ENDOROTOR

Investigational Plan

PROSPECTIVE, TRIAL EVALUATING THE SAFETY AND EFFECTIVENESS OF THE INTERSCOPE ENDOROTOR® RESECTION SYSTEM FOR DIRECT ENDOSCOPIC NECROSECTOMY OF WALLED OFF PANCREATIC NECROSIS (ENDOROTOR DEN TRIAL)

Protocol # CLIN 0047, Revision D, (31 August 2018)

A PROSPECTIVE, MULTI-CENTER, TRIAL TO EVALUATE THE SAFETY AND EFFECTIVENESS OF THE INTERSCOPE ENDOROTOR® RESECTION SYSTEM FOR DIRECT ENDOSCOPIC NECROSECTOMY OF WALLED OFF PANCREATIC NECROSIS

US FDA IDE # G180127

Sponsor:
Interscope Medical, Inc.
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Whitinsville, Massachusetts, USA 01605

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PROTOCOL SUMMARY

Study Title:	EndoRotor Direct Endoscopic Necrosectomy Trial
Protocol No.	CLIN 0047 / C
Study Design:	A prospective, single arm, open label, multi-center, trial to evaluate the safety and effectiveness of the Interscope EndoRotor® Resection System in subjects requiring direct endoscopic necrosectomy with walled off pancreatic necrosis (WOPN). Total enrollment 30 subjects with at least 15 enrolled in the US. Subjects will be debrided with the EndoRotor at least 2 days following initial stent placement with a maximum of 4 EndoRotor procedures. A minimum of 2 days is required between each EndoRotor procedure and all procedures need to be completed within a 14 (+7/-0) day period. Follow up is completed 21 (+/- 7) days after last EndoRotor debridement procedure.
Patient Population:	Subjects with confirmed walled off pancreatic necrosis requiring direct endoscopic necrosectomy
Objective:	To evaluate the EndoRotor's ability to safely remove non-viable/necrotic tissue for direct endoscopic necrosectomy in patients with walled off pancreatic necrosis.
Primary Endpoint:	The primary endpoint of this study is the freedom from major complications. The safety endpoint will include an assessment of the safety of the EndoRotor when performing endoscopic necrosectomy. For the purpose of this study, the safety evaluation shall include complications associated with endoscopic necrosectomy through the 21 (+/-7) day follow-up period. Potential endoscopic complications include perforation and bleeding.
Secondary Endpoints:	1. Successful clearance of necrosis in the collection being treated during direct endoscopic necrosectomy where success is defined as at least 70% of the necrotic debris in the collection being treated is removed based on CT evaluation of the cavity at the 21 (+/-7) day day follow up visit. 2. Assessment of total procedure time to achieve clearance of necrosis for all procedures 3. Assessment of adequacy of debridement 4. Assessment of total number of procedures to achieve clearance of necrosis. 5. Assessment of length of hospital stay and utilization. 6. SF-36 Questionnaire
Study Duration:	Total study duration is expected to be approximately 180 days assuming enrollment occurs in 90 days, subjects are followed and assessed at 21 (+/-7) days post procedure and allowing for 60 days for data collection and reporting.

Clinical Sites:	Up to 6 in the United States and 4 in the EU will enroll subjects.
Enrollment:	The sites will enroll a total of 30 subjects, 15 minimum from the US that meet all inclusion and exclusion criteria.

Inclusion Criteria:	1. Subjects who are ≥22; inclusive of males and females. 2. Patients with symptomatic pancreatic necrosis due to acute pancreatitis that have an indication to undergo endoscopic necrosectomy after having undergone EUS-guided drainage 3. Imaging suggestive of greater than or equal to 30% necrotic material 4. Walled off pancreatic necrosis size ≥6 cm and ≤22cm 5. Subject can tolerate repeated endoscopic procedures 6. Subject capable of giving informed consent. 7. Subjects with the ability to understand the requirements of the study, who have provided written informed consent, and who are willing and able to return for the required follow-up assessments through 21 (+/- 7) days, as indicated.
Exclusion Criteria:	1. Subject unable to give informed consent. 2. Subject is unwilling to return for repeated endoscopies. 3. Documented Pseudoaneurysm > 1cm within the WOPN 4. Intervening gastric varices or unavoidable blood vessels within the access tract (visible using endoscopy or endoscopic ultrasound). 5. Dual antiplatelet therapy or therapeutic anticoagulation that cannot be withheld for the procedure 6. Any condition that in the opinion of the investigator would create an unsafe clinical situation that would not allow the patient to safely undergo an endoscopic procedure (lack of medical clearance). 7. Pregnant or lactating women or women of childbearing potential who do not employ a reliable method of contraception as judged by the Investigator, and/or are not willing to use reliable contraception for the duration of study participation. 8. Patient is known to be currently enrolled in another investigational trial that could interfere with the endpoint analyses of this trial.
Primary Analysis:	Subjects enrolled in the study and who met all I/E criteria and are treated with the EndoRotor Device.
Study Device:	Interscope EndoRotor® Resection System

Regulatory Status:	EndoRotor® Resection System device is designed and manufactured in the United States for investigational use in the resection of walled off pancreatic necrosis. The FDA cleared the EndoRotor® under the Pre-market Notification, 510(k) program in April 2017 (K170120) for use in endoscopic procedures by a trained gastroenterologist to resect and remove residual tissue from the peripheral margins following endoscopic mucosal resection (EMR). The EndoRotor® is an approved product in Europe having received the CE Mark under MDD 93/42/EEC on Medical Devices Annex II, excluding Section 4.

Study Contacts

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Device Technical Support	Interscope Medical, Inc. Jeffery Ryan 617-360-1168 Ramon Franco Jr, M.D. 617-872-0128 Normal hours: Mon-Sat 7am to 6pm EST Emergencies (24 hours a day)
Data Monitoring Committee:	An Independent 3-Member Data Monitoring Committee – Members to be selected prior to study initiation
Clinical Research Organization - Study Management, Monitoring, Data Coordination, & Safety/Event Reporting	Alvamed, Inc. Eric Bannon, Acting Director, Regulatory and Clinical Affairs 1116 Great Plain Avenue, Needham, MA, USA 02492 Mobile: + 1 7 8 1 7 1 0 8 2 4 3 Email: ebannon@alvamed.com

Clinical Investigator Signature Page

The ENDOROTOR Study

Clinical Protocol: CLIN 0047, Version C, "Prospective Trial Evaluating the Safety and Performance of the Interscope EndoRotor® Resection System for the removal of walled off pancreatic necrosis". Prior to participation in the ENDOROTOR Study, the Clinical Investigator must obtain written approval from his/her Institutional Review Board (IRB). This approval must be in writing and must indicate the Study name, Protocol number, Institution(s) where the study will be conducted, any local regulations that apply to this trial, and the expiration date of the approval.

By signing below, I confirm that I will not enroll subjects in this study until IRB approval has been obtained at my site. I have signed an Investigator agreement and have completed all of the Sponsor requirements for training on the study and the Interscope EndoRotor® Resection System. I have read this protocol and agree to adhere to the protocol and study requirements. I will discuss this protocol and all related study material with the research team at my institution and ensure that they are fully informed regarding the study requirements and use of the EndoRotor® device. I will also ensure that the study is conducted in accordance with all applicable standards and regulations; including, but not limited to, the Declaration of Helsinki, Good Clinical Practices (GCP), FDA IDE regulations (21.CFR.812), the Sponsor, the IRB and any other applicable local or national requirements.

Clinical Investigator

_____ _____

Print Name Signature

_____

Date (dd/MMM/yyyy)

_____

Institution(s)/Location

1.0 INTRODUCTION & BACKGROUND

1.1 Introduction

The EndoRotor® Endoscopic Resection System is an automated mechanical endoscopic resection system for use in the gastrointestinal tract for benign neoplastic or pre-malignant tissue removal by interventional gastroenterologists and GI surgeons. The EndoRotor® System performs both tissue dissection and resection with a single device through an endoscope's instrument biopsy channel. A motorized rotating cutting tool driven by an electronically controlled console performs tissue resection. Because the system automatically suctions and cuts between 1000 and 1750 times a minute, resected tissue is immediately aspirated away from the resection site and collected onto a micron filter. Tissue collected on the filters can be used for pathological examination using standard methods.

Infected walled of pancreatic necrosis (WOPN) is a complication of acute pancreatitis. Direct endoscopic intervention is a means to remove the necrosis and improve patient recovery. Interscope completed direct endoscopic necrosectomy procedures in the European Union and believes that use of the EndoRotor will allow for a safe and effective direct endoscopic necrosectomy of WOPN. Current techniques employ the use of instruments not designed for the procedure such as endoscopic snares/jumbo forceps to blindly break up necrosis followed by endoscopic retrieval baskets to blindly grasp necrotic debris. In Europe, where the EndoRotor® has been used in human cases, it performed well in direct endoscopic necrosectomy. The EndoRotor's ability to resect tissue may provide faster rates of removal and less endoscopic procedures in this patient population.

In this study, Interscope will evaluate the EndoRotor's ability to remove walled off necrosis through direct endoscopic necrosectomy in patients requiring endoscopic necrosectomy. The study will be conducted at primary referral centers for this patient population.

1.2 Background

Acute pancreatitis is defined by sudden inflammation of the pancreatic gland, which functions to make insulin to control blood sugar levels and enzymes for the digestion of food. While the cause of acute pancreatitis can vary greatly among patients, severe cases can lead to development of life threatening complications, such as infected walled-off pancreatic necrosis (WOPN). Pancreatic necrosis is defined when more than 30% of the gland is affected by necrosis with 20% of patients requiring severe clinical course.[3] Of the 20%, one third (33.3%) of cases progress to infected necrosis with patient mortality ranging from 15-30%.[4] Should acute necrotic collections continue to progress, results may lead to the development of WOPN after 4 weeks time.

