# Self-sizing Radiofrequency ablation balloon for eradication of Barrett's esophagus: a randomized trial comparing two different treatment regimens

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Malignant and unspecified neoplasms gastrointestinal NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON45236

**Source**
ToetsingOnline

**Brief title**
Self-sizing RFA balloon for Barrett's :RCT two regimens

### Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

**Synonym**
Dysplasia in Barrett's esophagus, precancerous esophageal mucosa

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Barrett, Dysplasia, Radiofrequency Ablation

## Outcome measures

### Primary outcome

Percentage of endoscopically visual surface regression of BE epithelium at 3 months, as scored by two independent endoscopists blinded to the treatment regimen.

### Secondary outcome

1. Adverse events

2. Patient*s discomfort after RFA treatment

3. Procedure time

# Study description

### Background summary

Radiofrequency ablation is an established endoscopic technique for eradication of Barrett*s esophagus which has been investigated in a variety of study designs (including two randomized trials), and settings (US and EU, tertiary academic centers, community referral centers).
Radiofrequency ablation is associated with an acceptable safety profile, high rates of complete eradication of dysplasia and intestinal metaplasia, durability of effect, and a significant relative risk reduction for neoplastic progression. As a result, radiofrequency ablation is considered standard of care for patients with high-grade dysplasia, as well as for residual Barrett tissue after endoscopic resection of early cancer.
Currently, most patients undergo primary circumferential ablation with a balloon based electrode, the Barrx360 System, followed by additional focal ablation using a cap-based electrode, the Barrx90 System. The Barrx360 procedure starts with the introduction of a sizing balloon to measure the

internal esophageal diameter, because the ablation balloon comes in different sizes (18-31mm). The sizing balloon is used to take multiple measurements of the esophageal diameter and assists the endoscopist in choosing an ablation catheter with the appropriate diameter. Subsequently, the sizing balloon is removed and the BE segment can be treated with the ablation balloon. The advised standard treatment regimen for Barrx360 procedures consists of two ablation runs with extensive cleaning of the ablation zone after the first ablation (1x-clean-1x). The entire treatment procedure is time-consuming, as it consists of many different steps and requires multiple introductions and removals of the endoscope, sizing catheters and ablation balloons which are impractical and uncomfortable to the patient.
By incorporating the sizing balloon and the Barrx360 ablation balloon into a single device, the use of a separate sizing balloon and the need for having multiple sized balloon catheters are eliminated. The new Self Sizing RFA balloon catheter is a circumferential balloon catheter, and consists of a 4cm long bipolar electrode that is furled around a balloon. This single balloon catheter can unfurl in size ranges including 18-31mm, making it possible to size and treat the BE segment in a single step. Secondly, if the simplified ablation regimen (in which one ablation will be applied and the cleaning step is omitted) proves equally effective to the standard ablation regimen when using the Self Sizing balloon, the entire circumferential ablation procedure can be vastly improved (less time consuming and more comfortable for the patient).

## Study objective

The current study is designed to determine the most optimal treatment regimen for Barrett*s esophagus with early neoplasia, using the Self Sizing RFA balloon. In this study we will compare the standard ablation regimen (1x-clean-1x) with a simplified regimen (1x-no clean)

## Study design

If a patient is eligible for the study after one mapping endoscopy, and/or after endoscopic resection, and no abnormalities (visible lesions and/or severe stenosis) are observed during the endoscopy, the patient will undergo randomization.
Patients are randomly assigned to treatment with the standard protocol, the simple double ablation protocol or the simple single ablation protocol, using the Self Sizing RFA balloon catheter. Randomization is performed according to a computer-generated randomization sequence which is concealed from the researchers. Randomization is stratified according to prior endoscopic resection.
Randomization of eligible patients is performed on-site by the study coordinator during the endoscopic procedure after eligibility of the patient is confirmed. The study coordinator enrolls participants and assigns them to the

standard or one of the simple protocols by using the ALEA software.

Endoscopic resection at baseline
For patients with a visible abnormality mandatory endoscopic resection is performed. In case there is no suspicion on submucosal infiltration of the lesion the choice of ER technique will be left to the discretion of the endoscopist, with a preference for the ER-cap technique or endoscopic submucosal dissection (ESD) for elevated or depressed visible abnormalities and the multi-band mucosectomy (MBM) technique for flat type mucosal abnormalities. In case of suspicion on submucosal infiltration, the resection is preferably performed using the ER-cap or the ESD technique, since this will result in a larger and deeper resection specimen than with the MBM technique.
Prior to the ER procedure, the extent of columnar lined esophagus is documented according to the Prague C&M classification.
During the ER procedure, biopsies from the remaining Barrett*s segment (4Q/2cm) will be obtained immediately after the endoscopic resection, to evaluate the histological status of the remaining mucosa and to exclude the presence of cancer. Patients who show residual invasive cancer in these biopsies are not eligible for RFA.

Ablation procedure
Inspection of the Barrett*s segment and randomization.
The esophagus is evaluated using white light high-resolution endoscopy (WLE) and narrow band imaging (NBI). The extent of columnar lined esophagus is documented according to the Prague C&M classification and by taking still images with WLE+NBI at 1 cm intervals. In the absence of visible abnormalities and no severe stenosis, patients are subsequently randomized to circumferential ablation with the Self Sizing RFA balloon using the two simplified regimen or the standard ablation regimen.

