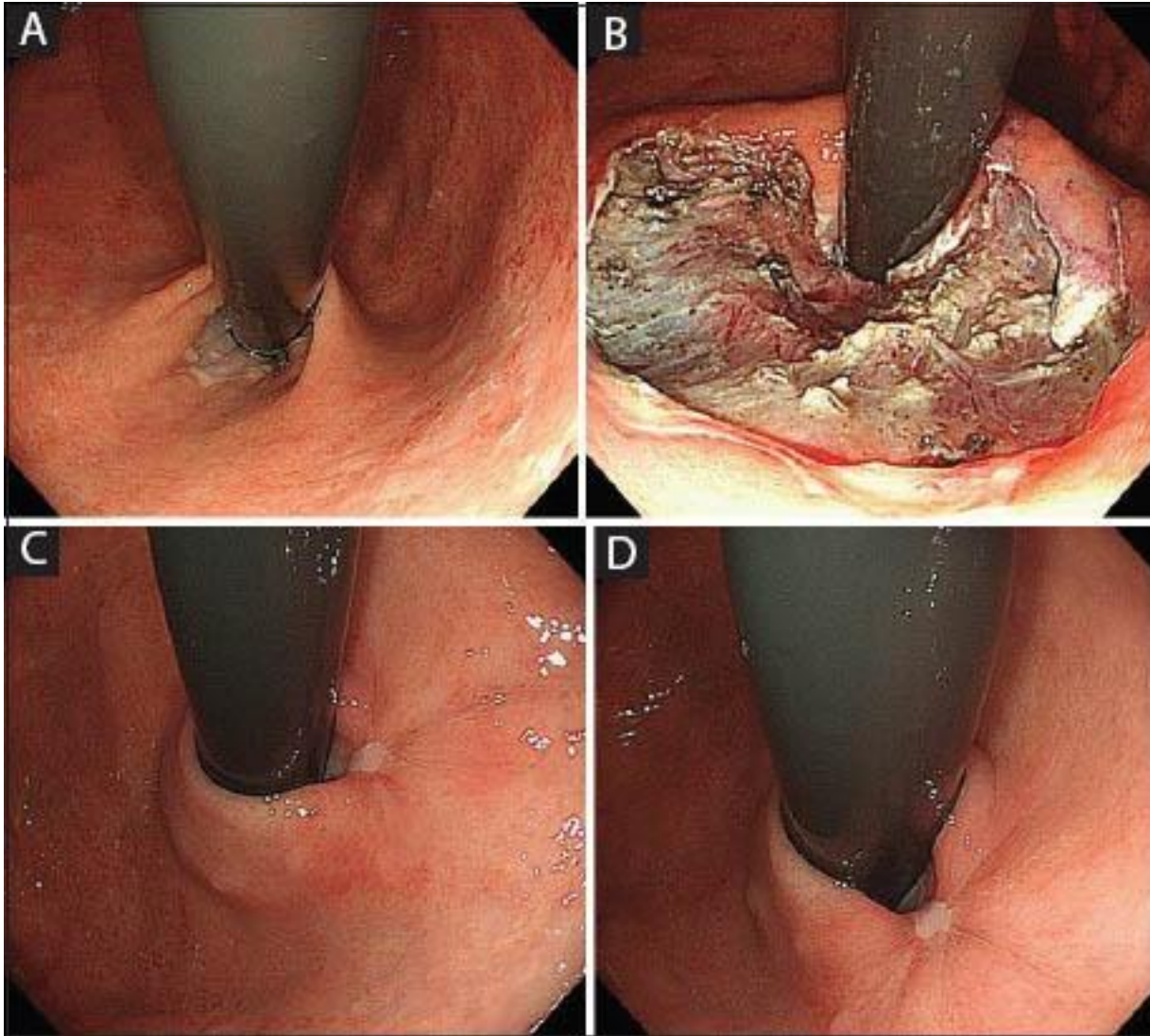
Endoscopic follow up of circumferential anti-reflux mucosectomy (ARMS) (retroflexed views). (A) Immediately after circumferential ARMS.

Approximately 2 cm-wide gastric cardia mucosa was circumferentially resected by cap-endoscopic mucosal resection method.

(B) Appearance at 3 years. A tight gastro-esophageal junction. Convergence of three gastric folds was observed along the lesser curve of the stomach.

(C) More than 10 years after circumferential ARMS. Appearance is similar to Fig. 3B.

(D) More than 10 years after circumferential ARMS (forward view). Chromoendoscopy with Lugol's solution demonstrated well-stained squamous epithelium with neither recurrence of esophagitis nor Barrett's esophagus. (for the courtesy of prof. Inoe)



Endoscopic follow up of crescentic anti-reflux mucosectomy (ARMS).

Before ARMS. Endoscopy in retroflexion demonstrated significant hiatal hernia (Flap valve score 3) but no sliding component. Chest pain and regurgitation were prominent in this case (DeMeester score 5) and symptoms were not controlled by double dose proton pump inhibitor.

(B) Immediately after procedure. Endoscopy in retroflexion showed two-thirds circumferential artificial ulcer. ARMS was centered at lesser curve and the **mucosal flap valve at greater curve was preserved**. (C) Appearance at 2 months. Mucosal valve was re-shaped and well-defined (Mucosal flap valve Grade 1).

(D) Alternative endoscopic view at 2 months. Mucosal valve as appeared as though "stitched" at the lesser curve of gastric cardia. (for the courtesy prof. Inoe)

## ANTI-REFLUX MUCOSECTOMY (**EARMS**) 2

The EARM procedure is emerging as a minimally invasive treatment option for patients with GERD. Reduced hospital stays and adverse events have been observed compared to conventional surgery (ARS/Anti Reflux Surgery), making the EARM procedure an attractive option for patients with GERD. **Long-term follow-up data with durable response tests are available for the radiofrequency method (RFA/Stretta) and for trans-oral fundoplication techniques (TIF and MUSE).** However, some **drawbacks with EARM** are remarkable. First of all, these devices were tested in selected patients with minimal esophageal inflammation and small hyatal hernia. Second, although the symptom response is reasonably good, objective data (such as EAET/Exposure Time of Esophagus to Acid) are less evident. Current literature suggests that EARM reduces EAET, but often do not normalize it. EAET normalization is undoubtedly a difficult objective to achieve, but can not be ignored due to possible long-term consequences such as Barrett's esophagus and esophageal adenocarcinoma. Likewise, the need to use PPI is reduced, but not completely eliminated, to a substantial percentage of patients undergoing endoscopic therapy. Finally, long-term data with some recently introduced EARM are not sufficient and there are no comparative studies between different endoscopic modes. Therefore, final data on the EARM procedure are not available.



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# EsophyX™ System with SerosaFuse™ Fastener

- They are called TIF (**Transoral Incisionless Fundoplication**) all endoscopic procedures, performing a fundoplication of the stomach, to the cardia level.
- The device creates a full-thickness fold, from serosa to serosa, and strengthens the sphincter esophageal-gastric.
- These procedures are less invasive alternatives of laparoscopy