The EndoRotor has been demonstrated to be a tool for safe and effective removal of pancreatic necrosis - due to its automated mechanical characteristics, which incorporate rotational cutting and suction for tissue removal in one inclusive device. An investigator-led series was completed by Marco Bruno, Arjun Koch et al at Erasmus Medical Center (Rotterdam, Netherlands) utilizing the EndoRotor in necrosectomy procedures to resect WOPN accessed via trans gastric fistulas created by luminal apposing metal stents (LAMS) and plastic stents (2 pig tails). The primary risk includes procedural bleeding and was tracked in the prospective series. While the device is used to resect necrotic tissue in the cavity perforation does not present a risk with no interaction with wall of pancreas and further there was no evidence of bleeding in the series. The EndoRotor demonstrated complete removal of pancreatic necrosis through various anastomosing stents in twenty-three (23) procedures of twelve (12) patients with no incidences of perforation or bleeding. An abstract of this series was accepted for Digestive Disease Week 2018 for poster with presentation and the investigators continue to treat patients for additional outcomes data. A pending manuscript is under peer review where the

authors presented their findings.

The investigators believe the EndoRotor provides a tool for safe and effective means at removal of necrotic debris in WOPN. Using the first series provides initial feasibility to evaluate the EndoRotor in a larger prospective cohort.

1.3 Literature Summary

Treatment of pancreatic necrosis has often been addressed through means of invasive surgery to remove the necrotic tissue, though within the last decade treatment has shifted dramatically to less invasive endoscopic treatments. One of the main limitations physicians face in addressing the removal of pancreatic necrotic tissue endoscopically is the lack of suitable instruments available to assist in the procedure execution. These limitations often result in time consuming procedures with marginal results often necessitating multiple procedures to reach desired patient outcomes. The use of direct endoscopic necrosectomy has been shown to be superior then endoscopic drainage alone for the treatment of WOPN with resolution in 88% of cases.[4] In high risk patients with pancreatic necrosis, studies have shown that minimally invasive endoscopic necrosectomy is associated with reduced mortality when compared to patients undergoing invasive surgical necrosectomy.[6]

2.0 Report of Prior Investigations

2.1 Summary of Prior Human Clinical Use

The EndoRotor® has been used in humans to resect walled off necrosis in 23 procedures in a post market series at Erasmus Medical Center located in Rotterdam, Netherlands, completed in an investigator lead case series utilizing the EndoRotor® to for direct endoscopic necrosectomy to resect walled-off pancreatic necrosis (WOPN). Investigators executed the procedures with the EndoRotor through various anastomosing stents, which included twenty-three (23) procedures in eleven (11) patients.

During an initial endoscopy, a trained gastroenterologist performed endoscopic ultrasound (EUS) guided transgastric drainage by creating a fistula from the stomach to directly access the adjacent WOPN site for collection. Two (2) double pigtail plastic stents and a nasocystic flushing catheter (n=9 subjects), or Luminal Apposing Metal Stents (LAMS, n=2 subjects), were positioned.

Due to deteriorating patient conditions shortly after initial endoscopy procedures, trained gastroenterologists determined is was necessary to proceed with necrosectomy of the WOPN. The first patient, Patient One, was treated approximately twenty-four (24) hours after the initial drainage procedure; a second endoscopy was carried out during which the fistula was dilated with a CRETM Balloon Dilator to 18 mm and was followed by initial attempts at necrosectomy with conventional instruments. Upon execution of necrosectomy with conventional instruments, the amount of necrotic tissue that could be removed was insufficient and clinical improvement was not observed. At this time, the attending gastroenterologist decided to proceed with an additional necrosectomy attempt utilizing the EndoRotor. Necrosectomy performed with the EndoRotor technique resulted in complete removal of all necrotic tissue and was achieved in two (2) sessions with no adverse events; patient was discharged 7 days after admission.

Subsequent patient treatment in the presented case series, Patient Two was approached using EndoRotor as a first line therapy for necrosectomy of WOPN achieving similar results. On average, two (2) sessions were required to remove the pancreatic necrosis. Reduction of required procedures to achieve favorable removal of

necrotic pancreatic tissue resulted in patient discharges within a few weeks versus an average of 6.2 sessions and almost twelve (12) weeks using conventional instrumentation as reported in literature.[9] An overview of patient demographics and medical history are presented in Table 1. It is noted that there was no device related adverse events.

Investigators participating in the EndoRotor case series concluded that initial experience with the EndoRotor in direct endoscopic necrosectomy procedures suggests that EndoRotor can safely and effectively remove pancreatic necrosis at a faster rate than that of conventional methods with no adverse events.

Patient	Age in years	Sex	Etiology	Infected necrosis PROVEN by culture	Size of first collection (diameter in mm)	Size of second collection (diameter in mm)	Stent placement†	Previous necrosectomy*	Necrosectomy using the EndoRotor**	EndoRotor version***	Mean procedure time in minutes	Procedure related adverse events
1	56	Female	Biliary	Yes	100	95	3 Pigtails	2	2	1	-	None
2	65	Male	Unknown	Yes	167	-	2 Pigtails	3	2	1	-	None
3	68	Male	Unknown	Yes	182	-	LAMS	1	7	1	56	None
4	43	Male	Biliary	Yes	141	20	2 Pigtails	0	2	1	33	None
5	67	Male	Biliary	Yes	130	-	2 Pigtails	0	1	1	32	None
6	71	Male	Biliary	Yes	78	43	LAMS	0	2	1	65	None
7	76	Female	Alcoholic	Yes	124	-	2 Pigtails	0	1	2	28	None
8	58	Male	Iatrogenic	No	220	-	3 Pigtails	0	3	2	43	None
9	51	Male	Alcoholic	Yes	84	-	LAMS	0	2	2	43	None
10	67	Female	Unknown	Yes	45	-	LAMS	0	2	1	60	None
11	66	Male	Unknown	Unknown	100	-	2 Pigtails	0	1	2	33	None

† *No stent dislodgement during the necrosectomy using the EndoRotor*

* *Number of previously performed endoscopic necrosectomy procedures with conventional instruments*

** *Number of performed endoscopic necrosectomy procedures using the EndoRotor*

*** *Version 1 is the regular EndoRotor, version 2 is the pancreas specific EndoRotor*

Mean age:	62.5 years
Mean collection size:	127 mm (±52.9)
Total number of EndoRotor procedures:	23 procedures
Mean EndoRotor procedure time:	43.7 minutes (±13.7)

Confidential *Version: 11 May 2018* *Drs. S.E. van der Wiel*

Table 1: Data Table from Van Der Wiel et al pending publication

Concurrently, the EndoRotor is used for its on-label indication facilitating the removal of peripheral margins in large endoscopic mucosal resection (EMR) and removal of a scarred base in EMR after incomplete resection with tissue persistence. In this indication the EndoRotor has been used in over 190 procedures in both clinical trials and commercial use. Investigators from NHS Kings College London and Queen Alexandria Hospital Portsmouth, United Kingdom have posters with presentation at DDW 2018. Both studies are being submitted for peer review publications.

In the Kings College Trial the effectiveness of large EMR was evaluated in 30 patients with the EndoRotor used to assess peripheral margins following EMR and use of magnification chrome endoscopy to ensure completeness of resection. There were no complications in this study. In 6 of 30 patients micro-adenoma was detected from margin specimen using EndoRotor where magnification chrome endoscopy showed no residual adenoma. Of these six (6) patients there were (0) recurrences at 3 month follow up.

In the Portsmouth trial 19 patients were evaluated in the initial experiences utilizing the EndoRotor in management of post EMR persistent adenoma with a scarred base. Investigators participating in this study hypothesized that the EndoRotor offered the capability to safely and effectively resect persistent adenoma in the immediate vicinity of the scar. Resection of such scar sites would ensure disease eradication and luminal preservation. Successful resection with EndoRotor would lead to the patient avoiding surgery and/or other invasive techniques such as full thickness resection.

Nineteen (19) patients were referred to Queens Alexandra Hospital, a tertiary center, following diagnosed tissue persistence following EMR. Scarred sites of the colon, in each of the nineteen (19) patients, were evaluated by physicians and found to have lesions determined difficult to resect and no longer amenable to EMR due to scarring from previous EMR. The EndoRotor was used to perform resection of the identified patient site and successfully demonstrated the ability to superficially resect the scarred areas. The procedure outcomes using the EndoRotor ensured muscle and luminal preservation in addition to disease eradication in fifteen (15) patients in twenty-one (21) procedures (1.4 procedure average) with no incidences of perforation or delayed bleeding; all patients were seen at follow up n=4 months. Study outcomes showed EndoRotor directly led to successful avoidance of surgery in 78.9% of patients.

Due to poor lesion access (i.e. requiring retrograde approach) two (2) patients (10%) were referred on for endoscopic submucosal dissection (ESD) and one (1) patient (5.2%) was treated with piecemeal EMR. One (1) patient 5.2% was referred on for surgery due to aggressiveness and phenotype of recurrence. Surgery was avoided in 18/19 (94.7%) of patients included in the study. There were no complications (perforations or delayed bleeding) and no device related adverse events associated with this study.

The EndoRotor is also the subject of US IDE G170106 trial investigating patients with refractory Barrett's Esophagus compared to continued ablative therapy. In the European Union investigators at Sana Clinic Offenbach, Germany evaluated the EndoRotor and their published manuscript, "Non-thermal ablation of non-neoplastic Barrett's esophagus with the novel EndoRotor resection device," appeared in a recent UEG journal where the authors concluded the EndoRotor as feasible for treatment of Barrett's mucosa.

The EndoRotor presents technique options for challenging intraluminal and extra-luminal procedures warranting further investigation for this trial.

2.2 Summary of Pre-Clinical (Animal) Testing

Animal testing of the EndoRotor® was conducted to evaluate the overall safety and performance of the device in an animal model. A summary of the study is presented below.

The objectives of this study were to evaluate the EndoRotor® system for performance of tissue resection in an animal model, with respect to safety:

- Assessment of tissue response acutely and at 2 weeks' post-resection utilizing standard light microscopy
- Clinical assessment of bleeding at sites of resection

In addition, the overall performance characteristics of the system were evaluated by multiple operators.

