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# Endoscopic full-thickness resection using an endoluminal-suturing device: a proof-of-concept study

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ABSTRACT

**Background and study aims** Endoscopic full-thickness resection (EFTR) is used to achieve R0 resection in difficult situations and as a way to overcome the limitations of endoscopic submucosal dissection. Multiple techniques have been described but adequate tools are still under evaluation. In this study, we evaluated the safety and feasibility of non-exposed endoscopic full-thickness resection using a novel endoscopic suturing device.

**Materials and methods** Full-thickness resections of gastric predetermined lesions were performed on five pigs using the Endomina platform. After creating virtual lesion >20 mm, sutures were placed around it using this triangulation platform. After tightening the knots, the bulging lesion, internalized into the gastric lumen, was cut with a needle knife.

**Results** R0 resections of large lesions (42 to 60 mm) were achieved in all cases. One perforation occurred and prompted us to improve the procedure by shortening the sutures for more maneuverability and reinforcing the suture line before section. Procedure duration dropped by 50 % between the first case and the fourth case. Histological analysis confirmed successful full-thickness resection of all resected specimens.

**Conclusion** EFTR using this triangulation platform seems feasible for lesions >20 mm. Additional possible improvements were identified to simplify the procedure before moving to human trials.

## Introduction

Endoscopic full-thickness resection (EFTR) is used to achieve RO resection and as a way to overcome the limitations of endoscopic submucosal dissection (ESD) in management of lesions arising or infiltrating the muscularis propria (subepithelial tumor [SET]) as well as non-lifting or partially-treated adherent lesions[1]. Multiple techniques have been described over time [2]. Exposed techniques, consisting of creating an open wound followed by secured closure, are already used in selected cases. These techniques include submucosal tunneling with endoscopic resection (STER) [3, 4], endoscopic submucosal excavation (ESE) [5], and endoscopic full-thickness resection with secondary closure (exposed EFTR) [6, 7].

Exposed EFTR was initially associated with safety problems, infection, and dissemination [8], leading to emergence of non-exposed techniques. Non-exposed techniques involve placing clips or sutures around the lesion before resection. For that purpose, dedicated clipping/snaring devices have been developed. These allow EFTR for small lesions but limitations still exist for targeting larger areas [9].

Therefore, although it has been proven over the last decade that endoscopic exposed techniques are now safe and feasible with limited risk of dissemination when performed by a skilled endoscopist [10], we decided to investigate a non-exposed technique to allow the procedure to be adaptable to larger areas. In this regard, suturing the site before resection might offer an alternative for larger resections, allowing better control of the operative field without insufflation issues and avoid risk of peritoneal seeding of malignant cells.

EFTR in the upper gastrointestinal tract is primarily indicated for gastrointestinal stromal tumors (GIST) without lymphadenectomy and solid lesions smaller than 3 cm that can be retrieved through the mouth. Other indications include epithelial tumors that are not candidates for ESD (either because of an ulcer scar or due to an invasion depth classified as M/SM1), tumors without lymph node involvement, early-stage gastric cancer that has developed from a benign ulcer, or early-stage gastric cancer in difficult locations (i. e. fundus) [2]. Guidelines on oncologic diagnosis and treatment (National Comprehensive Cancer Network, European Society for Medical Oncology) advise resection of GIST larger than 20 mm or that shows signs of malignancy.

Endomina is a triangulation platform used with an endoscope and suturing material (TAPES, EndoTools Therapeutics, Gosselies, Belgium) to create gastrointestinal suturing. It is used in obese patients for gastric reduction [11, 12] and has been evaluated for EFTR.

The aim of this study was to evaluate the safety and feasibility of non-exposed EFTR using this new full-thickness suturing device [11] on living pigs.

## Materials and methods

The study was approved by the Liège veterinary school ethical committee and included five Pietrain pigs. They were fasted for 24 hours before the intervention. Procedures were done under general anesthesia with intubation. Pigs received a single shot of antibiotic during the procedure and proton pump inhibitor (PPI) for 48 hours after.

Between November 2017 and July 2018, five pigs were enrolled. Their median weight was 25 kg (min 20; max 38 kg).

