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Efficacy of an assistive guide tube for improved endoscopic access to gastrointestinal lesions: an *in vivo* study in a porcine model

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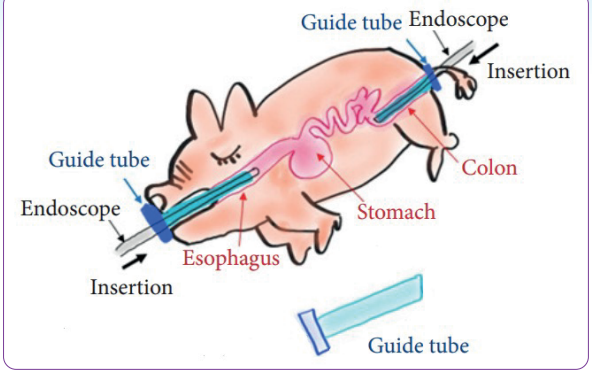
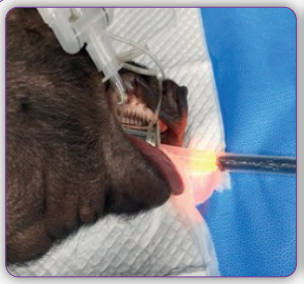
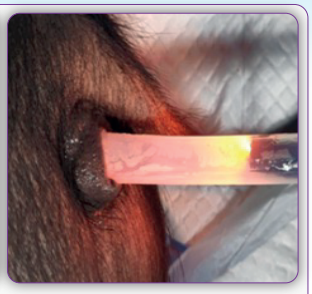




An iterative approach into the stomach through the guide tube



An iterative approach into the sigmoid colon through the guide tube

Guide tube-assisted endoscopic procedures are effective and safe for repeated endoscopic access in an *in vivo* porcine model.

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Background/Aims: Guide tube-assisted endoscopy for procedures that require repeated endoscopic access is safer and more effective than conventional endoscopy. However, its effectiveness has not been confirmed in animal studies. We assessed the usefulness of guide tube-assisted endoscopic procedures in an *in vivo* porcine model.
Methods: Five different guide tube-assisted endoscopic procedures were performed by experienced endoscopists on a pig weighing 32 kg. To evaluate the efficacy of these procedures, we compared the endoscopic approach time when a guide tube was used to that when it was not. Additional endoscopic procedures using a guide tube were performed, including multiple foreign body extractions, multiple polypectomies, and multiple submucosal dissections. To evaluate safety, we compared the insertion force into the proximal esophagus between the guide tube and conventional overtube methods.
Results: Using the endoscopic approach with a guide tube required a shorter average approach time to reach the three target lesions than when using the endoscopic approach without a guide tube ($p<0.001$). Compared to the conventional overtube method, the guide tube method produced a lower average resistance during insertion into the upper esophagus ($p<0.001$).
Conclusions: Guide tube-assisted endoscopic procedures are effective and safe for repeated endoscopic access in an *in vivo* porcine model.

Keywords: Access; Endoscopy; Guide tube; Methods

INTRODUCTION

Endoscopic procedures requiring repeated endoscope insertion are painful for the patient and difficult for the endoscopist.[1] Recently, overtubes, such as the Guardus overtube (US Endoscopy Group Inc.), which makes repeated endoscope insertion easier, have been produced for endoscopic procedures. However, fatal complications, such as intestinal perforation and pain associated with breakage of the rigid overtube material, can occur with overtube use.[2-6] Moreover, most overtubes have shallow insertional depths; therefore, inserting them into the distal portions of the intestinal tract, such as the cecum, is difficult.

In a previous study, we developed a guide tube that compensates for the disadvantages of rigid overtubes.[1] The guide tube was a soft silicone overtube. Various endoscopic procedures using a guide tube have been performed in a gastrointestinal simulator.[1] We observed that all guide tube-assisted endoscopic procedures were safer and more effective than conventional endoscopic techniques when performed using gastrointestinal simulators. However, because the gastrointestinal simulator does not produce peristaltic gastrointestinal movement, and the gastric and colonic lumens of the simulator are made of silicone, evaluating the risk of mucosal perforation using this test model was difficult. Therefore, in this study, we used an *in vivo* porcine model to overcome these limitations and evaluate the clinical outcomes of guide tube use.

