Novel device for blunt dissection in third space endoscopy: Preliminary animal study (with video)

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ABSTRACT

Background and study aims Blunt dissection is not commonly performed in flexible endoscopic procedures. We developed a novel blunt dissection device and evaluated its feasibility, safety, and potential effectiveness in third space endoscopy procedures.

Materials and methods The device consists of a cotton swab and a flexible shaft. To evaluate its functionality, creation of 4-cm submucosal tunnels in live swine stomachs was attempted by either blunt dissection using our device or sharp dissection using a standard monopolar knife. Data on factors such as completion rate, operating time, adverse events, necessity of submucosal injection, and dissected submucosal thickness were collected.

Results Eighteen submucosal tunnels were successfully created (sharp: 9, blunt: 9) by two experienced endoscopists and one novice endoscopist. Median operating time was significantly shorter in the blunt dissection group (239 vs. 429 s, $P = 0.008$). In the sharp dissection group, the experienced endoscopists did not cause any muscle layer injuries, but the novice endoscopist caused muscle layer injuries in all cases. In the blunt dissection group, neither experienced nor novice endoscopists caused muscle layer injuries. The blunt dissection group required significantly fewer submucosal injections (0 vs. 5, $P < 0.001$). Median dissected submucosal thickness was similar between the groups.

Conclusions Blunt dissection using our device was feasible, safe, and potentially effective in third space endoscopy procedures by shortening operating time, reducing submucosal injections, and potentially minimizing muscle layer injury.

Introduction

Third space endoscopy, also known as submucosal endoscopy, is a technique that tunnels into the space located between the mucosa and the muscularis layer of the gastrointestinal wall, and this allows therapeutic intervention, such as peroral endoscopic tumor resection including endoscopic submucosal dissection (ESD) and peroral endoscopic myotomy (POEM) [1, 2]. The first clinical application of third space endoscopy was POEM for treatment of esophageal achalasia, performed by Inoue in 2008 [3]. This has revolutionized the field of third space endoscopy, which is rapidly emerging as a minimally invasive alternative to conventional surgery [1, 2, 4]. The submucosa of the gastrointestinal tract is a layer of loose connective tissue that links the mucosa and the muscularis layer [5], but submucosal dissection is generally performed using electric-powered endoscopic knives in third space endoscopy procedures [1]. Serious adverse events (AEs) associated with use of electrocautery including intraoperative and/or delayed perforation, have been reported [6]. To avoid these AEs, a more atraumatic dissection technique is required.

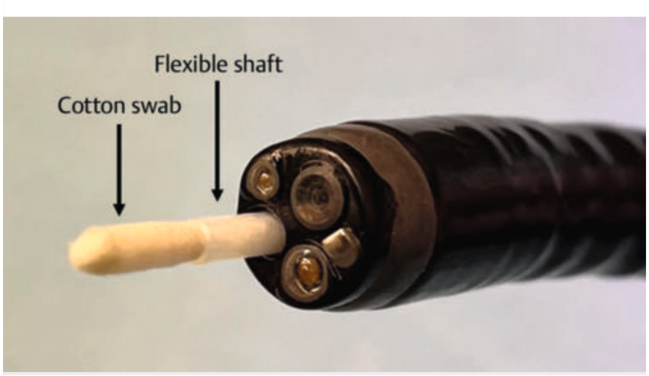
In this study, we report a new method of submucosal dissection using a cotton swab-type device that we have newly developed for flexible endoscopy. In surgical procedures, blunt dissection is accepted as an atraumatic fashion and is utilized in combination with "sharp dissection" using an electric scalpel or other energy device [7, 8], but that technique has not been widely performed in flexible endoscopic procedures. We hypothesized that blunt dissection is effective in third space endoscopy, and focused on the cotton swab, which is being used for blunt dissection in surgical procedures [9].

The aim of this study was to evaluate the feasibility, safety, and potential effectiveness of blunt dissection using our device in third space endoscopy procedures.

Material and methods

Device

The new device consists of a cotton swab and a flexible shaft (diameter: 2.6 mm, working length: 151 cm, cotton swab length: 10 mm) (▶ **Fig. 1**). It can be passed through the 2.8-mm biopsy channel of a standard flexible endoscope and air suction is possible as usual. Liquid suction is also possible but is compromised; full-power suction requires removal of the device.