## EsophyX™ System with SerosaFuse™ Fastener (2)

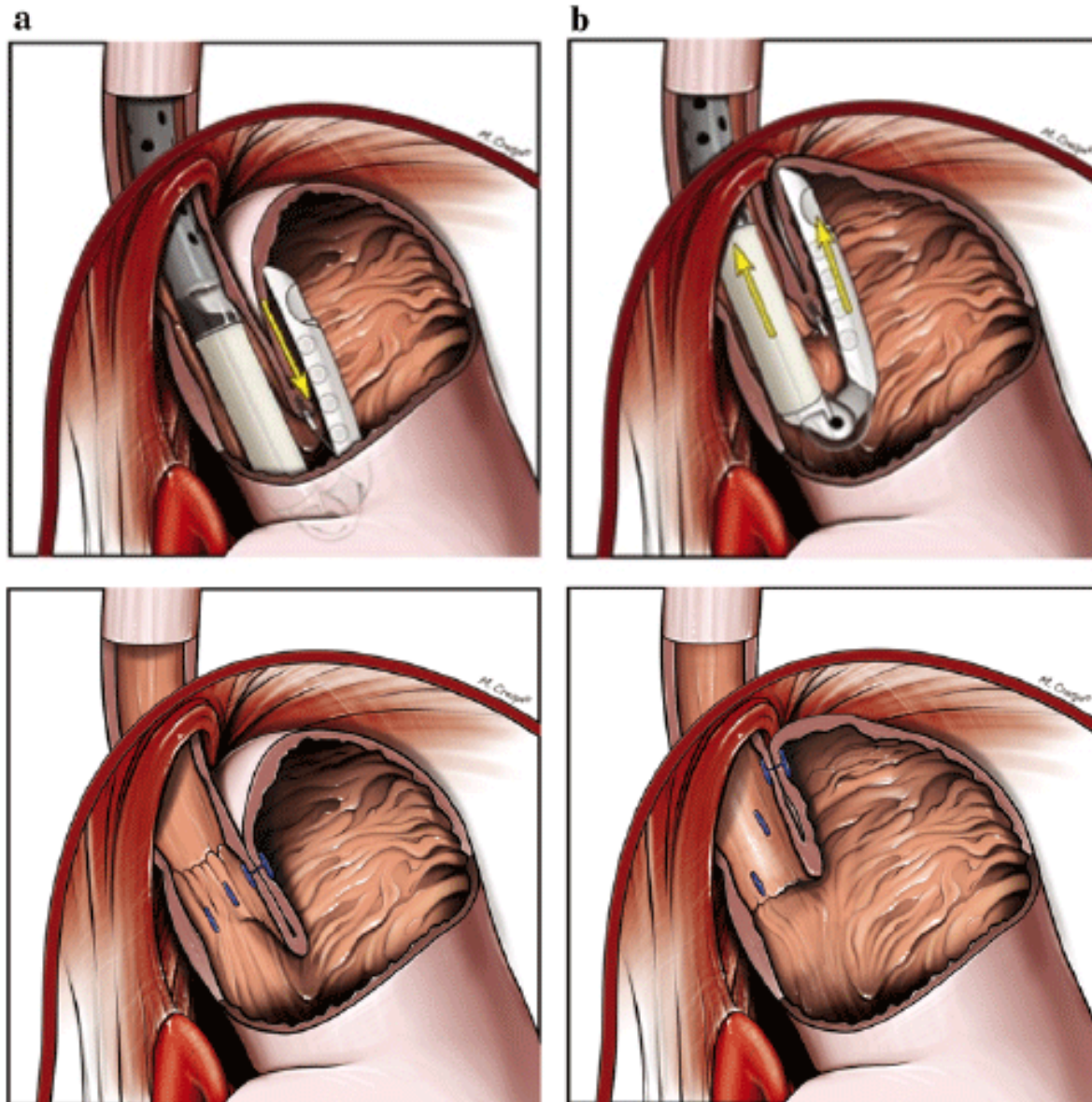
The **Esophyx** device, for the TIF method, which means Transoral Incisionless Fundoplication, is manufactured by EndoGastric Solution and allows the creation of a fundoplication esophago-gastric of 2-3 cm thick, for circumferential extension of 270°, capturing the mucosa tissue with 12 or more points of polypropylene suture. The device is used in combination with an endoscope flexible video, which provides the endoscopic visualization throughout the operation. *This necessity of double instrument makes complicated the procedure* and has meant that the technique has been partly abandoned in favor of a similar procedure, but using a single instrument, which allows the display and simultaneously the operation.

## EsophyX™ System with SerosaFuse™ Fastener (3)

The Esophyx proceedings showed, as many authoritative scientific journals have published, a good symptoms control, but for a short time, because the intervention does not allow the mobilization of the gastric fundus and the tension on the stitches causes, in the long run , their failure and the return to the status quo ante. It is known, moreover, that even surgical procedures, in many cases, are beset by recurrent, after years, but sometimes after a few months.



# ESOPHYX



# EsophyX™ System with SerosaFuse™ Fastener



Pre-operative



Intra-operative



Post-operative

## EsophyX™ System with SerosaFuse™ Fastener (4)

The ELF procedure (Endo-Luminal Fundoplication) can be tailored to the individual patient and his particular anatomy. The post-intervention [histological examinations](#) confirm that **EsophyX** creates a [valve, which incorporates the muscular wall of the fundus](#) of the stomach, made more solid by the development of collagen between the two layers of the fold. The [frenico-esophageal ligaments are incorporated](#) within the valve, stabilizing and increasing their holding, [anchoring it to the diaphragm](#). EsophyX reduces adverse events, frequent in surgical approach, such as dysphagia, pain and longer recovery times.

The [long-term studies](#), however, have dampened enthusiasm, in view of the [recurrence of the symptoms](#) and because of the [failure of the stitches](#). In fact, working endoscopically, it is not possible to release and mobilize the gastric fundus, which, for this reason, it exerts pressure and traction on packed sutures. [In the long run, therefore, the esophagogastric junction becomes again pathological.](#)

**Review** on Endoluminal Treatments for Gastroesophageal Reflux Disease (GERD)  
This statement was reviewed and approved **by the Board of Governors of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)** (September 2012)

**Laparoscopic fundoplication remains the gold standard** in interventions for GERD in both adults and children. Multiple studies document the long term success of laparoscopic Nissen fundoplication. Notwithstanding the successes of surgical fundoplication, patients and providers continue to search for increasingly less invasive approaches to GERD, especially emphasizing **techniques that seek to reduce the risks of dysphagia, bloating, and adverse outcomes sometimes associated with surgery.**

The review considers **two procedures based on an endoscopic platform (Esophyx and Stretta)** that provide alternatives to the pharmacologic and surgical treatment of GERD. In considering the clinical application of these and other alternatives to the effective therapy provided by laparoscopic fundoplication for patients with GERD, the reader is asked to consider the **degree of symptom relief** and **restoration of physiologic function** provided by each therapy, and further, to consider the implications of treatment failures related to endoluminal therapies.

Some endoluminal therapies may not offer the same degree of relief provided by surgery, but **might still represent viable alternatives for patients seeking relief from lifelong dependence on pharmacologic therapy, its cost, associated side effects, and long-term adverse outcomes.**

(2) **Review** on Endoluminal Treatments for Gastroesophageal Reflux Disease (GERD)  
This statement was reviewed and approved **by the Board of Governors of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)** (September 2012)

The **EsophyX device** has been studied across a broad range of adult patient populations, and reported in one adolescent study. Numerous published series have reported significant untoward events, although the safety profile for the procedure appears to be evolving in parallel with the procedural technique. **Results appear mixed with some series reporting disappointing outcomes, and others reporting promising short-term results;** yet, there still is a significant gap in the literature. The majority of available literature is significantly underpowered, mostly observational studies with routinely brief follow-up periods. There has been a paucity of sham controlled trials and studies that directly compare TIF (transoral incisionless fundoplication) with laparoscopic anti-reflux surgery. The device has been modified through multiple revisions, and the technique of the procedure has evolved as well; **long term data that will be available in the near future will most likely be based upon the first generation device and the TIF 1.0 technique.** The creation of the EsophyX database and registry will aid in future research important to making more meaningful recommendations with respect to placement of TIF (transoral incisionless fundoplication) in the treatment of patients with GERD. Further study in the pediatric population will be necessary to consider TIF a treatment option for children.

(3) **Review** on Endoluminal Treatments for Gastroesophageal Reflux Disease (GERD)  
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### **Recommendation for Esophyx:**

Long term data is not yet available for Esophyx. In short term follow-up, from 6 months to 2 years, Esophyx may be effective in patients with a hiatal hernia < 2 cm with typical and atypical GERD. Further studies are required to define optimal techniques and most appropriate patient selection criteria, and to further evaluate device and technique safety. **Quality of Evidence: (++)**. **GRADE Recommendation: Weak**

### **Stretta**

Mederi Therapeutics Inc. (Greenwich CT) acquired all rights to the Stretta system for the radiofrequency treatment of GERD, including its specialized catheters and radiofrequency (RF) generators. The FDA originally cleared Stretta for use in 2000 and issued an updated clearance on the RF generator in 2011. The transoral Stretta catheter system uses a proprietary algorithmic application of low power (5 Watts) RF energy and generates low tissue temperatures (65°C to 85°C) during a series of one-minute treatment cycles. Stretta therapy remodels the musculature of the lower esophageal sphincter (LES) and gastric cardia.



(4) **Review** on Endoluminal Treatments for Gastroesophageal Reflux Disease (GERD)  
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Clinical studies demonstrate that the **Stretta RF treatment results in significant reductions in tissue compliance and transient LES relaxations**. These mechanisms act to restore the natural barrier function of the LES as well as to significantly reduce spontaneous regurgitation caused by transient inappropriate relaxations of the sphincter.

#### **Conclusion of this review about Stretta**

More than 30 peer reviewed studies, including 4 adequately powered randomized, controlled studies, a comprehensive meta-analysis and multiple prospective clinical trials have documented the safety and efficacy of the Stretta procedure. Durable treatment outcomes to at least to 48 months also have been demonstrated in multiple studies, with significant reduction or elimination of medications used to treat the symptoms of GERD, as well as improvement in GERD QOL and symptom scores. **Stretta may be recommended as an appropriate therapeutic option** for patients with GERD who meet current indications and patient selection criteria and choose endoluminal therapy over laparoscopic fundoplication. Those criteria include:

Adult patients (age  $\geq 18$ ) with symptoms of heartburn, regurgitation, or both for  $\geq 6$  months who have been partially or completely responsive to antisecretory pharmacologic therapy.

