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A Prospective, Multi-Center Evaluation of the ECHELON CIRCULAR Powered Stapler in Left-Sided Colorectal Anastomoses

Protocol Number: ESC-16-002

Document	Effective Date
Original	05 May 2017
Amendment #1	19 July 2017
Amendment #2	10 January 2018
Amendment #3	29 October 2018

Sponsor: Ethicon Endo-Surgery, Inc.
4545 Creek Road
Cincinnati, OH 45242

Name of Finished Product: ECHELON CIRCULAR™ Powered Stapler

[redacted]

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Approvals:

[redacted]

This study will be performed in compliance with:

Good Clinical Practice (and in accordance with the Declaration of Helsinki), as well as all applicable local regulations.

INVESTIGATOR SIGNATURE

I have read, understood, and agree to:

- Ensure that the requirements for obtaining informed consent are met;
- Conduct the study in accordance with this protocol, including applicable local/state laws and regulations;
- Maintain the confidentiality of all information received or developed in connection with this protocol;
- Report all serious adverse events, as defined in the protocol, as soon as possible, but no later than 24 hours after becoming aware of the event;
- Adhere to the publication policy, as stated in the Clinical Study Agreement, for data collected during this study; and
- Ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed of their obligations in meeting the above commitments.

I will ensure that the Institutional Review Board (IRB)/Ethics Committee (EC) review complies with governmental requirements and will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB/EC all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without sponsor and IRB/EC approval of an amended protocol, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligation of Clinical Investigators and all other pertinent requirements of the Sponsor and government agencies.

_____ _____

Investigator Signature Date

_____

Printed Name of Investigator

PLEASE RETAIN A COPY FOR YOUR STUDY RECORDS

CLINICAL PROTOCOL SYNOPSIS

Objective(s):	**Primary:** To prospectively evaluate the intra-operative performance of the powered circular stapler used in left colectomy procedures in a post-market setting. **Secondary:** To assess surgeon workload, surgeon satisfaction, and proactive surveillance of safety of the powered circular stapler used in left colectomy procedures in a post-market setting.
Study Design:	Patients scheduled to undergo a left-sided colon resection, and who meet study entry criteria, may be enrolled. Investigators will perform each procedure using the ECHELON CIRCULAR™ powered stapler according to its instructions for use (IFU). ECHELON CIRCULAR™ powered staplers will be provided to all participating sites. There will be no blinding or planned interim analysis in this study. Procedures may be performed open or via minimally invasive surgery (MIS) according to institutional standard-of-care (SOC). Use of a hand port and robotic assistance are permissible providing the powered circular stapler is used to create the anastomosis. Conversion from laparoscopic to open surgery is permissible under the protocol at the surgeon's discretion for the patient's safety. Follow-up care will be documented at the first SOC post-operative visit to confirm healing of the anastomosis. The final scheduled study visit will occur 28 days post-procedure (routinely scheduled follow-up with surgeon). Follow-up by phone is permissible when an on-site visit is not planned or is more than six weeks post-operative.
Number of Subjects:	A total of 165 eligible subjects are planned to be enrolled in up to 12 sites to ensure at least 150 subjects complete the study. No formal hypothesis is being tested in this study, thus the sample size was not statistically sized through a power calculation, but rather is considered sufficient for a descriptive summary of stapler performance issues through confidence interval estimation and evaluation of safety. The sample size of 165 subjects is consistent with the amount of information that was planned to be collected on the powered stapler in the original study design and provides acceptable precision for estimation of the rate of stapler performance issues.
Diagnosis/Criteria for Inclusion:	1. Scheduled for colectomy with left-sided anastomosis performed with a circular stapler; 2. Willing to give consent and comply with all study-related evaluations; and 3. At least 18 years of age.

Diagnosis/Criteria for Exclusion:	Preoperative 1. Enrollment in a concurrent interventional clinical study that could impact the study endpoints; 2. Pregnancy; 3. Physical or psychological condition which would impair study participation; 4. Emergency surgery; 5. ASA Class ≥ IV; 6. The subject is judged unsuitable for study participation by the Investigator; or 7. Unable or unwilling to provide follow-up information post-procedure. Intraoperative 1. Undergoing multiple intraoperative synchronous colon resections; 2. Anastomosis not distal from splenic flexure of the colon; 3. Anastomosis of the colon not attempted; or 4. Subjects with any intraoperative findings identified by the surgeon that would preclude attempting an anastomosis with a circular stapler.
Test Product:	ECHELON CIRCULAR™ Powered Circular Stapler:
Reference Product:	No comparator product is being used in this study.

Product Code	Description	Diameter
CDH29P	ECHELON CIRCULAR™ Powered Stapler	29mm
CDH31P	ECHELON CIRCULAR™ Powered Stapler	31mm

Analysis of Effectiveness and Safety:	**Analysis of Effectiveness** The primary endpoint is the number of subjects in whom a stapler performance issue is observed, where a stapler performance issue is defined as a failure of the powered circular stapler (study device) to perform per its IFU. This includes but is not limited to difficulty placing or removing the stapler, stapler misfire/failure of the device to fully fire, staple line defects, incomplete or thin donuts, tissue damage, positive intraoperative leak test, detached components, unformed staples, or any other device failure. No formal hypothesis is being tested in this study. The primary endpoint of stapler performance issues will be summarized by counts and percentages and a 95% confidence interval will be calculated. Summary statistics as appropriate for continuous or categorical variables will be provided for assessments of surgical stress as measured by SURG-TLX and a surgeon satisfaction questionnaire. **Analysis of Safety** For this study, an adverse event is defined as any undesirable clinical occurrence in a subject that may be attributable to the study procedure or device used to create the colorectal anastomosis. Only AEs attributable to the device used to create the anastomosis or to the study procedure are to be recorded in the eCRF and reported to the Sponsor. All adverse events reported during the study will be coded to the Medical Dictionary for Regulatory Activities (MedDRA). Adverse events will be summarized with counts and percentages by MedDRA system organ class and preferred term. Device-related AEs and procedure-related AEs will also be summarized by MedDRA system organ class and preferred term. These summaries will also be presented for all serious adverse events reported during the study. AEs will also be summarized by maximum severity by MedDRA system organ class and preferred term.
Interim Analysis:	No interim analysis is planned.

