GERDX®-System

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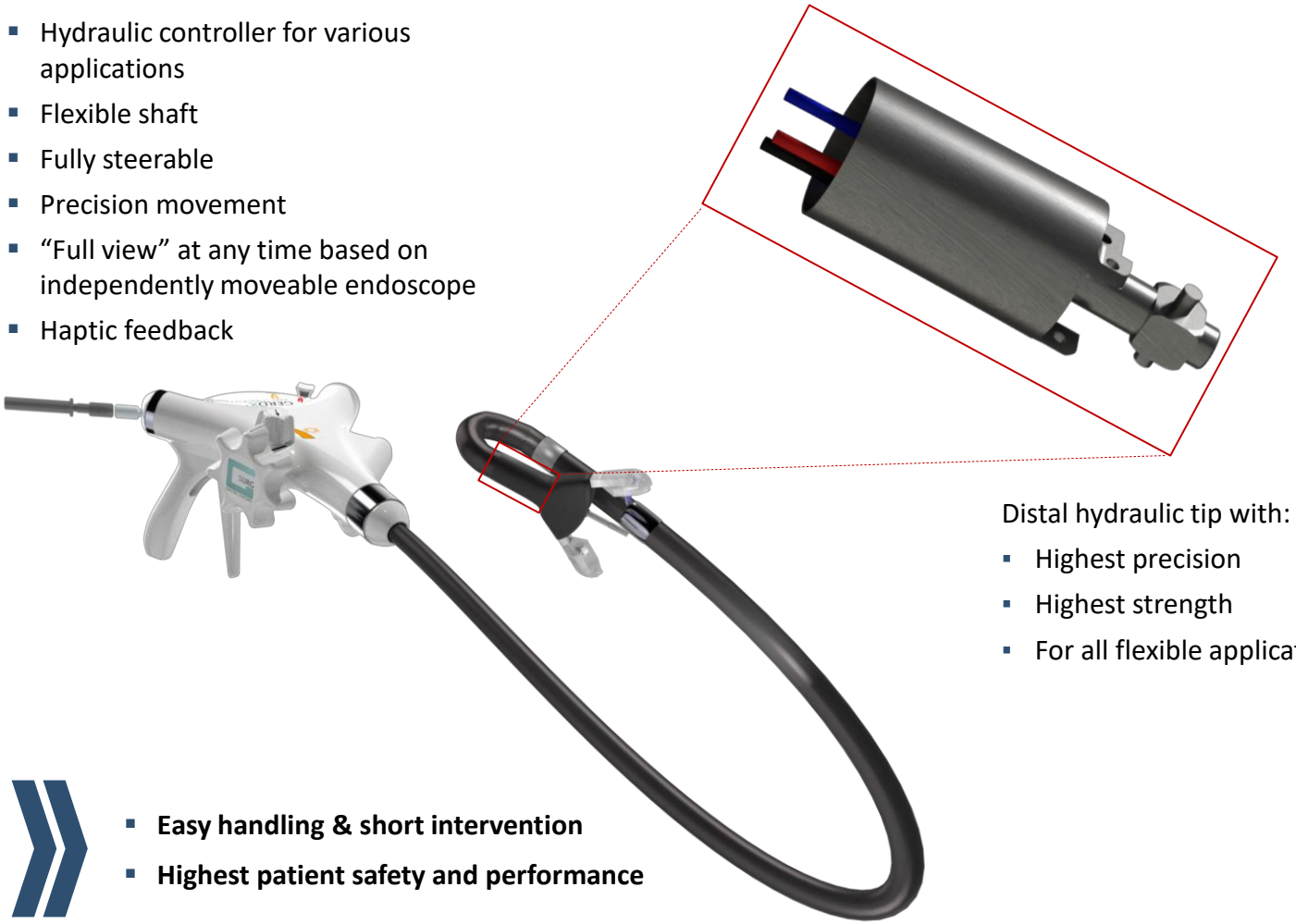
Agenda

1. A micro-hydraulic platform for tissue approximation, plication and fixation

GERDX®-System at a glance

Patented micro hydraulic technology

- Hydraulic controller for various applications
- Flexible shaft
- Fully steerable
- Precision movement
- “Full view” at any time based on independently moveable endoscope
- Haptic feedback



Distal hydraulic tip with:

