# A Prospective, Post-Market, Multicenter, Randomized Controlled Trial to Compare the Performance of the EndoRotor® System Versus Conventional Endoscopic Techniques for Direct Endoscopic Necrosectomy of Walled Off Necrosis

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To assess the performance of the EndoRotor, as compared to conventional endoscopic techniques, for direct endoscopic necrosectomy (DEN) of walled off necrosis (WON)

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Gastrointestinal therapeutic procedures |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON52160

**Source**
ToetsingOnline

**Brief title**
The RESOlVE Trial

### Condition

- Gastrointestinal therapeutic procedures

**Synonym**
encapsulated pancreatic necrosis, Walled-off pancreatic necrosis

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Stichting voor Lever en Maag-Darm Onderzoek (SLO)
**Source(s) of monetary or material Support:** Interscope Medical

## Intervention

**Keyword:** EndoRotor, Necrosectomy, Pancreas, Walled Off Necrosis

## Outcome measures

### Primary outcome

Primary endpoint: Mean total necrosectomy time to achieve resolution of WON.

Necrosectomy time is measured in minutes from the start of the debridement procedure to completion of the debridement procedure, including time to swap devices, and comprises the summation of the individual necrosectomy times in case of multiple procedures.

a. Resolution is defined as clinical improvement of WON symptoms precluding the need for additional endoscopic or surgical interventions.

d. Clinical improvement is defined according to the criteria used in the PANTER trial and TENSION trial.8,15 *Clinical improvement* was defined as:

i. Improved function of at least two organ systems (i.e. circulatory, pulmonary, renal) according to the Investigator*s medical judgement within 72 hours of the procedure, or;

ii. At least 10% improvement of two out of three parameters of infection (i.e. C-reactive protein, leucocyte count or temperature) within 72 hours of the procedure.

Deterioration of these parameters by other infectious causes (e.g. urinary tract infection) were excluded. Clinical failure was defined as the absence of clinical improvement or clinical deterioration.

**Secondary outcome**

The following secondary endpoints will be summarized using descriptive statistics. Any testing done to compare EndoRotor to conventional DEN will be considered hypothesis generating in nature.

1. The occurrence of all adverse events measured from the Index Procedure through the 6 Month Post Necrosectomy Follow-up Visit.

2. Conversion of DEN to surgery.

3. Length of hospitalization measured in days from the Index Procedure, including days in intensive care unit (ICU) vs. standard in-patient hospitalization.

4. Mean total cost of care per subject including: procedure costs, debridement devices used during the procedure, and inpatient hospital stay from the date of procedure to the date of discharge based on reimbursement fee structure expressed in US dollars, Euros or UK Pounds respectively.

a. Procedure costs will be based on the cost of an endoscopic retrograde cholangiopancreatography (ERCP) which covers room, X-ray, sedation, personnel, and other materials.

5. Percent reduction in WON collection volume (cm3) as assessed by contrast enhanced computed tomography (CECT) scan or magnetic resonance imaging (MRI) (Baseline vs. completion of necrosectomy).

a. Endoscopic ultrasound (EUS) may be used for imaging only when a subject is

contraindicated for MRI and CECT.

b. WON collection volume will be measured as follows:

i. Length = longest diameter in cm/mm in the axial plane (left - right)

ii. Width = the longest diameter in cm/mm (frontal - dorsal) in the same axial

plane as the length, perpendicular on the longitudinal axis.

iii. Height = longest diameter in cm/mm on coronal plane (cranial - caudal)

6. Procedure time measured in minutes from the point of per-oral scope

insertion to scope removal (scope-in / scope-out).

7.Total number of procedures required to achieve resolution of WON. Resolution

is defined using the definition in the primary endpoint.

8. Subject quality of life (QOL) as assessed by a SF-36 questionnaire performed

at Baseline, Discharge, and at the 1, 3, and 6 Month Post Necrosectomy

Follow-up Visits.