(5) **Review** on Endoluminal Treatments for Gastroesophageal Reflux Disease (GERD)  
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The procedure (**Stretta**) has not been studied and should not be applied in treating patients with severe esophagitis, hiatus hernias > 2 cm, long segment Barrett esophagus, dysphagia, or those with a history of autoimmune disease, collagen vascular disease, and/or coagulation disorders. Further studies are needed to evaluate the role of Stretta in children if it is to be considered a therapeutic option.

**Recommendation:**

Stretta is considered appropriate therapy for patients being treated for GERD who are 18 years of age or older, who have had symptoms of heartburn, regurgitation, or both for 6 months or more, who have been partially or completely responsive to anti-secretory pharmacologic therapy, and who have declined laparoscopic fundoplication.

**Quality of Evidence: (++++). GRADE Recommendation: Strong**



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# Bard EndoCinch Endoscopic Suturing System

The **EndoCinch** was the first form of intraluminal gastroplication, which has obtained the approval from the FDA in the United States, in 2006. The procedure, which takes its name from the instrument used, consists in capturing, **in a niche**, which is located in the final part of a special endoscope, part of the mucosa of the esophagogastric junction, where it is sewn to form folds. In this way, it reduces the cardial space, as happens in the surgical intervention (fundoplication procedure), creating these mucosal folds below the lower esophageal sphincter, with the sutures carried through the gastroscope. This method, like all endoscopic procedures, is burdened by the loss of long-term efficacy, due to the ineffective sealing of suture points.

## Bard EndoCinch Endoscopic Suturing System (2)

The same method was also used for obese patients, reducing the gastric lumen and putting in communication a gastric pouch, reduced in size, with the small intestine, obtaining an early sense of satiety, and simulating the surgery procedure of “sleeve gastrectomy”. Also this procedure presents the same drawback of the failure of the sutures tight.

As the procedure with Esophyx, EndoCinch also has the disadvantage of having to be carried out with two tools and the over-tube too, which makes the method complicated. The presence of the room, where it is sucked the mucosa of the esophagogastric junction, before applying the stitches, had hoped for a better grip of the same, as compared to other endoluminal procedures. But the clinical evidence does not support this point of view.

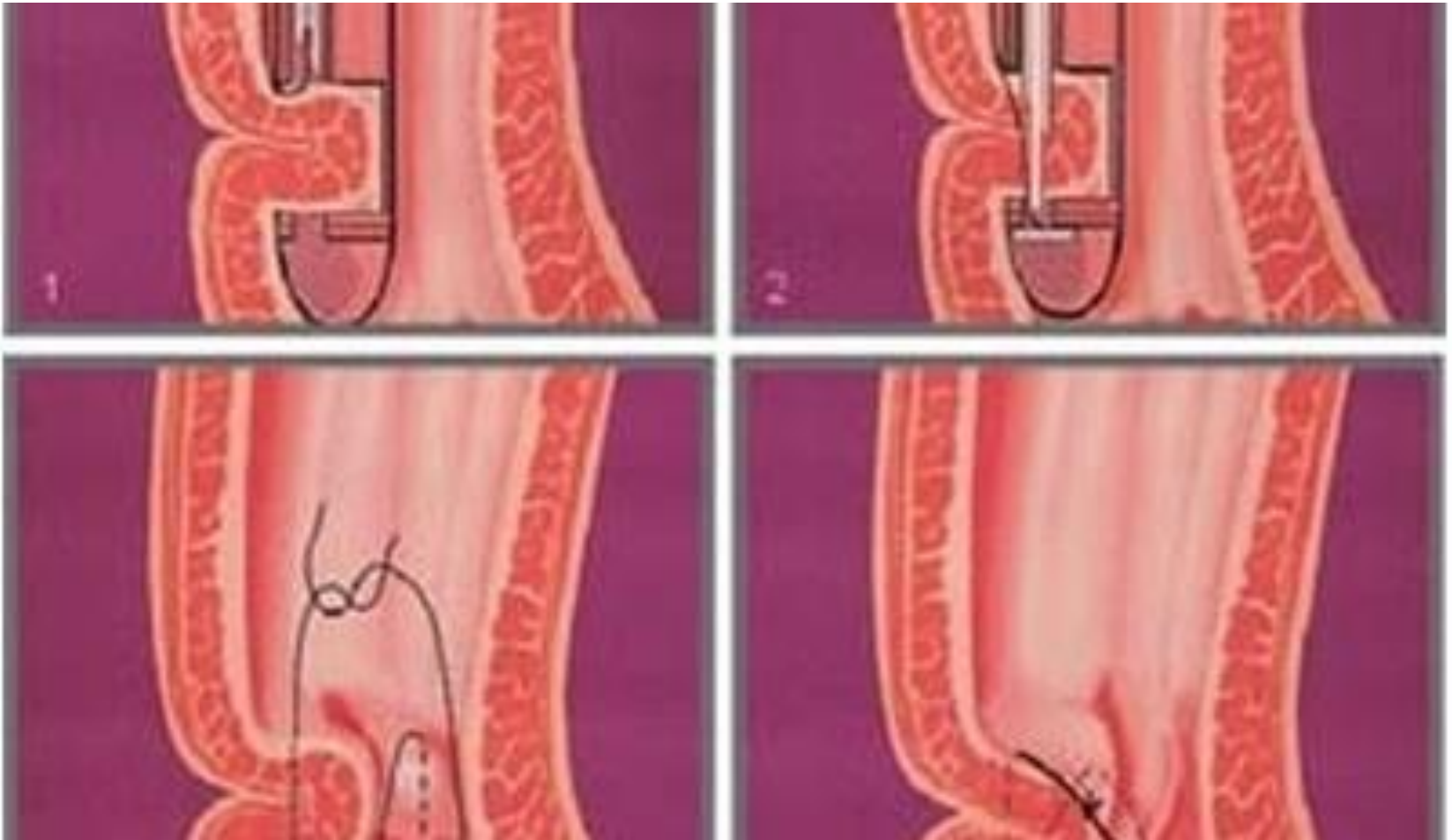
## Bard EndoCinch Endoscopic Suturing System (3)

- Effective in short-term follow-up period and the complication rate was relatively low
- Sutures were significantly lost within the 6-month follow-up period, thus necessitating reprocedure in about 25% of the patients.

# BARD Endocinch



Endocinch procedure: you see the **niche**, located in the final part of the endoscope



Gut. 2005 Jun; 54(6): 752–758.

Long term failure of endoscopic gastroplication (**EndoCinch**)

I Schiefke, A Zabel-Langhennig, S Neumann, J Feisthammel, J Moessner, and K Caca

**Patients and methods:** A total of 70 patients treated with **EndoCinch** at a single referral centre were studied prospectively. All patients were interviewed using a standardised questionnaire regarding their symptoms and medication prior to and 18 months after EndoCinch. In addition, follow up included endoscopy, 24 hour pH monitoring, and oesophageal manometry.

**Results:** The procedure was well tolerated **without major short or long term complications**. Eighteen months after EndoCinch, 56/70 patients (80%) were considered treatment failures as their heartburn symptoms did not improve or proton pump inhibitor medication exceeded 50% of the initial dose. Endoscopy showed all sutures in situ in 12/70 (17%) patients while no remaining sutures could be detected in 18/70 (26%). In 54 and 50 patients examined, respectively, no significant changes in 24 hour pH monitoring (median pH <4/24 hours, 9.1% v 8.5%;  $p=0.82$ ) or lower oesophageal sphincter (LES) pressure (7.7 v 10.3 mm Hg;  $p=0.051$ ) were observed while median LES length slightly increased (3.0 to 3.2 cm;  $p<0.05$ ).

**Conclusion:** Endoscopic gastroplication (**EndoCinch**) is a **safe and minimally invasive endoscopic treatment** for GERD with **reasonable short term results**. In contrast, **long term** outcome is **disappointing**, probably due to suture loss in the majority of patients. Therefore, technical improvements to ensure suture durability are mandatory before endoscopic suturing can evolve as a therapeutic option for GERD treatment.