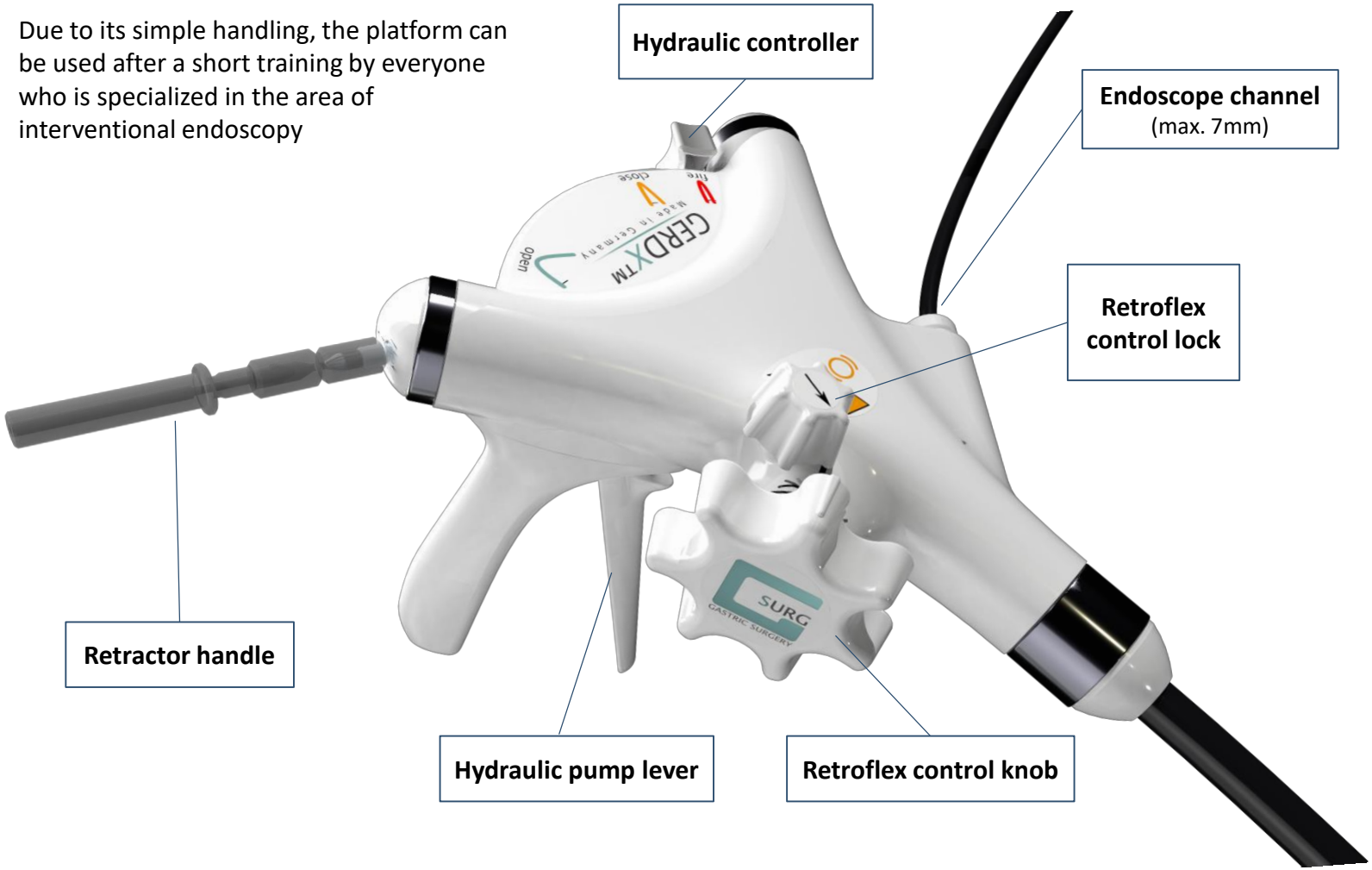
- Highest precision
- Highest strength
- For all flexible applications

- **Easy handling & short intervention**
- **Highest patient safety and performance**

