Coil

Interventional Clinical Study

Efficacy of Simplified Robot (FASTER)–Assisted Versus Conventional Endoscopic Submucosal Dissection (ESD) for Colorectal Lesions: A Prospective, Randomized, Controlled Trial

Protocol

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NCT number：NYSZYYEC2025K111R002

Version Date: October 11, 2025

Compliance Statement

In compliance with the Measures for Ethical Review of Life Science and Medical Research Involving Humans and the (Interim) Measures for the Administration of Investigator-Initiated Clinical Research Conducted by Medical and Health Institutions, as well as the Declaration of Helsinki, we undertake to conduct this study in accordance with this protocol. All study personnel must receive training, and the study may be implemented only after written approval by the Ethics Committee and written informed consent from participants have been obtained. Any protocol amendments must be re-reviewed and approved.

PROTOCOL SUMMARY

Study design (multiple selections allowed)	□ Case-control study □ Cohort study □ Cross-sectional study ☑Randomized controlled trial ☑ Blinding applied □ Other:
Study category (please tick according to project type)	**(Category A: High risk)** □ Gene-editing research □ Cell therapy research □ Implantable medical device research (including 3D printing) □ Class III new clinical technologies (proven safety and effectiveness; high technical difficulty and high risk) □ Research in special populations (children, pregnant women, persons with intellectual disability, patients with mental disorders, etc.) □ Off-label drug research (□ beyond indication □ beyond route □ beyond dose □ beyond age □ beyond contraindications □ beyond population □ other, specify:

	) □ Off-label device research (□ beyond indication □ beyond scope of use □ beyond contraindications □ beyond population □ other, specify:) □ Other (as judged by the investigator, specify:) (Category B: Moderate risk) □ **Post-marketing biologics research (preventive or therapeutic biologics)** □ Post-marketing therapeutic vaccine research □ Post-marketing orphan drug research □ Class II new clinical technologies (proven safety and effectiveness; certain technical difficulty; with certain medical and ethical risks) □ Other (as judged by the investigator, specify:) (Category C: Low risk) □ Research on drugs marketed for ≥5 years (including chemical drugs, generics, etc.) □ Research on marketed medical devices (including AI, imaging software, etc.) ☑Class I new clinical technologies (proven safety and effectiveness; low technical difficulty; virtually no ethical risk) □ Wearable devices (proven safety and effectiveness; low technical difficulty; virtually no ethical risk) □ Other (as judged by the investigator, specify:) □ Wearable devices (confirmed safety and effectiveness; low technical difficulty; almost no ethical risk) □ Other (as judged by the investigator, specify:)
Total number of cases	40 cases

Risk/benefit analysis	This study involves a relatively low level of risk. Potential risks include procedure-related complications such as gastrointestinal perforation, major bleeding, and infection, as well as device-related adverse reactions. We have established strict screening criteria and standardized operating procedures, and formulated emergency plans and postoperative follow-up to mitigate these risks. Meanwhile, this study may improve therapeutic outcomes for patients with colorectal lesions, shorten procedure time, and optimize the clinical workflow, providing scientific evidence for medical device development and medical progress.
Risk assessment	☑Not greater than minimal risk □ Greater than minimal risk Minimal risk: the probability and magnitude of anticipated harm or discomfort in the study are not greater than those ordinarily encountered in daily life, or during routine physical examination or psychological tests.

I. Background

Colorectal cancer is one of the leading malignancies worldwide in both incidence and mortality. In 2022, approximately 1.9 million new cases were diagnosed globally and about 904,000 patients died. Although historically higher in developed countries, incidence has continued to rise in Eastern Europe, Southeast Asia, and South America with economic transition and lifestyle changes. This trend is mainly attributed to dietary changes, sedentary behavior, and the increasing prevalence of obesity [1]. Therefore, early screening and precise treatment are of great importance for improving patient outcomes.

Endoscopic submucosal dissection (ESD) has been widely applied to treat superficial lesions of the gastrointestinal tract and is recommended by the European Society of Gastrointestinal Endoscopy (ESGE) for en bloc resection of colorectal lesions to ensure accurate pathological assessment and reduce the risk of local recurrence [2]. However, colorectal ESD still faces substantial anatomical and technical challenges. The right colon has a thin wall and is susceptible to tension; the transverse colon has sharp angulation and poor suspension; and the rectum is constrained by pelvic structures, resulting in a narrow operating space—factors considered high risk for perforation and muscular injury [3]. In addition, limited visualization of the submucosal layer and uneven tension distribution can prolong procedure time and increase complication risk [4]. Common traction techniques (e.g., clip-with-line, pulley, and

magnetic anchoring) can improve visualization to some extent, but most provide only unidirectional traction, require repeated repositioning, or rely on dedicated equipment, and thus do not meet the multidirectional traction needs of complex lesions [4]. Therefore, developing an assistive device that provides adjustable multidirectional traction and is compatible with a single-channel endoscope—thereby optimizing exposure and dissection efficiency while reducing complications—has become a key direction in the evolution of colorectal ESD.