▶ **Fig. 1** Our new flexible cotton swab.

Animals

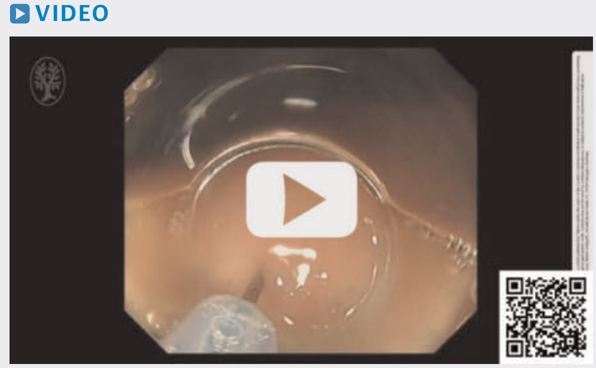
This study was approved by the Institutional Animal Care and Ethical Review Board (IVTeC Co. Ltd. Animal Welfare Committee, approval number: IVT23–16). All procedures were performed with 3-month-old female swine in a standard manner under general anesthesia. Each swine received pretreatment and was humanely euthanized upon completion of the experiment.

Endoscopic procedure

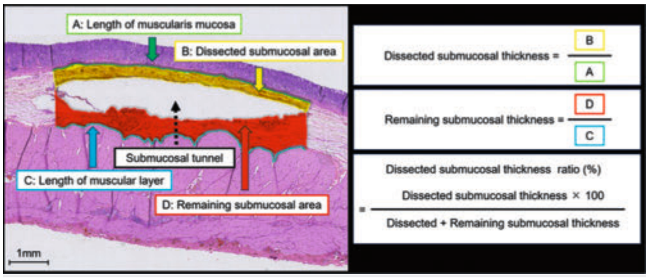
To evaluate performance of our device in third space endoscopy procedures, creation of submucosal tunnels in live swine stomachs was attempted by either blunt dissection using our device or sharp dissection using a standard monopolar knife [DualKnife J (KD-655 L), Olympus, Tokyo, Japan]. A high-frequency electrosurgical unit (VIO 300 D, ERBE Elektromedizin, Tübingen, Germany) was used with Swift coagulation mode, effect 3, 30 W setting. The procedures were conducted by two experienced endoscopists and one novice, who was an upper gastrointestinal surgeon and had only performed esophagogastroduodenoscopy surveillance. To standardize conditions, the location was restricted to upper or middle gastric body.

We performed the procedures with a single-channel endoscope (GIF-H290 T, Olympus, Tokyo, Japan). First, we measured 4 cm with a ruler and marked a goal by injecting indigo carmine into the submucosal layer. After injecting normal saline into the submucosal layer, a mucosal incision was made 4 cm proximal to the marked goal using a monopolar knife. Once an incision in the submucosal layer was made to create the entry hole, operating time measurement began. Subsequently, submucosal tunneling was performed using either our device or a monopolar knife, and the procedure was completed upon reaching the marked goal. During the procedures, injection of normal saline into the submucosal layer was allowed, if necessary. ▶ **Video 1** shows how our device is used for blunt dissection.

VIDEO



▶ **Video 1** A method of blunt dissection with our device.



▶ **Fig. 2** Pathological evaluation. We measured the length of the muscularis mucosa and the dissected submucosal area, and the dissected submucosal thickness was calculated by dividing the dissected submucosal area by the length of the muscularis mucosa. Similarly, the remaining submucosal area and length of the muscular layer were measured to calculate remaining submucosal thickness. In addition, the ratio of dissected submucosal thickness was determined by dividing the dissected submucosal thickness by the sum of the dissected and remaining submucosal thickness.

Data such as completion rate, operating time, AEs, necessity of submucosal injection, and dissected submucosal thickness were collected and compared between the sharp dissection and blunt dissection groups.

Pathological evaluation

The samples, including tunneling part, were obtained and fixed in 5% formalin. They were sectioned at 5-mm intervals for pathological evaluation. The tissue was then embedded in paraffin blocks and cut into 4-µm sections for hematoxylin and eosin staining. Images were digitized with a slide scanner (Ventana iScan HT, Roche Diagnostics, Sant Cugat, Spain), and the dissected submucosal area and the length of the muscularis mucosa were measured using an image analyzer (HALO software, Indica labs, Corrales, New Mexico, United States) (▶ **Fig. 2**).