1. A micro-hydraulic platform for tissue approximation, plication and fixation

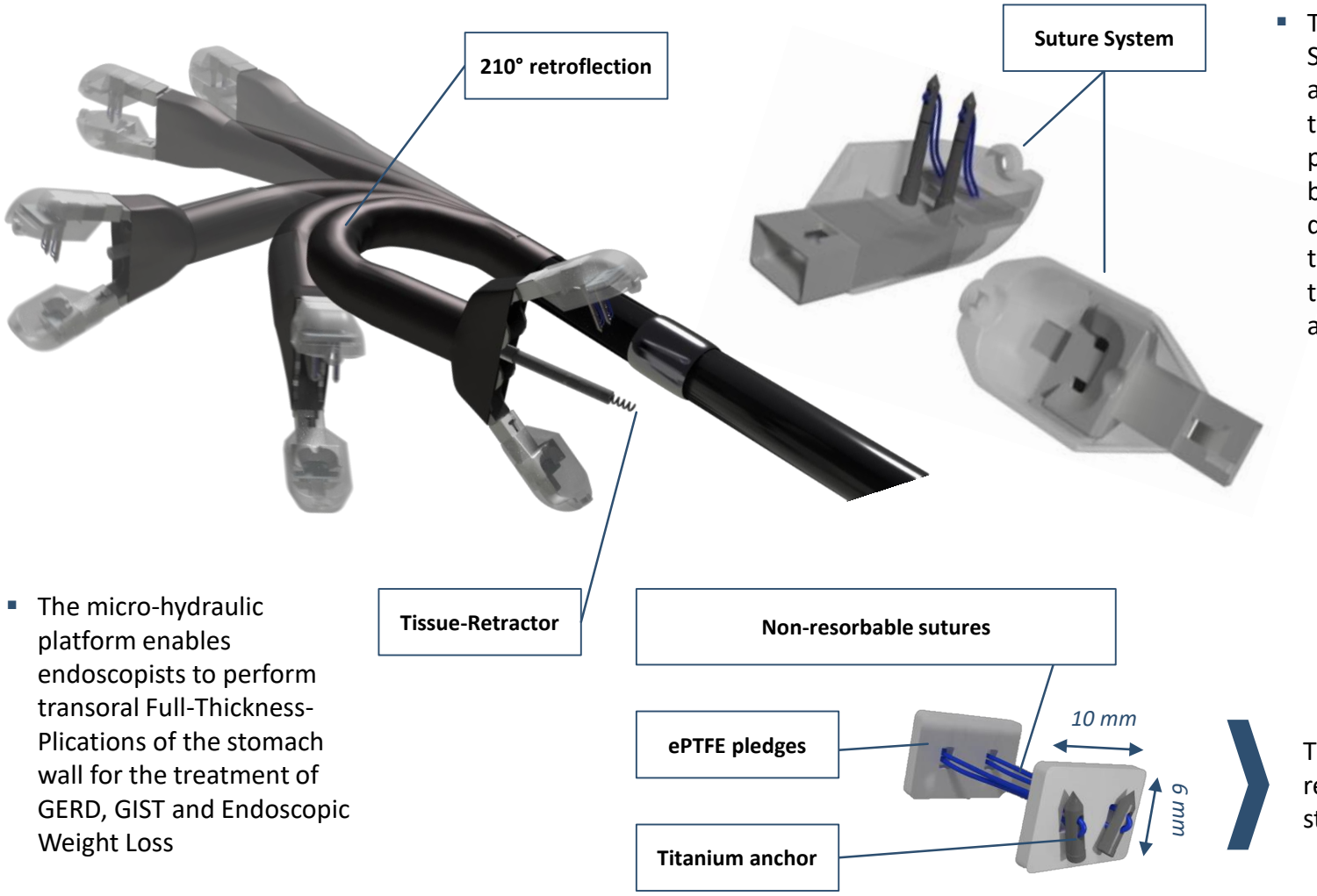
One controller for several applications

- Due to its simple handling, the platform can be used after a short training by everyone who is specialized in the area of interventional endoscopy



1. A micro-hydraulic platform for tissue approximation, plication and fixation

Components for GERD, GIST and EWL – Status: in use



- The Suture System contains a surgical suture, two ePTFE pledges (with a big surface for durable treatments) and two titanium anchors

- The micro-hydraulic platform enables endoscopists to perform transoral Full-Thickness-Plications of the stomach wall for the treatment of GERD, GIST and Endoscopic Weight Loss

