Endoluminal surgical triangulation 2.0: a new flexible surgical robot. Preliminary pre-clinical results with colonic submucosal dissection.

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Abstract

Background

Colorectal endoscopic submucosal dissection (ESD) is a challenging procedure, due to limitation of the existing tools. Our group has developed a robotized surgical flexible endoscopic platform. The tip of the scope opens to space the instruments and offer endoluminal triangulation. This robotic platform can be operated through an ergonomic and intuitive master interface, by a single operator. The aim of this study was to evaluate the feasibility of robotically-assisted colonic ESD in an acute porcine model.

Materials and Methods

Eight pigs (27-40kg) were involved in this study. ESDs were planned within 25cm from the anal verge, and were performed by a surgeon without previous experience with flexible endoscopy. The robot was introduced transanally after bowel preparation. Main steps of the ESDs were: target marking, mucosal lifting with 10% glycerol solution and total or partial mucosal precut followed by submucosal dissection. A combination of adapted teleoperated instruments (isolated tip knife, hook knife, plane grasper and teether grasper) was used. Specimens were inspected and measured.

Results

Out of a total of 18 ESDs, 12 were successfully completed. Six were aborted due to technical failure of the platform (n=3) or because of the occurrence of perforation (n=3). Among the completed procedures, 2 perforations and 1 system failure occurred, which were managed intraoperatively. There was no major bleeding. All complications/failures occurred during the first 12 cases, while the last 6 procedures were all uneventful, showing an evident learning curve effect, together with technical refinements. Mean size

of the removed specimens was $18.2 \pm 9.8 \text{ cm}^2$ and mean total procedure time was 73 ± 35.5 minutes.

Conclusions

Experimental colorectal ESDs using a new intuitive flexible surgical robot were feasible and suggested a short learning curve. Although some technical improvements are still required, the system might allow for wider adoption of complex endoluminal surgical procedures among interventional endoscopists.

Introduction

Endoscopic Submucosal Dissection (ESD) is an attractive minimally-invasive treatment option for gastrointestinal (GI) lesions with low metastatic potential. It provides high *en-bloc* resection rates even for large, laterally extended tumors. In Eastern countries ESD has become standard of care for early gastric cancer.[1, 2] However, ESD is generally a highly challenging technique and requires significant experience and skills to be carried out safely. Colorectal ESDs are even more difficult than gastric ones, with a steep learning curve [3], due to specific anatomical characteristics (presence of large tissue folds, peristaltic movements, thinner layers), presenting higher risk for complications.[4, 5] These characteristics limit the adoption of colorectal ESDs at large-scale level.

Current endoscopic technology is another important factor which has not been facilitating the widespread of these complex endoluminal surgical techniques. The most frustrating limitations within the GI lumen, from a surgical standpoint, are: lack of effective retraction, clear view and instruments' triangulation. The basic elements for surgery. In recent years, those limitations have been in the focus of innovation efforts at both technological and technical level [6-15]. However, the majority of proposed solutions have been mainly designed around the standard diagnostic flexible endoscopes, with no disrupting concepts or, at the extreme, by violating the minimally-invasive spirit. Without moving away from the standard endoscopic mindset, it is difficult to imagine a breakthrough in this specific surgical field.

As demonstrated by the advent of the concept of NOTES (Natural Orifice Transluminal Endoscopic Surgery), a strong paradigm shift, inducing cross fertilization between minimally-invasive surgery and endoscopy, is required [16]. In this surgical endoscopic perspective, our team - in collaboration with Karl Storz - has developed the Anubiscope®, a mechanical flexible surgical platform conceived for NOTES [17, 18] and

the Isiscope®, a shorter version for Laparo-Endoscopic Single-Site procedures.[19] Those platforms introduce the ability for instrument triangulation to flexible endoscopy. Recently, we have applied the device to colorectal ESDs and demonstrated the safety and efficacy in experimental setting, with clear advantages over the standard endoscopic approach.[20] The drawback of this mechanical platform is that it requires a fine-tuned cooperative work of two trained surgeons standing both around the endoscope.