The dissected submucosal thickness was calculated by dividing the dissected submucosal area by the length of the muscularis mucosa [10]. Similarly, the remaining submucosal area and the length of the muscularis layer were measured to calculate remaining submucosal thickness. In addition, the ratio of dissected submucosal thickness was determined by dividing the dissected submucosal thickness by the sum of the dissected and remaining submucosal thickness. The average dissected and remaining submucosal thickness, as well as the ratio of dissected submucosal thickness, were assessed for each tunnel and compared between the groups.

Statistical analysis

Statistical analyses were performed using a statistical software package (JMP ver. 17.1.0, SAS, Cary, North Carolina, United States). The results are presented as median (interquartile range). The Mann–Whitney U test and Pearson's Chi-square test were used to compare continuous and categorical variables, respectively. $P < 0.05$ was defined to be statistically significant.

Results

Nine submucosal tunnels were created in each group, totaling four swine. All procedures were successfully performed in both groups (completion rate = 100%). Overall operating time was 429 seconds (range, 323–452) in the sharp dissection group and 236 seconds (range, 177–376) in the blunt dissection group; operating time was significantly shorter in the blunt dissection group ($P = 0.008$) (▶ **Table 1**). Although no statistically significant differences were observed due to the small sample size, a similar trend was observed across all endoscopists (▶ **Table 2**). In the sharp dissection group, the experienced endoscopist did not cause any muscularis layer injuries, whereas the novice endoscopist caused muscularis layer injuries in all cases. In contrast, in the blunt dissection group, neither the experienced nor the novice endoscopists caused any muscularis layer injuries (▶ **Table 3**). There was no perforation and bleeding requiring coagulation in either group.

The median number of submucosal injections required during the submucosal dissection was five in the sharp dissection group, whereas the blunt dissection group did not require any submucosal injections ($P < 0.001$) (▶ **Table 1**, ▶ **Table 4**).

Dissected submucosal thickness was 372 µm (range, 302–447) in the sharp dissection group, and 457 µm (range, 371–566) in the blunt dissection group. The remaining submucosal thickness was 317 µm (range, 270–518) and 348 µm (range, 132–461) and the ratio of dissected submucosal thickness was 54% (range, 39–65) and 60% (range, 48–80). For each category, there was no significant difference between the groups (▶ **Table 5**).

▶ **Table 1** Overall outcomes.

	Sharp dissection	Blunt dissection	*P* value
Operating time (s)	429 (323–452)	236 (177–376)	**0.008**
Muscular layer injury	3/9 (33%)	0/9 (0%)	0.058
Bleeding*	0/9 (0%)	0/9 (0%)	
Perforation	0/9 (0%)	0/9 (0%)	
Number of submucosal injections	5 (3.5–7)	0 (0–0)	**< 0.001**

*Bleeding was defined as that requiring electrocoagulation.

▶ **Table 2** Operating time per endoscopist.

	Sharp dissection	Blunt dissection	*P* value
Experienced endoscopist 1	433 (355–453)	267 (189–404)	**0.047**
Experienced endoscopist 2	371 (315–426)	238 (125–351)	0.40
Novice endoscopist	446 (295–660)	189 (180–400)	0.175

▶ **Table 3** Muscularis layer injury per endoscopist.

	Sharp dissection	Blunt dissection	*P* value
Experienced endoscopist 1	0/4 (0%)	0/4 (0%)	
Experienced endoscopist 2	0/2 (0%)	0/2 (0%)	
Novice endoscopist	3/3 (100%)	0/3 (0%)	**0.014**

▶ **Table 4** Number of submucosal injections per endoscopist.

	Sharp dissection	Blunt dissection	*P* value
Experienced endoscopist 1	5 (3–7)	0 (0–0)	**0.005**
Experienced endoscopist 2	5 (3–7)	0 (0–0)	0.130
Novice endoscopist	5 (5–10)	0 (0–0)	**0.016**

▶ **Table 5** Submucosal thickness evaluation.