METHODS

Statement of animal ethics and animal care

This study was a preclinical trial performed in July 2019 using a 14-month-old pig weighing 32 kg as the *in vivo* porcine model for all tests (Fig. 1). Experiments were performed according to the regulations and guidelines provided by the committee. The description of this study follows the Animal Research: Reporting of *In Vivo* Experiments guidelines. The pig underwent fasting and intestinal cleansing a day before the procedure. On the day of the procedure, the animal was sedated with atropine sulfate (0.4 mg/kg) and xylene (2 mg/kg) and was then anesthetized through inhalation of 0.5% isoflurane. The target lesions for the endoscopic procedures were generated artificially as part of the porcine model. Two endoscopists from the SMG-SNU Boramae Medical Center, Seoul, Korea, participated in the study. The animal was sacrificed after the experiment according to the IACUC guidelines.

Devices and settings

In this study, we used a single-channel endoscope (GIF-Q260J; Olympus Co., Ltd.) for manipulation. Argon plasma coagulation (Olympus Co., Ltd.) and electrocauterization (VIO 300D; ERBE) were used to create the lesions. An insulation-tipped knife-2 (Olympus Co., Ltd.) was used for the lesion resection and submucosal dissection. A guide tube (SMG-SNU Boramae Medical Center; inner diameter, 13 mm; outer diameter, 15 mm; length, 25 cm) was used in the experimental tests. A conventional overtube (Sumitomo Bakelite Inc.; inner diameter:

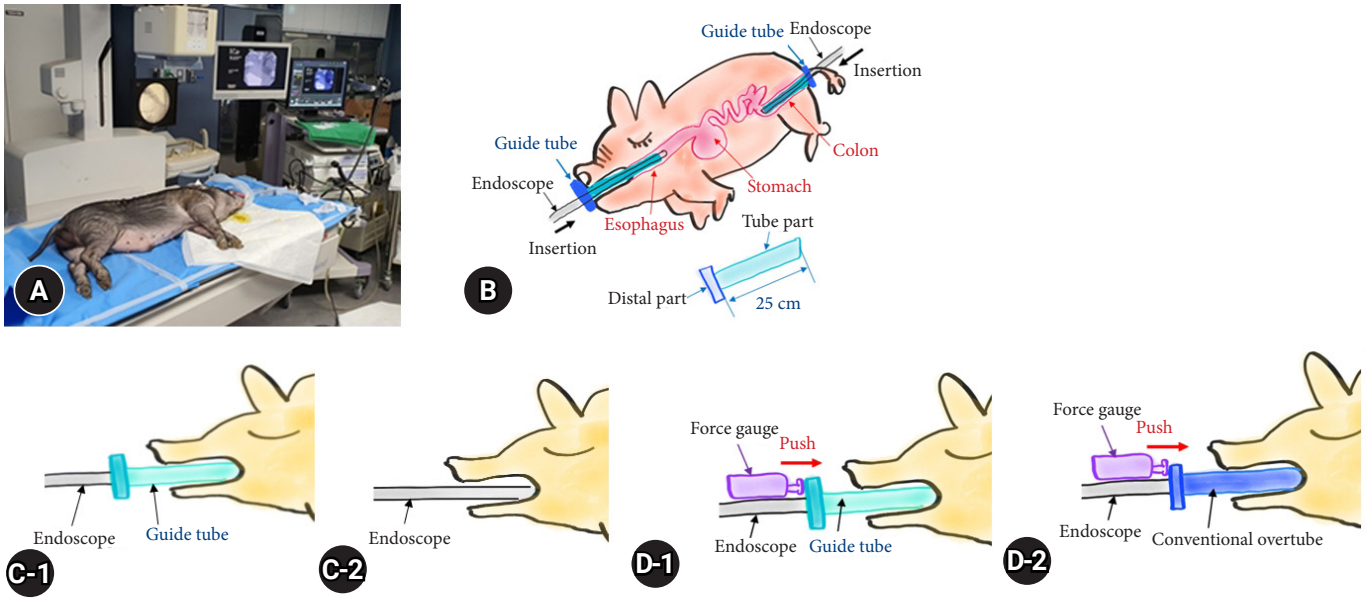

Fig. 1. (A) The *in vivo* porcine model and the animal room used for endoscopic procedures. (B) Schematic figure of the endoscope, guide tube, and porcine model in this experiment. (C) Measurement of the time for endoscopic approach with the guide tube and that for endoscopic approach without the guide tube. (D) Measurement of insertion force for the guide tube and conventional overtube methods.

15 mm; outer diameter: 18 mm) was used in the control tests (Fig. 2). A digital force gauge (ARTBULL) was used to measure insertion force.

Outcomes and data analysis

1) Efficacy evaluation of the guide tube

The primary measurement of outcome efficacy was the approach time(s) of endoscope insertion, defined as the time required to advance the endoscope from the upper incisors to the target sites, such as the esophagus, antrum, and sigmoid colon. Approach times were measured with a stopwatch in two groups as follows: a guide tube group, in which the endoscope was inserted into the target lesion through the guide tube (Fig. 1, C-1), and a control group, in which the endoscope was inserted into the target lesion without a guide tube (Fig. 1, C-2).