In recent years, robotic-assistance has gradually been applied in minimally invasive gastrointestinal therapy, particularly in laparoscopic surgery (e.g., the da Vinci Surgical System), where high-precision operation has been shown to improve procedural stability and surgeon control [5]. In the endoscopic field, systems such as the Master robot and STRAS have been used to enhance visualization and intraoperative precision [6, 7]. However, barriers related to cost and device compatibility remain, limiting widespread adoption.

FASTER is a simplified robotic endoscopic assistive system designed to provide continuous, adjustable, multidirectional traction during ESD, thereby improving visualization and procedural efficiency. Unlike conventional traction methods, FASTER can be used with standard single-channel endoscopes and does not require specialized platforms. In an ex vivo porcine stomach model, Yang Xiaoxiao et al. conducted a crossover study comparing FASTER-assisted ESD with conventional ESD and found that total procedure time for beginners was significantly shorter in the FASTER group (25.6 ± 7.8 min) than in the conventional group (38.9 ± 13.4 min; $P < 0.001$), while maintaining comparable safety and resection quality.

Nevertheless, robust clinical evidence on the safety and effectiveness of FASTER in real-world colorectal ESD is still lacking. Given the unique anatomical complexity of the colon and rectum and the higher technical demands of colorectal ESD, a prospective randomized controlled trial is warranted to systematically evaluate whether FASTER can shorten procedure time, improve efficiency, and reduce complications in colorectal lesions.

II. Objectives

1. Primary objective: To evaluate whether FASTER-assisted ESD reduces total ESD procedure time compared with conventional ESD for colorectal lesions.

2. Secondary objectives: To compare between the two groups (1) mucosal dissection time; (2) dissection speed; (3) R0 resection rate; (4) en bloc resection rate;

(5) complication rates (bleeding, perforation, muscular injury); and (6) flexibility/operability indicators of robotic manipulation.

III. Endpoints

1. Primary endpoint: Total ESD procedure time (min), defined as the cumulative time from submucosal injection to completion of submucosal dissection.

2. Secondary endpoints: (1) Mucosal dissection time (min); (2) Dissection speed (mm^2/min); (3) R0 resection rate; (4) en bloc resection rate; (5) Incidence of ESD-related complications (bleeding, perforation, muscular injury); (6) Robotic flexibility indicators (number of attempts needed for a first successful grasp and the number of accidental drops).

3. Safety endpoints: Device-related and procedure-related adverse events, including bleeding, perforation, muscular injury, infection, anesthesia-related events, and other unexpected events.

IV. Study Design, Methods, and Procedures

1. Study design

This is a single-center, prospective, randomized, controlled, open-label clinical study. A total of 40 eligible patients scheduled for colorectal ESD will be enrolled and randomized 1:1 to a FASTER-assisted ESD group (intervention group) or a conventional ESD group (control group).

Intervention group: During ESD, the endoscopist will attach the FASTER robotic arm to the tip of the endoscope. After submucosal injection and circumferential incision, the robotic grasper will provide continuous multidirectional traction on the lesion margin to optimize exposure and facilitate submucosal dissection.

Control group: A transparent distal cap will be attached to the endoscope tip. The lesion will be treated with conventional ESD following standard steps without robotic assistance.

All participants will be followed up during hospitalization, with daily assessments of vital signs, laboratory parameters, and adverse events until discharge.

2. Study methods

(1) Randomization

A random number table method will be used for 1:1 allocation. An independent statistician will generate the random sequence. Allocation will be concealed until enrollment to ensure scientific rigor and fairness.

After randomization, the intervention group will undergo FASTER-assisted ESD and the control group will undergo conventional ESD. The study coordinator will implement allocation according to the concealed sequence.

(2) Blinding/Unblinding

Given the nature of the intervention, blinding of operators is not feasible. Data analysts may be kept blinded to group allocation when appropriate. Unblinding, if needed for safety reasons, will be documented with reason and time.