9. Device deficiencies defined as an inadequacy of a medical device with

respect to its identity, quality, durability, reliability, safety, or

performance including malfunctions, use errors, and inadequate labelling.

# Study description

**Background summary**

Acute pancreatitis is a sudden inflammation of the pancreas. Although the cause of acute pancreatitis can vary widely between patients, severe cases can lead to the development of life-threatening complications. One of these complications is the development of infected necrotizing pancreatitis, in which part of the pancreas (pancreas) dies (necrosis) and this necrosis becomes infected (infecting). In walled-off pancreatic necrosis, the dead tissue must be removed by means of an operation, an "endoscopic necrosectomy". To remove the necrosis, instruments that have not been specifically developed for this

purpose are currently used (conventional instruments). Although it is almost always possible to remove the necrosis, the procedure often takes a long time and must be repeated several times. For this reason, we have long been looking for new instruments that facilitate the removal of dead tissue from the fluid collection and make it more effective.

The EndoRotor® (Interscope Medical, Inc., Whitinsville Massachusetts, USA) is a new automated mechanical endoscopic medical device designed for use in the gastrointestinal tract for tissue removal. Using the EndoRotor®, a motorized, rotating cutting tool, small pieces of tissue are cut, suctioned, and removed step by step.

In an earlier study, conducted at Erasmus MC in 2018, the EndoRotor® was used to treat patients with necrotizing pancreatitis. This study showed that the dead tissue could be removed with fewer treatments and that the patients recovered quickly after treatment with the EndoRotor®.
In a second study, conducted in 2019 at Erasmus MC and in various hospitals in the United States, a larger group of patients was treated with the EndoRotor®. This research also showed that the dead tissue could be removed safely and with fewer treatments. This indicated that the good results of the first study could also be achieved in other centers.

This new study is being conducted to directly compare the EndoRotor® system (the examination tool) with current conventional instruments for removing dead tissue in patients with walled-off pancreatic necrosis. The EndoRotor® system is expected to require fewer interventions than conventional instruments to remove dead tissue in the walled-off necrosis. In this current study, the subjects will be divided into two groups: one-half of the subjects (30 subjects) will be treated with the EndoRotor®, the other half of the subjects (30 subjects) will be treated with the conventional instruments. This allows us to directly compare the outcomes of the treatment and this is important before recommending this technique with the EndoRotor® even more widely to fellow doctors around the world as a safe and effective method for removing necrosis in patients with acute pancreatitis.

## Study objective

To assess the performance of the EndoRotor, as compared to conventional endoscopic techniques, for direct endoscopic necrosectomy (DEN) of walled off necrosis (WON)

## Study design

This study is a prospective, post-market, multicenter, randomized controlled trial to assess the performance of the EndoRotor, as compared to conventional endoscopic techniques, for direct endoscopic necrosectomy (DEN) of walled off

necrosis (WON).

A total of 60 subjects will be enrolled for this study.
Thirty subjects will be randomized to the EndoRotor arm (*study device*), and 30 will be randomized to the conventional DEN arm (*control device*). Subjects will be enrolled at 10-20 sites in the United States (US), United Kingdom (UK), The Netherlands, France, Italy, and Germany. It is anticipated that each site will enroll up to 10 subjects over a period of 9 months.
Each subject will be part of the study for approximately 7 months. The entire study is estimated to last approximately 16 months, including 9 months of enrollment plus 7 months of follow-up from the time the last subject is enrolled.

**Intervention**

2 days following the placement of EUS Guided Drainage and determination, if the study subject meets the I/E criteria, a direct endoscopic necrosectomy procedure can occur. Subjects will be randomized in a 1:1 ratio to the EndoRotor System or conventional DEN.

