STUDY PROTOCOL

A FEASIBILITY STUDY TO ASSESS RECTAL SENSITIVITY USING ELASTIC BALLOON DISTENSION VERSUS A RAPID RECTAL BAROSTAT BAG: IS THERE AN AGREEMENT IN LONDON CLASSIFICATION DIAGNOSES?

Assessing rectal sensitivity with elastic balloon distension versus rectal barostat

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ABBREVIATIONS

ARM – Anorectal Manometry

BSG – British Society of Gastroenterology

CDDFT – County Durham and Darlington Foundation Trust

CI – Chief Investigator

CRF – Case Report Form

CTIMP – Clinical Trial of an Investigational Medicinal Product

GCP – Good Clinical Practice

GI – Gastrointestinal

IBS – Irritable Bowel Syndrome

IBS-C – Irritable Bowel Syndrome Constipation Subtype

MRN – Medical Record Number

NUTH – Newcastle Upon Tyne Hospitals

PCF – Participant Consent Form

PI – Principle Investigator

PIS – Patient Information Sheet

QA – Quality Assurance

REC – Research Ethics Committee

SAE – Serious Adverse Event

STP – Scientist Training Programme

UEG – United European Gastroenterology

STUDY SUMMARY

Study Title	A feasibility study to assess rectal sensitivity using elastic balloon distension versus a rapid rectal barostat bag: is there an agreement in London classification diagnoses?
Short Trial	Assessing rectal sensitivity with elastic balloon versus rectal barostat
Study Design	Feasibility study, Non-CTIMP, Randomised Multi-site study
Study Participants	**Inclusion criteria:** • Aged over 18 years • Aged under 90 years • Male or nonpregnant female • Meets 1 or more of the following indications for anorectal physiology investigations: symptoms of constipation or disorder of evacuation, faecal incontinence, functional anorectal pain, faecal urgency and frequency of moving bowels, constant urge to move bowels. • Has had a previous lower gastrointestinal tract investigation (colonoscopy, flexible sigmoidoscopy, defecating proctogram, digital rectal examination, CT colon) in the past 2 years • Able to understand written and verbal English **Exclusion criteria:** • Creutzfeldt-Jakob disease • Pregnancy • Previous rectal surgery • Previous pelvic radiotherapy • Haemorrhoid banding in past 2 weeks • Haemorrhoidectomy in past 10 weeks • Reporting of change of bowel habits, rectal bleeding, or weight loss with no endoscopic investigations performed since symptoms commenced • History of inflammatory bowel disease • History of colorectal or anal cancer • Lack of capacity to consent • Over 90 years old • Under 18 years old • Currently or has been involved in a clinical trial investigational medicinal product study within 6 months prior to the start of the study. • Unable to understand written and/or verbal English

Planned Sample Size	30	
Planned Study Period	24 months	
	Objectives	*Outcome Measures*
Primary	To assess the feasibility of a definitive study which will compare two different measurement methods of rectal sensitivity. These measurement methods include the gold standard rectal barostat test and the more widely used elastic balloon distension test.	As this is a feasibility study, there are no primary outcome measures, only secondary outcome measures.
Secondary	• To assess whether they are any differences in rectal sensitivity diagnoses when using the London classification between the two methodologies (Elastic balloon test versus rectal barostat). • To assess the repeatability of the rectal barostat test. • To investigate whether patients with larger rectums require the elastic balloon to be inflated to a larger volume, before they feel an urge to defecate. • To determine whether the Laborie elastic balloon test or Medtronic elastic balloon test aligns better with the rectal barostat test. • To assess study participant eligibility, uptake and drop-out rate. • To assess study acceptability and tolerability. • To assess the costs per study of the two	• The London Classification diagnoses of each patient when rectal sensitivities are assessed using Laborie system elastic balloon distension versus the rectal barostat, and Medtronic system elastic balloon distension versus the rectal barostat. • Percentage of rectal capacity at each sensory threshold per test will be measured to assess repeatability • Total rectal volume (mL) measured using the rectal barostat will be recorded to assess correlation between capacity and balloon inflation (mL) at sustained urgency. • The number of patients who were eligible to participate in the study. • The number of patients who chose to participate in the study. • The number of patients who dropped out of the study. • The length of time required for the rectal barostat protocol and the elastic balloon distension protocol in clinic

	methodologies to help inform a definitive study (clinic time, analysis time and consumables).	• Costings of rectal barostat test comparison (costs of barostat bags and any additional staff time required) • Study acceptability and tolerability assessment.