3. Study procedures

Study flow chart

Item	Screening period	Procedure day	Follow-up period	
	-3 to 0 days	Intraoperative	During hospitalization	
Informed consent	X			
Demographics	X			
Inclusion/exclusion criteria	X			
Laboratory tests	X			
Electrocardiogram	X			
Colonoscopy	X			
Blood pressure, heart rate	X	X		
ESD procedural metrics		X		
Adverse events		X	X	X

(Note: Laboratory test results should be within 7 days prior to signing informed consent; colonoscopy results should be within 6 months prior to signing informed consent.)

V. Study Population

According to the 2019 guidelines of the Japan Gastroenterological Endoscopy Society (JGES), colorectal lesions meeting ESD indications will be included.

1. Inclusion criteria

(1) Age between 18 and 80 years.

(2) Patients with colorectal lesions scheduled to undergo endoscopic submucosal dissection (ESD) .

(3) Lesion characteristics meeting any of the following criteria: (1) Lesions unsuitable for en bloc resection using snare-based EMR, including non-granular type laterally spreading tumors (LST-NG), especially pseudo-depressed subtype (PD); lesions with type VI pit pattern (VI-type glandular opening configuration); carcinomas with superficial submucosal invasion (T1-SM); large depressed-type tumors; large protruding lesions suspected of malignancy, including nodular mixed-type granular LSTs (LST-G); other lesions unsuitable for en bloc resection using snare-based EMR; (2) Lesions with special background conditions, including mucosal tumors with submucosal fibrosis (caused by prior biopsy or mucosal prolapse due to peristalsis); sporadic tumors arising in the context of chronic inflammation (e.g., ulcerative colitis); local residual or recurrent early carcinoma following prior endoscopic resection;

(4) Willingness to participate in the study and provision of written informed consent.

2. Exclusion criteria

(1) Suspected deep submucosal invasive carcinoma based on endoscopic features；

(2) Lesions presenting with non-lifting signs, suggesting deep submucosal invasive carcinoma or tumors with severe submucosal fibrosis;

(3) Lesions extending to the appendiceal orifice, colonic diverticulum, or ileocecal valve;

(4) Pregnant women or women who may be pregnant; lactating women;

(5) Patients with coagulation disorders;

(6) Patients considered ineligible for specific reasons;

(7) Patients with contraindications to anesthesia and/or colonoscopy.

3. Lifestyle precautions

1. Smoking: Reduce or quit smoking to avoid impairment of intestinal mucosal microcirculation, delayed wound healing, and to reduce the risks of postoperative bleeding and perforation. 2. Alcohol: Avoid spirits and high-alcohol beverages to reduce chemical irritation to the intestinal mucosa and potential effects on coagulation. 3. Exercise: Begin ambulation early after surgery to promote gastrointestinal recovery; avoid vigorous exercise such as running, jumping, and weightlifting; low-intensity activities such as walking and yoga are allowed. 4. Diet: Avoid high-fiber, high-fat, spicy foods and carbonated drinks. Within 2 weeks after surgery, a lukewarm liquid or semi-liquid diet is recommended; gradually resume a regular diet after 2 weeks. 5. Prohibited medications: Avoid NSAIDs, antiplatelet agents, and anticoagulants; if use is necessary, notify the study team for evaluation. Proton pump inhibitors (PPIs) may be used postoperatively to prevent delayed bleeding, and polyethylene glycol (PEG) stool softeners are recommended to prevent constipation. 6. Additional treatments or surgery: If other bowel-related examinations (e.g., CT, ultrasound, follow-up endoscopy) or surgical interventions are needed, inform the study team in advance; the trial may be paused or the subject may withdraw.

4. Screening failure

Definition: Screening failure refers to subjects who have signed informed consent but do not meet the eligibility criteria or cannot complete baseline assessments, and therefore cannot be enrolled.

Management:

1. The reasons for screening failure must be recorded in detail, including failure to meet inclusion/exclusion criteria, incomplete baseline data, or

withdrawal of consent.

2. The subject should be informed of the screening failure and advised on standard medical management as appropriate.

3. Data management: Data from screening failures will not be included in the final analysis, but may be used for process optimization and subsequent feasibility assessment.

4. Follow-up: Some screening failures may be re-evaluated and may be rescreened for eligibility if their condition changes; the process should be documented.

5. Recruitment and retention strategy

This study will be conducted at Shenzhen Hospital of Southern Medical University. We plan to recruit 40 eligible patients scheduled for colorectal ESD via outpatient screening, inpatient ward referral, social media announcements, and patient education sessions, and randomize them 1:1 to the FASTER-assisted ESD group and the conventional ESD group using a random number table. To improve adherence and retention, the study team will maintain contact by phone, email, and WeChat, provide postoperative follow-up reminders, and offer health counseling related to colorectal lesions. For patients with slow recovery, additional health guidance and psychological support will be provided. As the study involves ESD, to ensure safety, minors and pregnant women will not be enrolled. All participants must sign written informed consent and fully understand the study objectives, methods, and potential risks. These measures aim to ensure smooth study conduct while safeguarding participants' rights and safety.

