# Confocal Laser Endomicroscopy before transurethral resection for optimizing Bladder Cancer diagnosis and treatment.

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Primary objectives: This study is two-fold and, therefore, has two primary objectives:1. Investigating the diagnostic accuracy of CLE (Cystoflex*F probe) during flexible cystoscopy for diagnosis and grading of urothelial carcinoma of the bladder.2....

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Renal and urinary tract neoplasms malignant and unspecified |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON55286

**Source**
ToetsingOnline

**Brief title**
CLETUR

### Condition

- Renal and urinary tract neoplasms malignant and unspecified
- Bladder and bladder neck disorders (excl calculi)

**Synonym**
bladder cancer, urothelial carcinoma of the bladder

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Stichting Cure for Cancer

## Intervention

**Keyword:** Bladder Cancer, Cancer, CLE, Confocal Laser Endomicroscopy

## Outcome measures

### Primary outcome

1. Overall accuracy, sensitivity and specificity of flexible probe CLE-based diagnosis (benign vs malignant) and grading (low-grade versus high-grade) in comparison with the histopathology of the resection specimen.

2. Overall accuracy, sensitivity and specificity of CLE-based assessment of the surgical radicality of the resection bed (radical versus irradical) in comparison with the histopathology of the biopsy of the resection bed.

### Secondary outcome

- Diagnostic accuracy of computer aided diagnosis based on CLE images compared to histopathology.

# Study description

### Background summary

Initial evaluation of gross hematuria consists of WLC. Urine cytology combined with contrast imaging of the upper urothelial tract is performed when a bladder tumour is seen. Follow up of NMIBC after initial treatment consists of similar steps. When a suspected lesion is visualized, a transurethral resection of the bladder tumor (TURBT) is performed for therapeutic and diagnostic purposes. TURBT is considered to be the gold standard for diagnosis of urothelial carcinoma of the bladder (UCB). High recurrence rates of UCB after TURBT are reported, leading to repetitive surgery and high costs. In certain cases of high grade UCB a second look TURBT has proven to be beneficial after primary resection to ensure radical resection. Furthermore, recent research suggests that active surveillance for low-grade bladder tumours is safe. Confocal laser endomicroscopy (CLE), a high resolution optical imaging technique that can be used in combination with endo-urological procedures, seems promising to improve diagnosis of urothelial cancer, possibly without the need for immediate

transurethral resection to obtain histological confirmation. CLE characteristics of UCB have been determined and validated using rigid probes, which are incompatible with flexible cystoscopes used for outpatient cystoscopies. With the present study, we aim to assess the diagnostic value of flexible probe based CLE for diagnosis and grading of UCB. Furthermore to possibly prevent second look TURBT in the future,an assessment of CLE features of the resection bed using a rigid CLE-probe will be performed.

## Study objective

Primary objectives:
This study is two-fold and, therefore, has two primary objectives:
1. Investigating the diagnostic accuracy of CLE (Cystoflex*F probe) during flexible cystoscopy for diagnosis and grading of urothelial carcinoma of the bladder.
2. To investigate the diagnostic potential of CLE (Cystoflex* UHD-R probe) for the assessment of the surgical radicality after transurethral resection of a bladder tumour (after TURBT)
Secondary objective:
- To validate a previously constructed convolutional neural network for computer aided assessment of CLE images for diagnosis and grading of UCB.

## Study design

This is a prospective, monocenter pilot study investigating the diagnostic accuracy of flexible pCLE. Furthermore it will assess the feasibility of CLE for assessment of the resection bed. Patients planned for TURBT will be asked to participate.

## Study burden and risks

Participants will not benefit directly from this study. We hypothesize, however, that the results of this study will contribute to improvements in the diagnostic and surgical procedure for UCB. Outpatient-based cystoscopy with the potential diagnostic certainty of CLE-based grade assessment may enable active surveillance in low-risk UCB, and thus may even lead to a reduction in surgical procedures. We will introduce a CLE probe before TURBT via the working channel of the flexible cystoscope and hold it in direct contact with the bladder tumour to obtain CLE images. Before image acquisition of the bladder tumour we administer fluorescein intravesical, which is a fluorescent dye, used regularly intravenously in ophthalmatology. Before image acquisition of the resection bed we administer fluorescein intravenously. In patients not at risk for a demonstrated allergic reaction to this dye, this is a safe procedure. Patients with a known allergic reaction to fluorescein cannot participate in this study. Patients will be exposed to approximately 20 minutes of extra surgery time and the introduction of a flexible cystoscope compared to regular TURBT. As a

result there is little burden to study participation for the patients. Adverse events are not expected based on previous experiences. The hospital*s internal protocol for standard clinical care and histopathologic evaluation are not going to be affected by the study protocol.

## Contacts

**Public**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
**Scientific**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

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

### Inclusion criteria

- papillary bladder cancer
- 18 years or older
- bladder that is accessible transurethral for cystoscopic follow up.

### Exclusion criteria

- allergy for fluorescein

## Study design

### Design

**Study type:** Observational invasive

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

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 06-01-2020 |
| Enrollment: | 60 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Generic name: | Confocal Laser Endomicroscopy |
| Registration: | Yes - CE intended use |

## Ethics review

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| Approved WMO Date: | 18-11-2019 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-06-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

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| Approved WMO Date: | 07-04-2021 |
| 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 | NL71360.018.19 |