1.0 BACKGROUND

The gastrointestinal tract contains an abundant supply of sensory nerve endings, including mechanoreceptors, chemoreceptors, and thermoreceptors, which allow for conscious perception of distension and contents[1]. This sensory function is vital in the rectum, the section of the GI tract responsible for the storage of faeces, as it allows for social control of defecation and the ability to delay the process until we are in a socially acceptable environment. Disturbances in sensory function have been associated with a number of functional GI disorders, such as irritable bowel syndrome (IBS), functional constipation, and faecal incontinence, in which patients can suffer with either rectal hyposensitivity or hypersensitivity, depending on the pathophysiology of their condition[2].

For example, patients with rectal hyposensitivity often suffer with chronic constipation or IBS-C (constipation subtype), and as a result do not experience a normal urge to defecate[3]. This can result in faeces sitting within the rectum for prolonged periods of time, which requires removal via the use of laxatives, transanal irrigation, or digital evacuation. Research has demonstrated that in individuals with diminished rectal sensitivity, abnormalities can either be due to alterations in afferent nerve pathways affecting the patient's sensation to stimuli, or increased rectal wall compliance[4]. Conversely, rectal hypersensitivity is associated with faecal urgency and incontinence, and commonly this patient cohort have poorly compliant and low capacity rectums that can contribute to their symptoms[5]. Some of these patient may feel sudden urges to defecate, but rather than having abnormalities with the rectal wall itself, instead have symptoms as a result of loose stool migrating from the rectum into the highly sensitive anal canal[6]. Therefore it can be useful to assess rectal sensitivity in these patient cohorts to further categorise the cause of their symptoms, and help to optimise treatment or management.

The most common assessment of rectal sensitivity in a clinical environment is made by gradually inflating an elastic balloon within the rectum, and measuring the volumes at which the patient reports their first sensation, their normal urge to defecate, and sustained urgency[7]. This is commonly performed in conjunction to anorectal manometry (ARM), which involves insertion of a catheter into the anorectum, and measuring pressure at rest and during specific manoeuvres to assess the function of the anal sphincters[8]. Most commercially available catheters for this test also contain the required elastic balloon to assess rectal sensitivities, which can be inflated manually or automatically by the equipment, depending on the model and the manufacturer. The advantages of assessing rectal sensitivities using the elastic balloon in conjunction with ARM is that it is fast and cheap, as it does not require a separate catheter being inserted for the additional test. However, the elastic properties of the balloon mean it is unsuitable to assess rectal compliance[9]. In our

services, we use two anorectal manometry systems across NUTH and CDDFT services. In NUTH we use a Laborie Solar High Resolution Manometry System with water-perfused catheters, and in CDDFT we use a Medtronic 3D Solid-State High Resolution Manometry System. Both systems are commercially available across the UK, and use a similar elastic balloon for inflation, however, they utilise different published normal ranges of sensory thresholds.

The rectal barostat is another, more comprehensive, device used to assess rectal sensitivity. It contains a polyethylene bag, which is inserted into the patient's rectum and inflated using a pneumatic pump either continuously or in phasic intervals[10]. Unlike the elastic balloon, the rectal barostat bag has infinite compliance whilst filling, which allows measurement of rectal compliance and total rectal volume, due to its ability to measure opposing pressure of the rectal wall. This protocol is more time-consuming, and for this reason is not routinely used in clinical practice, however it is considered the gold-standard of assessing sensory thresholds, and has the advantage of adding additional information about the biomechanical properties of the rectal wall[3].