6. Outcome assessments

(1) Efficacy assessment. Primary endpoint: 1) Total ESD procedure time (min): cumulative time from the start of submucosal injection to the end of submucosal

dissection. Timing will be recorded synchronously by intraoperative video and the operative record, and entered into the case report form (CRF) on the day of the procedure. Secondary endpoints: 2) Mucosal dissection time (min): time from the end of circumferential incision to complete lesion dissection, measured on intraoperative video and entered into the CRF after data compilation. 3) Dissection speed (mm^2/min): lesion area (mm^2) divided by dissection time (min). Lesion area measurement: the maximal long diameter (a, mm) and the maximal short diameter perpendicular to it (b, mm) will be measured intraoperatively or on the specimen. Area will be calculated using the ellipse formula: Area = $a \times b \times \pi/4$ (mm^2) and entered into the CRF. 4) Complete resection rate (R0): number of cases with negative pathological margins/total cases ×100%; entered into the database based on the pathology report. 5) En bloc resection rate: number of cases confirmed en bloc by intraoperative assessment and postoperative pathology review/total cases ×100%. 6) ESD-related complications (bleeding, perforation, muscular injury): ① Perforation rate: number of cases with endoscopically visible perforation intraoperatively or clinically plus radiologically confirmed perforation within 7 days postoperatively/total cases ×100%; determined jointly by the research nurse and attending physician; SAE report within 24 h if applicable. ② Bleeding rate: number of cases requiring endoscopic hemostasis intraoperatively or bloody stool within 24 h postoperatively with Hb decrease >2 g/dL/total cases ×100%; recorded in the operative record and 24 h AE/SAE log. ③ Muscular injury rate: number of cases with exposure or incision into the muscularis requiring clipping or suturing/total cases ×100%. 7) Robotic flexibility indices: number of attempts required for a first successful grasp and number of accidental drops. “Successful grasp” is defined as the grasper holding tissue with appropriate counter-traction and providing a good submucosal view.

(2) Safety assessment: Device-related malfunction, anesthesia-related events, and

other adverse events during and after the procedure will be recorded. Vital signs are considered stable when changes from baseline are <20%.

(3) Adverse event reporting and follow-up: Any adverse events will be recorded and managed according to protocol requirements. Serious adverse events must be reported within 24 hours.

VI. Study Intervention

1. Intervention

This study compares FASTER-assisted ESD (intervention group) with conventional ESD (control group) for colorectal lesions to evaluate safety and effectiveness. In the intervention group, the end effector of the FASTER robotic arm (EndoFaster; Robomed Medical Co., Ltd., Shenzhen, China) will provide continuous multidirectional traction of the lesion margin and allow real-time tension adjustment to optimize visualization for submucosal dissection. In the control group, submucosal dissection will be performed using conventional ESD. Other intraoperative steps will follow standardized procedures in both groups, including lesion marking, submucosal injection with normal saline plus indigo carmine, circumferential incision, and endoscopic hemostasis when necessary. All subjects will continue acid suppression with a PPI or P-CAB after surgery. A lukewarm liquid diet will start 6 hours postoperatively; if no discomfort within 24 hours, diet will gradually progress to semi-liquid and soft foods until discharge. During hospitalization, the following daily follow-up and assessments will be performed: 1) Vital signs (blood pressure, heart rate, temperature, respiration) and abdominal examination; 2) Laboratory monitoring (hemoglobin, white blood cell count, C-reactive protein); 3) Adverse event recording, including postoperative bleeding, perforation, muscular injury–related symptoms, and signs of infection. All assessments will be entered daily into progress notes and the CRF to

ensure data integrity and patient adherence.

2. Preparation/handling/storage/responsibilities

This study uses the FASTER robotic system and standard single-channel endoscopes. Storage, transport, and allocation must be strictly managed. Study medical devices should be stored at 5–30°C with relative humidity ≤93%. Temperature and humidity should be monitored and recorded during hospital storage to ensure appropriate conditions. Device transport will be coordinated by the study team using dedicated medical-device courier services, with transport temperature −40 to 55°C and humidity ≤93%. Upon arrival at the hospital, devices must be inspected/accepted and promptly stored.

Regarding device allocation, the intervention group will use FASTER-assisted endoscopy and the control group will use conventional standard endoscopy. Allocation will follow the randomized design with concealed assignment by an independent statistician to ensure scientific rigor and fairness. During the procedure, vital signs, whether the procedure proceeds smoothly, device compatibility, and any device-related adverse events must be recorded in detail and included in study analyses.