- Subjects randomized to the study device arm will undergo DEN using the 5.0 mm EndoRotor Catheter as per the system Instructions for Use (IFU).
Ideally, the entire EndoRotor procedure will be completed using the 5.0 mm catheter; however, if the procedure cannot be completed using the 5.0 mm catheter the 3.2 mm EndoRotor Catheter may be used. The reason for using the 3.2 mm catheter will be recorded on the applicable CRF.
Although the EndoRotor system will primarily be used to conduct the DEN procedure, conventional DEN instruments will be allowed to complete the procedure only if the Investigator is unable to do so with EndoRotor alone.
The type of conventional DEN instrument and reason for use will be captured on the applicable CRF.

- Subjects randomized to the control device arm will undergo conventional DEN as per the SOC. Investigators will choose conventional DEN instruments according to their preference.

**Study burden and risks**

The EnoRotor procedure poses no new risks to the patient than the commonly used mucosal resection techniques, As with all endoscopic resection devices, the most common risks are associated with the EndoRotor device or procedure include but are not limited to:
* Stent dislodgement
* Bleeding
* Delayed bleeding
* Perforation

* Pneumoperitoneum
* Infection
* Tissue damage

In addition to the risks listed above, the risks related to endoscopy and anesthesia should be explained to the subject.
All efforts will be made to minimize these potential risks by implementing Risk Minimization Actions which are:
* Selection of qualified Investigators and qualified investigational centers;
* Training the Investigators on proper technique for the EndoRotor System;
* Training the Investigators and on adherence to the study protocol and system IFU;
* Observation of procedures by the Interscope, Inc. and/or clinical personnel, as needed;
* Defining clear inclusion/exclusion criteria that ensure only appropriate subjects are enrolled and treated;
* Scheduled monitoring visits to the investigational site; and
* Regular communication with Investigator(s) and staff.

Each subject will be part of the study for approximately 7 months. The entire study is estimated to last approximately 16 months, including 9 months of enrollment plus 7 months of follow-up from the time the last subject is enrolled.
The patient will have to be available for the following:
* Informed Consent Process
* Baseline Visit
* EndoRotor Procedure or Conventional DEN Procedure
* Hospitalization
* During the Hospitalization Period subjects may require additional DEN procedures for treatment of WON. For both study arms, subjects will be assessed at 72 hours post necrosectomy to see if additional procedures are required.
* Discharge
* 1 Month Post Necrosectomy Follow-up Visit
* 3 Months Post Necrosectomy Follow-up Visit
* 6 Months Post Necrosectomy Follow-up Visit

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Patients 18 years of age or greater.
2. Patients with symptomatic pancreatic necrosis due to acute pancreatitis that have an indication to
undergo endoscopic necrosectomy after having undergone EUS-guided drainage.
a. Stent must be in place for a minimum of 2 days prior to the DEN procedure.
3. Patients who can tolerate repeat endoscopic procedures.
4. 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.
5. ASA classification < 5.

## Exclusion criteria

1. Documented pseudoaneurysm > 1 cm within the WON.
2. Subject unable or unwilling to provide informed consent.
3. Intervening gastric varices or unavoidable blood vessels within the WON access tract (visible using
endoscopy or endoscopic ultrasound).

4. Coagulation disorders or anti-coagulant therapy which cannot be discontinued (aspirin allowed).
5. Any condition that in the opinion of the Investigator would create an unsafe clinical situation or stent placement that would not allow the patient to safely undergo an endoscopic procedure.
6. 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.
7. Patient is enrolled in another trial that could interfere with the endpoint analyses of this trial.
8. Prior necrosectomy on existing collection.
9. Greater than 2 pancreatic / extra-pancreatic fluid collections.

# Study design

## Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 29-03-2021 |
| Enrollment: | 15 |
| Type: | Anticipated |

## Medical products/devices used

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|---|---|
| Generic name: | EndoRotor® System (Endoscope) |
| Registration: | Yes - CE intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 11-05-2021 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-05-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

| Register | ID |
|---|---|
| ClinicalTrials.gov | NCT03694210 |
| CCMO | NL75188.078.20 |