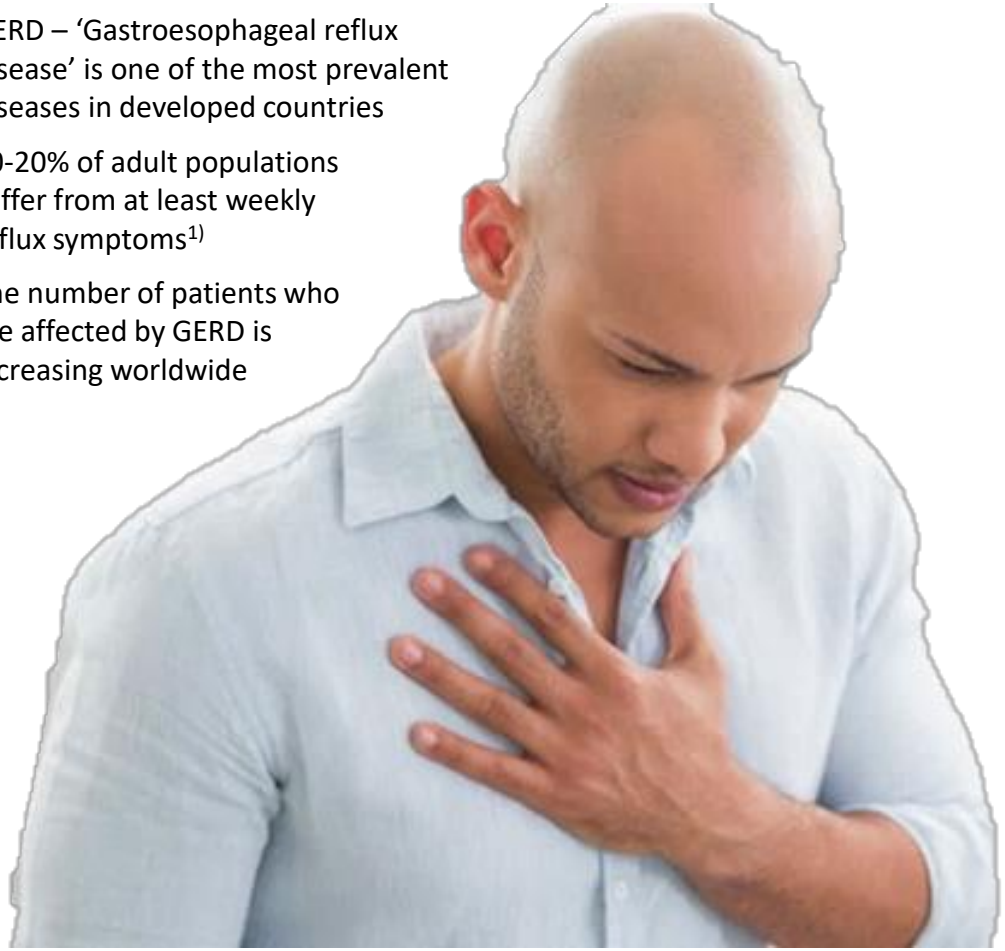
These parts remain in the stomach

Agenda

2.1 GERD – Gastro-esophageal reflux disease

Medical condition

- GERD – 'Gastroesophageal reflux disease' is one of the most prevalent diseases in developed countries
- 10-20% of adult populations suffer from at least weekly reflux symptoms[1)]
- The number of patients who are affected by GERD is increasing worldwide



Heartburn / chest pain

Higher risk of esophageal cancer from daily GERD[2)]

Bad breath / breathing problems

Irritation of the esophageal tissue

Dysphagia (swallowing)

1) Maxwell M Chait; Gastro-esophageal reflux disease: Important considerations for the older patients, 2) www.cancer.org/cancer/esophagus-cancer/causes-risks-prevention/risk-factors.html

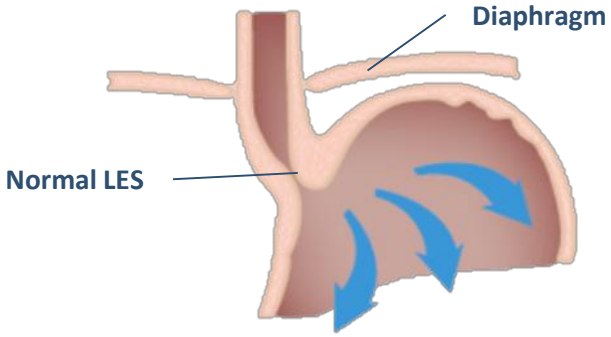
2.1 GERD – Gastro-esophageal reflux disease