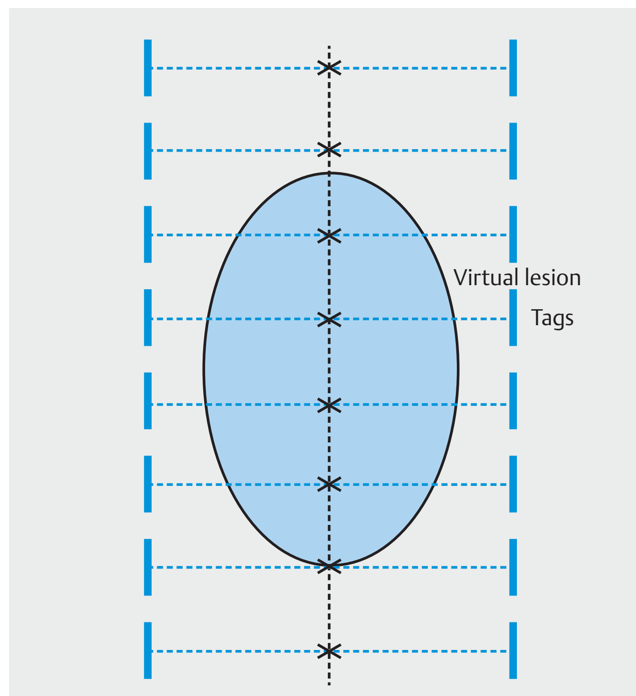
### Procedure

First, a gastroscopy was performed (GIF-Q160, Olympus, Tokyo, Japan) to clear the stomach. A virtual lesion was marked using a dual-knife (Olympus, Tokyo, Japan). The lesion was created in the fundus, on the greater curvature. The same localization was chosen in every pig to allow comparison. Then two Savary guidewires (Cook, Winston-Salem, North Carolina, United States) were left in the stomach.

Then, the Endomina system (Endotools SA, Gosselies, Belgium) was gently introduced over the guidewires into the stomach. The gastroscope followed the system to the stomach, the guidewires were retrieved, the platform was then opened, and the endoscope was inserted inside and fixed to it (▶ **Fig. 1**).

A 5Fr needle, preloaded with suture (TAPES, Endo Tools Therapeutics), was introduced into the flexible arm of the platform. This arm was bent perpendicular to the axis of vision of the endoscope. A grasping forceps (Raptor, US Endoscopy, Mentor, United States) was introduced into the working channel of the endoscope. The stomach wall was grasped with the forceps and pulled back between the two arms of the platform. The needle was pushed through the wall, visualized through a dedicated window on the other side of the device. A first tag, attached to suture and a pre-tied knot, was released. The needle was retracted, the first plicature was released and the second tag was released. The same steps were repeated until tags surrounded the entire lesion (▶ **Fig. 2**). Then, the pre-tied knot was grasped with a 6-mm snare (Endo-Flex GmbH, Voerde, Germany) and tightened until the plicature was firmly apposed. At this stage, the plicature involved one serosa-to-serosa apposition (▶ **Fig. 3a**).

▶ **Fig. 1** Device attached to an endoscope. On the top, the channel can be bent to an axis of 90 degrees. (Source: Endo Tools Therapeutics)




▶ **Fig. 2** Schema of the virtual lesion and placement of tags.

▶ **Fig. 3** **a** Tissue inside the device. The needle is piercing the tissue to release the first tag. **b** After placement of five pairs of tags, surrounding the lesion. **c** The bulging lesion after tightening the knots.

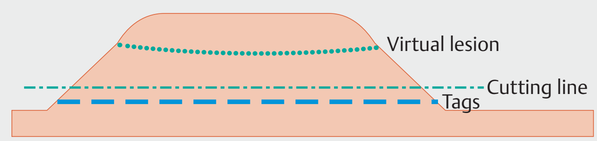
After careful evaluation of the bulging lesion, additional tags were placed to secure the lesion where needed (▶ **Fig. 3b**, ▶ **Fig. 3c**). Approximately 7 mm was taken from the piercing point to the margin of the lesion. Once every knot was tightened, the suture line was explored. If there was a distance of more than 10 mm between two tags, another suture was placed (▶ **Fig. 4**).

When the procedure was completed, the gastroscope was detached from the platform, the two arms of the platform were closed under visual control, and both devices were removed sequentially.

