Optical imaging techniques and breath analysis to evaluate the effect of Bronchial Thermoplasty (BT) for severe asthma

Published: 16-08-2022
Last updated: 30-01-2025

In this study we aim to use minimally invasive real-time techniques including OCT, HHGM, eNose and/or GC-MS for the evaluation of the effect of BT and determine response predictors. To evaluate innovative diagnostic techniques that might be able to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON51801

Source
ToetsingOnline

Brief title
OPTITHERM

Condition

- Respiratory disorders NEC

Synonym
Severe asthma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Medphot consortium

Intervention

Keyword: Breath analysis, Bronchial Thermoplasty, Optical coherence tomography, Severe asthma

Outcome measures

Primary outcome

- To obtain visual qualitative remodeling characteristics and quantitative measurements of OCT airway images and their 3-D reconstructions before and after BT and the non-treated ML.

- To obtain visual qualitative remodeling characteristics and quantitative measurements of ex-vivo HHGM images obtained from airway wall biopsies before and after BT and the non-treated ML.

- To identify and quantify ASM, ECM and inflammatory components in OCT images.

- To identify and quantify ASM, ECM and inflammatory components in HHGM images.

- To correlate OCT and HHGM images with histology results.

- To correlate OCT and HHGM images to clinical outcomes including responders / non - responders analysis

- To identify and quantify changes in VOCs by eNose and/or GC-MS before and after BT and correlate this to omics approaches in blood (and brushes if available) .

Secondary outcome

- To validate the ASM measurements by OCT in a larger number of patients, as has been done before in our previous work.

- To validate the distinctive patterns we have found in exhaled VOCs in

responders and non-responders to BT with GC-MS in a larger number of patients.

- To phenotype severe asthma and perform clinical outcome analyses that includes induced sputum, bronchial hyper-responsiveness (BHR, PC20 methacholine), forced expiratory volume in 1 second (FEV1) and fractional exhaled nitric oxide (FeNO) and molecular parameters including RNA-derived transcriptomes extracted from brushes.

- To evaluate the sub-acute effects of BT from the collected data at the last BT bronchoscopy 6 weeks after the first treatment procedure (BT1).

- To detect and evaluate the changes from measurements in the brushes and Bronchoalveolar lavage fluid (BALF) before and after therapy

- To detect and evaluate the differences from measurements in the brushes and BALF between the responders and non-responders.

- To evaluate the sub-acute effect of BT by analysing the biopsies, OCT measurements and HHGM images 6 weeks after treatment.

Study description

Background summary

Bronchial thermoplasty (BT) is a novel endobronchial treatment for severe asthma. The treatment is based on selective heating of the airways which aims to attenuate the airway smooth muscle (ASM) and airway remodeling. The reduction in ASM mass and changes in the structure of the airways have been shown in several histological studies. To assess and evaluate the ASM or other airway wall components like the extra cellular matrix (ECM), histological staining is the current gold standard. In the past years, less invasive and even more accurate techniques have been developed as diagnostic tools. At first, optical coherence tomography (OCT) is a minimal bronchoscopic invasive technique which generates high resolution, real-time cross sectional images of the airway wall. Secondly, higher harmonic generation microscopy (HHGM) is a relative new technique which enables assessment of the ECM components in airway

wall biopsies in several minutes of time without fixation and staining.
Thirdly, breathomics, which is analysis of volatile organic compounds (VOC*s) in exhaled breath, has great potential as a non-invasive test to monitor inflammation in the lungs. This can be done by using either an electronic nose (eNose) or gas chromatography-mass spectrometry (GC-MS).

Study objective

In this study we aim to use minimally invasive real-time techniques including OCT, HHGM, eNose and/or GC-MS for the evaluation of the effect of BT and determine response predictors. To evaluate innovative diagnostic techniques that might be able to monitor changes in the airways in severe asthma patients treated with BT, and to obtain more insight in the working mechanism and responder profile of BT.

Study design

This is an investigator-initiated, observational study where different monitoring techniques are evaluated (OCT, HHGM, and eNose and/or GC-MS) in comparison with histology and clinical parameters including asthma questionnaires and quality of life scores.

Study burden and risks

This study has a two-fold purpose; first to further unravel the working mechanism of BT in severe asthma and secondly gather more insight for a better patient selection. These objectives can only be achieved by linking patient-reported outcomes to airway structure/function, which is the principal aim of the study proposed.
The patient benefit of study participation is that he/she is offered a severe asthma treatment that is proven effective and safe long-lasting benefit but unfortunately not yet reimbursed in the Netherlands yet. Moreover, we are the only center which offer this treatment.
For study purposes we ask patients to undergo one extra bronchoscopy. This bronchoscopy is on top of a single standard screening bronchoscopy before BT and the bronchoscopy procedures for treatment. Before and after therapy airway sampling and OCT imaging is performed along with standard of care procedures such as sputum induction, pulmonary function tests and questionnaires. The bronchoscopies will be performed under deep sedation (midazolam and/or propofol) to minimize patient discomfort. Previous experiences in research bronchoscopies in severe asthma patients by our group and others have proven these procedures to be safe. To our opinion the burden one additional bronchoscopy is justified by the scientific insights that can be obtained in this important study in which a novel severe asthma treatment is offered that is otherwise not available.
For the OCT measurements we expect sedation time in the endoscopy suite to be

prolonged by 8 minutes. Based on our experiences with OCT in previous AMC initiated trials, and literature where OCT measurements of the airway wall are obtained, we state that imaging by OCT is safe and poses no risk for the patient. Images made by HHGM are ex-vivo and thereby are of no burden or risk to the patients. Another extra additional procedure in this study is the exhaled breath sampling, which is a non-invasive procedure, therefore the risks of this procedure are negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Patient is an adult, aged 18 years or older, and is scheduled to undergo (re-)BT treatment according to the Alair System directions for use, according to the BT registry protocol.
2. Patient is able to read, understand, and sign a written IC to participate in

this study and able to comply with the registry requirements.
3. Patient meets the inclusion criteria of the BT registry

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Use of investigative drugs or intervention trials in the 4 months prior to enrolment or during the duration of the study.
2. Any condition or compliance issue which in the opinion of the investigator might interfere with participation in the study.
3. Any exclusion criteria from the BT-registry

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2023
Enrollment:	15
Type:	Actual

Medical products/devices used

Generic name:	Optical coherence tomography
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	16-08-2022
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	NL80306.018.22