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Vagus nerve stimulation to improve bowel function after surgery

Submission date	Recruitment status	[X] Prospectively registered
07/10/2019	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/10/2019	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/10/2024	Surgery	

Plain English summary of protocol

Background and study aims
Ileus (lack of movement somewhere in the intestines that leads to a buildup and potential blockage of food material) is a common complication after colorectal surgery (surgery of the large bowel and rectum). It is characterised by a slow return of normal bowel function, giving rise to symptoms such as bloating, constipation, and vomiting. This increases the risk of other serious complications, reduces patient satisfaction, and increases healthcare costs.

We aim to test a new treatment to reduce Ileus in patients having colorectal surgery. Patients will self-administer a non-invasive nerve stimulator device (GammaCore) for five days before and after surgery. This will be a randomised study with some patients receiving "active" devices, and others receiving "placebo" (sham) devices.

Who can participate?
Patients aged over 18 years, planned to undergo elective, minimally-invasive (laparoscopic or robotic), colorectal surgery

What does the study involve?
For all patients, bowel function will be assessed via short, clinical consultations during their hospital admission. Participants will also be invited to participate in a series of optional sub-studies:
1. Assessment of inflammation after surgery - this will include a series of blood tests and abdominal fluid samples
2. Assessment of bowel motility - this will include a short MRI scan performed before and after surgery
3. Assessment of patient opinions of the treatment - this will include a short interview after hospital discharge

What are the possible benefits and risks of participating?
We hope that this new treatment will help to prevent ileus after surgery. However this is not certain and is the reason we are doing the study. The research may not directly benefit people who take part but it will help us to improve the recovery of bowel function in the future. As patients will receive an extra treatment compared to normal, there is a small chance of extra

side effects. These are considered mild and infrequent. If they do occur they typically resolve soon after using the device. Some possible effects are: mild lip twitch during stimulation, facial tingling, and mild irritation of the skin around the stimulation site.

Where is the study run from?
1. St. James's University Hospital, UK
2. Bradford Royal Infirmary, UK

When is the study starting and how long is it expected to run for?
November 2019 to April 2022 (updated 18/08/2021, previously: December 2021)

Who is funding the study?
National Institute for Health Research (NIHR), UK

Who is the main contact?
Stephen Chapman
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
42471

Study information

Scientific Title
Transcutaneous vagal nerve stimulation to reduce Ileus: A feasibility study (TRANSIT)

Acronym
TRANSIT

Study objectives

A definitive, phase-3, randomised controlled trial of patient-administered vagus nerve stimulation for the prevention of ileus is feasible

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/07/2019, North East - Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle-upon-Tyne, NE2 4NQ; +44 (0)207 972 249; nrescommittee.northeast-tyneandwearsouth@nhs.net), ref: 19/NE/0217

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Device

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Colorectal Surgery

Interventions
A feasibility RCT will be performed at two research sites. This will involve patients randomly assigned to four groups:
1. Pre-operative active stimulation and post-operative sham stimulation
2. Pre-operative sham stimulation and post-operative active stimulation
3. Pre-operative sham stimulation and post-operative sham stimulation
4. Pre-operative active stimulation and post-operative active stimulation

Patients will be approached about the study at their routine outpatient appointment by members of the clinical team. Verbal and written information will be provided and patients will be invited to take this home. With permission, they will be contacted 24 hours later to determine their decision to participate. They will be permitted to confirm their interest earlier than 24 hours if they wish, and their right to withdraw at any time will be emphasised strongly. Patients who confirm their interest (via telephone or at the time of approach) and satisfy all eligibility criteria will be invited to provide informed, written consent. Randomisation will take place immediately after consent via a 24-hour online randomisation service.

During the information-giving and consent processes, patients treated at the lead research site will be invited to enrol in several optional sub-studies. These are optional and not essential for participation in the main trial.
1. Inflammatory sub-study: this will involve a series of four blood tests and two abdominal fluid samples during surgery. Information about this sub-study will be included on the main trial information sheet and optional consent will be confirmed on the main trial consent form. Participation will be limited to the main study site, and no pre-specified limit on the number of participants will be set. Additional sub-study eligibility criteria will apply.
2. Bowel motility sub-study: this will involve a pre- and post-operative, non-contrast, MRI scan. The pre-operative scan will take place before hospital admission and the postoperative scan will take place during hospital admission. Information about this sub-study will be provided on a

supplementary information sheet and consent will be confirmed using a supplementary consent form at the same time as the main trial consent. Participation will be limited to the main study site, and recruitment will stop after 40 participants have been accrued. Additional sub-study eligibility criteria will apply.
3. Qualitative sub-study: this will involve a short, semi-structured interview with participants on hospital premises. Information about this sub study will be provided on a supplementary information sheet at the time of initial approach and consent will be confirmed using a supplementary consent form before discharge. Participation will be limited to the main study site and recruitment will stop once 20 participants have been accrued. No additional sub-study eligibility criteria will apply. Permission to audio record interviews will be acquired during the consent process and the recording will be transcribed by an authorised individual.

