# Long-term follow-up after RFA with or without prior EMR for early Barrett's neoplasia

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The aim of this study is to answer the question if RFA is an effective treatment modality in the long term, for patients with Barrett's esophagus containing HGIN or EC.

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

## Summary

### ID

NL-OMON36820

**Source**
ToetsingOnline

**Brief title**
5-year FU after RFA

### Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

**Synonym**
(early) esophageal cancer, Barrett's esophagus

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W,BARRX Medical Inc. 540 Oakmead Parkway Sunnyvale, CA 94085, USA

## Intervention

**Keyword:** Barrett's esophagus, Barrett's neoplasia, Long-term follow-up, Radiofrequency ablation

## Outcome measures

### Primary outcome

- Rate of complete histological remission of dysplasia and cancer

- Rate of complete endoscopic and histological eradication of IM

(including biopsies obtained from neosquamous mucosa)

### Secondary outcome

- Prevalence of subsquamous IM in neosquamous biopsies and ER-specimens

- Prevalence of IM below the Neo Z-line during 5-year follow-up visits

- Adverse events

# Study description

### Background summary

A relatively new form of endoscopic ablation therapy for Barrett's epithelium, is radiofrequency ablation (RFA), by using radiofrequency energy the mucosa can be ablated up to the superficial submucosa. Afterwards the mucosa regenerates with neo-squamous epithelium (NSE). In patients with non-dysplastic Barrett's esophagus (BE), RFA has been demonstrated to be safe and effective in the short- and long term (5 years) for eradication of IM, when applied for BE containing low-grade intraepithelial neoplasia (LGIN) results are similar, with favourable rates for complete eradication of dysplasia and IM. Furthermore, RFA is a modality with a low complication rate, low rate of esophageal stenosis and pre-existing genetic abnormalities in BE are absent in the NSE that regenerates after RFA.

To investigate whether RFA can be used effectively to treat patients with high-grade intra-epithelial neoplasia (HGIN) or early carcinoma (EC), in combination with endoscopic resection, two clinical trial studies (AMC-I and AMC-II) including 23 patients, were conducted at the Academic Medical Centre (AMC) in 2005/2006. Complete eradication of dysplasia and IM was achieved in

all patients. After a median follow-up of 14 months no recurrence of dysplasia or IM was observed. There were no adverse events or strictures and in none of the biopsies obtained from NSE buried Barrett glands were found.

Buried Barrett*s, a condition in which residual areas with IM are hidden underneath NSE is an issue to address when using ablation therapy. Ablative modalities like photodynamic therapy (PDT) or argon plasma coagulation (APC) are associated with high rates of buried Barrett*s (0-56%). Of concern is occult malignant progression of SSIM hidden underneath NSE and therefore not detectable during routine endoscopic inspection. This has been described in incidental case reports in patients who underwent treatment with APC and PDT. To assess whether or not RFA is associated with SSIM a separate study has been conducted in the AMC including the previously reported 23 patients at 2 years follow-up. Rigorous evaluation of the NSE after RFA was performed by taking biopsies, keyhole biopsies and ER specimens from the NSE to assess the presence of SSIM. In addition, pre-RFA cytology brushes from the BE segment and post-RFA cytology brushes from the NSE were used to evaluate eradication of genetic abnormalities pre- and post-RFA. No SSIM nor persisting genetic abnormalities were detected in any of the study subjects.