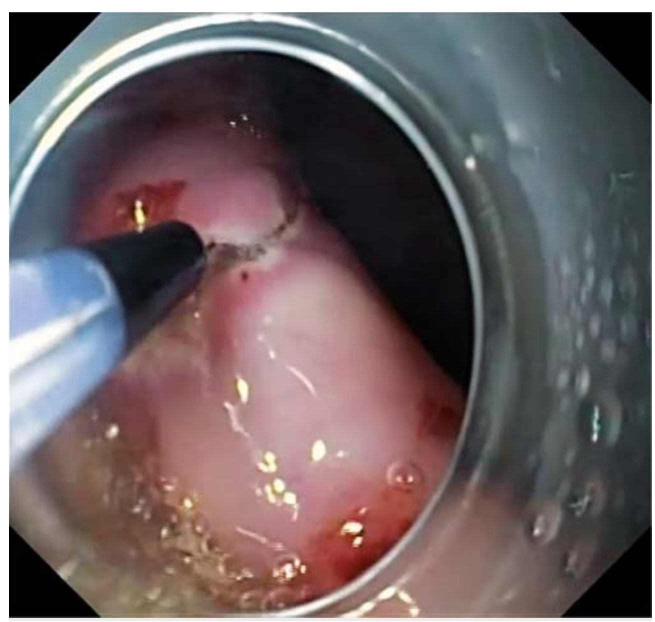
Lesion dissection was done using a straight cap (Olympus, Tokyo, Japan) and a Huibregtse needle knife papillotome (Cook, Winston-Salem, North Carolina, United States) (▶ **Fig. 5**).

After lesion resection, hemoclips (Olympus, Tokyo, Japan) were placed to secure the resection line, if necessary. (▶ **Fig. 6**, ▶ **Video 1**).

Pigs were left fasted for the rest of the day and fed a liquid diet for 2 days after the procedure.




▶ **Fig. 4** Schema of the bulging lesion before cutting.



▶ **Fig. 5** At the beginning of the dissection, using a straight cap (Olympus, Tokyo, Japan) and a Huibregtse needle knife papillotome.

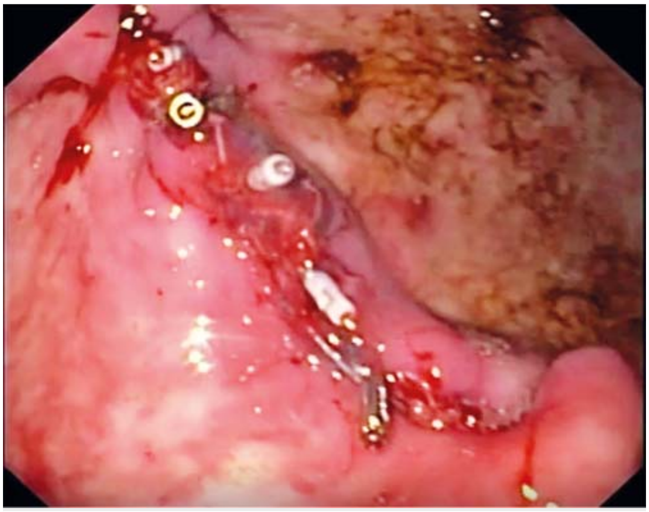
## Results

Procedure duration dropped from 3 hours 30 minutes for the first pig to 1 hour 40 minutes for the last one. Median sizes (range) of the resected specimens were 45 mm (42–60) × 30 mm (20–40). A median of eight sutures (range 6 to 10) were used per procedure (▶ **Table 1**). Outcomes are shown in ▶ **Table 2**.

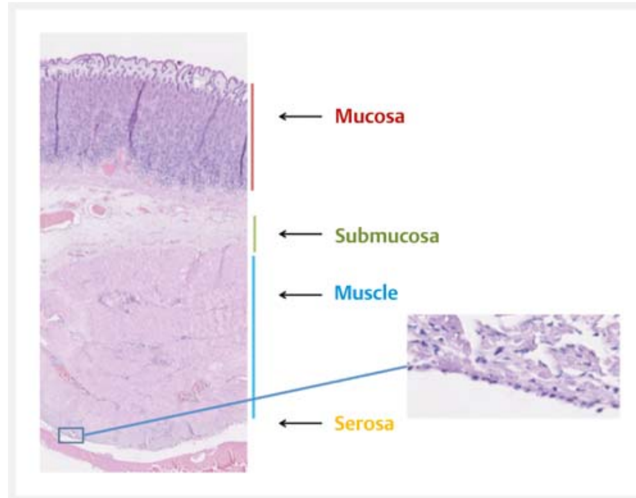
For the first pig, no complications occurred. Histological analysis proved the resection of a full-thickness specimen (▶ **Fig. 7**).