# Techniques

## A) Radiofrequency energy

**Stretta System**

## B) Injection or implantation techniques (obsolete?)

- **Gatekeeper** Reflux Repair System
- **Plexiglas** (polymethylmethacrylate) and **Durasphere**
- **Enteryx** procedure

## C) Mucosal resection

- Antireflux mucosectomy (**EARMS**)

## D) Endoscopic plication suturing (transoral incisionless fundoplication procedure)

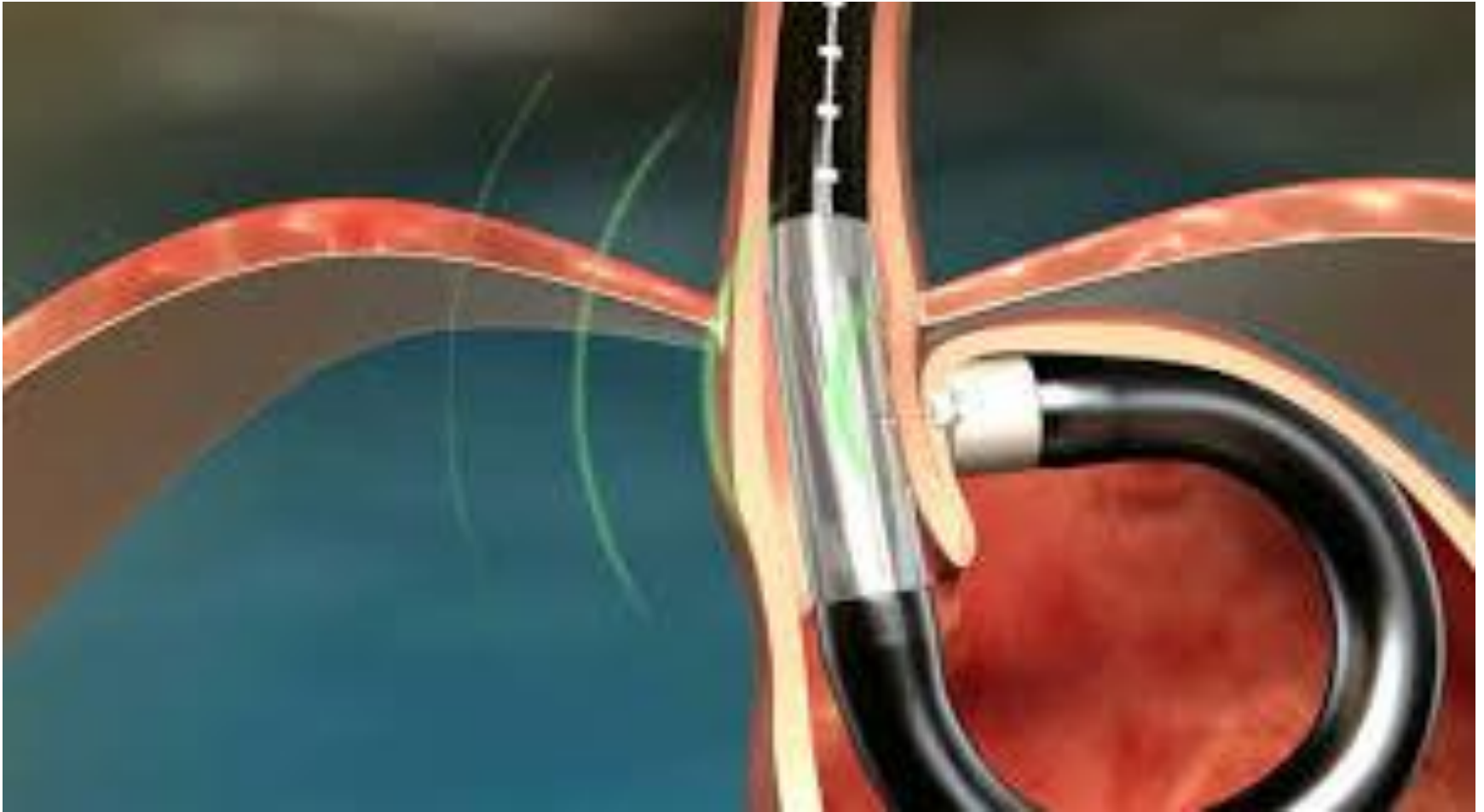
- **EsophyX™** System with SerosaFuse™ Fastener
- Bard **EndoCinch** Endoscopic Suturing System
- **MUSE** (Medigus Ultrasonic Surgical Endostapler)
- **GERD-X** Method



# MUSE (Medigus Ultrasonic Surgical Endostapler)

This method, similar to that used with the Esophyx, offers the advantage of a single tool, equipped with a stapler, Israeli ideation, MUSE, in which the presence of a mini-ultrasound on the tip, allows the identification of point exact, where the thickness of the lining of the esophageal-gastric junction is increased, allowing you to capture greater thickness of the mucous layer, safely operating. In other words, the operator runs a smaller risk of transmural mediastinal drilling, because he assesses, with the mini-ultrasound, the wall thickness, and he captures more tissue, making it more stable the stitches.

## MUSE (Medigus Ultrasonic Surgical Endostapler)



## Summary over endoscopic plication suturing

The safety and efficacy of endoscopic therapies for the treatment of GERD have not been established in the published medical literature. Current studies are generally of small to moderate size, lack adequate control or comparison groups, and provide only short-term follow-up. Further well-designed clinical trials with long-term follow up are required to establish that endoscopic therapies benefit health outcomes in patients with GERD by eliminating symptoms, preventing recurrence of symptoms or progression of disease, healing esophagitis, and reducing the need for pharmacologic therapy.

**Policy Number: SURGERY 025.21 T2**

**Effective Date: November 1, 2015**

**Minimally Invasive Procedures for Gastroesophageal Reflux Disease (GERD): Clinical Policy (Effective 11/01/2015)**

**1996-2015, Oxford Health Plans, LLC**

# Techniques

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NEW

## Endoscopic fundoplication with GERD-X

### The novelty of platelets.

From a couple of years (2014), though, the [new GERD-X system](#) applies the stitches, fired from the stapler, which have, at their ends, [two plates](#), of polytetra-fluoro-ethylene (PTFE), [which reinforce the suture and make it resistant to traction](#), exercised from the tissues. [These platelets](#), formed of the same material that is used in surgery to pack the wire mesh for hernia protection, [cement subsequently with the tissue](#), making it more stable plication.

Studies underway and those already performed with the previous Plicator of NDO Surg, similar to GERD-X, but not single-use, demonstrate [a greater hold over time of endoscopic plication with platelets](#), **COMPARABLE TO SURGICAL FUNDOPLICATION.**

The new Gerd-X tool is [disposable](#) and provides that, within it, a thin gastroscope of service passes, for visual control during the intervention.

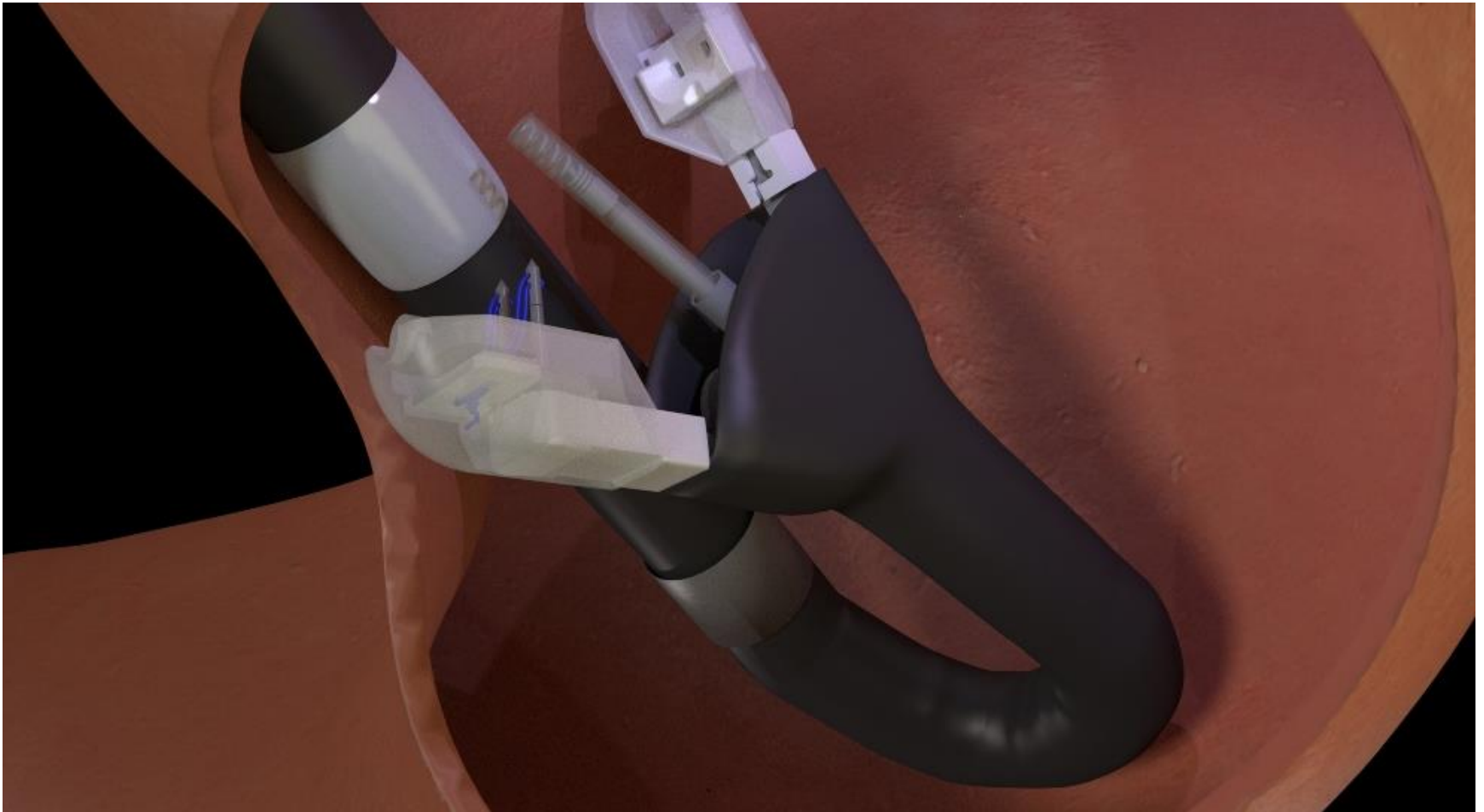
The Operator is facilitated by the [good maneuverability and by the micro-hydraulic technology](#), which enables fast and effective movements, with precise closure of the stapler.