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PROTOCOL-SPECIFIC ACRONYMS AND ABBREVIATIONS

Acronyms/Abbreviation	Terms
ACS NSQIP	American College of Surgeons National Surgical Quality Improvement Program
AE	Adverse Event
ASA	American Society of Anesthesiologists Physical Status Classification System
CFR	Code of Federal Regulations
CRA	Clinical Research Associate
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EES	Ethicon Endo-Surgery
GCP	Good Clinical Practices
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICD	Informed Consent Document
IFU	Instructions for Use
IRB	Institutional Review Board
LOS	Length of Stay
MIS	Minimally-Invasive Surgery
MM	Medical Monitor
OR	Operating Room
PI	Principal Investigator
RCRI	Revised cardiac index
SOC	Standard of Care
SURG-TLX	Surgery Task Load Index

ETHICS

Institutional Review Board/Ethics Committee
Participating investigators will ensure that this protocol, Informed Consent Document (ICD), ICD or protocol amendments, and if applicable, any other written information provided to the subjects that assist in the decision to participate are reviewed by an Institutional Review Board (IRB) or Ethics Committee (EC) that complies with governmental requirements. The approving IRB/EC will be responsible for the initial and continuing review and approval of this clinical investigation. Participating investigators will be required to promptly report to the IRB/EC as required by the IRB/EC's policies. Additionally, investigators will be required to refrain from making any changes in the clinical investigation plan without Sponsor and IRB/EC approval of an amended protocol, except where necessary to eliminate apparent immediate hazards to study subjects or others.

Applicable Regulations
This study will be conducted in compliance with Good Clinical Practice and in accordance with the Declaration of Helsinki, as well as any other applicable local and country regulatory requirements.

Subject Information and Consent
Regulations concerning the protection of subjects require that informed consent be obtained before a subject may participate in any clinical investigation.

An IRB/EC approved informed consent must be sought from each subject and must be appropriately documented in the subject's medical record prior to initiating the study. It is the Investigator's responsibility to obtain written informed consent from the subject, the Investigator may delegate this responsibility if appropriately documented.

The informed consent process involves the following: giving a subject adequate information concerning the study, providing adequate time for the subject to consider all available options, responding to the subject's questions, ensuring that the subject has comprehended this information and finally, obtaining the subject's written consent to participate in this study. All subjects in this study should be completely informed about the purpose, risks, benefits, and other pertinent details of this study. The informed consent process is careful to avoid the perception of any coercion or undue influence on, or inducement of, the subject to participate, and does not waive or appear to waive the subject's legal rights. The ICD is presented in native, non-technical language that is understandable to the subject.

Prior to a subject's participation in this study, an ICD will be signed and dated by the subject and person who conducted the consent discussion. The subject will be provided a copy of the signed ICD. The ICD and any other written materials provided to the subject to assist in the decision to participate must be revised whenever new information becomes available that may be relevant to their willingness to participate or continue participation in this study. Revision to the ICD and other written materials will receive IRB/EC approval before implementation. Each subject will be required to sign any amended ICD (as required by the IRB/EC) and will receive a copy of the signed ICD.

ADMINISTRATIVE REQUIREMENTS

This study is sponsored by Ethicon Endo-Surgery, Inc. (EES, Cincinnati, OH, USA) and will be conducted in up to 12 surgery centers in the United States and/or European Union under a single protocol approved by each participating site's IRB/EC prior to implementation. The principal investigator at each study site is a surgeon qualified by education, experience, and training to perform the study procedure and to assume responsibility for the conduct of this study.

The Data Management and Biostatistics groups of Ethicon Endo-Surgery, Inc. will be responsible for the analysis of data from this protocol. An Electronic Data Capture (EDC) system will be utilized by study site personnel to transfer study data from source records (the first point of clinical data capture) onto common electronic case report forms (eCRFs). This system is a web-based, secure electronic software application [redacted]r that is compliant with national and international Good Clinical Practice (GCP) data protection/data privacy and electronic record/electronic signature (e.g. 21 CFR Part 11) regulatory requirements.

Protocol Modifications

All protocol amendments must be issued by the Sponsor, signed and dated by the Investigator, and should not be implemented without prior IRB/EC approval, except where necessary to eliminate immediate hazards to the subjects or when the change(s) involves only logistical or administrative aspects of the study (e.g., change in monitor(s), change of telephone number(s)). The Investigator reports the protocol amendments to the IRB/EC as per their local requirements.

1.0 INTRODUCTION

Surgical staplers have been utilized in colorectal procedures since the early 20th century, with intraluminal staplers used to create the anastomosis since 1979.[1] Successful utilization of these devices, whether in open or laparoscopic procedures, requires extensive training and experience. Even with experience, device issues such as stapler misfire, incomplete firing, low surgeon satisfaction, etc., may occur. In a retrospective study of 349 colorectal resections, 67 (19%) procedures had some type of technical error.[2] The most frequently reported issues from the analysis were positive leak tests, difficulty placing or removing the stapler, and inadequate donuts. Surgeons may also experience psychological or physical stress during procedures due to complications, workload, or other factors.[3,4] Similarly, surgeon satisfaction with anastomotic procedures may be low for a variety of reasons, including need for multiple maneuvers, incomplete anastomosis, or excessive work effort.[5]

A powered circular stapler has been developed with improved stability, more evenly-distributed compression, and a significantly reduced force-to-fire.[6] It is expected that these design modifications will result in fewer technical issues associated with the device. This prospective clinical study will collect any performance issues in a post-market setting for the powered circular stapler in patients scheduled to undergo colectomy with left-sided colon anastomosis.

2.0 OBJECTIVE

Primary: To prospectively evaluate the intra-operative performance of the powered circular stapler used in left colectomy procedures in a post-market setting.

Secondary: To assess surgeon workload, surgeon satisfaction, and proactive surveillance of safety of the powered circular stapler used in left colectomy procedures in a post-market setting.