Once sensory thresholds have been measured, a diagnosis of normal, rectal hypersensitivity, rectal hyposensitivity, or borderline hyposensitivity is made according to the London Classification disorders of rectal sensation[11]. In this study we aim to identify whether patients receive the same diagnosis, according to the London Classification, regardless of whether the elastic balloon distension or rectal barostat is used. To achieve this, patients attending for their standard rectal sensitivity tests using the elastic balloon will be invited to repeat their study using the rectal barostat, and the diagnosis they receive (normal, hypersensitive, hyposensitive, borderline hyposensitive) will be compared. From this data, an indication of the clinical utility of the rectal barostat can be suggested, depending on whether a patient's diagnoses changes. As well as this, participants will be offered a questionnaire following their clinic appointment, which will include questions on their tolerability of each test, in order to gather information on the feasibility of a larger cohort study in the future.

2.0 RATIONALE

A recent service evaluation was conducted to compare the number of diagnoses of disorders of rectal sensitivity (n=70 per site) across NUTH and CDDFT services, in order to identify whether both pieces of equipment produce similar proportions. In NUTH, the majority of patients (91.4%) were diagnosed as normal, whereas in CDDFT, the majority of patients (65.7%) were diagnosed with rectal hypersensitivity. This suggests a possible difference in how each piece of equipment classifies patients, although the limitations such as two different cohorts of patients being studied, and the relatively small sample size should be acknowledged. This service evaluation supported the need for more research into our normal values and how we assess rectal sensitivity, and questioned whether a rectal barostat could be more appropriate.

There is little research directly comparing the assessment of rectal sensitivity using elastic balloon distension and the rectal barostat. A study by Sauter et al. (2014) assessed 26 healthy volunteers using both the elastic balloon inflation and barostat methodologies to assess rectal sensitivities, by recording volume inflated at first sensation, normal urge, and

sustained urgency. They found there was no agreement between the elastic balloon and barostat recorded volumes, however, this is possibly due to the difference in physical properties and shape at identical volumes, which the study failed to take into account[12]. There are currently no studies comparing the two devices in a symptomatic population, and no indication whether patients receive different diagnoses depending on what device is used to assess rectal sensitivity. Accurate and comprehensive assessment of disorders of rectal sensation to distension in symptomatic patients is vital, as studies have suggested patients with rectal hyposensitivity treated with biofeedback therapy improved their sensory thresholds and symptom severity[14], and sensory retraining is of greater utility when treating faecal incontinence than strength training alone[15].

This feasibility study will help investigate key variables required to inform a future definitive study, which will aim to determine whether patients receive a different diagnosis of rectal sensitivity dependent upon the test used. Moreover, a definitive study will address the potential impact of rectal sensitivity testing methodologies on patient outcomes.

2.1 Assessment and Management of Risk

There are some unavoidable burdens and risks to participants that will be explained fully in the Participant Information Sheet and prior to receiving informed consent to partake in the study. There is first the burden of time required from the patient, which is approximately 30 minutes additional to their standard anorectal physiology appointment time. To minimise this burden, the additional barostat test will be performed at the same time as their standard care appointment, to avoid additional travel costs and time. The barostat test also carries a risk of pain, discomfort, bleeding, and perforation of the rectum (<1 in 1000), the same as standard rectal sensitivity testing using the elastic balloon, which the patients will also be undergoing as part of their standard anorectal physiology appointment. To minimise pain and discomfort, lubrication is used to insert the catheter and the participant advised they can withdraw their consent at any point, and the test will be abandoned. To minimise the risk of bleeding, the test will be abandoned if there is any resistance during insertion of the catheter and participants are excluded from the study if they suffer from excessive or unexplained rectal bleeding. Any participants with risk factors of rectal perforation, such as previous pelvic surgery, pelvic radiotherapy, or inflammatory bowel disease are excluded from the study (according to exclusion criteria), and the barostat automatically deflates if pressure of the rectal wall exceeds 40 mmHg.

This trial is categorised as Type A (no higher than the risk of standard medical care).

3.0 OBJECTIVES AND OUTCOME MEASUREMENTS/ENDPOINTS

3.1 Primary Objective

To assess the feasibility of a definitive study which will compare two different measurement methods of rectal sensitivity. These measurement methods include the gold standard rectal barostat test and the more widely used elastic balloon distension test.