The **retractor of mucosa** serves to capture the appropriate amount of tissue, to obtain a full thickness plication, with a technique of **suck and shoot**, which brings the mucosa inside of the valves, where the points are pre-assembled, with the plates described. At this point we shoot the stapler and this operation is repeated two (or three) times, to obtain a 180 ° anterior fundoplication.

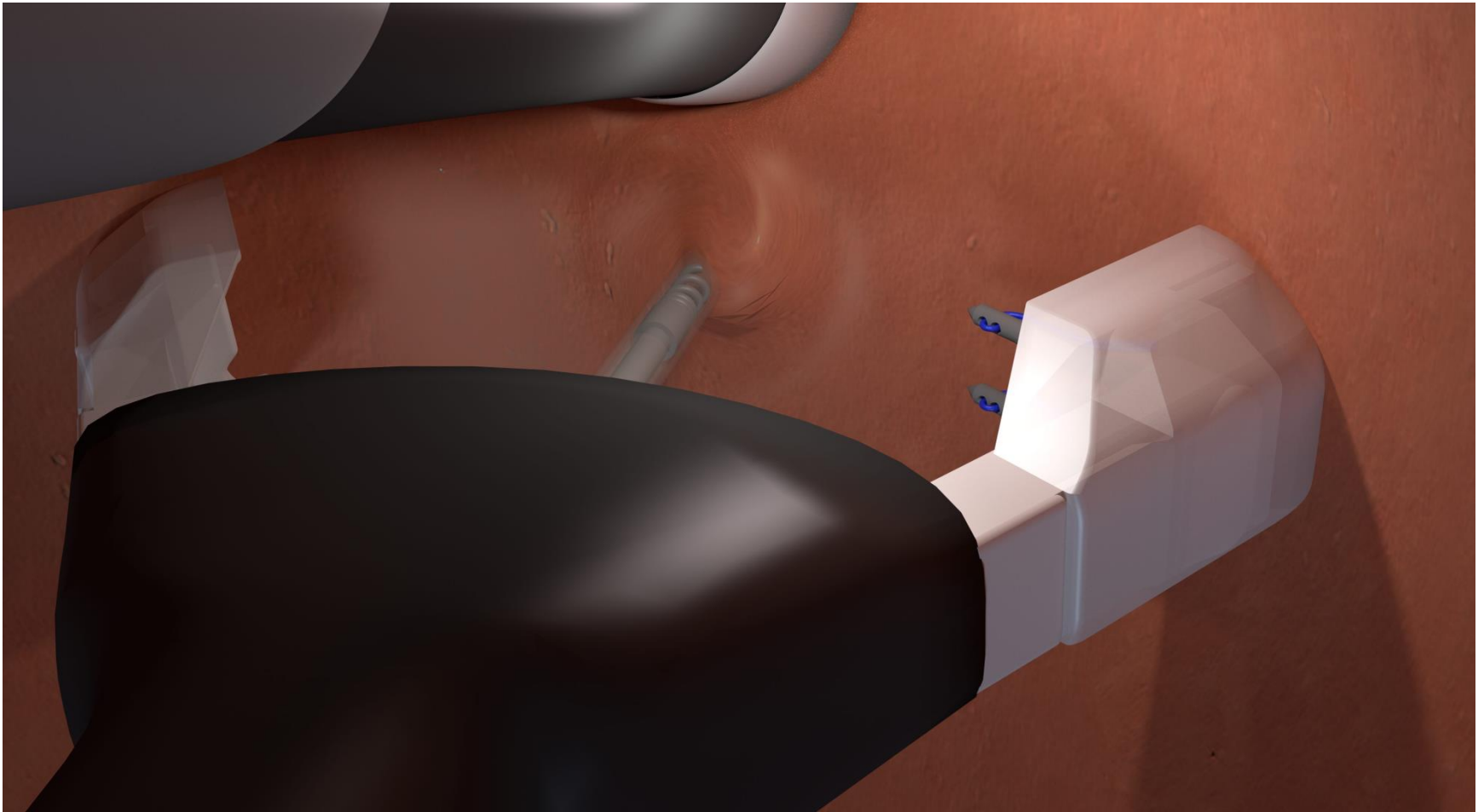


Il retrattore attira la mucosa a tutto spessore tra le valve del plicatore

The procedure begins with the placement of a guide wire, passed inside the operator channel of a gastroscope. [On the guide wire is advanced the applicator Gerd-X](#) and, subsequently, a pediatric ultrathin gastroscope is inserted into the channel of the applicator. Both the gastroscope that the Gerd-X are positioned at 180 ° retroversion. [Under visual control of the gastroscope camera](#), the [operator applies the sutures described](#), operating twice (or three times), in succession, the timing of the method.