2.1 PRIMARY ENDPOINT

The primary endpoint is the number of subjects in whom a stapler performance issue is observed, where a stapler performance issue is defined as a failure of the powered circular stapler (study device) to perform per its IFU. This includes but is not limited to difficulty placing or removing the stapler, stapler misfire/failure of the device to fully fire, staple line defects, incomplete or thin donuts, tissue damage, positive intraoperative leak test, detached components, unformed staples, or any other device failure.

2.2 SECONDARY ENDPOINTS

- Assessment of surgical stress (surgeon) associated with the procedure using the Surgery Task Load index (SURG-TLX)[7];
- Surgeon satisfaction questionnaire; and
- Surgeon grip strength using dynamometry (includes surgeon-reported age, height, and weight)

2.3 ADDITIONAL MEASUREMENTS / DATA COLLECTED

- Subject demographics and baseline characteristics;
- Subject height and weight;
- Relevant medical and surgical history (including diagnosis);

- If available, ICD-9 or ICD-10 codes, and subject insurance data;
- Documentation of pre-operative bowel prep and prophylactic use of antibiotics;
- Procedure approach (open, MIS);
- Procedure details (detailed in Section 3.17);
- Device usability/articulation questions (including robotic assistance);
- Occurrence of blood transfusion and rationale within the perioperative period;
- Outcome of intraoperative leak testing;
- Occurrence of device or procedure-related intraoperative and postoperative adverse events (including post-operative anastomotic leak);
- Length of hospital stay (LOS) from admission through discharge; and
- Details of discharge (skilled nursing facility, home, other - with rationale).

3.0 INVESTIGATIONAL PLAN

3.1 OVERALL STUDY DESIGN AND PLAN - DESCRIPTION

Patients scheduled to undergo a left-sided colon resection, and who meet study entry criteria, may be enrolled. In an effort to minimize selection bias, patients will be consecutively screened for enrollment. All subjects who meet entry criteria will be encouraged to enroll in the study. A subject will be considered enrolled once their anastomosis has been attempted with the powered circular stapler.

Procedures may be performed open or MIS according to institutional standard-of-care (SOC). Use of a hand port and robotic assistance are permissible providing the powered circular stapler is used to create the anastomosis. Conversion from MIS to open surgery is permissible under the protocol at the surgeon's discretion for the patient's safety. Follow-up care will be documented post-operatively to confirm healing of the anastomosis.

The final scheduled study visit will occur 28 days post-procedure (routinely scheduled follow-up with surgeon). Follow-up by phone for subjects is permissible when an on-site visit is not planned or more than six weeks post-operative.

3.2 ENROLLMENT

A subject will be considered enrolled once their anastomosis has been attempted with the powered circular stapler (defined as mobilization of colon). Investigators will be asked to include subjects scheduled for both open and MIS procedures. A total of 165 eligible subjects are planned to be enrolled in up to 12 sites (United States and Europe) to ensure at least 150 subjects complete the study. The planned maximum number of subjects enrolled at any site should not exceed 20% of the total number of subjects enrolled in the study. Enrollment above this threshold will require Sponsor approval.

3.3 INCLUSION CRITERIA

Subjects satisfying the following criteria will be eligible for participation in this study:

1. Scheduled for colectomy with left-sided anastomosis performed with a circular stapler;
2. Willing to give consent and comply with all study-related evaluations; and
3. At least 18 years of age.

3.4 EXCLUSION CRITERIA

Preoperative

1. Enrollment in a concurrent interventional clinical study that could impact the study endpoints;
2. Pregnancy;
3. Physical or psychological condition which would impair study participation;
4. Emergency surgery;
5. ASA Class ≥ IV;
6. The subject is judged unsuitable for study participation by the Investigator; or
7. Unable or unwilling to provide follow-up information post-procedure.

Intraoperative

1. Undergoing multiple intraoperative synchronous colon resections;
2. Anastomosis not distal from splenic flexure of the colon;
3. Anastomosis of the colon not attempted;
4. Subjects with any intraoperative findings identified by the surgeon that would preclude attempting an anastomosis with a circular stapler.

3.5 PRIOR AND CONCOMITANT THERAPY

Subjects may continue with their current medical care while in the study, including medications.

3.6 SCREENING FAILURES

All patients signing consent who do not have an anastomosis attempted with the powered circular stapler will be recorded as screen failures. The relevant electronic Case Report Form (eCRF) pages (demographics, reason for screen failure) will be completed for all screen failure subjects and the data will therefore be included in the study database.

3.7 REMOVAL OF SUBJECTS FROM STUDY

In accordance with the current revision of the Declaration of Helsinki and the Code of Federal Regulations, a subject has the right to withdraw from the study at any time for any reason without prejudice to his/her future medical care by the physician or the institution. Should a subject (or subject's legally authorized guardian/representative) decide to withdraw; all efforts will be made to collect any adverse events they have experienced, if applicable. Subjects who withdraw or are terminated early from the study may be replaced. Participation may be terminated prior to completing the study for any of the reasons listed below (reasons that do not fit the categories below will be documented as "other").

Withdrawal of Consent:
If a subject chooses to withdraw early from the study, the eCRF completion page should be completed. When a subject's participation is terminated prior to completing the study, the reason for withdrawal is to be documented on the eCRF and in the source documentation.

Surgical:
The Investigator must withdraw a subject intraoperatively for the following reasons:

- Anastomosis not distal from splenic flexure of the colon; or
- Anastomosis of the colon not attempted.

Death:

When possible, the cause of death will be documented.

Lost to follow-up:

A certified letter will be sent to the subject at their last known address, after a minimum of three attempts to reach the patient has failed. If communication via certified letter is unsuccessful, the patient will be considered lost to follow up.

Site Termination or Study Termination:
A site or study may be terminated. When this occurs all subjects at the site will be withdrawn and documented as early termination. Reasons for site or study termination may include, but are not limited to the following:

- Administrative concerns (e.g., inadequate patient enrollment,
- Investigator/institution non-compliance, change of business strategy, etc.);
- Safety Issues, including those due to non-compliance, which substantially affect the risk to benefit ratio of the study subjects at a site or for the study as a whole; or
- Regulatory Body Mandate(s).

