ISRCTN98760715 https://doi.org/10.1186/ISRCTN98760715

Subsensory sacral neuromodulation for incontinence

Submission date 04/09/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 25/09/2017	**Overall study status** Completed	
Last Edited 04/06/2024	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Faecal incontinence (FI) is when you do not have control over defecation. A relatively new treatment called sacral neuromodulation (SNM) is now commonly offered to adults suffering with FI. Suitable patients include those with faecal incontinence caused by childbirth, surgery, and advancing age. A battery powered unit is implanted into the lower back. This is connected to electrodes which rest on the nerves in the lower spine. This stimulator then continuously sends electrical impulses to the nerves and muscles that control the lower bowel (rectum and anus). The result is improved continence. Previous studies have reported a great benefit of SNM in some patients. Unfortunately, other patients can have little or no response. We are still unsure about how SNM restores bowel control, and we still do not know with certainty how effective SNM really is. SNM costs on average £10,000 per patient just for the equipment and is not without its risks and side-effects. It is therefore vital that these questions are answered. The aim of this study is to establish how SNM works and how well SNM works. These specialist tests will study their anal and rectal function as well as their corresponding brain activity.

Who can participate?
Adults aged 18-75 who have faecal incontinence.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive 16 weeks of therapy using the SNM and those in the second group receive 16 weeks of placebo (dummy) therapy. At the end of 16 groups the participants switch treatments. Participants are assessed for their quality of life and faecel incontinence symptoms. Participants are followed up to one year.

What are the possible benefits and risks of participating?
Participants may benefit from receiving a high standard of surgery using the latest technical optimisation and monitored scare. They are reimbursed for reasonable travel expenses. There are no major risks to participants above the standard risk of SNM therapy. SNM is an established therapy whose main attraction is non-invasiveness and safety compared to other surgical

procedures. The small period (3 months) without active therapy imposed by the crossover design is not deemed ‘harmful’ for a chronic and stable condition by the time surgical intervention is considered.

Where is the study run from?
This study is being run by Queen Mary University of London (UK) and takes place in several NHS specialist centres in the UK and in the EU.

When is the study starting and how long is it expected to run for?
April 2017 to February 2023

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

Who is the main contact?
1. Miss Eleanor McAlees
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Study website
www.blizard.qmul.ac.uk/subsonic.html

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
34463

Study information

Scientific Title
SUBsensory Sacral Neuromodulation for InContinence: Randomised double-blind efficacy and mechanism study of sub-sensory sacral (optimised) neuromodulation in adults with faecal incontinence

Acronym
SUBSoNIC

Study objectives
The aim of this study is to determine clinical effectiveness of sacral nerve-root stimulation: sacral neuromodulation (SNM) using a commercially-available implantable device, Medtronic Interstim ® in adults with Faecal Incontinence failing conservative treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
SUBsensory Sacral Neuromodulation for InContinence - SUBSoNIC, 13/09/2017, ref: 17/LO/1060

Study design
Randomised; Both; Design type: Treatment, Device, Complex Intervention, Surgery, Cohort study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Faecal incontinence

Interventions
In contrast to a traditional clinical trial, the design of this trial allows all participants to receive the treatment. This is possible by using a crossover design i.e. one where after implantation of the stimulator all participants receive a period of real therapy (SNM: device on but at an unperceived level of stimulation) compared to a period of sham (placebo) therapy. The effects of SNM can then be compared while both the patients and the research team are unaware of whether the stimulation is SNM or sham. This is called 'double-blinding' and is the gold standard for determining what the true effects of the treatment are.

Suitably eligible patients consenting to take part in the study undergo surgery to receive the SNM device (Medtronic Interstim II Model 3058) and be randomised to two equal groups (Group 1 and Group 2 above). Both groups receive 16 weeks with SNM and 16 weeks with SHAM (in different order). At the beginning and part way through (+6 weeks) each phase, participants attend a reprogramming of the SNM device. At the end of the 16 weeks they cross over to the other group (SNM to SHAM or SHAM to SNM). Assessments take the form of four week bowel diary and quality of life questionnaires/FI symptom scores. These are completed at baseline (prior to SNM implantation & randomisation) and at the end of each 16 week phase.

After completion of both 16 week phases (SNM & SHAM), all participants are then followed up to the one year time-point with all stimulators left SNM and patient decisive stimulation level.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Medtronic Interstim ®

Primary outcome measure
The reduction in FI events in SNM vs. SHAM using a 4 week bowel diary in paper format between 12 and 16 and between 28 and 32 weeks

Secondary outcome measures
A variety of quality of life questionnaire and bowel diary measures recorded at 16, 32 and 58 weeks:
1. E-event recorder including episodes of faecal material, leakage of flatus, urgency without incontinence, social and physical activity (see figure 4 below);

2. Other bowel diary measures: Urgency, Urge and passive faecal incontinence episodes, use of loperamide and social functioning;
3. Summative questionnaire assessments: St Mark's continence score52; OAB-Q SF score, FI QoL score53; International Consultation on Incontinence Bowel (SF-ICIQ-B) questionnaire54.
4. Viscerosensory bowel diary recording quality, site and intensity of defaecatory urge
5. Generic QOL: EQ-5D-5L
6. Likert scale of patient's global impression of treatment success (scale 0-10) and patient perception of group allocation (blinding success).
7. Electrode settings (inc. motor, first and habituated sensory thresholds), programming, & if applicable re-programming data
8. Adverse events and morbidity.