In addition, five non-participants of the main study will also be interviewed to explore reasons for non-participation. They will be approached with a dedicated information sheet and consent form. The interview will be conducted by an investigator who was not involved in the initial approach.

After providing consent for the main trial, participants will take part in a 20 minute training session on how to use the device. This will take place either at their routine pre-assessment appointment or a dedicated study visit (travel expenses reimbursed), according to patients' preference. This decision has been informed by our patient advisory group, who encourage a policy of flexibility for the timing of the training session. Participants of the bowel motility substudy will undergo their pre-operative MR scan at this time.

Participants will self-administer the device twice a day (morning and evening) for 5 days before and after surgery. Compliance will be recorded using self-reported diaries. On the day of surgery, each device will be collected and a newly allocated device will be provided according to the allocation schedule. This will be done irrespective of whether patients are due to retain the same type of device (active versus sham) in order to maintain blinding.

According to standard practice, It is expected that participants will be inpatients for at least 5 days. Participants' length of stay will not be extended for the purpose of completing study assessments. Adverse events will be recorded up to 30 days and will be explored by review of medical records and telephone follow up.

Intervention Type
Procedure/Surgery

Primary outcome(s)
As a feasibility study, the study does not have a primary defined outcome. Instead, it has a series of outcomes to
confirm or refute the feasibility of a definite RCT.

Measured at or up to 30 days after surgery:
Outcomes to inform progression:
1. Proportion of eligible patients identified from screening logs
2. Number of eligible patients randomised (per month), including reasons for approach failure
3. Adequacy of participant blinding according to a blinding poll (Bang Blinding Index)
4. Compliance to the study treatment schedule according to participant-reported diaries
5. Proportion of randomised participants lost to follow up
6. Incidence of serious and unexpected serious complications

Outcomes to explore clinical variability
1. Time to first passage of flatus
2. Time to first passage of stool
3. Time to first oral tolerance (tolerance of solid diet in the absence of vomiting for 12 hours)
4. Time to GI-2 (a composite of time to first oral tolerance and passage of first stool)

Key secondary outcome(s)
Outcomes for the optional sub-studies (lead site only) are described below.

Inflammatory response sub-study:
1. Serum interleukin (IL) 1-beta, IL6, and tumour necrosis factor (TNF)-alpha at time points:
1.1. Morning of surgery – after pre-operative stimulation schedule/prior to surgery
1.2. 2-4 hours after start of surgery – measured from time of "knife-to-skin"
1.3. 24 hours after start of surgery – measured from time of "knife-to-skin"
1.4. 72 hours after start of surgery – measured from time of "knife-to-skin"

2. Peritoneal fluid IL-6, IL1-beta, and TNF alpha at time points:
2.1. Start of surgery – estimated 0-30 minutes after "knife-to-skin"
2.2. End of surgery – estimated 2-4 hours after "knife-to-skin"

Small bowel motility sub-study:
1. Small bowel motility measured by assigning a validated GIQuant™ score to MR enterography scans

Completion date
30/04/2022

Eligibility

Key inclusion criteria
1. Aged > = 18 years
2. Able to provide written informed consent
3. Planned to undergo elective, minimally-invasive (laparoscopic or robotic), colorectal surgery

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment

Key exclusion criteria
Main trial:
1. Confirmed STEMI or NSTEMI) in the last 12 months
2. Known congestive heart failure (NYHA> 2)
3. Confirmed 2nd/3rd degree heart block, permanent atrial fibrillation, or previous VT/VF
4. Seizures or recurrent episodes of syncope (> 1) in the last five years
5. Cerebrovascular disease (transient ischaemic attack or cerebral vascular accident)
6. Previous vagotomy at any anatomical location
7. Confirmed diagnosis of chronic gastrointestinal inflammatory condition (Crohn’s disease or UC)
8. Confirmed diagnosis of neuro-endocrine tumour (such as carcinoid)
9. Existing gastrointestinal stoma (including ileostomy or colostomy)
10. Implanted electrical stimulator device
11. Structural abnormality of the neck anatomy which may impact on use of the device
12. Belonging to a vulnerable population (homeless, developmentally disabled, prisoner)
13. Pregnant, nursing or thinking of becoming pregnant during the study period

Inflammatory sub-study (lead site only):
14. Regular use of NSAIDs in the preceding 7 days or medical condition requiring oral/injectable steroids
15. Neoadjuvant chemoradiotherapy within 12 months prior to surgery

Small bowel motility sub-study (lead site only):
16. Non-MR compatible implants, prostheses, neurosurgical clips, or foreign bodies, precluding safe MR imaging
17. Claustrophobia, or other barrier to laying supine for 30 minutes

Date of first enrolment
01/11/2019

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St James's University Hospital
Leeds Teaching Hospitals NHS Trust
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Bradford Royal Infirmary
Bradford Teaching Hospitals NHS Foundation Trust
Duckworth Lane
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BD9 6RJ

Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: DRF-2018-11-ST2-049

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		12/10/2024	17/10/2024	Yes	No
Protocol article		21/07/2021	18/08/2021	Yes	No
HRA research summary			28/06/2023	No	No