In addition, the study team must ensure safe device use and provide standardized training for all medical staff to ensure consistency of clinical procedures. Any device malfunction or abnormality identified during use must be recorded immediately and reported to the study team to ensure smooth study conduct.

3. Concomitant therapy

During the study, permitted concomitant treatments include appropriate nutritional support, proton pump inhibitors, local anesthetics or low-dose opioids for pain control, antiemetics (e.g., ondansetron), probiotics, and psychological interventions. All concomitant medications and treatments must be recorded.

4. Emergency management

If unexpected situations require rescue, medical staff may provide targeted medications and treatments, including norepinephrine, ephedrine, or dopamine to raise blood pressure; desmopressin, thrombin, or intravenous transfusion to control severe bleeding; endoscopic titanium clips to close small perforations or surgery to manage large perforations; naloxone, endotracheal intubation, and mechanical ventilation for respiratory depression or asphyxia; and aspirin, nitroglycerin, and necessary cardiac interventional therapy for myocardial infarction. During resuscitation, intravenous access should be established, vital signs monitored in real time with a multifunction monitor, cardiopulmonary resuscitation (CPR) performed when necessary, and the emergency team involved for ICU transfer when required. All rescue processes must be documented in detail, including timing, clinical changes, drug doses and patient responses, and all monitoring data, procedural interventions, and imaging results should be archived to ensure data integrity and traceability.

VII. Discontinuation of Intervention / Subject Withdrawal and Study Termination

1. Discontinuation of study intervention

The study may be temporarily suspended under the following circumstances: occurrence of serious safety issues such as gastrointestinal perforation, major bleeding, or severe infection with an adverse event rate exceeding a pre-specified threshold; discovery of major protocol defects that prevent adequate assessment of device safety and effectiveness; or requests from regulatory authorities to protect participants' rights or to modify the study design.

The duration of suspension will depend on the situation and may be a short pause (e.g., 1–2 weeks) for adjustments or permanent termination. During suspension, data from enrolled participants will continue to be collected (e.g., symptom improvement and adverse event rates) to assess the impact on data integrity.

To restart the study, key safety or scientific issues must be resolved (e.g., optimizing device use, adjusting procedural workflow, or improving follow-up plans), and resumption is allowed only after approval by the ethics committee and regulatory authorities.

During intervention suspension, follow-up will continue. Participants will undergo symptom assessment and safety monitoring as scheduled; follow-up methods include telephone, WeChat, or outpatient visits. If participants experience adverse reactions or have medical needs, the study team will provide medical guidance or recommend appropriate treatment to ensure safety.

2. Discontinuation/withdrawal of subjects

Criteria for study termination (the trial will be terminated if any of the following occurs):

1) A serious safety issue occurs during the trial;

2) A major error is found in the clinical trial protocol;

3) The trial applicant requests termination of the trial;

4) The ethics committee requests termination of the trial;

5) The device regulatory authority requests termination of the trial.

For any subject who withdraws from the study for any reason, the reason must be recorded, including but not limited to:

1) Withdrawal of informed consent;

2) Sponsor terminates the study;

3) Serious adverse events affecting continued participation;

4) Major protocol violation/deviation;

5) Pregnancy;

6) Poor compliance;

7) Loss to follow-up;

8) The investigator and/or sponsor considers that the subject's medical condition may endanger the subject's safety or that continuing the study may harm the subject's health.

3. Loss to follow-up

To minimize loss to follow-up and reduce missing data, the study team will explain the importance of follow-up in detail at the outset, provide a clear schedule, and send regular reminders via phone, WeChat, email, and other means. Subjects must provide at least two alternate contacts to maintain communication if contact is lost. Remote follow-up options such as video calls or telephone interviews will be offered, with flexible scheduling to reduce loss due to distance or time constraints. For occasionally missing data, supplementation may be attempted via medical record review, subject interviews, or family inquiries. Statistical analyses will use intention-to-treat (ITT) principles and imputation methods as appropriate to mitigate the impact of missing data.

VIII. Detailed Study Procedures

1. All subjects must sign the informed consent form before screening. Subjects who pass screening may enter the study.

2. Subjects in the intervention and control groups will be treated according to the protocol: the intervention group will receive FASTER-assisted ESD and the control group will receive conventional ESD.

3. During the procedure, vital signs, whether the procedure proceeds smoothly (clinical feasibility of FASTER), the operator's experience, and any device-related adverse events will be evaluated and recorded and included in analyses.