The study was conducted at CBSET in Lexington, Massachusetts, USA as part of a Good Lab Practices (GLP) protocol, as well as for a preliminary research project in Germany at the Institut für Nutztiergenetik, Mariensee, Friedrich-Loeffler-Institut (FLI) Bundesforschungsinstitut für Tiergesundheitusing in live pigs[10]. The animal study was conducted under Good Laboratory Practice (GLP) guidelines. Six healthy, Yorkshire pigs underwent endoscopic procedures. The endoscopic procedure was carried out under general anesthesia with an appropriate endoscope inserted into the rectum and advanced into the colon for treatments, and also into the mouth and advanced into the esophagus and stomach for further treatments. The device was used to perform a series of tissue resections in each animal.

Over 120 resections were completed between the colon, stomach, and esophagus, and distributed across different sizes. Each resection site was scored by the endoscopist for bleeding as mild, moderate, or severe, and at least one resected tissue sample from each organ from each animal collected during the procedures, along with the native colon, stomach, and esophageal sites, were subject to histologic processing (paraffin) and staining (H&E). In addition, on the day the resections were conducted, performance characteristics of the EndoRotor® system were evaluated by two operators (physicians), in accordance with the acceptance criteria of the protocol, covering both performance and intended use.

Perforation and bleeding were the main safety criteria assessed. Other major endpoints were device performance/usability and histopathology. Perforation was noted in 2 (1.6%) of the colon resection sites, comparing favorably to the published rate of 2.3%. Bleeding was graded as mild (resolves in 2 minutes or less without intervention) in 79.5% of sites, as moderate bleeding (resolves in greater than 2 minutes without intervention) in 19.7% of sites, and one site (0.8% of sites) as severe bleeding (requires intervention to resolve the bleeding) which resolved after epinephrine administration. The bleeding rate that required intervention compares favorably to the rates for current interventional techniques published in the literature (0.8% vs. 1-16%). The study pathologist indicated that use of the EndoRotor® System for mucosal tissue resection in the porcine esophagus, stomach and colon was associated with favorable and clinically acceptable tissue responses. The EndoRotor® System received passing evaluation for all performance and intended use criteria by both physicians for the system usability assessment.

There is one published animal study[4] conducted in Germany. The study performed multiple upper and lower gastrointestinal endoscopic mucosal resections in three healthy live pigs. Animals were anesthetized and kept artificially ventilated while two physicians performed multiple qualitative mucosal resections on various sites of the pigs' esophagus, stomach, duodenum, and colon. Rapid resection of flat and slightly elevated mucosa up to several centimeters in size/diameter was performed. No major bleeding occurred during and after resections. When used properly, no gastrointestinal wall perforations occurred during superficial resections. Perforations in the colon were only observed when the device was deliberately pushed against deeper sub-mucosal layers or

when exceptional force was applied to penetrate the gastrointestinal wall. Histologic specimens showed complete mucosal removal at resection sites.

2.3 Summary of Design Verification and Validation Testing

In addition to pre-clinical animal testing, the Interscope EndoRotor® System has undergone extensive design verification and validation testing through a series of physical and mechanical performance tests on the catheter and console. Testing was conducted according to applicable US Food and Drug Administration requirements, requirements of the European Medical Device Directive, applicable ISO standards, and applicable test methods.

Testing of the catheter included sterilization validation with ethylene oxide residuals and pyrogenicity testing as well as biocompatibility testing. Shelf life testing and packaging validation and transport testing was conducted to support a 2-year shelf life for the packaged catheter. These tests included functional and simulated use testing which demonstrated conformance of the product with defined performance criteria out to 2 years.

Design verification testing performed on the console included power up and set up testing, foot pedal controls testing, functional testing, and torque testing. The console was also subjected to electrical safety and electromagnetic compatibility testing as well as evaluated for usability.

Summaries of the design verification and validation testing are provided in the Investigator's Brochure.

2.4 Summary and Conclusions

Review of the prior investigations of the EndoRotor® device demonstrate that the device is biocompatible when utilized as instructed. Bench testing demonstrates that the device meets performance specifications. Pre-clinical and clinical testing performed to date demonstrates that the device is safe and effective in removing mucosal tissue and lesions in both the upper and lower gastrointestinal tract.

3.0 Device Description - Interscope EndoRotor® Resection System

The EndoRotor Console® is a reusable device with disposable components (single-use, EndoRotor® catheter). The EndoRotor® cutting device is invasive and is in contact with mucosal membranes for less than 60 minutes. The EndoRotor® is manufactured in several lengths that conform to the lengths of the most popular endoscopes. The FDA cleared the EndoRotor® under the Pre-market Notification, 510(k) program in April 2017 (K170120) for use in endoscopic procedures by a trained gastroenterologist to resect and remove residual tissue from the peripheral margins following endoscopic mucosal resection (EMR). The EndoRotor® was granted the CE Mark in September of 2015.

All investigational devices will have the following label statement: CAUTION – Investigational Device. Limited by Federal law to investigational use.

3.1 Device Components

The Interscope EndoRotor® is a system comprised of the following core components:

- EndoRotor Console®: The system control unit housing the motor drive, peristaltic pump and pinch valve to provide rotation, irrigation, and vacuum regulation respectively. (Figure 1).
- Foot Pedal: Activates/deactivates cutter rotation/lavage and aspiration (suction).

- EndoRotor Catheter: The outer jacket of the cutter catheter serves as the delivery vehicle for the irrigation fluid that flows between the inner wall of the braid and outer wall of the torque coil. It also allows for outer cutter repositioning. The outer braided sheath is attached to the distal cutter at the end of the catheter. The torque coil transmits internal rotation to the inner cutter and is sealed with a shrink sleeve to contain aspiration. The rotation motion cuts tissue, which is simultaneously removed from the resection site by suction. The distal ends of the lavage and aspiration tubing are permanently affixed to the catheter (Figures 2-4).
- Collection Device: EndoRotor Specimen Trap® with pre-loaded micron filter. This custom trap is designed specifically to capture EndoRotor specimen.
- Polyp Filter: Filter Set includes 200 replacement filters that can be exchanged and placed within the EndoRotor Specimen Trap® to ensure collection of resected tissue

In addition, the device is not user programmable - it utilizes an off-the-shelf Maxon® electric motor built into the console that is not adjustable.

Figure 1. EndoRotor® Console

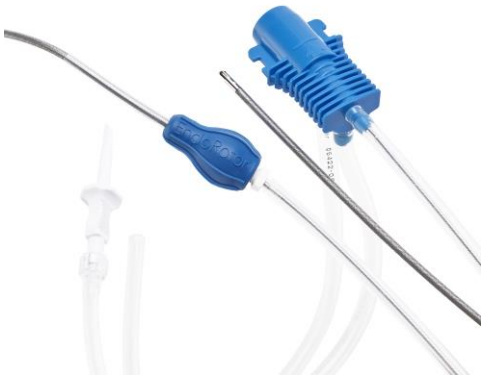

Figure 2. Tubing and Resecting Cutter Components

Figure 3. Disposable Resecting Cutter

Figure 4. Drawing of Resecting Cutter Deployed in Endoscope Working Channel

3.2 How Supplied

The EndoRotor Console®, power cord, and foot pedal are packaged together and supplied non-sterile. The EndoRotor Catheter is packaged separately, is intended for single use only and is provided sterile. The catheter is sterilized by Ethylene Oxide. The EndoRotor Specimen Trap® with pre-loaded micron filter is provided separately and is supplied non-sterile. Replacement filter sets are sold separately and are also nonsterile. Filters and filter sets are not required for this trial since tissue does not need to be collected for analysis.

3.3 Regulatory Status

The Interscope EndoRotor® Resection System is for investigational use only in the United States under this clinical protocol. The device is manufactured by Interscope, Inc. in the United States. Interscope has a quality management system in place that is in compliance with the US Food and Drug Administration's Quality System Regulation. The FDA cleared the EndoRotor® under the Pre-market Notification, 510(k) program in April 2017 (K170120) for use in endoscopic procedures by a trained gastroenterologist to resect and remove residual tissue from the peripheral margins following endoscopic mucosal resection (EMR). The FDA also approved US IDE G170106 comparing the safety and effectiveness of the EndoRotor with continued ablative therapy treating refractory Barrett's Esophagus. The EndoRotor® is sold throughout Europe.

3.4 Indication for Use

The Interscope EndoRotor® is intended for use in endoscopic procedures to resect and remove necrotic debris during direct endoscopic necrosectomy for WOPN.

3.5 Contraindications

None.

4.0 STUDY DESIGN

4.1 Study Objectives

The primary objective is to evaluate the EndoRotor®'s ability to safely remove non-viable/necrotic tissue for direct endoscopic necrosectomy in patients with walled off pancreatic necrosis

4.2 Overview of Study Design

A prospective, single arm, open label, multi-center, trial to evaluate the safety and effectiveness of the Interscope EndoRotor® Resection System in subjects requiring direct endoscopic necrosectomy with walled off pancreatic necrosis (WOPN). Total enrollment of 30 subjects with at least 15 enrolled in the US.

Subjects will be debrided with the EndoRotor at least 2 days following initial stent placement with a maximum of 4 EndoRotor procedures. A minimum of 2 days is required between each EndoRotor procedure and all procedures need to be completed within a 14 (+7/-0) day period. Follow up is completed to 21 (+/-7) days after first EndoRotor debridement procedure.

4.3 Primary Endpoint

The primary endpoint of this study is the freedom from major complications. The safety endpoint will include an assessment of the safety of the EndoRotor when performing endoscopic necrosectomy. For the purpose of this study, the safety evaluation shall include complications associated with endoscopic necrosectomy through the 21 (+/-7) day follow-up period. Potential endoscopic complications include perforation and bleeding.

4.4 Secondary Endpoints

- Successful clearance of necrosis in the collection treated during direct endoscopic necrosectomy where success is defined as at least 70% of the necrotic debris in the WOPN cavity is removed

based on CT evaluation of the cavity at the 21 (+/-7) day follow up visit.
- Assessment of total procedure time to achieve clearance of necrosis for all procedures
- Assessment of adequacy of debridement
- Assessment of total number of procedures to achieve clearance of necrosis
- Assessment of length of hospital stay and utilization
- SF-36 Questionnaire

4.5 Clinical Sites & Enrollment

Up to six (6) research sites in the United States and up to four (4) research sites in the European Union will participate in this trial. The sites will enroll a total of 30 subjects meeting all inclusion and exclusion criteria to reach a total of 30 evaluable subjects. Once the informed consent process is completed and final study eligibility has been confirmed, the patient will have the EndoRotor direct endoscopic necrosectomy.