3.2 Secondary Objectives

- To assess whether they are any differences in rectal sensitivity diagnoses when using the London classification between the two methodologies (elastic balloon distension test and rectal Barostat test).
- To assess the repeatability of the rectal barostat test.
- To investigate whether patients with larger rectums require the elastic balloon to be inflated to a larger volume, before they feel an urge to defecate.
- To determine whether the Laborie elastic balloon test or Medtronic elastic balloon test aligns better with the rectal barostat test.
- To assess study participant eligibility, uptake and drop-out rate.
- To assess study acceptability and tolerability.
- To assess the costs per study of the two methodologies to help inform a definitive study (clinic time, analysis time and consumables).

3.3 Outcome Measures

As this is a feasibility study, there are no primary outcome measures, only secondary outcome measures. These include:

- The London Classification diagnoses of each patient when rectal sensitivities are assessed using Laborie system elastic balloon distension versus the rectal barostat, and Medtronic system elastic balloon distension versus the rectal barostat.
- Percentage of rectal capacity at each sensory threshold per test will be measured to assess repeatability
- Total rectal volume (mL) measured using the rectal barostat will be recorded to assess correlation between capacity and balloon inflation (mL) at sustained urgency.
- The number of patients who were eligible to participate in the study.
- The number of patients who chose to participate in the study.
- The number of patients who dropped out of the study.
- The length of time required for the rectal barostat protocol and the elastic balloon distension protocol in clinic
- Costings of rectal barostat test comparison (costs of barostat bags and any additional staff time required)
- Study acceptability and tolerability assessment.

4.0 STUDY DESIGN

This is a feasibility study to test equivalence of elastic balloon distension to rectal barostat in diagnosing disorders of rectal sensitivity. This is a multi-site randomised study.

5.0 STUDY SETTING

Multicentre study. Research sites include:

- Newcastle Upon Tyne Hospitals NHS Foundation Trust (NUTH): Royal Victoria Infirmary, Medical Physics.
- County Durham and Darlington NHS Foundation Trust (CDDFT): University Hospital of North Durham, Medical Physics.

Patients identified at each site will undergo the study at the same site. Therefore, patients are not expected to travel between sites.

6.0 PARTICIPANT ELIGIBILITY CRITERIA

6.1 Inclusion Criteria

- Aged over 18 years
- Aged under 90 years
- Male or nonpregnant female
- Meets 1 or more of the following indications for anorectal physiology investigations:
    - Symptoms of constipation or disorder of evacuation
    - Faecal incontinence
    - Functional anorectal pain
    - Faecal urgency and frequency of moving bowels
    - Constant urge to move bowels
- Has had a previous lower gastrointestinal tract investigation (colonoscopy, flexible sigmoidoscopy, defecating proctogram, digital rectal examination, CT colon) in the past 2 years
- Able to understand both written and verbal English

6.2 Exclusion Criteria

- Creutzfeldt-Jakob disease
- Pregnancy
- Previous rectal surgery
- Previous pelvic radiotherapy
- Haemorrhoid banding in past 2 weeks
- Haemorrhoidectomy in past 10 weeks
- Reporting of change of bowel habits, rectal bleeding, or weight loss with no endoscopic investigations performed since symptoms commenced
- History of inflammatory bowel disease
- History of colorectal or anal cancer
- Lack of capacity to consent
- Over 90 years old
- Under 18 years old

- Currently or has been involved in a clinical trial investigational medicinal product study within 6 months prior to the start of the study
- Unable to understand written and/or verbal English

6.3 Number of Participants

In total 30 participants will be recruited for the study. 15 participants will be recruited at NuTH and 15 at CDDFT. Study recruitment will continue until complete study data has been obtained from 15 participants at each site.