Another issue to address is the presence of IM below the neosquamocolumnar junction (neo-SCJ). So far its clinical relevance remains debatable since it is unknown whether IM is a physiological finding or if it is the first sign of recurrence of Barrett. In a normal population IM can be detected in the cardia in up to 25% of patients and is not considered a premalignant condition. Studies and case reports have suggested that after thermal ablation therapy, the mucosal histology of the cardia undergoes a change, one study noting a rise in presence of IM from 8.5% pre-ablation to 28% post-ablation, and a rise of 5.3% for dysplasia. A previous study conducted in the AMC showed focal non-dysplastic IM in the cardia in two-thirds of patients with IM during follow-up evaluation after treatment with RFA. Several theories arise concerning development of IM. The first concerns an association with H. Pylori (HP) and IM elsewhere in the stomach. The second describes that repeated injury caused by the ablative method to the cardia, might generate a favourable condition in which cardiac dysplasia may arise. Another possibility is that the degree of damage to the cardia i.e. by acid and bile refluxate is already higher in patients treated for HGIN or cancer, accounting for a higher incidence of dysplasia in the cardia in dysplastic than non-dysplastic ablated Barrett. The risk of malignant progression of IM in the cardia seems lower than that of IM in (short-segment) BE. However the number of patients investigated so far remains small. Long-term data are necessary to evaluate behaviour of IM in the cardia. At the moment we believe that only dysplastic IM in the cardia should be treated.

**Study objective**

The aim of this study is to answer the question if RFA is an effective

treatment modality in the long term, for patients with Barrett's esophagus containing HGIN or EC.

## Study design

Endoscopic evaluation
All patients will be evaluated by an expert gastroenterologist at the AMC, who will record any visible abnormalities on a case record form (CRF); specific attention will be paid to the appearance of the neo-SCJ. Subsequently all patients will undergo an EUS and if necessary FNA, to exclude any abnormal regional lymph nodes, subsquamous growth or invasive growth of recurrent neoplasia, in patients who were previously treated for a (pre)cancerous condition.

Histopathological evaluation of neosquamous epithelium
At the follow-up endoscopy, 4Q/2cm biopsies will be taken from neosquamous epithelium. The neosquamous biopsies will be evaluated for the presence of intestinal metaplasia, dysplasia and subsquamous IM, by an expert GI-pathologist.

Histopathological evaluation of endoscopic resection specimens
Next to the biopsies, an endoscopic resection specimen from neosquamous epithelium will be obtained, by using the multi-band mucosectomy technique (MBM). ER has proved before to be an adequate method for detection of buried Barrett. 18 By using the multi-band mucosectomy (MBM) technique, a specimen can be obtained safely, and it can easily be used on areas previously treated with RFA.
The specimens will be evaluated for SSIM by an expert GI-pathologist, who will also score penetration depth of all ER-specimens on a standardized CRF.
The ER-specimen will be taken from an area with previous Barrett*s mucosa.
Prior to the MBM, 1-2 biopsies will be taken at the target site, to relate presence of SSIM in biopsies to the findings of the ER specimens.

Histopathological evaluation of biopsy samples below the neo-squamocolumnar junction
At least 4 quadrant biopsies will be taken from the area immediately distal to the neo-SCJ (within 5 mm); these biopsies will be evaluated for presence of intestinal metaplasia by an expert pathologist.
Furthermore at least 2 additional biopsies from antrum and corpus will be obtained to evaluate presence of HP and IM.

## Study burden and risks

In this study a regular follow-up endoscopy will be performed, with standard biopsy sampling. General risks associated with a gastroscopy are: mild irritation of the throat due to introduction of the endoscope, difficulties

swallowing and retrosternal pain. During follow-up endoscopy an endoscopic resection will be performed by using the multiband mucosectomy technique, minor bleeding may occur in 6% of the cases, usually easily managed with endoscopic hemostatic techniques. The additional risk of an EUS is rarely a perforation of the esophagus, which can be treated in a conservative manner or by surgical intervention.

## 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

- All eligible patients treated with RFA in the AMC-I/AMC-II/AMC-IV/EURO-I study (resp. MEC05/082 and MEC06/011, MEC 06/184, MEC 06/189), who are now being followed-up endoscopically in the AMC or referral centre in the Netherlands

- Written informed consent

### Exclusion criteria

- No justification for further follow-up due to (unrelated) comorbidity

## Study design

### Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 10-06-2011 |
| Enrollment: | 55 |
| Type: | Actual |

## Ethics review

Approved WMO

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| Application type: | First submission |
| 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 | NL34939.018.10 |