The indication

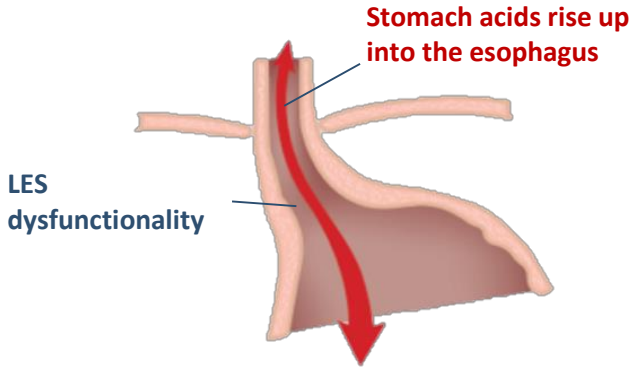
Introduction of GERD

- GERD is characterized mainly by heartburn and/or regurgitation
- GERD most commonly occurs when the **lower esophageal sphincter (LES)** opens spontaneously or does not close properly
- Left untreated, a persistent state of GERD may lead to **Barrett's esophagus**, a **precancerous condition** which can turn into esophageal cancer

Normal anatomy



Dysfunctional valve



Risk factors

- Obesity
- Hiatus hernia
- Smoking
- Aerated drinks e.g. Coca Cola
- Alcohol
- Coffee
- Fast food
- Spicy food
- Pregnancy
- Certain medications:
  - Asthma drugs
  - Calcium channel blockers
  - Pain killers
  - Sedatives
  - Antidepressants
- etc.

2.1 GERD – Gastro-esophageal reflux disease

Overview of treatments

Proton Pump Inhibitors (PPIs)

- Acid suppression medication
- Treatment might consist in successive long-term drug intake
- PPIs may cause gastro-intestinal and nutritional adverse effects

✓ Easy access
✓ Sufficient in weak cases
✗ Risk of side effects: gastric polyps, pneumonia, nausea, diarrhea, fatigue, headache, vitamin B_{12} deficiency, acid deficit, and dizziness
✗ Might cause addiction
✗ Very costly in the long run

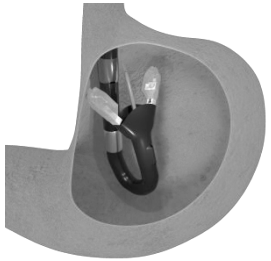
Laparoscopic surgeries

- **Fundoplication:** invented by Dr. Nissen and Toupet. The upper part of the stomach is wrapped around the lower end of the esophagus and stitched in place

✓ Effectiveness: However more then 50% of operated patients became long-term PPI users 10-15 years after surgery[2)]
✗ Invasive
✗ Longer hospitalization
✗ Risk of side effects: scars, dysphagia/and uncontrolled flatulence, vagus nerve injury, gas bloat syndrome

Endoscopic fundoplication

- **Transoral Full-Thickness-Plications** of the fundus (upper stomach wall) to create a mechanical barrier