4. During hospitalization, efficacy and complications will be evaluated and recorded.

5.1 Screening period:

All subjects must complete screening examinations before enrollment and be screened according to the inclusion/exclusion criteria.

（1）Sign the informed consent form;

（2）Record demographic data: date of birth, sex, initials, height, and weight;

（3）Medical history and physical examination (including vital signs, perianal inspection, and digital rectal examination);

（4）Other laboratory tests, such as complete blood count, coagulation profile, and infection panel;

（5）Preoperative assessment: electrocardiogram; preoperative colonoscopy (biopsy/pathology within 6 months; record lesion location, size, morphology, and Paris classification);

5.2 Treatment period: According to randomization, in the intervention group, at the start of the procedure the mechanical arm of the FASTER robot will be attached to the endoscope tip. ESD will then be performed following standard steps: 1) lesion marking; 2) submucosal injection with normal saline and indigo carmine; 3) circumferential incision. After submucosal injection and circumferential incision are completed, the mechanical arm is deployed and the end effector grasps and lifts the mucosal margin to allow clear visualization of the dissection plane, followed by submucosal dissection. Finally, the resected tissue will be retrieved using FASTER through the endoscope channel or a suction device.

In the control group, a transparent distal cap will be attached to the endoscope tip at the start of the procedure. Conventional ESD will be performed following standard steps: 1) lesion marking; 2) submucosal injection with normal saline and indigo carmine; 3) circumferential incision; 4) submucosal dissection; 5) tissue retrieval using a suction device. Vital signs and any procedure-related serious adverse events will be recorded for statistical analysis.

5.3 Follow-up period: All patients will be followed up during hospitalization. The following daily follow-up and assessments will be conducted: 1) Vital signs (blood pressure, heart rate, temperature, respiration) and abdominal examination; 2) Laboratory monitoring (hemoglobin, white blood cell count, C-reactive protein); 3) Adverse event recording, including postoperative bleeding, perforation, muscular injury–related symptoms, and signs of infection. Patients who develop symptoms such as bleeding, fever, or chest pain during follow-up should promptly undergo blood tests and, as needed, chest CT or colonoscopy to clarify the cause of complications.

IX. Observation, Recording, and Management of Adverse Events

1. Definition of adverse events (AE)

An adverse event (AE) refers to any unfavorable and unintended sign (including abnormal laboratory findings), symptom, disease, or injury occurring after the subject has signed informed consent and received study-related procedures, whether or not it is considered related to the study device.

2. Definition of serious adverse events (SAE)

A serious adverse event (SAE) refers to an AE that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, causes congenital anomaly/birth defect, or is otherwise deemed medically important.

1) Death;

2) Life-threatening events;

3) Hospitalization or prolonged hospitalization;

4) Persistent or significant disability/incapacity;

5) Congenital anomaly/birth defect;

6) Other medically important events as judged by the investigator.

3. Recording, collection, reporting, and management of AEs

(1) Collection, reporting, and management of AEs

AEs occurring from the time the subject signs the informed consent form until before use of the study device, and those related to protocol-specified procedures, must be recorded on the AE form.

AE records should include: description of the AE and all related symptoms, time of onset, severity, duration, relationship to the study device, measures taken, and final outcome/prognosis. AEs must be recorded using medical terminology; if symptoms and signs can be attributed to a common etiology, the diagnosis should be recorded where possible. Except for disease progression indicators, all clinical events and clinically significant laboratory adverse reactions may be managed with reference to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Treatment-emergent adverse reactions will be recorded by the investigator.

(2) Collection and reporting of SAEs

All SAEs occurring from the time the subject signs the informed consent form through hospitalization after completion of the study device procedure, regardless of cause or relationship to the device, must be reported using the SAE report form. If an SAE occurs, the investigator must immediately take appropriate measures to ensure subject safety, and submit a written report to the medical device clinical trial management department of the trial institution, which will issue a written notice to the sponsor. The management department shall, within 24 hours, submit written reports to the corresponding ethics committee and to the provincial/autonomous region/municipality food and drug administration department and the health authority where the trial institution is located. For deaths, the institution and investigator shall provide all required information to the ethics committee and the sponsor. For SAEs and device defects that may lead to SAEs, the sponsor shall, within 5 working days of

becoming aware, notify other participating trial institutions and investigators, and the management department shall promptly notify the institution's ethics committee. The initial report should include, as far as possible: report source, device name, SAE name, time of occurrence, severity, duration, relationship to the device, measures taken, and outcome.

(3) Pregnancy

Female subjects of childbearing potential must use effective contraception during the study and should avoid pregnancy.