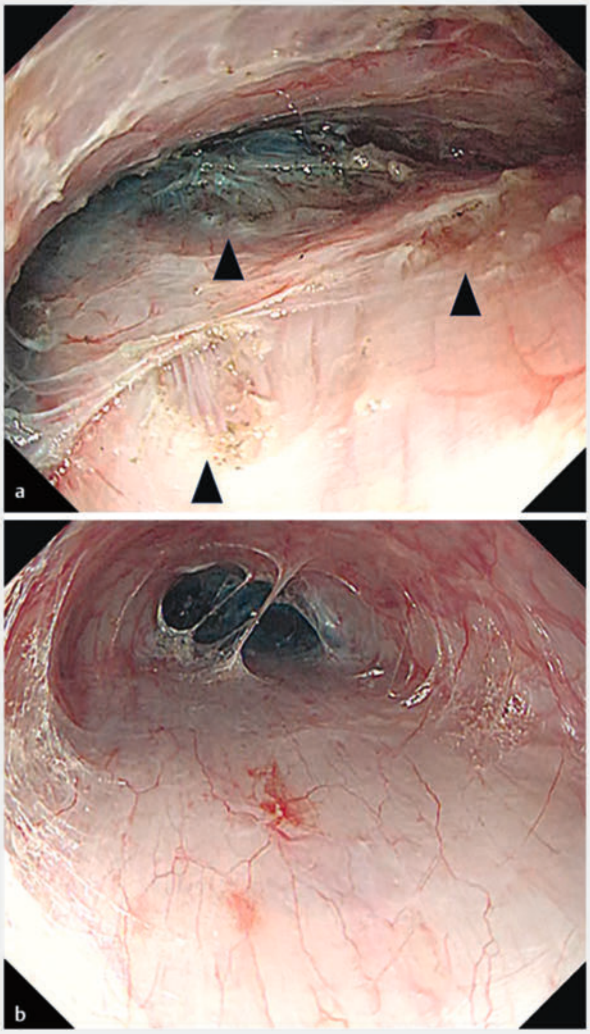
	Sharp dissection	Blunt dissection	*P* value
Dissected submucosal thickness (μm)	372 (302–447)	457 (371–566)	0.11
Remaining submucosal thickness (μm)	317 (270–518)	348 (132–461)	0.30
Dissected submucosal thickness ratio (%)	54 (39–65)	60 (48–80)	0.15

Macroscopic inspections of the submucosal tunnels performed by the novice are shown in ▶ **Fig. 3**. There were three muscularis layer injuries in the sharp dissection group (▶ **Fig. 3a**), whereas no such injuries were observed in the blunt dissection group (▶ **Fig. 3b**).

Discussion

In third space endoscopy, there have been reports of using a transparent cap for blunt dissection and developing multifunctional forceps to perform blunt dissection [11, 12], However, there are no reports worldwide of development of a dedicated device specifically for blunt dissection based on a cotton swab used in surgical procedures and comparison of it with existing methods [9]. The reason for adopting a cotton swab instead of forceps is that the roughness of the cotton surface is considered suitable for blunt dissection [13]. We developed the cotton swab for flexible endoscopy by adjusting the thickness and length of the cotton part to avoid obstructing the field of view, as well as adjusting the stiffness of the shaft. The development process, especially in producing a thinner cotton swab, involved technological challenges. Our previous experience with development of an ultra-thin (diameter: 3 mm) surgical cotton swab for laparoscopic surgery made us overcome those challenges [14].

In this study, we evaluated safety and effectiveness of blunt dissection using our device in submucosal dissection. Flexible endoscopic procedures such ase ESD and POEM have been gaining clinical acceptance worldwide [15, 16, 17], but they are still technically demanding [6, 17], and several AEs, such as perforation and bleeding, have been reported [15, 18, 19]. One way to prevent perforation may be to perform submucosal dissection without using electrocautery. In this study, because there was no muscularis layer injury in the blunt dissection group, blunt dissection using our device is considered to have safety advantages. Delayed perforation is another complication relating to flexible endoscopic procedures. The rate of delayed perforation is low (0.06%-0.45%) in ESD, but it often requires surgical intervention [20]. It is said that delayed perforation is associated with excessive use of electrocautery [20, 21]. In addition, cold polypectomy has been reported to reduce post-procedure perforation or bleeding compared with polypectomy with electrocautery and has rapidly spread worldwide [22]. Similar to cold polypectomy, our device does not generate any thermal spread



▶ **Fig. 3** Macroscopic inspections of interior of the submucosal tunnels that a novice performed. **a** Sharp dissection caused three muscularis layer injuries (arrowhead). **b** Blunt dissection did not cause such an injury.

due to electricity and it has a possibility of reducing delayed perforation.