4.6 Study Duration & Follow-Up

Total study duration is expected to be approximately 180 days assuming enrollment occurs in 90 days, subjects are followed and assessed at 21 (+/-7) days post procedure and allowing for 60 days for data collection and reporting.

4.7 Patient Population / Sample Size

This study is primarily designed as a safety evaluation and will enroll a total of 30 subjects. A minimum of 15 subjects will be enrolled at centers in the US. Although a primary efficacy and safety endpoint is specified, these endpoints are not statistically powered. However, for regulatory purposes, the data generated from this study is sufficient to demonstrate the benefit risk profile of the EndoRotor for this indication.

4.8 Subject Recruitment

The subjects will be recruited from the clinical practices of the investigators. Due to the number of patients with WOPN subjects they follow and are referred each month, there may not be a need to advertise. These centers are major referral centers for advanced cases such as WOPN. Subjects who require direct endoscopic necrosectomy will be told of the study and asked if they would be interested in participating.

4.9 Subject Screening

Following placement of stent and determination of need for necrosectomy study eligibility is confirmed and the patient will receive the EndoRotor® intervention. The patient will be enrolled upon insertion of the catheter into the endoscope. Screening shall include:

- Pregnancy test – within 1 day of the procedure.
- Medical clearance in advance of the procedure.
- WOPN resulting from necrotizing pancreatitis per high resolution vascular CT with the characteristics per the 2012 Revised Atlanta Classification.
- Imaging suggestive of greater than 30% necrotic material
- WOPN size ≥6 cm and ≤ 22 cm

4.10 Prior and Concomitant Therapy

Patients must have undergone EUS guided drainage procedure using LAMS or sinus tract fistula using plastic stents (pigtails) in order to enable access to the necrosis. Endoscopic confirmation after completion of

necrosectomy per contrast-enhanced CT will be obtained at 21 (+/-7) days following final DEN procedure. Subjects with walled off pancreatic necrosis are eligible for this study.

4.11 Informed Consent

Prior to the EndoRotor® procedure and enrollment in the ENDOROTOR study, written informed consent will be obtained in accordance with 21 CFR 50.20 and contain the information required by each of the eight basic elements of 21 CFR 50.25(a).

4.12 Inclusion Criteria

Candidates for this study must meet **ALL** of the following Inclusion criteria:

1. Subjects who are ≥22; inclusive of males and females.
2. Patients with symptomatic pancreatic necrosis due to acute pancreatitis that have an indication to undergo endoscopic necrosectomy after having undergone EUS-guided drainage
3. Imaging suggestive of greater or equal to 30% necrotic material
4. Walled off pancreatic necrosis size ≥6 cm and ≤ 22cm
5. Subject can tolerate repeated endoscopic procedures
6. Subject capable of giving informed consent.
7. Subjects with the ability to understand the requirements of the study, who have provided written informed consent, and who are willing and able to return for the required follow-up assessments through 21 (+/-7) days, as indicated.

4.13 Exclusion Criteria

Subjects will not be included in the study if **ANY** of the following exclusion criteria are met:

1. Subject unable to give informed consent.
2. Subject is unwilling to return for repeated endoscopies.
3. Documented Pseudoaneurysm > 1cm within the WON
4. Intervening gastric varices or unavoidable blood vessels within the access tract (visible using endoscopy or endoscopic ultrasound).
5. Dual antiplatelet therapy or therapeutic anticoagulation that cannot be withheld for the procedure
6. Any condition that in the opinion of the investigator would create an unsafe clinical situation that would not allow the patient to safely undergo an endoscopic procedure (lack of medical clearance).
7. Pregnant or lactating women or women of childbearing potential who do not employ a reliable method of contraception as judged by the Investigator, and/or are not willing to use reliable contraception for the duration of study participation.
8. Patient is known to be currently enrolled in another investigational trial that could interfere with the endpoint analyses of this trial.

4.14 Study Withdrawal & Lost to Follow Up

Study participation is voluntary and subjects may withdraw their consent at any time. **ALL** enrolled subjects and their status in the study will be included in the study reports.

- **Treated and Study Criteria Not Met:** Subjects who are enrolled and treated, but who are later discovered to not meet all of the study criteria, will remain in the study and complete all of the study testing and follow-up requirements. A protocol deviation will be completed for study subjects who are

found to be ineligible after enrollment. These subjects may be excluded from the Per Protocol analysis depending upon the nature of the protocol deviation.

- **Patient Withdrawal:** Participation in any clinical investigation is voluntary and a patient is allowed to discontinue their participation at any time. Subjects may withdraw at their own discretion with or without reason and without any impact on their continued medical care. If a patient voluntarily withdraws from the study, no additional medical data will be collected, and the patient will not continue in the study.
- Subjects who withdraw from the study will not be replaced; however, if a patient withdraws their consent **BEFORE** being treated with the study device (before insertion of the catheter into the endoscope), and/or before the 21 (+/-7) day follow-up, he or she will not be included in the analysis.

- **Investigator Termination:** The site Investigator may terminate the patient's procedure if it is in the patient's best interest not to continue; however, the patient is withdrawn from the study and will not be included in the analysis.

- **Lost-to-Follow-up:** A patient who does not complete follow-up requirements and does not officially withdraw from the study is considered lost-to-follow-up. This does not apply to missed visits where the patient misses one of the follow-up contact time points but completes the subsequent one. In order to consider a patient lost-to-follow-up, site personnel should make all reasonable efforts to locate and communicate with the patient. All attempts to contact the patient must be recorded in the study notes, including the date, time, and name of site personnel who have attempted to contact the patient.

5.0 STUDY PROCEDURES

5.1 Overview of Study Procedures

Refer to **Appendix 1** for a Schedule of Study Assessments.

5.1.1 Baseline Evaluation

The following baseline evaluations will be assessed and recorded on all subjects who provide written informed consent:

- Demographic information and medical history including risk factors
- Pregnancy test within 1 day of the procedure
- Assessment against Inclusion/Exclusion criteria
- Medical clearance before the procedure
- Contrast-enhanced, high resolution vascular CT demonstrating at least 30% of necrotic debris in walled off necrosis
- Quality of life per SF-36 questionnaire

5.1.2 Baseline Demographics and Relevant Medical History

The subject's demographic information and relevant medical history will be documented in the subject's source medical record and on the appropriate case report form (CRF). This will include the subject's:

- Age
- Gender

- Height
- Weight
- Race and Ethnicity Information
- Relevant medical history
- Physical Examination

5.2 Laboratory Tests

Results from the subject's following laboratory tests will be documented in the subject's source medical record and on the appropriate CRF:

- Urine pregnancy test if female of child-bearing age within 1 day of procedure

5.3 Index Procedure

5.3.1 Eligibility

The Investigator will verify informed consent and confirm the subject meets all inclusion / exclusion criteria. The Investigator, or designee, will record in the subject's source medical record that informed consent was verified, and all inclusion / exclusion criteria were confirmed prior to the index study procedure.

5.3.2 Imaging

Current standard of care for diagnosis of WOPN in patients requires contrast enhanced, high resolution vascular CT scan. Imaging should fall within the following characteristics, per the 2012 Revised Atlanta Classification and can be completed up to 2 weeks in advance of the procedure:

- Heterogeneous with liquid and non-liquid density with varying degrees of loculations (some may appear homogeneous)
- Well defined wall
- Location intra-pancreatic and/or extra-pancreatic

5.3.3 Screen Failures

Enrolled subjects failing to meet inclusion / exclusion criteria at the time of index procedure will not be treated with the EndoRotor® device and; therefore, are classified as screen failures. Any baseline study data captured in the CRFs will be collected. Only subjects in whom the EndoRotor® catheter will be followed and study data analyzed.

5.3.4 Index Procedure

The investigators shall follow the technique described by the manufacturer's instructions as provided in the Instructions for Use. Following stent placement and once the clinician determined removal of necrotic debris should be completed, direct endoscopic necrosectomy of the WOPN will be performed within 2 weeks of enrollment with video documentation of the necrotic debris at start of the procedure. For patients with LAMS, a therapeutic gastroscope must be able to pass through the LAMS necessitating a minimum stent diameter to accommodate the gastroscope such as a 15mm. If a LAMS is used, it must be removed within 60 days per manufacturer's labeled instructions for use.

The EndoRotor® will be set-up and used to resect the WOPN. The resection is removes all accessible necrotic debris wherever the endoscope can provide access. No resection is performed on the pancreatic wall during this procedure. Multiple debridement procedures can be performed to remove necrotic tissue as required.

The EndoRotor® is set to either High Speed (1700 RPM) or low speed (1000 RPM) based on user preference and the vacuum is set to between 550 mmHg of negative pressure. The endoscopist will start the EndoRotor® motor using the left foot pedal and will activate the cutting by depressing and holding the right pedal down for as long as he wants to resect. The technique is repeated until the entire gross visible necrotic debris has been removed to present a cavity clear of necrosis.

5.3.5 Procedural Details

Following placement of EUS guided drainage and determination of the subjects meeting I/E criteria a direct endoscopic necrosectomy procedure can be performed at least 2 days following the EUS guided drainage. During the index procedure the EndoRotor® will be set-up and used to resect all visible and accessible necrotic debris. No resection is performed on the pancreatic wall during this procedure. Multiple procedures can be performed to remove necrotic tissue as required.

Details of the subject's index procedure will be documented in the subject's source medical record and on the appropriate CRF, including:

- Date of Procedure
- Method and Type of Sedation
- Verification of resection results
- Time of endoscope insertion and beginning of EndoRotor use
- An estimate of the percent reduction of the necrosis achieved with the EndoRotor based on endoscopic images
- Time the Procedure was Completed (end of EndoRotor use and time endoscope removed)
- Lot and Serial Number of the EndoRotor® console and catheter
- Any Adverse Events

5.3.6 Post-Procedure Evaluations

Subjects will be discharged from the hospital upon satisfactory completion of all post-procedure recovery requirements as defined by the investigational site's standard protocol and satisfactory resolution of subjects WOPN status.

