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Understanding Raman signatures in colorectal cancer

Submission date	Recruitment status	[ ] Prospectively registered
28/01/2023	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
15/02/2023	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
04/06/2025	Cancer	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Bowel cancer is one of the commonest cancers worldwide. Early diagnosis is vital for improving outcomes but challenging as symptoms are not specific and are common to other non-cancer conditions. The current gold standard for diagnosis of bowel cancer is colonoscopy. However, colonoscopy is not without risk and services are under huge pressure due to increasing demand causing long waiting times for the patients who need it most. In collaboration with Swansea University, we have developed a blood test that works by shining a laser light onto a blood sample and measuring how much light is scattered off molecules in that sample. This creates a unique 'fingerprint' result that is specific to cancer. Our early results show that the test is very good at identifying patients with a high likelihood of having bowel cancer. We aim to understand the underlying causes of the differences between the blood sample fingerprints measured in patients with and without bowel cancer. By better understanding the origin of the signals, the accuracy of the test could be improved, leading to better cancer detection. The study will achieve this by tracking the patterns measured in the blood test from the blood samples back to the tumour. This will include investigating the role of the gut organisms that inhabit the bowel, the effect of the fasting state, lipids and bowel preparation on the results of the blood test.

Who can participate?
Adult participants with a diagnosis of bowel cancer, significant bowel disease requiring an operation, patients who undergo routine lipid, or procedures requiring bowel preparation and control participants

What does the study involve?
Participants will undergo blood tests and provide faecal samples. For patients having an operation as part of their care, a small portion of tissue that has been removed will be studied.

What are the possible benefits and risks of participating?
The team believe that by better understanding the origins of these signals, the accuracy of the blood test can be improved as well as studying its limitations (e.g. whether the test needs to be done only when fasted, if it maintains accuracy in patients with very high cholesterol levels and if bowel preparation medication affects this test). Participants will undergo investigations /treatments that are in line with current standards of care. For the majority of participants, the

risk associated with participating is that of an additional blood test, which will be minimised if the blood test is done at the same time as other blood tests. For a subset of participants undergoing glucose tolerance testing, risks include multiple tests at different time points and the risk of low blood sugar from fasting. This will be minimised by having trained staff supervise the test.

Where is the study run from?
Swansea Bay University Local Health Board (UK)

When is the study starting and how long is it expected to run for?
June 2021 to July 2026

Who is funding the study?
Cancer Research Wales (UK)

Who is the main contact?
Prof Dean Harris, dean.a.harris@wales.nhs.uk (UK)

Contact information

Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
303620

Central Portfolio Management System (CPMS)
52480

Study information

Scientific Title
Mechanisms and Origins of Spectral Signatures: defining colorectal cancer/polyp/adenoma detection by Raman spectroscopy

Acronym
RAMAN-MOSS

Study objectives
Spectral signatures defining colorectal cancer and polyp/adenomas originate from metabolites that are produced due to changes in metabolic pathways, and driver mutation pathways and are influenced by the gut microbiome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 31/01/2022, Hampstead Research Ethics Committee (Ground Floor, Temple Quay House, Health Research Authority, BS1 6PN, UK; +44(0)2071048345; hampstead.rec@hra.nhs.uk), ref: 21/PR/1616

Primary study design
Observational

Study design
Single-centre prospective observational cohort study with a laboratory component

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Early detection of colorectal cancer

Interventions
There are five sub-studies in this project to investigate the different explanations for differences in the Raman signal seen in the blood of people with/without polyps/colorectal cancer.

Sub-study A (Metabolomics and genomics) - existing serum samples and tissue samples from patients recruited to the existing study "Raman spectroscopy and colorectal cancer" (IRAS 146942 REC reference 14/WA/0028). Serum samples will be analysed with mass spectrometry and RNA extracted from tissue samples for analysis.

Sub-study B (Gut microbiome) - participants with a known diagnosis of bowel cancer or significant bowel disease undergoing bowel resection and healthy controls will be recruited. For participants who will be undergoing bowel resection, blood and faecal samples will be collected at two-time points - at enrolment or prior to surgery and at their first follow-up appointment 6-8 weeks after surgery. All sampling can be done during clinic or routine hospital visits where possible. In addition, a small portion of bowel tissue will be collected from the section of the bowel that has been removed. For controls, only a single blood and faecal sample is required at the time of recruitment. Raman spectroscopy will be carried out on blood, faecal, tissue and cell media. Mass spectrometry will be carried out on blood, faecal samples and cell media. Additional tests include 16s rRNA sequencing for faecal samples (for profiling of bacteria) as well as an inflammatory panel and genomic tests on cells. There is the potential to then use organoids derived from patient tissue to study the effects of gut bacteria using co-culture techniques.

Sub-study C (Fasting state) - All participants (25 cancer, 25 control) will be required to undergo an oral glucose tolerance test. They will be required to fast prior to the test (at least 4-6 hours without food). On arrival, they will have a blood sample taken following which they will be given a sugary drink. They will have subsequent blood tests at 30 mins, 60 mins, 90 mins, 120 mins and 4 hours following consumption of the sugary drink. The blood samples will be analysed with Raman spectroscopy and any differences in the signal between participants with and without bowel cancer measured.

Sub-study D (Lipid) - A single serum sample will be analysed with Raman spectroscopy and correlated with the results of participants' lipid tests as well as medication to better understand the limitations of Raman spectroscopy for this particular application in blood with very high lipid levels.