The second pig was not well prepared. The stomach was full of straw and unclean before starting the intervention. Also, the spacing between the tags was too wide to allow for safe resection after tightening the knot, and a perforation occurred during the specimen resection. Despite efforts to close the perforation, the pig died.

This prompted us to improve our procedure. First, pig fasting was reinforced with a liquid diet for 24 hours before surgery, to avoid difficulties and complications due to an unclean stomach. Second, the suture line was reinforced at potential weak points before cutting. If two tags were too distant (i. e. > 10 mm), another was placed in between. Finally, the length of the tag chains was shortened from 100 mm to 60 mm to



▶ **Fig. 6** At the end of the resection, hemoclips are placed to further secure the resected line.





▶ **Fig. 7** Histological analysis shows full-thickness resection.

**Video 1** Non-exposed endoscopic full-thickness resection of a pretend lesion using endomina in vivo. Following the steps described from ▶ **Fig. 3** to ▶ **Fig. 6**.

▶ **Table 1** Animal and surgical characteristics.

| Pig | Weight (kg) | Time (hour) | Size (mm) | Sutures (number) | Dead or Alive |
|---|---|---|---|---|---|
| 1 | 20 | 03:30:00 | 40 × 30 | 6 | Alive |
| 2 | 30 | 04:30:00 | 60 × 40 | 6 | Dead |
| 3 | 25 | 03:30:00 | 45 × 25 | 9 | Alive |
| 4 | 25 | 01:40:00 | 42 × 30 | 10 | Alive |
| 5 | 38 | 01:40:00 | 55 × 20 | 8 | Alive |

▶ **Table 2** Outcomes.

| Pig | Complete resection rate* | Technical success | Complication |
|---|---|---|---|
| 1 | Yes | Yes | No |
| 2 | Yes | Yes | Yes (perforation) |
| 3 | Yes | Yes | No |
| 4 | Yes | Yes | No |
| 5 | Yes | Yes | No |

* Complete resection rate defined by negative lateral margin and histological confirmation of full-thickness wall involving MP and serosa.

ease maneuverability and tightening, as well as to improve the bulging.

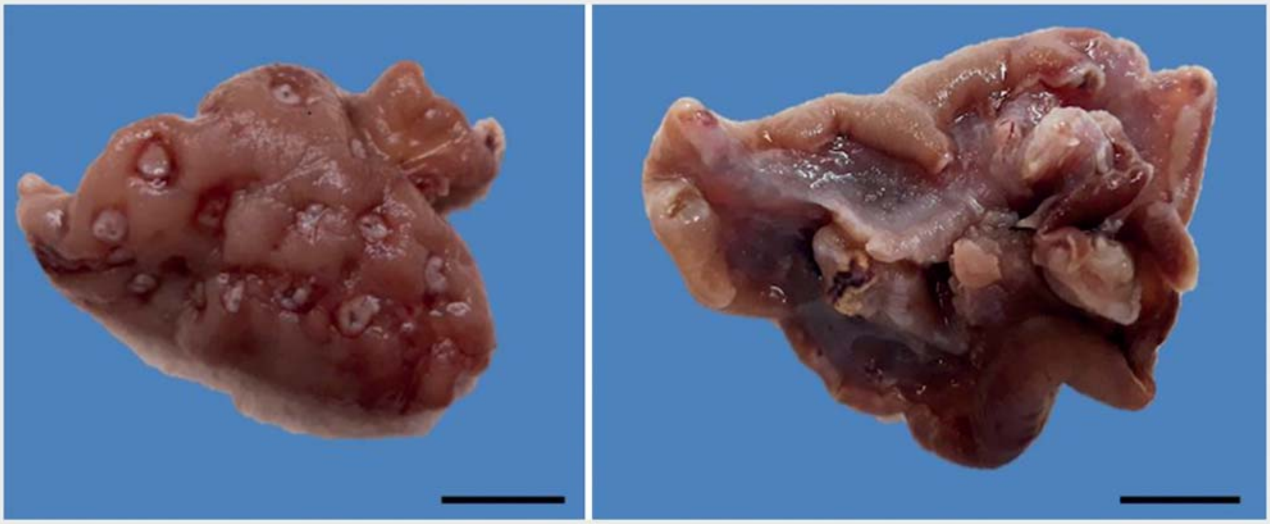
After these changes were implemented, procedures on the next three pigs were done successfully without any complications. Macroscopic and histological analysis of all specimens proved that successful full-thickness resections were achieved (▶ **Fig. 8**).