7.0 STUDY PROCEDURES

7.1 Recruitment

Referrals from Consultant Gastroenterologists or Colorectal Surgeons to the GI Physiology Service at NUTH or CDDFT for anorectal physiology studies will be screened for study eligibility, according to the inclusion and exclusion criteria. This will be performed by trained healthcare scientists or a trainee clinical scientist (NHS STP) under supervision. The team performing the screening and all study procedures are the same individuals that would usually be involved in the standard care of the patient.

During standard care a standard anorectal physiology patient information leaflet (PIL) and appointment letter is sent to the patient. The standard appointment letter states that the patient can call the GI physiology secretary to make an appointment for their standard anorectal physiology test or the patient can be called by the GI physiology secretary to make an appointment.

As part of the research study eligible patients will also be sent a study patient information sheet (PIS) alongside the standard anorectal physiology PIL and appointment letter. The patient will then receive a telephone call from an investigator of the research team (GI physiology team), a minimum of 5 days following postage, to determine whether they would like to participate in the study. If they are willing to participate an appointment will be made, which will include their standard clinic appointment. Full eligibility will be assessed once informed consent has been given at their clinic appointment. For patients who do not want to participate they will continue with standard care and a standard anorectal physiology appointment will be made.

7.2 Screening Logs

7.2.1 Pre-Screen Log

Participants identified by researchers who accept a PIS will be included on the pre-screening log. This log will provide the following information:

- Patient initials
- Sequential screening number
- Date of when potential study eligibility was determined by researcher upon referral for anorectal physiology
- Site (NUTH or CDDFT)
- Eligibility based on clinical history (yes/no)
- Initial screening via telephone outcome (recruited, declined/reason given)
- Clinic discussion with researcher outcome (recruited, declined/reason given)

7.2.2 Participant Identification Log

Participants recruited to the study will be documented within the participant identification log, which will include the following information:

- Participant name
- Participant initials
- Screening number
- Subject number
- NHS number
- MRN (medical record number)
- Confirmation of eligibility
- Date of consent
- Personal details (address, phone number, email address)
- Withdrawal (yes, no/when and why)

The researcher will use a checklist to determine clinical eligibility. If recruited, patients will be assigned a Case Report Form (CRF).

7.3 Consent

Participants eligible for the study will be sent a PIS alongside a standard anorectal physiology PIL and appointment letter.

The eligible participants will then receive a telephone call from the study team (GI physiology team, who are the patient's direct care team) and will be asked whether they would like to participate. If they would like to participate an appointment will be made which includes both the research study elements and standard care.

At the appointment the researcher will outline what the research study entails, what risks are involved, and they will give the participant an opportunity to ask questions and have them answered satisfactorily. If the participant agrees to participate at that stage the researcher will continue with the informed consent process and complete the Participant Consent Form (PCF). Once the consent form has been signed by both the participant and the researcher, the appointment will proceed. A copy of the consent form will be given to the participant, and the original copy will be stored in the site file. Participants can withdraw their consent at any point during the study, including after data has been collected.

7.4 Randomisation

All participants will have the rectal barostat test, but the order of tests will be changed per patient to avoid bias on the order of tests influencing the results. Patients will either receive procedure A or procedure B:

- **Procedure A:** Anorectal manometry, elastic balloon distension, endoanal ultrasound, rectal barostat
- **Procedure B**: Rectal barostat, endoanal ultrasound, anorectal manometry, elastic balloon distension

The basic details (e.g. short title, study overview) of the study will be registered with the online randomisation software, Sealed Envelope (https://www.sealedenvelope.com/).The simple randomisation service for non-commercial clinical studies will be selected. At each site a secure NHS email address accessible only to the research team will be used to perform each randomisation. The unique participant randomisation number will be entered into the software. The software will then automatically randomise to procedure A or procedure B. A copy of the randomisation is also automatically emailed. The email containing the randomisation allocation will be printed out and saved as part of the SIF.

Randomisation will occur once informed consent has been obtained and the study eligibility of the participant has been confirmed.

7.5 Assessments

7.5.1 Digital Rectal Examination

Digital rectal examination will be performed before anorectal physiology appointments begin as per standard care and according to local procedure.