Sub-study E (Bowel preparation) - participants will be recruited pragmatically into each of the four groups; Picolax + Metronidazole, Picolax +Metronidazole+Neomycin, Moviprep or control. Participants in the 3 bowel preparation groups will undergo a blood and faecal sampling prior to starting bowel preparation and repeat blood and faecal sampling following the consumption of bowel preparation. Controls will only be required to provide a single blood and faecal sample at enrolment.

The blood samples will be analysed with Raman spectroscopy and differences in the signal before and after the consumption of bowel preparation as well as the effects seen between the different types of bowel preparation taken will be analysed. Faecal samples will be sent for gut bacteria profiling with 16s rRNA testing to study the differences between pre-and post-consumption of bowel preparation and antibiotics.

Intervention Type
Mixed

Primary outcome(s)
Spectral signatures defining CRC and polyp/adenoma detection measured using Raman spectroscopy of study samples in the laboratory at one timepoint (unless otherwise specified in specific sub-study)

Key secondary outcome(s)
Secondary outcomes will be assessed in the laboratory at one timepoint:
1. Sub-study A (Metabolomics and Genomics) - Metabolites that correspond to peaks seen in the Raman spectra in serum samples and tissue samples from patients measured using mass spectrometry and RNA extracted from tissue samples for analysis
2. Sub-study B (Gut microbiome) - Metabolites related to pathobionts in the samples from participants with colorectal cancer, polyps/adenoma. Variables measured using Raman spectroscopy on blood, faecal, tissue and cell media, mass spectrometry on blood, faecal samples and cell media, 16s rRNA sequencing on faecal samples and an inflammatory panel and genomic tests on cells. Organoids derived from patient tissue will also be used to study the effects of gut bacteria using co-culture techniques. Samples were collected at two timepoints - at enrolment or prior to surgery and at their first follow-up appointment 6-8 weeks after surgery.
3. Sub-study C (Fasting state) - Ideal fasting time for the oral glucose tolerance test measured using the Raman test at baseline, and 30, 60, 90 mins, and 4 hours
4. Sub-study D (Lipids) - Level of lipaemia in serum measured using Raman spectra
5. Sub-study E (Bowel preparation) - Colorectal cancer/polyp/adenoma signal in the serum of patients measures using Raman spectroscopy

Completion date
02/07/2026

Eligibility

Key inclusion criteria
1. Aged 18 years old and over

2. For sub-study A (Metabolomics), informed consent has been obtained for RAMAN-CRC (Groups 1-4) and provided blood serum for Raman spectroscopy and has a corresponding tissue biopsy or resection collected as the standard of care in archives

3. For sub-study B (Gut microbiome):
3.1. Has a confirmed diagnosis of colorectal cancer, benign/inflammatory conditions requiring surgery/biopsies at colonoscopy OR normal colonoscopy/previous history of complete surgical removal of colon and rectum for the control group
3.2. Informed consent obtained for the RAMAN-MOSS study
3.3. Able and willing to provide blood serum and faecal samples
3.4. Corresponding tissue biopsy/resection collected as the standard of care (for CRC and benign /inflammatory bowel disease groups only)

4. For sub-study C (Fasting state study):
4.1. Has a confirmed diagnosis of CRC (for CRC group)
4.2. Has normal colonoscopy (for the control group)
4.3. Informed consent obtained for the RAMAN-MOSS study
4.4. Able and willing to undergo oral glucose tolerance test
4.5. Able and willing to provide blood serum samples for Raman spectroscopy

5. For sub-study D (Lipid study):
5.1. Known diagnosis of hyperlipidaemia and referred to hyperlipidaemia clinic
5.2. Informed consent obtained for the RAMAN-MOSS study
5.3. Able and willing to provide blood serum sample for Raman spectroscopy

6. For sub-study E (Bowel preparation and Antibiotics study):
6.1. Referred for colonoscopy for investigation of bowel symptoms OR under colonoscopy surveillance programme OR undergoing surgical resection
6.2. Fit for bowel preparation
6.3. Informed consent obtained for the RAMAN-MOSS study
6.4. Able and willing to provide blood serum and faecal samples

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Aged 17 years old and under
2. Unwilling/unable to consent to trial participation

3. Patients from vulnerable groups (defined as lacking the capacity to freely give informed consent)
4. Unwilling/unable to provide blood/faecal/tissue samples required for the study
5. Additional for sub-study C (Fasting state):
5.1. Glucose tolerance test (OGTT) contraindicated
5.2. Diagnosis of diabetes
6. Additional for sub-study E (bowel preparation and antibiotics):
6.1. Unfit for bowel preparation or colonoscopy
6.2. Allergy to bowel preparation and/or antibiotics

Date of first enrolment
22/09/2022

Date of final enrolment
02/05/2026

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Swansea Bay University Local Health Board
One Talbot Gateway, Seaway Drive
Seaway Parade Industrial Estate
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SA12 7BR

Sponsor information

Organisation
Swansea Bay University Health Board

ROR
https://ror.org/04zet5t12

Funder(s)

Funder type
Charity

Funder Name
Cancer Research Wales

Alternative Name(s)
Ymchwil Canser Cymru, CRW

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be made available upon request from the Chief Investigator, Prof. Dean Harris (dean.a.harris@wales.nhs.uk). Informed consent from participants was required and obtained. Only pseudonymised data relevant to the study is shared with researchers. All identifiable data is held by their routine clinical care team/NHS research team recruiting the patient. Any identifiable data especially relating to medical records and genetic data will not be shared.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No