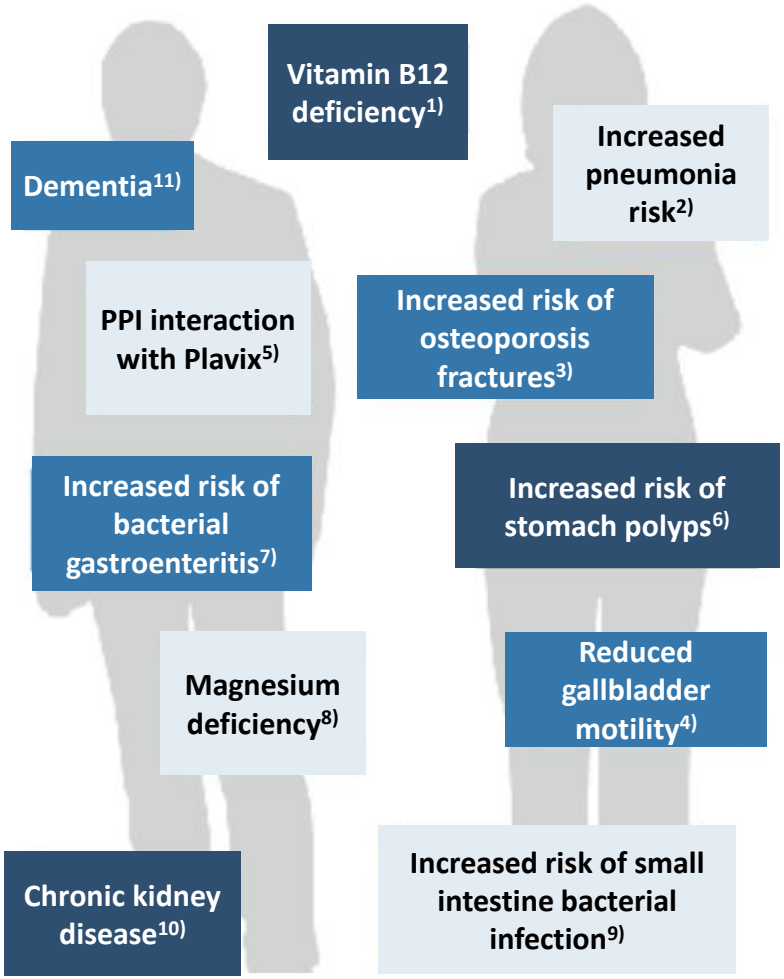
✓ Incisionless
✓ GERD procedures is reversible
✓ Short procedure
✓ Long-term effectiveness
✓ Currently 1 night stationary, potentially ambulant
✗ Post procedure: Temporary sore throat, abdominal pain, chest pain
✗ Currently not recommended for hiatal hernia > 2cm

27% of PPI users are not satisfied[1)] → **High aversion by patients due to dimension of treatment** → **New technology** allows a **patient friendly** method and creates a **new market**

1) John Plevris (2012), "Problem-based Approach to Gastroenterology and Hepatology";
2) A. Lodrup et al.: Use of proton pump inhibitors after anti-reflux surgery: a nationwide register-based follow-up study, GUT 2014; 63; 1544-1549)

2.1 GERD – Gastro-esophageal reflux disease

Published risks observed with PPI use



1) Dharmarajan, TS, et. al., 2008 Mar; 9(3):162-7.
2) Eom, CS, et. al., 2011 Feb 22;183(3):310-9.
3) Targownik, LE, et. al., 2008 Aug 12; 179(4): 319-26.
4) Cahan, MA, et. al. Surg Endosc 2006 Sep; 20(9):1364-7.
5) Ho, PM, et. al., JAMA 2009 Mar 4;301(9):937-44.
6) Jalving, M, et. al., Aliment Pharmacol Ther. 2006 Nov 1;24(9):1341-8.
7) García Rodríguez LA, et. al.;Clin Gastroenterol Hepatol. 2007 Dec;5(12):1418-23.
8) Cundy T, Dissanayake A.; Clin Endocrinol (Oxf). 2008 Aug;69(2):338-41.
9) Lombardo, L. et. al.; Clin Gastroenterol Hepatol. 2010 Jun;8(6):504-8.
10) Lazarus B, et al; JAMA Intern Med. 2016 Feb 1;176(2):238-46.
11) Gomm W et al; JAMA Neurol. 2016 Feb 15. doi: 10.1001/jamaneurol.2015. 4791.

2.1 PPI vs. Laparoscopy vs. GERDX®

Comparison

	Proton Pump Inhibitors (PPIs)			Laparoscopy	Endoscopy
	OTC	Prescribed generics	Prescribed brands		
Targeted	✗ Not severe enough for any surgery	✓ These patients should consider an endoscopic intervention	✓	(✓) Depending on contra indications	✓

- Since GERD is a chronic disease instead of an acute illness, it causes **significant costs for the healthcare systems and private households** due to the required long-term disease management
- **Direct costs associated** with the disease include costs of
  - ✗ PPIs
  - ✗ physician office and hospital visits
  - ✗ surgical costs
  - ✗ costs resulting from the disease, such as Barrett's esophagus and esophageal adenocarcinoma
  - ✗ costs of side effects caused by PPI long-term intake

- With an endoscopic intervention
  - ✓ a more invasive laparoscopic surgery and a
  - ✓ potentially lifelong consumption of pharmaceuticals can be avoided or
  - ✓ at least the dose of PPIs can be significantly reduced
- The endoscopic intervention is
  - ✓ very patient friendly short procedure
  - ✓ improves quality-of-life at a
  - ✓ very attractive ‘price-performance’ ratio