Several techniques for improving efficacy have been tested using a guide tube. Multiple foreign body extractions (pork meat: 10 pieces, each measuring 2 cm in diameter), multiple polypectomies (stomach and colon polyps: three each, each measuring 1 cm in diameter), and multiple submucosal dissections (gastric lesions: three, each measuring 2.5 cm in diameter) were performed using the guide tube. Procedure time was not measured in any of the above mentioned procedures.

Safety evaluation of the guide tube

The primary measurement of safety outcome was the insertion force required for guide tube insertion. We selected the proximal esophagus, an area where mucosal perforation frequently occurs during the insertion of an overtube, as the site for assessing the resistance experienced during insertion of each tube. To measure the insertion force, we pushed the distal part of the overtube using a force gauge (SF-100; digital force gauge). The insertion force (kgf) was measured in two groups: the guide tube group, in which the guide tube was inserted into the proximal esophagus (Fig. 1, D-1), and the control group, in which a conventional overtube was inserted into the proximal esophagus (Fig. 1, D-2). The force of insertion in the sigmoid colon was not measured. Radiographs were checked to locate the perforations 3 hours after the guide was inserted into the esophagus and sigmoid colon 50 times for each time.

Statistical analysis

All statistical analyses were conducted using the IBM SPSS software ver. 21.0 (IBM Corp.). Continuous variables are presented as mean±standard deviation. Student *t*-test was used for statistical analysis, and significance was determined at $p<0.05$.

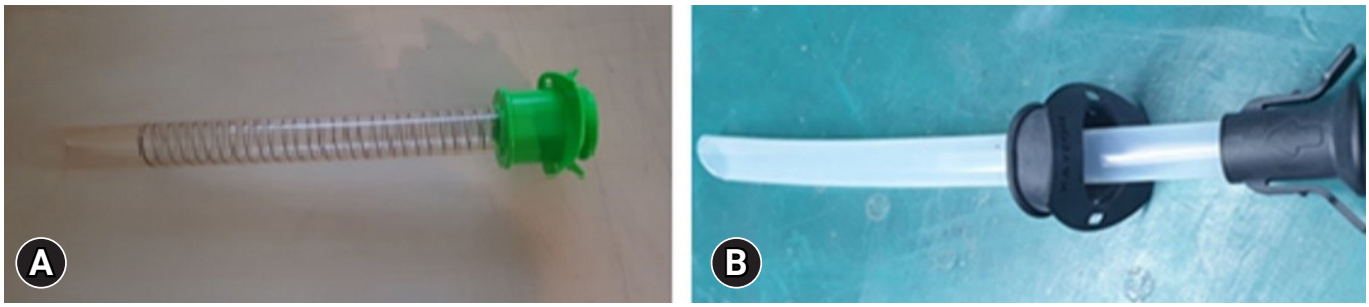

Fig. 2. The two types of overtubes used. (A) A conventional overtube. (B) A guide tube (silicone overtube).

Ethical statements

The animal experiments were approved by the Institutional Animal Care and Use Committee of KNOTUS (KNOTUS IACUC 19-KE-453).

RESULTS

Efficacy evaluation

The efficacy of the guide tube for endoscopy was demonstrated using an *in vivo* porcine model. Compared to the conventional endoscopic approach, the guide tube-assisted endoscopic approach had a shorter approach time to reach the distal esophagus (3.35±0.38 seconds and 7.90±0.74 seconds, respectively, $p<0.001$), antrum (6.16±0.62 seconds and 20.60±2.59 seconds, respectively, $p<0.001$), and sigmoid colon (2.95±0.43 seconds and 8.15±0.75 seconds, respectively, $p<0.001$) (Table 1).

Multiple foreign body extractions, polypectomies, and submucosal lesion dissections were successfully performed. A guide tube was used to remove multiple foreign bodies (pork meat: 10 pieces, each measuring 2 cm in diameter), perform multiple snare polypectomies (stomach and colon polyps: three of each, measuring 1 cm in diameter), and perform multiple submucosal dissections (gastric lesions: three, measuring 2.5 cm in diameter) (Fig. 3).

Safety evaluation

Less resistance was encountered during the insertion of the guide tube into the upper esophagus compared to the resistance measured during the insertion of the conventional overtube (0.96±0.10 kg and 1.49±0.09 kg, $p<0.001$) (Table 2). Perforation was not observed on follow-up radiographs obtained 3 hours after the guide tube was inserted 50 times for each time in the esophagus and sigmoid colon (Fig. 4).