Pregnancy testing (e.g., urine/serum hCG) should be performed for women of childbearing potential at screening as appropriate.

If pregnancy occurs during the study, it must be reported promptly. Follow-up should continue to document pregnancy outcome, and the subject should be withdrawn from the study as appropriate.

(4) Criteria for AE severity assessment

The investigator will grade AE severity according to the five-grade criteria of NCI CTCAE v5.0:

Grade 1 (Mild): asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.

Grade 2 (Moderate): minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL.

Grade 3 (Severe): medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL.

Grade 4 (Life-threatening): urgent intervention indicated.

Grade 5 (Death): death related to AE.

(5) Other responsibilities of investigators during SAE follow-up

Investigators should arrange appropriate examinations and treatments based on the subject's condition, actively follow up the course and outcomes of the event, update SAE information in a timely manner, and complete follow-up reports until the event is resolved or stabilized.

X. Data Management

1. Data management

(1) Investigators must ensure that data are true, complete, and accurate.

(2) Any corrections to study records must be made by drawing a line through the original entry, writing the corrected data in the margin with the reason, and signing and dating by the investigator; erasures or overwriting are not permitted.

(3) Laboratory test items must be complete.

2. Data recording and document retention

Data on the CRF should be recorded using subject codes; subjects may be identified only by subject code or initials.

Data will be managed using Excel. The process includes data entry, source data verification, quality control query resolution, database lock, and data export. After confirming no outstanding queries, all parties will sign the database lock application form, and the data manager will lock the database. After database lock, the data manager will export the analysis database for statistical analysis. Locked data cannot be edited. Issues identified after lock may be corrected in the statistical analysis program after confirmation.

XI. Data Safety Monitoring

A Data Safety Monitoring mechanism will be implemented. The study team will regularly review safety data and adverse events and report to the ethics committee as required.

XII. Statistical Analysis

1. Sample size determination

Based on the effect size reported by Yang Xiaoxiao et al. in a crossover study comparing FASTER-assisted ESD with conventional ESD in an ex vivo porcine stomach model (total procedure time for beginners: 25.6 ± 7.8 min in the FASTER group vs 38.9 ± 13.4 min in the conventional group; $P < 0.001$), we set a two-sided significance level $\alpha = 0.05$ and power $1-\beta = 0.90$ ($\beta = 0.10$). PASS 15 software was used to estimate sample size based on a two-independent-sample t-test model, yielding 16 subjects per group. Allowing for a 20% loss-to-follow-up rate, the final sample size is 20 subjects per group, for a total of 40 subjects. This approach is consistent with commonly used methods in clinical trials; however, given differences between ex vivo models and real clinical settings in procedural difficulty and time variability, we plan an interim sample size re-estimation after 50% enrollment to adjust for the observed effect and variance and ensure adequate statistical power.

2. Definition and selection of analysis sets

Full Analysis Set (FAS): includes all randomized subjects who received the assigned intervention, analyzed according to the intention-to-treat (ITT) principle.

Safety Set (SS): includes all subjects who underwent the procedure and have at least one post-baseline safety assessment.

Per-Protocol Set (PPS): includes subjects who completed the study without major protocol deviations.

3. Statistical methods

Statistical analyses include: (1) Description of case distribution and baseline characteristics; (2) Comparison of feasibility and safety indicators; (3) Comparison of

efficacy indicators and postoperative outcomes/complications.

4. Statistical software and general requirements

- All statistical analyses will be performed using SPSS version 27.
- Continuous variables will be described using mean, standard deviation, median, maximum, and minimum.
- Categorical variables will be described using frequency and percentage.
- For the primary study endpoints (safety, effectiveness, postoperative outcomes, and complications), chi-square tests will be used for statistical comparisons as appropriate.

XIII. Ethical Principles and Requirements for Clinical Research

The clinical study will comply with the Declaration of Helsinki and relevant regulations in the People's Republic of China, including requirements on informed consent, privacy protection, free participation and compensation, risk control, protection of special populations, and compensation for research-related injury. The study will be implemented only after approval of this protocol by the Ethics Committee. Before enrollment, investigators must fully and comprehensively explain to the subject and/or their legal representative the purpose, procedures, and potential risks of the study, and obtain written informed consent. Subjects must be informed that participation is entirely voluntary, that they may refuse or withdraw at any stage without discrimination or retaliation, and that their medical care and rights will not be affected. The informed consent form will be retained as a study document for inspection. Participants' privacy and data confidentiality will be strictly protected.

XIV. Study timeline

November 2025–March 2026: Complete patient recruitment, randomization, and

treatment.

April 2026–July 2026: Complete follow-up and data statistical analysis.