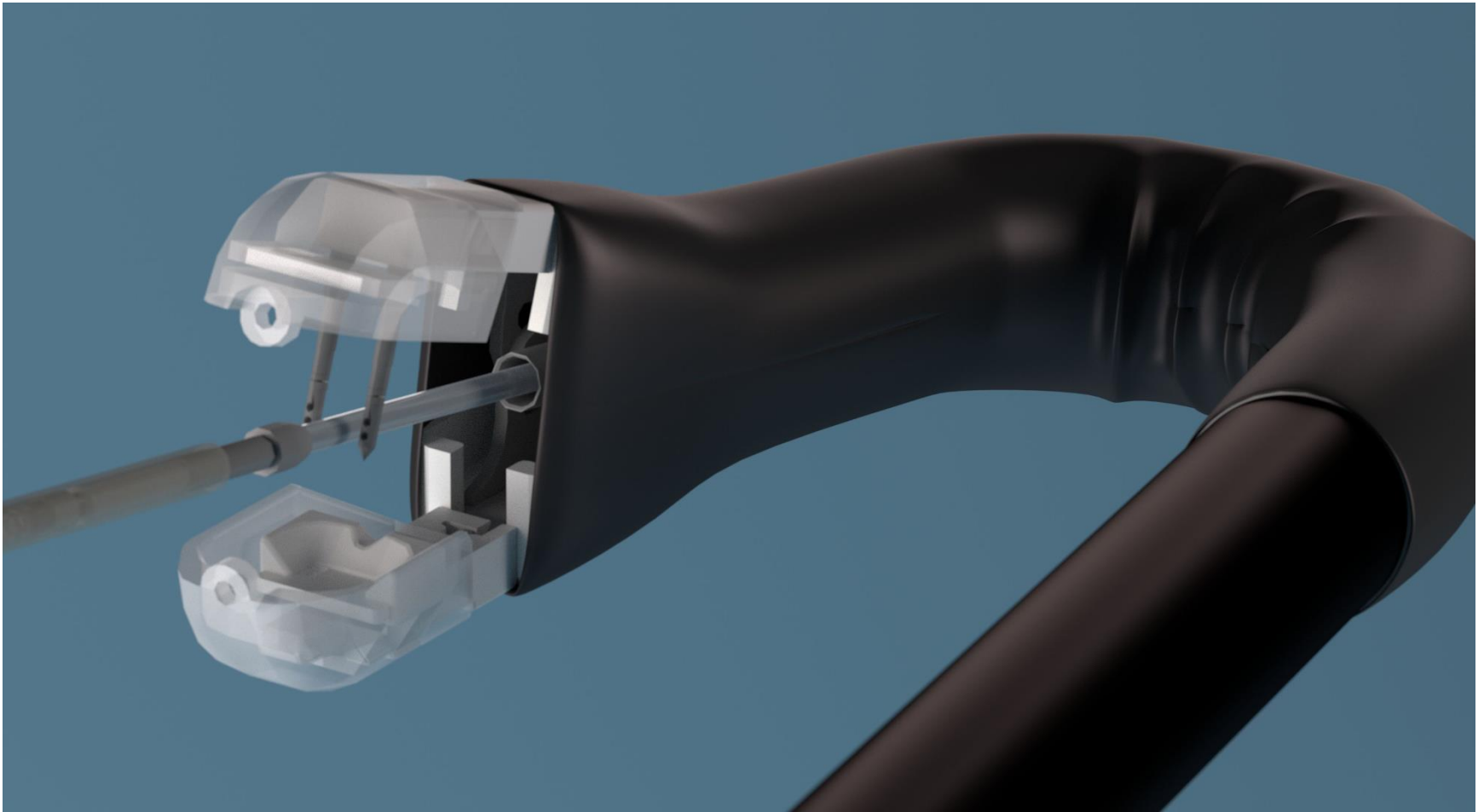


The **retractor of mucosa** serves to capture the appropriate amount of tissue.





Retractor leads the mucosa inside the valve, where there are the points pre-assembled with the plates described.



# GERD-X procedure

Clinical studies, to which I refer, show a **minimal complication rate** (only one case of bleeding, of 37 patients, treated conservatively with endoscopy and blood transfusion). They **not occurred organ perforation or post-procedural stenosis**. The subsequent checks and the follow-up have shown, with appropriate score, **a clear improvement in the quality of life** and a **reduction of the phenomena of reflux**, evaluated with reliefs of Impedance-pH-metry and manometry.

The advantages of the endoluminal endoscopic procedures, **compared to surgery**, are the **reduction of operative complications** (perforations, bleeding, post-procedure stenosis), the **reduced period of hospitalization**, the **simplicity** of the intervention, with the **possibility of repeating, or of switching to surgery**, in case of ineffectiveness.

## Endoscopic full-thickness plication for the treatment of gastroesophageal reflux disease using multiple Plicator implants: 12-month multicenter study results.

D. von Renteln, I. Schiefke, K.H. Fuchs, S. Raczynski, M. Philipper, W. Breithaupt, K. Caca, H. Neuhaus.  
**Surg Endosc (2009) 23:1866–1875**

The full-thickness Plicator\* (Ethicon Endosurgery, Sommerville, NJ, USA) was developed for endoscopic treatment of gastroesophageal reflux disease (GERD). The goal is to restructure the antireflux barrier by performing sutures at full thickness of the cardia sphincter. To date, studies using this device have involved the placement of a single suture to create the plication. The purpose of this study was to evaluate the 12-month safety and efficacy of this procedure using multiple implants to restructure the gastroesophageal (GE) junction.

***\*THE NDO PLICATOR (NDO SURG) IS THE PRECURSOR OF GERD-X (G-SURG).***

Methods. A multicenter, prospective, open-label trial was conducted at four tertiary centers. Eligibility criteria included symptomatic GERD (GERD Health-Related Quality-of-Life (GERD-HRQL) questionnaire, off of medication), and pathologic reflux (abnormal 24-h pH monitoring) requiring daily proton pump inhibitor therapy. Patients with Barrett's epithelium, esophageal dysmotility, hiatal hernia >3 cm, and esophagitis (grade III or greater) were excluded. All patients underwent endoscopic full-thickness plication with linear placement of at least two transmural pledged sutures with plates in the anterior gastric cardia.

## **(2) Endoscopic full-thickness plication for the treatment of gastroesophageal reflux disease using multiple Plicator implants: 12-month multicenter study results.**

D. von Renteln, I. Schiefke, K.H. Fuchs, S. Raczynski, M. Philipper, W. Breithaupt, K. Caca, H. Neuhaus  
**Surg Endosc (2009) 23:1866–1875**

Results of this study. Fortyone patients were treated. Twelve months post treatment, 74% of patients demonstrated improvement in GERD-HRQL scores by >50%, with mean decrease of 17.6 points compared with baseline (7.8 vs. 25.4,  $p < 0.001$ ). Using an intention-to-treat model\*, 63% of patients had symptomatic improvements of >50%, with mean GERD-HRQL decrease of 15.0 (11.0 vs. 26.0,  $p < 0.001$ ). The need for daily proton pump inhibitor (PPI) therapy was eliminated in 69% of patients at 12 months on a per-protocol basis, and 59%, on an intention-to-treat basis. Adverse events included post-procedure abdominal pain (44%), shoulder pain (24%), and chest pain (17%). No long-term adverse events occurred.

Conclusions of the study. Endoscopic full-thickness plication using multiple Plicator implants can be used safely and effectively to improve GERD symptoms and reduce medication use.

\* *ITT intention to treat analysis is statistical analysis which, for the assessment, is based upon the initial treatment intent and not on the actual treatment administered. They are considered all patients, even those who have abandoned the experiment and not only those who have completed the study. Different is per-protocol analysis.*

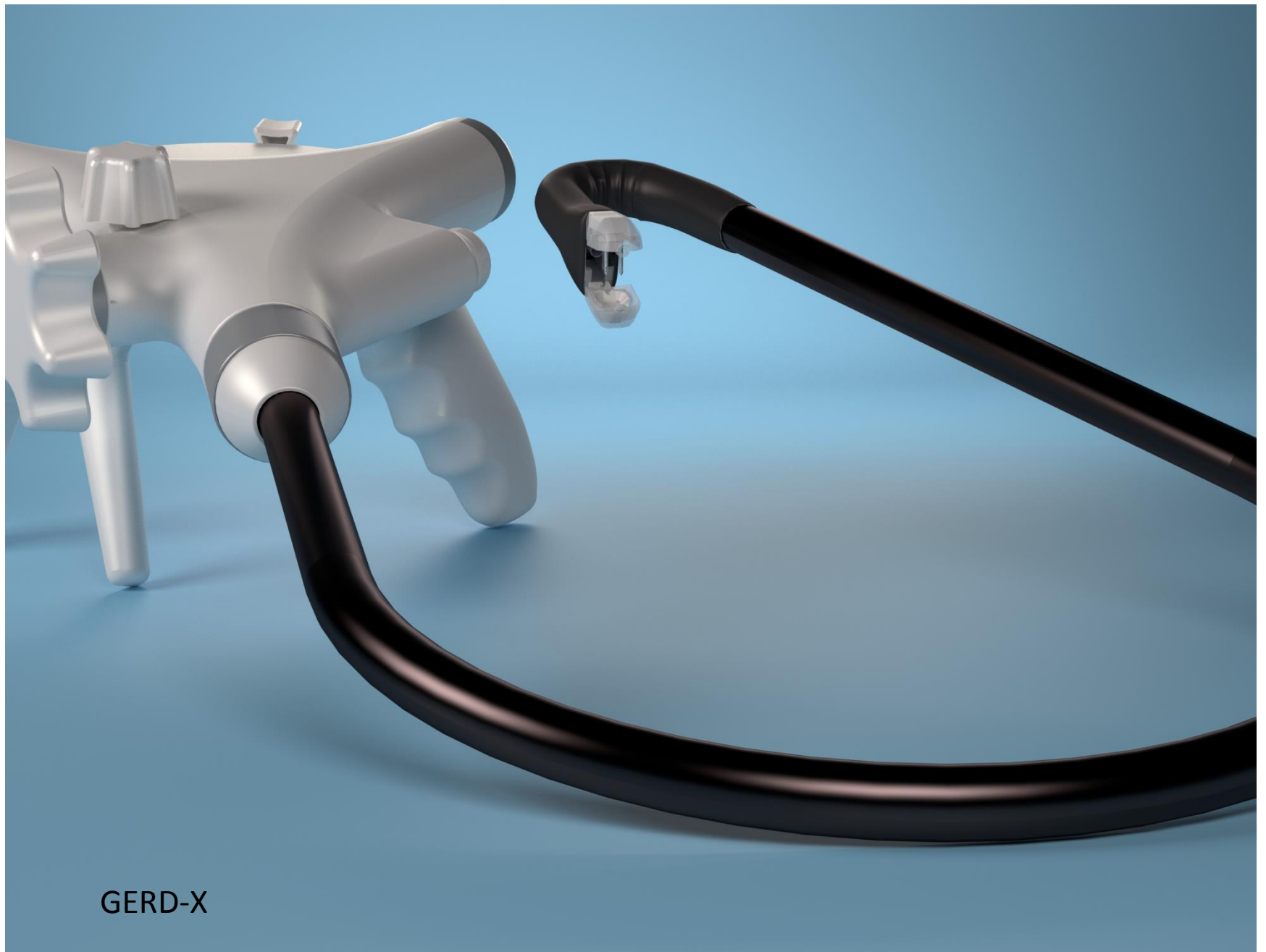
## Endoscopic full-thickness plication versus laparoscopic fundoplication: a prospective study on quality of life and symptom control