DISCUSSION

Endoscopic procedures performed using current endoscopic platforms are limited by the narrow and complex gastrointestinal tract. Only small objects can be removed through an endoscope channel with a diameter of <3.2 mm. Therefore, repeated endoscopic insertion is required to remove multiple large polyps or foreign bodies.[7,8] Repeated endoscopic insertions are difficult for both patients and endoscopists. Several overtube devices have been designed to facilitate endoscopy.[6,9,10] However, the use of overtubes is limited owing to complications such as pharyngeal and esophageal perforations, pneumomediastinum, variceal rupture, and tracheal compression. Recently, a novel shape-locking overtube (ShapeLock) was developed to facilitate repeated endoscopic insertions.[11,12] However, the prohibitive cost and complexity of the device limits its use.

The guide tube was made of silicone and named based on its proposed use to provide a guided path to various gastrointestinal lesions during endoscopy procedures. The silicone fabrication of the guide tube reduces the mucosal trauma caused by the rigid materials used to make conventional overtubes. The guide tube is useful in difficult gastrointestinal endoscopic procedures. It can be used to remove large, sharp foreign bodies such as fish bones, blades, or mussel shells; can be easily adapted for use with specialized procedures such as repetitive endoscopic submucosal dissections or endoscopic mucosal dissections of multiple large polyps; and provides a pathway for endoscopic drainage of bulk food material or blood for patients with gastroparesis or gastrointestinal bleeding.

The development and experimentation with endoscopic accessory devices are essential for advancing the diagnosis and treatment of gastrointestinal disorders. This preclinical trial aimed to evaluate the efficacy of the guide tube as an endoscopic accessory device for improving the accessibility of

Table 1. Comparison of times of endoscopic approaches to target sites (*in vivo* porcine model)

	Approach through the guide tube (*n*=10, two endoscopists) (sec)	Approach without the guide tube (*n*=10, two endoscopists) (sec)	*p*-value
Distal esophagus	3.35±0.38	7.90±0.74	<0.001
Antrum	6.16±0.62	20.60±2.59	<0.001
Sigmoid colon	2.95±0.43	8.15±0.75	<0.001

Values are presented as mean±standard deviation.