The Investigator has the right to terminate their participation at any time. Should this be necessary, procedures for termination will be provided by the Sponsor.

3.8 STUDY PROCEDURES

3.9 PROCEDURE DESCRIPTION(S)

Colectomy with left-sided circular stapler anastomosis will be performed in keeping with the surgeon's standard practice.

Procedure Overview

The patient is prepped and draped in the lithotomy position. Abdominal cavity access is obtained via laparotomy or laparoscopy and the peritoneal cavity is explored. The section of interest in the colorectum is identified and exposed. A thorough exploration of the abdominal cavity is performed. The colon and liver surface are examined for any lesions. Adequate exposure of the left colon and mesenteric vessels is obtained, and anatomical landmarks identified.

The inferior mesenteric artery (IMA) is identified, isolated and divided. The left ureter is identified and preserved. The presacral space is entered and the rectum mobilized as appropriate. The mesentery is divided and distal transection of the colorectum is performed with linear stapler(s). The left colon is mobilized along the white line of Toldt and the mesentery is divided as needed for adequate resection and tension-free anastomosis. The inferior mesenteric vein (IMV) is ligated and divided.

If splenic flexure mobilization is needed, the patient is placed in a reverse Trendelenburg position. The omentum is freed from the transverse and descending colon. The colon is mobilized up and around the splenic flexure the lesser sac is entered. The colonic mesentery is dissected off the retroperitoneum and extended laterally toward the splenic flexure, with care taken not to injure to the splenic vessels. The IMV is taken below the ligament of Treitz.

After colon mobilization and distal division, a site is selected for proximal transection. A purse-string suture is placed in the proximal portion of the colon, an anvil is placed and secured by tying the purse-string suture. The stapler is passed transanally and the stapler trocar is brought out through the distal colorectal stump. The stapler and anvil are coupled and the device is closed and fired. The device is withdrawn and the tissue donuts from the anastomosis are inspected. A leak test with air insufflation in to the rectum is completed. Once anastomotic integrity is confirmed, hemostasis is secured. The patient's abdomen is closed and wounds are dressed.

3.10 GUIDELINES FOR DOCUMENTING STAPLER PERFORMANCE ISSUES

As described in Section 2.1, the primary endpoint for this study is the number of subjects in whom a stapler performance issue is observed for the powered circular staplers used to create the anastomosis in left-sided colectomy procedures. Under this protocol, stapler performance issues are defined as failure of the powered circular stapler (study device) to perform per its IFU. This includes but is not limited to difficulty placing or removing the stapler, stapler misfire/failure of the device to fully fire, staple line defects, incomplete or thin donuts, tissue damage, positive intraoperative leak test, detached components, unformed staples, or any other device failure.

The following data will be captured for each occurrence of a stapler issue:

- Procedure step (preparation of device for use, device deployment, intraoperative inspection of staple line, post-operative adverse event);
- Stapler Issue;
- Action taken; and
- Whether action resolved issue (Y/N).

3.11 IDENTITY OF STUDY PRODUCTS

No investigational devices will be tested in this study. The ECHELON CIRCULAR™ Powered Staplers will be used in accordance with product labeling and IFU will be included in the study.

3.12 TEST PRODUCT: ECHELON CIRCULAR™ POWERED CIRCULAR STAPLER

Product Code	Description	Diameter
CDH29P	ECHELON CIRCULAR™ Powered Stapler	29mm
CDH31P	ECHELON CIRCULAR™ Powered Stapler	31mm

ECHELON CIRCULAR™ Powered Staplers are sterile, single-patient use surgical instruments used throughout the alimentary tract for end-to-end, end-to-side and side-to-side anastomoses. The device utilizes a curved shaft, an ergonomic handle with an integrated motor and battery power to cut and staple simultaneously to create an anastomosis. The instruments are packaged with a battery pack installed prior to use.

ECHELON CIRCULAR™ Powered Staplers will be provided to all participating study sites. Surgeons will go through standard in-servicing prior to using the powered device. Powered staplers will be tracked using shipping receipt and device accountability logs. All product returns will be managed by contacting the Sponsor.

The Investigator, upon receipt of the clinical supplies will:

- Conduct an inventory;
- Upon confirmation that all materials arrived intact, complete and sign and date the Packing List for Clinical Supplies packing list included with the shipment. The Sponsor should be contacted immediately if any materials are damaged or missing from the shipment;
- After signature and date, promptly return the packing list to the Sponsor; and
- Retain a copy of the signed and dated Packing List for the Investigator's records.

Powered staplers provided for the study must be kept in a secure area and used only for treating subjects enrolled in the study. The study device inventory must be available for periodic inspection/verification.

3.13 REFERENCE PRODUCT

No comparator product is being used in this study.

3.14 SCHEDULE OF EVENTS

Table 1

Study Activity	Visit 1	Visit 2	Visit 3
	Screening	Procedure through Discharge	Post Procedure (28 days ± 14 days)[f]
Informed consent	X		
Demographic information[a]	X		
Medical/surgical history[b]	X	X	
Inclusion/Exclusion Criteria	X	X	
If available, ICD-9 or ICD-10 codes, and insurance information		X	X
Surgeon questionnaires and measures[c]		X	
Pre-operative details, including time of hospital admission		X	
Procedure details[d]		X	
Evaluation of anastomotic donuts, with intra-operative photo documentation		X	
Device use details[d]		X	
Concomitant Procedures		X	
Need for blood transfusion		X	
Adverse Events (related to device or procedure)		X	X
Concomitant medications associated with captured adverse events		X	X
Evaluation for anastomotic leak[e]		X	X
Date and time of hospital discharge		X	
Unscheduled Visits (if applicable)			X
Subject Readmission (if applicable)			X
Subject exited from study			X

a. See Section 3.16 for details of Demographic data collection;
b. See Section 3.16 for details of Medical/Surgical History data collection;
c. SURG-TLX, surgeon satisfaction questionnaire, surgeon grip strength;
d. See Section 3.17 for details of device and procedure-related data collection;
e. If post-operative anastomotic leak indicated, followed to resolution, stable state, or end of study (whichever occurs first); and
f. May be conducted by phone if subject cannot complete office visit.