7.5.2 Endoanal Ultrasound

Participants from NUTH will have endoanal ultrasound performed as per local procedure using a BK3000 system with a 20R3 9052 transducer. Participants from CDDFT will have endoanal ultrasound performed as per local procedure using a BK Specto system with a 20R3 9052 transducer. Endoanal ultrasound will be performed as per standard care.

7.5.3 Anorectal Manometry and Rectal Sensitivity Testing

Participants from NUTH will have anorectal manometry and rectal sensitivity tests as per local procedure using a Laborie Solar High Resolution Manometry System with water-perfused catheters. Participants from CDDFT will have anorectal manometry and rectal sensitivity tests as per local procedure using a Medtronic 3D Solid-State

High Resolution Manometry System. These tests are performed as per standard care, however rectal sensitivity testing will be performed twice more as part of non-standard care.

7.5.4 Rectal Barostat

Participants from NUTH and CDDFT will have the rectal barostat test performed as per local procedure as part of non-standard care.

7.5.5 Rectal Sensitivity Testing Questionnaire

Participants will receive a questionnaire at the end of their appointment to assess their tolerability to each test. This will take 5 minutes to complete post-appointment to be completed in the waiting room and handed to reception. The completed questionnaires will be collected by a researcher post-clinic.

7.6 Withdrawal

Participants may withdraw from the study at any point. If this occurs, the reason for withdrawal if provided by the participant will be documented in the participant's CRF and the Study Recruitment log. Any study related identifiable information will be destroyed (not including the consent form). However, non-identifiable study information up to and including the point of withdrawal will be retained.

7.7 End of Study

End of study is defined as the final visit of the final participant. The study can be terminated by the investigators or sponsor at any time for clinical or administrative reasons.

7.8 Data Analysis

To investigate whether London Classification diagnoses differs when using the rectal barostat compared to elastic balloon distension, a binary indicator will be used to determine the percentage of patients who's diagnoses were in agreement. To examine this closer, a Fisher's exact test will be used to determine whether the difference in number of diagnoses between the elastic balloon distension and rectal barostat reaches a significance level of p=0.05.

To assess repeatability of sensory thresholds at first sensation, normal urge, and sustained urgency of the rectal barostat, an intraclass correlation coefficient will be calculated for each test.

To identify whether there is a correlation between total rectal capacity and the volume of the elastic balloon at the sensory threshold of sustained urgency, a Pearson's correlation will be calculated to test the strength of the relationship between these variables.

8.0 DATA COLLECTION

8.1 Source Data Documentation

Source data associated with the study is anticipated to include information on consent, demographics, medical history, adverse events, and communications. Source data relating to results of the elastic balloon inflation and rectal barostat tests will be recorded in the participant's CRF.

A source data log will kept in the site file, to include the origin and destination of data, date of data transfer, individuals with access to the source data, and the type of document.

8.2 Case Report Forms

Each participant will be allocated a CRF containing anonymised source data relating to the participant's involvement in the study. The CRF will be stored in the site file.

8.3 Access to Data

Direct access will be granted to authorised representatives from NUTH and CDDFT and regulatory authorities to permit trial-related monitoring, audits, and inspections, in line with participant consent.

9.0 SAFETY REPORTING

Elastic balloon distension and rectal barostat tests are low risk investigations that are performed routinely in clinical practice. If any adverse events were to occur during the study the sponsor will be notified immediately of the patient's ID, the event that occurred, review of causality, and whether the event is resolved or ongoing. If the adverse event is believed to have been as a result of the research study, it will be reported on local incident reporting systems. The adverse events will also be recorded in the adverse events log and on the participant's CRF within the Trial Master File.

Any Serious Adverse Event (SAE) occurring as a result of the study will be reported by the CI to the REC within 15 days of the event occurring. The National Health Service Health Research Authority Non-CTIMP Safety Report to REC form should be used to do this. Any

SAE will also be included in the Annual Progress Report to the REC. Further, any SAE related to the research study procedures will also be reported to the Study Sponsor.

10.0 SPONSORSHIP, MONITORING, AND AUDIT

The CI will monitor the informed consent process to ensure that consent forms are appropriately counter signed at both sites. The research team will also conduct internal monitoring to ensure the study is run in line with Good Clinical Practice (GCP). The study may fall under the sponsor's QA audit programme as per NJRO-QA-SOP-001 and data will be made available if requested.