Mechanistic outcomes
1. Advanced anorectal physiology
2. Anocortical neurophysiology

Overall study start date
01/04/2017

Completion date
28/02/2023

Eligibility

Key inclusion criteria
1. Adults aged 18-80 (updated 25/07/2019, previously: 75)
2. Meet Rome III and ICI definitions of FI (recurrent involuntary loss of faecal material that is a social or hygienic problem and not a consequence of an acute diarrhoeal illness)
3. Failure of non-surgical treatments to the NICE standards. Minimum NICE standard includes; diet, bowel habit and toilet access addressed. Medication e.g. loperamide, advice on incontinence products, pelvic floor muscle training, biofeedback and rectal irrigation should be offered if appropriate.
4. Minimum severity criteria of 8 FI episodes in a 4 week screening period (this is important to exclude patients who might thence have zero FI episodes during baseline evaluations)
5. Ability to understand written and spoken English or relevant language in European centres (due to questionnaire validity)
6. Ability and willingness to give informed consent

All participants will have been determined as clinically suitable for SNM based on clinical evaluation and subsequent multidisciplinary team discussion (as mandated by NHS England specialist commissioning guidance) or equivalent guidance in other participating EU countries.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
Planned Sample Size: 90; UK Sample Size: 80

Total final enrolment
39

Key exclusion criteria
A standard list of exclusions (disease variants; surgical fitness, specific contraindications to implantation) will be used. Note that these are routine clinical exclusions to the use of SNM rather than participation in the research. For completion:
1. Known communication between the anal and vaginal tracts
2. Prior diagnosis of congenital anorectal malformations
3. Previous rectal surgery (rectopexy/resection) performed < 12 months ago (24 months for cancer)
4. Present evidence or past history of full thickness rectal prolapse
5. Prior diagnosis of chronic inflammatory bowel diseases
6. Displays symptoms of chronic constipation with over-flow incontinence
7. Structural abnormality of the pelvic floor leading to clear evidence of obstructed defaecation based on examination and/or imaging
8. Symptoms of significant evacuatory dysfunction based on Obstructive Defecation Syndrome Score > = 8
9. Presence of active perianal sepsis (including pilonidal sinus)
10. Defunctioning loop or end stoma in situ
11. Diagnosed with neurological diseases, such as diabetic neuropathy, multiple sclerosis and Parkinson's disease
12. Current or future need for MR imaging based on clinical history
13. Complete or partial spinal cord injury
14. Bleeding disorders e.g. haemophilia, warfarin therapy
15. Pregnancy or intention to become pregnant during the study period
16. Not fit for preferred method of anaesthesia
17. Anatomical limitations that would prevent successful placement of an electrode including congenital abnormalities
18. Psychiatric or physical inability to comply with the study protocol (inc. e-diary assessments) at investigator discretion
19. Required to drive for long periods of time for example lorry drivers, taxi drivers and delivery drivers.

Date of first enrolment
01/10/2017

Date of final enrolment
23/06/2022

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
The Royal London Hospital
Whitechapel Road
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Study participating centre
Addenbrooke's Hospital
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal as well as:
1. Study participants and carers: feedback to individual participants, users and carers who have been involved in, or otherwise contributed to, the trial);
2. Charity links and patient groups: results of the studies will be disseminated using the strong web-based and media infrastructure already developed by the Charity Bowel and Cancer Research (B&CR). This infrastructure includes the B&CR website (www.bowelcancerresearch.org which has 2,500 unique web visitors monthly), social media e.g. Facebook site (12,000 followers and), Twitter, and a public relations officer (a free-lance journalist who is employed by B&CR for one day per week who will help develop and edit press releases: 50 local and national news publications in 2012). B&CR is dedicated to breaking down the taboos concerning discussion of bowel problems such as incontinence. B&CR and several of the applicants have links with other

patient organisations and charities e.g. Core, GI Blues, Ileostomy Association and the Bladder and Bowel Foundation;
3. Local health service providers including developing clinical commissioning groups via specially convened local meetings and written reports
4. NIHR collaboration: the CI is Director of the Bart's NIHR HTC for GI disease. Results will be disseminated by the HTC newsletter/website to all 90 UK industrial and all 25 clinical colorectal centres.

Intention to publish date
31/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from the Pragmatic Clinical Trials Unit Data Sharing Committee, pctu-data-sharing@qmul.ac.uk Anonymised individual level data without prior consent in line with the Data Protection Act will be available subsequent to the final report and publication made by the CI /lead authors. Data will be made available only following a successful application and data sharing agreement with PCTU. The PCTU supports appropriate data sharing to maximize the value of research data, including for patient and public benefit.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2	27/07/2017	26/10/2017	No	Yes
Protocol article	protocol	26/06/2018		Yes	No
HRA research summary			26/07/2023	No	No
Basic results		04/06/2024	04/06/2024	No	No