3.15 VISITS

3.16 VISIT 1 – SCREENING

Subjects presenting will be evaluated according to the local investigator's preferred practice. Subjects will be selected for a surgical procedure based on the preoperative investigations and the local investigator's interpretation of the clinical picture.

Eligible subjects will be provided with the study information, including the ICD.

The following screening activities will occur prior to the study procedure:

- Review and execution of the ICD
- Review/collection of inclusion/exclusion criteria and determination as to whether the subject is eligible for participation
- Collection of demographic information
  - Year of birth, gender, ethnicity, height and weight
- Review and collection of relevant medical/surgical history
  - Medical condition requiring study procedure
  - Any emergency room visits in previous six months
  - ASA score
  - Co-morbid conditions such, diabetes, smoking, condition requiring steroid use, etc.
  - Prior radiation therapy/chemotherapy (presence or absence),
  - Presence/absence of metastasis
  - Tumor details, including staging information

3.17 VISIT 2 – SURGICAL PROCEDURE THROUGH DISCHARGE

Pre-procedure

The following is obtained prior to the surgical procedure:

- Surgeon grip strength (includes surgeon-reported height, weight, and age)
- Update to medical /surgical history
- Confirm inclusion and exclusion criteria
- Date and time of hospital admission
  - Pre-operative antibiotics (IV)
- Documentation of pre-operative bowel prep

Intraoperative

Data collected during procedure:

- Surgeon glove size
- Surgical approach (open, MIS, robotic assistance)
- Conversion to open, if applicable (with rationale)
- Duration of procedure (first incision to skin closure, includes creation of anastomosis)
- Occurrence of mobilization of splenic flexure

- Devices and cartridges used
- Details of anastomosis (type, approximate distance from anal verge, use of adjunct)
- Visual assessment of the anastomotic donuts with intra-operative photo documentation (see Section 3.19)
- Endoscopic assessment of anastomotic staple line
- Technical issue(s) with circular stapler
- Intraoperative complications associated with procedure or device
- Presence / absence of diverting stoma and rationale
- Anastomotic leak assessment according to site SOC (including actions taken if leak present)
- Concomitant procedures (defined as any medical or surgical procedure beyond activities associated with primary study procedure)
- Occurrence of blood transfusion
- Concomitant medication usage associated with AEs
- If available, ICD-9 or ICD-10 codes, and insurance information
- Surgeon assessments (questionnaires)

Postoperative

Post procedure assessments will be completed from operating room (OR) discharge through hospital discharge:

- Date and time of hospital discharge, including post-discharge accommodation (skilled nursing facility, home, other)
- Additional procedures (any medical procedure)
- Adverse Events
  - Includes surgical site infections requiring intervention
  - If anastomotic leak, includes clinical aspect, treatment, and outcome
- Concomitant medication usage associated with AEs

Clinical Anastomotic Leak Information

The Investigator and study staff will follow all subjects for potential signs and symptoms associated with an anastomotic leak. Clinical suspicion of anastomotic leak will be confirmed visually (intra-operative) or by diagnostic imaging according to the clinician's best judgment for patient care.

Anastomotic Leak Documentation

In this protocol, anastomotic leak is defined as a defect at the circular stapler anastomotic site (including suture and staple lines of neorectal reservoirs and crossing linear staple lines) leading to a communication between the intra- and extraluminal compartments.[8] This may be a clinical or radiological diagnosis, or both. The following information will be documented for an AE of clinical anastomotic leak:

- Date of onset
- Method of diagnosis
- Severity of anastomotic leakage (Grade A - C)
- Specific intervention/remediation
- Visual or diagnostic confirmation information:
  - Date of confirmation
  - Method or modality of confirmation
- Relationship to procedure and devices used in procedure
- Whether the AE was serious or not
- Action taken
- Whether the subject remained in the hospital longer or was rehospitalized
- Outcome/ resolution date (followed to resolution, stable state, or end of study (whichever occurs first))

3.18 VISIT 3 - POST-PROCEDURE VISIT

A follow-up visit will occur 28 days (± 14 days) post-procedure and the following will be conducted/obtained:

- Documentation of any unscheduled visit or hospital readmission (if applicable)
- Additional procedures associated with the primary procedure (e.g., reoperation due to anastomotic leak)
- Adverse events (related to the procedure / device)
- Concomitant medication usage associated with adverse events
- Subject exited from study

If a subject does not have a follow-up office visit with the investigator/surgeon or is more than six weeks post-operative. a phone call from the site to the patient or treating physician for confirmation of presence / absence of adverse events is acceptable.

3.19 INTRA-OPERATIVE PHOTO DOCUMENTATION AND SPONSOR ASSESSMENT

If possible, intra-operative photo documentation of the anastomotic donuts should be taken as local institutional policy allows. The photo will be a close-up (approximately 10 inches above the tissue) taken after the inspection of the donuts. The photo should be of both proximal (may still be on anvil) and distal donuts, an overhead view, on a flat surface, and labeled appropriately with the Subject ID and date of collection only. The photo will be uploaded to the eCRF as either jpeg or pdf file. This photo will be considered source documentation as well as the CRF. Each photo taken will be reviewed and assessed by the Sponsor (physician at the Sponsor who is not associated with the study) to evaluate the quality of the donuts created and/or to determine if either donut appeared thin or incomplete.

4.0 DATA MANAGEMENT AND INTEGRITY

4.1 DATA COMPLETION AND RECORD KEEPING

Source Documents

Source documents are documents on which information regarding subjects is first recorded, including printed, optical, or electronic documents. Investigator subject files or hospital records generally are the basis of source document information. This includes but is not limited to, original subject files; hospital/clinic records; original recordings /tracing; digital images from automated instruments (e.g., cameras); radiographs; device accountability records; photographic negatives; and records kept at the investigation site, at the laboratories and at other departments involved in the clinical investigation.

Source documents must be retained by the Investigator as part of the subject's permanent medical record. The information in the source documents is used to complete the eCRFs. All information captured on the eCRFs should be completely and accurately supported in source documentation. Any additional information relevant to the study should be included in the source documents. In particular, any deviations from the protocol or procedures should be recorded in the source documents. The Investigator will retain originals of all source documents, subject consent forms, and study data.