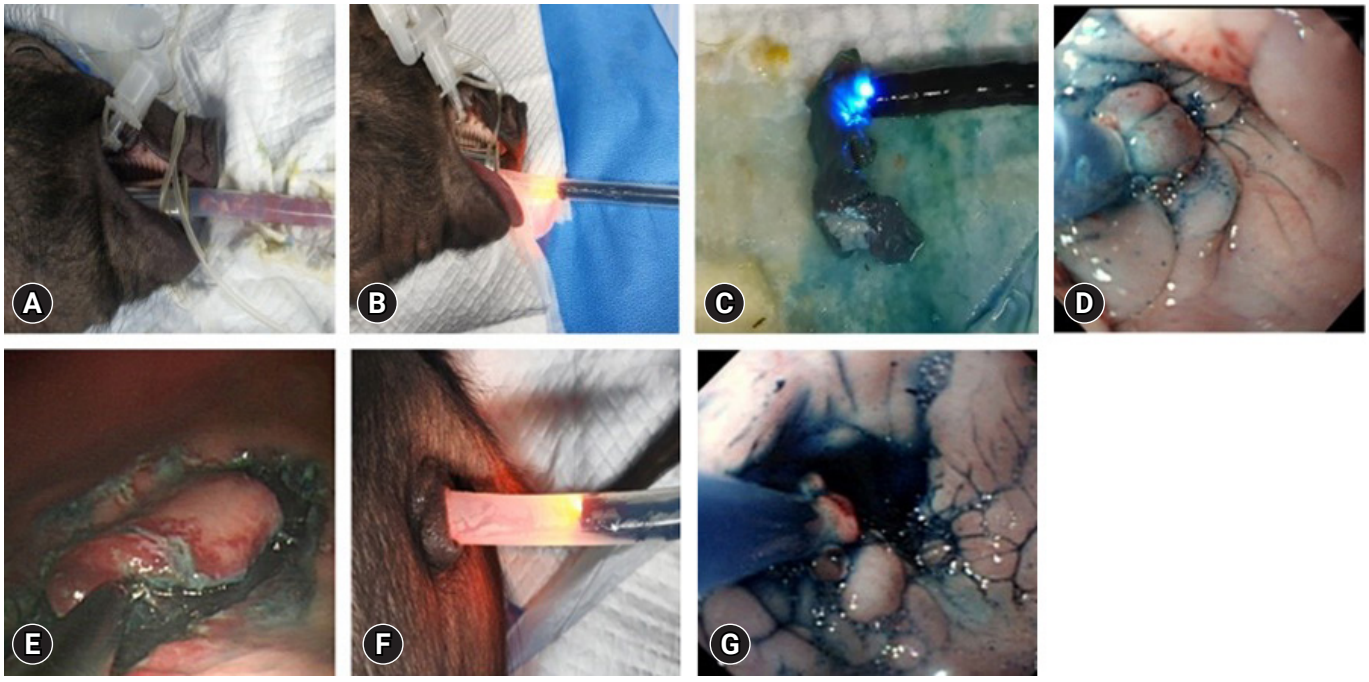

Fig. 3. Endoscopic procedures using the guide tube. (A) Ten pork pieces, measuring 2 cm in diameter, were inserted. (B) An iterative approach into the stomach through the guide tube. (C) A pork piece measuring 2 cm in diameter was removed through the guide tube. (D) Endoscopic mucosal resection of multiple gastric polyps. (E) Endoscopic submucosal dissection of multiple gastric polyps. (F) An iterative approach into the sigmoid colon through the guide tube. (G) Endoscopic mucosal resection of multiple colonic polyps.

Table 2. Comparison force for insertion into the proximal esophagus (*in vivo* porcine model)

	Guide tube (*n*=10, two endoscopists)	Conventional overtube (*n*=10, two endoscopists)	*p*-value
Proximal esophagus (kg)	0.96±0.10	1.49±0.09	<0.001

Values are presented as mean±standard deviation.

gastric lesions. To minimize animal use in the evaluation of the guide tube, we used a human simulator device for testing in a previous study.[1] In the current study, we performed various experiments in a short period without complications using only one pig. Endoscopic procedures that required repeated endoscopic access were performed faster, easier, and safer with the guide tube-assistive device than with a conventional endoscopic overtube. Compared to the conventional endoscopic method, all endoscopic procedures performed with the guide tube had shorter approach times and encountered lower resistance to endoscope advancement. Multiple foreign body extractions, polypectomies, and submucosal dissections were easily performed using guide tube-assisted endoscopy. Furthermore, mucosal perforation did not occur during any of the guide tube-assisted procedures.

This study has several limitations. First, it was a single-center,

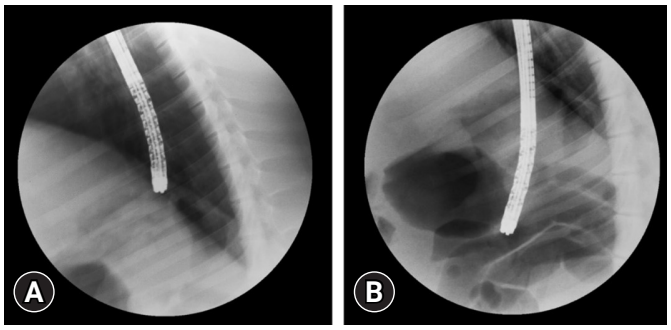

Fig. 4. Abdominal radiographs taken after the guide tube-assisted endoscopic procedures revealed no evidence of tissue perforation. (A) The stomach. (B) The colon.

preliminary study based on few swine experiments. Nevertheless, this experimental bias was minimized by conducting several pretests using realistic animal model simulators. Second, due to the anatomical differences between the porcine and human gastrointestinal systems, the guide tube-assisted endoscopy results may not be the same for human patients as they were for the animal used in this preclinical study. Therefore, long-term evaluation of this endoscopic technique in human patients is needed. Lastly, the time required for efficacy-related procedures, such as multiple foreign body extractions, polypectomies, and submucosal lesion dissections, was not measured because of limited research funding.

In conclusion, this study was designed to test the efficacy and safety of endoscopy using a guide tube. Despite the limitations of this study, our results demonstrated that guide tube-assisted endoscopy was effective and safe for performing procedures requiring repeated endoscopic access in an *in vivo* porcine model. Large-scale human studies are required for further clinical implementation.

Conflicts of Interest

The authors have no potential conflicts of interest.

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Author Contributions

Conceptualization: DSL, JSB, SGK; Data curation: DSL, JWK, SGK; Formal analysis: KLL, JBJ, YJJ, HWK; Funding acquisition: DSL; Methodology: DSL, JSB, SGK; Supervision: JSB, SGK, JWK; Writing–original draft: DSL, JSB, SGK, JWK, KLL, JBJ, YJJ; Writing–review & editing: DSL, JSB, SGK, HWK.

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