Early detection of cancer onset based on sensing field cancerization at the organ level in the alimentary tract using an integrated Raman/scattering modality for endoscopic real-time in vivo measurements

Published: 14-04-2022
Last updated: 16-11-2024

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Ethical review	Approved WMO
Status	Completed
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON51792

Source
ToetsingOnline

Brief title
The SENSITIVE study

Condition

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

Synonym
oesophageal and colorectal (adeno-)carcinoma and premalignant stages

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Horizon 2020 project van de Europese Unie

Intervention

Keyword: Field cancerization, GI endscopy, Raman spectroscopy, Scattering spectroscopy

Outcome measures

Primary outcome

To assess the in vivo safety of a Scattering/Stimulated Raman Spectroscopy

integrated modality during GI endoscopy

We aim to assess the safety through the registration of AEs, SAEs, and SUSARs.

Secondary outcome

To assess the feasibility of a Scattering/Stimulated Raman Spectroscopy

integrated modality for real-time in vivo assessment of field cancerization in

GI tissue in BE patients and in patients suspected of colorectal polyps;

We aim to assess the feasibility of in vivo Stimulated Raman spectroscopy and

scattering measurements through correlation of the measurements to;

• Histopathology examination of the tissue from the targeted biopsies

• Results of endoscopic examination and histopathological examination from the

clinical biopsies of the involved organ (i.e., Barrett*s esophagus or colon).

• Validation of the endoscopic in vivo SRS measurements by the spontaneous

Raman spectroscopy measurements.

Study description

Background summary

Patients with Barrett*s esophagus and Lynch syndrome (LS) are known to be at risk of developing respectively esophageal adenocarcinoma (EAC) and colorectal carcinoma (CRC). Therefore, both these patients are subject to regular endoscopic surveillance examinations in order to detect these tumors during their premalignant stages and subsequently enable early endoscopic intervention. However, these time-consuming screening programs have an empirical basis and thus, individual patients are either examined too little or too much. In addition, satisfying results of these programs are impeded by relatively high miss rates of neoplasias in these patients as they exhibit solely subtle morphological changes. Interestingly, nanoarchitectural changes in cells and tissue throughout the whole organ occur as elements of field cancerization before neoplastic lesions become manifest in the gastrointestinal tract. Thus, detection of field cancerization in the tissue could prompt further endoscopic examination of the whole organ and allow real-time in vivo tissue diagnosis. Through the integration of biophotonics in optical imaging, an approach is created that allows a label-free visualization of the smallest alterations in the tissue of interest in a non-destructive manner. Through integration of Raman spectroscopy and scattering spectroscopy into one modality, detailed information upon the biochemical composition and tissue structure on a nanoscale can be respectively obtained. Therefore, this Raman/scattering integrated modality would be able to measure the intracellular processes and nanoarchitectural changes that are associated to field cancerization. Therefore, we hypothesize that detection of field cancerization in the GI tract could be performed during endoscopy by performing Raman and scattering measurements. In the context of the SENSITIVE project, an investigational medical device was developed that integrates probe-based Raman and scattering measurements for endoscopic purposes: the SENSITIVE system. In addition, a spontaneous Raman spectroscopy device (SRM1 device) was developed specifically for this study to validate the SRS measurements. During preclinical ex vivo studies, we have established that scattering and Raman measurements were able to discriminate between non-field cancerized tissue and field cancerized tissue. Considering these results, we aim to assess the safety of in vivo Raman/scattering during endoscopy. Secondly, we to assess the feasibility of this approach measurements to determine field cancerization in the alimentary tract during endoscopy through the SENSITIVE system. Therefore, we assess the precision of the stimulated Raman spectroscopy measurements of the SENSITIVE system by performing spontaneous Raman measurements with the SRM1

device.

Study objective

The primary objective involves the safety of in vivo Raman/scattering during endoscopy. Therefore, we will assess safety parameters (AEs, SAEs, SUSARs). Secondary objective involves the feasibility of the probe-based scattering/(stimulated) Raman spectroscopy integrated system (The SENSITIVE system and SRM1 device respectively) to enable real-time in vivo detection of field cancerization in the GI tract in patients with BE and in patients that are at risk of developing CRC. Therefore, we will correlate the scattering and Raman measurements to both histopathology and additional ex vivo analysis of the targeted biopsies. Furthermore, we will correlate the measurements to the endoscopic diagnosis of the organ (esophagus or colon), and the histopathological diagnosis of other clinical biopsies that are obtained during the endoscopic procedure.

Study design

Study design: The study concerns a non-randomized, non-blinded, prospective, phase I medical device study.

An interim analysis will be conducted by the investigators involved in this study after the first 15 patients. The interim analysis will include the assessment key safety parameters: AEs, SAEs and SUSARS.

Secondary, we will assess the feasibility of Raman/scattering measurements for distinguishing Raman spectra and scattering properties between morphologically aberrant and morphologically non-aberrant tissue.

If these criteria are met, we will continue the inclusion up to 60 patients.

Intervention

Patients that are scheduled for a diagnostic or therapeutic endoscopic procedure and have provided informed consent will undergo Raman and scattering measurements during endoscopy. Preparations for endoscopy and the endoscopy procedure itself will be performed according to the dedicated clinical routine. After evaluation of the mucosa under white light illumination and narrow band imaging, the mucosa will be rinsed and Raman and scattering measurements will be performed of the spot of interest using a fiber that is passed through the working channel of a normal endoscope (this approach is comparable to the approaches that we employ during our studies of fluorescence molecular endoscopy (of which we have performed >200 procedures). First we will perform Raman measurements with the SENSITIVE system, and subsequently with the SRM1 device. After measurements, targeted biopsies will be taken for histopathology

analysis, immunohistochemistry and FGmRNA-profiling.

Study burden and risks

Patients are not required to pay an extra visit to the UMCG for study procedures. Clinical indication for endoscopic procedure is necessitated and measurements will be performed during endoscopic examination. In order to verify the in vivo measurements, extra biopsies will be obtained of tissue that has been measured. Overall, the study procedures will take around 20 minutes per patient. We consider the risk for patients to participate in the study to be negligible. There is no direct diagnostic or treatment benefit for the patients as the procedures are conducted according to standard clinical guidance. No decisions in the context of clinical care will be based upon study findings.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Scheduled for either a gastroscopy in the context of a Barrett*s esophagus or a colonoscopy in the context of colorectal polyps;
• Age of 18 years or older;
• Written informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Patients with simultaneous neoplasia elsewhere in the GI tract;
• Patients with a medical history head and neck or lung cancer;
• Patients with a history of endoluminal ablative therapy or radiation therapy;
• Patients younger than 18 years
• Other medical conditions of the esophagus or colon that potentially can disturb measurements of the SRS/scattering spectra such as (eosinophil) esophagitis, inflammatory bowel disease or a medical history of radiation therapy;
• Physical or mental disorders that comprise the ability of the patient to give informed consent.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-07-2022

Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	Endoscopic probe for integrated Raman/scattering measurements during endoscopy (SENSITIVE system) an
Registration:	No

Ethics review

Approved WMO Date:	14-04-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-06-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NCT05247346
CCMO	NL79647.042.22