Adverse events will be recorded in the subject's source medical record and on the appropriate CRF as they are observed.

In addition, hospital utilization will be tracked including total days to discharge and number of procedures completed.

5.4 Subject Follow-Up

If at any point during post-procedure subject follow-up, a subject's clinical presentation jeopardizes the safety or welfare of the subject, the Investigator should act in the best interests of the subject, utilizing any and all means judged medically necessary.

5.4.1 Follow-Up Scenarios

There are several scenarios with respect to each individual subject's timeline relative to the severity and volume of WOPN requiring direct endoscopic necrosectomy.

Scenario 1 – Adequate removal of necrotic debris at index procedure. The subject undergoes a

treatment and returns in 21 (+/-7) days for follow-up.

Scenario 2 – Removal of necrotic debris requiring a maximum of 4 endoscopic debridement procedures. The subject undergoes additional treatment(s) with a minimum of 2 days between treatments over a 14 (+7/-0) day period based on endoscopic verification that less than 70% of the necrotic debris has been removed. The subject returns in 21 (+/-7) days following the last debridement procedure performed.

5.4.2 Follow-up Visit 21 Days (± 7 days)

All subjects will return to the clinic for the 21 (+/-7) day visit as determined from the last EndoRotor procedure. Results of the following study procedures will be recorded in the subject's source medical record and on the appropriate CRF:

- CT Scan Imaging: Record results and the percent resolution of necrotic debris in the collection being treated
- Surveillance endoscopy (only if clinically required) whereby physician can use local standard of care to continue to treat the patient if required
- Physical Exam
- SF-36 Questionnaire

All subjects will exit from the study after this visit; however, all subjects should be followed according to the Investigator's clinical standard practice guidelines for safety.

5.4.3 Unscheduled Visits

The subject may return to the outpatient clinic or phone the physician for any reason in their judgment, or in the judgment and upon request of the Investigator. Should such visit(s) occur, the Investigator will record all unscheduled visit findings, phone calls, endoscopy and laboratory results in the subject's source medical record and on the appropriate CRF.

5.5 Post Procedure Imaging

Subjects will receive a contrast enhanced, high resolution vascular CT Scan per standard of care at the 21 (+/-7) day follow up visit. The CT will also be used to measure the effectiveness endpoint to validate disease clearance in the collection being treated.

6.0 Risks / Benefits Assessment

6.1 Risks to the Patient

The EndoRotor procedure poses no new risks to the patient than the commonly used mucosal resection techniques. As with all endoscopic resection and ablation devices, the most common risks are perforation and bleeding requiring intervention. Other commonly known risks to direct endoscopic necrosectomy removal include the following:

- Stent dislodgment
- Delayed bleeding occurring after the patient has been discharged requiring hospitalization and intervention
- Undiagnosed perforation resulting in free air in the peritoneum post-procedure

Risks related to endoscopy include:

- Bleeding
- Infection
- Damage to GI tract and surrounding tissue

Risks related to anesthesia include:

- Post operative confusion
- Heart attack
- Pneumonia
- Stroke

These are all common to established mucosal resection / ablation techniques and endoscopists are well practiced in handling these events. There are no additional risks that are particular to the EndoRotor® mechanical resection device.

6.2 Mitigation Measures to Minimize Risk

All efforts will be made to minimize these potential risks by:

- Selection of qualified investigators and a qualified investigational center;
- Training the Investigator(s) on proper technique for EndoRotor® technique;
- Observation of procedures by the Interscope, Inc. and/or clinical personnel;
- Defining clear inclusion/exclusion criteria that ensure only appropriate subjects are enrolled and treated;
- Ensuring that the treatment and follow-up of subjects is consistent with current medical practice;
- Careful monitoring of adverse events, serious adverse events and device malfunctions by an Independent 3-Member Data Monitoring Committee and Interscope, Inc.;
- Scheduled monitoring visits to the investigational site; and
- Regular communication with Investigator(s) and staff.

6.3 Potential Benefits to the Patient

The potential benefits of the EndoRotor® device are as follows:

- May result in less time to resolution of WOPN
- Complete removal of necrotic debris requiring less treatments

7.0 STATISTICAL METHODS

7.1 General Principles

While this protocol does specify primary and safety endpoints, these are not meant to define subject and study success. Instead, the results of this evaluation will be used to establish the safety and efficacy profile of the EndoRotor Procedure and to evaluate the effect size for powering future clinical investigations.

Nominal and ordinal variables for each time period will be presented using frequencies and percent of patients in each category. Interval and ratio variables for each time period will be presented using means and standard deviations, median, quartiles, and minimum and maximum. For variables collected at multiple follow-up time periods, tables, which include change from baseline, will be presented at each follow-up visit.

Distributions of each continuous variable will be assessed prior to analysis and examined for normality. Data with interval or ratio scales to be analyzed that are not normally distributed will be analyzed using non-parametric statistics. Statistical tests will be performed using two-sided significance levels of 5% unless otherwise specified.

7.2 Analysis Populations

Study Population: The study population includes all subjects consented at the site. Within this population there are Screened, Safety and Treated populations.

Screened: This population includes all subjects that meet the inclusion and exclusion criteria as specified in the protocol.

Safety: This population includes all subjects in whom the EndoRotor procedure was attempted. Subjects will be analyzed according to the treatment received.

Treated: This population includes all subjects that successfully received the EndoRotor debridement procedure.

7.3 Sample Size

This study will enroll a total of 30 subjects. Sample size determination is based on the nature and objective of this study and not statistical considerations. The data will be sufficient to provide an assessment of the safety profile of the EndoRotor for DEN in WOPN as well as provide initial efficacy data to support an evaluation of the benefit/risk profile.

7.4 Statistical Analysis

7.4.1 Demographic and Baseline Characteristics

Demographic and baseline data will be summarized using summary statistics of sample size, mean, standard deviation, median, quartiles, min and max for continuous variables and proportions and frequency of patients for categorical values. Demographics will be presented for the following analysis populations:

7.4.2 Safety Analysis

All safety data will be displayed and analyzed using descriptive statistical methods. No formal inferential analysis is planned for safety comparisons. The safety endpoint is the absence of any device or procedure related serious significant adverse events (SAEs) within the 21 (+/-7) days following EndoRotor procedure. These will be presented overall and by system organ class and preferred term (PT). This will be conducted on the Safety analysis set overall. Subjects who experience more than one event in a given System Organ Class (SOC) and PT will be counted once within that SOC and PT. The total number of events and the number and percentage of subjects with each event will be reported.

Adverse Events: AEs, SAEs and UADEs will be coded using MedDRA. Treatment Emergent AEs, SAEs and UADEs are defined as events starting or worsening after start of the procedure. The number and percent of patients with Treatment Emergent AEs, SAEs and UADEs will be summarized overall and by primary SOC and preferred term (PT). Subjects who experience more than one event in a given SOC and PT will be counted once within that SOC and PT.

The number and percent of subjects with treatment emergent AEs, UADEs and SAEs will be further presented by severity and by relationship to the device or procedure. In tabulating the severity of AEs on a per subject basis, the greatest severity will be assigned to a subject should there be more than one occurrence of the same AE with different reported severities. Relationship will be categorized as unrelated, possibly, probably and definitely related. The highest level of association will be reported for subjects with different relationships for the same AE.

7.4.3 Effectiveness Analysis

Effectiveness Analysis will be assessed via the following secondary endpoints:

- Successful clearance of necrosis in the collection being treated during direct endoscopic necrosectomy where success is defined as at least 70% of the necrotic debris in the WOPN cavity is removed based on CT evaluation of the cavity at 21 (+/-7) day follow up visit.
- Assessment of total procedure time to achieve clearance of necrosis for all procedures
- Assessment of adequacy of debridement
- Assessment of total number of procedures to achieve clearance of necrosis
- Assessment of length of hospital stay and utilization
- SF-36 Questionnaire

7.5 Missing Data

Missing data within this subject cohort is expected to occur at a low rate. All efforts will be made to prevent the occurrence of missing data. Site training and regular monitoring will help to minimize missing data. Due to the sample size and nature of this pilot study, there will be no imputation of missing data. In other words, analyses will be based only on available data.

8.0 INVESTIGATOR RESPONSIBILITIES

The Site Investigators are responsible for signing the Investigator agreement prior to the commencement of the study and for ensuring that this trial is conducted according to this clinical protocol, Good Clinical Practice (GCP) Guidelines, the Declaration of Helsinki, US FDA requirements and any other local, or IRB requirements that apply to Clinical Investigations at their center.

It is the also the Investigator's responsibility to ensure that all sub-investigators and staff assisting with this study have the appropriate qualifications and that they complete training on the investigational devices and study procedures and that patient confidentiality is respected.

8.1 Institutional Review Board (IRB) Approval

The Investigator at each site is responsible for securing IRB approval for this study protocol and the Informed Consent documents prior to any patient enrollment. The local IRB for each specific institution or for multiple institutions must review and approve this study protocol and the specific Informed Consent forms to be used at that site **prior** to enrollment of the first patient. The Sponsor **must** also review and approve the final Informed Consent documents prior to their use. The Sponsor and/or their designated CRO must receive a copy of any IRB correspondence, as well as the final approval letter and the final approved Informed Consent from each IRB. Investigators are also responsible for submitting and obtaining a continuing review (at intervals not greater than once a year) of the study by their IRB.

The Investigator or clinical site staff will not make amendments to this protocol or the Informed Consent forms without **PRIOR** written approval from the Sponsor. All approved amendments must then be submitted to the local IRB and the FDA, as appropriate for approval.

8.1.1 Withdrawal of Approval

If the Investigator's IRB withdraws their approval to conduct this study for any reason, the Investigator **must** notify the Sponsor and their designated CRO as soon as possible, but in no event later than **five working days** after the withdrawal of the approval.