Stavros A. Antoniou • Oliver O. Koch • Adolf Kaindlstorfer • Kai U. Asche • Johannes Berger • Frank A. Granderath • Rudolph Pointner  
**Surg Endosc (2012) 26:1063–1068**

... This study aimed at *comparatively evaluating the effectiveness of endoscopic plication and laparoscopic fundoplication* in terms of quality of life and symptom control. ... 60 patients with documented GERD were randomly assigned to undergo either endoscopic plication or laparoscopic fundoplication. Quality-of-life scores and symptom grading were recorded before treatment and at 3 and 12-month follow-up. Outcomes were compared with the statistical significance set at a  $p$  value of 0.05. ...

**Results of this study:** Twenty-nine patients from the endoscopic group and 27 patients from the operative group were available at follow-up. *Quality-of-life scores showed a substantial and similar increase for both groups after treatment.* Symptoms of *heartburn* ( $p < 0.02$ ), *regurgitation* ( $p < 0.004$ ), and *asthma* ( $p = 0.03$ ) were significantly improved in the endoscopic group, whereas *laparoscopic fundoplication was more effective in controlling symptoms of heartburn* ( $p < 0.01$ ) and *regurgitation* ( $p < 0.05$ ), compared to the endoscopic procedure.

**Conclusions of the study:** *Endoscopic plication and laparoscopic fundoplication resulted in significant symptom improvement with similar quality-of-life scores* in a selected patient population with GERD, whereas *operative treatment was more effective in the relief of heartburn and regurgitation, at the expense of higher short-term dysphagia rates.*



GERD-X

# Studies: Full-Thickness-Procedure

Pleskow D., Rothstein R., Kozarek R., Haber G., Gostout C., Lo S., Hawes R., Lembo A.: **Endoscopic full-thickness plication for the treatment of GERD: Five-year long-term multicenter results.**

Surg Endosc (**2008**) 22:326–332

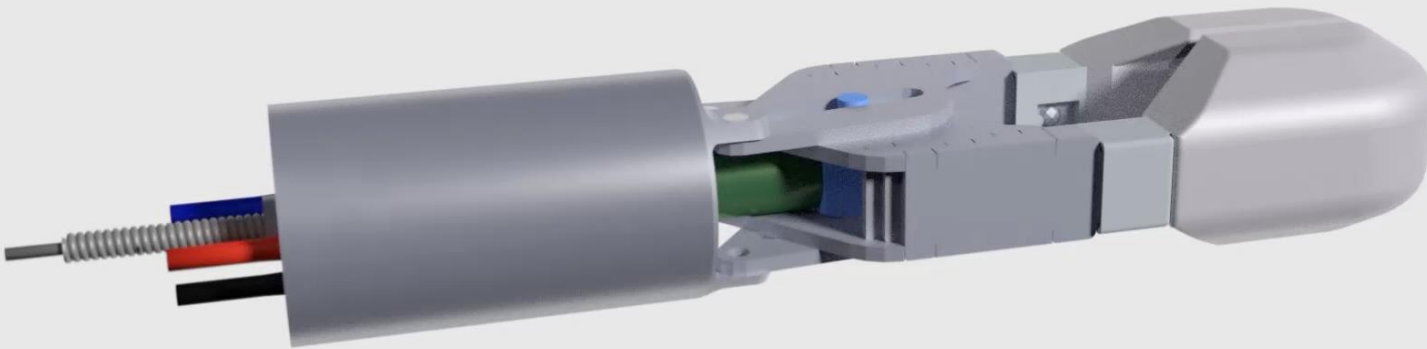
**Results:** Of the subjects who were PPI dependent prior to treatment 67% (20/30) remained off daily PPI therapy at 60 months and 5-year median.

GERD health-related quality of-life (HRQL) scores show significant improvement from baseline off-meds scores (10 versus 19,  $p < 0.001$ ).

Additionally, 50% (16/32) of subjects achieved > 50% score improvement in GERD-HRQL. No new adverse events were identified and all device-related events occurred acutely. These results were comparable to the results seen at 36 months follow-up.

**Conclusions of the study:** Endoscopic full-thickness plication can reduce GERD symptoms and medication use for at least 5-years post procedure with no long-term adverse events post treatment.

# Microhydraulic system



Microhydraulic Platform: GERDX by G-SURG GmbH



## **Subjective and objective data on esophageal manometry and impedance pH monitoring 1 year after endoscopic full-thickness plication for the treatment of GERD by using multiple plication implants.**

Oliver O. Koch, Adolf Kaindlstorfer, Stavros A. Antoniou, Georg Spaun, Rudolph Pointner, Lee L. Swanstrom.

**GASTROINTESTINAL ENDOSCOPY Volume 77, No. 1 : 2013**

Background: Subjective and especially objective data after endoluminal full-thickness gastroplication are scarce. Objective: To **evaluate symptoms and reflux activity 12 months after gastroplication by using**

**multichannel intraluminal impedance monitoring**. Design: Open-label, prospective, single-center study.

Setting: Tertiary referral hospital in Zell am See, Austria.

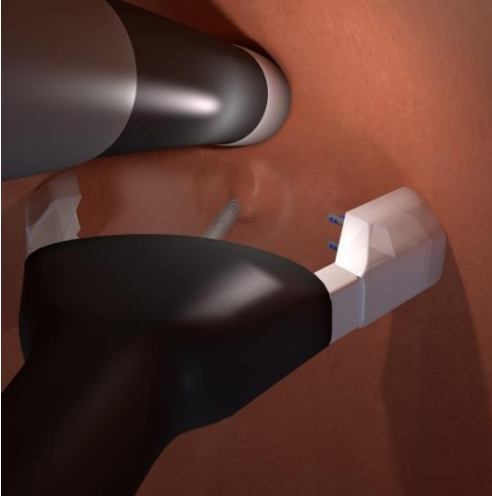
Patients: Subjects **without hiatal hernias** with documented GERD and persistent or recurrent symptoms **despite treatment with a proton pump inhibitor**.

Interventions: A total of 36 patients underwent endoscopic full-thickness gastroplication **with 1 or more Plicator implants**.

Main Outcome Measurements: Mean Gastrointestinal Quality of Life Index and reflux-specific symptom scores significantly improved on follow-up ( $P < .01$ ). **Atypical reflux, gas/bloating, and bowel dysfunction, specific symptom scores as well as belching and dysphagia scores improved**. Twenty-two patients returned for esophageal manometry and multichannel intraluminal impedance testing 1 year after surgery. **DeMeester scores decreased** from 20 to 10 ( $P < .029$ ). The median numbers of total, acid, proximal, upright, and recumbent reflux episodes were all significantly reduced ( $P < .05$ ). **Manometric data were virtually unchanged**. The percentage of **patients taking proton pump inhibitors** on daily basis after the procedure **was 11.5%**. There was only 1 postprocedure incident (bleeding) that required intervention. Three of 36 patients (8.3%) were considered treatment failures because of persistent symptoms and were assigned to undergo laparoscopic fundoplication. Limitations: No randomized comparison with a sham procedure or laparoscopic fundoplication; short follow-up interval.

Conclusions of this study: **Endoscopic plication is safe and improves objective and subjective parameters at 1-year followup**, without side effects seen after laparoscopic fundoplication. Further studies on the clinical merit of this procedure in specific patient populations are warranted.