11.0 ETHICAL AND REGULATORY CONSIDERATIONS

11.1 Research Ethics Committee (REC) Review and Reports

Before commencement of the trial, approval will be sought from the REC for the study protocol, informed consent forms and patient information leaflets. Any substantial amendments to the protocol will be submitted for review by the REC, and will not be implemented until a favourable opinion has been granted. Any correspondence with the REC will be retained in the Investigator Site File, and it is responsibility of the Chief Investigator's to produce the annual reports as required, and notify the REC of the end of the study. If the study is ended prematurely, the Chief Investigator will notify the REC, and include reasons for premature termination. Within one year following the end of the trial, the Chief Investigator will submit a final report with the results, including publications, to the REC.

11.2 Amendments

Protocol amendments must be reviewed and approved by the CI, PIs and the study team. All amendments must also be reviewed and approved by the Study sponsor. Major amendments must also be reviewed and approved by the REC.

11.3 Protocol Compliance

Planned deviations from the study protocol are prohibited. Any accidental protocol deviations must be adequately documented and reported to the Chief Investigator immediately. Deviations from the protocol that are found to frequently reoccur are not acceptable, and could be classified as a serious breach.

11.7 Notification of Serious Breaches to the Protocol

A 'serious breach' is defined as a breach likely to effect to a significant degree:

(a) The safety or physical or mental integrity of the participants
(b) The scientific value of the trial

The sponsor will be notified immediately of any case where the above definition applies during the study.

11.8 Data Protection and Patient Confidentiality

11.8.1 Data Management

Management of data will be in line with GCP, with access to data only being granted to those involved in the research study, and to monitors, auditors, and inspectors. All researchers will be up to date with mandatory information governance training and GCP eLearning.

Clinical data collected during the study will be stored within their CRF, and physical copies will be stored in the Trial Master File. Patient identifiable data will be stored in the Trial Master File and a Microsoft Excel Spreadsheet will be used to collate information from the CRF for data analysis. Any electronic transfer of data will be via encrypted email accounts.

11.8.2 Data Confidentiality

Newcastle Upon Tyne Hospitals NHS Foundation Trust is the sponsor for this study and will act as the data controller. Research will be conducted in line with Caldicott Principles, General Data Protection Regulation (2018) and GCP. Encrypted, password-protected NHS IT devices will be used within local sites.

Standard care documents not used as part of the study e.g. Anorectal physiology consent form, patient worksheet, patient assessment form and Tristel disinfection logs will be scanned, saved on NHS IT devices and then paper copies destroyed.

Electronic anorectal manometry physiology source data including the raw data from the elastic balloon distention test will be saved locally on NHS devices as per standard care. The results from the anorectal physiology elastic balloon distension test will be noted in the participant CRF.

The electronic source data from the rectal barostat balloon distension test will be anonymised and stored as part of the study. However, the results of the barostat test will be made available to the referrer and stored on the patient record. If the participant withdraws consent after the rectal barostat test is performed then these results will not be made available to the referrer or stored on the patient record.

11.8.3 Study Retention Record

All documents relating to the study will be kept for 5 years from the study end point. Permission will be sought from the sponsor before any information is destroyed. This is in alignment with NuTH Archiving SOP.

11.9 Conflicts of Interest

There are no conflict of interests to declare for this study.

11.10 Indemnity

Newcastle Upon Tyne Hospitals NHS Foundation Trust will cover indemnity for the design, management, and conduct of the study.

12.0 DISSEMINATION PLANS

The results of the study are intended to be disseminated via a poster, which will be submitted for conferences including the British Society of Gastroenterology (BSG), and the United European Gastroenterology (UEG) annual conferences. The research also be circulated across the Association of Gastrointestinal Physiologists via the newsletter NewWave, and written with the intent to publish to open-access peer-reviewed journals, to contribute to scientific and clinical communities.

13.0 REFERENCES

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14.0 APPENDICES