Standard ablation regimen:
After mapping and randomization, the Barrett*s segment is flushed with the mucolytic agent acetylcysteine (1%) followed by flushing with tap water. The Self Sizing RFA balloon (GI Solutions Covidien, Sunnyvale, CA) is then introduced and positioned at the desired treatment zone. The device is inflated, and the electrode unfurls until the electrode contacts the esophageal wall. Under visual control the BE is ablated (10 J/cm2 at 300 Watt) working proximal to distal using visual repositioning. A small overlap (i.e. <1cm) between ablation zones is allowed. After the first ablation pass, the endoscope is removed followed by removal of the ablation catheter. The coagulum is cleaned off the balloon catheter. The endoscope is reintroduced to irrigate and suction the ablation zone. A distal attachment cap may be attached to the tip of the endoscope to gently wipe of the coagulum from the ablated segment. After irrigating and suctioning the debris away as much as possible, the ablation zone is cleaned by forcefully flushing water through a spraying catheter. The stomach is emptied and deflated, the endoscope is removed and the ablation catheter is reintroduced to repeat the ablation. After this second ablation no

additional cleaning of the ablation zone is required. First, the endoscope is removed, followed by careful removal of the ablation catheter.

Simplified single ablation regimen:
The Barrett segment will be cleaned with water through the waterjet channel of the endoscope. Flushing with the mucolytic agent acetylcysteine (1%) is not performed. The Self Sizing RFA balloon (GI Solutions Covidien, Sunnyvale, CA) is then introduced and positioned at the desired treatment zone. The device is inflated, and the electrode unfurls until the electrode contacts the esophageal wall. Under visual control the BE is ablated (10 J/cm2 at 300 Watt) once. After deflation, the balloon is advanced distally to ablate subsequent zones with a single ablation in an identical way. There is no cleaning step.

Medication and discharge regimen
All patients will be on a maintenance dose of a proton pump inhibitor (by preference esomeprazole) at a dosage of 40 mg twice a day during the whole treatment period and follow-up. This medication is supplemented with ranitidine 300 mg at bedtime and sucralfate suspension three times a day (after each meal and prior to bedtime) for a period of two weeks following all RFA procedures.
Further treatment and follow-up
At 3 months, the first post-treatment endoscopy will be performed with white light high-resolution endoscopy (WLE) and NBI. Still images with WLE+NBI will be obtained at 1-cm intervals throughout the extent of the original Barrett*s segment, to assess the percentage of endoscopically visible surface regression of BE. Further treatment and follow-up are performed according to standard guidelines. Repeat RFA treatment will be performed at 2-3 months intervals with a maximum of two Barrx360 and three Barrx90 ablation sessions. For all patients, at least one Barrx90 ablation will be performed for circumferential ablation of the squamocolumnar junction.
After complete removal of BE is achieved, patients will be scheduled for surveillance endoscopy after six months, twelve months and annually thereafter with WLE plus NBI and 4-quadrant biopsies from the gastric cardia (immediately below the neosquamocolumnar junction).

## Intervention

Radiofrequency ablation to eradicate Barrett's mucosa

## Study burden and risks

The ablation procedure with the self-sizing balloon will be less complicated, because sizing of the inner esophagus will not be performed as done in the RFA procedure according the general guidelines. Less number of introductions of the gastroscope are needed and the procedure time will shorten. During the procedure with self-sizing balloon accurate imaging before and after the ablation will increase the procedure. The two simple regimens will be even

shorter than the standard procedure with the self-sizing balloon. The balloon and endoscope will only be introduced once instead of twice.
We expect no additional risk for patients participating in the study than for patients undergoing the regular ablation.
Study patients will be asked to fill out a diary for the first 30 days after the RFA treatment. The diary consists of a list with pain symtoms.

## Contacts

**Public**
Academisch Medisch Centrum

Herestraat 4
Leuven B-3000
NL
**Scientific**
Academisch Medisch Centrum

Herestraat 4
Leuven B-3000
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

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

### Inclusion criteria

1. Patients aged 18-85 years, with biopsy proven LGD, HGD or EC in a BE after local expert pathology review.
2. Scheduled circumferential ablation for BE with flat LGD, HGD, or for BE after prior endoscopic resection (ER) for lesions containing HGD or EC (<2 cm and <50% of the

circumference).
3. Pretreatment biopsies and/or ER specimens reviewed by a local expert pathologist.
4. Written informed consent

### Exclusion criteria

1. Patients with a BE segment < 2cm or >15 cm prior to ER.
2. Any prior endoscopic ablation treatment.
3. Significant esophageal stenosis prior to initial treatment, preventing passage of a therapeutic endoscope OR any prior endoscopic dilatation for esophageal stenosis.
4. Presence of esophageal varices.
5. Anti-coagulant therapy (apart from aspirin or NSAID) that cannot be discontinued prior to ER or RFA, OR uncorrectable hemostatic disorders.
6. In case of prior ER: patients with ER of multiple lesions in a single ER session are not eligible, if one of the resections measures more than the aforementioned size criteria, OR if resections of different lesions are not separated by a free circumferential segment of at least 1 cm.
7. In case of prior ER: a specimen showing carcinoma with positive vertical resection margins, deep submucosal invasion (>T1sm1), poorly or undifferentiated cancer (G3 or G4), or lymphatic/vascular invasion.
8. In case of prior ER: invasive cancer in any of the biopsies obtained at high-resolution endoscopy after ER.
9. An interval >6 months between the last high-resolution endoscopy with biopsies and RFA.
10. An interval < 6 weeks between ER and RFA.
11. Patients unable to give informed consent.

## Study design

### Design

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| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 14-09-2015 |
| Enrollment: | 80 |
| Type: | Actual |

## Medical products/devices used

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| Generic name: | self-sizing RFA balloon |
| Registration: | Yes - CE intended use |

# Ethics review

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|---|---|
| Approved WMO Date: | 05-02-2015 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 17-07-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-03-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-05-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# 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 |
| --- | --- |
| CCMO | NL51663.018.14 |