August 2026–November 2026: Complete manuscript preparation.

XV. Key References

[1] BRAY F, LAVERSANNE M, SUNG H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. CA Cancer J Clin, 2024, 74(3): 229-63.

[2] PIMENTEL-NUNES P, LIBâNIO D, BASTIAANSEN B A J, et al. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022 [J]. Endoscopy, 2022, 54(6): 591-622.

[3] YAMAMOTO K, SHIMODA R, OGATA S, et al. Perforation and Postoperative Bleeding Associated with Endoscopic Submucosal Dissection in Colorectal Tumors: An Analysis of 398 Lesions Treated in Saga, Japan [J]. Intern Med, 2018, 57(15): 2115-22.

[4] NAGATA M. Device-assisted traction methods in colorectal endoscopic submucosal dissection and options for difficult cases [J]. World J Gastrointest Endosc, 2023, 15(4): 265-72.

[5] UYAMA I, KANAYA S, ISHIDA Y, et al. Novel integrated robotic approach for suprapancreatic D2 nodal dissection for treating gastric cancer: technique and initial experience [J]. World J Surg, 2012, 36(2): 331-7.

[6] YEUNG B P, CHIU P W. Application of robotics in gastrointestinal endoscopy: A review [J]. World J Gastroenterol, 2016, 22(5): 1811-25.

[7] PHEE S J, REDDY N, CHIU P W, et al. Robot-assisted endoscopic submucosal dissection is effective in treating patients with early-stage gastric neoplasia [J]. Clin Gastroenterol Hepatol, 2012, 10(10): 1117-21.

[8] YANG X X, FU S C, JI R, et al. A novel flexible auxiliary single-arm transluminal endoscopic robot facilitates endoscopic submucosal dissection of gastric lesions (with video) [J]. Surg Endosc, 2022, 36(7): 5510-7.

[9] JI R, YANG J L, YANG X X, et al. Simplified robot-assisted endoscopic submucosal dissection for esophageal and gastric lesions: a randomized controlled porcine study (with videos) [J]. Gastrointest Endosc, 2022, 96(1): 140-7.

[10] CUI C, LU X, ZUO X L, JI R. Endoscopic submucosal dissection of early gastric angle cancer by using a simplified robot-assisted device for traction [J]. Endoscopy, 2024, 56(S 01): E49-e50.

[11] TURIANI HOURNEAUX DE MOURA D, AIHARA H, JIRAPINYO P, et al.

Robot-assisted endoscopic submucosal dissection versus conventional ESD for colorectal lesions: outcomes of a randomized pilot study in endoscopists without prior ESD experience (with video) [J]. Gastrointest Endosc, 2019, 90(2): 290-8.

Participant Signature Page

Efficacy of Simplified Robot (FASTER)–Assisted Versus Conventional Endoscopic Submucosal Dissection (ESD) for Colorectal Lesions: A Prospective, Randomized, Controlled Trial

Informed Consent Statement:

I have been informed of the purpose, background, procedures, risks, and potential benefits of this study. I have had sufficient time and opportunity to ask questions, and I am satisfied with the answers provided.

I have also been informed whom to contact if I have questions, wish to report difficulties or concerns, have suggestions about the study, want further information, or wish to offer assistance to the study. I understand that I may choose not to participate in this study, or may withdraw from the study at any time during the study without giving any reason. In addition, the investigators have not used deception, inducement, coercion, or other means to force me to agree to participate in the study. I understand that if my condition worsens, or I experience a serious adverse reaction, or my study physician believes that continuing participation is not in my best interest, he/she may decide to withdraw me from the study. The sponsor or regulatory authorities may also terminate the study during the study period without obtaining my consent. If this occurs, the physician will notify me in a timely manner and the study physician will discuss my other options with me.

I have read this informed consent form and agree to participate in this study. I will receive a copy of this informed consent form bearing the signatures of both myself and the investigator.

Participant signature: Date:

Contact phone number:

Legal representative signature: Relationship: Date:

Contact phone number:

(Note: If the participant lacks or has limited capacity to act, such as inclusion of vulnerable groups with mental disorders or impaired consciousness, the legal representative must sign in the space below.)

Independent witness signature: Date:

Contact phone number:

(Note: An independent witness signature is required only when the participant may have decision-making capacity but is unable to read the text (e.g., illiterate, visually impaired). When a witness is present, the investigator should, if possible, retain video documentation as evidence of informed consent.)

I have accurately explained this document to the participant, he/she has read this informed consent form accurately, and I confirm that the participant had the opportunity to ask questions and voluntarily agreed.

Investigator signature: Date：

Contact phone number：