Robotic technology has already been taken to this field to develop new concepts in order to tear down current barriers between flexible endoscopy and an efficient, safe and feasible endoluminal surgery.[21, 22]

To improve our mechanical platform, we called robotic science resources to optimize performances and ergonomics. In a collaborative work with the ICube laboratory in Strasbourg, the Isiscope® served as a base to produce the STRAS robot (Single-access Transluminal Robotic Assistant for Surgeons).[23-25] The STRAS is a master-slave system that can be operated through a very intuitive control interface, in an ergonomic fashion by a single operator. The aim of this study was to evaluate the feasibility of colon submucosal dissection in acute porcine model using the STRAS robot.

Materials and methods

The master-slave robotic STRAS system

The STRAS is based on the Isisscope® therapeutic platform (Karl Storz Endoskope, Tuttlingen, Germany). This is a special 50 cm long flexible endoscope with a maximal shaft diameter of 18mm. The shaft houses two 4.2mm working channels for operative instruments and one 2.8mm working channel for conventional flexible endoscopic instruments. The motorized main operative module has a four-way deflection tip and it is translated and rotated as well. The tip of the endoscope is equipped with two opening arms to offer endoluminal triangulation for the instruments (**Figure 1**). The robotic operative instruments are either purely mechanical or electric with three or four degrees of freedom (DOF) each. The available tools are graspers with different profiles, an isolated tip knife and a hook knife (**Figure 2**). Overall the system has 10+1 DOF. The platform is teleoperated through a very intuitive master interface in an ergonomic fashion by a single operator (**Figure 3**).

Set up and manipulation of the system

The slave unit is composed of a carrier cart and the detachable flexible endoscope. The slave cart is rollable and houses the electronic system and the endoscope rack. The rack adjusts the height as well as the translation of the surgical platform. The slave unit is set close to the operation table and can be teleoperated remotely from undefined distance. As a first step the portable motorized endoscope is inserted into the rectum manually, with the tip oriented by a built-in joystick, under endoscopic visual control (**Figure 4/A**). Once the target area is reached the portable platform is reattached to the slave rack and the operating tools are inserted (**Figure 4/B and C**). Pneumorectum is created by CO₂ insufflation to open the surgical space. If required, the clamshell arms can contribute to the stability of the operative field. Once the endoluminal view is established, the

endoscope is positioned for the first steps of the surgery through the master control. From this point on, manipulation of the system is entirely done by the master console surgeon. The 2.8 mm working channel is served mainly for insufflation, suction and as an access for additional instruments (e.g. endoscopic injection needle) if needed. On this prototype the insufflation, suction and lens cleaning functions of the endoscope are controlled by an assistant at the patient site. The robotic instruments can be changed if needed during the operation. After the procedure is completed the platform can be removed by moving the slave carrier back (**Figure 4/D**).

Animals

Eight pigs (*Sus scrofa domesticus*, ssp large white) weighting 27–40 kg were included in this non survival study. The study protocol was approved by the Institutional Ethical Committee on Animal Experimentation (ICOMETH n°38.2011.01.018), and animals were managed in accordance with French laws for animal use and care as well as the European Community Council directive no. 2010/63/EU. Animals were fasted for 24 h before the procedure with free access to water. Ketamine (20 mg/kg) and azaperone (2 mg/kg, Stresnil; Janssen-Cilag, Beerse, Belgium) were administered intramuscularly 10 minutes before the procedure as premedication. Induction of anesthesia was achieved using intravenous propofol combined with rocuronium (0.8 mg/kg). Anesthesia was maintained with 2 % isoflurane after endotracheal intubation of the animal in a supine position. Rectal cleansing was performed until the effluent turned clear. All pigs were humanely euthanized immediately after the procedures by intravenous injection of a lethal dose of potassium chloride.

Procedures

All procedures were performed by a general surgeon (AL) who acted as a “test pilot” mainly because of his lack of exposure to flexible endoscopy. He did NOT do pilot test prior to the study.