# Discussion

EFTR is complementary to endoscopic submucosal dissection (ESD) and third-space endotherapy for management of gastrointestinal tumors (submucosal tunneling resection, per-oral endoscopic tumor resection). ESD leads to high rates of R0 resection [13] but can be challenging in cases of submucosal fibrosis or submucosal cancer with a higher risk of perforation [14]. Third-space endoscopy carries risk of peritoneal seeding and may become difficult in cases of insufflation leakage. EFTR has the ability to overcome these limitations. Moreover, histopathological analysis can be potentially more accurate [15]. However, EFTR is still at an early stage of development.

Two techniques have been described, exposed and non-exposed EFTR, but some challenges still have to be resolved [2].

This in vivo pig study evaluated the safety and feasibility of using EFTR to tackle lesions larger than those amenable to re-



▶ **Fig. 8** Macroscopic analysis shows that all dots are inside the specimen (left) with full-thickness resection (right).

section after clip placement. The steps to achieve EFTR were initially designed using a simple suturing device for tissue apposition. In one of the animals, a perforation occurred and led to improvement of the technique and minor modifications of the materials used. Specifically, the suture line was further secured before resection and tag chains were shortened for ease of use. After these changes were implemented, the procedures that followed were successful and no other complications occurred. Procedure duration was dramatically reduced with increased experience.

A major advantage of this technique is that lesion length is not a limitation. The suture line can be adjusted to a lesion of any length. However, endoscopic extraction through the mouth limits the size of solid lesions to approximately 30 mm [2]. Other potential benefits of the non-exposed EFTR technique may include its limited risk of cancer cell dissemination, an operating field that remains accessible with no insufflation issues, and a low risk of peritonitis from gastric juice leak. One disadvantage of the technique is that maneuverability can be challenging in some situations because of the stiffness of both the device and the endoscope together, a feature which would require further material developments.

We decided to use a precut needle knife, usually used for precut papillotomy, because its length was adapted to cut a large amount of tissue. Indeed, a quick cut involving all the tissue from mucosa to serosa on each side is probably best to avoid bleeding (and to open the resected area more widely in case of perforation). In ESD, when a perforation occurs, opening the submucosal space more widely is recommended to ensure a better view and to be able to catch both edges of the perforation. Knives developed for ESD are probably also suitable for this procedure but research to develop dedicated materials would be welcome.

Non-exposed EFTR has a good chance of becoming a method of choice in selected cases of gastrointestinal tumor management. In this procedure, the lesion is secured with a full-thickness device before cutting [2]. The technique requires serosa-to-serosa apposition. In the colon, it seems that over-the-scope-clip (OTSC) devices are highly reliable for small lesions. Recently Schmidt et al [16] described full-thickness resection in the colon using an OTSC device (FTR device, Ovesco Endoscopy GmbH, Tüebingen, Germany). The R0 resection rate was 76.9 % in 181 patients. However, maximum lesion size should not exceed 2 cm in order to be accessible by this therapy.

On the other hand, for gastric lesions, full-thickness suturing devices are still experimental [17]. In another publication, Dobashi et al [18] described EFTR with the Overstitch device (Apollo Endosurgery, Austin, Texas, United States) on pig stomachs. This proof-of-concept study is interesting and further data are expected. The Double-Armed Bar Suturing System (DBSS) is another device that achieves full-thickness sutures. Mori et al. [19] reported the safety and efficacy of this device on porcine stomachs.

Our study supports the concept of non-exposed EFTR as a potential therapeutic method for management of larger lesions with a new suturing device. Improvements in the technique during this animal study show that non-exposed EFTR using Endomina for tissue apposition seems feasible and allows safe resection. Further technical developments are in progress to simplify the procedure, improve maneuverability, and move to initial human use.

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## Competing interests

Drs. Huberty and Deviere are shareholders in Endotools SA, which was initially a startup of the Université Libre de Bruxelles where they have appointments.

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