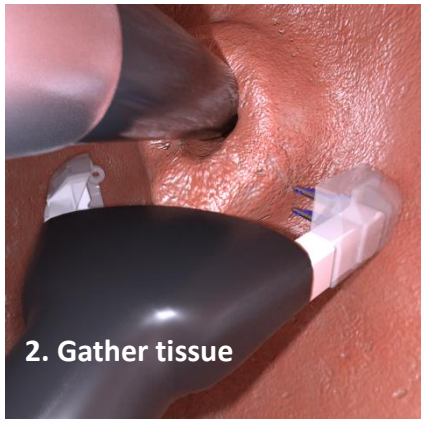
1) “Choosing a PPI To Treat Heartburn, Acid Reflux & GERD”, Consumers Union and Consumer Reports Best Buy Drugs (2013); 2) Prices for laparoscopy and endoscopy are estimated averages, the actual costs per country might significantly deviate

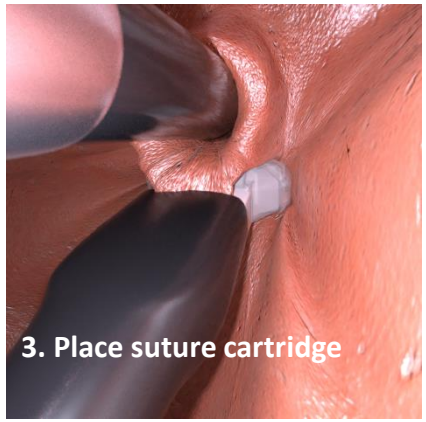
2.1 GERD procedure

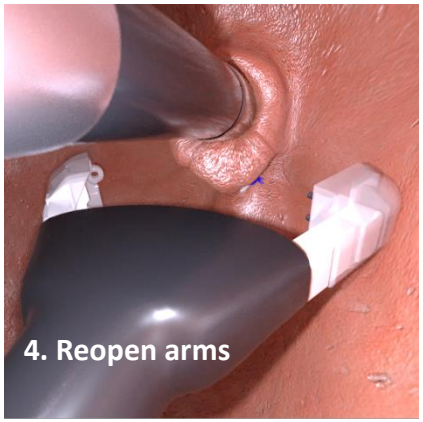
Endoplication with GERDX-System

- The GERDX® including an endoscope is inserted at deep sedation or full-anesthesia into the stomach
- Two suture systems are placed for:
  - gastro-gastric plication
  - tight closure of cardia
  - rebuild the flap valve
- Permanent restoration of the barrier to reflux

- The GERDX® enables:
  - full thickness plication
  - exact, intuitive positioning
  - gather large volumes of tissue
- by positioning the sutures with pledges exactly, safe and – as it is a full-thickness-procedure – durable
- The procedure is intuitive, easy to use and completed within approx. 20 minutes







1) Georg Spaun, Linz, Austria, 2016 Peroral full thickness suturing for the treatment of GERD using the GERDX®

3. GERDX®-System: Summary

Comments on NDO Plicator publications

- **Previous studies were performed with only one suture until 2008** (e.g. the clinical paper – Endoscopic full thickness 5 years data by Pleskow et al). An exception to this is the study done by Renteln et al. which was published in 2007. They used 2 sutures. In the following years 2008 and 2009 Renteln et al published studies with at least 2 placed sutures (publ. #6 & #10). In all subsequent studies, at least 2 sutures were set.
- **Patient selection was significantly less accurate in the 2000s than it is today** (due to poorer measuring instruments such as 24-hour multichannel impedance ph monitoring). In addition, the Hill classification which is used today, allows a better patient selection.
- Khajanchee et al. published a study (publ. #9) in 2009 in which a statistical determination of the **success factors** of a Plicator application was made. As Yashodan pointed out, there was **no corresponding focus on these patients in previous Plicator studies**.
- If the NDP Plicator would be used **today**, taking the above mentioned factors into account (multiple sutures, **improved patient selection** through **better measure procedures** and knowledge of success factors), **this alone should improve the already good results of the Plicator procedure**. **"*In conclusion, patient selection is critical in determining who will achieve success.*"** (Khajanchee publ. #9)
- Furthermore the **GERDX® is characterized by additional constructional advantages** compared to the NDO Plicator™ System incl. **simplified handling, high-precision suturing, single-use**, … which should lead to a further improvement of the NDO Plicator™ results.