Electronic Data Capture

An electronic data capture (EDC) system will be utilized by site personnel to transfer data from source records (medical records and/or source document worksheets) onto common eCRFs. This system is a web-based, secure electronic software application [redacted] s compliant with national and international GCP data protection/data privacy and electronic record/electronic signature (e.g., 21 CFR Part 11) regulatory requirements. The EDC system will be used to facilitate the collection of all data at the site. Designated site personnel will be responsible for entering patient data into the EDC system. All external and Sponsor internal users will be trained on the EDC application at a level dependent on their planned function. An EDC digital User Manual will be available under the help menu [redacted] in the collection and entry of source data into the electronic casebook.

[redacted] staffed by the outsourced vendor will also be available to respond to site and monitor questions.

Data Collection

Each EDC eCRF will be completed by the PI or PI's designee. Every effort should be made to respond to all monitoring and/or data management questions on each eCRF as completion of the data is required by the protocol. A unique ID number will identify each subject. The subject's unique ID number will be visible on each eCRF. At no time should the subject name appear on the eCRFs.

All data should be recorded accurately and completely. The Investigator is responsible for reviewing and approving each completed eCRF. Assurance of overall review and approval will be documented by the Investigator electronically signing each subject's electronic

casebook.

Data Correction

Required data corrections to eCRFs will be prompted via automated electronic edit checks and/or queries manually created by Sponsor reviewers. The change(s), individual making the change(s), and time the change(s) were made to the eCRFs will be automatically captured in the audit trail [redacted].

Data Privacy

The collection, use, and disclosure of all personal data, including subject health and medical information, are to be maintained in compliance with applicable personal data protection and security laws and regulations that govern protected health information and the informed consent given by each subject. When collecting and processing such personal data, appropriate measures are to be taken to maintain the confidentiality of patient health and medical information and to prevent access by unauthorized persons.

Record Retention, Inspection, and Custody

The PI must maintain all documentation related to the study until notified by the Sponsor. The PI will allow representatives of the Sponsor, the FDA, or other government regulatory agencies to inspect all study records, eCRFs, and corresponding portions of the subject's office and/or hospital medical records at regular intervals during the study. These inspections are to verify adherence to the protocol, integrity of the data being captured on the eCRFs, and compliance with applicable regulations.

Study reports will not identify subjects by name. These reports may be submitted to the FDA and/or regulatory authorities.

If custody of the clinical study records is transferred, notice of such a transfer should be given to the Sponsor no later than 10 working days after the transfer occurs.

4.2 MEDICAL DICTIONARY CODING

Medical dictionary coding of medical history and verbatim AEs captured on eCRFs will be performed using a coding thesaurus algorithm. The Medical Dictionary for Regulatory Activities and World Health Organization Drug Dictionary will be used after data entry and query resolution, via auto-encoding and interactive coding processes.

4.3 DATA QUALITY ASSURANCE

Steps to be taken to assure the accuracy and reliability of data include the selection of qualified investigators and appropriate sites, review of protocol procedures with the Investigator and associated personnel prior to the study, and periodic monitoring visits by the Sponsor. The Sponsor will review eCRFs for accuracy and completeness during on-site monitoring visits; any discrepancies will be resolved with the Investigator or designees, as appropriate.

Investigator Training

Prior to screening subjects for this study, the PI, sub-Investigators, study coordinators, and other designated staff (as applicable) will be provided information on study execution, data collection, and procedures specific to this clinical protocol.

Monitoring

This study will be monitored by the Sponsor to ensure:

- The rights and well-being of the subjects are protected;
- Reported data is accurate, complete, and verifiable from source documents where utilized; and
- The conduct of the study is in compliance with the currently approved protocol/amendment(s), applicable GCPs, and with applicable local/regional regulatory requirements.

The extent and nature of monitoring will be predetermined and agreed to by the Sponsor and investigators. Monitors will comply with established written standard operating procedures as well as procedures (i.e., monitoring plan) specified by the Sponsor for monitoring this study as characterized in the monitoring plan.

4.4 PROTOCOL DEVIATIONS

A deviation (any activity conducted outside the parameters established by the protocol) can be identified from a number of sources. Potential sources for identification of deviations include but are not limited to: a member of the Investigator's staff, a Sponsor representative during monitoring visits, or a member of the data management or statistical groups when entering or analyzing data. Regardless of the source, it is crucial to document the deviation. The PI will report protocol deviations to the IRB as required by the IRB/EC procedures.

5.0 STATISTICAL METHODS PLANNED IN THE PROTOCOL AND DETERMINATION OF SAMPLE SIZE

5.1 STATISTICAL AND ANALYTICAL PLANS

The Sponsor Data Management and Biostatistics groups will be responsible for the analysis of data from this protocol. A comprehensive and detailed Statistical Analysis Plan will be finalized prior to database lock to supplement the statistical design and analysis described in this section.

Categorical variables will be summarized descriptively by frequencies and associated percentages. Continuous variables will be summarized descriptively by number of subjects, mean, standard deviation, median, minimum, and maximum. Confidence intervals will also be provided for procedure-related variables.

5.2 STUDY DESIGN

This prospective open-label, multicenter, clinical study will evaluate the intra-operative performance of the powered circular stapler used in left colectomy procedures in a post-market setting.

5.3 TREATMENT ASSIGNMENT

Upon site initiation, subjects will have procedures completed using the powered stapler, as described in Section 3.9.

5.4 INTERVAL WINDOWS

No interval windows are specified for this study given the short-term nature of follow-up.

5.5 PRIMARY ENDPOINT AND ASSOCIATED HYPOTHESES

The primary endpoint is the number of subjects in whom a stapler performance issue is observed, where a stapler performance issue is defined as a failure of the powered circular stapler (study device) to perform per its IFU. This includes but is not limited to difficulty placing or removing the stapler, stapler misfire/failure of the device to fully fire, staple line defects, incomplete or thin donuts, tissue damage, positive intraoperative leak test, detached components, unformed staples, or any other device failure.