The surgeon was allowed to practice with the robotic system on bench top a total of 30 minutes before the study. The main steps of the procedures were the follows: after bowel preparation, target areas were marked at different levels up to 25 cm from the anal verge. Intention was made to mark and remove 3 to 5 cm diameter specimens. After marking the target areas the mucosa was lifted by submucosal injection of 10% glycerol solution (Cooperation Pharmaceutique, Melun, France) mixed with few drops of methylene blue (**Figure 5/A and B**). For submucosal injections a 23G injection therapy needle (Interject™ Contrast, BostonScientific, MA, USA) was used. The marked and lifted areas were then completely precut around the marks or only a small mucosal incision was made. As a last step the target areas were dissected at the submucosal level and then removed (**Figure 5/C to G**).

To assess the feasibility of a hybrid approach in the first case the marking and precut was made by using a conventional flexible gastroscope (Silverscope® 13821 PK, Karl Storz, Tuttlingen, Germany) and a triangle tip (TT) electrosurgical knife (KD-640L, Olympus, Tokyo, Japan). However, it was felt to be too time consuming for the study surgeon and it was abandoned.

In case of pneumoperitoneum a Veres needle was inserted into the abdominal cavity to decrease the pressure. The distal colon was harvested and the operation sites were inspected for injuries from both outside and inside as well. Specimens were inspected, expanded on a corkboard with pins, measured and stored in 2% buffered formalin for further pathologic evaluation (**Figure 5/H and I**).

All the procedures were video recorded through the surgical platform's video camera.

Data were either recorded on data collection sheets during the procedures or after reviewing the recorded videos. Total procedure time was defined as time elapsed between insertion of the platform into the anal canal and complete removal of the mucosal specimen. Dissection time was defined as the time required for submucosal dissection after a complete precut or if precut was not made the time elapsed from the first mucosal cut to specimen removal. Procedural speed was calculated from the total procedural time and size of the removed specimen.

The procedures were then retrospectively divided into three equal groups in order to represent the learning curve, procedural and technological refinement.

Results

Total of 18 ESDs were attempted and 12 were successfully completed. Total of 5 (27.7%) perforations occurred whereof one was closed by using a flexible endoscopic hemostatic clip through the platform allowing the operator to finish the procedure, and another one which had no effect on the procedure. Total of 4 system failures occurred. Three procedures were aborted because of technical difficulties. In one case the robot was repaired intraoperatively. All surgical and technological complications occurred during the first 12 procedures. There was no major bleeding. In all animals pneumoperitoneum in some degree developed irrespectively to a presence or lack of perforation.

The mean size of the removed specimens was $18.2 \pm 9.8 \text{ cm}^2$ and mean time required per total procedure was 73 ± 35.5 minutes. The mean pure dissection time was 49.6 ± 35.1 minutes.

There was a remarkable improvement in the performance during the study. From the first 6 cases only 2 could be completed due to major complications – surgical or technological - while from the last 6 procedures all were complete and no complication occurred. The mean procedural speed was almost two times higher in the last group than in the first ($0.186 \text{ cm}^2/\text{min}$ vs. $0.344 \text{ cm}^2/\text{min}$). The mean procedural time and size of dissected surface in the first and last groups were 100.5 ± 7.78 vs. 60.8 ± 27.9 minutes and 18.6 ± 12.2 vs. $21.05 \pm 9.78 \text{ cm}^2$ respectively. Table 1 shows the study data in details.

Discussion

Endoscopic submucosal dissection provides endoluminal surgical treatment option for premalignant or early malignant lesions of the gastrointestinal tract with a high en bloc resection rate.[26, 27] In spite of the growing number of patients diagnosed with earlier stage malignant disease in the Western World adoption of colorectal ESD is relatively slow. This is - besides the limited training opportunities - related to the technical difficulties, consequent higher procedural complication risks and long operation time. Robotic technology may break this barrier by providing technically facilitated working environment. In the present animal study we have demonstrated the feasibility of colorectal ESD by using our ergonomic master-slave robotic endoluminal surgical platform.

The origin of technical difficulties of ESD is the lack of effective retraction to provide wide and clear exposure of the targeted layer. There are numerous different traction systems published for gastric and colorectal ESDs proposing clips with lines, magnetic anchors, external forceps, clips with rubber rings, sinkers, double endoscopes or even percutaneous instruments.[6-15, 28] The drawbacks of these systems are that they either need multiple intubation of the endoscope and difficult to set up, they are not independent from the motions of the endoscope, they are invasive, they can be used only in certain locations, they need continuous patient repositioning or require two endoscopists to operate.