8.2 Informed Consent

The Investigator is responsible for ensuring that all local, national, GCP, Declaration of Helsinki, and US FDA guidelines and regulations are met when completing the informed consent process. Written, informed consent is to be obtained whenever possible for each patient **prior** to treatment. Additional details regarding the informed consent process are also available in the Section 4.8 Screening and Enrollment of this protocol.

8.3 Clinical Data Collection

Electronic Case Report Forms (eCRFs) will be used to collect complete and accurate records of the clinical data from this study according to the Good Clinical Practices (GCP) requirements. The Investigator and/or study staff under his/her direction is responsible for accurately recording the clinical data for this study and entering the data into the CRF and upload to the Sponsor's secure web server in a timely manner. The required form / report and timeframes are provided in **Table 1** below:

Table 1. Form/Report and Required Submission Timeframe

Form/Report	Required Submission Timeframe
Enrollment/Treatment Notification	Enter onto CRF and upload to Sponsor's secure web server **within 48 hours.**
Baseline and Treatment CRFs	Enter onto CRF and upload to Sponsor's secure web server **within 7 days** of the index procedure.
Discharge Data	Enter onto CRF and upload to Sponsor's secure web server **within 7 days of discharge.**
Follow-up Forms	Enter onto CRF and upload to Sponsor's secure web server **within 7 days** of follow-up visit.
Serious Adverse Events	Notify Sponsor via email **within 24 hours** of knowledge. Enter onto CRF and upload to Sponsor's secure web server within **7 Days** of knowledge.
Adverse Events	Enter onto CRF and upload to Sponsor's secure web server **within 7 days** of knowledge.
Device malfunction / Failure	Notify Sponsor via email **within 48 hours** of knowledge. Enter onto CRF and upload to Sponsor's secure web server **within 48 hours** of knowledge.
Deviations from the CIP	Enter onto CRF and upload to Sponsor's secure web server **within 7 days** of knowledge.

8.4 Device Accountability

The Sponsor will ship investigational devices only to the designated Investigators participating in this study following internal requirements, FDA IDE Conditional Approval and IRB approval. All Investigators will be responsible for providing a secure storage location for the investigational devices, supervising investigational device use, and the disposal and/or return of the investigational devices as instructed by the Sponsor. In addition, all Investigators will maintain records to document the receipt, use and disposition of all investigational devices received by their site. The Sponsor, designated monitor and/or CRO will also maintain

records of all shipments and disposition of the investigational devices. The Sponsor and/or their authorized CRO will routinely inspect the clinical site inventory records for device accountability at the clinical sites participating in this trial.

8.5 Clinical Site Records

Records to be maintained by the Investigator and research staff include:

- Clinical trial investigational plan and all amendments
- Signed clinical trial agreement
- Investigator agreements
- IRB approval letter, including informed consent documents
- IRB membership list
- Correspondence relating to the trial
- CVs for all investigators and key personnel
- Clinical monitor sign-in log
- Patient screening / enrollment log
- Training log
- Device accountability log
- Delegation of Authority log
- Lab certification and lab test normal ranges
- Reports (includes annual reports, final reports from investigator and sponsor)

The following records must be maintained for each patient enrolled in the trial:

- Signed Patient Informed Consent Form
- All completed eCRFs
- Supporting documentation of any complications and Serious Adverse Events

Interscope recommends that the investigator retain copies of procedure reports, procedure notes and the results of any interventional procedures that occur after the endoscopy procedures.

8.6 Investigator Reports

8.6.1 Serious Adverse Events (SAEs) & Unanticipated Adverse Events (UAEs)

The Investigators will report by telephone, email or eCRF any SAEs or UAEs as soon as possible, (within 24 hours) of the Investigator becoming aware of the event, to the Sponsor and the CRO. Additionally, SAEs and UAEs should be reported to the IRB and/or FDA (if applicable) per the clinical site guidelines. The Serious Adverse Event form is to be uploaded to the Sponsor's secure web server within 7 days of the event. The contact information for reporting SAEs and UAEs is provided in the Study Contact section of this protocol.

8.6.2 Device Malfunctions

The Investigators will report any Device Malfunction that occurs to Interscope as soon as possible, or within 48 hours of the Investigator becoming aware of the event. The report may be made by telephone, email or eCRF. Additionally, when a device malfunction occurs, or is suspected to occur during treatment, the Investigator must keep the device in a safe storage facility until an investigation can be completed and/or the designated monitor or a Sponsor representative directs the Investigator or study staff to return the device to Interscope for investigation.

8.6.3 Deviations from the Investigational Plan

The Investigator must notify Interscope and/or the CRO of any deviation from the Investigational Plan by completing the eCRF. The Investigator should also notify the IRB and/or FDA as required per their local requirements. This notice must occur as soon as possible, but in no case longer than five working days after the Investigator becomes aware of a serious deviation. Serious deviations include those that involve the informed consent process, the inclusion/exclusion criteria of the study or any deviation that involves or leads to a serious adverse event in a study participant.

8.7 Clinical Site Reports

Investigators are required to prepare and submit to Interscope complete, accurate and timely reports on this investigation when necessary according to **Table 2** below:

Table 2. Responsibilities for Preparing and Submitting Reports

Type of Report	Prepared by Investigator for	Time of Notification
Enrollment/Treatment Notification	Interscope	Within 48 hours. Automatic email notification is sent to Interscope.
Serious adverse events	Interscope, IRB	Within 24 hours of knowledge of event
Unanticipated complications	Interscope, IRB	If serious or life threatening within 24 hours of knowledge of event
Patient withdrawal	Interscope	Within 10 working days
Withdrawal of IRB approval	Interscope	Within 5 working days
Annual progress report (Enrollment, SAE/UADE reports)	Interscope, IRB	Submitted annually
Protocol Deviations	Interscope, IRB	Within 7 working days
Informed consent not obtained from patient	Interscope, IRB	Within 5 working days
Final report	Interscope, IRB	Within 3 months

Other information upon the request of the IRB, FDA, or Interscope	As appropriate	As requested

8.8 Investigator's Final Report

Upon completion or termination of the Interscope Study the principal investigator must submit a final written report to Interscope and the IRB as required by the IDE regulations. The report must be submitted within 3 months of completion or termination of the trial. The investigator's final report will include a summary of the enrollment, SAE and UADE reported during the trial and overall impression of study outcomes.

8.9 Deviations from Protocol

The investigator will not deviate from the protocol without the prior written approval of Interscope except in medical emergencies or in unforeseen, isolated instances where minor changes are made that will not increase the patient's risk or affect the validity of the trial. In medical emergencies, prior approval for protocol deviations will not be required; however, Interscope's CRO must be notified within 5 days of the incident.

8.10 Site Record Retention Policy

Records and reports will remain on file for a minimum of two (2) years after the latter of either the completion/termination of the investigational trial or the date the investigational device receives FDA clearance. They may be discarded upon notification by Interscope. To avoid error, the principal investigator should contact Interscope before the destruction of any records and reports pertaining to the trial to ensure they no longer need to be retained.

In addition, Interscope should be contacted if the principal investigator plans to leave the investigational site so that arrangements can be made for transfer of records and the remaining follow-up (if any) in the study.

8.11 Investigator Access to the Data and Publication Policies

At the conclusion of the trial, a multicenter publication/presentation reporting the primary results will be prepared and presented at a major medical meeting. A multicenter publication will also be prepared for publication in a reputable scientific journal. The publication of results from any single center experience within the trial is not allowed until the multicenter results have been prepared, presented and submitted for publication (normally 1 year following the completion of the study). The analysis of other pre-specified and non-pre-specified endpoints will be performed by Interscope. For purposes of timely abstract presentation and publication, such secondary publications will be delegated to the appropriate principal authors, and final analyses and manuscript review for all multicenter data will require the approval of the Interscope. The ENDOROTOR study will be registered with Clinicaltrials.gov per applicable requirements.

9.0 SPONSOR RESPONSIBILITIES

9.1 Role of Interscope

As the study Sponsor, Interscope, Inc. is responsible for the overall conduct and quality of the study, including the assurance that the study complies with the appropriate standards and regulations that apply to medical device clinical investigations. Interscope will also ensure adherence to the Sponsor general duties as outlined by GCP standards and the US FDA standards. Additionally, the Interscope study management will ensure that qualified monitors are monitoring the study according to the protocol, GCP standards and study regulations, and that the Informed Consent process is followed per each site's local and US FDA requirements.

9.2 General Duties (21 CFR 812. 40)

Interscope general duties, either directly or as delegated to its CRO, consist of submitting the IDE application to FDA and obtaining FDA approval for the IDE prior to shipping devices, selecting qualified investigators and clinical sites, ensuring that each site has obtained IRB approval prior to shipping devices to that site, ensuring proper clinical site monitoring and GCP compliance, and ensuring that informed consent is obtained for each enrolled patient.

Interscope will also ensure adherence to the FDA regulations and the Sponsor general duties (21 CFR 812.40), selection of investigators (21 CFR 812.43), monitoring (21 CFR 812.46), supplemental applications [21 CFR 812.35 (a) and (b)], maintaining records [21 CFR 812.140 (b)], and submitting reports [21 CFR 812.150 (b)].

Interscope will collect quality data that satisfies federal regulations including serious unanticipated adverse events and deviations from the protocol. Interscope will prepare written progress reports and a final study report at the completion of the study.

9.3 Selection of Clinical Sites & Investigators

Interscope will select qualified clinical sites and Investigators who are experienced in interventional endscopic ultrasound, endoscopic ultrasound guided pancreatic fluid collection drainage and walled off necrosectomy debridement. The Investigator must work with an IRB to oversee the rights, safety and welfare of the study participants. The clinical site must also have an adequate patient population and the appropriate staffing and equipment to meet the requirements of the study protocol and the expected enrollment time frames. In addition, the clinical site must have staff dedicated to required data capture, entry and required study record keeping. All sites will be pre-qualified by the Sponsor or its CRO. Financial disclosures will be collected from all investigators during the site qualification process.

Interscope will ship devices only to participating investigators, obtain a signed Investigator's Agreement and provide the investigators with the information necessary to conduct the study.