No formal hypothesis will be tested in this study.

5.6 ANALYSIS SETS

The primary analysis of safety and effectiveness endpoints will be performed on the Full Analysis Set, defined as all subjects who are enrolled in the study and have an anastomosis attempted with the powered circular stapler. A Per Protocol analysis set will be defined as all subjects who had an anastomosis completed with the powered circular stapler and no major protocol deviations. Effectiveness analyses will be repeated for the Per Protocol Set.

5.7 SAMPLE SIZE JUSTIFICATION

A total of 165 eligible subjects are planned to be enrolled in up to 12 sites to ensure at least 150 subjects complete the study. No formal hypothesis is being tested in this study, thus the sample size was not statistically sized through a power calculation, but rather is considered sufficient for a descriptive summary of stapler performance issues through confidence interval estimation and evaluation of safety. The sample size of 165 subjects is consistent with the amount of information that was planned to be collected on the powered stapler in the original study design and provides acceptable precision for estimation of the rate of stapler performance issues. Available literature suggests that stapler performance issues are observed in 15% to 20% of subjects in whom a circular stapler is used, and a sample size of 165 subjects will provide a margin of error for a one-sided 95% confidence interval that does not exceed 5.1% for estimation of the true rate of stapler performance issues. This margin of error will be even smaller should the expected rate be lower than 15% to 20%.

Further, in consideration of rare AEs that may occur, for an event that occurs at a rate of, for example, 1.5%, then in a sample of 165 subjects, the probability of observing at least 1 event is greater than 90% under a binomial probability model. Thus, this sample size provides a high probability of observing rare events if they do occur and provides reasonable assurance that the absence of such events in the study is not a result of too few subjects being studied, should none be observed.

5.8 ANALYSES TO BE CONDUCTED

Disposition of Study Subjects

Subject disposition will be summarized using counts and percentages. The number and percentage of subjects completed and discontinued along with the specific reasons for discontinuation will be tabulated .

Demographic and Baseline Characteristics

Summary statistics will be provided for patient demographics and pre-operative surgical characteristics.

Primary and Secondary Endpoint Analyses

The primary endpoint of stapler performance issues will be summarized by counts and percentages and a 95% confidence interval will be calculated.

Summary statistics as appropriate for continuous or categorical variables will be provided for assessments of surgical stress as measured by SURG-TLX, and a surgeon satisfaction questionnaire.

Analysis of Safety

All AEs collected will be summarized with counts and percentages by MedDRA system organ class and preferred term. Device-related AEs and procedure-related AEs will also be summarized by MedDRA system organ class and preferred term. These summaries will also be presented for all serious adverse events reported during the study. All AEs will also be summarized by maximum severity by MedDRA system organ class and preferred term. The number and percentage of subjects requiring blood product transfusions will be summarized. Concomitant procedures and concomitant medications will be listed for all subjects.

Handling of Dropouts or Missing Data

All analyses will be performed only on subjects undergoing the surgical procedure (colorectal anastomosis attempted with a powered circular stapler) and only observed data will be analyzed. There will be no imputation of missing data for any parameters or for early terminated subjects.

Data Monitoring Committee

No data monitoring committee is planned for this study.

Multicenter Studies

No adjustment for center is planned in the statistical analysis. However, center specific analyses may be conducted pending within-center sample size to understand the effect that surgeon techniques and site standard of care may have on the overall results.

Analysis of Subgroups

Subgroup analyses are planned to be performed for prior radiation therapy/chemotherapy (presence or absence), procedure approach (open vs. laparoscopic), and indication for surgery (diverticulitis, neoplasm, etc.). Summary statistics for the procedure-related parameters will be provided for each subgroup. Further subgroups may be defined pending the distributions of baseline demographic and clinical characteristics.

6.0 RISKS AND BENEFITS OF THE STUDY

All procedures will be performed per site standard-of-care. This study may or may not provide any benefits to the subject. No risks will be introduced to subjects outside of those that are already inherent in these types of procedures.

7.0 ADVERSE EVENTS

7.1 DEFINITIONS

Adverse Event
Adverse events will be collected from the time an attempt is made to use the powered circular stapler device. For this study, an AE is defined as any undesirable clinical occurrence in a subject that may be attributable to the study procedure or device used to create the colorectal anastomosis. Only AEs attributable to the device used to create the anastomosis or to the study procedure are to be recorded in the eCRF and reported to the Sponsor.

Expected Morbidity/Anticipated Adverse Events
An expected morbidity/procedural complication is defined as an AE that is known to be common or usual in nature, severity, or incidence during left-sided colon surgery. A list of expected AEs (anticipated) that may occur during this study are listed in Appendix II.

Serious Adverse Event
It is the Investigator's responsibility to determine the "seriousness" of an AE using the protocol defined terms below. A serious adverse event/injury is an AE that results in one or more of the following for this study:

- Life-Threatening: The subject was at imminent risk of dying at the time of the adverse event.
- Permanent Impairment: An adverse event that resulted in permanent impairment of a body function or permanent damage to a body structure.
- Necessitated Intervention: An adverse event that resulted in a condition that necessitated medical or surgical intervention to preclude permanent impairment of a body function or damage to a body structure.
- Required in-patient or prolonged hospitalization.
- A persistent or significant disability or incapacity.
- Resulted in Death: An adverse event that resulted in the subject's death.

Note: "Death" should not be reported as an adverse event. The cause of death should be reported as an adverse event. The only exception is "Sudden Death" when the cause is unknown. NOTE Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.

Severity of Adverse Events
It is the Investigator's responsibility to assess the severity of an AE. A change in severity may constitute a new reportable AE.

The following guideline should be used to determine the severity of each adverse event:

- **MILD:** Awareness of signs or symptoms, but does not interfere with the subject's usual activity, or is transient which resolves without treatment and with no sequelae.
- **MODERATE:** A sign or symptom, which interferes with the subject's usual activity.
- **SEVERE**: Incapacity with inability to do work or usual activities.

Relationship of Adverse Events

It is the Investigator's responsibility to assess the relationship between all AEs and the study procedure or circular staplers used in the study. Only AEs attributable (relationship of possibly, related, or unknown) to a device or the study procedure are to be recorded in the eCRF and reported to the Sponsor.