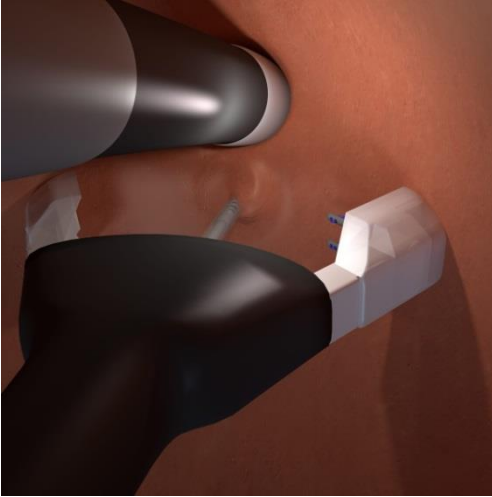
# Indication I:GERD-Procedure



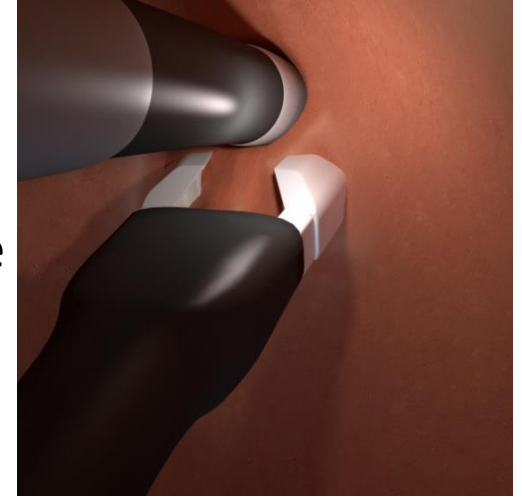
Drill Helix

Retractor of mucosa

# Indication I:GERD-Procedure

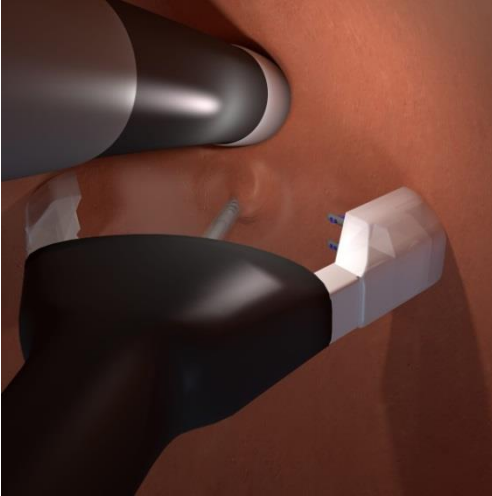


Drill Helix

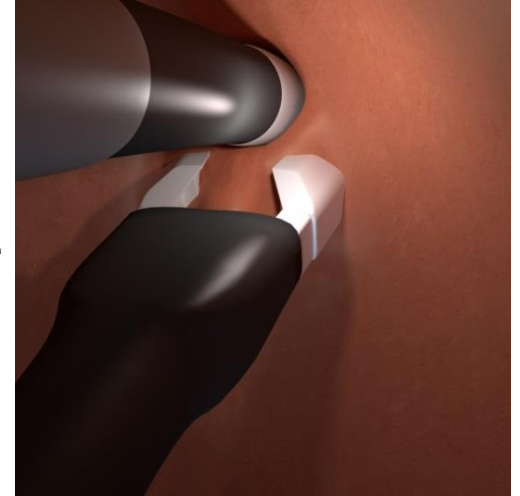


Gather Tissue

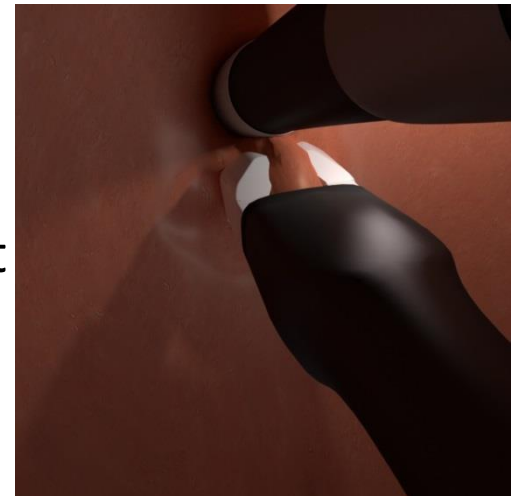
# Indication I:GERD-Procedure



Drill Helix

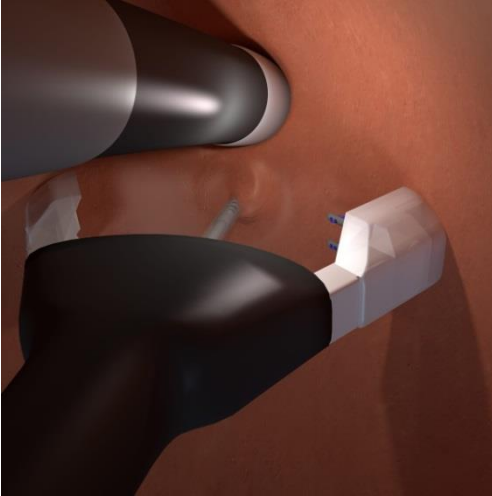


Gather Tissue

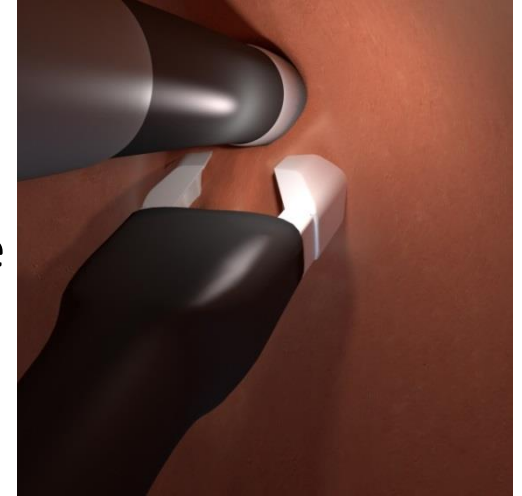


Place Implant  
of stitches

# Indication I:GERD-Procedure



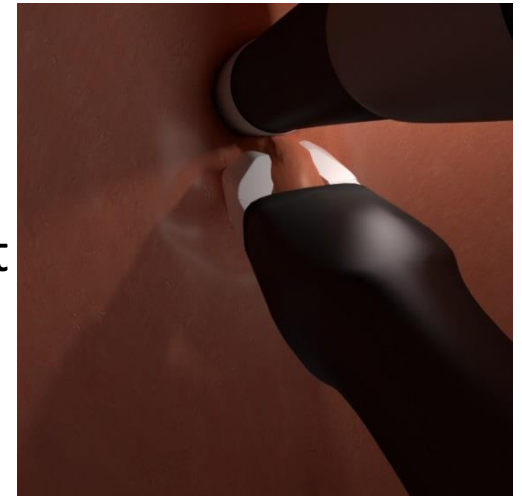
Drill Helix



Gather Tissue



Reopen Arms



Place Implant

# Long-term results of ALL endoscopic procedures

Chen et al. (2009) conducted a systematic review that included 33 studies examining 7 endoscopic procedures (*Stretta procedure, Bard EndoCinch, Wilson-Cook Endoscopic Suturing Device, NDO Plicator, Enteryx, Gatekeeper Reflux Repair System and Plexiglas*). Of the three procedures that were compared with sham controls (*Stretta procedure, Bard EndoCinch and Enteryx*), patient outcomes in the treatment group were either as good as, or significantly better than, those of control patients in terms of heartburn symptoms, QOL, and medication usage. However, for the two procedures, that were compared with laparoscopic fundoplication, *Stretta procedure* and the *Bard EndoCinch device*, outcomes for patients in the endoscopic group were conflicting. Some patients in the endoscopic group experienced comparable outcomes as patients undergoing the laparoscopic approach, while others experienced inferior outcomes. *The authors concluded that there is insufficient evidence to determine the safety and efficacy of endoscopic procedures for GERD, particularly in the long term* (Chen et al., 2009).


“Systematic review of endoscopic treatments for gastro-oesophageal reflux disease”

D. Chen, C.Barber, P.McLoughlin, P. Thavaneswaran, G.G.Jamieson and G. J. Maddern

British Journal of Surgery 96 (2):128-36 · February 2009

# Take home message

- In most cases, the **medical management** of gastro-esophageal reflux disease is preferable and more accepted by the Patients.
- In non-responders, in cases where PPI therapy is problematic and in cases where the young age of the patient is unaware of the chronic use of drugs, the **indication for surgical therapy** is appropriate.
- **Laparoscopic fundoplicatio** offers greater guarantees of long-term success, at the expense of greater operational risk and a failure to repeat the intervention shortly.
- STRETTA and EARMS methods **fibroize the esophageal mucosa**, with good probability of resolution, even in the long run.
- Injecting and implanting techniques presented problems of adverse events and are not effective in long-term.
- The **endoscopic fundoplication**, although partially less effective than laparoscopic fundoplication, finds its space, as appropriate physiopathologically remedy, if only as a bridge to laparoscopic surgery.



The GERD-X platelets

**Thanks for your attention**