Complex manual multitasking platforms can overcome the difficulty of intraluminal retraction. They were developed originally in the era of NOTES for intra-abdominal use and some of them were successfully applied to perform operations within the GI lumen. The advantages of these multi-channel systems are that they provide retraction by allowing multiple instrument usage; they are stable and usually control bendable tools.

Many of them showed advantages when using within the upper GI tract. The R-scope (Olympus, Tokyo, Japan) was originally designed to improve endoluminal surgical performance at difficult location of the stomach. The drawback of the device is that it requires two or three persons to operate the endoscope with the end effectors in harmony. [29, 30] The EndoSamurai (Olympus, Tokyo, Japan) is a 15 mm modified double channel endoscope with handles similar to laparoscopic instruments. The working channels continue in two short, independent arms that can be moved only into a mild angle. The platform is stabilized by a locking overtube which is manipulated by a second operator to keep the endoscope always stable in a desired position.[31] The Incisionless Operating Platform (USGI, USA) incorporates four large-size working channels; one for a 4-6 mm flexible endoscope and three (4-7 mm) channels for special articulated instruments.[32] The manipulation of the platform requires a well synchronized work of two skilled operators.

Our group in collaboration with Karl Storz has been previously developed two flexible endoscopic manual platforms for NOTES (Anubiscope®) and for single-port intra-abdominal surgery (Isiscope®) and recently successfully applied it for rectal ESD.[17-20] These platforms combine the capabilities of a flexible endoscope with the advantages of laparoscopy resulting in a highly efficient system. A pair of intuitive, strong and bendable instruments is used in triangulation allowing the operator to work precise and distant from the target area in a well exposed operation field. However, the fact that their operation requires a strong cooperative work of two surgeons makes the device control more challenging.

To overcome this limitation a robotized version of the Isiscope® has been recently developed. This master-slave system – called STRAS - provides all the advantages of the mechanical platform and can be operated remote through a very intuitive master interface by a single operator. There has been only one robotic flexible endoscopic multitasking platform developed and demonstrated feasibility to perform complex intraluminal tasks in the gastrointestinal tract. The MASTER is one of the first robotic surgical endoscopic systems. It was conceived to be used tandem with a commercially available double-channel flexible endoscope. The operating arms are placed on the top of a dedicated flexible endoscope (Olympus 2T160) and they are controlled by a surgeon through the master interface from a distance. The flexible endoscope itself is held and manipulated by the endoscopist standing at the patient bedside. Five human gastric submucosal dissections were successfully carried out to show feasibility and safety.[33] The advantage of the STRAS® over the MASTER is that after set up its manipulation requires only one surgeon. A new concept for single operator endoluminal surgery has been recently published.[34]

Another advantage of our robotic platform is that besides the two bendable instruments there is a 2.8 mm working channel for conventional flexible endoscopic tools. This prevents the necessity of multiple endoscope intubations when an extra tool is needed - injection needle, hemostatic clips etc. We found this channel very useful also for electrical devices cleaning by using a small brush. The control cables of the MASTER's slave unit are running into the working channel of the flexible carrier endoscope blocking the access for other instruments.

During more complex procedures robotic tool exchange may be necessary. The operative tools of our system can be detached from the driver motor and relatively easily replaced by another one without changing the position of the platform. The spectrum of robotic

tools for the STRAS allows the surgeon to optimize the instrumentation to the operative situation. There is an actuator-driven master-slave system called ViaCath which controls two interchangeable articulated robotic instruments with 7 DOF each.[35]

Variety of the tools may also facilitate the adoption of flexible endoscopic robotic platforms. These systems should be easy to adopt not only for complex clinical situations but also for both endoscopists and surgeons. The procedures of the present study were performed by a surgeon with initially very limited flexible endoscopic experience. Complex flexible endoscopic procedures require both excellent technical skills and knowledge of intramural anatomy. Robotic technology reduces the technical challenges interventional endoscopists are facing with and may facilitate to understand GI intramural anatomy easier for inexperienced operators. The last six procedures in the current study were carried out safer, faster while larger mucosal pieces were removed, compare to the first phase of the experiment. This suggests that the unique feature of the STRAS (ability to bimanual manipulate triangulated instruments in distance by a single surgeon - an environment similar to laparoscopy) allows an easy adaption of complex endoluminal procedures with shorter learning curve for even those with very small flexible endoscopic experience.