Blunt dissection facilitated the procedure by significantly reducing operating time and need for submucosal injections compared with sharp dissection. The number of submucosal injections was approximately five in the sharp dissection group, which alone cannot account for the difference in operating time. The distance achieved by sharp dissection gain is limited by the length of the active knife, which is much shorter what can be achieved with blunt dissection. In blunt dissection, the length of dissection is adjusted by the stroke, depending on surgeon judgment. For example, in an avascular area, a single stroke can gain a longer dissection distance. This is likely the reason for the difference in operating time between the two groups.

Although submucosal injections were not required during blunt dissection, our study does not recommend avoiding them injections. We have found that injection of tumescent liquid facilitates blunt dissection in surgical procedures [23, 24]. Thus, if submucosal injection is necessary to achieve an adequate field of view and ensure safety, we would not hesitate to use it in combination with blunt dissection.

It is important to note that a novice endoscopist was able to complete the procedures without causing muscularis layer injury or perforation using our device. The European Society of Gastrointestinal Endoscopy (ESGE) suggests that training in ESD should be considered only by fully trained endoscopists. In addition, performing at least 20 ESD procedures in animal and/or ex vivo models is recommended before human practice, with no perforation in the last 10 training cases [25]. POEM is also a technically demanding procedure [26]. Experienced endoscopists who trained on animal models have reported requiring a learning curve of 25 cases [27]. Thus, mastery of ESD and POEM requires time, effort, and resources, but our device may contribute to reducing the learning curve by facilitating the procedure and making the technique more accessible.

To utilize our device for ESD, evaluation of the dissected submucosal thickness was essential. We conducted microscopic evaluations and observed that dissected submucosal thickness and ratio of dissected submucosal thickness were similar in both groups. This finding suggests that, from the perspective of cancer resection, blunt dissection using our device has the potential to provide treatment comparable to sharp dissection.

This study evaluated third space endoscopy procedures, demonstrating our device's potential usefulness in POEM and the dissection phase of ESD. However, the situation we examined did not fully replicate an ESD situation, so we are planning to conduct another study to evaluate the effectiveness of our device especially in ESD.

Blunt dissection cannot cut the mucosa or achieve hemostasis, and thus, it is impossible to complete procedures like ESD or POEM with it alone. Therefore, it needs to be used in combination with electric knives. Our plan is to use electric knives to incise the mucosa, followed by submucosal dissection with our device. When large blood vessels are encountered, we coagulate them using electric knives. Our device was able to dissect connective tissue without damaging large blood vessels in the swine model. However, in the case of bleeding, the operative field is typically washed with water and suctioned to identify the bleeding site. It may be effective to attempt compression of the bleeding site with our device to reduce blood flow prior to electrocautery. Currently, it is necessary to switch between our device and electric knives. However, developing a blunt dissection device that integrates electrocautery functionality could be considered in the future.

There are several limitations to our study. First, this study was a preclinical trial using a swine model, which is known to be associated with less bleeding [28]. In addition, submucosal dissection may be easier in a swine model than in humans, potentially resulting in conditions that do not precisely replicate those in human subjects. Third, the number of trials was limited. The fourth limitation is the small number of novice participants, making it difficult to determine the usability for all novices. Finally, we were not able to evaluate delayed complications such as delayed perforation because we sacrificed the swine models on the day of the experiment.

Conclusions

Blunt dissection using our novel cotton swab-type device was feasible, safe, and may be an attractive alternative for third space endoscopy procedures. It reduced operating time and need for submucosal injections, and potentially minimized muscularis layer injury without increasing bleeding or perforation, while maintaining the dissected submucosal thickness.

Conflict of Interest

Shota Fujii is a full-time employee of Sanyo CO. Ltd. The remaining authors have no conflict of interest to declare.

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