9.4 Investigator & Staff Training

Training of the Investigators and clinical study staff is the responsibility of the Sponsor, Chief Medical Officer, designated monitors and/or the CRO. Training may be conducted during an Investigator meeting, a site initiation visit, or appropriate training venues. Investigators and study staff will undergo training on the study devices and study protocol prior to participating in the study. Training may encompass didactic information regarding the study devices as well as hands-on practice. Study enrollment will not be opened until all training has been completed and documented on the training log. Procedural technique and experience with the Interscope device will be assessed by the Trainer during the first case at each site. Observations during the cases will also be discussed with the Investigator and study staff. Study and support staff at the clinical site will also be trained on the study protocol, eligibility criteria, the Instructions for Use, and proper storage of the device and supplies.

9.5 Monitoring

The assigned CRO will monitor the study and will select or designate clinical monitors who are qualified by training and experience, to monitor and oversee the conduct of the ENDOROTOR study. The clinical monitors will follow the Sponsor's standard operating procedure for monitoring and the Monitoring Plan to be written on a risk-based approach for this study. The Monitoring Plan will require evaluation of compliance with the

protocol, GCP compliance, FDA regulations, and any specific recommendations made by the site's IRB and the signed Investigator and Study Agreements. Periodic phone contacts, site visits, and intermittent remote visits will be conducted to ensure that the protocol is being followed. The clinical monitor(s) will also verify that the electronic Case Report Forms (eCRFs) are in agreement with the source documentation and other records.

On-site and intermittent remote monitoring of all study sites will be frequent enough to ensure continued acceptability of the data by assessing compliance of the site to the Investigational Plan, adherence to the data collection procedures, and maintenance of study records. If necessary, appropriate corrective action will be taken to ensure adherence to the study protocol.

For record verification purposes, the monitor and/or authorized Sponsor representative will be provided access to hospital records, original laboratory data, and other records and data as they relate to the study and as agreed to with the Investigator prior to the initiation of the trial. The Investigator will also make available to the clinical monitor all regulatory documents, all completed CRFs, informed consent documents, source documentation and other relevant records for all enrolled subjects at the site. It is important that the Investigator and other relevant site personnel are available for consultation with the clinical monitors during the monitoring visits and that sufficient time is devoted at the site to the monitoring process.

If the Sponsor and/or their authorized representatives becomes aware that an Investigator is not complying with the study protocol, the Investigator Agreement, the Declaration of Helsinki, GCP standards, applicable privacy standards, or any condition of the study imposed by the IRB or the FDA, the Sponsor or their authorized representatives will immediately secure compliance or discontinue further shipments of the study devices. An inability to secure compliance and/or to complete an investigation into the factors that are inhibiting compliance may result in the Investigators termination from the study by the Sponsor.

Study close-out visits will be conducted after the final follow-up visit is completed at each site. Following the resolution of any outstanding data discrepancies and adverse events, the remaining investigational study devices will be the collected and returned to the Sponsor. A final study report will be generated and submitted to the Investigator and the appropriate study oversight authorities. Study document retention requirements will be reviewed with each site during the close-out visit.

9.6 On-Site Audits

In accordance with GCP and US FDA requirements, a Sponsor or CRO representative may request access to all study records, including source documents, for inspection and duplication. In the event that an Investigator is contacted by a regulatory agency or local IRB in relation to this study, the Investigator will notify the Sponsor or designated monitor/CRO as soon as possible.

The Investigator and/or designees must be available to respond to reasonable requests by authorized Sponsor, CRO and regulatory agency representatives during the monitoring and inspection process. The Investigator must provide the Sponsor and CRO with copies of all correspondence that may affect the review of the current study (i.e. Inspection Observations) or their qualification as an Investigator in clinical studies conducted by the Sponsor. The Sponsor will provide any needed assistance to the clinical site for regulatory audits.

9.7 Records & Record Retention

The Sponsor and/or designated monitor/CRO will maintain copies of correspondence, Investigator

Agreements, clinical data, device shipments, clinical events (AEs, SAEs, and UAEs), adverse device effects and other records related to the clinical trial and supporting documentation, and other records and reports related to this clinical study.

The Sponsor, core Laboratories and clinical sites will maintain the study records until 2 years after the final study report is completed, or longer if required by local or national regulatory agencies. The Sponsor and/or CRO will notify each site regarding the regulatory requirements for record retention during the study close-out visit.

9.8 Sponsor Reports

Interscope, Inc. will submit the required FDA reports identified in 21 CFR 812.150 (B). This includes unanticipated adverse device effects, withdrawal of IRB or FDA approval, current Investigator list (every 6 months), annual progress reports, recall information, final reports and protocol violations.

9.8.1 Study Data Reports

All information and data generated in association with the study will be held in strict confidence and remains the sole property of the Sponsor. The Investigator agrees to use this information for the sole purpose of completing the study and for no other purpose without prior approval of the Sponsor.

Upon receipt of the final study data and the final reports from each center, the Sponsor will complete a final study report. Copies of the final report will be provided to each Investigator.

9.9 Supplemental Applications

As appropriate, the Sponsor will submit changes to the study protocol to the FDA and to the Investigators to obtain IRB re-approval.

9.10 Coverage of Patient Expenses

The treated subjects will not be compensated for their time during the trial. The Sponsor may provide reimbursement for modest out-of-pocket patient costs associated with travel, parking, or other expenses associated strictly with completing the protocol requirements of this study that would not normally be covered under routine medical coverage for the patient's underlying medical condition if such reimbursement is approved in writing by the local IRB prior to study enrollment.

10.0 QUALITY ASSURANCE & ETHICAL STANDARDS

The study will be conducted according to the Declaration of Helsinki, Good Clinical Practice Guidelines (GCP), US FDA regulations, and any additional IRB requirements that apply to clinical investigations of medical devices. As the study Sponsor, Interscope has the overall responsibility for the conduct of the study, including the assurance that the study is in compliance with these guidelines, standards and requirements.

10.1 Medical Monitor

To meet the ethical responsibilities and standards for research subjects, the Medical Monitor (Sponsor's Chief Medical Officer) will review all adverse events, serious adverse events, unanticipated adverse device effects, and in conjunction with the engineering department any device performance report, failure or malfunction that could potentially impact the treatment of, or the clinical outcomes of subjects enrolled in the study. In the event that further investigation is required for any significant clinical or device performance issue that is identified in the trial the Medical Monitor or Sponsor's Regulatory Representative will initiate a corrective and

preventative action (CAPA) procedure within the Interscope Quality Management System to further investigate and resolve the occurrence.

10.2 Safety Monitoring & Study Termination

The Medical Monitor will closely monitor current medical practice, device performance, and the occurrence of and rate of occurrence of adverse events, serious adverse events, and unanticipated adverse device effects to determine if there is an unreasonable risk to the study participants. If warranted, the study protocol may be amended, and/or the study may be suspended or terminated early.

An independent Data Monitoring Committee (DMC) consisting of at least three members will review serious adverse events and safety endpoint events. Adjudication of adverse events will be conducted according to a Data Monitoring Committee Charter to be approved by the Sponsor and the DMC. The Charter will include:

- Stopping rules
- Planned Safety Reviews: Safety reviews will occur at predetermined intervals
- Unplanned Safety Reviews: Any safety concerns that arise during the trial will be brought to the attention of the IPA. A full DMC meeting can be called at the discretion of the DMC Chairperson. The DMC Chairperson may also request additional data reviews when considered necessary to monitor the progress of the trial.
- DMC reports are to include:
    - Rates of recruitment, ineligibility, noncompliance, protocol violations and dropouts, overall and by study site;
    - Completeness and timeliness of data;
    - Duration of follow-up and early study discontinuation;
    - Baseline characteristics and demographics;
    - Medical History;
    - Device data;
    - Adverse Events;
    - Serious Adverse Events; and
    - Unanticipated Adverse Device Effects
    - A significant difference in safety or effectiveness between the EndoRotor and the control devices
    - Decision on continuing or stopping the study based on safety and effectiveness of the study device and the control devices

The stopping rules for the study are as follows:

> The study will be suspended in the event of an occurrence of a perforation, pancreatic leak, or procedural bleeding related to the EndoRotor debridement procedure that is not amenable to endoscopic intervention. If the DMC and FDA determine that the event was not related to the EndoRotor debridement procedure the study will be allowed to resume.

The DMC will be determined prior to the study and records of event review will be documented and maintained in the study records. The DMC will be completely independent of the Sponsor and the ENDOROTOR study. The Sponsor may terminate Investigator and site participation in the study if there is evidence of an Investigator's failure to maintain adequate clinical standards or evidence of continued serious protocol deviations.

10.3 Data Management

All required data for this clinical study will be recorded via a validated database. This database complies with GCP requirements, laws and regulations applicable to the conduct of clinical trials, ISO 14155, and 21 CFR 11 (US Code of Federal Regulations) pertaining to the use of electronic records and signatures. System training for all research coordinators and Investigators will be conducted through instructor-led training supported with an on-line training module.

Incoming data will be frequently reviewed to identify inconsistent or missing data and any adverse events. Investigators are responsible for the accurate completion and timely submission of the data collected during this trial. Any data issues are to be promptly addressed with the Investigator by the study manager, designated monitor/CRO and/or Sponsor.

Clinical procedures have been established to ensure that complete, accurate and timely data are submitted, that protocol requirements are followed and that adverse events are correctly reported and investigated. Investigators are to maintain all source documents as required by the protocol, including laboratory results, supporting medical records and signed Informed Consent forms. The source documents will be verified during regular monitoring visits to ensure that the clinical data is complete and accurate.

10.4 Adverse Events & Definitions

A complication is defined as any clinical finding that has the potential to become clinically significant in the opinion of the investigator. A complication may progress in the level of clinical significance and become classified as an adverse event. All complications shall be recorded on the CRFs.