The future clinical adoption of flexible endoluminal surgical systems— mechanical or robotic – will be determined besides of safety, efficacy and ergonomics by their ability for suturing. Reliable and easy intraluminal suturing through a flexible endoscopic platform is one of the most awaited task that such platforms should accomplish. Robotics may facilitate to overcome this challenge. Single port surgery also holds a big promise for flexible platforms especially for those with suturing capacity.

Conclusions

Experimental colorectal ESDs using a new STRAS intuitive flexible surgical robot were feasible and suggested a short learning curve. Although some technical improvements are still required, the system might allow for wider adoption of complex endoluminal surgical procedures among interventional endoscopists.

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Figure legends

Figure 1. The operating tip of the robotic platform.

The instruments are passing through a 4.2 mm channel. Two arms on the side are opening (red arrow) to provide optimal position for the robotic instruments to be used in triangulation. The black arrow indicates the exit of a 2.8 mm working channel for regular endoscopic tool on the middle lower part of the endoscope's tip.

Figure 2. Instrumentation of the system

The currently available robotized tools: fenestrated and teeth graspers, electric hook and an insulated tip knife.

Figure 3. The master interface with the intuitive controllers.

The master unit is set remote from the patient. The intuitive control interface allows the surgeon to comfortably operate the system and provides a continuous feedback about the actual position of the tools.

Figure 4. Device set-up and removal

A. The device is dismounted from the slave rack and inserted hand controlled into the rectum under direct visual control. **B.** After insertion the platform is secured on the slave rack with a single motion. **C.** The robotized instruments are consisted of a proximal motor and a flexible shaft with a bendable distal tip and are loaded one by one. **D.** After the procedure is completed the platform is removed from the rectum by rolling the whole slave unit back.

Figure 5. The main steps of the procedure.

A. As a first step the target area is marked by using an electrical instrument. **B.** The mucosa is lifted with a stained 10% glycerol solution using a regular endoscopic injection needle passing through the 2.8 mm working channel. **C.** First a small mucosal cut is made. **D.-G.** The mucosa is dissected in small steps without the need of a mucosal precut. The grasper provides a wide mucosal retraction that allows the surgeon to do precise dissection from a distance having a wide field of view.

Table 1. Detailed operative data of the overall study. Improvement in procedural performance is clearly visible by comparing the results of the first and last 6 interventions.

Procedure No	Procedure completed	Perforation	System failure	Size of dissected area (cm ²)	Procedure time (min)
1	Yes	No	No	5.1x5.3 (27.3)	106
2	No	No	Yes	NA	NA
3	No	Yes	No	NA	NA
4	No	Yes	No	NA	NA
5	Yes	Yes	No	4.0x2.5 (10)	95
6	No	No	Yes	NA	NA
Average/ Total	2	3	2	(18.6)	100
7	Yes	Yes*	Yes**	5.2x4.1 (21.3)	128
8	Yes	No	No	4.5x5.0 (22.5)	55
9	Yes	No	No	3.5x2.4 (8.4)	107
10	No	Yes	No	NA	NA
11	Yes	No	No	1.5x1.5 (2.2)	18
12	No	No	Yes	NA	NA
Average/ Total	4	2	2	(13.6)	77
13	Yes	No	No	3.4x3.1 (10.5)	30
14	Yes	No	No	3.3x2.8 (9.2)	39
15	Yes	No	No	5.5x4.7 (25.8)	92
16	Yes	No	No	6.3x5.5 (34.6)	84
17	Yes	No	No	6.1x4.2 (25.6)	82
18	Yes	No	No	5.4x3.8 (20.5)	38
Average/ Total	6	0	0	(21.0)	61
Overall Average/ Total	12	5	4	(18.2)	73

* - This perforation was closed by using a flexible endoscopic hemoclip; ** - The system had been repaired on site; **NA**- non applicable