The following guidelines should be used in determining the relationship of an adverse event to a device, study procedure, or other causality:

- **Possibly** – A clinical event (including abnormal laboratory result) that presents an unlikely association between device/procedure, which cannot be ruled out with certainty, but could also be explained by alternative etiology;
- **Related** – A clinical event (including abnormal laboratory result) that presents a strong temporal relationship between device/procedure, in which an alternative etiology is unlikely; or
- **Unknown** – A clinical event (including abnormal laboratory result) that cannot be determined to be related or unrelated to device/procedure given the information obtained.

7.2 REPORTING PROCEDURES FOR ADVERSE EVENTS

7.3 RECORDING ADVERSE EVENTS

The Investigator will record all device- or procedure-related AEs considered attributable (relationship of possibly, related, or unknown) to the powered circular stapler or to the procedure in the source documents and associated eCRF. The site must complete the AE CRF within two weeks of becoming aware of an event and SAE eCRF within 72 hours of becoming aware of the event. Supporting SAE documentation should be de-identified and emailed to the Clinical Study Lead.

Standard medical terminology should be used when recording AEs. In addition, the following information should be recorded:

- Onset Date
- Resolution date or date of death
- Severity of the event
- Action Taken
- Event Status (ongoing at study end or resolved)
- Relationship of AE to a surgical device used in the study
- Relationship of AE to the study procedure
- Indication of whether the event is serious

Data related to SAEs will be collected until event resolution, or until the event is considered stable, or until all attempts to determine the resolution of the event are exhausted. All AEs that are unresolved at study completion (or early termination) will be recorded as ongoing at study end.

The Investigator will be required to assess if the SAE is considered anticipated (Appendix II) and if the event involved a product complaint. The report of an SAE by a site does not constitute an admission that study personnel or the user facility (hospital/clinic) caused or contributed to the event. The study site is also responsible for submitting to the reviewing IRB/EC according to their IRB/EC procedures.

The Investigator will be required to assess if the SAE is considered anticipated (Appendix II) and if the event involved a product complaint. The report of an SAE by a site does not constitute an admission that study personnel or the user facility (hospital/clinic) caused or contributed to the event. The study site is also responsible for submitting to the reviewing IRB/EC according to their IRB/EC procedures.

7.4 SAFETY MONITORING AND REPORTING

If any serious and unexpected AEs occur during the study, all PIs will be notified by the Sponsor within 72 hours of learning of the event.

8.0 PRODUCT COMPLAINTS

8.1 PRODUCT COMPLAINT DEFINITION

A product complaint is defined as any written, electronic or oral communication that alleges deficiencies related to the identity, labeling, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution (21CFR 820.3 (b)). A product complaint may or may not be associated with an AE/SAE.

8.2 REPORTING PRODUCT COMPLAINTS

All product complaints related to devices in the procedure shall be documented throughout the clinical investigation.

Product complaints related to an Ethicon-manufactured circular stapler must be reported to the Sponsor in a timely manner and no later than 24 hours after becoming aware of the event. When a sponsor representative becomes aware of a product complaint, the Product Complaint Team must be notified within 24 hours after becoming aware of the event. The Product Complaint Form must be emailed to the Sponsor Customer Complaint team at the following email address:

[redacted]

[redacted]

One copy of the processed form should be kept on-site and the device should be retained. Sponsor representatives will organize collection of the device for evaluation as needed.

9.0 REFERENCE LIST

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3. Andersen LP, et al. Psychological and Physical Stress Among Experienced and Inexperienced Surgeons During Laparoscopic Cholecystectomy. Surg Laparosc Endosc Percutan Tech 2012;22:73–78.

4. Pinto A, Faiz O, Bicknell C, Vincent C. Surgical complications and their implications for surgeons' well-being. British Journal of Surgery. 2013; 100:1748–1755.

5. Kono E, Tomizawa Y, Matsuo T, Nomura S. Rating and issues of mechanical anastomotic staplers in surgical practice: a survey of 241 Japanese gastroenterological surgeons. Surg Today. 2012;42:962–972.

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7. Wilson MR, Poolton JM, Malhotra N, Ngo K, et al. Development and validation of a surgical workload measure: the surgery task load index (SURG-TLX). World J Surg. 2011;35(9):1961–1969.

8. Rahbari NN, Weitz J, Hohenberger W, Heald RJ, etal. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. Surgery. 2010; 147(3):339-51.

10.0 APPENDIX I: SPONSOR CONTACT INFORMATION

[redacted]		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

11.0 APPENDIX II: ANTICIPATED ADVERSE EVENTS

Associated with left-sided colon resection and General Anesthesia	
Air/Gas Embolism	Ischemia
Abcess	Jaundice
Adhesions	Leak
Anastomotic Leak	Lethargy
Bleeding	Leukocytosis
Bowel obstruction	Liver Failure
Bradycardia	Mesenteric Infarction
Cardiac Arrhythmia	Mesenteric Ischemia
Constipation	Myocardial Infarction
Deep Venous Thrombosis	Nausea
Dehydration	Nutrient Deficiency
Diarrhea	Obtundation, Depressed Level of Consciousness
Disseminated Intravascular Coagulation (DIC	Oliguria
Coagulopathy	Pain (increased/severe/chronic)
Discharge of feces through drain	Peritonitis
Dizziness	Pneumonia
Electrolyte Imbalance	Pulmonary Embolism
Dysphagia	Renal Failure
Evisceration	Respiratory Failure
Headache	Respiratory Insufficiency
Fistula	Stenosis
Headache	Stricture
Hematuria	Systemic Inflammatory Response
Hemorrhage	Tachycardia
Hypernatremia	Thromboembolic Event
Hyperphosphatemia	Thrombosis
Hypertension	Transient Ischemic Attack (TIA)
Hypotension	Tightness of the chest, Angina
Hypoxia	Urinary Retention
Incisional Hernia	Urinary Tract Infection (UTI)
Ileus	Volume Depletion, Hypovolaemia
Infection / wound infection	Vomiting