Adverse Events (AEs) are clinical findings that result in an untoward medical event.
Please record all AEs on the CRFs. Adverse Events will be further classified as Serious Adverse Events (SAEs) if the event:

- Is life threatening or fatal;
- Results in permanent impairment of a body structure or function;
- Results in congenital anomalies/birth defects
- Requires or prolongs hospitalization; or
- Requires medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

Note: Hospitalization is defined as any initial admission (even if less than 24 hours) to a healthcare facility as a result of a precipitating clinical adverse effect; to include transfer within the hospital to an intensive care unit. Hospitalization or prolongation of hospitalization in the absence of a precipitating, clinical adverse effect (e.g., for a preexisting condition not associated with a new adverse effect or with a worsening of the preexisting condition; admission for a protocol-specified procedure) is not, in itself, a serious adverse effect. The following definitions for rating severity of adverse events will be used:

Mild: Awareness of signs or symptoms, but easily tolerated; are of minor irritant type; causing no loss of time from normal activities; symptoms would not require medication or a medical evaluation; signs or symptoms are transient.

Moderate: Interferes with the subject's usual activity and/or requires symptomatic treatment.

Severe: Symptom(s) causing severe discomfort and significant impact of the subject's usual activity and requires treatment.

AEs or SAEs will also be classified as to their relationship to the device, as follows:

Not Related: The event is due to an underlying or concurrent illness or effect of another device, drug or intervention and is not related to the investigational device, procedure or general surgery.

Possible: The event has a strong temporal relationship to the use of the investigational device, procedure or general surgery, and an alternative etiology is equally or less likely.

Probable: The event has a strong temporal relationship to the use of the investigational device, procedure or general surgery and another etiology is unlikely or significantly less likely.

Definite: An event that can only be attributed to the use of the investigational device, procedure or general surgery.

Not Assessable: The event's relationship to the use of the investigational device, procedure or general surgery cannot be assessed.

If an AE or SAE is determined to be probably or definitely related to the investigational device and has not been previously anticipated, the clinical finding would further be classified as an unanticipated adverse device effect (UADE). A UADE is defined as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects."

SAEs that are determined to be probably or definitely related to the investigational device are referred to as device-related serious adverse events (DRSAEs). The protocol definitions for "device failure", "device malfunction", and "technical observation" are provided below:

Device Failure: A device has failed if it does not perform according to the Instructions for Use provided with the device and as a result, negatively impacts the treatment, when used according to this protocol. A device failure that causes or contributed to a serious adverse event would be classified as a DRSAE.

Device Malfunction: A device malfunction is an unexpected change to the device that is not contradictory to the labeling and may or may not affect the performance of the device. A device malfunction is not considered to be a DRSAE unless it causes or contributes to a serious adverse event. **Technical Observation:** Malfunction or complaint with a medical device that has the potential to, but may or may not result in, a negative clinical consequence to the patient.

> **Note:** A device failure or device malfunction is considered to be a DRSAE if it causes or contributes to a SAE.

Any Device Failure, Device Malfunction or Technical Observation must also be documented in the CRFs.

10.5 Reporting of Adverse Events

All adverse events, including SAE's and UADE's, will be monitored from the time of enrollment through the

study exit. A description of the event, including the start date, resolution date, action taken, and the outcome shall be provided, along with the Investigator's assessment of the relationship between the AE and the study device and procedure.

All AE's should be followed until the event is resolved or judged to be clinically stable. The clinical site should plan to provide additional, relevant AE follow-up information to the Sponsor upon request.

All SAEs, DRSAEs, and UADE's must be reported to the Sponsor and/or CRO and the primary Investigator at the site **within 24 hours** of the Investigator becoming aware of the event. Additionally, the Investigator should notify their IRB, and local/national authorities as required, within their specified timeframes. The Sponsor and CRO will decide whether all of the local Investigators need to be informed immediately, or whether this can be postponed until the next regularly scheduled study update.

A completed SAE CRF **must** be uploaded to the Sponsor's secure web server **within 7 days of the event**. The minimum required data to be recorded for an SAE includes: date of event, type of event, duration of event, severity, seriousness, action taken, outcome, causality and relationship to the Interscope device and procedure. In the case of a DRSAE, whenever possible, the device involved in the failure or malfunction is to be returned to Interscope for analysis.

10.6 Privacy and Confidentiality

Privacy and confidentiality of subjects will be maintained throughout the Interscope ENDOROTOR trial. A unique identification code will be assigned to each patient participating in this trial. Access to the patient's medical records will be limited to authorized personnel of the Sponsor, their designated CRO, clinical site study staff and authorized regulatory authorities as required by the EC and/or local or national agencies. Any data that may be published in abstracts or scientific journals, and/or presented at medical meetings will reference a unique patient code and will not reveal the patient's identity. The Sponsor and their representative (CRO) will make every reasonable effort to protect the confidentiality of the subjects participating in this study.

11.0 STUDY DATA REPORTING AND PROCESSING

11.1 Data Entry, Cleaning and Editing

Development of a validated database for the trial will be performed by Interscope and/or its CRO. Interscope will also be responsible for auditing the database and confirming the overall integrity of the data.

Single data entry into the database will be done by Interscope and/or its CRO. All study records and CRFs will be subjected to initial inspection during routine monitoring visits for omitted data, gross data inconsistencies, and deviations. Any deficiencies or deviations will be resolved by the site. Any discovered errors are referred to the clinical site research coordinator for correction through a Data Clarification Form.

11.2 Final Data Analyses

All exported datasets for analyses by SAS will undergo a final data cleaning procedure using SAS programmed logical routines unique to each exported dataset.

12.0 BIBLIOGRAPHY

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3. Van der Wiel et al, Erasmus Medical Center; A Novel tool for fast and effective removal of pancreatic necrosis. Digestive Disease Week 2018. Poster Number TU1440-A
4. Kumar, et al. Direct Endoscopic Necrosectomy Versus Step-Up Approach for Walled-Off Pancreatic Necrosis: Comparison of Clinical Outcome and Health Care Utilization, Pancreas. 2014 November ; 43(8): 1334–1339. doi:10.1097/MPA.0000000000000213.
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6. Seifert, H., et al, Transluminal endoscopic necrosectomy after acute pancreatitis: a multi-centre study with long-term follow-up (the GEPARD Study); Gut 2009 58: 1260-1266 originally published online March 11, 2009 doi: 10.1136/gut.2008.163733

APPENDIX 1 – SCHEDULE OF STUDY ASSESSMENTS

A schedule of study assessments is provided below.

	Baseline	**Index Procedure (Day 0)[2]**	**Procedures 2 through 4 14 (+7/-0) Days[3]**	**Discharge**	**21 (±7) Days[4]**
Confirm Eligibility	**X**	**X**			
Informed Consent	**X**				
Demographics	**X**				
Medical History	**X**				
Physical Examination	**X**				**x**
SF-36	**X**				**x**
Pregnancy Test[1]	**X**				
EndoRotor® Procedure		**X**	**X**		
CT Imaging (Standard of Care)	**X**				**X**
Adverse Event Assessment		**X**	**X**	**X**	**X**

[1] Urine pregnancy test for female of child bearing potential within 1 day of procedure.
[2] The index procedure must be done within 2 weeks of enrollment with outpatient video documentation of before and final results from procedure.
[3] Procedures 2 through 4 at 14 (+7/-0) days is not required if there is at least 70% removal of accessible necrotic debris in the collection being treated.
[4] Visit based on 21 (+/-7) days from last EndoRotor procedure

APPENDIX 2 - DEFINITIONS

Adverse Device Effect (ADE): An adverse device effect is defined as any untoward adverse event related to the use of an investigational or unintended response to a medical device.

NOTE 1: This definition includes adverse events resulting from insufficient or inadequate Instructions for Use, deployment, installation, operation, or any malfunction of the medical device. This definition includes any event resulting from insufficiencies or inadequacies in the Instructions for Use or the deployment of the device or any event that is a result of user error.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the medical device.

Adverse Event (AE): An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the study device/procedure.

Anemia: Decrease from baseline in red blood cells, hemoglobin, or total blood volume that is associated with hemodynamic changes or requires transfusion, or a drop in hematocrit to below 30%. Any documented anemic event requiring ≥2 units PRBCs will be considered an SAE.

Bleeding Complication at Index Procedure: Bleeding requiring intra-procedure intervention is not considered a serious adverse event and while it can occur it can be managed intra procedurally.

Death: (divided into 2 categories)

A. Cardiac death is death due to any of the following:

1. Acute myocardial infarction.
2. Cardiac perforation/pericardial tamponade.
3. Arrhythmia or conduction abnormality.
4. Stroke within 30 days of the procedure or stroke suspected of being related to the procedure.
5. Death due to complication of the procedure, including bleeding, vascular repair, transfusion reaction, or bypass surgery.
6. Any death for which a cardiac cause cannot be excluded.

B. Non-cardiac death is a death not due to cardiac causes (as defined immediately above).

Delayed Bleeding: Bleeding occurring after the patient has been discharged requiring hospitalization and intervention.

Bleeding that occurs post-procedure requiring intervention.

Device Failure: A device that is used in accordance with the Instructions for Use, but does not perform according to the Instructions for Use and negatively impacts the treatment.

Device Malfunction: A malfunction of a device is an unexpected change to the device that is contradictory to the Instructions for Use and may or may not affect device performance. Includes damage, stress fracture or other failure as observed at the procedure.

Endoscopy: An examination or procedure using an endoscope to examine the inside of the alimentary tract.

Infection, systemic: Systemic infection documented by positive lab culture or clinical evidence, requiring medical treatment to treat and resolve.

Perforation: Puncture of the alimentary tract.

Serious Adverse Device Effect (SADE): A serious adverse device effect is defined as an adverse device effect that results in any of the consequences characteristics of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune.

Serious Adverse Event (SAE): A serious adverse event (SAE) is defined an adverse event that:

- led to death,
- led to a serious deterioration in the health of the subject, that either resulted in:
- a life-threatening illness or injury, or
- resulted in a permanent impairment of a body structure or a body function, or
- required in-patient hospitalization or prolongation of existing hospitalization, or
- resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function, or,
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the study plan without serious deterioration in health, is not considered a serious adverse event.

Sepsis: Organ dysfunction, hypoperfusion, or hypotension in the presence of a known or suspected infection.

Unanticipated Adverse Device Effect (UADE): A UADE is an event that occurs that has not been expected to occur with the device or during the course of the study procedures and has not otherwise been identified as a possible risk in the clinical investigations.